HOW THE REPORT ON CARCINOGENS USES SCIENCE TO MEET ITS STATUTORY OBLIGATIONS, AND ITS IMPACT ON SMALL BUSINESS JOBS

HEARING

BEFORE THE

SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT

COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY

JOINT WITH THE

SUBCOMMITTEE ON HEALTH CARE AND TECHNOLOGY

COMMITTEE ON SMALL BUSINESS

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Wednesday, April 25, 2012

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HOW THE REPORT ON CARCINOGENS USES SCIENCE TO MEET ITS STATUTORY OBLIGATIONS, AND ITS IMPACT ON SMALL BUSINESS JOBS

WEDNESDAY, APRIL 25, 2012

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT,
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY,
JOINT WITH THE
SUBCOMMITTEE ON HEALTHCARE AND TECHNOLOGY,
COMMITTEE ON SMALL BUSINESS,
Washington, DC.

The Subcommittees met, pursuant to call, at 10:01 a.m., in Room 2318 of the Rayburn House Office Building, Hon. Paul Broun [Chairman of the Investigations and Oversight Subcommittee] presiding.

Committee on Science, Space, and Technology
Subcommittee on Investigations & Oversight
and
Committee on Small Business
Subcommittee on Healthcare and Technology

How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs

Thursday, April 25, 2012
10:00 a.m. to 12:00 p.m.
2318 Rayburn House Office Building

Witnesses

Panel I:
Dr. Linda S. Birnbaum, Director, National Institute of Environmental Health Sciences & National Toxicology Program, U.S. Department of Health and Human Services

Mr. Charles A. Maresca, Director of Interagency Affairs, Office of Advocacy, U.S. Small Business Administration

Panel II:
Dr. James S. Bus, Director of External Technology, Toxicology and Environmental Research and Consulting, The Dow Chemical Company

Dr. L. Faye Grimsley, Associate Professor, Tulane School of Public Health and Tropical Medicine, Department of Global Environmental Health Sciences

Ms. Bonnie Webster, Vice President, Monroe Industries, Inc.

Ms. Ally LaTourelle, Esq., V.P. Government Affairs, Bioamber, Inc

Mr. John E. Barker, Corporate Manager, Environmental Affairs, Safety and Loss Prevention, Strongwell Corporation

Dr. Richard B. Belzer, President, Regulatory Checkbook

U.S. House of Representatives

Committee on Science, Space, and Technology
Subcommittee on Investigations & Oversight

and

Committee on Small Business
Subcommittee on Healthcare and Technology

HEARING CHARTER

"How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"

Wednesday, April 25, 2012
10:00 a.m. – 12:00 p.m.
2318 Rayburn House Office Building

PURPOSE

On April 25, the Committee on Science, Space, and Technology Subcommittee on Investigations & Oversight, and the Committee on Small Business Subcommittee on Healthcare and Technology, will hold a hearing to examine the Report on Carcinogens (RoC). This joint hearing will provide Members an opportunity to understand how the U.S. Department of Health and Human Services' (HHS) National Toxicology Program (NTP), an interagency program administered by the National Institute of Environmental Health Sciences (NIEHS), produces the RoC. Given the interest generated by the 12th RoC last year, and particularly as NTP embarks on preparations for the 13th RoC, the committees are interested in understanding the history of the RoC, how NTP uses science to meet its statutory obligations, and the RoC's impact on stakeholders, particularly small businesses.

BACKGROUND

The RoC's Legislative History

The RoC is a biennial report mandated by Congress to identify substances[1] that may pose a hazard to human health by virtue of their carcinogenicity. Although the law[2] originally called for annual reports, the reporting was made biennial in 1993.[3]

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[1] NTP Website, *Since You Asked – 12th Report on Carcinogens*, available at: http://www.niehs.nih.gov/news/sya/sya-roc/index.cfm; (hereinafter NTP Website – Since You Asked); NTP defines substances as "agents, substances, mixtures, or exposures (collectively called substances) that may potentially put people in the United States at an increased risk for cancer. Listed in the RoC are a wide range of substances, including metals, pesticides, drugs, and natural and synthetic chemicals."

[2] P.L. 95-622, (Community Mental Health Centers Act, Amendments), available at: http://history.nih.gov/research/downloads/PL95-622.pdf.

Congress passed the law establishing an annual RoC in 1978 as a consequence of oversight hearings on the National Cancer Institute (NCI). The concept of an annual report was raised by witnesses who testified that no agency maintained a comprehensive list of carcinogenic chemicals at the time. Congressman Andrew Maguire of New Jersey introduced legislation that initially required NCI to publish a report with a list of all known or suspected carcinogens.[4] The report was to include three elements:

- *a list of all known or suspected carcinogens;*
- *information concerning the nature of exposure and number of individuals exposed; and*
- *an evaluation of the efficacy of existing regulatory standards designed to control suspected carcinogens.*[5]

He hoped the report would "educate the public, serve as a point of reference for scientists and regulators, and evaluate the activities of the regulatory agencies, who are not immune to pressure from the outside."[6]

Congressman Maguire's bill was folded into a different bill[7] sponsored by Florida Congressman Paul Rogers, Chairman of the Committee on Interstate and Foreign Commerce Subcommittee on Health and the Environment. Chairman Rogers' bill expanded on Congressman Maguire's bill and transferred the responsibility to produce the report to the then-Department of Health, Education, and Welfare, now the Department of Health and Human Services. Ultimately, Congress passed the Senate version of these proposals,[8] which made some changes to the House language, including a critical edit to **better reflect the intent of the legislators in what they expected of the annual report**. Specifically, the Senate bill change included:

> *"a replacement of the phrase 'suspected carcinogens' with 'substances...reasonably anticipated to be carcinogens,' in order to make it absolutely clear in the statute that there must be reasonable ground for designating a substance as a putative carcinogen."*[9]

Chairman Rogers further clarified the "regulatory importance of the Annual Report"[10] by stating that the:

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[3] P.L. 103-43, (National Institutes of Health Revitalization Act of 1993), available at: http://history.nih.gov/research/downloads/PL103-43.pdf.

[4] H.R. 10190, the Cancer Prevention Act, introduced by Rep. Andrew Maguire (D-NJ), December 1, 1977, available at: http://www.congress.gov/cgi-lis/bdquery/D?d095:1:./temp/~bdMhBZ:@@@L&summ2=m&:dbs=n:|/billsumm/billsumm.php?id=2|.

[5] U.S. Congress, Office of Technology Assessment, "Identifying and Regulating Carcinogens," OTA-BP-F1-42, Washington, DC: U.S. Government Printing Office, November 1987 (hereinafter OTA Report).

[6] Ibid.

[7] H.R. 12347, the Biomedical Research and Research Training Amendments, introduced by Rep. Paul Rogers (D-FL), April 25, 1978, available at: http://www.congress.gov/cgi-lis/bdquery/D?d095:1:./temp/~bdJjb7:@@@L&summ2=m&:dbs=n:|/billsumm/billsumm.php?id=2|.

[8] S. 2450, the Biomedical Research Extension Act, introduced by Sen. Edward Kennedy (D-MA), January 27, 1978, available at: http://www.congress.gov/cgi-lis/bdquery/D?d095:1:./temp/~bdjAJk:@@@L&summ2=m&:dbs=n:|/billsumm/billsumm.php?id=2|.

[9] Congressional Record, Volume 124 – Part 28, October 14, 1978.

[10] OTA Report, *supra*, note 5.

> *"intention of the legislation was that listing in the annual report would be a first step in regulation, one triggering a review by the agencies responsible for enforcing various laws regulating carcinogens."*[11]

These changes, including the 1993 update to a biennial reporting schedule, form the background of the current law. *(Appendix 1).*

The RoC is a cumulative document of substances listed in one of two categories, as either "known" to be a human carcinogen, or "reasonably anticipated" to be a human carcinogen. (Appendix 2). Each edition of the report includes substances listed in past reports, in addition to the new substances in the most recent version, along with any changes to the status of previously listed substances. Since the law's inception in 1978, only twelve reports have been published in the 31 years between the first RoC in 1980, and the 12th in 2011. The 12th RoC lists 240 substance profiles – 54 listed as "known" carcinogens and 186 as "reasonably anticipated" to be carcinogens.[12] Over the course of the 12 reports, only nine substances have been delisted from the report (*see Appendix 3*) and a similar number have moved from the "reasonably anticipated" to be a carcinogen list to the "known" to be a carcinogen list.

Federal Chemical Assessment Programs

There are multiple federal agencies that produce a variety of chemical assessment reports with which the House Science, Space, and Technology Committee is familiar. For example, the Agency for Toxic Substances & Disease Registry (ATSDR), another HHS agency, performs certain functions that are congressionally-mandated. ATSDR conducts:

> *"public health assessments of waste sites, health consultations concerning specific hazardous substances, health surveillance and registries, response to emergency releases of hazardous substances, applied research in support of public health assessments, information development and dissemination, and education and training concerning hazardous substances."*[13]

Notably, this Committee has held several hearings on the U.S. Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS) program, which maintains a database of chemicals that provide a hazard identification and dose-response analysis. This information, when combined with estimates of exposure, allow regulatory agencies to produce a risk assessment.

While the Report on Carcinogens is also a source for decision-making by regulatory agencies at the federal and state levels, the NTP states that the RoC is a:

> *"hazard identification document and does not present quantitative assessments of the risks of cancer associated with exposure to these substances. Thus a listing in the RoC*

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[11] Ibid.

[12] U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program, *Report on Carcinogens*, Twelfth Edition, 2011, available at: http://ntp.niehs.nih.gov/ntp/roc/twelfth/roc12.pdf (hereinafter 12th RoC).

[13] ATSDR Website, *About ATSDR*, available at: http://www.atsdr.cdc.gov/about/index.html.

> *only indicates a potential hazard and does not estimate cancer risks to individuals associated with exposures in their daily lives."*[14]

Notwithstanding NTP's disclaimer, the RoC does not operate in a vacuum. Last year's release of the 12th edition of the RoC demonstrated this fact with the coverage it received, particularly in reference to its upgrade of formaldehyde from a "reasonably anticipated" carcinogen to a "known" carcinogen, and a first-time listing of styrene as a substance "reasonably anticipated" to cause cancer. The styrene listing even resulted in a lawsuit against HHS,[15] and caused concerns for businesses that use the substance who questioned the scientific rationale behind the listing.

Concerns about the RoC, identified in public comments and during listening sessions last year as NTP commenced preparations for the 13th RoC, include among others: a policy of soliciting, but not responding to public comments; lack of independence in its peer review process; lack of clarity in its definitions as to what constitutes a substance to be listed as either "reasonably anticipated" or "known" to cause cancer; cherry picking studies to support its listings; ignoring certain statutory requirements; and a failure to keep up with advances in modern methods of evaluating carcinogenicity. [16]

Beyond these science and process concerns about NTP, for stakeholders such as the small businesses testifying today, the consequences of a listing in the RoC are severe, as effects include: increased compliance costs to meet additional regulations; a freeze on new hires or new investments in the business because of uncertainties associated with a RoC listing; confusion to consumers and employees about the true health risks of a substance listed in the RoC; and insurance concerns relative to workers' compensation policy coverage being raised or dropped.

It is particularly noteworthy that the release of the 12th RoC last year was delayed in part due to a National Academy of Sciences' review of EPA's IRIS assessment of formaldehyde. The Academies:

> *"strongly questioned EPA claims that exposure to formaldehyde can result in increased risk of a leukemia and other cancers that had not previously been associated with formaldehyde, asthma, and reproductive toxicity."*[17]

NTP disagreed with the Academies' assessment, and attached an addendum to the 12th RoC claiming that:

> *"[b]ecause the NAS document is not an independent hazard assessment, it has limited applicability to the NTP's RoC evaluation of formaldehyde. The RoC evaluation involved a multistep comprehensive assessment of the literature, and resulted in a narrative justification for the NTP's conclusions that was developed independently from*

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[14] NTP Website: Since You Asked, *supra*, note 1.
[15] *SIRC v. Sebelius*, June 14, 2011, available at: http://www.styrene.org/news/pdfs/06-16-11-SnyderDeclaration.pdf.
[16] NTP Website, *Background Information on Development of the Process for Preparation of RoC*, available at: http://ntp.niehs.nih.gov/?objectid=13BBADB8-AFDA-7523-3C14A341F04C9BBC (hereinafter NTP Website – Background Information).
[17] Maria Hegstad, "NAS Sets Back EPA Proposal For Strict Formaldehyde Risk Assessment," *Environmental NewsStand*, April 8, 2011, available at: http://insideepa.com/20110408236040 7/EPA-Daily-News/Daily-News/nas-sets-back-epa-proposal-for-strict-formaldehyde-risk-assessment/menu-id-95.html.

> *the EPA IRIS assessment. Neither the NTP listing process nor the justification for the listing of formaldehyde in the RoC was reviewed by the NAS."*[18]

This disagreement ultimately led Congress to direct the National Academy of Sciences to review the 12th RoC's classification of formaldehyde and styrene.

ISSUES

Definitions of "Known" and "Reasonably Anticipated" *(Appendix 2)*

There is a great deal of uncertainty in NTP's listing criteria for deciding how substances should be categorized. To be a "known" carcinogen, NTP requires there be an **undefined** "sufficient evidence of carcinogenicity from studies in humans."[19] To be a "reasonably anticipated" carcinogen requires "limited evidence of carcinogenicity from studies in humans."[20] It is unclear what constitutes "limited evidence."

Such ambiguity causes enormous confusion, as critics have argued that NTP:

> *"reserve[s] to itself the discretion to consider whatever information it wants, to exclude whatever information it wants, and to evaluate that information in accordance with whatever ad hoc criteria it wants to apply."*[21]

Moreover, without any data identifying levels of exposure or the circumstances under which a RoC substance is cancerous, any listing in the document appears hazardous to the average person. Further confusing the issue is NTP's disclaimer that a:

> *"listing in the Report on Carcinogens does not by itself mean that a substance will cause cancer. Many factors, including the amount and duration of exposure, and an individual's susceptibility to a substance, affect whether a person will develop cancer."*[22]

NTP Response to Public Comments

While NTP solicits public comments during the preparation of the RoC, it does not, practically speaking, respond to them. As part of the 12th RoC, NTP did respond to select comments, but only after the 12th RoC was published.

Soliciting public comments is merely half the process – the more critical half requires replying to them. Such an action could be of great value not only to those who submit comments, but also to NTP as it would provide a level of transparency to the RoC by demonstrating to commenters and

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[18] Addendum to the 12th Report on Carcinogens, available at: http://ntp.niehs.nih.gov/ntp/roc/twelfth/addendum.pdf (hereinafter RoC Addendum).
[19] NTP Website, *Listing Criteria*, available at: http://ntp.niehs.nih.gov/?objectid=03C9CE38-E5CD-EE56-D21B94351DBC8FC3 (hereinafter NTP Website – Listing Criteria).
[20] Ibid.
[21] Dr. Richard Belzer, "The Report on Carcinogens – What Went Wrong and What Can be Done to Fix It," January 2012, available at: http://cei.org/sites/default/files/Richard%20B%20Belzer%20-%20The%20Report%20on%20Carcinogens.pdf (hereinafter Belzer Paper).
[22] NTP Website - Since You Asked, *supra*, note 1.

review panel members exactly how NTP has considered the comments. As it stands now, one will have to take NTP's word that it considers comments because the 13th RoC makes no accommodation for responding to comments – that step has been removed since the last RoC. *(Appendix 4 and 5).*

It bears highlighting that in a November 16, 2004 'prompt' letter from the Office of Management and Budget (OMB) to the National Institutes of Health (NIH), the Administrator of the Office of Information and Regulatory Affairs (OIRA) echoed similar concerns after noting the "six distinct information quality correction requests [under the Information Quality Act] related to either the NTP Report on Carcinogens or to the NTP review process for individual substances."[23]

Under the federal Information Quality Act (IQA)[24] and the implementing guidelines,[25] federal agencies are required to maximize the quality, integrity, utility and objectivity of the information they disseminate.[26] Scientific information must be reproducible and transparent, and sound statistical and research methods must be used to develop analytical results.[27]

To "instill public confidence in the NTP process and Report on Carcinogens,"[28] the OIRA Administrator suggested:

> *"[W]hen NTP receives comments from the public on substances being reviewed for listing or delisting in the Report on Carcinogens, NTP should prepare a response-to-comments document and make this document available to the public in a timely manner. The Report on Carcinogens already acknowledges that 'opportunities for public comment and participation are an integral part of the review process.' To fully realize the value of the comment process, NTP should prepare and disseminate a response-to-comments document before completion of a substance's review. This document would improve the transparency of the process and assure the public that their perspectives have not only been sought but also considered. Moreover, the discipline of preparing this document will ensure that the scientists responsible for the Report on Carcinogens have systematically considered and addressed all the significant scientific comments that NTP has received. It would also be desirable for this document to be made available before an NTP review committee evaluates a particular substance. With this structure, the members of these important committees will also have the benefit of both the insights of the public and the NTP's responses to these comments."*[29]

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[23] Letter from OIRA Administrator Dr. John D. Graham to NIH Director Dr. Elias A. Zerhouni, November 16, 2004, available at http://www.reginfo.gov/public/prompt/nih_ntp111604.pdf (hereinafter OIRA Letter to NIH); "'Prompt' letters are a mechanism created in 2001 that OIRA uses to pro-actively suggest issues that agencies might address." OIRA Q&A's, available at http://www.whitehouse.gov/omb/OIRA_QsandAs.

[24] Treasury and General Government Appropriations Act for Fiscal Year 2001, Pub. L. No. 106-554, § 515, 114 Stat. 2763A-153 to 2763A-154, 44 U.S.C. § 3516 note (2000).

[25] Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies, 67 Fed. Reg. 8452 (Feb. 22, 2002) (hereinafter OMB IQA Guidelines); HHS Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated to the Public, available at http://aspe.hhs.gov/infoquality/Guidelines/index.shtml; NIH Guidelines for Ensuring the Quality of Information Disseminated to the Public, available at http://www.aspe.hhs.gov/infoquality/Guidelines/NIHinfo2.shtml.

[26] OMB IQA Guidelines, 67 Fed. Reg. at 8452.

[27] Ibid.

[28] OIRA Letter to NIH, *supra*, note 23.

[29] Ibid.

Peer Review Transparency

Part of the process for the 13th RoC includes peer review of the draft RoC Monograph by an NTP Peer Review Panel. Although the schematic (*Appendix 4*) identifies these peer review panels as federally chartered advisory groups, several concerns have been raised about them, including the charge questions - what they will be and where they will come from - and the extent of public input into their formulation.[30] It is also unclear whether these advisory groups fit Federal Advisory Committee Act (FACA) criteria such as membership balance, objectivity, and accessibility to the public.[31]

Concerns also exist over the NTP's Board of Scientific Counselors (BSC), which are involved twice during the 13th RoC process - once to review the "draft concepts for substances proposed for evaluation," (*Appendix 4*) and then again when it is "present[ed] information regarding the peer review and revised draft RoC Monograph." (*Appendix 4*). The use of the word 'present' is unclear, as it suggests the BSC may not be given the option to review, comment, and provide feedback on the revised draft RoC Monograph.

Administration Guidance on Regulatory Process

On January 20, 2009, President Obama's then-Chief of Staff Rahm Emanuel issued a memo to the heads of executive departments and agencies on regulatory review. The following language in the memo is of interest to this hearing:

> *"As used in this memorandum, 'regulation' has the meaning set forth in section 3(e) of Executive Order 12866 of September 30, 1993, as amended; this memorandum covers 'any substantive action by an agency (normally published in the Federal Register) that promulgates or is* ***expected to lead to the promulgation of*** *a final rule or regulation, including notices of inquiry, advance notices of proposed rulemaking, and notices of proposed rulemaking.'"*[32] *(emphasis added).*

NTP's position is that the RoC is a "science-based, authoritative public health communicated tool, not a regulatory document."[33] But the Emanuel memo specifically covers actions by agencies that 'promulgate or is **expected to lead to the promulgation of** a final rule or regulation.' Arguably, the RoC is covered in this definition because NTP acknowledges that

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[30] NTP Website – Background Information, *supra*, note 16.

[31] Wendy R. Ginsberg, "Federal Advisory Committees: An Overview," *Congressional Research Service*, (R40520), January 24, 2011, available at: http://www.crs.gov/Products/R/PDF/R40520.pdf; "FACA defines an 'advisory committee' as 'any committee, board, commission, council, conference, panel, task force, or other similar group, or any subcommittee or other subgroup thereof' that is 'established by statute or reorganization plan,' 'established or utilized by the President,' or 'established or utilized by one or more agencies.' All advisory bodies that fit this definition, however, are not necessarily entities that must adhere to FACA."

[32] Memo from Rahm Emanuel, Assistant to the President and Chief of Staff, to Heads of Executive Departments and Agencies, January 20, 2009 (effective after 12:00pm), available at: http://www.whitehouse.gov/sites/default/files/omb/assets/information_and_regulatory_affairs/regulatory_review_01_2009.pdf.

[33] Memo from NIEHS and NTP Director Linda Birnbaum, to HHS Secretary Kathleen Sebelius, "Follow-up Information on the Report on Carcinogens, Twelfth Edition," December 2, 2010.

"[c]ertain regulatory agencies have chosen to base certain of their regulatory actions on a listing of a substance in the *Report on Carcinogens*."[34]

Moreover, applying the principles of the Emanuel memo to the RoC would also appear to honor the legislative intent of the law creating the RoC, when then-Chairman Rogers explained that the:

> *"intention of the legislation was that listing in the annual report would be a first step in regulation, one triggering a review by the agencies responsible for enforcing various laws regulating carcinogens."*[35]

Interagency Review and Decision-Making

Typically, substances listed in the RoC are selected after an interagency committee reviews the nominations.[36] This rather informal - and closed - process involves a scientist-representative from each of nine designated agencies, yet, once a substance goes through an interagency review early in the RoC process, it is almost certain to be listed in the final report. It is very rare for a substance to be reviewed and not recommended for a listing. The 12th RoC identifies three substances - over the course of twelve reports in 31 years - that were "formally considered for listing by the NTP and, after evaluation by the Report on Carcinogens review groups, were recommended not to be listed in the Report on Carcinogens."[37] When one considers that the 12th RoC contains 240 substance profiles, it raises questions about the role of public comments and review groups in the RoC.

Strength-of-Evidence vs. Weight-of-Evidence

Two common approaches in how scientific studies are assessed and evaluated include a strength-of-evidence (SOE) approach and a weight-of-evidence (WOE) approach. One of our witnesses, in recent public comments before the Board of Scientific Counselors regarding NTP's proposed revisions to the process for preparation of the RoC explained the issue thus:

> *"Although the draft [of the 13th RoC] speaks of addressing 'all information that may bear on a listing decision' and 'integrat[ing] the overall body of evidence,' it lacks a defined commitment to employing a weight-of-evidence approach to data evaluation. Such evaluations provide a systematic approach to describing how varied data contribute to the questions at hand, which for the RoC, means the considerations leading to potential human carcinogenicity classification. Thus, it is not sufficient to simply 'integrate' all data that argue for a listing, as is represented by the strength-of-evidence approach used*

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[34] Ibid.
[35] OTA Report, *supra*, note 5.
[36] Process for Preparation of the Report on Carcinogens, NTP, available at: http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf; (hereinafter NTP's RoC Preparation Process); "Interagency review is invited from agencies represented on the NTP Executive Committee, including the Consumer Product Safety Commission, Department of Defense, Environmental Protection Agency, Food and Drug Administration, National Cancer Institute, National Center for Environmental Health/Agency for Toxic Substances and Disease Registry, National Institute of Environmental Health Sciences, National Institute for Occupational Safety and Health, and Occupational Safety and Health Administration."
[37] 12th RoC, *supra*, note 12.

> *in past Report on Carcinogen reviews and which remains implied in the proposed revisions. Rather, a weight-of-evidence review demands a visible commitment to, and articulation of, standardized data presentation and analysis of all countervailing evidence, and weighs the associated strengths and weaknesses of those data in supporting listing classifications."*[38]

Moreover, the National Research Council of the National Academies had the following to say about a WOE approach in its review of EPA's formaldehyde assessment last year (*Appendix 6*):

> *"A weight-of-evidence approach such as that provided in EPA's RfC [Reference Concentration] Methodology (U.S. EPA, 1994) or in EPA's proposed guidelines for carcinogen risk assessment (U.S. EPA, 1999a) should be used in assessing the database for an agent. This approach requires a critical evaluation of the entire body of available data for consistency and biological plausibility. Potentially relevant studies should be judged for quality and studies of high quality given much more weight than those of lower quality. When both epidemiological and experimental data are available, similarity of effects between humans and animals is given more weight. If the mechanism or mode of action is well characterized, this information is used in the interpretation of observed effects in either human or animal studies. Weight of evidence is not to be interpreted as simply tallying the number of positive and negative studies, nor does it imply an averaging of the doses or exposures identified in individual studies that may be suitable as points of departure (PODs) for risk assessment. The study or studies used for the POD are identified by an informed and expert evaluation of all the available evidence (EPA 2002b, Pp 4-11 to 4-12)."*[39]

Studies considered for a RoC listing do not follow a WOE system as NTP does not identify a WOE framework to characterize the value, or 'weight,' of studies considered in determining a substance's carcinogenicity.

The RoC's Statutory Obligations

RoC Schedule

NTP has had a difficult time meeting its publication schedule. The 1st RoC was published in 1980, two years after the law's enactment, which initially called for an annual report. Although the 2nd RoC came out in 1981, the 3rd RoC was published in 1983 and the 4th was largely unavailable until 1986.[40] The 1993 change in the law allowing for biennial publications has not led to a more timely schedule considering the six years that lapsed between the publication of the 11th RoC in 2005 and the 12th last year.

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[38] James S. Bus, Ph.D., DABT, ATS, The Dow Chemical Company, Public Comment to the Board of Scientific Counselors re: National Toxicology Program Proposed Revisions to the Process for Preparation of the Report on Carcinogens, December 15, 2011, available at: http://ntp.niehs.nih.gov/NTP/About_NTP/BSC/2011/December/PublicComm/Bus20111215.pdf.

[39] "Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde," National Research Council of the National Academies, April 8, 2011 (hereinafter NAS Formaldehyde Report).

[40] OTA Report, *supra*, note 5.

Significant Number of Persons Exposed

The RoC is required to list substances *"to which a significant number of persons residing in the United States are exposed." (Appendix 1).* While the 12th RoC acknowledges the statutory requirement, it goes on to say:

> *"Some substances that have been banned or restricted in use (e.g., safrole, arsenical pesticides, and mirex) are listed either because people who were previously exposed remain potentially at risk or because these substances still are present in the environment."*[41]

No indication is given as to what constitutes a significant number of persons, nor how the substances listed in the 12th RoC impact such an undefined significant number of persons residing in the U.S.

Nature of Exposure and Number of Persons Exposed

The RoC is required to provide *"information concerning the nature of such exposure and the estimated number of persons exposed to such substances." (Appendix 1).* NTP falls short of meeting these statutory requirements, claiming:

> *(a) that four of its participating agencies "are responsible for regulating hazardous substances and limiting the exposure to and use of such substances,"*[42] *and*
> *(b) "[b]ecause little information typically is available, estimating the number of people who could be exposed and the route, intensity, and duration of exposure for each substance is a difficult task."*[43]

In ignoring these requirements, NTP explains that the RoC is a hazard identification document only because:

> *"the listing of substances in the RoC only indicates a potential hazard and does not establish the exposure conditions that would pose cancer risks to individuals in their daily lives."*[44]

NTP further offers in the 12th RoC that:

> *"other types of information, such as data on use, production, and occupational or environmental exposure, can be used to determine whether there is (or was) exposure in the United States, and this information is included in each substance profile."*[45]

But, as critics have pointed out, this may not be sufficient:

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[41] 12th RoC, *supra*, note 12.
[42] Ibid.
[43] Ibid.
[44] Ibid.
[45] Ibid.

> *"The requirement to quantify the number of persons exposed serves a critical purpose, which is to ensure that the NTP focuses on high-priority substances and is not distracted by minutiae. As for the nature of exposure, it is reasonable to infer that Congress intended the NTP to focus on environmental and occupational cancer risks because it was these circumstances on which Congress was focused at the time it enacted the law. The NTP does not estimate the actual number of persons exposed...it relies on mass and volume indicators in lieu of exposure indices."*[46]

How a Federal Standard for a Substance Decreases the Public Health Risk

The RoC is required to provide *"a statement identifying for each effluent, ambient, or exposure standard established by a Federal agency with respect to a substance contained in the list under subparagraph (A), the extent to which, on the basis of available medical, scientific, or other data, such standard, and the implementation of such standard by the agency, decreases the risk to public health from exposure to the substance." (Appendix 1).*

The RoC addresses this requirement by:

> *"providing in each profile a summary of the regulations and guidelines, if any, that are likely to decrease human exposure to that substance. Some of these regulations and guidelines have been enacted for reasons other than the substance's carcinogenicity (e.g., to prevent adverse health effects other than cancer or to prevent accidental poisoning of children). These regulations are included in the profiles because reduction of exposure to a suspected or known carcinogen is likely to reduce the risk for cancer."*[47]

While the above might be helpful information, it lacks the analysis the law requires of the RoC, which would be to connect the *"effluent, ambient, or exposure standard established by a Federal agency"* and the *"extent to which, on the basis of available medical, scientific, or other data, such standard, and the implementation of such standard by the agency, decreases the risk to public health from exposure to the substance." (Appendix 1).*

NTP's explanation for not meeting this requirement is that it is "beyond the scope of this report to provide detailed information or interpretation concerning the implementation of each regulatory act, and no attempt is made to do so."[48]

Route of Exposure/Mechanism of Action/Mode of Action

According to NTP's listing criteria:

> *"Conclusions regarding carcinogenicity in humans or experimental animals are based on scientific judgment, with consideration given to all relevant information. Relevant information includes, but is not limited to, dose response, route of exposure, chemical structure, metabolism, pharmacokinetics, sensitive sub-populations, genetic effects, or*

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[46] Belzer Paper, *supra*, note 21.
[47] 12th RoC, *supra*, note 12.
[48] Ibid.

> *other data relating to **mechanism of action or factors that may be unique to a given substance.**"*[49] *(emphasis added).*

Yet, in the Addendum to the 12th RoC, NTP says:

> *"**Appreciation of 'mode of action,'** or an understanding of how exposure to a given substance might lead to cancer, is an important piece of supporting evidence, but **is not a requirement for listing in the RoC.**"*[50] *(emphasis added).*

Analyzing these two comments side-by-side, it appears as though NTP can pick and choose parts of its listing criteria to apply to the studies that exist on any given substance. It is worth referencing EPA's "*Guidelines for Carcinogen Risk Assessment*" to understand the significance of mode of action. EPA emphasizes that:

> *"In evaluating an agent's mode of action, it is usually not sufficient to determine that some event commences upon dosing. It is important to understand whether it is a necessary event that plays a key role in the process that leads to tumor development versus an effect of the cancer process itself or simply an associated event."*[51]

A recent article on NTP's decision to list styrene in the 12th RoC has this to say about mode of action:

> *"risk assessors need to understand as best they can the 'mode of action' (MOA) by which a substance acts biologically within and upon an organism. In many cases, this understanding will help confirm that humans are likely to react the same way as the test animal. But in some cases, this will show that what happened in the test animal is unlikely to happen in humans because of the differences between the species."*[52]

The article further explains that such is the case with styrene, because:

> *"Tumors in laboratory animals have been observed in only one species - mice - and the known plausible biological mechanism by which styrene could cause cancer is specific to the mouse lung and is not relevant to humans."*[53]

Delisting a Substance

There are no guidelines on the process for delisting a substance beyond a mention that one can nominate a substance for delisting in the same way that one nominates a substance for listing in a RoC. However, it is not easy to delist a substance once it is on the RoC, as it takes years, if not decades, to accomplish, and even then, it may not really be delisted. For example, saccharin,

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[49] NTP Website – Listing Criteria, *supra*, note 19.
[50] RoC Addendum, *supra*, note 18.
[51] EPA, "Guidelines for Carcinogen Risk Assessment," March 2005, available at: http://www.epa.gov/osa/mmoaframework/pdfs/CANCER-GUIDELINES-FINAL-3-25-05[1].pdf
[52] Julie E. Goodman, Lorenz R. Rhomberg and Robyn L. Prueitt, "Why Styrene Should Not be Classified as a Human Carcinogen And Does Not Belong in the NTP's 12th Report on Carcinogens," *Bloomberg BNA Daily Environment Report*, March 12, 2012, available at: http://www.gradientcorp.com/alerts/pdf/Styrene.pdf.
[53] Ibid.

which was last listed in 1998 in the 8th RoC, was first listed in the 2nd RoC in 1981 as 'reasonably anticipated' to be a human carcinogen.[54] More interesting is the attempt to delist glass wool, which was first listed in 1994 in the 7th RoC. As described in a December 14, 2011 letter from SBA's Office of Advocacy to the Director of the Office of the Report on Carcinogens:

> *"After more than ten years of research, glass wool was nominated for delisting in 2004. However, instead of delisting the substance the NTP modified the substance profile which excluded certain varieties of glass wool that are 'not biopersistent' in the lung.*
>
> *In the 12th RoC glass wool does not appear either as a delisted substance or as a listed substance, causing additional confusion. The listing to 'delisting' process for glass wool took more than 20 years."*[55]

RoC and IARC

The International Agency for Research on Cancer (IARC) is part of the World Health Organization (WHO). IARC's mission is to "coordinate and conduct research on the causes of human cancer, the mechanisms of carcinogenesis, and to develop scientific strategies for cancer prevention and control."[56] Through international Working Groups, IARC prepares and publishes:

> *"critical reviews and evaluations of evidence on the carcinogenicity of a wide range of human exposures. The[se] Monographs represent the first step in carcinogen risk assessment, which involves examination of all relevant information in order to assess the strength of the available evidence that an agent could alter the age-specific incidence of cancer in humans."*[57]

It is easy to make comparisons between the RoC and IARC's cancer Monographs, given that they're both hazard identification documents, and in the case of the RoC, is largely considered to be influenced by IARC's work. Unlike the RoC however, IARC maintains five categories for classifying its substances:

- *Group 1: Carcinogenic to humans – 107 agents;*
- *Group 2A: Probably carcinogenic to humans – 63 agents;*
- *Group 2B: Possibly carcinogenic to humans – 271 agents;*
- *Group 3: Unclassifiable as to carcinogenicity in humans – 509 agents; and*
- *Group 4: Probably not carcinogenic to humans – 1.*[58]

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[54] 12th RoC, *supra*, note 12.
[55] Letter from Winslow Sargeant, Chief Counsel for Advocacy, to Ruth Lunn, Director, Office of the Report on Carcinogens, December 14, 2011, available at: http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/PublicComm/SBA20111214.pdf.
[56] International Agency for Research on Cancer website, available at: http://www.iarc.fr/ (hereinafter IARC Website).
[57] IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Preamble, 2006, available at: http://monographs.iarc.fr/ENG/Preamble/CurrentPreamble.pdf.
[58] IARC Website, *supra*, note 56.

The RoC has the two categories – "known" to be carcinogenic and "reasonably anticipated" to be carcinogenic. *(Appendix 2).*

While the IARC's five cancer classification categories appear to provide more flexibility and clarity than the RoC, the IARC process also has its own limitations, as, like the RoC, it too is a hazard identification document.

Impact on Small Business

The listing or upgrade of a substance in the RoC has both immediate and long-term impacts on small businesses and creates an atmosphere of uncertainty.[59] While NTP claims the RoC is not a regulatory document, federal and state agencies and state legislators use the RoC as a basis for regulatory and legislative actions without conducting or requiring more comprehensive risk assessments. Small businesses concerned about increased compliance costs due to regulations triggered by the recent listing of styrene are delaying making investments and holding off on hiring additional employees.[60] Some small business owners are also concerned that the increased operating costs may force them to move their facilities outside of the United States.[61]

Federal agencies rely on the information provided in the RoC[62] and use it as a substantive source of information to make regulatory decisions. Under the Occupational Safety and Health Administration's (OSHA) existing Hazardous Communication Standard (HCS), safety data sheets (SDSs) and labeling requirements are triggered by a RoC listing.[63] OSHA recently revised the HCS but retained the requirement that RoC listings be included on SDSs.[64] Small businesses that have hazardous chemicals in their workplace are required to use the SDSs to inform and train employees.[65] In addition, OSHA-regulated laboratories must adopt special procedures for a substance that is listed in the RoC.[66] EPA's reliance on the 11th RoC led it to add 16 chemicals listed in the RoC to its list of toxic chemicals subject to reporting under section 313 of the Emergency Planning and Community Right-to-Know Act of 1986 and section 6607 of the Pollution Prevention Act of 1990.[67]

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[59] Mike Verespej, "Congressmen ask for review of styrene safety," *Plastics News*, November 9, 2011, http://plasticsnews.com/headlines2.html?id=23645 (hereinafter Verespej Article).

[60] Ibid.

[61] Ibid.

[62] Addition of National Toxicology Program Carcinogens; Community Right-to-Know Toxic Chemical Release Reporting, 75 Fed. Reg. 72,727, 72,729, November 26, 2010 (hereinafter Community Right-to-Know); The EPA has stated that the "RoC is an excellent and reliable source of information on the potential for chemicals covered therein to cause cancer in humans." Ibid.

[63] 29 C.F.R. § 1910.1200 (2011).

[64] U.S. Department of Labor, Occupational Safety & Health Administration, Modification of the Hazard Communication Standard (HCS) to conform with the United Nations' (UN) Globally Harmonized System of Classification and Labeling of Chemicals (GHS), available at: http://www.osha.gov/dsg/hazcom/hazcom-faq.html. OSHA modified and published the revised Hazardous Communication Standard on March 26, 2012. Hazardous Communication,77 Fed. Reg. 17,574 (March 26, 2012) (to be codified at 29 C.F.R. pts. 1910, 1915, and 1926). The new regulatory requirements will be phased in between December 1, 2013 and June 1, 2016. Ibid. at 17,582. Employers must be in compliance with the existing or revised HCS, or both, during the phase-in period.

[65] Hazardous Communication, 77 Fed. Reg. 17,574, 17,577 (March 26, 2012) (to be codified at 29 C.F.R. pts. 1910, 1915, and 1926).

[66] 29 C.F.R. § 1910.1450(e)(viii) (2011).

[67] Community Right-to-Know, *supra*, note 62.

On the state-level, a number of worker and community right-to-know and regulatory requirements in other states are also automatically triggered.[68] The listing of a substance in the RoC triggers California Proposition 65, the Safe Drinking Water and Toxic Enforcement Act of 1986.[69] States may also propose new standards as a result of a substance listing. Citing the recommendation of an NTP expert panel in the 12th RoC, California's Office of Environmental Health Hazard Assessment (OEHHA) recently published its Draft Public Health Goal for Styrene in Drinking Water.[70]

In addition to the regulatory burdens, a listing may also cause confusion as to the true public health risk posed by a substance, which can have an economic impact on small business. As previously mentioned, the NTP states that "listing of substances in the RoC only indicates a potential hazard and does not establish the exposure conditions that would pose cancer risks to individuals in their daily lives."[71] However, this disclaimer may not allay the concerns that any exposure to the substance has the potential to cause cancer and lead to legislative action to protect the public's health.

In 2010, Colorado state legislators, concerned about chemicals that cause cancer or reproductive toxicity in personal care products, introduced a bill that in part defined "chemical identified as causing cancer or reproductive toxicity" as a substance listed in the RoC.[72] The legislation would have banned all sales and distribution of personal care products that contain a substance listed in the RoC as "known" or "reasonably anticipated" to be a carcinogen.[73] Among those substances is methyleugenol, a naturally occurring substance present in a number of essential oils including rose, hyacinth, anise, basil, and citronella, which was originally listed in the 10th RoC as reasonably anticipated to be a human carcinogen.[74] The ban would have been enforced through a private right of action that would have allowed citizens to bring an action against a manufacturer.[75] Small businesses found in violation of the law would have been subject to civil penalties of $5,000 for a first offense and $10,000 for subsequent offenses.[76]

The listing of Styrene in the 12th RoC has the potential to impact a substantial number of small businesses as thousands of companies across the country use the substance.[77] For example, over 3,000 small and medium-sized companies represented by the American Composites Manufacturers Association use styrene-polyester resin and glass fiber to manufacture a variety of

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[68] *See* 010-00 ARK. CODE. R. 012 (2012); 105 MASS. CODE REGS. 670.010 (2011); MINN. R. 5206.0100 (2011); N.J. ADMIN. CODE § 12:100-7.7 (2012); 34 PA. CODE § 323.5 (2012).

[69] CAL. HEALTH & SAFETY CODE § 25249.5-25249.13 (2012).

[70] OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT, CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY, PUBLIC HEALTH GOALS FOR CHEMICALS IN DRINKING WATER, STYRENE 2 (2010). OEHHA recommended a Public Health Goal of 0.5 parts per billion (ppb) (0.5 micrograms/liter) for styrene in drinking water (a much lower level than the federal EPA maximum contaminant level goal of 100 ppb (0.1 milligrams/liter).

[71] 12th RoC, *supra*, note 12.

[72] H.B. 10-1248, 67th Gen. Assem., 2d Sess. (Colo. 2010) (hereinafter CO Bill).

[73] Ibid.

[74] 12th RoC, *supra*, note 12.

[75] CO Bill, *supra*, note 72.

[76] Ibid.

[77] American Composites Manufacturers Association Questions and Answers about Styrene, January 21, 2010, available at http://www.acmanet.org/ga/advocacy/Questions&Answers-about-Styrene.pdf.

products including: major components for wind and solar energy; ballistic panels that protect our troops; residential bathtubs, showers, and countertops; recreational boats; and light-weight components that improve the fuel economy of cars, trucks, and mass transit vehicles.[78] The industry estimates that manufacturing plants that use styrene or styrene-derived products employ 500,000 people.[79]

An Oregon composites manufacturer that uses styrene believes that the RoC listing of styrene affected its insurance coverage. Miles Fiberglass and Composites' workers' compensation insurance policy, which was up for renewal in 2011, was dropped, and the small business is now paying $144,000 annually, as compared to its previous rate of $73,000.[80]

Companies are also concerned about potential litigation which may drive up insurance costs. A recent article noted that "[a]ttorneys are primed for a wave of toxic torts over exposure to formaldehyde, which U.S. regulators identified as a 'known carcinogen' last summer."[81]

Legal Challenges, and Agency Comments

Various RoC listings have also been subject to challenges by affected businesses and trade associations in the courts.[82] Before the 12th RoC was finalized, the Chief Counsel for Advocacy of the U.S. Small Business Administration sent a letter to the Secretary of the Department of Health and Human Services citing small business concerns about the NTP process.[83] In 2011, after the 12th RoC was finalized, the Chief Counsel for Advocacy again wrote to the Secretary of Health and Human Services and outlined the potential economic impact on small businesses of a RoC listing, concerns with the 12th RoC review process, and concerns about the proposed changes for the 13th RoC.[84] The Chief Counsel for Advocacy:

> *"urge[d] the HHS to review and evaluate the RoC's purpose and objectives and to consider whether, if substantial changes cannot be made, the RoC should continue to play a role in the federal government's chemical risk assessment program."*[85]

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[78] Ibid.
[79] Ibid.
[80] Verespej Article, *supra*, note 59.
[81] Erin Fuchs, "Formaldehyde Cancer Link Could Spur Modest Tort Wave," *Law 360*, April 17, 2012.
[82] *See Tozzi v. U.S. Dep't of Health & Human Servs.*, 271 F.3d 301 (D.C. Cir. 2001); *The Fertilizer Inst. v. U.S. Dep't of Health & Human Servs.*, 355 F. Supp. 2d 123 (D.D.C. 2004); *Synthetic Organic Chem. Mfrs. Ass'n v. U.S. Dep't of Health & Human Servs.*, 720 F. Supp. 1244 (W.D. La. 1989).
[83] Letter from Winslow Sargeant, Chief Counsel for Advocacy to Kathleen Sebelius, Sec'y of Health & Human Servs, December 1, 2010, available at http://www.sba.gov/sites/default/files/hhs10_1201.pdf.
[84] Letter from Winslow Sargeant, Chief Counsel for Advocacy to Kathleen Sebelius, Sec'y of Health & Human Servs, November 22, 2011, available at http://www.sba.gov/sites/default/files/Advocacy_Comment_Letter-Report_On_Carcinogens.pdf. Advocacy resent this letter to Ruth Lunn, Director, Office of the Report on Carcinogens, on December 14, 2011.
[85] Ibid.

WITNESSES

Panel I:

- **Dr. Linda S. Birnbaum**, Director, National Institute of Environmental Health Sciences & National Toxicology Program, U.S. Department of Health and Human Services
- **Mr. Charles A. Maresca,** Director of Interagency Affairs, Office of Advocacy, U.S. Small Business Administration

Panel II:

- **Dr. James S. Bus**, Director of External Technology, Toxicology and Environmental Research and Consulting, The Dow Chemical Company
- **Dr. L. Faye Grimsley,** Associate Professor, Tulane School of Public Health and Tropical Medicine, Department of Global Environmental Health Sciences
- **Ms. Bonnie Webster**, Vice President, Monroe Industries, Inc.
- **Ms. Ally LaTourelle**, Esq., V.P. Government Affairs, Bioamber, Inc
- **Mr. John E. Barker**, Corporate Manager, Environmental Affairs, Safety and Loss Prevention, Strongwell Corporation
- **Dr. Richard B. Belzer**, President, Regulatory Checkbook

APPENDIX 1[86]

History of the RoC - Congressional Mandate (1978)

In response to concerns from people within the United States regarding the relationship between their environment and cancer, in 1978 the U.S. Congress mandated, as part of the Public Health Service Act, (see Section 301(b)(4), as amended)[11], that the Secretary, Health and Human Services (HHS), publish a biennial report which contains:

A. a list of all substances
    i. which either are known to be carcinogens or may reasonably be anticipated to be carcinogens and
    ii. to which a significant number of persons residing in the United States are exposed;
B. information concerning the nature of such exposure and the estimated number of persons exposed to such substances;
C. a statement identifying
    i. each substance contained in the list under subparagraph (A) for which no effluent, ambient, or exposure standard has been established by a Federal agency, and
    ii. for each effluent, ambient, or exposure standard established by a Federal agency with respect to a substance contained in the list under subparagraph (A), the extent to which, on the basis of available medical, scientific, or other data, such standard, and the implementation of such standard by the agency, decreases the risk to public health from exposure to the substance; and
D. a description of
    i. each request received during the year involved
        I. from a Federal agency outside the Department of Health, Education, and Welfare for the Secretary, or
        II. from an entity within the Department of Health, Education, and Welfare to any other entity within the Department, to conduct research into, or testing for, the carcinogenicity of substances or to provide information described in clause (ii) of subparagraph (C), and
    ii. how the Secretary and each such other entity, respectively, have responded to each such request.

[86] NTP Website, *History of the RoC*, available at: http://ntp.niehs.nih.gov/?objectid=03CA7EEA-CBAA-EB17-20B4B2C329C5DDCF.

APPENDIX 2[87]

NTP Listing Criteria for the RoC

The criteria for listing an agent, substance, mixture, or exposure circumstance in the RoC are as follows:

Known To Be Human Carcinogen:

There is sufficient evidence of carcinogenicity from studies in humans,* which indicates a causal relationship between exposure to the agent, substance, or mixture, and human cancer.

Reasonably Anticipated To Be Human Carcinogen:

There is limited evidence of carcinogenicity from studies in humans,* which indicates that causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding factors, could not adequately be excluded,

or

There is sufficient evidence of carcinogenicity from studies in experimental animals, which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors (1) in multiple species or at multiple tissue sites, or (2) by multiple routes of exposure, or (3) to an unusual degree with regard to incidence, site, or type of tumor, or age at onset,

or

There is less than sufficient evidence of carcinogenicity in humans or laboratory animals; however, the agent, substance, or mixture belongs to a well-defined, structurally related class of substances whose members are listed in a previous Report on Carcinogens as either known to be a human carcinogen or reasonably anticipated to be a human carcinogen, or there is convincing relevant information that the agent acts through mechanisms indicating it would likely cause cancer in humans.

Conclusions regarding carcinogenicity in humans or experimental animals are based on scientific judgment, with consideration given to all relevant information. Relevant information includes, but is not limited to, dose response, route of exposure, chemical structure, metabolism, pharmacokinetics, sensitive sub-populations, genetic effects, or other data relating to mechanism of action or factors that may be unique to a given substance. For example, there may be substances for which there is evidence of carcinogenicity in laboratory animals, but there are compelling data indicating that the agent acts through mechanisms which do not operate in humans and would therefore not reasonably be anticipated to cause cancer in humans.

**This evidence can include traditional cancer epidemiology studies, data from clinical studies, and/or data derived from the study of tissues or cells from humans exposed to the substance in question that can be useful for evaluating whether a relevant cancer mechanism is operating in people.*

[87] NTP Website – Listing Criteria, *supra*, note 19.

APPENDIX 3[88]

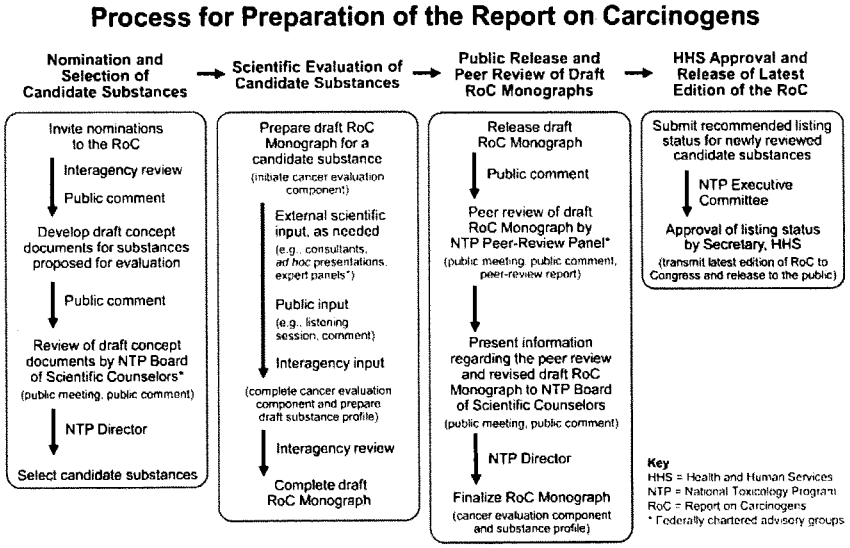
Substances Delisted from the Report on Carcinogens

Substance Name	CAS Number	Last Listing	Reason for Delisting
Chloramphenicol	56-75-7	*known*	Human data considered inadequate
Aramite	140-57-8	First RoC (1980) *reasonably anticipated* Fourth RoC (1985)	No U.S. residents exposed
N,N-Bis(2-chloroethyl)-2-naphthylamine (Chlornaphazine)	494-03-1	*known*	No U.S. residents exposed
Cycasin	14901-08-7	Fourth RoC (1985) *reasonably anticipated*	No U.S. residents exposed
Methyl iodide	78-88-4	Fourth RoC (1985) *reasonably anticipated*	Reevaluated by IARC; evidence now considered equivocal
5-Nitro-*o*-anisidine	99-59-2	Fourth RoC (1985) *reasonably anticipated*	Insufficient evidence of carcinogenicity
p-Nitrosodiphenylamine	156-10-5	Fifth RoC (1989) *reasonably anticipated*	Insufficient evidence of carcinogenicity
Ethyl acrylate	140-88-5	Fifth RoC (1989) *reasonably anticipated*	See following profile
Saccharin	81-07-2	Eighth RoC (1998) *reasonably anticipated* Eighth RoC (1998)	See following profile

[88] 12th RoC, *supra*, note 12.

APPENDIX 4[89]

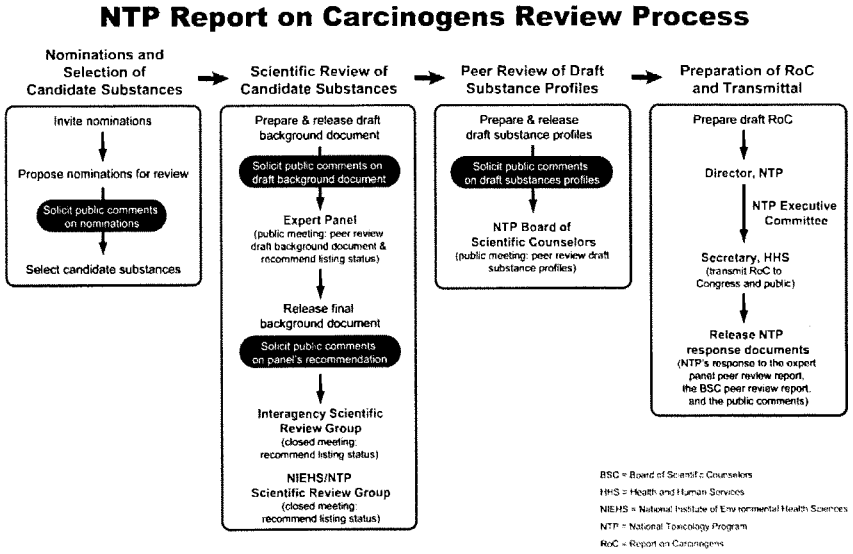
Schematic of the Process for the 13th Report on Carcinogens



[89] NTP Website, *Process for the Preparation of the Report on Carcinogens*, (13th RoC), available at: http://ntp.niehs.nih.gov/?objectid=3756DE0C-FA7A-404B-3F72194C30ABD961.

APPENDIX 5[90]

Schematic of the Process for the 12th Report on Carcinogens



[90] NTP Website, *Review Process for the 12th Report on Carcinogens*, available at: http://ntp.niehs.nih.gov/?objectid=03C9C7CF-CF9E-913D-882FBAB402BADA19.

APPENDIX 6[91]

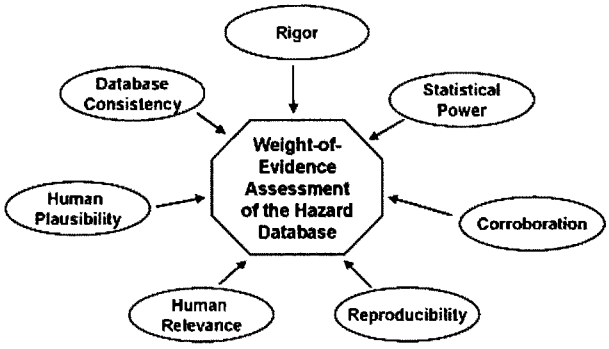


FIGURE 4-5 Conceptual view of a weight of evidence (WOE) assessment. This figure illustrates the critical considerations within a WOE assessment of toxicity data.

- **Rigor** is the degree of proper conduct and analysis of a study; greater weight is generally given to more rigorous studies.
- **Statistical Power** is the ability of a study to detect effects of a given magnitude.
- **Corroboration** means that specific effects are replicated in similar studies, similar effects are observed under varied conditions and /or similar effects are observed in multiple laboratories.
- **Reproducibility** means that an effect is observed in multiple species by various routes of exposure.
- **Relevance to Humans** means that similar effects are observed in humans or in a species taxonomically related to humans or at doses similar to those expected in humans.
- **Plausibility to Humans** is the determination of whether a similar metabolism, mechanisms of damage and repair, and molecular target of response could be expected to occur in humans, based on an evaluation of the biologic mechanism of a toxic response in animals.
- **Database Consistency** is the extent to which all of the data are similar in outcome and dose (exposure-response) and are operating under a single biologically plausible assumption (mode of action).

Source: Adapted from Gray et al. 2001, EPA 2006, Pp 29-30.

[91] NAS Formaldehyde Report, *supra*, note 39.

Chairman BROUN. Committee on Science, Space, and Technology, Subcommittee on Investigations and Oversight, and the Committee on Small Business, Subcommittee on Healthcare and Technology will come to order. Good morning, everyone. Welcome to today's joint hearing entitled, "How the Report on Carcinogens Uses Science to Meet Its Statutory Obligations and Its Impact on Small Business Jobs."

In front of you are packets containing the written testimony, biographies, and truth in testimony disclosures for both of today's witness panels. Before we get started, since this is a two-panel joint hearing involving two House Committees, Subcommittees, I want to explain how we will operate procedurally so that all Members understand how the question-and-answer period will be handled. We will take testimony from the first panel and then proceed with a question-and-answer period. During the question-and-answer period, we will alternate between the two Committees, starting with the Science Committee majority and then the Science Committee minority. We will then call on the Small Business Committee majority, followed by the Small Business minority. If there is not a Member of one of these Committees present, we will continue to alternate between the majority and minority Members and allow all Members an opportunity for questioning before recognizing a Member for a second round of questions, if we get to a second round.

We will recognize those Members of either Subcommittee present at the gavel in order of seniority on their respective Committee, and those coming in after the gavel will be recognized in their order of arrival.

After the first panel has been excused, we will take testimony from the second panel and then undertake a question-and-answer period in the same fashion as with the first panel.

I now recognize myself for five minutes for an opening statement.

I would like to extend a strong, warm welcome to my colleagues from the Small Business Committee and thank them for their participation in this joint hearing today.

The Science, Space, and Technology Committee has a history of conducting oversight hearings on agencies and programs that produce chemical assessments. While we have delved into the work performed by the Agency for Toxic Substances and Disease Registry and the EPA's IRIS Program on more than one occasion, this is the first time I have had the opportunity to hearing from the director of HHS's National Toxicology Program on the subject of the Report on Carcinogens, also known as the RoC.

I view today's hearing as a learning opportunity for our Committees so that we may better understand the work performed by NTP as it publishes its report on carcinogens.

As a legislator, I am very concerned with protecting public health and safety. I can think of few greater responsibilities that we have as public servants. As a physician, I take this responsibility even more seriously. When substances are found to be harmful, we should make every effort to minimize the public's exposure. We also have a responsibility to ensure that these determinations are appropriate and not arbitrary or capricious and are communicated correctly.

While taking the most cautious and precautionary approach to making these determinations may seem like the right thing to do, this method may actually do more harm than good. When concerns and fear are promoted with little actual risk, commerce, small businesses, and everyday citizens are impacted with no appreciable benefit to their safety.

It is often repeated that RoC does not assess risk, just hazards, and it is not a regulatory action, and therefore, it is not required to meet more rigorous standards. While this may be true, it unfortunately is not the whole story. These assessments are highly influential scientific assessments that influence regulatory actions at the earliest stages. When the law that established the RoC was passed, its stated intent was, "to be a first step in regulation."

Because the RoC has such great import, it is critical that these reports reflect the best available science. The recent release of the 12th RoC demonstrates how confusing this process can be. In a report published last April on the EPA IRIS assessment of formaldehyde, the National Academy of Sciences stated, "strongly question EPA's claims that exposure to formaldehyde can result in increased risk of leukemia and other cancers that had not previously been associated with formaldehyde, asthma, and reproductive toxicity."

Yet two months after the Academy's reports, the NTP issued the 12th RoC with an upgrade in the listing of formaldehydes to a known carcinogen, based in part on claims similar to those made by EPA and dismissed the Academy's report in an addendum. Since then, concerns have been raised about how the RoC is developed and how its findings are communicated.

Last winter, the Small Business Administration's Office of Advocacy sent a letter to HHS, as well as to NTP, urging HHS, "to review and evaluate the RoC's purpose and objectives and to consider whether, if substantial changes cannot be made, the RoC should continue to play a role in the Federal Government's Chemical Risk Assessment Program."

This is a surprisingly forthright comment and one that Congress should not take lightly. Separately, in the Omnibus Appropriations Bill passed last December, Congress directed the Academies to review the 12th RoC's listing of two of its substances, and I look forward to reading that report when it is published, hopefully soon.

Although the RoC is not a regulation, by its own admission, "the RoC can be used by regulatory agencies and others for decision making." That makes this a very influential document, because a RoC listing has real-world implications, and we will hear about some of those implications from the small business witnesses on our second panel.

Ultimately, we have to ensure that the public has the best information possible in order to protect their health.

[The prepared statement of Mr. Broun follows:]

OPENING STATEMENT
The Honorable Paul Broun, M.D. (R-GA), Chairman
Science, Space, and Technology Committee, Subcommittee on Investigations and Oversight
Joint Hearing with
Small Business Committee, Subcommittee on Healthcare and Technology
"How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"

Wednesday, April 25, 2011

I'd like to extend a warm welcome to my colleagues from the Small Business Committee, and thank them for their participation in this joint hearing today.

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I view today's hearing as a learning opportunity for our committees so that we may better understand the work performed by NTP as it publishes its Report on Carcinogens.

As a legislator, I am very concerned with protecting public health and safety. I can think of few greater responsibilities we have as public servants. As a physician, I take this responsibility even more seriously. When substances are found to be harmful, we should make every effort to minimize the public's exposure. We also have a responsibility to ensure that these determinations are appropriate, are not arbitrary or capricious, and are communicated correctly.

While taking the most cautious and precautionary approach to making these determinations may seem like the right thing to do, this method may actually do more harm than good. When concerns and fear are promoted with little actual risk, commerce, small businesses, and everyday citizens are impacted with no appreciable benefit to their safety.

It is often repeated that the RoC does not assess risk, just hazards, and it is not a regulatory action, and therefore it is not required to meet more rigorous standards. While this may be true, it unfortunately is not the whole story. These assessments are highly influential scientific assessments that influence regulatory actions at the earliest stages. When the law that established the RoC was passed, its stated intent was "to be a first step in regulation."

Because the RoC has such great import, it is critical that these reports reflect the best available science. The recent release of the 12th RoC demonstrates how confusing this process can be. In a report published last April on the EPA IRIS assessment of formaldehyde, the National Academy of Sciences:

> "strongly questioned EPA claims that exposure to formaldehyde can result in increased risk of a leukemia and other cancers that had not previously been associated with formaldehyde, asthma, and reproductive toxicity."

Yet two months after the Academies' report, NTP issued the 12th RoC with an upgrade in the listing of formaldehyde to a "known" carcinogen, based in part on claims similar to those made by EPA, and dismissed the Academies' report in an addendum. Since then, concerns have been raised about how the RoC is developed and how its finding are communicated.

Last winter, the Small Business Administration's Office of Advocacy sent a letter to HHS as well as to NTP, urging HHS:

> "to review and evaluate the RoC's purpose and objectives and to consider whether, if substantial changes cannot be made, the RoC should continue to play a role in the federal government's chemical risk assessment program."

That is a surprisingly forthright comment, and one that Congress shouldn't take lightly. Separately, in the omnibus appropriations bill passed last December, Congress directed the Academies to review the 12th RoC's listing of two of its substances, and I look forward to reading that report when it's published.

Although the RoC is not a regulation, by its own admission, "the RoC can be used by regulatory agencies and others for decision making." That makes this a very influential document because a RoC listing has real world implications, and we will hear about some of those implications from the small business witnesses on our second panel. Ultimately, we have to ensure that the public has the best information possible in order to protect their health.

I now yield to Chairwoman Ellmers.

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Chairman BROUN. Now, I ask unanimous consent that we add a number of letters from various groups to the record. These have been shared with the minority in advance of the hearing.

Without objection, so ordered.

[The information may be found in Appendix 2.]

Chairman BROUN. I now recognize the Chair of the Committee on Small Business, Subcommittee on Health and Technology, for five minutes and her opening statement. Mrs. Ellmers.

Chairwoman ELLMERS. Good morning, and I thank Chairman Broun for working with me and my staff on this very important issue. I thank all of our witnesses for being here today, and I am looking very much forward to your testimony.

We are here today to learn about the Report on Carcinogens and the impact it has on small businesses across America. According to the National Toxicology Program, this report is intended to be a science-based, public health communication tool. However, the Report on Carcinogens has been used by federal and State agencies as a regulatory document, using its listing of substances as a basis for regulatory and legislative action.

Each year, small businesses with less than 20 employees are burdened with compliance regulations that cost them 36 percent more per employee than their larger counterparts. Despite the economic downturn, the regulatory burden on small businesses continues to grow. Increasing regulations mean small businesses must dedicate more money, time, and resources by complying with regulations instead of doing what they do best, creating jobs and innovating new products.

The Federal Government has an important duty in researching and identifying substances that could cause harm and hazards in the public health. But at the same time, our government must recognize the adverse consequences of requiring businesses to call a substance a human carcinogen without definitive evidence. It is irresponsible and could lead to unnecessary strain for small businesses. The regulatory uncertainty this is causing has already resulted in small businesses delaying hiring new employees and is causing many small businesses to hold off on making important investment decisions.

Scientists, small businesses, and their representatives are now raising concerns about the quality of this analysis and the process used to list these substances in the Report on Carcinogens. Specifically, questions have been raised regarding the peer review process. Reports have shown that this process has failed to meet the independent and objective standards that would justify the overbearing burdens being placed on local economies and businesses, not to mention the insufficient public comment procedures that remain lacking.

The Report on Carcinogens was originally mandated by Congress in 1978, to help aid the research and prevention of many cancers. Although there have been many major breakthroughs in the scientific understanding of cancers and its causes, the process that the National Toxicology Program currently uses to identify carcinogens has not kept up with the pace of scientific developments. Despite warnings that the National Toxicology Program review process for the report must be improved, there are new concerns that

the process for the next report has made only minor substantive changes and is merely a rearranging of the deck chairs.

Small businesses continue to fear the ramifications of this report. When the government publishes scientific information that negatively impacts private businesses, the government has the duty and responsibility to ensure that the information is the product of an objective and scientifically sound process.

Again, I want to thank each one of our witnesses today for their participation, as well as Chairman Broun and the Science Committee for hosting us today. I look forward to working with all of you on this very important issue.

Mr. Chairman, I would like to take a moment to say that I have included one letter from a small business in my district as well as a letter to the Office of Advocacy, November 22, 2011, to the letter of Department of Health and Human Services as part of my opening statement for the record.

I yield back.

[The prepared statement of Mrs. Ellmers follows:]

Opening Statement of Chairwoman Renee Ellmers
Subcommittee on Healthcare and Technology
"How the Report on Carcinogens uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"
April 25, 2012

Good morning. I want to thank Chairman Broun for working with me on this joint hearing, and would like to thank our witnesses for being here today. We look forward to your testimony.

We're here today to learn about the Report on Carcinogens and the impact it has on small businesses across America. According to the National Toxicology Program, this report is intended to be a science-based, public health communication tool. However, the Report on Carcinogens has been used by federal and state agencies as a regulatory document - using its listing of substances as a basis for regulatory and legislative action.

Each year, small businesses with less than 20 employees are burdened with compliance regulations that cost them 36 percent more per employee than their larger counterparts. Despite the economic downturn, the regulatory burden on small business continues to grow. Increased regulations mean small businesses must dedicate more money, time, and resources to complying with regulations instead of doing what they do best – creating jobs and innovating new products.

The federal government has an important duty in researching and identifying substances that could cause harm and hazards to public health. But at the same time, our government must recognize the adverse consequences of requiring businesses to call a substance a human carcinogen, without definitive evidence. It is irresponsible and could lead to unnecessary strain for small businesses. The regulatory uncertainty this is causing has already resulted in small businesses delaying the hiring new employees and is causing many small businesses to hold off on making important investment decisions.

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The Report on Carcinogens was originally mandated by Congress in 1978 to help aid the research and prevention of many cancers. Although there have been major breakthroughs in the scientific understanding of cancer and its causes, the processes that the National Toxicology Program currently uses to identify carcinogens has not kept pace with scientific developments. Despite warnings that the National Toxicology Program review process for the report must be

improved, there are new concerns that the process for the next report has made only minor substantive changes and is merely a rearranging of the deck chairs.

Small businesses continue to fear the ramifications of this report. When the government publishes scientific information that negatively impacts private businesses, the government has the duty and responsibility to ensure that the information is the product of an objective and scientifically sound process.

Again, I want to thank each of our witnesses for their participation, as well as Chairman Broun and the Science Committee for hosting us today. I look forward to working with you on this important issue. I yield back.

Chairman BROUN. Without objection, they will be entered into the record at this point.

[The information may be found in Appendix 2.]

Chairman BROUN. The Chair now recognizes my good friend from New York, Mr. Tonko, for an opening statement. You are recognized for five minutes.

Mr. TONKO. Thank you, Mr. Chair, and welcome to our witnesses.

Usually I begin my statement by thanking you for having the Subcommittee examine a topic of importance and for inviting witnesses who bring a variety of perspectives and expertise to the subject at hand.

Unfortunately, I am sorry that I am unable to do that today. We did not agree in all particulars of the last Subcommittee hearing, but I compliment you for inviting a balanced slate of witnesses to inform us on renewable energy tax provisions. When the Subcommittee is in a learning mode, such balance reflects well on the Subcommittee and highlights that we are truly interested in coming to a complete understanding of a policy issue.

Today's hearing is very disappointing. In theory, we are examining the National Toxicology Program's 12th Report on Carcinogens. In reality, we are hearing the objections of one industry to the listing of one chemical. There is virtually no balance here today, in my opinion. Five of the six witnesses invited by the majority are aligned closely with the styrene industry and the American Composite Manufacturers Association.

Certainly we should hear from the businesses with an interest in this report. Their concerns about the implications of the report for their businesses are legitimate issues for us to, indeed, consider. But in this matter, I would also expect us to bring other concerned voices into the room to ensure that we have a complete, complete picture of how the report and this program are viewed by all interested parties.

If we were going to fully examine the deep issues this hearing purports to tackle, I would have expected to hear from veterans' groups, environmental justice groups, workers, and distinguished public health experts with intimate knowledge of the NTP and the Report on Carcinogens. No such individuals were called by the majority. To the degree there is any divergent voice heard today, it is because of the minorities' sense of obligation to try to provide some balance.

I could have recommended witnesses such as retired Marine Corps Master Sergeant Jerry Amsfinger and Ms. Erin Brockovich, who worked with veterans and communities that have been harmed by chemical exposure and fought for years to get toxicity information into the public policy arena. I could have recommended a fleet of distinguished science policy experts, such as Dr. Phil Landrigan of Mount Sinai Medical College, or you could stay with the beltway, within the beltway and invite Dr. Lynn Goldman, Dean of the George Washington University School of Public Health and Dr. Jennifer Sass of the Natural Resources Defense Council.

In addition, the structure of this hearing suggests that small businesses are hurt uniformly and primarily by documents such as the RoC. The picture is far more complicated than that. I could

have recommended a host of small business leaders who would have made it clear that their business is expanding and taking market share away from petrochemical manufacturers because public tastes are, indeed, changing.

The shift away from substances that cannot be easily recycled or composted is a process that gained a full head of steam long before the 12th Report on Carcinogens was drafted. I am attaching to my statement letters we have received from a wide variety of groups asking that this Subcommittee examine the claims of the styrene industry with a critical eye and that we understand how important the work of the NIEHS is to protecting public health.

Out of fairness, I want to ask you, Mr. Chair, to commit to a second hearing that would expand the scope of the voices we hear on this important matter. The issues are too important to treat in such an imbalanced way. The Investigations and Oversights Subcommittee must be viewed as impartial and thorough and should build a complete record that includes more than allegations into lawsuit the styrene industry has brought against NIEHS. A second hearing would allow us to correct the impression that we will dance to any single-interest tune. I stand ready to work with you to shape such a hearing at your earliest convenience.

There is one final issue I want to raise. Because the government is subject to an ongoing lawsuit in which Dr. Birnbaum as the director of NIEHS has a direct role, she may not be able to answer some questions here today. It would be grossly unfair for Members to try to use this forum to build the record to assist the industry in its lawsuit against the government by asking questions of Dr. Birnbaum that she cannot answer and then treating her as if she is trying to be evasive.

So I ask that you be especially sensitive to the legal implications of this hearing and protect Dr. Birnbaum in situations where she has been counseled not to comment. Last week's joint hearing was marred by abusive conduct towards a witness. I know you found the behavior distasteful, and I find it unacceptable. Tough questions are fair game, but we should stand together to ensure that things do not move from being tough and probing to being personally abusive. I don't know whether the NIEHS or the styrene industry is right or wrong on the matters before us. I do not believe we have done enough work on this matter, nor invited a diverse enough set of witnesses to reach any meaningful conclusions today.

The letters I am attaching to my statement asks us to believe that the styrene industry is wrong, and the Committee is biased in its approach. They may or may not be right on the first issue, but their second criticism is valid. To restore the perception of our independence and objectivity, we desperately need another hearing and a different set of witnesses. I hope we can work together on that hearing, Mr. Chair, and then we can bring, begin to come to a fuller understanding of the complex questions that are, indeed, before us.

I yield back.

[The prepared statement of Mr. Tonko follows:]

Opening Statement of
Rep. Paul D. Tonko, Ranking Member
Subcommittee on Investigations and Oversight
Committee on Science, Space, and Technology

Hearing on:
How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs

April 25, 2012

Mr. Chairman: Usually, I begin my statement by thanking you for having the Subcommittee examine a topic of importance and for inviting a slate of witnesses who bring a variety of perspectives and expertise to the subject at hand. I am sorry that I am unable to do that today. We did not agree in all particulars regarding the scope of the last Subcommittee hearing, but I compliment you for inviting a balanced slate of witnesses to inform us on renewable energy tax provisions. When the Subcommittee is in a learning mode, such balance reflects well on the Subcommittee and highlights that we are truly interested in coming to a complete understanding of a policy issue.

Today's hearing is very disappointing. Although the title indicates we are examining the process and result of the National Toxicology Program's biennial production of the Report on Carcinogens, we are really examining the objections of one industry to the listing of one chemical. There is virtually no balance here today. Five of the six witnesses invited by the Majority are aligned closely with the styrene industry and the American Composite Manufacturers Association.

Certainly, we should hear from industry scientists and businesses with an interest in the activities of federal agencies that impact their businesses. Their concerns about the implications of this listing for their businesses are legitimate issues for us to consider. But in this matter, I would also expect us to bring other concerned voices into the room to ensure we have a complete picture of how the 12th Report on Carcinogens, the National Toxicology Program is developed and viewed by all interested parties.

If we were going to fully examine the deep issues this hearing purports to tackle, I would have expected to hear from veterans groups, environmental justice groups, workers, and distinguished public health experts with intimate knowledge of the NTP and the RoC. No such experts were called by the Majority. To the degree there is any divergent voice to be heard today it is because of the Minority's sense of obligation to try to provide some balance.

I could have recommended witnesses such as retired Marine Corps Master Sergeant Jerry Ensminger and Ms. Erin Brockovich who work with veterans and communities that have been harmed by chemical exposure and have fought for years to get toxicity information into the public policy arena; I could have recommended a fleet of distinguished science policy experts such as Dr. Phil Landrigan of Mt. Sinai Medical College, or you could stay within the beltway and invite Dr. Lynn Goldberg, Dean of the GWU School of Public Health and Dr. Jennifer Sass of the Natural Resources Defense Council.

In addition, the structure of this hearing suggests that small businesses are hurt uniformly and primarily by documents such as the RoC. The picture is far more complicated than that. I could have recommended a host of small business leaders who would have made it clear that their business is expanding and taking market share away from petrochemical manufacturers. Public tastes are changing, and the shift away from substances that cannot be easily recycled or composted is a process that gained a full head of steam long before the 12th Report on Carcinogens was drafted.

The matters before the Subcommittee are too complex to think that two Minority witnesses can somehow balance the account presented to Members by 5 witnesses aligned with the styrene manufacturers.

I am attaching to my statement letters we have received from a wide variety of groups asking that the Subcommittee examine the claims of the styrene industry with a critical eye, and that we understand how important the work of the NIEHS is to protecting public health.

Out of fairness, I want to ask you Mr. Chairman, to commit to a second hearing that would expand the scope of the voices we hear on this important matter. The issues are too important to treat in such an unbalanced way. The Investigations and Oversight Subcommittee must be viewed as impartial and thorough, and should build a complete record that includes more than the allegations in the lawsuit the styrene industry has brought against NIEHS. A second hearing would allow us to correct the impression that we will dance to any single interest's tune. I stand ready to work with you to shape such a hearing at your earliest convenience.

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To restore the perception of our independence and objectivity, we desperately need another hearing and a different set of witnesses. I hope we can work together on that hearing Mr. Chairman. Then, we can begin to come to a fuller understanding of the complex questions before us.

Chairman BROUN. Thank you, Mr. Tonko. I want to remind my good friend from New York that of the letters that you just asked to be admitted into the record, we have already admitted those into the record from our side all except for, I think but one of those, and we just have so many people, and this is about process and not about any given entity or chemical. It is about how the process goes on.

Thank you, sir. I appreciate that.

The Chair now recognizes my good friend from Louisiana, Mr. Richmond, for an opening statement. Sir, you are recognized for five minutes.

Mr. RICHMOND. Thank you, Mr. Chairman.

It is undisputed that chemicals are a part of our daily lives from the food that we eat, the products in our homes, and in our children's toys. In a great majority of their uses, they improve our lives.

However, in a few instances they can be dangerous. To address this, the National Toxicology Program issues a Report on Carcinogens which lists substances that may cause cancer. The report now identifies 240 substances that are either known or are likely human carcinogens. For consumers, this gives them information they can use to make informed decisions. For employers, it can help them to protect the workers. For all of us, this report can lead to cleaner air and water. By identifying substances that may heighten the risk of cancer, the public is made aware of potentially life-threatening chemicals in our everyday lives.

As new chemicals are created and additional uses are found for existing ones, companies are able to make their products stronger, more durable, and a better value for the consumer. As this process evolves, it remains a top priority to understand not only what is in them but how they may affect us, our children, and the environment.

The rapid pace of scientific discovery in the United States makes doing so even more important. With this degree of innovation also comes a strong sense of corporate responsibility that we are fortunate to have in this country. It is important to remember that no business wants to put its employees or the public in danger. Safe products and a hazard-free work environment are in a company's own self-interest and simply make good business sense.

With that in mind, the report's designation of substances as a carcinogen can only significantly impact small businesses. For some firms, listing a chemical that they use, even in minimal amounts, has the potential to stigmatize their products and their business. Unlike their large counterparts, small firms rarely have teams of attorneys and research personnel in house to mitigate the impact of such a listing. Instead they must hire expensive outside consultants or shift resources from production to regulatory compliance, slowing growth and job creation.

Given these concerns there is a need to examine the report and how it is prepared. During today's hearing, I hope to examine how rigorous the listing process is and how open it is to external critique. Sound scientific analysis and methods, as well as public comment and peer review, are key to the legitimacy of the report.

Transparency is also essential for businesses affected by a listing. They should have an opportunity to give their input throughout the process, especially at those points which try final listing decisions.

I am also looking forward to hearing testimony on the revised process for the 13th report, which HHS recently issued in January. These procedures are at the heart of many of the issues that we will examine today. It is my hope that we can explore whether or not this new process increases transparency in public input.

The Report on Carcinogens is an important source of information on substances that may cause cancer in humans. It remains vital for consumers, businesses, and government alike. The listing of these substances gives the public and decision makers a necessary resource to evaluate the safety of where we live, work, and our children play. Ensuring that this is the most credible scientific approaches and uses, processes that are open and clear, is essential not only to our Nation's public health but also to the economic viability of many small businesses.

I would just say as a Member whose new footprint represents the largest petrochemical footprint in the United States Congress, that the concerns go both ways, and I think that the more information you have, the more knowledge that you have, the better that we can protect our citizens, our families, our children.

So with that, Mr. Chairman, I would yield back.

[The prepared statement of Mr. Richmond is not available.]

Chairman BROUN. Thank you, Mr. Richmond.

I would like to remind my colleagues on both sides at today's hearing we have invited two Administration witnesses and two witnesses suggested by the minority. Our committee rules only require one minority witness. We thought it was important to allow a variety of opinions. Half the witnesses that are here today either represent the Administration or were invited by the minority. We are trying to be very candid and fair with, again, this is about process and not about any individual entity.

If there——

Mr. TONKO. Mr. Chair, I understand that there is only one Administrative representative here, and that would be Dr. Birnbaum. Thank you.

Chairman BROUN. There is a small business advocacy witness from Small Business Administration.

Mr. TONKO. With their testimony reviewed by the leadership of that agency, I believe. Is that correct? It is an independent office.

Chairman BROUN. Thank you. Let us go ahead. If there are Members who wish to submit additional opening statements, your statements will be added to the record at this point.

At this time I would like to introduce our witnesses. First is Dr. Linda Birnbaum, the Director of National Institute of Environmental Health Science and National Toxicology Program at the U.S. Department of Health and Human Services.

Madam Chairwoman, would you like to introduce our other witness?

Chairwoman ELLMERS. Yes. Thank you, Mr. Chairman. I am going to introduce Mr. Charles Maresca. He is the Director of Interagency Affairs in the Small Business Administration's Office

of Advocacy. The Office of Advocacy monitors federal agencies' compliance with the Regulatory Flexibility Act or RFA, as amended by the Small Business Regulatory Enforcement Fairness Act and represents the views and interests of small businesses before federal agencies.

Mr. Maresca, I am looking forward to your testimony.

Chairman BROUN. Thank you, Mrs. Ellmers. I would like to thank the Chairwoman for being here and us doing this together.

We will now begin hearing from our witnesses. As our witnesses should know, spoken testimony is limited to five minutes each, after which the Members of the Committee will have five minutes each to ask questions.

It is the practice of the Subcommittee on Investigations and Oversight to receive testimony under oath, and we will use that practice today here as well.

Do any of you have—either of you have any objections to taking an oath?

Okay. Let the record reflect that both witnesses are willing to take the oath by shaking their head in a normal fashion, side to side. You also may be represented by counsel. Do either of you have counsel here today?

Let the record reflect that neither has counsel here today.

Now, if you will please both stand and raise your right hand. Do you solemnly swear to affirm and tell the whole truth and nothing but the truth, so help you God?

Be seated, please. Let the record reflect that both witnesses have taken the oath.

Dr. Birnbaum, you are now recognized for five minutes.

STATEMENT OF DR. LINDA S. BIRNBAUM, DIRECTOR, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES AND NATIONAL TOXICOLOGY PROGRAM, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. BIRNBAUM. Good morning. I am Linda Birnbaum, Director of the National Institute of Environmental Health Sciences, part of the National Institutes of Health, and I am also Director of the National Toxicology Program, also known as the NTP. It is my pleasure to appear before you today to discuss the Report on Carcinogens.

The report is required by biennially under the Public Health Service Act and issued by the Secretary of Health and Human Services. The Secretary has delegated responsibility for preparing the report to the NTP.

In the United States, approximately one in two men and one in three women will develop cancer in their lifetime. We have both a legal and a moral obligation to identify substances in our environment that are cancer hazards and to communicate this information to ensure that people can choose to live and work in safe environments.

The Report on Carcinogens is a science-based, public health document that provides information about the relationship between the environment and cancer. The report lists a wide range of sub-

stances, including metals, pesticides, drugs, natural and synthetic chemicals, and biological agents that are considered cancer hazards for people in the United States.

A listing in the report indicates a potential hazard for cancer. Many factors, including the amount and duration of exposure and an individual's susceptibility to a substance affect whether a person will develop cancer. The Report on Carcinogens is not a risk assessment document. It is not a regulatory document.

However, the report does provide decision makers and the public with information they can use to make decisions about exposures to cancer-causing substances. The Public Health Service Act stipulates that the report lists substances in one of two categories.

The first is known to be carcinogens. The second category is reasonably anticipated to be carcinogens. These categories are based on criteria approved by the HHS secretary in 1996 that was a product of a thorough and public review.

For a substance to be listed in the known category, there must be sufficient evidence from studies in humans that indicates a causal relationship between the substance and human cancer. Briefly, for a substance to be listed in the reasonably anticipated category, any one of three scenarios may apply. One, limited evidence of cancer from human studies, or two, sufficient evidence of cancer from animal studies, or three, evidence that the substance is in a class of substances already listed in the report or that it causes biological effects known to lead to cancer in humans.

The decision by the NTP to list a substance in the Report on Carcinogens is based on scientific judgment with consideration of all relevant research data and input from advisory groups and the public. For each listing, the report includes a substance profile with information on cancer studies that justifies the listing. The profile also provides information about use, production, potential sources of exposure, and any current federal regulations to limit exposures.

Each edition of the report is cumulative and includes substances newly reviewed, along with those listed in all previous editions. The first report was released in 1980. The most recent 12th report in June, 2011. Anyone may nominate a substance for listing in or removal from the report. The multistep process to prepare the 12th report included expert advisory reviews, independent external peer review, and drew upon the science expertise of federal agencies including NIH, CDC, FDA, EPA, OSHA, and the Consumer Product Safety Commission.

The process also increased opportunity for public review and input. In fact, public comments were solicited on six separate occasions.

The NTP is now moving forward with preparation of the 13th report. We have changed some elements to enhance transparency and efficiency in the process but still maintain rigorous, independent, external peer review, and multiple opportunities for public input. Among the changes to enhance transparency, we will now prepare a single literature review document that systematically assesses all relevant literature and explains how the entity reaches its conclusions for its proposed listing recommendation. This document will be disseminated for public comment prior to public external scientific peer review.

We believe that the Report on Carcinogens is and will remain an important public health document that improves the public and decision makers, provides, and empowers the public and decision makers with information about cancer hazards.

I appreciate this opportunity to discuss the report and would be happy to answer any questions. Thank you.

[The prepared statement of Dr. Birnbaum follows:]

Testimony

Before the Science, Space, & Technology Committee's Subcommittee on Investigations and Oversight and the Small Business Committee's Subcommittee on Healthcare and Technology
United States House of Representatives

The Report on Carcinogens

Statement of
Linda Birnbaum, Ph.D., D.A.B.T., A.T.S.
Director, National Institute of Environmental Health Sciences, National Institutes of Health, and Director, National Toxicology Program
U.S. Department of Health and Human Services

Good afternoon, I am pleased to appear before you today to present testimony on the Report on Carcinogens. I am Linda Birnbaum, Director of the National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health (NIH), and Director of the National Toxicology Program (NTP). The NTP is an interagency program headquartered at the NIEHS. Both NIEHS and NTP are part of the U.S. Department of Health and Human Services.

The Report on Carcinogens is an informative, science-based public health document, required biennially under the Public Health Service Act[1] and approved and published by the Secretary of Health and Human Services. The Secretary has delegated responsibility for preparation of the Report on Carcinogens to the NTP.

The Report on Carcinogens identifies agents, substances, mixtures, or exposure circumstances, collectively known as "substances," that are considered cancer hazards for people living in the United States. It is not a risk assessment document. A listing in the Report indicates a potential hazard for cancer, but does not estimate cancer risks that individuals may face when encountering listed substances in their daily lives. Many factors, including the amount and duration of exposure and an individual's susceptibility to a substance, affect whether a person will develop cancer.

Reducing exposures to cancer-causing substances is important to protect public health. The Report provides health regulatory and research agencies, scientific and medical communities, and the public with information they can use to make decisions about exposures to cancer-causing substances. The Report is not a regulatory document.

The Public Health Service Act stipulates that the Report list substances in one of two categories defined by statute: *known to be carcinogens* or *reasonably anticipated to be*

[1] Section 301(b)(4) of the Public Health Service Act, as amended

carcinogens. The Report lists a wide-range of substances including, metals, pesticides, drugs, natural and synthetic chemicals, and biological agents such as certain viruses. For each listed substance, the Report includes a substance profile that provides information from cancer studies that provide justification for the listing and information about use, production, potential sources of exposure, and any current Federal regulations to limit exposures.

Each edition of the Report is cumulative and includes substances newly reviewed in addition to those listed in the previous edition. The first Report was released in 1980 and the 12th edition was released in June 2011. It has 240 listings. This includes 54 listings in the *known* and 186 listings in the *reasonably anticipated carcinogens* categories.

The NTP invites anyone in the public and private sectors to nominate a substance for listing in or removal from the Report. The NTP has followed an established process to evaluate substances for listing, which has been reviewed periodically. In April 2007, the NTP published the process for preparation of the 12th Report on Carcinogens. In preparation for the 12th Report, the process used for the 11th Report was revised to increase peer review and the opportunity for public involvement and to address guidance issued in the Office of Management and Budget Information Quality Guidelines for Peer Review. Information about the process is available on the NTP website (http://ntp.niehs.nih.gov/ntp/roc/twelfth/ReviewProcess.pdf).

For preparation of the 12th Report, we followed a multi-step process that included expert advisory reviews, independent external peer review, and multiple opportunities for public involvement. Three scientific advisory groups, including an external expert panel, selected by the NTP from recognized authorities with relevant expertise and knowledge from the public and private sectors, and two governmental review groups, whose members were appointed by the participating agencies, examined the literature relevant to the carcinogenicity of each substance

under review. We drew upon the scientific expertise of Federal agencies including NIH, the Centers for Disease Control and Prevention, the U.S. Food and Drug Administration, the U.S. Environmental Protection Agency, the Consumer Product Safety Commission, and the Department of Labor's Occupational Safety and Health Administration.

The process for the 12th Report included many opportunities for public input. Public comments were solicited:

- on substances nominated for review;
- on the draft background documents that summarized all relevant publicly available, peer-reviewed scientific literature from human, experimental animal, and mechanistic studies, as well as information on exposure, chemical and physical properties, use, and production;
- on the external scientific expert panels' recommendation on whether to list the substances; and
- on the draft substance profiles that ultimately appear in the Report.

The public also had an opportunity to provide oral testimony at external, scientific expert panel meetings and at meetings of the NTP Board of Scientific Counselors. All public comments were posted on a website and distributed to the expert advisory groups for consideration in their deliberations.

Beginning with the 3rd Report in 1983, the NTP has used established criteria to evaluate the scientific evidence on each substance under consideration to determine whether to recommend listing the substance as a *known* or *reasonably anticipated carcinogen,* or to not list it in the Report. The Report on Carcinogens listing criteria have been reviewed and revised

periodically since they were developed. The current criteria, approved by the Secretary of Health and Human Services in 1996, were the product of a thorough and public review.[2]

The listing criteria specify the level of evidence that must be met in order for a substance to be listed in the Report in either category. For a substance to be listed in the *known* category, there must be sufficient evidence from studies in humans that indicates a causal relationship between exposure to the substance and human cancer. In brief, for a substance to be listed in the *reasonably anticipated* category, the level of evidence can be based on one of three scenarios:

1) limited evidence of carcinogenicity from studies in humans or

2) sufficient evidence of carcinogenicity from studies in experimental animals or

3) evidence that a substance is a member of a class of substances already listed in the Report or that it causes biological effects known to lead to the development of cancer in humans.

The conclusion to list a substance in the Report is based upon scientific judgment with NTP giving consideration to all relevant data and to input from the advisory groups and the public.

If new scientific information becomes available once a substance is listed, it can be nominated for re-review including to upgrade the listing from *reasonably anticipated* to *known carcinogen*, to refine identification of the listed substance, or to remove the substance from the Report.

The NTP is now moving forward with preparation of the 13th Report. We have maintained rigorous, independent, external peer review and multiple opportunities for public

[2] National Toxicology Program Fiscal Year 1996 Annual Plan. U.S. Department of Health and Human Services. NIH Publication No. 96-4168.

input in the review process. To enhance transparency and efficiency and to better enable us to complete the Report with the statutory biennial time frame, we have added the following steps:

- making more transparent how the NTP reaches its conclusions concerning the listing recommendation for a substance under review by combining the scientific information, its assessment, and the listing recommendation in a single document,
- providing more flexibility in the approaches the NTP might use to obtain external scientific and public input during a substance's evaluation, and
- separating the substances under review from a specific Report edition so that the list of substances is dynamic and the review process is continuous between editions.

We sought public input on the proposed review process for the 13th Report through solicitation of written comments and a public listening session. Taking into consideration public comments, we proposed these revisions to the NTP Board of Scientific Counselors in December 2011 at a public meeting. The NTP Board of Scientific Counselors endorsed the changes.

We finalized the Report review process in January 2012, posted it to the Report website, and announced its availability in the Federal Register.[3] We are now beginning work on the 13th Report.

The Report on Carcinogens empowers the public with information that allows them to reduce exposure to cancer hazards. Thank you for the opportunity to provide information about the Report. I would be happy to answer any questions.

[3] 77 Fed. Reg. 1707, January 11, 2012

Chairman BROUN. Thank you, Dr. Birnbaum.
Mr. Maresca, you are now recognized for five minutes.

**STATEMENT OF MR. CHARLES A. MARESCA,
DIRECTOR OF INTERAGENCY AFFAIRS,
OFFICE OF ADVOCACY,
U.S. SMALL BUSINESS ADMINISTRATION**

Mr. MARESCA. Chairman Broun, Ranking Member—Chairwoman Ellmers, Ranking Member Tonko, Ranking Member Richmond, Members of the Committees, good morning. Thank you for the opportunity to appear before you today to discuss small business concerns with the Department of Health and Human Services Report on Carcinogens.

As Director of Interagency Affairs at the Office of Advocacy at the U.S. Small Business Administration, I manage a team of attorneys that works with small businesses and Federal Government agencies during the rulemaking process to reduce regulatory burdens on small business.

Chief Counsel for Advocacy Winslow Sergeant wrote in a letter to HHS on November 22, 2011, that small businesses have two primarily concerns with the report, that substances have been listed in the RoC based on potentially inaccurate scientific information and that the peer review and public comment processes should be improved.

Accurate and credible scientific assessments are vital for small businesses. Listing a substance in the report has the potential to curtail the use of the substance. This may lead to substantial adverse economic impacts for small businesses that use that substance, including increased costs of insurance and Workers' Compensation premiums.

Further, when the Federal Government incorrectly lists a substance as a carcinogen or as a potential carcinogen, small businesses may experience lasting negative economic impacts.

Also, technical labels can be misinterpreted and confuse the public about the true lead to questions about the true nature of the risk to health and safety. For example, although the report lists substances as reasonably anticipated to be a human carcinogen or known to be a human carcinogen, the caveat states that the listing of substances in the report only indicates a potential hazard and does not establish the exposure conditions that would pose cancer risks to individuals in their daily lives. The important distinction between hazard and risk is not understood by most consumers. Consumers and small businesses are likely to be more aware of whether the substance is listed than of the caveat.

Small businesses are concerned with the soundness of the science underlying listing decisions. First, because it is a hazard-based listing, not a risk-based listing, the report has little value for estimating actual cancer risk to the general public even though the listings appear to indicate that there is a cancer risk. Second, NTP's weight-of-evidence analysis does not appear to account for inconsistent or contradictory data.

A more robust weight-of-evidence analysis would consider all scientific data, including contradictory or inconsistent data.

Small businesses are also concerned with the report's preparation process. The 12th RoC process did not provide sufficient opportunity for meaningful peer review or public comment. The peer reviewer process did not include adequate dialogue between NTP and the peer reviewers, nor did NTP provide adequate response to peer review or public comments.

Although on paper the 12th RoC preparation process included several opportunities for public comment, small businesses found that NTP did not respond meaningfully to their comments. Because public comment is the primary method by which small businesses can contribute to the report's preparation process, it is important that such opportunities be meaningful.

Finally, Advocacy is concerned with NTP's recent review of the 12th RoC preparation process for three reasons. First, the review process needs improvement. Second, the review of the 12th RoC preparation process was a process-based review only and did not address substantive scientific concerns, and, third, the new preparation process for the upcoming 13th RoC should bolster opportunity for peer review or require NTP response to peer review and public comment.

Advocacy commends two positive changes that resulted from the 12th RoC review process, including an additional opportunity for public comment and two additional opportunities for interagency comment.

Small business relies on credible and reliable science. NTP's review of the 12th RoC demonstrates that it is aware that there are concerns with the RoC. However, NTP needs to make further improvements in order to ease concerns. To the extent that NTP can improve the scientific reliability as well as the peer review and public comment processes for the report, there will be a measurable burden reduction on small businesses.

I would like to thank you once again for inviting me to speak to you today. I commend the Committee's interest in improving and fostering legitimacy in the report's listings, and I would be happy to respond to questions.

[The prepared statement of Mr. Maresca follows:]

Advocacy: the voice of small business in government

Testimony of

Charles Maresca
Director of Interagency Affairs
Office of Advocacy
U.S. Small Business Administration

U.S. House of Representatives
Committee on Small Business and
Committee on Science, Space, and Technology

Date:	April 25, 2012
Time:	10:00 a.m.
Location:	Room 2318 Rayburn House Office Building Washington, D.C.
Topic:	How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs

Created by Congress in 1976, the Office of Advocacy of the U.S. Small Business Administration (SBA) is an independent voice for small business within the federal government. The Chief Counsel for Advocacy, who is appointed by the President and confirmed by the U.S. Senate, directs the office. The Chief Counsel advances the views, concerns, and interests of small business before Congress, the White House, federal agencies, federal courts, and state policy makers. Issues are identified through economic research, policy analyses, and small business outreach. The Chief Counsel's efforts are supported by offices in Washington, D.C., and by Regional Advocates. For more information about the Office of Advocacy, visit ***http://www.sba.gov/advocacy****, or call (202) 205-6533*

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www.sba.gov/advocacy

Chairman Graves, Chairman Hall, Ranking Member Velázquez, Ranking Member Johnson, Members of the Committees: good morning and thank you for the opportunity to appear before you today to discuss small-business concerns relating to the Department of Health and Human Service's Report on Carcinogens (RoC).

As Director of Interagency Affairs at the Office of Advocacy (Advocacy), I manage a team of attorneys who works with small businesses and federal government agencies during the rulemaking process to reduce regulatory burdens on small businesses. Advocacy is an independent office within the U.S. Small Business Administration (SBA) that speaks on behalf of the small-business community before federal agencies, Congress, and the White House. The views in my testimony do not necessarily reflect the views of the Administration or the SBA and this statement has not been circulated to the Office of Management and Budget for clearance.

After reaching out to small businesses, Chief Counsel for Advocacy Winslow Sargeant submitted a letter to the Department of Health and Human Services (HHS) on November 22, 2011, conveying small-business concerns with the Report on Carcinogens, Twelfth Edition (12^{th} RoC). These concerns are primarily twofold: that substances have been listed in the RoC based on inaccurate scientific information, and the peer review and public comment processes need improvement.

The Report on Carcinogens serves an important federal purpose. Small businesses and the public rely on the scientific integrity and rigorous process underlying the chemical risk characterizations the report contains. To this end, Advocacy continues to strongly support the President's call for sound science. The President's 2009 Memorandum on Scientific Integrity states "Science and the scientific process must inform and guide decisions of my Administration … The public must be able to trust the science and scientific processes informing public policy decisions." This memorandum was later followed by Executive Order 13563 which states that "Our regulatory system must protect public health, welfare, safety, and our environment, while promoting economic growth, innovation, competitiveness, and job creation."

Accurate and credible scientific assessments are vital for small businesses that provide products derived from chemicals in the marketplace. Listing a substance in the RoC has the potential to substantially curtail its use. This is also true when a substance is mislabeled as a carcinogen, or even as a potential carcinogen.

In this instance, small businesses may experience economic hardship. These include the following:

- Reduced demand for the product in American and international markets by businesses and consumers;
- an increase in the likelihood of additional regulations;
- an increase in the cost of insurance and worker's compensation premiums;
- increasing sourcing costs; and
- increased tort litigation.

Technical labels used in the RoC can be misinterpreted and lead to questions about the true nature of risks to health and safety. For example, although the RoC lists substances as "reasonably anticipated to be a human carcinogen" or "known to be a human carcinogen," the RoC includes the caveat that "listing of substances in the RoC only indicates a potential hazard and does not establish the exposure conditions that would pose cancer risks to individuals in their daily lives."[1] In other words, a listing in the RoC flags a potential hazard but does not mean that the substance presents a risk to human health. However, this distinction is not conveyed to or understood by consumers. Consumers and businesses are likely to be more aware of whether the substance is listed than the disclaimer.

As this caveat highlights, the RoC listings are based on a hazard assessment, which is an assessment of anything that can cause harm, and not a risk assessment, which can provide an estimate of the number of persons who may be harmed and the degree of that harm.

[1] National Toxicology Program, U.S. Department of Health and Human Services, Report on Carcinogens, Twelfth Edition (2011), p 3.

Many chemicals, such as styrene and formaldehyde, occur naturally in the environment in food, our bodies, and water, but in much smaller doses than would cause cancer. The RoC's use of the hazard assessment does not indicate the dose or conditions needed to cause cancer in humans.

Advocacy has met and spoken with small businesses who have experienced some of the impacts listed above. For example, some small businesses have already reported that the 12th RoC's listing of styrene as "reasonably anticipated to be a human carcinogen" has led to increases in insurance and worker's compensation costs.

Further, while the RoC is not itself a regulatory document and was not meant to form the basis of regulations, some entities use the RoC to inform their rulemaking. For example, the RoC has led to additional regulation in California, where under Proposition 65, the Safe Drinking Water and Toxic Enforcement Act, a listing in the RoC may trigger a listing in California.

Small businesses seek to improve the scientific practices supporting the RoC listings. First, because it is a hazard-based listing, not a risk-based listing, the RoC has little value for estimating actual cancer risk to the general public even though the listings appear to indicate that there is a cancer risk. Second, the National Toxicology Program's (NTP) weight-of-evidence analysis does not appear to account for inconsistent or contradictory data.

Regarding the listing of styrene as "reasonably anticipated to be a human carcinogen" one recent European Union review of the styrene health effects database determined that styrene should not be classified or regulated as a carcinogen. [2] A second report in 2009 by a blue-ribbon panel of internationally recognized epidemiologists concluded that the "available epidemiologic evidence does not support a causal relationship between styrene

[2] European Chemicals Agency, *European Union Risk Assessment Report: Styrene* (2008), *available at* http://echa.europa.eu/doc/trd_substances/styrene/rar/trd_rar_uk_styrene.pdf.

exposure and any type of human cancer."[3]

Further, the University of Alabama's Dr. Elizabeth Delzell, a styrene researcher, argues that there "is not sufficient science to conclude that styrene causes lymphoma, leukemia or other cancers."[4] Also, the International Agency for Research on Cancer decided to list styrene as a "possible" and not a "probable" carcinogen in a 2002 review.[5]

The RoC's listing of formaldehyde as "known to be a human carcinogen" for leukemia contradicts the National Academy of Sciences' (NAS) recent independent review of the Draft Integrated Risk Information System's (IRIS) Review of Formaldehyde. NAS found that the Environmental Protection Agency's own IRIS scientific evaluation of formaldehyde did not support EPA's conclusion that formaldehyde caused blood cancers. It is not clear if any of these reports or studies were factored into the RoC listing determinations for styrene and formaldehyde.

NTP could strengthen its scientific data and increase credibility by adopting a more robust weight-of-evidence analysis to ensure that the full range of scientific studies are considered so that the RoC decisions are made with the most comprehensive and accurate scientific analysis. Such an analysis would be more transparent and would ensure greater scientific credibility.

Small businesses are also concerned with the 12th RoC's preparation process, particularly regarding peer review and public comment. The 12th RoC process did not provide sufficient opportunity for meaningful peer review. According to small businesses, there was inadequate dialogue between NTP and the peer reviewers, lack of peer reviewer

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[3] Boffetta *et al*, Epidemiologic Studies of Styrene and Cancer: A Review of the Literature, 51 J *Occup Environ Med.* 1275, 1275-87 (2009).

[4] Letter from Elizabeth Delzell, researcher, University of Alabama, to Barbara Shane, executive secretary, Board of Scientific Counselors, National Toxicology Program (Feb. 5, 2009), *available at* http://www.box.net/shared/static/slm4m8tp7a.pdf.

[5] International Agency for Research on Cancer (IARC), World Health Organization (WHO), *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Some Traditional Herbal Medicines, Some Mycotoxins, Naphthalene and Styrene*, (2002), *available at* http://monographs.iarc.fr/ENG/Monographs/vol82/mono82-9.pdf.

access to public comments, inadequate time and resources to perform the review, and inadequate NTP response to peer review comments.

Although the 12th RoC preparation process included several opportunities for public comment, small businesses found that NTP disregarded or did not respond meaningfully to their comments. Because public comment is the primary method by which small businesses can contribute to the RoC's preparation process, it is important that such opportunities be meaningful and include timely response to public comment.

Small businesses are concerned with NTP's recent review of the 12th RoC preparation process for three reasons: the review process needs improvement; the review of the 12th RoC preparation process was a process-based review only and did not address any substantive scientific concerns; and the new preparation process for the upcoming 13th RoC should bolster opportunity for peer review or require NTP response to peer review and public comment.

Notably, the 12th RoC review process has resulted in two positive changes: One additional opportunity for public comment and two additional opportunities for interagency comment have been added.

Advocacy commends the improvements NTP has made. Advocacy looks forward to working with NTP to improve the review process. Specifically, the review process should address the substantive scientific concerns involving the weight-of-evidence analysis. The process should also increase the number of peer review opportunities and provide for meaningful dialogue and NTP response to peer review and public comments.

Considering continued scientific advances in both the understanding and control of potentially carcinogenic substances, it also is important for NTP to have a robust process for reviewing substances for delisting. Small businesses seek to improve the process by which chemicals are listed and delisted.

This need to improve the process is highlighted by the attempt to delist glass wool which was listed as "reasonably anticipated to be a human carcinogen" in the 7th RoC published in 1994. In 2004, after ten years of research, North American Insulation Manufacturers Association nominated glass wool for delisting. The matter was not concluded until the publication of the 12th RoC. However, instead of delisting the substance in the 12th RoC, NTP modified the definition of glass wool to exclude certain types of glass wool that are "not biopersistent" in the lung. In the 12th RoC, glass wool is still listed as "certain glass wool fibers (inhalable)." This process of "delisting" non-biopersistent glass wool fibers took over 20 years.

Small business relies on accurate, credible, and reliable science. NTP's review of the 12th RoC demonstrates that it is aware that there are concerns with the RoC. However, NTP needs to make further improvements in order to ease concerns. To the extent that NTP can improve the substantive underlying science, the preparation process, and the clarity of the listings of the RoC, there will be an important and measurable burden reduction on small businesses.

I would like to thank you once again for inviting me to speak to you today. I commend the Committees' interest in improving the RoC, as well as reducing uncertainty in the RoC listings and fostering their legitimacy.

Chairman BROUN. Thank you, Mr. Maresca. We are going to give you that opportunity in just a second. I thank you all for your testimony.

Reminding Members that Committee rules limit questions to five minutes. The Chair will, at this point, open the first round of questions, and I recognize myself for five minutes.

Dr. Birnbaum, NAS's review of the 12th RoC listing of styrene and formaldehyde regarding that, last year Congress directed HHS to contract with the National Academies to review two of the 12th RoC's determinations. What is the status of this review, and when will HHS direct NAS to move forward with the review?

Dr. BIRNBAUM. The Office of the Assistant Secretary of Health was charged with that, with contracting with NAS. I understand they are in the process of developing that contract with the Academy. They expect it to be in place by the fall.

Chairman BROUN. Okay. So can we be assured that it will be in place by the fall?

Dr. BIRNBAUM. This is the responsibility for the Assistant Secretary of Health. They are working on it. They are doing everything they can to complete it by the end of this fiscal year, September 30.

Chairman BROUN. Very good. Thank you so much. I certainly look forward to that being completed.

Mr. Maresca, is the RoC a highly influential scientific assessment?

Mr. MARESCA. The RoC is the first step in regulations that depend on science. Yes.

Chairman BROUN. The written testimony submitted by witnesses on the second panel have indicated that roughly 250,000 jobs are associated with just one substance. OMB considered the scientific assessment to be, "highly influential if it could impact public or private sector by more than $500 million in one year," or is, "novel, controversial, or precedent setting or has significant interagency interests."

Do you consider the RoC to be a highly influential statement in those regards?

Mr. MARESCA. Mr. Chairman, I do not know how it would be, how the impact would be calculated. I do know that it is influential among, within the agencies.

Chairman BROUN. Okay. Very good. Again, Dr. Birnbaum, the 13th RoC will contain a new category called candidate substances. Stakeholders are already concerned that a listing as reasonably anticipated inappropriately stigmatized substances without sufficient evidence as evidenced by the attention RoC has received over the past year.

How will HHS prevent substances from being stigmatized simply by adding to this lower-level category without any justification or review?

Dr. BIRNBAUM. I am sorry, Mr. Broun, but I am not aware of our adding any additional categories. The Congress in its wisdom gave us two categories, known and reasonably anticipated. Candidate substances are these chemicals or the substances or the biological agents that may be considered under the RoC. A candidate substance is not a category of carcinogen.

Chairman BROUN. Okay, but will this be published with the RoC, or is it going to be an interagency or within the agency as a—just a process of looking at potential substances?

Dr. BIRNBAUM. Anyone can nominate candidate substances for evaluation in the Report on Carcinogens process. The first step in that nomination will be that candidate substances will be, information will be gathered on them and an expert group will review that nomination to decide whether there is enough information, and that will also include public comments at that point in time to go forward with a full-scale evaluation.

Chairman BROUN. Okay. Very good. Dr. Birnbaum, what action should consumers take in response to a substance listing in the RoC?

Dr. BIRNBAUM. Reducing exposure to cancer-causing agents is important to public health and the Report on Carcinogens provides important information on substances that might pose a potential cancer risk, and individual's knowledge is power, and individuals can make decisions about what hazards that they can or are willing to be exposed to.

Chairman BROUN. One of the substances that are proposed for consideration in the 13th RoC is shiftwork involved light, involving light at night. Does this mean that people who work the third shift, including those in 24-hour places like a police station, the hospital should perhaps start thinking about limiting their exposure to the substances listed in this report?

Dr. BIRNBAUM. There is always a balance between risk and benefit, and there is growing new scientific information that indicates that shift work may, in fact, have health consequences, including cancer.

Chairman BROUN. So we are going to outlaw working at night, I guess, if somebody takes that tact.

My time has expired.

Now I will recognize Mr. Tonko for five minutes.

Mr. TONKO. Thank you, Mr. Chair.

Now, I care about businesses in America, as I am certain everyone on the panel does, and I am also deeply concerned, however, about the impact of carcinogens on the lives of children, workers, sailors, soldiers, our veteran's community, and the public health professionals who work with them. Those voices are missing from today's hearing, as I earlier stated.

Dr. Birnbaum, if you could give us insight into the other stakeholders in the work of the National Toxicology Program that we should be hearing from and why they would care about the information and the data you assemble.

Dr. BIRNBAUM. Thank you, Mr. Tonko. I think it would be very important that we heard from some of the expert scientists who actually were involved in the conduct of these studies. I think that their expert, unconflicted advice would be very important to understanding the impacts that some of these compounds may have, have the potential to have on human health. I think the general population, public health experts, workers, but to me, I think it would be very important that you heard from the scientists who actually were involved in these studies.

Mr. TONKO. We highlighted some of those in that stakeholder category. Beyond what I made mention, are there others you would list that might be included as stakeholders?

Dr. BIRNBAUM. The National Toxicology Programs reporting carcinogens is intended as a public health document, and so it informs all stakeholders. I think it is very important, and many small businesses, in fact, are very interested in making sure that their workers are safe.

Mr. TONKO. Uh-huh, and today we are hearing allegations that the process used for the 12th RoC was not transparent. Can you briefly explain how public comments and public input were considered during the listing process?

Dr. BIRNBAUM. So public comments were taken six times during the preparation of the 12th Report on Carcinogens. There were four opportunities for written comments. All those written comments were not only posted on the Web for information, they were all provided to the different expert panels each time for their consideration. There were also two opportunities for oral public comment, both at different public meetings that were held to discuss the RoC. All the public comments were looked at. The peer panels and the expert panels discussed those public comments, and the NTP took them all into consideration in its final determination.

Mr. TONKO. Now, I also believe there may be some confusion about what the Report on Carcinogens is and what the Report on Carcinogens is not. Do you consider the RoC to be a regulatory document? And if not, why not?

Dr. BIRNBAUM. The RoC is not a regulatory document. It is a hazard assessment document. It looks at all the information, and I think that is important to state. It looks at all the information, both positive and negative, that is all evaluated and then the information which supports the determination of whether the compound has the potential to cause cancer, either as a known or reasonably anticipated carcinogen, is compiled to make the public health document, which is the substance profile part of the Report on Carcinogens. All of the information, however, positive and negative and all the discussion about it are available on the Website.

Mr. TONKO. And do you think the general consensus out there is that it, indeed, is not regulatory? Do you hear from groups or individuals?

Dr. BIRNBAUM. Yes. I think that it is understood by the scientific experts and most of the community that it is not a regulatory document.

Mr. TONKO. Okay. Again, I think that as you have indicated with your comments here, the balance that we need to strike as a Subcommittee in order to have an in-depth and fair and balanced review would require that we hear from these other stakeholders and then and only then can we come up with a meaningful assessment of the NTP and the RoC.

And so I appreciate your input, and Mr. Chair, I will yield back with, again, the request that we put together the efforts to host yet another hearing that would provide additional parties so as to strike with a full balance.

Chairman BROUN. Well, thank you, Mr. Tonko. I want to remind my good friend that this is about the process, not about the evalua-

tion of any specific substance, and we have included in the record six, I think, of the seven letters that you have indicated, and so they are part of this record, and we are just trying to look at the process in this hearing, not whether a given substance should be included or not included. We are just looking at the process and what, how that process affects any given entity.

So I thank you, and we will just, you and I can work together as we go forward.

Mr. TONKO. Mr. Chair, if I might just suggest that developing the comments of those who have presented letters, many of us, having them more fully develop their thought on the process would be, indeed, helpful.

Chairman BROUN. Well, thank you, Mr. Tonko, and I want to remind you that I am a physician, and I am concerned about these, and Mrs. Ellmers is also a registered nurse, and she is concerned. She has been in the health care field for a long period of time.

So both of us as Chairs are really interested not only in this process but also in protecting my patients and her patients also.

Mr. TONKO. Well, for us non-health care professionals on the panel, as for us engineers, we want data and be able to assemble data and problem solve as engineers do.

Chairman BROUN. Again, sir, this is about the process of developing the RoC.

Now recognize Chairman Ellmers for five minutes.

Chairwoman ELLMERS. Thank you, Mr. Chairman.

I would like to start, Mr. Maresca, just for clarification purposes, to be clear, the Office of Advocacy is part of the U.S. Small Business Administration, a federal agency. Is this correct?

Mr. MARESCA. That is correct.

Chairwoman ELLMERS. Okay. The federal agency or the chief counsel for the federal agency who heads the Office is an appointee of President Obama. Is that correct?

Mr. MARESCA. That is correct.

Chairwoman ELLMERS. Thank you. Mr. Maresca, starting with the questions that I have for you on this issue, why did the Office of Advocacy decide to send a comment letter to the National Toxicology Program regarding the Report on Carcinogens?

Mr. MARESCA. We did hear from a number of small businesses and their representatives that there was a problem with the 12th RoC. When we looked into it, we realized that there was going to be an impact on small business as a result of the listing of those substances, and as a result we sent that letter.

Chairwoman ELLMERS. All right. What does Advocacy think the National Toxicology Program can do to improve the Report on Carcinogens? What would be your input on that?

Mr. MARESCA. Well, as we said in our letter, we think that they can do a weight-of-evidence analysis during the process, looking more completely at the contradictory data as well as the data that supports the listing. We think that they can also improve the peer review and public comment process by including in those stages some response to the public comment and to the peer review.

Chairwoman ELLMERS. Thank you, Mr. Maresca, and Dr. Birnbaum, on that last response from Mr. Maresca, what do you do with the public comments? Do you respond to all the public com-

ments, and to what point in the process does this occur? Before or after the Report on Carcinogens is published?

Dr. BIRNBAUM. Thank you for the question, Mrs. Ellmers. The public comments come at different stages as I said before, and we listen to them, we consider them. They often lead to changes in what we determine or modifications in how we do things. For the 12th report, we did respond to all the public comments at the time that the document was released. For the 13th report, we intend to have the public comments actually discussed at the expert peer review meeting.

Chairwoman ELLMERS. Now, as the NTP develops the 13th edition of the Report on Carcinogens, do you think that the potential regulatory consequences of listing a substance should be considered? Now, I know, you know, as you have pointed out that this is a hazard assessment document, but because sometimes it seems to be used as this, do you think that this might improve it if we did look at the potential regulatory consequences?

Dr. BIRNBAUM. Our charge from the Congress is to evaluate the potential for compounds to be a known carcinogen or reasonably anticipated carcinogen. Our charge is not to consider regulatory consequences.

Chairwoman ELLMERS. Okay. When new studies are published that provide additional scientific information regarding a substance already listed as a known carcinogen or reasonably anticipated to be a carcinogen, does the NTP review the new information and reexamine the listing decision?

Dr. BIRNBAUM. If new information becomes available that might question the listing or cause a change in the listing, NTP will, if it is nominated to us or we self-nominate, we will begin to the process of evaluating and it can alter the listing about whether something can actually be removed from the list or downgraded or revised.

Chairwoman ELLMERS. With your response, one of the issues that has been raised is the timeframe that we are talking about. How quickly does the NTP review and reexamine the listing decisions, and does it take months or years?

Dr. BIRNBAUM. It would depend upon the topic and the compound and the amount of new data that becomes available and how important that new data is. But I can tell you that even at the times of the external peer review and response to public comments can have an impact on how we might list or not list a compound.

Chairwoman ELLMERS. Thank you very much to both of you for your responses, and I yield back the remainder of my time.

Chairman BROUN. Thank you, Mrs. Ellmers.

I now recognize my good friend from Louisiana, Mr. Richmond. I sure hope that the crawfish never get on the RoC. Mr. Richmond, you are recognized for five minutes.

Mr. RICHMOND. Well, we certainly have an interest in formaldehyde considering the tens of thousands of trailers that contain formaldehyde that our people in Louisiana lived in after the storm.

Dr. Birnbaum, the specific—and I want to just give you a chance to respond to the specific concerns which the 12th RoC process did not provide sufficient opportunity for meaningful peer review, and there was inadequate dialogue between NTP and the peer review-

ers, lack of peer reviewer access to public comments, inadequate time and resources to perform the review and inadequate NTP responses to peer review comments.

Dr. BIRNBAUM. I am sorry that you have had some misinformation if you heard that there was inadequate time for peer review, that the peer reviewers did not receive the public comments. All that was—is not true. In fact, the information was provided to all of them. There was extensive time for great peer review of all of the information. We held a special expert panel dealing with the issue of formaldehyde carcinogenesis.

Mr. RICHMOND. And Mr. Maresca, before I get to you, Dr. Birnbaum, and I am trying to apply this to, you know, sometimes we speak in theory up here and sometimes I try to get it to reality. I remember growing up and my grandfather and all of his brothers owned funeral homes, which are, you know, the very basic of small businesses, and I noticed after he passed and years when I went back, I noticed that the embalming room, the door to the embalming room now has a big sign that says wear protective gear and formaldehyde may cause cancer.

Well, my brother and all of his—I mean, my grandfather and all of his brothers who owned funeral homes and who were embalmers all developed a sense of cancer. Is this something that would come from NTP or at least a warning sign, or is that what we are talking about here? Yes.

Dr. BIRNBAUM. NTP does not provide the warning signs.

Mr. RICHMOND. Right.

Dr. BIRNBAUM. It provides some of the information. NTP first listed formaldehyde as reasonably anticipated to be a human carcinogen in 1980. It then updated it in the 12th report to known carcinogen based upon a series of epidemiology studies in people, looking at thousands of workers in different occupations. Embalmers were one of those occupations. Embalmers, garment workers, and chemical workers and in all cases there was a relationship between the extent of the exposure, the duration of the exposure, how high the exposure was to formaldehyde, and the carcinogenic response, which appeared to be myeloid leukemia in those studies.

Mr. RICHMOND. And just taking those examples and wearing my lawyer hat and small business side and all the other hats, it would seem to me that that information gives everybody an opportunity to act. It gives employers the ability to warn employees, it gives the chemical manufacturer the ability to warn suppliers and people who are going to use it, and or take necessary action to cover themselves from unnecessary liability and to protect the public at the same time.

Is that the goal of what we are trying to do here?

Dr. BIRNBAUM. Again, we are providing the information that decision makers and the public can use to protect health, and OSHA does take the NTP information and requires, for example, that if something is reasonably anticipated to be a human carcinogen, it does require labeling information, and it requires that to be on their material safety data sheets.

Mr. RICHMOND. Mr. Maresca, now I will give you the same opportunity to respond to the critiques of the 12th report if you want to do that.

Mr. MARESCA. The—well, our response to the critiques is that we do believe the science could be improved and that the peer review process and public comment process could be improved. We do know that OSHA, that a listing in the RoC would require changes, a new listing to the RoC would require changes to manufacturers' safety data sheets.

Mr. RICHMOND. And I guess the ultimate question, at some point a decision is going to have to be made one way or the other no matter how much peer review you have and no matter how much, you know, it is almost like being a judge and listening to two dozen experts on each side who are both advocating opposite positions, and at some point someone has to make a decision.

How much do we allow for the back and forth until we are satisfied that the people who are charged with making a decision have to make a decision?

Mr. MARESCA. Well, I think more than what we have now is the quick answer to your question. A little bit more response to peer reviews, for example, more dialogue between the Agency and the public, more dialogue among the peer reviewers.

Mr. RICHMOND. Thank you, Mr. Chairman. I see that I am out of time. I yield back.

Chairman BROUN. Thank you, Mr. Richmond.

I now recognize Mr. Miller for five minutes.

Mr. MILLER. Thank you, Mr. Chairman. I do know Dr. Birnbaum. She—I don't think she lives in my district. She lives in my area, and I have seen her on many occasions, and I know her reputation, which is excellent, and I know the reputation of the scientific work done at NIEHS, and that is excellent, and I have relied upon her judgment on some occasions and have always found her judgment to be sound.

Mr. Maresca.

Mr. MARESCA. Uh-huh.

Mr. MILLER. In my 20s I spent a year at University, as they would say, in London. I am not a gifted natural athlete. I think I am on the right slope of the athleticism bell curve, but the curve is still really fat where I am. But I like playing pick-up basketball, and a buddy I went to school with, the buddy I was at University with, played pick-up basketball, but I heard about a pick-up game among Americans living in London at an American school on Sunday afternoons. I showed up, and they let me play, but it quickly became apparent that I was just way, way out of my depth. And between the games I overhead the conversations, and everyone else in the game was actually living in Europe because they were playing European pro ball.

Mr. Maresca, that is probably how you should feel sitting today beside Dr. Birnbaum in talking about the subject that is before us. Dr. Birnbaum has her Master's and her Ph.D. in microbiology. She has published 700—more than 700 peer reviewed publications, book chapters, abstracts, reports. They appear—her own original research is entirely in the area of public health effects of chemical exposures. She is an adjunct faculty member both in public health, toxicology, environmental sciences at the University of North Carolina, Chapel Hill, my alma mater, an excellent institution as well

as a nearby university of lesser reputation. And you are a lawyer. Isn't that right?

Mr. MARESCA. That is correct.

Mr. MILLER. And the agency that you head, the office that you head is not a science policy office, and you are not a scientist. Isn't that right?

Mr. MARESCA. That is correct.

Mr. MILLER. Okay, and it is not the task of your agency to protect public health or the quality of the environment, environmental quality. Isn't that right?

Mr. MARESCA. That is correct.

Mr. MILLER. Okay. Do you have scientists who performed an independent assessment of the claims of the styrene industry about the evaluation of the scientific literature and any irregularities in the scientific process?

Mr. MARESCA. We do not.

Mr. MILLER. Okay. Is there anything that you have said in your testimony today that—we know the styrene industry has spent close to $1 million dollars in lobbying in just the last two years on this issue. Is there anything that you said in your testimony today that differs in any detail from the criticisms of the styrene industry?

Mr. MARESCA. I am not as familiar with the, all of the criticisms of the styrene industry. They were among the small businesses who did come to our office to suggest that there were problems with the 12th RoC.

Mr. MILLER. Okay. So your testimony today, your criticisms have come to you from the styrene industry. Is that correct?

Mr. MARESCA. In part. Yes.

Mr. MILLER. Okay, and you—according to your newsletter and actually the styrene industry's lobbying arms newsletter, claimed credit for this hearing today, for having obtained this hearing.

But your newsletter said that you had a round table discussion of NIHES—NIEHS Report on Carcinogens and that representatives from the American Chemistry Council and Regulatory Checkbook were there. Was anyone from NIEHS there?

Mr. MARESCA. I do not believe so.

Mr. MILLER. Okay. Was Dr. Belzer, who will testify on the next hearing, was he at that——

Mr. MARESCA. I believe he was.

Mr. MILLER. Okay, and Mr. Tonko's statement today includes—he added to it a small business owner's statement that they actually manufacture, I wouldn't have thought of the styrene industry as being a small business, but there is someone who is developing another form of packing material from mushrooms, and he says that actually what you are advocating for today is hurting their interests. Were they included in the round table?

Mr. MARESCA. I am not familiar with that letter, so I couldn't tell you.

Mr. MILLER. Okay. Mr. Chairman, I will yield back my last 11 seconds.

Chairman BROUN. Glory be. Thank you so much, Mr. Miller. By the way, I did not know that Dr. Birnbaum was a professional basketball player in Europe, and I appreciate you bringing that to our

attention, and I would also like to remind my friend if you had looked at the second panel, there is Dr. Bus, who is a toxicologist, who will be presenting to us today also.

So now I recognize my good friend, Mr. McNerney, for five minutes.

Mr. MCNERNEY. Thank you, Mr. Chairman, and I thank you for holding a hearing that is not specifically designed to bash the Administration.

Dr. Birnbaum, can you tell us what evidence the National Toxicology Program used in listing styrene as a reasonably anticipated to be a carcinogen?

Dr. BIRNBAUM. There were over, between 400 and 500 papers that were——

Chairman BROUN. Dr. Birnbaum, your microphone.

Dr. BIRNBAUM. Sorry. There were over 400 to 500 papers or more that were looked at in the background document that were involved in assessing the health effects of styrene. There were many—there were three groups of expert witnesses who reviewed it, plus our Board of Scientific Counselors. There were votes taken at all of the expert groups, and of the 32 votes, 30 were for listing styrene. Thirty-one of the 32 were for listing styrene, and of those 31 there were actually several votes for listing it as a known carcinogen.

Mr. MCNERNEY. So you wouldn't consider that to be a controversial issue within the review groups?

Dr. BIRNBAUM. I think not. I think the only discussion among one of the review groups was should it be listed as known or reasonably anticipated.

Mr. MCNERNEY. Well, the Report on Carcinogens lists many different substances that are known to be human carcinogens or reasonably anticipated to be human carcinogens. Why do you believe that the styrene and the formaldehyde in particular have generated so much controversy? If I may ask.

Dr. BIRNBAUM. I think these are high-volume use compounds, but we have had controversy on some of our listings in the past as well.

Mr. MCNERNEY. Thank you. One of the things that I hear complaining from the industry groups is that there were public comments, and there were no response to those comments. How many public comments were there? Would it have overwhelmed the resources of your department to try to respond to each one of those comments?

Dr. BIRNBAUM. Yes.

Mr. MCNERNEY. Thank you. Mr. Maresca claims, and this is still for Dr. Birnbaum, that several studies refute your listing of styrene as a reasonably anticipated to be a human carcinogen. Can you explain the discrepancies between the studies, your studies and the studies of the other side?

Dr. BIRNBAUM. We looked at all of the studies, both the studies that demonstrated an association in humans for styrene and where some of the negative studies. Our conclusions were that the evidence in humans was limited. We also, though, found that styrene is a carcinogens in experimental animals by two routes of exposure by both oral and inhalation, and we also found that styrene is well

known to be metabolized to a chemical called styrene oxide, and that can be found circulating in the blood of workers who are using styrene, and we have also found chromosomal aberrations. Those are genetic problems in the blood of workers who are exposed to styrene.

So listing it as reasonably anticipated was based not on one of the three potential criteria to put it in that category but upon all three.

Mr. MCNERNEY. Does this listing apply to public use of styrene or to workers in styrene production or both?

Dr. BIRNBAUM. All the human studies involve highly exposed workers.

Mr. MCNERNEY. So using a styrene cup is not really going to expose you to unnecessary cancer risks.

Dr. BIRNBAUM. We are not concerned about any styrene that might leak from a polystyrene cup.

Mr. MCNERNEY. Thank you for your direct answers, and I yield back.

Chairman BROUN. Thank you, Mr. McNerney.

I want to thank the witnesses for you all's valuable testimony and the Members for your questions. The Members of this, of either Committee may have additional questions for either of you, and we will ask you to respond to those questions in writing as expeditiously as you possibly can.

Mr. TONKO. Mr. Chair. Point of clarification.

Chairman BROUN. Certainly.

Mr. TONKO. I am just wanting to clarify, and I am doing this via the document from the Office of Advocacy from the SBA, and in their coversheet with testimony, they offer a letter to Secretary Sebelius at HHS, indicating that as Advocacy, as an independent body within the United States Small Business Administration, the views expressed by Advocacy do not necessarily reflect either the position of the Administration or the SBA.

So I think that is important to clarify, and also in——

Chairman BROUN. I think that letter, I think you already have——

Mr. TONKO. Right.

Chairman BROUN. It is submitted, and so you can ask any further questions by writing if you don't mind because we need to forge ahead.

The record will remain open for two weeks for additional comments from Members, not to cut you off, but it will remain open so that you can make other comments. Witnesses are excused. We will move to our second panel. Thank you so much for participating today.

And if the second panel will take your seats very quickly, we would appreciate it.

While they are being seated, at this time I would like to introduce our second panel. First is Dr. James S. Bus. He is the Director of External Technology, Toxicology, and Environmental Research and Consulting for the Dow Chemical Company. Ms. Ally LaTourelle, Esquire, is the Vice President for Government Affairs at Bioamber, Incorporated, and Dr. Richard Belzer is the President of Regulatory Checkbook.

And I recognize Chairwoman Ellmers for introducing the remaining witnesses.

Chairwoman ELLMERS. Thank you, Mr. Chairman.

I would like to introduce Dr. Grimsley, who was invited to testify by my colleague, Ranking Member Richmond. She is a Certified Industrial Hygienist. She is currently on special leave from Tulane University School of Public Health and Tropical Medicine, where she is an Associate Professor.

Chairman BROUN. Thank you, Mrs. Ellmers.

As our witnesses should know. Oh, I am sorry.

Chairwoman ELLMERS. I apologize.

Chairman BROUN. Go right ahead. I thought you had finished.

Chairwoman ELLMERS. This process is a little different than what we have in Small Business, so I——

Chairman BROUN. That is quite all right.

Chairwoman ELLMERS. I would also like to introduce Bonnie Webster, who is the Vice President of Monroe Industries in Avon, New York. Monroe Industries is a cast polymer company that manufactures high-end custom showers and vanity tops and has seven employees.

I would also like to introduce John Barker. He is Corporate Manager of Environmental Affairs, Safety and Loss Prevention for Strongwell Corporation, which is headquartered in Bristol, Virginia. Strongwell Corporation manufactures ballistics panels and bridge beams and platforms and employees 465 people in their three facilities.

Dr. Grimsley, Ms. Webster, and Dr. Barker, we very much look forward to your testimony today, and I yield back now, Mr. Chairman.

Chairman BROUN. Thank you, Mrs. Ellmers.

As our witnesses should know, spoken testimony is limited to five minutes each, after which the Members of the Committee will have five minutes each to ask questions.

As I noted before, it is the practice of the Subcommittee on Investigations and Oversight to receive testimony under oath, and we will use that practice here today.

Do any of you have an objection to taking an oath?

Okay. Very good. Let the record reflect that all witnesses are willing to take the oath. You also may be represented by legal counsel. Do any of you have counsel here today?

Okay. Let the record reflect that none of the witnesses have counsel.

Now, if you would each would please stand and raise your right hand. Do each of you solemnly swear and affirm to tell the whole truth and nothing but the truth, so help you God?

Okay. Please be seated. Let the record reflect that all witnesses have taken the oath.

I now recognize Dr. Bus for five minutes.

STATEMENT OF DR. JAMES S. BUS, DIRECTOR OF EXTERNAL TECHNOLOGY, TOXICOLOGY, AND ENVIRONMENTAL RESEARCH AND CONSULTING, THE DOW CHEMICAL COMPANY

Dr. BUS. Good morning. My name is Dr. James Bus. Over my career as a toxicologist, I have served as the President of the Society of Toxicology and served on science advisory bodies of the National Academy of Sciences, the EPA, the FDA, and the NTP. I am here today as a concerned scientist and represent the Styrene Information and Research Center, of which my employer, the Dow Chemical Company, is a founding member.

I, Dow, and the styrene industry are keenly interested in protecting the health and safety of workers, customers, and the public. Objective, evidence-based reviews of the scientific research are essential elements in our decision making about products and facilities.

The NTP is globally recognized as an authoritative body. Chemical classifications in its RoC carry significant consequences for businesses, large and small, including regulatory actions and commercial impacts.

Thus, it is essential that the RoC classifications represent the highest quality scientific evaluations. My comments today focus on three shortcomings of the NTP's RoC process and are based in part on issues revealed in recent RoC evaluations, including styrene.

First, the RoC process is almost entirely ad hoc and lacks explicit criteria necessary to assure consistency and transparency. Importantly, NTP's RoC process is completely silent about criteria needed to guide scientific evaluations at several key process stages.

For example, draft monographs provide the primary rationale for RoC classifications. Yet the recently updated RoC process states that monograph reviews only include, "external scientific input as needed, for example, consultants, ad hoc presentations, expert panels."

A 2011 NAS assessment of the EPA review of formaldehyde details a number of scientific best practices for assessments of chemicals in general and points out that ad hoc review processes cannot be relied on to produce scientifically valid assessments.

Indeed, evidence-based approaches are now being used by other institutions such as the Institute of Medicine.

Second, the RoC process lacks adequate checks and balances, including peer review and addressing outside or conflicting data. NTP's new process limits review by its Board of Scientific Counselors to NTP's initial draft concept document, which is akin to an outline of what the NTP's review intends to examine. Peer review of the critical draft monographs by external panels is left entirely to the discretion of the NTP, including the key steps of expert panel member selection and identification of review charge questions.

In addition, interagency review of draft monographs is reduced to providing inputs that will only be considered at the discretion of the NTP and are not further shared with the expert panels or the public.

Finally, draft monographs are presented to the NTP Board of Scientific Counselors for information only, denying this senior advisory panel any meaningful peer review. This is not transparent or credible peer review.

Finally, the RoC fails to employ scientific best practices, relies on outdated approaches, and has not adopted recent NAS recommendations. The NAS has specifically outlined several fundamental best practices necessary to assure that the processes for toxicology-related assessments of chemicals are evidence based, objective, and scientifically credit. The process used to prepare the RoC falls considerably short of those objectives.

For example, NTP has previously stated that RoC reviews are based on strength of evidence as compared to the more comprehensive weight of evidence analyses used by groups such as the Institute of Medicine. The RoC heavily favors finding supporting NTP's proposed listing position while contrary findings are seldom given much weight.

Although external public comment is solicited, NTP has stated as a matter of policy it will no longer offer any written response, thereby masking the existence of different scientific views.

In summary, the current RoC process falls well short of producing evidence-based decisions. I urge Congress to oversee a thorough assessment of the RoC, ideally through an NAS review, to ensure that any future RoC listings are evidence based, provide accurate public health information, and reflect the highest scientific standards in its processes and to begin to determine the RoC's fundamental relevancy going forward. This will increase the public's and industry's confidence in the RoC listings and their applications to science-informed decision making.

Thank you.

[The prepared statement of Dr. Bus follows:]

Written Testimony provided to the U.S. House of Representatives'
Committee on Science, Space & Technology, Subcommittee on Investigations & Oversight
and
Committee on Small Business, Subcommittee on Health Care & Technology

Joint Hearing: "How the *Report on Carcinogens* Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"

James S. Bus, PhD, DABT, ATS
The Dow Chemical Company
April 25, 2012

Presenter

My name is Dr. James Bus. I am employed as Director of External Technology, Toxicology and Environmental Research and Consulting, by The Dow Chemical Company (Midland, Michigan).

Since receiving my Ph.D. from Michigan State University in 1975, I have:

- Authored or co-authored more than 100 scientific papers, reviews and books in my field.
- Served as the president of the Society of Toxicology and the American Board of Toxicology, and currently am the president of the Academy of Toxicological Sciences.
- Been a member of the National Academy of Sciences (NAS) Board of Environmental Sciences and Toxicology.
- Served as a member of the Science Advisory Boards of the US Environmental Protection Agency (EPA), US Food and Drug Administration (FDA) and the US National Toxicology Program (NTP).

Executive Summary

I am here today as a concerned scientist and represent the Styrene Information and Research Center, of which my employer is a founding member, and I very much appreciate the opportunity to provide these comments regarding concerns about the scientific integrity of the processes the NTP uses in the development of the *Report on Carcinogens (RoC).*

I, Dow, and the styrene industry are keenly interested in protecting the health and safety of workers, customers and the public. Objective, evidence-based reviews of scientific research are essential elements of our decision making about our products and facilities.

The National Toxicology Program (NTP) is globally recognized as an "authoritative body;" chemical classifications in its *Report on Carcinogens* carry significant consequences for businesses large and small, including regulatory actions and commercial impacts. Thus, it is essential that *RoC* classifications represent the highest quality scientific evaluations.

The primary issues with the process NTP used for the 12th *RoC*, and with the new process NTP implemented for future *RoC* assessments, are expanded upon in these comments. However, these concerns may be summarized by highlighting the following key points I hope the Joint Committees will please consider:

1) **The *RoC* is *Ad Hoc* and lacks explicit criteria needed to assure its reviews of scientific information are transparent and scientifically consistent.**

   While NTP prides itself on an effective *RoC* assessment process, the fact is that the process is – by NTP's own admission – largely *ad hoc* and does not document the fundamentally required specifics of the scientific approach NTP uses to assess the data on which its carcinogen listings are based.

Additionally, it is completely silent about criteria needed to guide scientific evaluations at several key process stages. For example, draft "Monographs" provide the primary rationale for *RoC* classifications. Yet the recently updated *RoC* process states reviews of the Monographs only include "external scientific input, **as needed** (*e.g.*, consultants, *ad hoc* presentations, expert panels)" **(emphasis added).**

A 2011 NAS assessment of the EPA review of formaldehyde details a number of scientific best practices for assessments of chemicals in general and points out that *ad hoc* review processes cannot be relied on to produce scientifically valid assessments; indeed, evidence based approaches are now being used by other institutions such as the Institute of Medicine.

2) **The *RoC* process lacks adequate checks and balances, including peer review and addressing outside/conflicting data.**

Although NTP insists that public comments are repeatedly solicited, and considered, the reality is that NTP's main approach to outside input is posting comments in an on-line docket. NTP has not dealt with public comments or sought peer review opinions on data contradictory to its conclusions. For the 12th *RoC*, NTP provided only minimal response to public comments after the Secretary had signed-off on the final *Report*. For the new *RoC* process NTP has clearly indicated, **as a matter of policy**, that it no longer will respond to public comments at all.[1]

In addition, NTP's current process limits review by its own Board of Scientific Counselors (BSC) to NTP's initial draft "concept document," which is akin to an outline of what NTP's review intends to examine. Peer review of the critical draft Monographs by external Expert Panels is left entirely to the discretion of the NTP, including the key steps of selection of expert panel members and identification of review charge questions.

Finally, interagency peer review of draft Monographs is reduced to providing "inputs" that will only be considered at the discretion of NTP and are not further shared with the Expert Panels or the public. Towards the end of the process, draft Monographs are simply presented to the NTP BSC for its information only, denying this senior advisory body from any meaningful peer review of the Monograph.

3) **The *RoC* process does not employ scientific best practices, relies on outdated approaches and has not adopted recent NAS recommendations.**

Both past and current *RoC* assessment processes fly in the face of scientifically accepted hazard assessment procedures – *i.e.*, an evidence-based approach to weighing the full body of data.

NTP acknowledges it used the outmoded "strength of evidence" approach in the 12th *Report on Carcinogens*,[2] essentially utilizing only data that support a conclusion of carcinogenicity. In fact, other regulatory bodies that employ the more scientifically robust evidence-based assessment process have reached opposing conclusions on substances NTP has listed as carcinogens.

NTP's process for the 12th *RoC*, as well as its new process, ignored clear and pertinent direction from the National Research Council's National Academy of Sciences (NAS) regarding several fundamental best practices necessary to assure that toxicology-related assessments of chemicals are conducted in an evidence based, objective and scientifically credible manner. In the case of formaldehyde for the 12th *RoC*, NTP dismissed NAS' conclusions that NTP's approach in classifying formaldehyde was scientifically inaccurate.

In summary, the current *RoC* process falls well short of producing evidence-based listing decisions.

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[1] NTP Board of Scientific Counselors Meeting, 15 Dec 2011, statement of Dr. John Bucher. The statement referred to can be found at 6:15 minutes of the recording that is available at https://www.box.com/shared/static/ea274f5a6547994936ac.wma.

[2] "Peer Review of Draft Substance Profiles for the 12th *Report on Carcinogens*," slide 6 of presentation by Mary S. Wolfe of NTP to the NTP Board of Scientific Counselors Meeting, 24 Feb 2009; available at http://ntp.niehs.nih.gov/files/Wolfe20090224.pdf.

Additionally, the current *RoC* program does not address the original intent of Congress to identify only serious carcinogen concerns. NTP instead seemingly attempts to justify listing all substances nominated for consideration. Further, the *RoC* program is now duplicative of other federal carcinogen classification programs which use more robust assessment practices and which have been put in place since the *RoC* program began.

Given the above facts, I strongly urge Congress to oversee a thorough assessment of the current *RoC* program (ideally through an NAS review of the *RoC*), and to begin an ongoing evaluation to determine the *RoC's* fundamental relevancy and to ensure that any future *RoC* listings are evidence-based, provide accurate public health information and reflect the highest scientific standards in its processes.

This will increase the confidence of the public and industry in the *RoC's* listings and their application to science-informed decision-making.

Background

The *Report on Carcinogens* (*RoC*) is a Congressionally mandated report that lists substances that the Secretary of Health and Human Services (HHS) has determined are "known" or "reasonably anticipated" to cause cancer and to which significant numbers of Americans are exposed. The HHS Secretary has delegated responsibility for preparation of the *RoC* to the staff of the National Toxicology Program (NTP), which is housed administratively at the National Institute of Environmental Health Sciences (Research Triangle Park, NC). The Congressional directives for the *RoC* are sparse (see page fourteen of these comments), and NTP has managed this program without meaningful oversight.

NTP has attempted to provide the public with some perspective about its *RoC* listings by stating:

> "A listing in the *RoC* does not by itself establish that a substance will cause cancer in an individual. Many factors, including the amount and duration of an exposure, and an individual's susceptibility to a substance, impact whether a person will develop cancer or not. Formal risk assessments, that take into account these factors, are the purview of the appropriate federal, state, and local health regulatory and research agencies."[3]

NTP has published 12 editions of the *RoC* – the 11th Edition was issued in 2004, and the 12th Edition was published June 10, 2011.[4]

The NTP is globally recognized as an "authoritative body," and chemical classifications in the *RoC* carry significant consequences for businesses large and small, including regulatory actions (*e.g.*, OSHA Hazard Communications Standard labeling requirements, TSCA reporting requirements and California's Proposition 65)[5] and commercial impacts.

Because objective, evidence-based reviews of scientific research are essential elements of both informing the public about the potential risks which may be associated with individual substances and decision making by industry about its products and facilities, the reality of these impacts make it essential that *RoC* classifications represent the highest quality scientific evaluations.

My comments focus on three key shortcomings in the process NTP uses to prepare and develop its *RoC* assessments, and are based in part on issues revealed in the review of styrene in the recent 12th *RoC*, namely:

- **The *RoC* is *Ad Hoc* and lacks explicit criteria needed to assure its reviews of scientific information are transparent and scientifically consistent.**
- **The *RoC* process lacks adequate checks and balances, including peer review and addressing outside/conflicting data.**
- **The *RoC* process does not employ scientific best practices, relies on outdated approaches and has not adopted recent NAS recommendations.**

Each of these shortcomings is discussed in more detail in the following pages.

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[3] NTP's "Questions & Answers about the *RoC*, What does a listing in the *RoC* Mean?" Available at http://ntp.niehs.nih.gov/go/7249.
[4] *Report on Carcinogens* 12th Edition; available at http://ntp.niehs.nih.gov/go/roc12.
[5] NTP's "Questions & Answers about the *RoC*, What does a listing in the *RoC* Mean?" Available at http://ntp.niehs.nih.gov/go/7249.

The *RoC* is *Ad Hoc* and lacks explicit criteria needed to assure its reviews of scientific information are transparent and scientifically consistent.

The NAS expert panel members who prepared a 2011 assessment[6] of the EPA Integrated Risk Information System (IRIS) review of the chemical formaldehyde expressed concern about the fact that, in preparing its formaldehyde assessment, EPA referred to its own guidelines but did not follow them, employing instead what appeared to be a largely *ad hoc* process.[7]

Chapter seven of the NAS report lays out a "Roadmap" in which the Panel details a number of scientific best practices for assessments of chemicals in general and points out that *ad hoc* review processes cannot be relied on to produce scientifically valid assessments.

These concerns indirectly but convincingly call into question the validity of the process NTP used to conduct each of the assessments published in the 12th *RoC*. Even though NAS criticized some of the conclusions of EPA's draft IRIS review, the IRIS process is designed to rely on EPA's well-described, detailed and extensive evidence-based guidelines, which include its "Guidelines for Carcinogen Risk Assessment."[8]

In contrast, NTP's process for the *Report on Carcinogens* is almost entirely *ad hoc*. For example, the *Report on Carcinogens* has no supporting guidelines for carcinogen hazard or risk assessment and its listing criteria are filled with ambiguous non-scientific terms and are devoid of any details of how data are to be evaluated to apply the listing criteria.

NTP's newly revised *RoC* process, which is described in a brief five-page document titled "Process for Preparation of the *Report on Carcinogens*,"[9] includes a series of bureaucratic steps but is completely silent about the scientific processes that should occur at each state of the process. In fact, NTP itself characterizes parts of the new *RoC* process as "*ad hoc*." Given the lack of specific procedures and the fact that so many of the *RoC* process steps are completely at NTP's discretion, the overall process is, in effect, *ad hoc*.

To describe how external peer review input is supposed to occur, this document simply includes a footnote on page three that links to an NTP webpage for "Special Emphasis Panels." Following this link on NTP's website reveals:

> "The NTP uses ad hoc scientific experts, referred to as special emphasis panels (SEPs), as needed, to provide independent scientific peer review and advice on targeted issues. Such issues include the strength of the scientific evidence of the potential for harm from specific environmental or occupational exposures, the identification of toxicology knowledge gaps and data needs, and the evaluation of new/revised alternative toxicological methods of multi-agency interest that might improve or reduce, refine or replace the use of animals. These panels help ensure transparent, unbiased, and scientifically rigorous input to the program for its use in making credible decisions about human health hazards, setting research and testing priorities, and evaluating test methods for toxicity screening. The *Report on Carcinogens*, Office of Health Assessment and Translation and the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods use SEPs to conduct evaluations. Special emphasis meetings are typically announced and open to the public."[10]

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[6] *Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde*, Board on Environmental Studies and Toxicology, National Research Council of the National Academies, 189 pages, 2011, National Academies Press, Washington, D.C; available at http://www.nap.edu/catalog/13142.html.

[7] *Ibid.*, p. 80.

[8] *Guidelines for Carcinogen Risk Assessment*, Risk Assessment Forum, United States Environmental Protection Agency, 166 pages, 2005; available at http://www.epa.gov/raf/publications/pdfs/CANCER_GUIDELINES_FINAL_3-25-05.PDF.

[9] *Process for Preparation of the Report on Carcinogens*, 11 Jan 2012; available at http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.

[10] *Special Emphasis Panels*, last updated 2 May 2011, http://ntp.niehs.nih.gov/go/166, accessed on line 20 Apr 2012.

Furthermore, a key step of the NTP process includes preparation of a draft "Monograph" which contains NTP's primary scientific rationale for its *RoC* classification decisions. However, a flowchart of the *RoC* process published by NTP states the Monograph is reviewed by "external scientific input, **as needed** (*e.g.*, consultants, ***ad hoc*** presentations, expert panels)"[11] **(emphasis added).**

NTP's process provides no criteria for how or when "external scientific input" is to be solicited or if and when it may be needed. Equally important, no criteria are provided for identification of the critical studies upon which the assessment detailed in the Monograph is to be based, how these studies will be evaluated, how studies that NTP considers to be critical will be selected or how consistent and transparent evidence-based evaluations of the overall body of scientific evidence can be assured, all matters that the NAS panel explicitly identified as necessary in its Chapter seven "Roadmap" in its review of the IRIS formaldehyde assessment.

NTP's review of formaldehyde for the 12th *RoC*, found that exposure to this substance was associated with leukemia, and on that basis NTP's panel voted to recommend that formaldehyde be listed as a "known carcinogen" in the *RoC*. Yet the NAS panel that reviewed formaldehyde found that the available data do not support a leukemia concern.[12] The NAS panel suggested that only an inadequate assessment of the data could result in a leukemia finding for formaldehyde. NTP has subsequently responded to the NAS review, dismissing its relevance to NTP's review of formaldehyde by highlighting the small differences between the nature of the EPA and NTP reviews.[13]

In summary, since the EPA formaldehyde review used an *ad hoc* process that resulted in a scientifically unsupported conclusion for formaldehyde, it follows that the NTP process for formaldehyde is also suspect. By extension, NTP's process is therefore generally suspect with respect to its ability to implement transparent, credible and evidence-based reviews. In the view of the NAS formaldehyde panel's Chapter seven, a process this *ad hoc* cannot be relied on to produce scientifically valid assessments.

The *RoC* process lacks adequate checks and balances, including peer review and addressing outside/ conflicting data.

Before discussing the lack of an adequate peer review process at NTP for the *Report on Carcinogens*, it is important to understand what appropriate and effective peer review consists of.

According to a 2004 bulletin published by the White House's Office of Management and Budget (OMB):

> "Peer review is one of the important procedures used to ensure that the quality of published information meets the standards of the scientific and technical community. It is a form of deliberation involving an exchange of judgments about the appropriateness of methods and the strength of the author's inferences. Peer review involves the review of a draft product for quality by specialists in the field who were not involved in producing the draft."[14]

The OMB Bulletin further indicates:[15]

- "The peer reviewer's report is an evaluation or critique that is used by the authors of the draft to improve the product. Peer review typically evaluates the clarity of hypotheses, the validity of the research design, the quality of data collection procedures, the robustness of the methods employed, the appropriateness of

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[11] *Process for Preparation of the Report on Carcinogens*, 11 Jan 2012, Figure 1; available at http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.
[12] *NAS Formaldehyde Review*, *op. cit.*, pp. 108-110, 112.
[13] *Addendum to the 12th Report on Carcinogens*, National Toxicology Program, 30 Nov 2011; available at http://ntp.niehs.nih.gov/ntp/roc/twelfth/Addendum.pdf.
[14] *Final Information Quality Bulletin for Peer Review*, Executive Office of the President, Office of Management and Budget, p. 4, 16 Dec 2004; available at http://www.whitehouse.gov/sites/default/files/omb/memoranda/fy2005/m05-03.pdf.
[15] *Ibid.*, pp. 3-4.

the methods for the hypotheses being tested, the extent to which the conclusions follow from the analysis, and the strengths and limitations of the overall product."

- "Peer review should not be confused with public comment and other stakeholder processes. The selection of participants in a peer review is based on expertise, with due consideration of independence and conflict of interest."

Simply stated, effective peer review provides needed checks and balances, is conducted by "specialists in the field who were not involved in producing the draft" and is scientifically essential "to ensure…the quality of published information" and "to improve the product."

The Obama Administration has more recently reinforced a similar theme in several of its directives relation to the use of scientific information and scientific integrity. For example:

- A January 18, 2011 Executive Order by President Obama further directed that "[r]egulations shall be based, to the extent feasible and consistent with law, on the open exchange of information and perspectives among…affected stakeholders in the private sector, and the public as a whole."[16]
- A December 17, 2010 memo by the Director of the White House Offices of Science and Technology Policy, directs heads of executive departments and agencies to ensure that their scientific programs are based on "…honest investigation, open discussion, refined understanding, and a firm commitment to evidence.".[17]
- A March 9, 2009 "Memorandum on Scientific Integrity" to the heads of executive departments and agencies states "[t]he public must be able to trust the science and scientific process informing public policy decisions. Political officials should not suppress or alter scientific or technological findings and conclusions." It also says "[w]hen scientific or technological information is considered in policy decisions, the information should be subject to well-established scientific processes, including peer review where appropriate…"[18]

In contrast to these policies, the NTP process does not conform to the President's directives and advocacy in favor of transparency, integrity and sound science In contract, NTP's current review process, is starkly different from President Obama's directives relating to the use of science as well as OMB's description of peer review:

- **NTP's Board of Scientific Counselors (BSC)**

  In the past, the BSC's review served as both a peer review and a check and balance to the NTP office. With the exception of the 12th *RoC*, the BSC was asked to critically review NTP's scientific reasoning and then to vote on the NTP's recommendation found in the draft Monograph. Over the years, on three occasions, the BSC overturned the NTP's draft recommendation as a result of its peer review.[19] For the 12th *RoC*, the BSC had a more limited role due to a change in NTP policies was not asked to vote on NTP's listing decision.[20]

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[16] Improving Regulation and Regulatory Review, Executive Order 13563 of January 18, 2011, Federal Register, v. 76, no. 14, pp, 3821-3823; available at http://www.gpo.gov/fdsys/pkg/FR-2011-01-21/pdf/FR-2011-01-21.pdf.

[17] Memorandum for the Heads of Executive Departments and Agencies, Memorandum: Scientific Integrity, 17 Dec 2010; available at http://www.whitehouse.gov/sites/default/files/microsites/ostp/scientific-integrity-memo-12172010.pdf.

[18] *Memorandum on Scientific Integrity*, Administration of Barack. H. Obama, 9 Mar 2009; available at http://regs.dot.gov/requirements/DCPD-200900137.pdf.

[19] *12th Report on Carcinogens, Appendix C*; available at http://ntp.niehs.nih.gov/ntp/roc/twelfth/roc12.pdf, p. 470 (lists these substances); the outcomes of the BSC deliberations can be found by reviewing the documents related to each review (available on request from NTP).

[20] *NTP Report on Carcinogens Review Process*, last updated 3 Oct 2011, http://ntp.niehs.nih.gov/go/29353, accessed 20 Apr 2012.

In the newly announced process, review by the BSC is limited to its initial draft "concept document,"[21] which is akin to an outline of what NTP's review intends to consider for a particular substance.

As a nearly final process step, NTP is also to "present information"[22] to the BSC about each draft Monograph and any reviews by an NTP Special Emphasis Panel (if convened). This step appears to be intended simply to inform the BSC in a public forum about NTP's conclusions, and it denies this senior advisory body any opportunity to conduct a peer review of the draft Monograph.

As a result, NTP will not use the BSC as a peer review body in the future.

- **Interagency Review**

  Draft Monographs have historically been subject to interagency peer review, but the results of these reviews have not been made public. These reviews were formalized as a part of NTP's process and gave experienced scientists at other Federal agencies with an interest in substances under review the opportunity to provide NTP with a critical peer review of the draft Monographs.

  For the 12th *RoC*, this process involved "...an interagency scientific review group..." which was "...provided with all relevant information (including the background document, the expert panel report, and any public comments received to date) on the candidate substances and asked to apply the listing criteria to this information and make a recommendation on the listing status of the candidate substance."[23] As with previous *RoC* reviews, the deliberations and results of this interagency review were not made public.

  In addition, in the case of styrene in NTP's 12th *RoC*, the meeting of one of the review panels was scheduled just four days following the close of the comment period; this made it exceptionally unrealistic to imagine that the reviewers would be able to appropriately consider the public comments received by NTP.

  NTP's flowchart of its most recent *RoC* review process still includes "Interagency Input" and "Interagency Review" as line items.[24] However, while in the past, this review was formalized when NTP "provided all relevant information" to its interagency partners, interagency "input" is now "invited" and any input received is "considered," along with input from other stakeholders.

  In essence, NTP has reduced interagency review to one of several stakeholder processes it uses to gather information. This is not peer review, however, as explained in OMB's 2004 Bulletin on Peer Review, which says "[p]eer review should not be confused with public comment and other stakeholder processes."[25]

  The bottom line is that NTP is free to do what it pleases with this "input," as NTP's process includes no formal guidelines for addressing such input.

- **Special Emphasis Panels**

  As previously referenced in these comments, NTP clearly states that its Special Emphasis Panels are, "*ad hoc* scientific experts..." who serve "...as needed, to provide independent scientific peer review and advice on targeted issues."[26]

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[21] *Process for Preparation of the Report on Carcinogens*, 11 Jan 2012, p.2; available at http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.
[22] *Process for Preparation of the Report on Carcinogens*, 11 Jan 2012, Figure 1; available at http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.
[23] *NTP Report on Carcinogens Review Process*, last updated 3 Oct 2011, http://ntp.niehs.nih.gov/go/29353, accessed 20 Apr 2012.
[24] *Process for Preparation of the Report on Carcinogens*, 11 Jan 2012, Figure 1; available at http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.
[25] *OMB Peer Review Bulletin, op. cit.*, p. 4.
[26] *Special Emphasis Panels*, last updated 2 May 2011, http://ntp.niehs.nih.gov/go/166, accessed on line 20 Apr 2012.

In addition, NTP states that "[m]embers of NTP panels are scientists with relevant expertise and knowledge selected by the NTP from the public and private sectors. The final selection of membership is based upon providing a balanced and unbiased group of highly qualified individuals."[27]

For the *RoC*, such panels are instructed to determine "...whether the scientific evidence is adequate for applying the listing criteria..."[28] Special Emphasis Panels are included in the current NTP *RoC* process description and flowchart, but under different names:[29]

- NTP seeks "external scientific input, as needed" as it completes its draft Monograph.
- The *RoC* process includes a near-final step of "peer review of draft *RoC* Monograph by NTP Peer-Review Panel."

When each of these steps is first mentioned in the description of the updated *RoC* process and flowchart, they are footnoted with a reference to NTP's "*ad hoc*" and "as needed" Special Emphasis Panels.

The above descriptions of NTP's listing criteria and the roles of its Special Emphasis Panels seem similar to how OMB's 2004 Bulletin describes the peer review process. However, as explained beginning on page eleven of these comments, in its past practices, NTP has failed to adhere to evidence-based approaches which meet "...the standards of the scientific and technical community" and which assure that peer reviewers are "...not involved in producing..." NTP's draft Monographs.

At the present time, however, even the need for peer review of the critical draft Monographs by any non-NTP body, including NTP's self-described "*ad hoc* expert panels," is left entirely to the discretion of the NTP; this total discretion extends to the essential steps of selecting expert panel members who have appropriate expertise and identifying the review charge questions, which guide the reviews.

- **Role of the HHS Secretary**

The statue which created the *Report on Carcinogens* requires that the Secretary of Health and Human Services approve the publication of the listing decisions in the *Report on Carcinogens*.[30]

- In the 12th *RoC*, the Secretary received briefing papers from NTP and held meetings with members of the public who objected to the recommendations in the draft report. This provided some level of supervision of NTP's decisions.
- Under the new process for future assessments, the *Report* signed by the Secretary is afforded secondary importance by the fact that the NTP will publish the results of its assessments on the Internet for the public to begin using immediately upon completion and then every two years send forward the assessments completed up to that point for formal publication in the *Report on Carcinogens*.[31]
- It is hard to imagine that the Secretary would be inclined to overrule one of these assessments that had already made available to the public on the Internet up to 2 years previously.

This process change has now given the Director of the NTP full authority to write the assessments, subject them to some form of peer review to a panel of NTP's own choosing, complete the report, and publish it on the Internet without any supervision or review by any person outside of direct organizational control of the NTP Director.

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[27] *Process for Preparation of the Report on Carcinogens*, 11 Jan 2012, page 3, footnote 7; available at http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.
[28] *Ibid.*, p. 4.
[29] *Process for Preparation of the Report on Carcinogens*, 11 Jan 2012, Figure 1; available at http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.
[30] Public Services Health Act, as amended,§301(b)(4); available at http://energycommerce.house.gov/108/pubs/109_health.pdf.
[31] *Process for Preparation of the Report on Carcinogens*, 11 Jan 2012; available at http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.

For a *Report* that has such important potential consequences for public health and the economy, this lack of proper checks and balances is inappropriate.

To summarize, NTP selects the scope of work for each Monograph, creates its Monographs in-house with limited external input or oversight, selects its own review committees "as needed," and approves and publishes the final content on the Internet.

In addition to the general issues that NTP's *Report on Carcinogens* has with its peer review process, as outlined above, the case of styrene in the 12th *RoC* also reveals a very specific concern about NTP's approach to peer review:

- NTP's current description of its *RoC* process include the following statement about peer review:

  "...all scientific information used to evaluate the potential carcinogenicity of a candidate substance must come from peer-reviewed, publicly available sources." Similar descriptions have been in place for some time at NTP.[32]

- Unfortunately, while this statement is clear, NTP did not follow it during its review of styrene during the 12th *RoC*. As part of NTP's styrene review, NTP reinterpreted two studies in ways that differed from the study authors' peer reviewed published conclusions. As a result, NTP was able to claim that styrene met its listing criteria and subsequently classified styrene as "reasonably anticipated to be a human carcinogen" in the 12th *RoC*.

  The styrene industry challenged NTP's approach in its public comments and testimony at public meetings to no avail.[33] Additionally, when NTP was questioned about its reinterpretation of these studies by two Members of Congress,[34] NTP, in a meeting with the Congressmen, first said that NTP could not conduct a peer review because the novel statistical analysis "was submitted to NTP over the phone."[35] In response to a written question, NTP later baldly stated that "no formal analysis of the results of any epidemiology study was presented as part of this process."[36]

None of the above reflects either transparent or credible peer review, and do not meet even the minimum standards of transparency, collaboration and participation which the Obama administration recognized in its 2009 memorandum about scientific integrity.[37]

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[32] *Ibid.*, p. 3.
[33] Letter from Jack Snyder, Styrene Information and Research Center, to Linda Birnbaum, Director of NTP, 22 Oct 2009; available at http://ntp.niehs.nih.gov/ntp/roc/twelfth/2009/Styrene/SIRC20091022.pdf.
[34] Questions 5 and 6, letter from John Shadegg and Rick Boucher, Congressmen, to Linda Birnbaum, Director of NTP, 22 Oct 2010.
[35] Question 5, letter John Shadegg and Rick Boucher, Congressmen, to Linda Birnbaum, Director of NTP, 22 Oct 2010.
[36] Reply to Question 6, letter to The Honorable John Shadegg from Linda Birnbaum, Director of NTP, 20 Dec 2010.
[37] *Memorandum on Scientific Integrity*, Administration of Barack. H. Obama, 9 Mar 2009; available at http://regs.dot.gov/requirements/DCPD-200900137.pdf.

The *RoC* process does not employ scientific best practices, relies on outdated approaches and has not adopted recent NAS recommendations.

As previously noted in these comments (see page five), the National Academy of Sciences has specifically outlined some fundamental best scientific practices which are necessary to assure that toxicology-related assessments of chemicals are conducted in an evidence based, objective and scientifically credible manner.

These current best practices are detailed in Chapter seven of the NAS formaldehyde panel's report, which provides a "roadmap" for preparing hazard and risk assessments. In the view of the NAS panel, the roadmap provides the most effective process for developing the most scientifically valid assessments.

The NAS panel observed that successful approaches for reviewing and evaluating scientific data have several common elements, namely:

1. Transparent and explicitly documented methods;
2. Consistent and critical evaluation of all relevant literature;
3. Application of a standardized approach for grading the strength of evidence;
4. Addressing peer review and public comments; and
5. Clear and consistent summative language.[38]

The *Report on Carcinogens'* failure to meet these tests is especially egregious with regard to the first four:

1. Transparent and documented methods

As previously described on pages five and six of these comments, NTP's *RoC* process, while arguably open to the public, is *ad hoc* and lacks the explicit criteria needed to assure a consistent and transparent process.

2. Consistent and critical evaluation.

The NAS report specifically discussed the importance of a including a systematic, tabular analysis ("evidence table") of all the relevant studies as a specific best practice in conducting scientifically valid assessments.

The NAS report states that such tables should "...summarize the details and findings [of the research studies] in evidence tables. Typically, such tables provide a link to the references, details of the study populations and methods, and key findings. They are prepared in a rigorous fashion with quality-assurance measures, such as using multiple abstractors (at least for a sample) and checking all numbers abstracted."

Examining NTP's approach to its review of styrene for the 12th *RoC* is helpful in evaluating NTP's process:

- During the time that styrene was being reviewed by NTP but before the 12th *RoC* was finalized, several letters from various of Members of Congress were sent to NTP regarding NTP's styrene review. One of these letters, authored by then Congressmen John Shadegg (R-AZ) and Rick Boucher (R-VA), asked NTP to provide answers to eleven specific questions about the styrene review. One of these questions requested than NTP provide the Congressmen with a list of studies that supported a link between styrene and cancer and specifically how the data from these studies supported a cancer concern.[39]

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[38] *NAS Formaldehyde Review*, *op. cit.* p. 157.
[39] Question 7, letter from John Shadegg and Rick Boucher, Members of Congress, to Linda Birnbaum, Director of NTP, 22 Oct 2010.

- NTP's reply to this letter did not provide the requested analysis. Instead, it referred to NTP's preliminary Styrene Background Document that "includes more than 500 studies." NTP further stated that the analysis of the studies was "complex," implying that it was not feasible for NTP to provide the requested study-by-study analysis.[40] Additionally, the published Styrene Substance Profile in 12th *RoC* does not include a table of this nature.[41]

This is just one example of how the process NTP used to prepare the *RoC* falls considerably short of this specific best practice as recommended by NAS.

3. Standardized approach to grading evidence.

The NAS panel identified a weight-of-the-evidence approach as a vital component of any standardized approach to evaluating scientific evidence so that the evaluation results in a balanced toxicity assessment.[42] This approach requires the use all the relevant data to develop the most plausible hypothesis regarding potential human toxicity.

In contrast, for the *RoC*, NTP uses a strength-of-the-evidence approach for its assessments. Such assessments differ from a weight-of-the-evidence review in that their conclusions are based primarily on data which supports an adverse effect ("positive data"). Even if there is a substantial body of data which fails to support an adverse effect ("negative data"), NTP typically does not use this data to as a counter-weight to the positive data. NTP may, as they often state, "consider" the negative data, but they do not "use" it.

This interpretation of the *RoC* process is supported by a number of examples, three of which follow:

- During a public 2010 NTP Board of Scientific Counselor's meeting, Dr. Gloria Jahnke of NTP presented and explained the NTP draft profile for glass wool fibers.

  Following this presentation, Dr. Mitzi Nagarkatti of the University of South Carolina School of Medicine (a member of the BSC panel), asked Dr. Jahnke: "I'm just wondering whether there were not studies on other animals such as mice, or they were done and found not to be carcinogenic."

  Dr. Jahnke replied: "The inhalation study of monkeys was negative. So, I'm not recording negative data here; I am recording data that supports our call. So that's why you didn't see it."[43]

- During a public 2009 NTP Board of Scientific Counselor's meeting regarding styrene and several other chemicals which were subsequently listed in the 12th *RoC*, a senior NTP official stated that *RoC* reviews are based on a "strength of the evidence" approach.[44]

- In a summary of a paper that reviews NTP's listing of styrene in the 12th *RoC* and is currently "In press" in the journal *Human and Ecological Risk Assessment,* the authors conclude:

  > "The NTP classification of styrene as 'reasonably anticipated to be a human carcinogen' based on 'limited' evidence of carcinogenicity in humans, 'sufficient' evidence in animals, and supporting mechanistic data is not scientifically supported, given that the available data do not meet these criteria. Styrene should not have been listed as 'reasonably anticipated to be a human carcinogen' in the NTP's 12th *Report on Carcinogens.*"[45]

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[40] Reply to Question 7, letter to The Honorable John Shadegg from Linda Birnbaum, Director of NTP, 20 Dec 2010.
[41] *12th Report on Carcinogens, Styrene*, pp. 383-391, 2011; available at http://ntp.niehs.nih.gov/ntp/roc/twelfth/roc12.pdf.
[42] *Ibid.*, pp. 151-166.
[43] NTP Board of Scientific Counselors Meeting, June 21, 2010. The discussion referred to can be found at 12:30 minutes of the recording that is available at www.box.net/shared/static/sxqzg12pkr.mp3.
[44] "Peer Review of Draft Substance Profiles for the 12th *Report on Carcinogens*," slide 6 of presentation by Mary S. Wolfe of NTP to the NTP Board of Scientific Counselors Meeting, 24 Feb 2009, http://ntp.niehs.nih.gov/files/Wolfe20090224.pdf.
[45] Goodman, J.E., Rhomberg, L., "Why Styrene Should Not Be Classified as a Human Carcinogen And Does Not Belong in the NTP's 12th *Report on Carcinogens*," *Daily Environment Report*, BNA, 12 Mar 2012; available at http://www.gradientcorp.com/alerts/pdf/Styrene.pdf.

4. Addressing peer review and public comments.

The NAS Panel's "New IRIS assessment process" includes seven specific steps; step five of this new process is described as "Revise Assessment: Address peer review and public comments; prepare response to comments document."[46]

Although external public comment is solicited as an element of NTP's *RoC* process, NTP has stated, **as a matter of policy**, it will not offer any written response to such inputs for future *RoC* reviews.[47] This is in direct contradiction to the best practices articulated by the NAS Panel; this also minimizes the existence of differing scientific viewpoints. Several additional examples of NTP's failure to consider public and peer review comments evident from the styrene review are outlined below:

- Dr. Elizabeth Delzell, the author of a study that was inappropriately used to support NTP's classification of styrene in the 12th *RoC*, wrote a letter to NTP in which Dr. Delzell complained that NTP applied a novel statistical manipulation to her peer reviewed published data to change the result of the study and to incorrectly suggest a cancer concern for styrene, and that NTP had also improperly interpreted other studies.[48]

  In the same exchange of letters between Members of Congress[49] and NTP referred to on page eleven of these comments, NTP was asked about this situation. NTP first responded that it was unaware of Dr. Delzell's letter, even though it had long been posted to NTP's *RoC* docket; when made aware of Dr. Delzell's letter, NTP responded that it would be addressed at the completion of the *RoC* review,[50] well after its consideration could have any impact on the outcome of the *RoC* review.

- NTP did provide a response to certain issues raised by the public (including Dr. Delzell's questions), at the same time the final *RoC* was released, on June 10, 2011.[51] However NTP's response, which is simply "too little, too late," is critically flawed in two ways:

  1. NTP's response to comments came well after any opportunity for them to have any influence, if justified, on the outcome of the *RoC* review.
  2. NTP failed to respond at all to many additional public comments, as a matter of policy.[52]

  Each of these flaws is contrary to the best practices outlined in the OMB Bulletin on Peer Review and the NAS Panel's recommendations.

- In the same exchange of letters referred to earlier, NTP was asked more generally about how NTP would respond to scientific input received as part of the public comment process relating to the 12th *RoC*. NTP's response was similar to their response to Dr. Delzell, except that NTP went on to add that the various review groups were "provided access" to public comments "prior to their meetings"[53] related to the 12th *RoC* process.

  However, simply making information "available" to reviewers by posting it to a publicly-available docket or via some other mechanism is inconsistent with best practices. Such reviewers are often volunteers with limited time availability, and it is the role of review's sponsor to make this process efficient and to bring potentially conflicting areas of data interpretation to the attention of reviewers.

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[46] *NAS Formaldehyde Review, op. cit.* p. 154.
[47] NTP Board of Scientific Counselors Meeting, 15 Dec 2011, statement of Dr. John Bucher. The statement referred to can be found at 6:15 minutes of the recording that is available at https://www.box.com/shared/static/ea274f5a6547994936ac.wma.
[48] Letter from Dr. E. Delzell, University of Alabama to Dr. B. Shane, NTP, .5 Feb 2009; available at http://ntp.niehs.nih.gov/files/20090205Delzell.pdf.
[49] Question 8 in letter from John Shadegg and Rick Boucher, Members of Congress, to Linda Birnbaum, Director of NTP, 22 Oct 2010.
[50] Response to Question 8 in letter to The Honorable John Shadegg from Linda Birnbaum, Director of NTP, 20 Dec 2010.
[51] *NTP Response to Issues Raised in the Public Comments for Candidate Substances for the 12th Report on Carcinogens*, National Toxicology Program, 50 pages, 2011; available at http://ntp.niehs.nih.gov/ntp/roc/twelfth/2011/ResponsePublicComments2011.pdf.
[52] *Ibid.*, p. 1.
[53] Response to Question 10 in letter to The Honorable John Shadegg from Linda Birnbaum, Director of NTP, 20 Dec 2010.

Review

In summary, NTP's process for the *RoC* fails four of the National Academy of Sciences Panel's for quality hazard assessments:

- NTP's data evaluation methods are not well documented and are not employed consistently or transparently.
- From the early stages of a review, all but the data supporting a cancer concern are largely ignored.
- There is no standardized approach for grading scientific evidence.
- NTP's policy going forward is to NOT provide comments on public input and NTP "considers" input from the public but seldom actually uses it.

Oversight of the *RoC* by the Congress is needed now.

In creating the *Report on Carcinogens,* the U.S. Congress sought to identify those substances that are "known" or "reasonably anticipated to be" human carcinogens. The statutory language is brief.

Within the scientific context of carcinogen classification, the statutory phrase "reasonably anticipated to be a human carcinogen" is neither plain nor clear, but the Joint House-Senate Comparative Summary provides guidance.

> "...the phrase 'suspected carcinogens' [was replaced] with 'substances...reasonably anticipated to be carcinogens', in order to make it absolutely clear in the statute that there must be reasonable ground for designating a substance as a putative carcinogen."[54]

The final legislative language was a clear departure from earlier proposals that would have expansively listed substances as "suspect" carcinogens based on much looser criteria, such as "sound theoretical grounds."[55]

NTP has strayed from its legislative mandate by interpreting "reasonably anticipated" to mean suspect or theoretical carcinogens. This dilution of the basic evaluation criteria has led to excessive hazard identifications not intended by Congress.

NTP updated its *RoC* process in January 2012.[56] The changes made by NTP have weakened its process for reviewing scientific data even further by:

- Removing the long-standing authority of the Board of Scientific Counselors to peer review NTP substance assessments;
- Removing NTP's responsibility to respond at any time to public comments;
- Making the way in which peer review will be conducted *ad hoc* and entirely within the discretion of the authors of the assessment; and
- Effectively removing the Secretary of Health and Human Services from supervising NTP's *RoC* assessments before they are made public on the Internet.

In addition, in today's difficult economic climate, Congressional oversight could result in a substantial savings for the Federal budget. Congress may want to consider whether or not the *Report on Carcinogens* is redundant and should either be combined with other assessment functions or possibly sunset.

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[54] Joint House-Senate Comparative Summary and Explanation of Title II of H.R. 12460 and H.R. 12347, as Reported by the Committee on Interstate and Foreign Commerce, the Senate Bill, S. 2450, and the House Amendment in the Nature of a Substitute. 124 Congressional Record H38657 (1978) (statement of Rep. Rogers).

[55] 124 Congressional Record H34938 (1978) (statement of Rep. Rogers).

[56] *Process for Preparation of the Report on Carcinogens,* 11 Jan 2012; available at http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.

This idea is supported by the fact that there is a great deal of redundancy among the hazard and risk assessment activities of the Federal government as applicd to chemicals.

- When the *Report on Carcinogens* was first authorized in 1978, it was unique in its functions; however, othcr, more thorough, hazard assessment programs have outstripped it in terms of quality and usefulness.
- At the present time, however, seven different Federal agencies, including NTP, perform hazard and/or assessments on chemicals, including two other agencies within HHS alone – FDA and ATSDR – that overlap NTP's mission related to the *Report on Carcinogens*.
- Since 2011, just for the chemical styrene, four reviews have recently been completed or are currently underway, namely:
  - 2011 – National Toxicology Program's *Report on Carcinogens*.
  - 2011 – Agency for Toxic Substances and Disease Registry's Toxicological Profile.
  - 2012 – United States Environmental Protection Agency's IRIS Assessment.
  - 2012 – EPA's office of Chemical Safcty and Pollution Prevention Review – announced, but start date is uncertain.

Summary

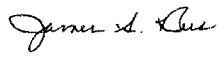
As demonstrated in the preceding pages of this testimony, the current *RoC* process falls well short of producing evidence-based listing decisions. Simply stated, the current process for the *Report on Carcinogens*:

- Lacks explicit criteria needed to assure a consistent and transparent assessment process.
- Does not meet even minimum standards of peer review and ignores nearly all public comments.
- Fails to use many current scientific best practices

Conclusions

I urge Congress and these Committees to actively oversee a thorough assessment of the *RoC* – ideally through an NAS review – to ensure that any future *RoC* listings are evidence-based, provide accurate public health information and reflect the highest scientific standards in its processes, and to begin to determine the *RoC's* fundamental relcvancy going forward. This will increase the public's and industry's confidence in the *RoC's* listings and their application to science-informed decision-making.

Respectfully submitted,



James S. Bus, PhD, DABT, ATS
Director of External Technology, Toxicology and Environmental Research and Consulting
The Dow Chemical Company

Chairwoman ELLMERS [presiding]. Thank you, Dr. Bus.

I would now like to introduce Dr. Grimsley for five minutes. Thank you.

TESTIMONY OF DR. L. FAYE GRIMSLEY, ASSOCIATE PROFESSOR, TULANE SCHOOL OF PUBLIC HEALTH AND TROPICAL MEDICINE, DEPARTMENT OF GLOBAL ENVIRONMENTAL HEALTH SCIENCES

Dr. GRIMSLEY. Good morning. My name is Faye Grimsley. I am Associate Professor of Global Environmental Sciences, Tulane University. I am currently on special leave as a Yerby Visiting Associate Professor, Department of Environmental Health, Harvard School of Public Health. My testimony today will focus on the process of the NTP Program's RoC, the impact of the Report on Carcinogens on jobs, and why the National Toxicology Program is important.

First of all, the process involves a number of peer reviews first by Expert Panel; second, by Interagency Scientific Review Group; third, the NIEHS/NTP Scientific Review Group; and finally, review by the NTP Board of Scientific Counselors. Comments from the public are solicited during steps one through three of the process. When the Expert Panel meets to review the background documents and NTP Board of Scientific Counselors meets to review draft substance profiles, the public is invited to attend. Closed meetings are held when listing or removal status recommendations are made for selected substances. Although there are a number of closed meetings to discuss and recommend listing status of specific substances, the review process is transparent and open to the public for criticisms and opinions during the review process.

The impact of the NTP RoC process on jobs. We know that according to NIOSH it is well documented that associations between occupational exposures and cancer exists. From an environmental health scientist point of view and an industrial hygienist, the NTP process is a valuable resource of information and is often cited and referred when carcinogenic information is needed. Any chemical substance listed by the RoC will impact the health of workers and the public. The review process should consider what impact this will have on businesses of all sizes. Whenever new regulations or standards are introduced, use of state-of-the-art technologies and practices to protect worker health may be beyond resources of small businesses. Small entities often have limited resources. Agencies charged with health and safety of the public and workers should anticipate and provide assistance and resources to these entities to relieve any additional strain of compliance.

Most health and safety personnel, regardless of company size, would agree that additional requirements are involved when new chemicals are designated as a carcinogen or potential carcinogenic agent, but the benefits of knowing that readily available lists of carcinogenic chemicals relieve some of the burden of identifying one category of toxic substances which workers have a potential for exposures and adverse health effects if needed.

Why the NTP is important to public health: with more and more chemicals being developed and used by society and in the workplace, databases that contain toxicity and health and safety information developed by the NTP process, and others will continue to be used by a number of companies, organizations, and agencies for toxicity assessment and decision making to address public health issues. Development of exposure limits and carcinogenic classifications is even, is a challenge.

When workers and community members are unaware of the potential toxic health hazards in their work environment and communities, this makes them more vulnerable to injury and diseases. It is important to provide them with information and references to assist in anticipating and recognizing hazards and the health effects associated with carcinogens in the workplace and the community. If a chemical or agent lacks toxicological and carcinogenic data, it is difficult to conduct exposure assessment in public health and worker populations, which makes it difficult to respond to affected populations concerns and fears of long-term health effects.

For example, in the aftermath of Hurricane Katrina, the public was very concerned about the copious amounts of mold exposure and potential health effects. The NTP played an instrumental role in gathering knowledge and coordinating potential research questions that could help address the impact of mold and mycotoxin and exposures and health effects.

Potential exposures to chemicals occur in homes and communities. Scientists have the daunting task of combining and assessing data from laboratory studies and information from human population epidemiologic studies to determine a substance's cancer causing ability. Systematic processes are needed to assess toxicity and hazards associated with these chemicals. Given the limitations of oversight sometimes placed on federal agencies, the NTP is uniquely positioned to lead various types of reviews and investigations of chemicals that are of concern across different aspects of public health.

Thank you.

[The prepared statement of Dr. Grimsley follows:]

Testimony of L. Faye Grimsley
Associate Professor, Department of Global Environmental Health Sciences, Tulane University School of Public Health and Tropical Medicine
before
The Subcommittee on Healthcare and Technology Joint Hearing with Committee on Science, Space, & Technology Subcommittee on Investigations & Oversight on
"How the Report on Carcinogens uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"

April 25, 2012

Chairwoman Ellmers, Ranking Member Richmond, Chairman Broun, Ranking Member Tonko, and Members of the Subcommittees, I appreciate your inviting me to testify on "How the Report on Carcinogens uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs." My name is Faye Grimsley, Associate Professor of Global Environmental Health Sciences, Tulane University School of Public Health and Tropical Medicine. I am on special leave from Tulane this semester and currently appointed as Yerby Visiting Associate Professor, Department of Environmental Health, Harvard School of Public Health.

My testimony today will focus on the following:

1) The overall process of the National Toxicology Program's Report on Carcinogens
2) The impact of the Report on Carcinogens on Jobs
3) Why the National Toxicology Program is Important to Public Health

Process of the NTP's Report on Carcinogens

The Report on Carcinogens (RoC) is prepared by the National Toxicology Program Director, and then submitted through the Secretary of Health and Human Services (HHS) to Congress and public every 2 years. The Report on Carcinogen Process involves 4 major steps: 1) Nomination and Selection of Proposed Substances, 2) Scientific Review of Selected Substances, 3) Preparation of Draft Specific Substance Profiles for Peer Review, and 4) Preparation and Release Draft Report on Carcinogens. The process involves a number of peer reviews first by Expert Panel, second by Interagency Scientific Review Group, thirdly the NIEHS/NTP Scientific Review Group, and final review by the NTP Board of Scientific Counselors. Comments from the public are solicited during steps 1-3 of the process. When the Expert Panel meets to review background documents and NTP Board of Scientific Counselors meets to review draft substance

profiles the public is invited to attend. Closed meetings are held when listing or removal status recommendations are made for selected substances. Although there are a number of closed meetings to discuss and recommend listing status of specific substances, the review process is transparent and open to the public for criticisms and opinions during the review process.

The 12th RoC, the latest edition, was published on June 10, 2011. The 13th RoC is under development. For each listed substance, the RoC contains a substance profile, which provides information on: 1) Cancer studies that support the listing—including those in humans, animals, and on possible mechanisms of action; 2) Potential sources of exposure to humans; and 3) Current Federal regulations to limit exposures.

NTP and Other Carcinogen Classifications and Reports: There are several other agencies, programs, and organizations that test and list agents based on carcinogenicity. Agents are classified/categorized using a criteria based on evidence of carcinogenicity. The NTP list chemicals in two categories, Known to Be Human Carcinogen or Reasonably Anticipated to be Human Carcinogen. The Twelfth Report on Carcinogens include 54 profiles for substances listed as known to be human carcinogens and 186 profiles for substances listed as reasonably anticipated to be human carcinogen. NTP categories are similar to other published carcinogen listings such as the International Agency for Research on Cancer (IARC), which is the most widely used and referenced system for classifying carcinogens, has 5 categories: Group 1- Carcinogenic to humans; Group 2A- Probably carcinogenic to humans; Group 2B- Possibly carcinogenic to humans; Group 3-Unclassifiable as to carcinogenicity in humans; and Group 4- Probably not carcinogenic to humans. In the past 30 years, the IARC has evaluated the cancer-causing potential of more than 900 likely candidates, placing them into one of the above groups. Only a little over 100 are classified as "carcinogenic to humans."

The EPA uses a rating system similar to that of IARC when describing the cancer-causing potential of a substance and has 5 categories: Group A- Carcinogenic to humans; Group B- Likely to be carcinogenic to humans; Group C- Suggestive evidence of carcinogenic potential; Group D- Inadequate information to assess carcinogenic potential; and Group E- Not likely to be carcinogenic to humans. The American Conference of Governmental Industrial Hygienist (ACGIH) assigns each chemical or agent to one of the following 5 categories for carcinogenicity: A1 - Confirmed human carcinogen; A2 - Suspected human carcinogen; A3 - Confirmed animal carcinogen with unknown relevance to humans; A4 - Not classifiable as a human carcinogen; and A5 - Not suspected as a human carcinogen.

NTP Description: The National Toxicology Program is an entity within the National Institute of Environmental Health Sciences (NTP). The program's physical offices and laboratories are located in Research Triangle Park, North Carolina. The Program was established in 1978 under the Carter Administration and has undergone transformation to align with changing institutional priorities and public health needs. The program is known and recognized as a national and international authority on testing chemicals and agents which are toxic and may

pose a threat to the health of the public and specific worker populations. The process used for testing is based on applying scientific toxicology principles and is an interagency program with collaborative efforts among various health and regulatory agencies across the United States. Agencies include but not limited to the Centers for Disease Control and Prevention (CDC)/ National Institute for Occupational Safety and Health (NIOSH), and National Center for Toxicological Research (NCTR) of the Food and Drug Administration (FDA). The NTP has four main goals: 1) to coordinate toxicology testing programs with the federal government; 2) to strengthen the science base in toxicology; 3) to develop and validate improved testing methods; and 4) to provide data information to health and regulatory agencies, medical and scientific communities, and the public.

Impact of NTP RoC Process on Jobs

According to NIOSH and published literature, it is well-documented that associations between occupational exposures and cancer exist, it is estimated that approximately 20,000 cancer deaths and 40,000 new cases of cancer each year in the United States are attributable to occupation; additionally, it is estimated that less than 2% of chemicals in commerce have been tested for carcinogenicity.

From an environmental health scientist point of view, the NTP process is a valuable resource of information and is often cited and referred when carcinogenic information is needed. Any chemical substance listed by the RoC will impact the health of workers and the public. The review process should consider what impact this will have on businesses of all sizes. Whenever new regulations or standards are introduced, use of state –of- the art technologies and practices to protect worker health may be beyond resources of small businesses. Small entities often have limited resources. Agencies charged with health safety of the public and workers should anticipate and provide assistance and resources to these entities to relieve any additional strain of compliance. In 2006, small firms with less than 500 employees accounted for 99% of the 26.8 million businesses in the United States.

Most health and safety personnel regardless of company size, would agree that additional requirements are involved when new chemicals are designated as a carcinogen or potential carcinogenic agent, but the benefits of knowing that readily available lists of carcinogenic chemicals relieves some of the burden of identifying one category of toxic substances which workers have a potential for exposures and adverse health effects is needed. According to Cherry, "There is a need to set exposure limits so that there is a balance between the risks that workers are exposed to and the costs of averting these risks."

Why the NTP is Important to Public Health

A concern from workers and communities regarding chemicals and substances which cause or is associated with cancer is still voiced around the world. Keeping workers safe from harmful agents is a daunting and challenging job. Development of exposure limits and carcinogenic classifications is even more challenging. The American Cancer Society reference and list chemicals from the International Agency for Research on Cancer (IARC) and U.S. National Toxicology Program (NTP) and emphasizes that testing and determining if something can cause cancer is difficult. Cancer is caused by a number of environmental factors and exposures from lifestyle (e.g., tobacco use), workplace chemicals, household chemicals, pollution and medical treatments.

With more and more chemicals being developed and used by society and in the workplace, databases that contain toxicity and health and safety information developed by the NTP process and others will continue to be used by a number of companies, organizations, and agencies for toxicity assessment and decision making to address public health issues. Given the thousands of chemicals that need to be tested, and resources allotted, there are limitations to how many chemicals can be tested by carcinogenic agencies, in 1998 the NTP had resources and the capacity to consider and evaluate only 10-20 compounds. Since inception, The NTP has evaluated more than 2,500 substances for adverse health effects related to general toxicity, reproductive and developmental toxicity, genotoxicity, immunotoxicity, neurotoxicity, metabolism, respiratory illnesses, and carcinogenicity. The primary means of research and testing are performed using rodent models in short-term studies for up to thirteen weeks and long-term studies for up to two years.

The NTP is recognized by the American Public Health Association (APHA) as one of the agencies that play a role in protecting the public's health from harmful chemical exposures. The NTP coordinates the toxicological research efforts across 5 agencies (ATSDR, CDC-NCEH, FDA, NIOSH, and NIEHS) within the Department of Health and Human Services (HHS). A chemical safety responsibilities matrix developed by the APHA identifies the NTP as playing a key role in protecting workers and researching chemicals.

When workers and community members are unaware of the potential toxic health hazards in their work environment and communities, this makes them more vulnerable to injury and diseases. It is important to provide them with information and references to assist in anticipating and recognizing hazards and the health effects associated with carcinogens in the workplace and community. If a chemical or agent lacks toxicological and carcinogenic data, it is difficult to conduct exposure assessment in public health and worker populations which makes it difficult to respond to affected populations concerns and fears of long-term health effects

and outcomes. For example, in the aftermath of Hurricane Katrina, the public was very concerned about the copious amounts of mold exposure and potential health effects. The NTP played an instrumental role in gathering knowledge and coordinating potential research questions that could help address the impact of mold and mycotoxin exposures and health effects.

The NTP Process has played a role in in the field of public health specifically in the areas of occupational hygiene and environmental health. One important aspect of protecting workers and the health of communities is conducting public health and exposure assessments to determine the hazard of the chemical and to determine the amount present.

For example, when the ATSDR conduct public health assessments to identify possible harmful exposures and to recommend actions needed to protect public health, toxicological data used to determine potential health effects in these public health assessments is compiled mainly from the ATSDR's toxicological profiles and other compilations of toxicological data including resources such as the U.S. Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS) database, International Agency for Research on Cancer (IARC) Monographs, and National Toxicology Program (NTP), as well as some non-governmental resources and textbooks. According to the ATSDR, public health assessments differ from the more quantitative risk assessments conducted by regulatory agencies, such as EPA. When conducting public health assessments, ATSDR considers the same environmental data as EPA, but focuses more closely on site-specific exposure conditions, specific community health concerns, and any available health outcome data to provide a more qualitative, less theoretical evaluation of possible public health hazards.

When environmental health scientists, industrial hygienists, occupational safety and health professionals, and other public health practitioners conduct an exposure assessment, information is needed to evaluate potential toxicity of chemicals. Information from several agencies and organizations are used as resources for this toxicity evaluation, these include the Occupational Safety and Health Administration (OSHA), American Conference of Governmental Industrial Hygienist (ACGIH), National Institute for Occupational Safety and Health (NIOSH), American Industrial Hygiene Association (AIHA), Environmental Protection Agency (EPA), National Toxicology Program (NTP), International Agency for Research on Cancer (IARC), Material Safety Data Sheets (MSDS), and Agency for Toxic Substance Disease Registry (ATSDR).

In summary, potential exposures from chemicals can occur in workplaces, homes and communities. Scientists have the daunting task of combining and assessing data from laboratory studies and information from human population epidemiologic studies to determine

a substance's cancer causing ability. Systematic processes are needed to assess toxicity and hazards associated with these chemicals. There is a need for more research and testing given the number of chemicals used by individuals on a daily basis. The NTP is one of many organizations, agencies, and programs that are aware of the public's concern related to chemicals that can cause or likely to cause cancer. The NTP report on carcinogen review process uses a scientific approach to gather and synthesize data, to make decisions that is in the best interest of the public's health, and to provide documents and reports that can be used to assist with identifying health hazards and disease prevention. The NTP should continue to solicit feedback and respond to input from interested stakeholders who may be affected by recommendations related to carcinogen classifications. Given the limitations of oversight sometimes placed on federal agencies, the NTP is uniquely positioned to lead various types of reviews and investigations of chemicals that are of concern across different aspects of public health.

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Chairwoman ELLMERS. Thank you, Dr. Grimsley.
I will now introduce Ms. Webster for five minutes. Thank you.

TESTIMONY OF MS. BONNIE WEBSTER,

VICE PRESIDENT,

MONROE INDUSTRIES, INCORPORATED

Ms. WEBSTER. Thank you, Chairman Broun, Chairwoman Ellmers, Ranking Member Tonko and Ranking Member Richmond for the opportunity to testify before you today. My name is Bonnie Webster, and I am the Vice President of Monroe Industries in Avon, New York. My husband, John, is here with me today and together we run the company. We have seven employees but often hire two to three more seasonally to meet demand. We are a cast polymer company and use styrene-based resin to manufacture high-end custom showers and vanity tops.

We are a small operation, but we do go to great lengths to reach the highest level of safety. In 1999, we built a new facility away from residential areas because styrene, like any chemical, has the potential to be harmful when misused. We ensure that every employee uses a respirator and other safety equipment. Unlike larger companies we do not have the ability to employ a full-time occupational safety staff, however, we bring in consultants annually to address OSHA matters and ensure that even with small resources we are compliant and safe.

Our company works hard to lessen the environmental impact of our production. We have created Robal Glass, a product that uses half the amount of resin. Robal Glass uses a bio-based resin and recycled glass for which we have won an EPA Environmental Quality Award. Our products have a life cycle of well over 20 years and are designed to last the duration of the home.

Despite our hard work to be on the cutting edge of the composites industry, we are very concerned that the listing of styrene in the 12th Report on Carcinogens make it very difficult for us to stay in business.

Currently there is only one company that will insure us. Should we be dropped by that company, like other composite companies whose coverage has been terminated by long-term carriers, it will be impossible for us to continue to make an affordable product. Today's mentality when it comes to liability lawsuits is who can we sue next. We cannot afford to be next and remain in business. If the poor science that informed the RoC listing begins to inform the EPA or OSHA regulations, our concerns will only worsen.

Our worries are not unique only to Monroe. Many state air pollution regulatory programs will look at the RoC listing and set styrene ground level exposure limits based on a presumption of carcinogens, and this will make it impossible for composite manufacturers in these states to get or renew operating permits.

In light of the uncertainty presented by the styrene listing in the RoC, we have no plans to expand our production or increase our number of employees. We hope with this economy we will be able to maintain the business that we have now. Compared to many other companies in the cast polymer subset of the composite's in-

dustry, we are in a better position than most because our products are totally customized and therefore, very difficult to import.

The current environment has made it nearly impossible for high-production cast polymer fabricators to compete. Surrounding countries do not have the regulations and additional costs that we have here. Unlike larger composite manufacturers who do not have the luxury, if you can call it that, of moving production offshore, if this trend continues, we will have no choice but to liquidate our companies.

There is a significant environmental benefit to using our engineered composite products over natural stone products and other materials that should be considered. Granite, for example, is mined in South America and often shipped to China to be polished before shipping, being shipped back to the U.S. to be fabricated. The environmental impact of the transportation aspect alone is considerable. The fact that our engineered surfaces are fully manufacturable in the United States, in addition to being partially constituted of recycle components, makes them a very green product.

The RoC has hidden in the shadows pretending only to be harmless input to the public health agencies. It has been largely unsupervised by the Congress, unreachable by the Courts, and not carefully supervised by senior officials in their respective agencies. Yet its actions have every bit as much of an impact as regulations which in contrast are subject to the Administration Procedure Act.

Our industry is asking that Congress reform the way the Federal Government analyzes the risk of chemicals to make it a more transparent, inclusive, and scientific process. Please consider these reforms that will ensure that federal programs like the Report on Carcinogens leads to valuable assessments that help rather than harm American business and the American worker.

Thank you very much for your time.

[The prepared statement of Ms. Webster follows:]

Statement of Bonnie Webster, Monroe Industries

Science and Small Business Joint Hearing on the *Report on Carcinogens*

April 25, 2012

1. Thank you Chairman Broun, Chairwoman Ellmers, Ranking Member Tonko, and Ranking Member Richmond for the opportunity to testify before you today. My name is Bonnie Webster and I am the Vice President of Monroe Industries in Avon, NY. My husband John is here with me today and together we own the company. We have seven employees but often hire 2-3 more seasonally to meet demand. We are a cast polymer company and use styrene-based resin to manufacture high-end custom showers and vanity tops.

2. We are a small operation but we go to great lengths to reach the highest level of safety. In 1999 we built a new facility away from any residential areas. Because styrene, like any chemical, has the potential to be harmful when misused we ensure that every employee uses a respirator and other safety equipment. Unlike larger companies we do not have the ability to employ full-time occupational safety staff. However, we bring in consultants annually to address OSHA matters to ensure that even with small resources we are compliant and safe.

3. Our company works hard to lessen the environmental impact of our production. We have created Robal Glass a product that uses half the amount of resin. Robal Glass uses a bio based resin and recycled glass for which we won an EPA Environmental Quality Award. Our products have a lifecycle of well over 20 years and are designed to last the duration of the home.

4. Despite our hard work to be at the cutting edge of the composites industry we are very concerned that the listing of styrene in the 12th *Report on Carcinogens* could make it very difficult for us to stay in business.

5. Currently there is only one company that will insure us. Should we be dropped by that company, like the many other composites companies whose coverage has been terminated

by their long-time carriers, it will be impossible for us to continue to make an affordable product. Today's mentality when it comes to liability law suits is "Who can I sue next?" We cannot afford to be next and remain in business. We are also very concerned about our worker's compensation insurance, as many composites companies have been under increased scrutiny since the inclusion of styrene in the 12th *RoC*. Some have been threatened to have their coverage revoked. If the poor science that informed the *RoC* listing begins to inform EPA or OSHA regulation our concerns will worsen.

6. Our worries are not unique only to Monroe Industries. Many state air pollution regulatory programs will look at the *RoC* listing and set styrene ground-level exposure limits based on a presumption of carcinogenicity, and this will make it impossible for composite manufacturers in these states to get or renew operating permits. Most composite manufacturers are required under the Clean Air Act to post a public notice every 5 years when they renew their operating permits. In many cases, plant neighbors will find a reference to the *RoC* listing on the Internet and will incorrectly but understandably believe that the permits should not be renewed.

7. In light of the uncertainty presented by the styrene listing in the *RoC* we have no plans to expand our production or increase our number of employees. We hope we will be able to maintain the business that we have now. Compared to many other companies in the cast polymer subset of the composites industry we are in a better position than most because our products are totally customized and, therefore, very difficult to import. The current environment has made in nearly impossible for many high production cast polymer fabricators to compete. Surrounding countries do not have the regulations and additional costs that we have here. Unlike larger composites manufacturers, cast polymer fabricators do not have the luxury, if you can call it that, of moving production offshore. If this trend continues we will have no choice but to liquidate our companies.

8. There is a significant environmental benefit to using our engineered composite products over natural stone products that should be considered. Granite, for example, is mined in South America and, often, shipped to China to be polished before being shipped to the United States for customization. The environmental impact of the transportation aspect of

that alone is considerable. The fact that our engineered surfaces are fully manufacturable in the United States in addition to being partially constituted of recycled components makes them a very green product.

9. The *RoC* has hidden in the shadows, pretending only to be harmless input to public health agencies. It has been largely unsupervised by the Congress, unreachable by the courts, and not even carefully supervised by the senior officials in their respective agencies. Yet, its actions have every bit as much an impact as regulations, which in contrast are subject to the Administrative Procedure Act, are held accountable for responding to public comments, are scrutinized by the Congress, and can be challenged appropriately in Court.

10. Our company, like many in our industry, is a very tight knit entity. I would never want to see any of our employees hurt and if I believed that there was any genuine threat of styrene causing cancer then I would not be here today. The fact is that flawed science has led to a flawed conclusion that has fallen on the backs of small business. The viability of our entire industry is at risk, one that employs over 250,000 people in the United States – the vast majority of which in small businesses.

11. Our industry is asking that Congress reform the way the federal government analyzes the risk of chemicals to make it a more transparent, inclusive, and scientific process. Please consider these reforms that will ensure that federal programs like the *Report on Carcinogens* lead to valuable assessments that help, rather than harm, American business and the American worker.

12. Thank you very much for your time.

Chairwoman ELLMERS. Thank you, Ms. Webster.

I would like to introduce Ms. LaTourelle now for five minutes. Thank you.

TESTIMONY OF MS. ALLY LATOURELLE, ESQUIRE,

VICE PRESIDENT GOVERNMENT AFFAIRS,

BIOAMBER, INCORPORATED

Ms. LATOURELLE. Thank you, Mrs. Chairman. Chairman Broun, Chairwoman Ellmers, Members of the Committee, Ranking Member Tonko, and Ranking Member Richmond, thank you for the invitation to speak today. This is the first time I have been before a committee, so I would like to, if I may, enter my written testimony into the record and summarize those points here for you today.

Chairwoman ELLMERS. Without objection.

Ms. LATOURELLE. Thank you. My name is Ally LaTourelle. I am the Vice President of Government Affairs for a company called Bioamber. We are a renewable chemical company. My work with Bioamber includes renewable chemical manufacturing project finance, federal, State, and local financial incentive analysis, renewable chemical and economic policy development, and I currently head global sustainability. It is a start-up.

I am also a former investment advisor, both for private individuals on private companies in the clean tech sector and for public companies. So my perspective is a little bit different than the other members of the panel.

Bioamber, just to start, is a next-generation chemicals company. We have a proven proprietary process that uses economically viable, sustainable feedstocks rather than oil and coal and natural gas to produce platform chemicals. These chemicals are used for a diverse range of applications.

For example, we produce a non-toxic, bio-based succinic acid. This is used in many applications from food additives to fabrics, and we do so at lower cost.

We have also developed bio-based butanediol, a technology that will be deployed at our first commercial scale facility in Ontario, Canada, along with the succinic acid. Now, in combination these two chemicals put together make what is called a modified polybutylene succinic, and this is a resin similar to what we just heard about.

This—I did bring some samples here I would just like to show so that we can get a practical feel for what we produce. This is the modified PBS as it comes out. It goes into extrusion machines. This type of plastic is stamped into very familiar objects, coffee cup lids, and our technology is special because it gives heat resistance. Not only is it biodegradable within 90 days, but you also have heat resistance, which is a very difficult property to engineer.

Respectfully, I would like to present a few different reactions to the issues of concern before the Committee today, from the perspective of a renewable chemistry company. Like Dr. Bus, I, too, question the fundamental relevancy of the RoC to small business, but from a different perspective, and my next statement is in no way challenging the science or the importance of the RoC itself. We find

ongoing reporting of carcinogens has a negligible impact on competition in the face of industry-wide 21st century business concerns.

The ad hoc nature of global chemical regulations is not detrimental to our small business, and it is not a shock. I would like to just remind you that the World Health Organization in its International Agency for Research on Cancer moved styrene, for example, from not classifiable to possibly carcinogen to humans in 1987. So the impacts of this information should have already come to the floor. They reviewed that assessment in 1994 and in 2002, and came up with the same conclusions. The U.S. Agency for Toxic Substances and Disease Registry pointed to that report in 2007, and the EPA has regulated styrene already in drinking water where it has been found.

To be fair, Canada has found styrene to be non-toxic. However, I would like to point out that this in no way, even though we make a direct substitution for styrene, has in no way impacted our decision to commercialize, to get to commercial scale in Canada. Last year in California, for example, a total ban of styrene was considered.

These regulations are essentially ongoing discussions, but they really take a backseat to the larger concerns of the 21st century. We have cost concerns related to energy supply price increases. We have shipping and supply chain costs mentioned by Ms. Webster associated with radical swings in the price of oil. We have increased demands for transparency, and the chemical industry is bringing science and innovation to design products that avoid these concerns, as well as toxicity. Our chemical process design takes 51 percent less energy to run than the incumbent petrochemical players. That means there is a 205 percent energy efficiency that occurs pound for pound. In our adipic acid technology, for example, it takes 205 percent more energy to create a petrochemical adipic acid.

Chairman BROUN. Ms. LaTourelle, if you would, your time has expired, so if you would wrap up quickly, I would appreciate it.

Ms. LATOURELLE. Oh, yes. I am sorry.

Chairman BROUN. We would appreciate it.

Ms. LATOURELLE. My apologies.

Just to wrap up, I would also like to suggest that regulations themselves lead to innovation. If we cannot identify the problems and if we do not have access to information, we cannot find the solutions. Large chemical partners also support a shift in this industry to safer alternatives. Familiar names from our strategic and innovation partner list are Dupont, Cargill, Lanxess, Mitsubishi Chemical, Mistui.

I would also like to point out that retail regulation and consumer drive is a bigger concern to us than any of the other things mentioned.

In conclusion, the environmental concerns, the 21st century concerns are quantifiable. Something like the RoC really takes a backseat in terms of small business to competitive answers that are readily available.

Thank you for your time.

[The prepared statement of Ms. LaTourelle follows:]

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Chairman Paul Broun, M.D.,
House Committee on Science, Space and Technology
Subcommittee on Investigations and Oversight
2321 Rayburn House Office Building
Washington, DC 20515

Chairwoman Renee Ellmers
House Committee on Small Business
Subcommittee on Healthcare and Technology
2361 Rayburn House Office Building
Washington, DC 20515

April 24, 2012

Joint Hearing: How the Report on Carcinogens Uses Science to Meet its Statutory Obligations and its Impact on Small Business Jobs.

Chairman Broun, Chairwoman Ellmers, and other members of the Committee,

Thank you for the invitation to speak today. This is the first time I've been before the Committee. With your permission, I will submit my written testimony and then briefly summarize it for you.

My name is Ally LaTourelle. I am the Vice President of Government Affairs for BioAmber, a renewable chemical company. My work with BioAmber includes renewable chemical manufacturing project finance; federal, state and local financial incentive analysis; and renewable chemical and economic policy development. In addition, I manage BioAmber's global sustainability initiatives.

BioAmber is a next generation chemicals company. BioAmber's proven, proprietary process uses economically-viable, sustainable feedstocks to produce platform chemicals for a diverse range of chemical applications.

For example, we produce a non-toxic, biobased succinic acid that is used in many applications from food additives to fabrics, and we can do so at lower cost than succinic acid produced using traditional methods. In addition to biobased succinic acid, we have developed biobased butanediol (BDO) technology that will be deployed at our first commercial scale facility in Ontario, Canada.

In combination, these two chemicals make a polymer, or plastic, modified polybutalene succinate (mPBS) that is used in numerous applications, including building materials. The technology enables a 100% biobased route to the polymer, making this non-toxic, biobased alternative to petrochemicals "drop in" ready to existing manufacturing equipment. This polymer is high temperature heat resistant, yet also biodegradable within 90 days.

Respectfully, I would like to present a few different reactions to the issues of concern before the committee today.

THE REPORT ON CARCINOGENS (ROC) PROVIDES A LOGICAL BASIS FOR SOLUTIONS BASED INNOVATION

The Report on Carcinogens (ROC) that styrene is "reasonably anticipated" to be carcinogenic is not

detrimental to our small business, nor was it a shock. While ongoing reporting is important to the consumer, those industry stakeholders most concerned with sustainability have already responded to issues in these reports using innovative solutions.

Possible toxicity of styrene has been reported since the mid 1980's when the World Health Organization's International Agency for Research on Cancer (IARC) moved Styrene from "not classifiable" to "possibly carcinogenic to humans" in 1987.[1] It considered styrene again and found the same conclusion in 1994 and 2002. Styrene as a "possible human carcinogen" was also identified in 2007 by the Agency for Toxic Substances and Disease Registry at the US Department of Health and Human Services in a toxicology facts sheet.[2] The US EPA already regulates styrene after detection of the chemical in drinking water which leached into groundwater supply from spills and products that biodegraded in landfills. And where Health Canada concluded that styrene is "non-toxic" and therefore not regulated by Environment Canada and Public Works, California has considered a total ban on polystyrene containers as recently as last year.

Clearly, perceived risk of a direct competitor's product will drive business our way, since our mPBS is a direct replacement for styrene in some applications. However, we know that consumers are already on alert and this update on the US Report on Carcinogens will not guarantee our success. All chemical companies face the larger concerns of the 21st Century, and that is where our business acumen is focused. We are focused on cost concerns related to energy supply price increases, shipping and supply chain costs associated with radical swings in the price of oil, and increased demands for transparency from a more health and environmentally conscious consumer base.

These larger drivers have been the real boon for our small business. Our renewable chemical production design is 51% less energy consumptive than incumbent processes. Our adipic acid process provides an 84% emission reduction compared to petro-derived adipic acid. Our biobased succinic acid is non-toxic and non-hazardous. These benefits amount to real cost reductions that garner competitive advantage in the market place.

All that said, there is a definitive need for the Report on Carcinogens (ROC) and reports like it because they spur innovative solutions. This has clearly been the case with the green chemistry industry. In addition, these reports provide critical information for businesses to determine their strategic path while giving consumers tools to make more informed choices.

Separating the two issues – reporting for informational purposes and market response – is critical. From my perspective, the market is sorting this business out in the right way. It is putting downward pressure on the businesses that are bringing less value to the market (suspected harmful products) and responding with higher costs to insure them. And, in turn, it is responding favorably to the businesses that are implementing innovation spurred in part by readily available data of reports like the ROC. This is exactly what we want, especially where human health is concerned. We want businesses to respond as soon as the health risk is identified, or fail.

Business owners must learn to take the health of workers and product safety more seriously. If they are currently feeling economic pain, in my professional opinion, at least in this particular case, it is deserved. This is the right market response with regard to health risks.

As long as the Federal Government ignores the Toxic Chemical Safety Act reform and allows chemical companies to put products on the market without proving that the chemicals used to make them are safe, reports like the ROC are critical. A higher standard of care must be taken by businesses with regard to chemical products. After bankruptcy, a business owner or corporation can start again. After cancer, a consumer or worker might not be so lucky.

AD HOC REGULATION LEADS TO SUPPLY CHAIN RISKS AND CONSUMER DEMANDS FROM THE INDUSTRY FOR TRANSPARENCY; SAFER ALTERNATIVES MITIGATE THIS RISK

Irregularity of regulatory regimes is part and parcel of our business today. As a small chemical and

[1] http://www.styrene.org/regulatory/intl_regulation.html
[2] ATDSR Styrene CAS# 1000-42-5

manufacturing company, we are connected to a global supply chain and manage the irregularity of regulatory regimes as well as ad-hoc chemical reporting across the globe.

Sony learned a hard lesson in the late 90's when shipping Playstations for distribution across Europe during the holiday buying season. A component of their product contained a material that was banned in the specific country where the distribution was to originate. They were prevented from distributing their product to the rest of Europe and lost hundreds of millions of dollars. In response to this 21st Century business challenge, where component parts are shipped globally for assembly in one country before going to another, our customers and partners are looking to avoid disruptions altogether in their supply chains.

We are innovating applications with less toxic materials in order to withstand this increasing transparency and meet the demand for safer, environmentally favorable alternatives. Our own mPBS can be used as a non-toxic, non-off-gassing replacement binder in construction materials. This advantage captures a segment of a green building materials market that is expected to grow from $7 billion in 2009 to $230 billion by 2030. This amounts to an annualized growth rate in the sector of 18% per year.[3]

LARGE COMMERICAL PARTNERS SUPPORT A SHIFT IN THIS INDUSTRY TO SAFER ALTERNATIVES

The growing market demand for lower cost alternatives and technology readiness at commercial scale in biobased chemicals has many forward thinking incumbent chemicals businesses looking to biobased chemical production for growth in their portfolios. We have enjoyed an increase in valuation as a privately held company, our workforce has increased by 450%, and many of our strategic and innovation partners are familiar names: Dupont, Cargill, Lanxess, Mitsubishi Chemical, Mistui. Lanxess, for example, has strategically partnered with us to produce non-phthalate esthers (as in PVC piping). I believe that we are not an anomaly in this growing industry, but that we are at the beginning of a dramatic shift toward biobased alternatives.

We are providing our partners with new low cost processes, innovative high performance materials and competitive pricing. This amounts to market entry and economic sustainability. But we also provide them with an answer to the larger 21st Century concerns regarding energy consumption, environmental degradation and toxicity. From my perspective, these partners are making not the 'right' choice but the sound business decision. They are focused on long term risk mitigation and increased value creation in a changing business landscape.

They are not fighting against the current changes. Our partners are remaining competitive by accepting the shift in the fundamentals of business and customer preferences. They have moved on to innovating new solutions as they should in a market-based society. An argument can be made that decreasing information regarding toxicity and other potential risks stifles innovation and science. If the problem is ignored, a solution will not emerge.

"RETAIL REGULATION" DRIVEN BY CONSUMER DEMAND PICKS UP WHERE GOVERNMENT LEAVES OFF – CONSUMERS ARE THE ULTIMATE REGULATORS

The rising tide of consumer demand for products with a better environmental and toxicological profile has far surpassed "trend" status. In 2009 JD Ford & Company Investment Bankers reported that the $600 billion global health and wellness industry has held up well in the face of the global economic downturn. Health & wellness' share of the food, beverage and healthcare market has grown significantly and is expected to continue to do so. The American Sustainable Business Council, a growing coalition

[3] The Economic Benefits of a Green Chemical Industry in the United States. Renewing Manufacturing Jobs While Protecting Health and the Environment. James Heintz and Robert Pollin, Political Economy Research Institute, Univ. Of Mass; Blue Green Alliance.

over 120,000 business and more than 200,000 business leaders, reports that in an independent poll released in February 2012 by Lake Research, 80% of small business owners were in favor of disclosure and regulation of toxic substances that are used in products.

In 2010, DuPont surveyed more than 800 customers globally in industries spanning food and agriculture, transportation, chemicals and manufacturing, plastics, packaging and electronics to better understand if there is long-term demand for sustainable products. 89% of the customers surveyed said that delivering products with environmental benefits is a long-term market opportunity. And 95% of those surveyed reported customer demand as a key driver for developing products with an enhanced environmental footprint. "The results of this survey reinforce our belief that there is broad market demand for products with an enhanced environmental profile and that demand is coming from customers," DuPont Vice President and Chief Sustainability Officer Linda J. Fisher told participants at the New York Stock Exchange and Yale Green Summit in 2010. She continued, "This trend is here to stay and offers significant growth opportunities for companies which can deliver sustainable solutions. DuPont, with its market-driven science and broad global industry reach, can help address this growing trend."

ENERGY AND ENVIRONMENTAL COST CONCERNS TRUMP THE ONGOING REPORTING OF THE ROC FOR PETROCHEMICALS

Ninety-seven percent of all products -- building materials, fabrics, food service ware, computer parts, auto parts -- almost everything we use in life is made from chemicals. The U.S. chemical industry is the largest industry in the world and, as reported by the Berkeley National Laboratory, consumes approximately 20% of the total industrial energy in the US.[4] It is one of America's oldest industries responsible for 11% of US industrial production with a value estimated at $720B per year. However, oil producing countries increasingly build the manufacturing value chain in proximity to their petrochemical feedstocks. This has reduced US chemical jobs by 12% since 2002.[5] While some petrochemical industries attack the science behind the ROC and other reports, others are starting to avoid toxicity altogether by collaborating on alternatives and problem solve the larger issues – like energy costs. Increases in energy prices mean increases in the cost to produce materials and lower margins.

We currently produce succinic acid at a 3,000 metric ton capacity or demonstration scale and will break ground on a commercial plant with capacity for 35,000 Metric Tons on May 16th. Biobased succinic acid is cost competitive at commercial scale even with oil prices dropping to $50 per barrel.

Increased regulation of emissions in the chemical and materials industry is a driver to our small business. While incumbent players are required, for example, to employ expensive abatement technology in the production of the chemical adipic acid – a main ingredient of Nylon - because of carcinogenic N0x emissions, our biobased adipic acid technology will reduce emissions by 84.5%. In addition, by comparison, this technology uses 51.2% less energy and no fossil resources as feedstocks. This lack of correlation to the price of oil creates the competitive cost to market entry.

Many more changes in business fundamentals are to come. We are actively preparing for the following and believe these actions reduce risks and costs, and increase value across a full spectrum of current challenges:

Supply Chain scrutiny and demands for increasing transparency across suppliers.
An expectation of analysis of water stress risk.
Energy supply price volatility.
Transportation price volatility.

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[4] *Energy Use and Energy Intensity of the US Chemical Industry;* Ernst Worrell, Dian Phylipsen, Dan Einstein, and Nathan Martin, Energy Analysis Department, Environmental Energy Technologies Division, Ernest Orlando Lawrence Berkeley National Laboratory, University of California, Calfironia 94720, April 2000.

[5] "Biobased Chemicals and Products, A New Driver of US Economic Development and Green Jobs," BIO, March 2010.

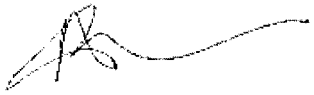
BioAmber
CHEMISTRY

Climate change risk planning.
Life Cycle Analysis requirements from customers.
Environmental Product Declaration development in multiple applications.
Meeting emergent business standards like the Carbon Reporting Initiative.

Our innovations underscore both the critical need and consumer support for reports like the Report on Carcinogens. With this information, we can transition away from the use of toxic chemicals and pave the way to a better, safer future. We think this makes long-term economic sense.

Thank you for your time and attention and for this opportunity to bring to you the small business perspective of a renewable chemical company.

Sincerely,



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Chairman BROUN. Thank you, Ms. LaTourelle.
Mr. Barker, you are recognized for five minutes.

STATEMENT OF MR. JOHN E. BARKER, CORPORATE MANAGER, ENVIRONMENTAL AFFAIRS, SAFETY AND LOSS PREVENTION, STRONGWELL CORPORATION

Mr. BARKER. Thank you, Chairman Broun, Chairwoman Ellmers, Ranking Member Tonko, and Ranking Member Richmond, for the opportunity to testify before you today. My name is John Barker. I am Corporate Manager of Environmental Affairs at Strongwell Corporation. And I would also like to introduce my colleague, David Ring, who is with us from Strongwell.

Strongwell employs 465 people with facilities in Bristol, Virginia; Abingdon, Virginia; and Chatfield, Minnesota. Our primary raw materials are styrene, resins, and reinforcements, which we use to make many products, including ballistic panels, having shipped over 150,000 to protect American troops and soldiers in Iraq and Afghanistan. We also manufacture bridge beams, platforms being used increasingly to reduce the lifecycle cost and improve sustainability of infrastructure.

Like any chemical such as styrene, it is critical to follow the safety guidelines. At Strongwell, we pride ourselves in our proactive safety programs. Each facility has a Plant Safety Committee and an excellent safety record. Our employees are trained periodically on each chemical that we use, with all employees being retrained at least annually. We ensure that all employees have both the protective equipment and knowledge they need to safely use the chemicals that are a part of our production.

By nearly every count, when following the proper safety guidelines, styrene is a safe chemical. Many studies from both the private and public sectors alike speak to the absence of a threat of cancer when using styrene. And regardless, the National Toxicology Program listed styrene as a reasonably anticipated carcinogen in the 12th Report on Carcinogens. The listing of styrene in the RoC is of significant concern to Strongwell and the composites industry in general. For one thing, the idea of "reasonably anticipated" has caused great confusion among our employees, their families, and members of our communities.

We have taken a very proactive approach of informing employees about the ruling and other studies about styrene toxicity. We have gone over this matter in depth with city councils of both Bristol, Virginia, and Bristol, Tennessee, and have taken community leaders on tours of our facilities to fully explain our safety practices. We have spent millions of dollars on emissions reductions and have pushed toward direct injection molding, which lessens the exposure of workers to styrene.

And Dr. Bus has explained the scientific problems behind the listing of styrene in the Report on Carcinogens. Let me tell you about some of the problems it is causing to business. As a company, Strongwell has gone to great lengths for many years to have a strong and positive relationship with our community. For example,

we assist the local fire department in their annual training and we provide assistance in maintaining their equipment. Lately, we have been receiving anonymous phone calls saying things like, "you do know that styrene causes cancer, don't you?" This tells us that people believe the flawed science used in the assessment of styrene and it makes it difficult to maintain an open and fair relationship with our community.

A Google search of styrene toxic tort returns a list of many law firms that now claim to specialize in styrene injury suits. Styrene was not a business opportunity for these law firms a year ago. Because we self-insure, styrene—or Strongwell has had to place a significant amount of money into reserves to protect ourselves against potential liability lawsuits. The money that we must reserve for liability purposes could be used for investment and job creation and expansion if it weren't for this listing.

As I mentioned previously, Strongwell manufactures many important products and these are just a small example of the thousands of applications of composite products. Styrene is an essential chemical component of this manufacturing for which there is no reasonable replacement. Resins based on other chemicals do exist but they are usually far more expensive and not nearly as well understood in terms of health effects on humans.

Likewise, we are very concerned about the potential regulatory burden that could be placed on our operations should the RoC listing form the basis of regulatory changes. Changes to the regulations already in effect by OSHA and EPA could cause the cost of compliance to increase substantially. Further, focusing on a matter that should be of no concern will make it harder for employees to get full attention to the safety issues that are important.

Because there is no legitimate substitute for styrene and because the cost of liability and compliance could increase astronomically, there is a concern that the federal treatment of styrene could draft composites jobs offshore. And by the way, this is not just a concern for Strongwell but for the entire industry that employs over 250,000 people.

Chairman BROUN. Mr. Barker, if you could wrap up very quickly. You have overstated your five minutes, so please finish quickly.

Mr. BARKER. Okay. We do have international competition and we support reforms with the RoC process. And finally, I would like to say that while I am speaking here today, we have got 50 second-graders from a local elementary school touring our plant in Bristol, Virginia, and if we believed that styrene posed any threat of cancer, we would never allow those children from our community to our facility.

Thank you very much for the opportunity to provide these comments.

[The prepared statement of Mr. Barker follows:]

Statement of John Barker, Strongwell Corporation

Science and Small Business Joint Hearing on the *Report on Carcinogens*

April 25, 2012

1. Thank you Chairman Broun, Chairwoman Ellmers, Ranking Member Tonko, and Ranking Member Richmond for the opportunity to testify before you today. My name is John Barker. I am the Corporate Manager of Environmental Affairs at Strongwell Corporation. I would also like to introduce my colleague David Ring from Strongwell who is here with me today. Strongwell employs 465 people with facilities in Bristol, Virginia, Abingdon, Virginia, and Chatfield, Minnesota. Our primary raw materials are styrene, resins and reinforcements which we use to make many products including ballistic panels, having shipped over 150,000 to protect American soldiers in Iraq and Afghanistan. We also manufacture bridge beams and platforms being used increasingly to reduce the lifecycle cost and improve the sustainability of infrastructure.

2. Like any chemical such as styrene it is critical to follow safety guidelines. At Strongwell, we pride ourselves in our proactive safety programs. Each facility has a plant safety committee and an excellent safety record. Our employees are trained periodically on each chemical that we use with all employees being retrained at least annually. We ensure that all employees have both the protection equipment and knowledge they need to safely use the chemicals that are a part of our production.

3. By nearly every account, when following the proper safety guidelines styrene is a safe chemical. Many studies from both the private and public sectors alike speak to the absence of a threat of cancer when using styrene. Regardless, the National Toxicology Program listed styrene as a "reasonably anticipated carcinogen" in the 12th *Report on Carcinogens.*

4. The listing of styrene in the *RoC* is of significant concern to Strongwell and the composites industry in general. For one thing, the idea of "reasonably anticipated" has caused great confusion for our employees, their families, and members of the community. We have taken a proactive approach of informing employees about the ruling and other studies about styrene toxicity. We have gone over this matter in-depth with the city councils of Bristol, Virginia and Bristol, Tennessee and have taken community leaders on tours of our facilities to fully explain our safety practices. We have spent millions of dollars on emission reductions and have made a push toward direct injection molding which lessens the exposure of workers to styrene.

5. Dr. Bus has explained the scientific problems behind the listing of styrene in the *Report on Carcinogens.* Let me tell you about the problems it is causing to business:

    a. As a company, Strongwell has gone to great lengths for many years to have a strong and positive relationship with our community. For example, we assist the local fire department with their annual training and provide assistance in maintaining their equipment. Lately, we have been receiving anonymous phone calls saying things like "You do know that styrene causes cancer, don't you." This tells us that people believe the flawed science used in the assessment of styrene and it makes it difficult to maintain an open and fair relationship with the community.

    b. A Google search of "styrene toxic tort" returns a list of many law firms that now claim to specialize in "styrene injury suits"; styrene was not a business opportunity for these law firms a year ago. Because we self-insure, Strongwell has had to place a significant amount of money into reserves to protect ourselves against potential liability lawsuits. The money that we must reserve for liability purposes could be used for investment and job expansion if it weren't for this styrene listing.

6. As I mentioned previously, Strongwell manufactures many important products and these are just a small example of the thousands of applications of composite products. Styrene is an essential chemical component of this manufacturing for which there is no reasonable replacement. Resins based on other chemicals do exist, but are far more expensive and not nearly as well understood in terms of health effects on humans.

7. Likewise, we are very concerned about the potential regulatory burden that could be placed on our operations should the *RoC* listing form the basis of regulatory changes. Changes to the regulations already in effect by OSHA and EPA could cause the cost of compliance to increase substantially. Further, focusing on a matter that should be of no concern will make it harder for employees to give full attention to the safety issues that are important.

8. Because there is no legitimate substitute for styrene and because the costs of liability and compliance could increase astronomically, there is a concern that the federal treatment of styrene could drive composites product jobs off-shore. By the way, this is not just a concern for Strongwell, but also for the entire industry that employs over 250,000 people.

9. Our competitors in Mexico, China, Canada, South America and Japan do not face the same regulatory barriers. Even Denmark, and other countries in the EU, welcome composites manufacturing, because they recently looked carefully at the styrene data and determined that it's not a carcinogen.

10. Our industry association is proposing modest commonsense reforms, which could be enacted legislatively or administratively, and which would dramatically improve the scientific quality *RoC*. We feel our suggested reforms could also serve as a model for improving the quality of Federal science in other areas. Without these changes and without a reexamination of the listing of styrene our entire industry, one on the cutting edge of innovation, is in jeopardy.

11. While I am speaking with you today a group of 50 second graders from a local elementary school are touring the Strongwell plant in Bristol, Virginia –including the daughters of our two top executives. If we believed that styrene posed any threat of cancer we would never allow children from our community, much less our families, to be exposed.

12. Thank you very much for the opportunity to provide these comments.

Chairman BROUN. Thank you, Mr. Barker.
And now, I will recognize Dr. Belzer for five minutes.

STATEMENT OF DR. RICHARD B. BELZER, PRESIDENT, REGULATORY CHECKBOOK

Dr. BELZER. Thank you, Chairman Broun. I thank you for the opportunity to testify again today. I am Richard Belzer, President of Regulatory Checkbook, a nonpartisan, nonprofit organization whose mission includes the promotion of quality improvements in science, economics, and information quality.

In August of 2011, I was asked by the Competitive Enterprise Institute to conduct a short study trying to explain why the RoC had become so intensely controversial. Regulatory Checkbook received an honorarium of $5,000 for a completed published paper. CEI put no substantive constraints on my work. Subsequently, Regulatory Checkbook supplied an additional $5,000 of unrestricted resources.

My research shows that the RoC is not a high-quality scientific work product and there are two fundamental reasons why. This may be a little harder for you to see than I had anticipated. I apologize. When Congress wrote the RoC's authorizing legislation in 1978, it asked for a scientific compendium of substances carcinogenic to humans but did not ask for this in a scientific language. This you may or may not be able to quite read. The task was to list all substances which are either known to be carcinogens or may reasonably be anticipated to be carcinogens. And I will get to the second item in a moment.

But science does not know or reasonably anticipate things. Science cannot tell you whether a number is significant. These are not scientific words; they are the words of lawyers. Given the opportunity, therefore, the NTP has exchanged its white lab coat of science for something of a bureaucratic imperative of maximizing the number of substances listed. The NTP has achieved this by maximizing its flexibility to use or reject scientific information however it sees fit. Thus, while the NTP's listing determinations have scientific content, they are not scientific determinations.

The NTP defines a known human carcinogen as follows—and this is an actual verbatim description of it. A lot of attention has been focused on this—the footnote. I want to focus on something different. I want to focus on a comma midway through the first sentence. And the comma is important, because in English grammar everything that follows this comma is called a parenthetical element. It can be removed from the sentence without changing the sentence's meaning. Therefore, the NTP's definition for a known human carcinogen can be shown much more succinctly as follows, which is "there is sufficient evidence of carcinogenicity from studies in humans." Everything else is subordinate to that.

This definition is tautological and utterly opaque. It is tautological because it must be true. It goes without saying that for every substance defined as a known human carcinogen by the NTP, the evidence was at least sufficient in the judgment of the NTP. It is utterly opaque, however, because no one outside the NTP knows what makes evidence sufficient.

Now, a similar story can be told regarding the definition of "reasonably expected" human carcinogen. A comma is located in the same place. Everything that follows that comma can be eliminated without altering the meaning of the criterion or the sentence.

So we have "sufficient evidence," we have "limited evidence," we have in one case "less than sufficient evidence." All these terms used by the NTP are legal terms. They are not scientific terms. So while the Congress seems to have asked for a scientific compendium, what the NTP appears to produce is legislative determinations and it does this in a way that makes it look like they are scientific. Biology words are often used, for example. But the determinations themselves cannot be scientific because the definitions are themselves not scientific.

Now, return with me for just a moment to the—an earlier slide. There is a second clause, ii, and it is part of the definition of what the statute requires for a substance to be listed and that is that the substance has to meet the first test of being known or reasonably anticipated. It also has to be a substance to which a significant number of persons residing in the United States are exposed. That is in the law. To the best of my knowledge and reading through the listing decisions, the NTP does not do this. It doesn't actually fulfill that second prong of the requirement for a listing.

There are ways of going about that. The NTP could define a significant number of persons residing in the United States. It could then define a de minimis cancer risk, and then it would have to go about a scientific task of estimating the number of persons exposed. Now, I don't believe that the NTP has done any of these three steps. The first two are strictly policy related. Science again can't speak to whether a number is significant or it can't speak to what constitutes de minimis cancer risk. But science can be used to estimate the number of persons exposed.

Chairman BROUN. Dr. Belzer, if you could go ahead and wrap up, please, sir.

Mr. BELZER. I am sorry. I apologize.

What can be done—I provided in my written testimony a number of different reforms that Congress could consider that would improve the scientific content of RoC and make it more useful for public policy purposes, for small businesses, for big business, for consumers, for anyone. The problem with the RoC now is that it stands as a document that does not actually have the scientific content that Congress had intended 35 years ago when it wrote the law.

Thank you very much.

[The prepared statement of Dr. Belzer follows:]

REGULATORY
CHECKBOOK

Written Testimony of

Dr. Richard B. Belzer
President
Regulatory Checkbook

Joint Hearing on

"How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"

Before the

House Committee on Science, Space, & Technology
Subcommittee on Investigations & Oversight
and
House Committee on Small Business
Subcommittee on Healthcare & Technology

April 25, 2012

PO Box 319
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REGULATORY CHECKBOOK

INTRODUCTION

Chairman Broun, Chairwoman Ellmers, Ranking Members Tonko and Richmond, thank you for inviting me to testify on the *Report on Carcinogens*, which the National Toxicology Program attempts to publish biennially. I am Dr. Richard B. Belzer, president of Regulatory Checkbook, a nonpartisan and nonprofit organization whose mission includes the promotion of quality improvements in science, economics, and information quality. I have been president of Regulatory Checkbook since its founding in 2001.

Regulatory Checkbook does not lobby or take public positions on substantive legislation or rule making. Our sparsely populated niche is to seek improvements in the quality of scientific information, risk assessment and economic analysis used in support of regulatory decision-making, regardless of whether it tends to support or oppose specific regulatory actions.

No one has compensated Regulatory Checkbook or me for my testimony today.

In August 2011, I was asked by the Competitive Enterprise Institute (CEI) to conduct a short study of why the RoC has become so intensely controversial. CEI offered to pay Regulatory Checkbook an honorarium of $5,000 for a completed, publishable paper. CEI put no substantive constraints on my work. Subsequently, Regulatory Checkbook supplied an additional $5,000.

CEI published my report in January 2012. A longer, working paper written for future submission to a scholarly journal is available on my personal web site at rbbelzer.com.

Before this hearing was scheduled, CEI arranged for a Capitol Hill briefing on chemical policy and regulation. The briefing will include my monograph and two other papers. So, I will be back to talk about this subject again on Monday, April 30th, from 2:00 to 3:00 p.m. in Room 2322. Obviously, if Members still have questions at the end of today's hearing and the time to stop by, I would be honored to answer them in that less formal setting. As I understand it, there will be free snacks and refreshments, so the room may be full of staff.

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The Results of My Research

My research shows that the RoC is not a high-quality scientific work product. There are two major reasons why.

First, when Congress wrote the RoC's authorizing legislation in 1978, it asked for a scientific compendium of substances carcinogenic to humans but it did not ask for this in scientific language:[1]

> The Secretary shall publish a biennial report which contains—
>
> (A) a list of all substances
>
> (i) which either are known to be carcinogens or may reasonably be anticipated to be carcinogens and
>
> (ii) to which a significant number of persons residing in the United States are exposed;
>
> (B) information concerning the nature of such exposure and the estimated number of persons exposed to such substances;

Figure A: Statutory Directive for the Report on Carcinogens

This disconnect set the stage for today's hearing. Science does not "know" or "reasonably anticipate" things. Science cannot tell you whether a number is "significant." These are not scientific words. They are the words of lawyers.

Second, given the opportunity, the NTP has happily exchanged the starched white lab coat of science for the bureaucratic imperative of maximizing the number of substances listed. The NTP has achieved this by maximizing its flexibility to use (or reject) scientific information however it sees fit. Thus, while the NTP's listing determinations have scientific content, they are not scientific determinations.

[1] 42 U.S.C. § 241(b)(4)(A)(i)-(ii).

To start, the NTP had to create its own criteria for listing substances in the RoC, and the way it did so made sure that science would always be the junior partner.

The NTP defines a "known" human carcinogen as follows:

> There is sufficient evidence of carcinogenicity from studies in humans,* which indicates a causal relationship between exposure to the agent, substance, or mixture, and human cancer.
>
> *This evidence can include traditional cancer epidemiology studies, data from clinical studies, and/or data derived from the study of tissues or cells from humans exposed to the substance in question, which can be useful for evaluating whether a relevant cancer mechanism is operating in humans.

Figure B: "Known human carcinogen"

People get distracted by the footnote. Let's ignore it and focus on what is really important: the comma midway through the first sentence:

> There is sufficient evidence of carcinogenicity from studies in humans,* which indicates a causal relationship between exposure to the agent, substance, or mixture, and human cancer.
>
> *This evidence can include traditional cancer epidemiology studies, data from clinical studies, and/or data derived from the study of tissues or cells from humans exposed to the substance in question, which can be useful for evaluating whether a relevant cancer mechanism is operating in humans.

Figure C: "Known human carcinogen"

In English grammar, everything that follows this comma is called a "parenthetical element." It can be removed from the sentence without changing the sentence's meaning.[2] Therefore, the NTP's definition for a

[2] U.S. Government Printing Office Style Board. Style Manual: An Official Guide to the Form and Style of Federal Government Printing Washington, D.C.: U.S. Government Printing Office, 2008, 201, Rule 8.40 on comma usage ["to set off parenthetic words, phrases, or clauses"].

"known" human carcinogen can be shown much more succinctly, as follows:

> There is sufficient evidence of carcinogenicity from studies in humans

This definition is tautological and utterly opaque. It is tautological because it must be true: it goes without saying that for every substance deemed a "known" human carcinogen by the NTP, the evidence was at least "sufficient." It is utterly opaque because no one outside the NTP knows what makes evidence "sufficient."

We do not know if the NTP requires evidence of human carcinogenicity to be "beyond a reasonable doubt" (say, ≥95%), or whether a "preponderance of the evidence" will do, a likelihood greater than 50%. Indeed, the NTP's evidentiary standard could be well below a 50% likelihood. For all we know, the NTP might be applying a "beyond reasonable doubt" standard in which the null hypothesis is the substance is presumed to be a carcinogen, and thus it is the duty of negative evidence to show that there is less than 5% chance that the substance is not a carcinogen. Or maybe even a 1% chance.

A similar story can be told regarding the definition of a "reasonably expected" human carcinogen. The definition has the same comma located in the same place. Everything following the comma is a parenthetical element, and it may be deleted without changing the meaning of the definition.

"Sufficient evidence," "limited evidence," "less than sufficient evidence"—all these terms used by the NTP are legal terms, not science. What the Congress seems to have asked for was a scientific compendium. What the NTP produces is legislative determinations. It produces these legislative determinations in a way that looks

scientific—biology words are often used, for example—but the determinations themselves cannot be scientific because the definitions have no scientific content.

The NTP Does Not Comply with a Crucial Element of the Law

Return with me for a moment to my second slide, the one showing the statutory directive the NTP is supposed to implement:

> The Secretary shall publish a biennial report which contains—
>
> (A) a list of all substances
>
> (i) which either are known to be carcinogens or may reasonably be anticipated to be carcinogens and
>
> (ii) to which a significant number of persons residing in the United States are exposed;
>
> (B) information concerning the nature of such exposure and the estimated number of persons exposed to such substances;

Figure D: Statutory Directive for the Report on Carcinogens

So far, we have discussed only the first clause in subparagraph (A). To be listed, a substance also must satisfy the test in the second clause: "a significant number of persons residing in the United States" must be exposed to it.

The text refers to human exposure, so to comply with the law, the NTP must investigate and estimate the extent of human exposure in the United States. This cannot be done merely by estimating the mass or volume of production or use. It also cannot be done by relying on historical data (such as "persons who were exposed sometime in the past") or data from another country (such as "persons exposed in China"). The law is clear: It must be actual human exposure, occurring now, in the United States.

1. Define "a significant number of persons residing in the United States";
2. Define a *de minimis* cancer risk level; and
3. Estimate for each candidate substance the number of persons in the United States exposed above the *de minimis* cancer risk level.

Figure E: Steps Required to Implement 42 U.S.C. § 241(b)(4)(B)

This text box shows the steps that must be taken to implement clause (B). Two of the three steps are strictly policy determinations—the definition of a "significant" number of persons, and the definition of a *de minimis* cancer risk level. The third—estimation of the number of persons residing in the United States actually exposed above the *de minimis* cancer risk level—is strictly scientific.

To the best of my knowledge, the NTP has performed none of these tasks. Indeed, the NTP appears to functionally ignore this requirement for listing.[3] It would be an interesting research project to determine how many of the 240 listed substances do not meet the statutory test for listing because actual human exposure in the United States is lacking.

For those substances that pass both prongs of the statutory requirement for listing, the law requires the NTP to include "information concerning the nature of such exposure and the estimated number of persons exposed to such substances."[4] The NTP does not perform this task, either. I am unaware of any substance listing that includes an objective estimate of the number of persons exposed and at what level.

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[3] In the 12th RoC, the NTP acknowledges that "[t]he RoC is required to list only substances to which a significant number of people living in the United States are exposed" (p. 4). The NTP defends its continued inclusion of substances for which actual U.S. exposure is unambiguously trivial because "people who were previously exposed remain potentially at risk or because these substances still are present in the environment." Both justifications are contrary to the plain text of the law, which says nothing about risk and requires listings to be limited to where the number of actually exposed persons residing in the U.S. is "significant."

[4] 42 U.S.C. § 241(b)(4(B).

What Can Congress Do?

An obvious starting point is to figure out a way to compel the NTP to perform all of the tasks set forth in statute—to limit listings to substances "to which a significant number of persons residing in the United States are exposed," and to objectively estimate the numbers of persons exposed. The NTP would comply in a New York minute if the public had standing to challenge its listing decisions, a right that to the best of my knowledge it does not have.

More generally, if Congress wants the RoC to become a useful scientific compendium about human carcinogens, it will need to upgrade the statutory language to make it scientific. I present six ideas in my monograph:

1. **Direct the NTP to make its determinations conditional on exposure or dose.** The NTP completely ignores exposure or dose in making its determinations. That severely undermines the practical utility of the RoC and arguably renders its determination useless or misleading.
2. **Direct the NTP to include potency in its listing decisions.** The NTP makes no distinction between strong and weak carcinogens. Relative potency matters. It is misleading to report substances with the same carcinogenicity label when their capacity to cause cancer—at the same dose—varies by orders of magnitude.
3. **Replace problematic risk descriptors or provide guidance concerning how to interpret them.** Congress should abandon its reliance on nonscientific descriptors such as "known" and "reasonably anticipated." If you want a scientific compendium, ask for one in the language of science, not law.
4. **Direct the NTP to establish a strictly scientific weight of evidence (WoE) scheme.** Nobody knows how the NTP weighs evidence because the NTP won't tell us. Enough. Direct the NTP to devise a new WoE scheme that is transparent, reproducible, and strictly science-based. Give the public the right to challenge it in court if it's not strictly scientific.
5. **Sunset listings to encourage revision.** The current process is anti-scientific because it encourages the NTP to review each substance once, then bolt the door to prevent the intrusion of inconvenient, new scientific knowledge.
6. **Direct the NTP to affirmatively comply with applicable Information Quality Guidelines.** The information quality framework requires information to be objective and presented in an objective manner. The NTP doesn't comply. Petitioning for correction is ineffective because there is no penalty for noncompliance. Give the public the right to challenge

These reforms would help restore the NTP as a scientific agency and get it out of the business of legislating policy through the back door.

Conclusion

Last fall, a real scientific controversy arose because a team of physicists using the Large Hadron Collider at the European Center for Particle Physics reported that they had measured neutrinos moving slightly faster than the speed of light.[5] So what's the big deal? Well, if

[5] T. Adam, N. Agafonova, A. Aleksandrov, O. Altinok, P. Alvarez Sanchez, A. Anokhina, S. Aoki, A. Ariga, T. Ariga, D. Autiero, A. Badertscher, A. Ben Dhahbi, A. Bertolin, C. Bozza, T. Brugière, R. Brugnera, F. Brunet, G. Brunetti, S. Buontempo, B. Carlus, F. Cavanna, A. Cazes, L. Chaussard, M. Chernyavsky, V. Chiarella, A.

it was true, then Albert Einstein was wrong. And that would be a big deal.

Certain of Einstein's theories are believed to be true—let's call them "known"—because they have been subjected to countless experiments and never been refuted. Until now, apparently. As *Time's* Michael Lemonick wrote:

> Physicists have a stock phrase they trot out whenever someone claims to have made an astounding new discovery about the universe. "Important," they say, "if true."[6]

This group of scientists behaved as if their result was true and that obtaining credit for their discovery was the most important thing. (This is a phenomenon we see all the time, when a research group, a university, or a scholarly journal rushes to issue a press release in order to garner headlines.)

Chukanov, G. Colosimo, M. Crespi, N. D'Ambrosio, G. De Lellis, M. De Serio, Y. Déclais, P. del Amo Sanchez, F. Di Capua, A. Di Crescenzo, D. Di Ferdinando, N. Di Marco, S. Dmitrievsky, M. Dracos, D. Duchesneau, S. Dusini, J. Ebert, I. Efthymiopoulos, O. Egorov, A. Ereditato, L.S. Esposito, J. Favier, T. Ferber, R.A. Fini, T. Fukuda, A. Garfagnini, G. Giacomelli, M. Giorgini, M. Giovannozzi, C. Girerd, J. Goldberg, C. Göllnitz, D. Golubkov, L. Goncharova, Y. Gornushkin, G. Grella, F. Grianti, E. Gschwendtner, C. Guerin, A.M. Guler, C. Gustavino, C. Hagner, K. Hamada, T. Hara, M. Hierholzer, A. Hollnagel, M. Ieva, H. Ishida, K. Ishiguro, K. Jakovcic, C. Jollet, M. Jones, F. Juget, M. Kamiscioglu, J. Kawada, S.H. Kim, M. Kimura, E. Kiritsis, N. Kitagawa, B. Klicek, J. Knuesel, K. Kodama, M. Komatsu, U. Kose, I. Kreslo, C. Lazzaro, J. Lenkeit, A. Ljubicic, A. Longhin, A. Malgin, G. Mandrioli, J. Marteau, T. Matsuo, N. Mauri, A. Mazzoni, E. Medinaceli, F. Meisel, A. Meregagli, P. Migliozzi, S. Mikado, D. Missiaen, K. Morishima, U. Moser, M.T. Muciaccia, N. Naganawa, T. Naka, M. Nakamura, T. Nakano, Y. Nakatsuka, V. Nikitina, F. Nittia, S. Ogawa, N. Okateva, A. Olchevsky, O. Palamara, A. Paoloni, B.D. Park, I.G. Park, A. Pastore, L. Patrizii, E. Pennacchio, H. Pessard, C. Pistillo, N. Polukhina, M. Pozzato, K. Pretzl, F. Pupilli, R. Rescigno, F. Riguzzia, T. Roganova, H. Rokujo, G. Rosa, I. Rostovtseva, A. Rubbia, A. Russo, O. Sato, Y. Sato, J. Schuler, L. Scotto Lavina, J. Serrano, A. Sheshukov, H. Shibuya, G. Shoziyoev, S. Simone, M. Sioli, C. Sirignano, G. Sirri, J.S. Songa, M. Spinetti, L. Stanco, N. Starko, S. Stellacci, M. Stipcevic, T. Strauss, S. Takahashi, M. Tenti, F. Terranova, I. Tezuka, V. Tioukov, P. Tolun, N.T. Tran, S. Tufanli, P. Vilain, M. Vladimirov, L. Votano, J.-L. Vuilleumier, G. Wilqueta, B. Wonsak, J. Wurtz, C.S. Yoon, J. Yoshida, Y. Zaitsev, S. Zemskova, A. Zghiche, "Measurement of the neutrino velocity with the OPERA detector in the CNGS beam," ArXiv.org, November 17, 2011. Available at http://arxiv.org/pdf/1109.4897v2.pdf.

[6] Michael D. Lemonick, "Was Einstein Wrong"? A Faster-than-Light Neutrino Could Be Saying Yes," Time, September 23, 2011. Available at http://www.time.com/time/health/article/0,8599,2094665,00.html.

But the physics community insisted on determining first whether the claims were true before discarding Einstein and virtually everything learned since his day. They reviewed the experiment that yielded the astounding result. They performed more experiments. They did this over and over. And they discovered that the astounding result purportedly overturning Einstein was the result of a loose cable. In late March, the leading physicists responsible for claiming to have refuted Einstein have resigned, their careers left in ruins.

Human carcinogenesis is much less certain. Hardly anything at all is "known" in the way Einstein's special theory of relatively is "known." So if the NTP applied a scientific standard of confidence for the definition of a "known" human carcinogen, the RoC would be a very thin pamphlet. And every few years, one of the few "known" human carcinogens would have to be removed from the pamphlet because new scientific knowledge rendered the previous conclusion scientifically untenable.

For the RoC to ever produce useful information about human carcinogens, the authorizing statute will have to be changed. Legalese will have to be replaced with the language of science. The NTP must be directed to stick to science, and its incentives to practice bureaucratic self-aggrandizement must be eliminated. Only then will it be possible for the RoC have any practical value for informing decisions.

I look forward to answering any questions you might have.

Chairman BROUN. Thank you, Dr. Belzer.

I appreciate you all's testimony. For you all that are not southern, y'all is plural for all y'all.

I remind Members that Committee rules limit questioning to five minutes. The Chair at this point will open the first round of questions and I recognize myself for five minutes.

Now, my first question is to Dr. Bus and Dr. Belzer. Written testimony submitted for this hearing indicates that roughly 250,000 jobs are associated with just one substance. OMB considers the scientific assessment "highly influential" if it could impact the public or private sector by more than $500 million in one year or is "novel, controversial, or precedent setting or has significant interagency interest." Do you consider the RoC to be a highly influential scientific assessment, Dr. Bus?

Dr. BUS. Yes, indeed. In fact, as I pointed out in my testimony, the outputs from the report on carcinogens are directly translated in some regulatory environment such as California and other locations around the globe in terms of moving forward with regulatory action. So although they are not regulatory actions themselves, they serve as the foundation for it.

Chairman BROUN. And bring about regulations? Okay. Dr. Belzer.

Dr. BELZER. It is—I have not looked at the economic consequences of the RoC in any way. I have looked at the amount of intense energy devoted to attempting to get good quality science out of the RoC. Based on that, I would draw the inference it is highly influential.

Chairman BROUN. Very good. Dr. Bus, you argue that the NTP does not apply a weight of the evidence review of substances, yet I understand that the Assistant Director of NTP at the December 15, 2011, meeting of the Board of Scientific Council has made it clear that NTP has always considered the full body of evidence for every chemical and that all the studies are listed in the background document. Are you really saying that you just disagree with how they weighed those studies?

Dr. BUS. Absolutely not. In fact, the testimony as presented by Dr. Bucher indicated that, yes, they do perhaps consider all the evidence but really what is more important is the process by which the evidence is evaluated. So, for instance, in the recent NAS review of the formaldehyde document, that is where the National Academy of Sciences really outlined a roadmap for how scientific data should be evaluated with respect to assessments of the toxicology of chemicals. And they really emphasize that they should take a weight-of-evidence approach, which is not just a recitation of the numbers of studies that are out there but really a broad-based critical analysis of how you identify the studies, how those studies are used, how they are to be interpreted, and where they are to be employed. So there is a dramatic difference between a weight-of-the-evidence approach versus just simply listing the numbers of studies that are out there.

Chairman BROUN. Very good. Hopefully, we will have that contract put in place and the Academy can go forward.

Dr. Belzer, in your testimony you state that the risks' descriptors "known" and "reasonably anticipated" are confusing. Can you tell

us why this legal language which appears in the statute is confusing and is not appropriate for use in describing the cancer risk that a substance may possess or pose?

Dr. BELZER. Well, as I noted in my oral testimony, the term "known" or the phrase "reasonably anticipated," these are just not terms that scientists use. Scientists deal with theories and with hypotheses and they test them. But to say that something is known in science is very difficult. I am not sure what level of confidence Congress intended in 1978 for this idea of "known human carcinogen." One possible interpretation that Congress intended would be like "'beyond a reasonable doubt," something like that. And it would be useful to know if that is the standard the NTP is using. The NTP doesn't—has not, to the best of my knowledge, disclosed how it interprets this language. What is the likelihood that a chemical is a human carcinogen? What is enough to be "reasonably anticipated?" Scientists can't answer that question but the NTP is making policy decisions. Presumably, they should be able to answer that question.

Chairman BROUN. Thank you, Dr. Belzer.

Dr. Bus and Dr. Belzer, do you believe that the RoC truly reflects the intent of the law that created it? Dr. Bus.

Dr. BUS. I believe with the status of "reasonably anticipated" and "known," the intent clearly is to identify chemicals that the public should in fact take direct attention to. And if—with that degree of significance associated with those classifications, I believe the public is best served if, in fact, it has confidence that the scientific evaluations that underpin those classifications are based upon the highest quality scientific evaluation that can be done. And those principles have been outlined, as I have mentioned before, are really centered on evidence-based approaches to evaluation of the data, which really promotes a structured, organized way of looking at the data that gives you a consistent evaluation of the data from the chemical and that builds assurance with the public that, in fact, the evaluations that are put forward by the Report on Carcinogens in fact can be trustworthy and used for science-informed decision making.

Chairman BROUN. Thank you, Dr. Bus. I am not sure that that truly answered whether it follows the intent of the law. And Dr. Belzer, my time is expired, so if you would just include that in your written answers.

So now, I recognize Mr. Tonko, my friend, for five minutes.

Mr. TONKO. Thank you, Mr. Chair.

Ms. LaTourelle and all of our witnesses, thank you for joining us today. But to Ms. LaTourelle, recently I toured a company started by a couple of graduates of Rensselaer Polytechnic Institute in my district, and they invented a process with the help of the campus incubator to use mushrooms and agricultural byproduct to grow packing material to replace polystyrene. They are enjoying real success and finding interested partners in old line businesses that welcome these products to reduce their own carbon footprint and meet customer preferences. It seems to me that consumers are ahead of some companies about what they want in products. As important as the Report on Carcinogens may be to some, it is irrelevant to the preexisting surge in demand to move away from petro-

chemical-based products. Could you elaborate a little on consumer demand as a driver for the change in these given areas?

Ms. LATOURELLE. Certainly. Consumer demand basically picks up where government regulations leave off or where government regulation is absent. The move toward greener—however you categorize that, essentially products that have more environmental benefit, use less energy, are nontoxic, and use renewable resources—are so in demand that companies like DuPont, for example, in 2010 surveyed 800 of their customers globally and DuPont's customer base is—it spans food and agriculture, transportation, chemicals, manufacturing, plastics—they understand that there is a long-term demand for these products and alternatives because of the larger drivers on the business and they look to their customers to be sure that there is going to be a ready market.

Eight-nine percent of the 800 customers surveyed said that delivering products with environmental benefits is a long-term market opportunity, and those are the customers that sell products directly to consumers. Ninety-five percent of those surveyed reported customer demand is a key driver for developing products.

I would also like to point out that there is such an incredible shift in the marketplace to these types of alternatives that companies like SC Johnson have created their own metrics through which they screen chemicals to use in their products. Theirs is called a Green Screen. Staples has been actively dialoguing with their suppliers. They have goals regarding how much renewable products they sell and they are working with their suppliers to find ways in which products can be less toxic and less harmful to the environment. Wal-Mart is a great example. They have reduced their packaging and found that essentially what it did is it made their shipments almost double in size because the reduction in packaging allowed them to ship more, and this has saved them millions of dollars in transportation costs.

Mr. TONKO. Thank you. Now, you heard the testimony of the Office of Advocacy from SBA, and it struck me that they are very aggressive intervention into this case based on lobbying from the styrene industry amounts to a government office picking winners and losers in the market. Based on what you have learned, does it appear that they are working in the interest of green chemistry firms?

Ms. LATOURELLE. No. Clearly, green chemistry is—let me put it this way. The ship has sailed. Green chemistry is here. The alternatives are here. For governments to be determining what is going to happen in the green chemistry industry, it is too late. We certainly advocate for more incentives to get to commercial scale so that our respected colleagues on this panel can supply customers with these products. We are seeing more job creation coming out of green chemistry. For government to be inserting itself and disputing the process of a document like the RoC to me is disruptive to the larger issues of the availability of toxicology in general. Consumers get their information from many different sources, this being just one of them. Yes, it is influential. It influences the customer base, but we are already well beyond concerns of a document like this.

Mr. TONKO. Thank you so much. I yield back, Mr. Chair.

Chairman BROUN. Thank you, Mr. Tonko.

Now, I recognize Chairman Ellmers for five minutes.

Chairwoman ELLMERS. Thank you, Mr. Chairman.

My first question is for Ms. Webster. If your company had to replace styrene with another substance, would you still be able to sell your products at a competitive price and how would that impact your bottom line?

Ms. WEBSTER. No, I would not be able to be competitive. It would make it easier——

Chairman BROUN. Microphone, please, ma'am.

Ms. WEBSTER. It would make it definitely easier for imported products to come into the United States. I do have a bio-based resin that I do use. That has actually gotten us more business. People do like the aspects of us going green, but no, the cost of the other resins that do not have styrene are very cost-prohibitive. And we have looked at vinyl esters and epoxies and things like that. It is just not cost-effective. It will increase imports.

Chairwoman ELLMERS. It will increase imports and then, obviously, if you were to—and this is just me throwing this out there—if you were to use another product, obviously that cost would be passed on to the consumer.

Ms. WEBSTER. Absolutely.

Chairwoman ELLMERS. My other question for you is you had mentioned in your testimony that you, you know, obviously as a small business you don't have the resources for a Regulatory Compliance Officer, is that correct?

Ms. WEBSTER. Yes.

Chairwoman ELLMERS. Okay. So who in your company is the person that is responsible to be complying with the federal regulatory process?

Ms. WEBSTER. We hire a company to come in, they do a walkthrough, they do training, they do training on the forklifts and things like that. Once a year, they come in and go through the plant, they let us know if there is any issues, they pat us on the back, and knock on wood, we haven't had any problems. So we hire somebody to come in to do that.

Chairwoman ELLMERS. My next question—thank you, Ms. Webster. I do want to add one last thing and you may not feel comfortable answering this and if you don't, that is fine. Is that a very costly endeavor, having someone have to actually come in and help you in that process?

Ms. WEBSTER. It runs—it is going up every year——

Chairwoman ELLMERS. Um-hum.

Ms. WEBSTER [continuing]. But it runs—it is just under $1,000 but I think it is based on how many employees you have.

Chairwoman ELLMERS. I see. Thank you. Thank you for that, Ms. Webster.

For Mr. Barker, I have a couple questions for you. Do you feel that the Report on Carcinogens is helping or hindering you in creating a safer workplace?

Mr. BARKER. At this time I would have to say that it is a hindrance, although I think at this point not as great as it is likely to be. And from that hindrance it distracts our employees from the real concerns that they should be dealing with on a day-to-day

basis, wearing the proper protective equipment, being concerned about the physical hazards they work with, and they are distracted because of the concern about getting cancer from styrene that the NTP has said is reasonably anticipated to be a carcinogen. So they are concerned about that. And we are concerned that the further we go with this as awareness grows, the more distracted they will become.

Chairwoman ELLMERS. And my last question for you is, now, it is our understanding that Strongwell participated in a public comment process of the 12th RoC. Is that correct?

Mr. BARKER. That is correct.

Chairwoman ELLMERS. Can you tell us whether or not your comments were responded to by the NTP?

Mr. BARKER. Our comments as far as I know were not responded to.

Chairwoman ELLMERS. Okay. And I would like to just, for the record, point out—and there again, in the previous panel, Dr. Birnbaum had stated to the best of her knowledge that all comments had been responded to. But I do have an additional question—thank you, Mr. Barker—for Dr. Belzer. In your testimony, you noted that the NTP completely ignores exposure or dose in making its determinations. And why is it important for exposure or dose to be considered when providing information to the public about substances that have the potential to cause cancer? I am sorry. Dr. Belzer.

Dr. BELZER. Sorry, it wasn't clear who you were addressing.

Chairwoman ELLMERS. I am sorry, no. I apologize.

Dr. BELZER. The public has an obvious need for information on chemicals or substances that could cause cancer but the dose at which those substances might cause cancer is very important. If it is something that happens at extraordinarily high doses and it happens in animals under laboratory conditions, that is an important fact but that is very different than happening at environmental exposure levels. This is the type of thing that people ought to have access to. I think that improving the targeting of the information so that—well, in 1978 I think there was a general notion that either a substance caused cancer or it didn't and that seemed to be the prevailing state of knowledge at the time. But that is not correct. Things are more far more complicated than that. And the NTP is quite capable of being more discriminating and to provide information that is more dose-relevant so that people have that information as well as the current worst-case scenario.

Chairwoman ELLMERS. Great. Thank you so much. Thank you for all of your comments and your testimony. Thank you.

I yield back.

Chairman BROUN. Thank you, Mrs. Ellmers.

I now recognize Mr. Richmond for five minutes.

Mr. RICHMOND. Thank you, Mr. Chairman. It appears to me now that this is a styrene hearing. And with that, let me just start with—I have heard a lot of testimony about—that there is no legitimate substitute, the benefits of it, and I guess my question—I will start with you, Ms. Webster. Let us assume that NTP is right and styrene is a carcinogen. Now what?

Ms. WEBSTER. My company will most likely liquidate, and I will have to find another job.

Mr. RICHMOND. So if it is in fact—if it in fact causes cancer, would—with substantial exposure, then it pretty much kills your business?

Ms. WEBSTER. The risk of liability that we would be faced with, I wouldn't be able to sleep at night. I go to work every day feeling good about what I do and if this comes out as listed as an anticipated carcinogen, I am not going to feel good about what I do.

Mr. RICHMOND. And I guess my question is what if they are right? What if it does cause cancer?

Ms. WEBSTER. I guess I would like to see the scientific data. The research papers that I have seen and read is not showing that.

Mr. RICHMOND. And Mr. Barker, I guess I would pose the same question to you. What if they are right and a high level exposure to it could cause cancer?

Mr. BARKER. Well, first of all, let me say that we are genuinely concerned about our employees and about our community, and we do not want our employees to get cancer from exposure to styrene. But I think this is part of the problem that Dr. Belzer was talking about. So they are right. To what degree? What is the risk? And that to me is the whole crux of the problem. Here the NTP has said that styrene is reasonably anticipated to be a carcinogen.

Mr. RICHMOND. Um-hum.

Mr. BARKER. So how much exposure do you have to have to get cancer? Is it 50 parts per million for 10 years, 20 years? Is it 500 parts per million for eight hours? None of that has been discussed. And so that is—our problem right now is our employees, all they hear is this stuff causes cancer and there is a great deal of uncertainty. And we feel like there is just not a need for that uncertainty at this point. Now, if they were to come back and say, you know, something quantitative like, you know, there is pretty high risk you are going to get cancer if you work in this environment at 50 parts per million for 10 years, then, you know, we wouldn't—that would be unacceptable. Then we would start looking at engineering alternatives and possibly, you know, other materials.

Mr. RICHMOND. And I guess my major concern and it is before my day and—but it reminds me, at least as I did a little research on it of the argument over asbestos or lead in paint and gas——

Mr. BARKER. Sure.

Mr. RICHMOND [continuing]. And all of those things and effects on it, and now we are down the road and we still have asbestos in a number of things because we just didn't stop or recognize it early enough. But I ask and defer to Dr. Grimsley, I know that with BP and the chemicals we use to treat the oil spill, the dispersants, they are doing some sort of a study to see—and they are using exposure. So how can exposure be included and do you think that is a necessary first step in just saying it is likely to or could lead to cancer?

Dr. GRIMSLEY. Yes. I am serving on the Scientific Advisory Board for the NIEHS in the Gulf Worker study and they are looking at different types of exposures, some of the dispersants and some of the hydrocarbons that were related to that. The exposure component is a very important piece that the NIEHS is actually looking

at. It is always one of the first steps that you want to do in exposure assessments is to actually have good data and to have good estimates about the exposures. And so they are going through and doing that important step in order to identify if you are going to actually have some type of health outcome that is related to any particular type of exposure—if it is a low exposure, if it is a medium exposure, if it is a high exposure.

Mr. RICHMOND. And can that be done with styrene? Or where are we in the process of that?

Dr. GRIMSLEY. Well, I think, Ms. LaTourelle, she has already alluded to the point that some of the other agencies have already listed styrene as a carcinogenic agent. I used to work as an industrial hygienist at Texaco. I used to work as an industrial hygienist at International Paper and at bigger companies and smaller companies, we try to encourage what we call the ALARA, As Low As Reasonably Achievable. If you have exposure limits, you avoid exceeding the exposure limits, but most definitely try to keep the exposures down as low as possible, then, that is one of the things we strive for.

Chairman BROUN. The gentleman's time has expired.

Mr. RICHMOND. Mr. Chairman, I see that my time has expired and, Mr. Chairman, if you will allow me, I just wanted to recognize that Dow is in my district and they are doing a wonderful job and they are expanding. And I went and watched their first responders and their safety mechanisms so I am not implying that anybody is not concerned about the health of their employees, but the question becomes what if NTP is right and other people are wrong? And I yield back.

Chairman BROUN. Thank you, Mr. Richmond.

As much as my colleagues on the Democrat side would like to make this a hearing about styrene, holding a hearing on the RoC process, which is what this hearing is all about without discussing substances recently listed would be totally irresponsible and we need to fully evaluate the process. And that is what this is all about and specific substances just serve as case studies. They are not—this is not about styrene as much as my colleagues on the Democratic side would like to make it be. This is about the process. The title of this hearing is "How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs." So that is the reason that folks are here.

So now I recognize Mr. Miller for five minutes.

Mr. MILLER. I thank the Chairman for that clarification, but the styrene industry's lobbyists do take credit for having scheduled this hearing.

Mr. Barker and Ms. Webster, you have both said in your testimony that insurance costs might go up, policies might be canceled for firms that use styrene-based products or use styrene in their processes. Is that something you are supposing might happen or do you actually know of any instances where companies have in fact lost coverage or been charged more in premiums because of—they—because they used styrene either in their products or in their processes so we could check with those companies and the insurance companies directly for more information about that?

Ms. WEBSTER. I was on a conference call about six weeks ago. There was a woman—John Schweitzer might be able to get me her name—I think her name was Laurie who was—she was dropped by her insurance carrier and the next carrier that picked her up, the costs were quadruple.

Mr. MILLER. Okay. Can you get—I mean, Laurie is not enough to go on.

Ms. WEBSTER. Yeah, I know. The call was about six weeks ago.

Mr. MILLER. Mr. Barker, do you have—do you know personally of any companies that have in fact been dropped or had their premiums raised?

Mr. BARKER. I am aware of the same company I think that Ms. Webster is talking about.

Mr. MILLER. Okay. Can you get us Laurie's last name and——

Mr. BARKER. Yes.

Mr. MILLER [continuing]. Contact information——

Mr. BARKER. Sure.

Mr. MILLER [continuing]. As well? And I would hope that we could get from her the names of the companies——

Mr. BARKER. Sure.

Mr. MILLER [continuing]. Or rather the names of the insurance companies.

Mr. Barker, in your testimony you said that you had done a Google search for styrene toxic tort and there were 12 firms that had been—that were advertising to handle styrene toxic torts since the 12th RoC came out. Our staff did the same research and found that actually only one of those mentioned the RoC in—on their Website, and I actually called some of those firms and it appeared that all but one—or maybe all of them had actually been doing styrene toxic torts well before the RoC. There were plenty of people in the scientific community including toxicologists who—public health experts who believe that styrene was a carcinogen before it was recognized—before the RoC. Are you aware that actually there were lawyers who were handling styrene toxic torts before the RoC, and in fact the RoC does not appear to have changed that?

Mr. BARKER. Yes.

Mr. MILLER. Okay. You were aware that that has been going on right along?

Mr. BARKER. Yes.

Mr. MILLER. Okay. Not new, not because of RoC, right along?

Mr. BARKER. Right.

Mr. MILLER. Okay. And finally, Mr. Barker, I know that there was a miscommunication between our staff—our Democratic staff and you yesterday. They sent a request for information in two emails to the address that had—to which your invitation to appear had been sent and did not get a response. Will you provide the information that they asked for for the record? And could you also just kind of tell us what happened now for the record?

Mr. BARKER. Well, I was on my way here——

Mr. MILLER. Okay.

Mr. BARKER [continuing}. And didn't have access to email.

Mr. MILLER. All right. But you will provide us that information?

Mr. BARKER. Yes.

Mr. MILLER. All right. Well, Mr. Chairman, I think you said glory be before when I yielded back 12 seconds. I will yield back a minute and 20 now.

Chairman BROUN. Hallelujah. As Mr. Miller knows, I have always tried to be very liberal with you, as well as other Members of our Committee and have enjoyed serving——

Mr. MILLER. A tendency that does not show up in many other areas.

Chairman BROUN. Well, I try to be very lenient with everybody. But I also want to remind Mr. Miller that this Committee is not responsible for what outside entities state. This is still about process. This is not trying to exonerate or vilify any particular entity or industry and this is about the process. That is what I would hope to be as a scientist, as a physician, I am very concerned for my patients and for all Americans about potential exposure to anything that may cause people harm. And so I share my Democratic colleagues' concern about the health of all Americans and this is not to try to hold up any industry in either regard as to exonerate them. It is about process and it is not to try to vilify anybody. So thank you, Mr. Miller. I appreciate it.

Now, I recognize my friend, Mr. McNerney, for five minutes.

Mr. MCNERNEY. Thank you. And I do thank the witnesses for coming forth today. It is not easy.

Ms. LaTourelle, you have significant experience with green chemistry businesses, and jobs are, of course, a big deal to us here in Congress. Would you address job creation and the green chemistry production as opposed to the traditional petrochemical production businesses?

Ms. LATOURELLE. I would be happy to. And I would like to recommend the source from which the statistics that I am about to share are derived, that is the economic benefits of a green chemical industry in the United States, renewing manufacturing jobs while protecting health and the environment. I think that is something we can all get behind. This is a report by the BlueGreen Alliance, which is an organization that has environmental concerns and also labor concerns.

It states that using similar input-output analysis, they estimate that spending a million dollars on traditional plastics production would generate 4.3 jobs while spending a million dollars on bioplastics would generate an estimated 6.9 jobs. It is a pretty significant impact. The American Sustainable Business Council represents 120,000 sustainable businesses. They represent 200,000 sustainable business leaders and they are also a ready source for job creation. They have access to many green businesses, if you would like to know more.

Mr. MCNERNEY. Thank you. Nice answer.

I understand from your testimony—think I understand from your testimony—I am going to ask for your verification that 21st century businesses—for 21st century businesses, the RoC should have a little impact. Was that what you intended, and is it because of energy efficiency, public perceptions and so on? What are the sort of reasons for that, if I am correct?

Ms. LATOURELLE. Well, first, 21st century businesses have much larger concerns than a report like the RoC. I mean as I said be-

fore—sorry to mention styrene again—has been identified since 1987. These are concerns that businesses should have already vetted. They are not assessing the risk appropriately. I am not saying that the RoC has no place for us. It is clearly an important document. However, its impact on small business is questionable because, in any event, these types of documents should be drivers of innovation to find solutions——

Mr. MCNERNEY. That is great. That leads to my next question. I only have a limited amount of time.

Ms. LATOURELLE. Sorry.

Mr. MCNERNEY. You say that regulations spur innovation, and I have heard that from other witnesses in other hearings, and I just want to direct the next question to Mr. Barker. Would you say that the 12th RoC, which may lead to regulations, has led to innovation at Strongwell?

Mr. BARKER. Not the RoC at this point, but I would agree to some extent that some regulation can lead to innovation, yes.

Mr. MCNERNEY. Thank you.

Dr. Grimsley, would you address the controversy between strength of evidence and weight of evidence?

Dr. GRIMSLEY. I am not quite sure what some of the procedures that are associated with the evidence, the weight of evidence and the strength of evidence, especially how some of the agencies go about looking at those, if they have a systematic process. I know they have a systematic process. The American Conference of Governmental Industrial Hygienists, the EPA, the NTP, when they go through and they actually look at the data that is available, I do know they have some type of system but I can't speak to exactly what—is it high, medium, low and to what extent those strengths of evidence are.

Mr. MCNERNEY. All right. Dr. Bus, let me just ask you a simple question. Was your objective today to throw down on the validity of the 12th RoC and 13th RoC? Is that your basic objective here today?

Dr. BUS. My objective is to make sure that we have the highest quality science evaluation supporting these very important decisions such as classifications of carcinogens. And I strongly believe as a result of our experiences with styrene and other chemicals that what we have witnessed—that there is a significant need for refinement of the RoC process. And if those processes are considered and, we believe, as I proposed, a review by the National Academy of Sciences to conduct a review of those processes, in the end we will result—we have a process that will deliver classification decisions that we can have far greater confidence in not only as an industry but also as the public, which is the ultimate recipient of that information.

So I am a strong believer that, yes, in fact the examples of some of the chemicals that have gone through the RoC reveal significant flaws in the process that can be solved. And certainly with the advice of the NAS or other advisory bodies, we could end up with a process which delivers science that truly is useful for informing decision making.

Chairman BROUN. The gentleman's——

Mr. MCNERNEY. So in other words this——

Chairman BROUN [continuing]. Time is expired and so we will go forward.

And I thank you all for—all you all for you all's testimony here today. Members of either Committee may have additional questions for you all, and we ask for you to please respond very expeditiously in writing. The record will remain open for two weeks for additional comments from Members. You all are excused. I appreciate you all's participation.

The hearing is now adjourned.

[Whereupon, at 12:25 p.m., the Subcommittees were adjourned.]

ANSWERS TO POST-HEARING QUESTIONS

ANSWERS TO POST-HEARING QUESTIONS

Responses from Dr. Linda S. Birnbaum were not submitted.

U.S. House of Representatives

Committee on Science, Space, and Technology
Subcommittee on Investigations & Oversight
and
Committee on Small Business
Subcommittee on Healthcare and Technology

QUESTIONS FOR THE RECORD

"How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"

Wednesday, April 25, 2012

Dr. Linda S. Birnbaum, Director,
National Institute of Environmental Health Sciences & National Toxicology Program,
U.S. Department of Health and Human Services

Questions submitted by Dr. Paul Broun, Chairman, House Science, Space and Technology, Subcommittee on Investigations & Oversight and Rep. Renee Ellmers, Chairwoman, House Small Business Subcommittee on Healthcare and Technology

1) In late March, pursuant to language in the conference report accompanying the appropriations bill Congress passed last December, the National Academies of Science (NAS) sent a proposal to Dr. Howard Koh, the Assistant Secretary for Health at HHS, outlining the scope of a scientific peer review of the 12th Report on Carcinogens' determinations related to formaldehyde and styrene. You were cc'd on that correspondence.

   About a month ago, the Academies' contract office received an e-mail from HHS saying the agency would issue a Request for Proposal (RFP).

   Following up on questions posed to you during the hearing, could you please provide a status update of the Academies' proposal to HHS, specifically addressing the following questions:

   A) Why did HHS send the Academies an RFP?
   B) Does HHS always issue RFPs for work with the NAS? Please provide examples of previous RFPs for work done by NAS.
   C) Was there something in the Academies' proposal that concerned the Agency?
   D) Is HHS planning to modify the Academies' proposal - and thus by default modify Congress' intent - by identifying different task items in the RFP?
   E) When will HHS fund the Academies' project as directed by Congress?

2) In response to a question about a recent roundtable discussion on the RoC sponsored by the Small Business Administration's Office of Advocacy, Mr. Maresca stated no one from NIEHS attended.
   A) Were representatives of the NTP invited to attend and participate in the Office of Advocacy's March 16, 2012 roundtable on environmental issues at which the NTP's Report on Carcinogens was discussed?
   B) If yes, why didn't a representative from NTP attend?

3) Last year, in Chapter 7 of its review of EPA's Draft IRIS Assessment of Formaldehyde, the National Academies of Science emphasized the importance of weight-of-evidence evaluation in hazard identification.
   A) While this report was directed at EPA, have you read Chapter 7? Do you believe that its recommendations are relevant to the RoC? Do you believe that the RoC meets any of the recommendations of that Chapter, and if so, which one(s)?
   B) Does NTP plan to develop a consistent weight-of-evidence framework so that data from all relevant studies - both positive and negative studies - can be systematically reviewed, given appropriate weight, and integrated in a manner that provides a robust understanding of the mode of action?

4) The RoC statute directs NTP to include substances in the report that are "known" or "reasonably anticipated" human carcinogens.
   A) "Known" is a pretty high standard in science. Presumably it does not mean 100% certainty. What is the minimum probability needed to designate a substance as a "known" human carcinogen?
   B) What about a "reasonably anticipated" human carcinogen? What is the minimum probability necessary to designate a substance as "reasonably anticipated" to cause cancer?

5) In the NTP's listing criteria, a "known" human carcinogen is defined as one in which "[t]here is sufficient evidence of carcinogenicity from studies in humans..."
   A) How does NTP define "sufficient" evidence?
   B) Is this definition listed somewhere that is accessible to the public, so that we can tell in advance with a high degree of certainty what is "sufficient" evidence and what is not? If so, please provide that location.

6) In the NTP's listing criteria, one way for a substance to be deemed a "reasonably anticipated" human carcinogen is if "there is limited evidence of carcinogenicity from studies in humans..."
   A) How does NTP define "limited" evidence?
   B) Is this definition listed somewhere that is accessible to the public, so that we can tell in advance with a high degree of certainty what is "limited" evidence and what is not? If so, please provide that location.

7) The RoC statute also requires, as a condition for listing, that "a significant number of persons residing in the United States [must be] exposed."
   A) How does NTP develop this number?

8) In the twelve RoCs developed over the past 31 years, how many substances have been upgraded from the "reasonably anticipated" list to the "known" list?
   A) How many have been delisted in 31 years?
   B) How long did it take to delist these substances?

9) Once the criteria for "reasonably anticipated" or "known" are met, does NTP evaluate new data that may contradict a listing?
   A) Let us pose a hypothetical: if there are reports published this year in peer reviewed journals showing that styrene-induced mouse lung tumors are not relevant to humans, and that a multi-decade update to a large study with highly exposed workers shows no styrene-related cancer, will NTP remove styrene from the RoC?

10) How many times - and please provide specific examples - has NTP ***not*** listed an item in the RoC as a direct result of comments provided by the public?

11) How many of the substances in the 12th RoC listed as "reasonably anticipated to be human carcinogens" fall under the International Agency for Research on Cancer's (IARC) Group 2A which are "probably carcinogenic to humans?"
   A) How many of the substances in the 12th RoC listed as "reasonably anticipated to be human carcinogens" fall under IARC's Group 2B which are "possibly carcinogenic to humans?"

12) The process for the 13th RoC that NTP issued in January 2012 is five pages long, including a process flow chart. Conversely, in 2005, the U.S. Environmental Protection Agency issued a 166-page "Guideline for Carcinogen Risk Assessment," providing explicit detail on how carcinogen assessments should be conducted.
   A) Understanding that the RoC is not a risk assessment document, does it not seem odd that an agency as deeply rooted in science as the NTP believes that it can document in five pages the process it uses to conduct highly scientific assessments on substances that may have expansive and complex databases?

13) Regarding the criteria NTP uses to produce all RoCs, where do these established criteria come from?
   A) How often are they reviewed?
   B) When was the last time they were updated?
   C) Was any peer review conducted to ensure the scientific rigor of the criteria?

14) In the process for the 13th RoC, NTP will seek public comment on (1) nominations to the RoC; (2) draft concept documents for substances proposed for evaluation; (3) cancer evaluation components; and (4) draft Monographs for candidate substances. However, NTP removed any requirement to develop a written response to public comments.
   A) Why did NTP remove the requirement - which existed in the 12th RoC - to respond to public comments in writing?

B) How does NTP plan to ensure that public comments are adequately considered and responded to substantively?

15) In response to a question asking if NTP responds to all public comments, you stated that "for the 12th Report we did respond to all the public comments at the time the document was released." However, John Barker from Strongwell Corporation testified that Strongwell had participated in the public comment process for the 12th RoC and to his knowledge, NTP had not responded to Strongwell's comments. In addition, when asked, "[w]ould it have overwhelmed the resources of your department to try to respond to each one of those comments," you responded "Yes."
   A) Please explain these apparent discrepancies.
   B) How many public comments did NTP receive regarding the 12th RoC?
   C) Did NTP respond to all the public comments it received during the development of the 12th RoC?
   D) How did NTP respond to public comments? Did it merely acknowledge receipt of the letters, or did NTP respond to the substantive concerns raised by commenters?
   E) Attachment A is a copy of a May 27, 2009 letter from you to John Tickle, the President of Strongwell Corporation, acknowledging receipt of his May 18, 2009 letter to NTP relative to styrene. How many of your responses are similar to the attached letter? Please identify who received acknowledgment letters similar to the attached letter.
   F) How many people received letters that addressed the substance of their comments? Please identify those recipients.

16) In response to a question about public comments, you stated that for the 13th RoC, you "intend to have the public comments actually discussed at the expert peer review meeting."
   A) Please elaborate on that, addressing for example, how many days peer reviewers would have to review the comments prior to the peer review meeting, and how much time would be spent discussing the public comments at the meeting.

17) In your written testimony, you say that the 12th RoC was "revised to increase peer review and the opportunity for public involvement and to address guidance issued in the Office of Management and Budget Information Quality Guidelines for Peer Review." A 2004 "prompt" letter from the Office of Information and Regulatory Affairs to NIH included some specific suggestions about responding to comments, such as:

> *"To fully realize the value of the comment process, NTP should prepare and disseminate a response-to-comments document before completion of a substance's review. This document would improve the transparency of the process and assure the public that their perspectives have not only been sought but also considered."*[1]

[1] Letter from OIRA Administrator Dr. John D. Graham to NIH Director Dr. Elias A. Zerhouni, November 16, 2004, available at http://www.reginfo.gov/public/prompt/nih_ntp111604.pdf.

A) How did NTP accommodate those OIRA suggestions, especially when comments in the 12th RoC were responded to *after* the document was published, and for the 13th RoC, there's no mention of responding to comments at all?

18) In your written testimony, you talk about multiple opportunities for public involvement in the 12th RoC, and you explain that the process involved an independent external peer review and two governmental review groups.
   A) Please explain how the involvement of the two governmental groups (the Interagency Scientific Review Group and the NIEHS/NTP Review Group), whose meetings were closed to the public, contribute to "increased peer review and the opportunity for public involvement?"
   B) Who selects the external expert panel members? Who decides their charge questions? Do these expert panels comply with Federal Advisory Committee Act (FACA) requirements such as membership balance, objectivity, and accessibility to the public?[2]

19) In discussing the 12th RoC in your written testimony, you talk about opportunities for the public to "provide oral testimony at external, scientific expert panel meetings and at meetings of the NTP Board of Scientific Counselors [BSC]."
   A) How much time did the expert panel and BSC have to review and analyze these public comments?
   B) Regarding the BSC - who selects those members? Who decides their charge questions? Do these expert panels comply with Federal Advisory Committee Act (FACA) requirements such as membership balance, objectivity, and accessibility to the public?[3]
   C) Do these panels comply with OMB peer review guidelines?

20) In its revised process for the 13th RoC, NTP indicates that each draft Monograph will be reviewed by a peer review panel.
   A) Will NTP create separate peer review panels for each substance under review?
   B) What criteria will NTP use to choose experts to serve on a peer review panel?
   C) Will the public be given an opportunity to comment on the proposed members of the panel and the proposed charge questions?

21) We understand that it is the policy of the NTP to choose its own expert panels to peer-review NTP's Report on Carcinogens hazard assessments. This seems in stark contrast to the independence we see in the peer review of scientific articles submitted for publication in peer-reviewed journals. For example, if you were to submit an article for publication in a peer-reviewed journal, the editor of that journal, not you, would choose the peer reviewers of your article, and the editor would independently judge whether or not you

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[2] Wendy R. Ginsberg, "Federal Advisory Committees: An Overview," *Congressional Research Service*, (R40520), January 24, 2011, available at: http://www.crs.gov/Products/R/PDF/R40520.pdf; "FACA defines an 'advisory committee' as 'any committee, board, commission, council, conference, panel, task force, or other similar group, or any subcommittee or other subgroup thereof' that is 'established by statute or reorganization plan,' 'established or utilized by the President,' or 'established or utilized by one or more agencies.' **All advisory bodies that fit this definition, however, are not necessarily entities that must adhere to FACA.**" (emphasis added.)

[3] Ibid.

responded adequately to the critiques from these peer reviewers. This system helps assure the independence and objectivity of the scientific process.

A) Why isn't this same kind of independent review applied to the work of the NTP?
B) How does the NTP avoid the perception of choosing panels that will rubber-stamp NTP's work?

22) The revised process for the 13th RoC states that NTP "may defer or terminate the review of a candidate substance for the RoC at any time if relevant information becomes available that warrants its reconsideration."

A) What criteria will NTP use to make that determination?

23) Attachment B is taken from a recent document explaining the RoC and the process for the 13th RoC. It identifies a "separate list of candidate substances from a specific RoC edition." Please explain how this list will be different from any other list, such as a list of substances nominated for review in the 13th RoC, or a list selected for a cancer evaluation or RoC Monograph?

A) In your response to a question about this subject in the hearing, you said you were unaware of any additional RoC categories - please explain how this new list of candidate substances is not a new category?
B) How will HHS prevent substances from being stigmatized simply by being added to this lower category without any justification or review?

24) The RoC lists substances that pose a potential hazard for cancer without including the estimated "cancer risks that individuals may face when encountering listed substances in their daily lives." How useful is this information to the public?

25) How does NTP adapt to advances in scientific methodologies as new methods and principles of study, evaluation, and analysis are discovered and established by the scientific community?

26) HHS' webpage notes that NTP received a request on October 26, 2009 from the Styrene Information and Research Center concerning the RoC Background Document for Styrene. NTP responded to the request on December 23, 2010, 14 months later. NTP then received an appeal on February 11, 2011, which was responded to on June 8, 2011, four months later.

A) HHS' guidance on Request for Corrections is to respond 60 to 90 days - why did it take so long to respond to the styrene RFCs?
B) Is this response rate typical?

27) In response to a question during the hearing, you indicated that NTP "looked at" 400 to 500 studies on styrene. However, in the final assessment, NTP relied on only a hand-full of studies to justify its listing decision on styrene.

A) Please elaborate on what you meant by "looked at." As part of your response, please describe how NTP assures that all scientific information impacting RoC reviews is consistently and transparently considered for its merits in assuring a high quality, evidence-based evaluation.

B) It appears that NTP does not have any published guidelines regarding how it "looks at" all studies on a particular chemical. How is the public to present any alternate views of how these studies should be interpreted and assessed as a group when NTP does not appear to disclose its methods or its thinking with regard to this matter?

C) How is the public to have confidence that NTP is following anything more than an *ad hoc* assessment of these studies?

28) In response to a question during the hearing, you stated that "there were three groups of expert witnesses who reviewed [the health effects of styrene], plus our Board of Scientific Counselors. There were votes taken at all of the expert groups, and of the 32 votes, 30 were for listing styrene."

A) A vote clearly was documented in the Expert Panel process, yet that Panel consisted of only 11 members. Please identify who cast the other 21 votes. As part of the response, please provide the names of everyone who voted, and how they voted, relative to the styrene listing.

29) Among the reviewers you noted on the Expert Panel for the styrene listing was Dr. Lauren Ziess of the California Environmental Protection Agency (CalEPA). Within roughly 10 days of NTP issuing its Styrene Background Document, the CalEPA office directed by Dr. Ziess issued a draft styrene technical document for its Public Health Goal program. Stakeholders have noted a similarity between the NTP and California documents in that the CalEPA document likewise focused on positive data, ignored or dismissed large amounts of the negative/null data, and did not substantively consider mode of action data. The CalEPA styrene document also concluded that styrene should be considered a "probable" human carcinogen -- essentially the same as "reasonably anticipated."

A) Given that Dr. Ziess concurrently had overseen an assessment of styrene that already had concluded styrene was a "probable" carcinogen, do you believe Dr. Ziess was in a position to openly and objectively provide input to the Expert Panel?

30) Does NTP have formal guidance or offer training to Expert Panel members regarding potential conflicts of interests (COI) associated with their participation on Expert Panels?

A) Does NTP require signed COI statements to be provided by Expert Panel members?

B) Does NTP staff make any effort to ascertain that COI might be present beyond the signed COI statements of Expert Panel members alone? For example, what steps do NTP staff take in cases where Expert Panel members have previously commented on studies and/or have a direct and personal connection to them?

31) In the case of the review of styrene for the 12th RoC, your staff appeared to reinterpret the data from a study by Dr. Elizabeth Delzell to support a listing of styrene. Dr. Delzell subsequently wrote NTP[4] objecting to the re-interpretation of her peer-reviewed data.

[4] Letter from Elizabeth Delzell, Sc.D., to Barbara Shane, Executive Secretary, NTP, BSC, NIEHS, Feb. 5, 2009

A) Did you, or a member of the NTP staff, ever formally mention this objection from Dr. Delzell to Secretary Sebelius? If yes, please explain when, in what context, and provide all supporting documents; if no, please explain why not.
B) In addition, in an October 22, 2010 letter from former Congressmen Rick Boucher and John Shadegg, you were questioned about a comment made in a meeting with them relative to the Delzell data that the reason it should not be peer reviewed was because it was "submitted to NTP over the phone." Your response to the Congressmen's letter does not address this comment at all. Please elaborate on this comment beginning with whether you, or someone on the NTP staff, made the comment, and if so, in what context. If you, or NTP staff, did not make the comment, then please state that for the record.

32) In response to a question regarding why you thought the listings of styrene and formaldehyde have generated controversy, you stated that they were high-volume use compounds but "we have had controversy on some of our listings in the past as well."
A) Please list all the substances that have been controversial in the past.
B) Please describe all actions NTP has taken as a result of controversies from substance listings.

33) How many full time dedicated NTP staff do you have who work on producing the RoC?
A) Please describe their background and job description.
B) How many contractors - full time and part time - did NTP hire for the 12th RoC?
C) Please provide the statement of work associated with this procurement.

34) What was the total cost of producing the 12th RoC? In your response, please provide a line-item breakdown of the amounts.
A) Please estimate the costs for the 13th RoC? Please provide a similar line-item breakdown as above with the estimated costs.

35) Is there any action that Congress can or should take that can help NTP with publication of the RoC, or are you satisfied with the current law, process and accompanying reports? For example, should Congress change the part of the law that requires the RoC to be published biennially?

Attachments

ATTACHMENT A

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, N.C. 27709
Website: www.niehs.nih.gov

May 27, 2009

Mr. John Tickle
President
Strongwell Corporation
400 Commonwealth Avenue
Bristol, Virginia 24201

Dear Mr. Tickle:

Thank you for your May 18 letter from Mr. Bill Kreysler and you. I appreciate you contacting me with your concerns regarding the proposed listing of styrene in the 12th Report on Carcinogens (RoC) as *reasonably anticipated to be a human carcinogen* and the impact it has on your companies.

The NTP understands the importance of effectively communicating information about the 12th RoC and all new listings when the report is published. We will work to ensure that our disseminations clearly explain the listing categories and what a listing in the RoC means, so that the public understands that a listing in the RoC is not regulatory although it may prompt regulatory agencies to consider limiting exposures or uses of a substance. Currently, the NTP has a "Questions & Answers about the RoC" on its Website (http://ntp.niehs.nih.gov/go/7249) that specifically addresses these topics.

The NTP is using an established, multi-step process that includes input from independent scientific panels and the public (*http://ntp.niehs.nih.gov/go/29353*), as well as specific criteria (*http://ntp.niehs.nih.gov/go/15209*) to evaluate styrene for the 12th RoC. We would welcome receiving from industry any peer-reviewed, publicly available publications for our consideration in this evaluation.

The RoC is an important public health document and I appreciate your interest in this matter.

An identical letter has been sent to Mr. Bill Kreysler.

Sincerely,

Linda S. Birnbaum

Linda S. Birnbaum, Ph.D., D.A.B.T., A.T.S.

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ATTACHMENT B

Enhance efficiency and transparency of the process and enable NTP to better meet the legal mandate for biennial release of the report

1. Separate list of candidate substances from a specific RoC edition

- List of candidate substances is dynamic
  - Not linked to specific RoC edition; accommodates adding new candidate substances or changing priority of ones on the list
  - Proposed listings for next RoC edition are those completed in the current RoC cycle. Other substances stay on list for future edition, allowing continuous review process between RoC editions

11

RESPONSE TO QUESTIONS FOR THE RECORD
for Charles A. Maresca

Responses to Questions submitted by Dr. Paul Broun

Question 1:

What is the role of the U.S. Small Business Administration's Office of Advocacy?

Answer 1:

The Office of Advocacy (Advocacy) is an independent voice for small business within the federal government. Advocacy was created by Congress in 1976 and is directed by the Chief Counsel for Advocacy, who is appointed by the president and confirmed by the U.S. Senate.

Advocacy produces independent economic research on small business and the economy, and represents small businesses before the federal agencies, the White House, and Congress.

The Regulatory Flexibility Act (RFA) and Executive Order 13272 require federal agencies to determine the impact of their rules on small entities, consider alternatives that minimize small entity impacts, and make their analyses available for public comment. Advocacy attorneys work with federal regulators to ensure that these obligations are met and convey how small entities might be disproportionately impacted by federal regulatory actions.

As the independent voice for small business, Advocacy also frequently is involved in non-regulatory matters affecting small business.

Question 2:

Were representatives of the National Toxicology Program (NTP) invited to attend and participate in the Office of Advocacy March 16, 2012 roundtable on environmental issues at which the NTP's Report on Carcinogens was discussed? Did a representative from NTP attend?

Answer 2:

Dr. John Bucher, the director of the National Toxicology Program (NTP), received both written and verbal invitations to participate in a July 28, 2011 roundtable on RoC, which included a discussion of styrene. He declined to participate. The Advocacy Environmental Roundtable regularly invites participation from government agencies and Environmental Protection Agency (EPA) officials frequently appear at Advocacy roundtables. During 2011, Advocacy had several discussions with the Department of Health and Human Services (HHS) and NTP personnel about RoC.

Question 3:

Based upon the Office of Advocacy's experience with the regulatory process, please explain the value of the public comment process.

Answer 3:

The public comment process is valuable because it ensures that all stakeholders can participate in the rulemaking process. This process was strengthened by Executive Orders 13563, 13579, 135609, and recently 13610. Further, public comments maximize the amount of information available to the agency on which to base its rule.

Advocacy has extensive experience with the regulatory process through its involvement with agency rulemakings. This experience has provided Advocacy with first-hand knowledge of the importance of the public comment process, and the need for public participation in government rulemaking and other activities that affect the public. Further, because public comment is the primary method by which small businesses can contribute to the RoC's preparation process, it is important that such opportunities be meaningful and include timely response by the agency to the public comment.

Not only does the public comment process afford all interested stakeholders an opportunity to participate in rulemakings that will have a direct impact on them, but it also provides the agencies with important and useful information they might not have been aware of or could not access. During agency rulemakings, agencies frequently request additional information through the Federal Register on certain aspects of the rule. Without the public comment process most agencies cannot assess accurately impacts of a rulemaking on stakeholders before finalization of the rule.

Question 4:

What concerns does the Office of Advocacy have with the public comment process used by the NTP?

Answer 4:

Advocacy's concerns with the public comment process used by NTP are threefold. First, NTP did not provide response to public comments until after the publication of the 12th RoC. There was no opportunity for the public to address NTP's responses.

Second, it is unclear whether NTP or the Expert Panel seriously considered the numerous public comments which outlined the differences between the NTP findings and the findings of other federal and international science bodies. In NTP's response to comments document released following the publication of the 12th RoC, NTP indicates that it did not respond to all comments. NTP writes, "The NTP did not respond to comments on (1) the final background document, (2) the review process, or (3) non-technical or non-scientific issues, and only responded to specific issues for the expert panel report that are applicable to the final substance profile." To produce a

thorough response to comments NTP should address all comments, especially those comments pertaining to such important issues as the final background document and the review process.

Third, NTP has removed the requirement to respond to public comments for the current 13th RoC preparation process entirely. A public comment process cannot be meaningful without responses to comments. Not responding to comments decreases the transparency of the preparation process and creates the impression that NTP does not truly consider public comments.

Question 4(A):

If an agency merely acknowledges receipt of public comments, does the Office of Advocacy consider that an adequate response?

Answer 4(A):

No.

Question 4(B):

If not, what kind of response to comments shows that an agency has considered substantive concerns and issues raised by interested parties?

Answer 4(B):

To show that an agency has considered the substantive concerns and issues raised by all interested stakeholders, an agency should provide both substantive written responses to comments as well as further opportunities for stakeholders to respond to NTP comments. Response to comments should resemble a dialogue between the agency and its stakeholders. Response should be provided by NTP throughout the process.

Question 5:

What concerns does the Office of Advocacy have with the RoC's delisting process?

Answer 5:

Advocacy is concerned that either there is no established delisting process or that if there is an established process, the process is not transparent. As outlined in Advocacy's written testimony, it took 12 years to delist glass wool as "reasonably anticipated to be a human carcinogen."

Moreover, instead of delisting the substance in the 12th RoC, NTP modified the definition of glass wool to exclude certain types of glass wool that are "not biopersistent" in the lung. In the 12th RoC, "certain glass wool fibers (inhalable)" is still listed. Both NTP and the public would be better served if NTP would establish and publish a robust and explicit delisting procedure.

Question 6:

Please discuss the effects of multiple agencies producing substance hazard characterization and risk assessments.

Answer 6:

Multiple agencies producing chemicals assessments may lead to confusion for all stakeholders: the public, businesses and the government. This confusion is attributable to agencies employing different labels and labeling systems. It is most acute, however, when one agency labels a chemical as a carcinogen while another does not. Although these programs purport to use different scientific methods and serve different purposes, this is not obvious to the public. Given the enormous public resources devoted to understanding chemicals among various agencies, it makes sense to place resources into the most robust practices.

Responses to Questions submitted by Rep. Brad Miller

Question 1(A):

In response to a question at the hearing, you stated:
"We did hear from a number of small businesses and their representatives that there was a problem with the 12th RoC. When we looked into it, we realized that there was going to be an impact on small business as a result of the listing of those substances, and as a result we sent that letter [comment letter to the National Toxicology Program regarding the Report on Carcinogens]."

A) Please provide a complete account of all contacts from any kind of businesses or their representatives regarding the 12th RoC. Please provide a list that:
   i. shows date of contact;
   ii. method of contact;
   iii. the name of the person and the company, association or other firm that the person was with;
   iv. the nature of their communication (in support of proposal or process, against proposal or process, concerned, however you want to characterize it).

Answer 1(A):

There are many ways that Advocacy performs outreach with small businesses. One of the most significant ways is through roundtables.

Advocacy held three roundtables where the RoC was discussed. RoC was formally on the agenda for roundtables on the July 29 2011, and March 16, 2012, and was raised by participants on May 5, 2011.

On average 50 individuals, small-business trade organization representatives, businesses and science consultants attend Advocacy Environmental roundtables to listen to the speakers and to

participate in the ensuing discussion. Advocacy estimates in total about 80 people were involved in the RoC-related roundtables. A list is provided below.

Advocacy also reaches out to trade associations and directly to small businesses through email, telephone calls, and in-person meetings. Small businesses and trade associations also will contact the office to discuss issues impacting their firms.

Advocacy staff met with styrene users on November 16, 2011. This included Ms. Lori Miles-Luchak, president of Miles Fiberglass and Composites Management and members of the American Composites Manufacturing Association. Advocacy met with representatives of styrene users from The Policy Navigation Group on January 20, 2012 and subsequently had several telephone conversations with them.

Advocacy staff also attended via teleconference the RoC Review Process listening session on November 29, 2011 and the NTP's Board of Scientific Counselor's meeting on December 15, 2011.

Advocacy staff attended a March 22, 2012 workshop on Capitol Hill focused on how the federal government uses scientific data to make hazard and exposure assessments for certain chemicals and other substances, and the regulatory and non-regulatory impacts of these assessments on the marketplace. During this time Advocacy spoke with the Napthalene Council and the Kitchen Cabinet Manufacturers Association for their perspectives on the RoC's listing of naphthalene and formaldehyde, respectively.

Advocacy has not been contacted by small businesses or small-business representatives that are in support of the RoC process.

Environmental Roundtable Participants

Name	**Affiliation**
Theresa Pugh	American Public Power Association
Jamie Conrad	Conrad Counsel
Laura Brust	American Chemistry Council
Diane Schumacher	Schumacher Partners
Randy Schumacher	Schumacher Partners
Dick Titus	Kitchen Cabinet Manufacturers Association
David Dunlap	Koch Industries
Charlie Grizzle	Grizzle Co.
Tawny Bridggford	National Mining Association
Laurie Holmes	American Forest and Paper Association
Darrel Smith	
Rich Bozek	Edison Electric Institute
Stephanie Castorina	IPC
Timothy Serie	American Coatings Association
Therese Cirone	The Chorine Institute

Ann Mason	American Chemistry Council
Richard Belzer	Regulator Checkbook
Jane Luxton	Pepper Hamilton
William Walsh	Pepper Hamilton
Jeff Hannapel	The Policy Group
David Fisher	Star Power
Phil Wakelyn	Consultant
Norman Birchfield	EPA
Steve Via	EPA
Steven Lamm	Consultants in Epidemiology and Occupational Health
Heidi King	House Energy and Commerce Committee
Troy Hillier	Policy Navigation
Dan Moss	Society of Chemical Manufacturers and Affiliates
Fern Abrams	IPC
Ellie Zahirieh	SBA
Burleson Smith	United Fresh
Mark Collatz	Adhesive and Sealant Council
Tim Hunt	American Forestry and Paper Association
Lisa Goldberg	Aerospace Industries Association
John Schweitzer	American Composite Manufacturers Association
Chuck Elkins	IPC
Jack Snyder	Styrene Information Research Center
Bob Reiley	Comcast
Bob Fronczak	Association of American Railroads
John Arnett	Kelley Drye & Warren
Keith Holman	National Lime Association
Tony Russo	National Lime Association
Anne LeHuray	Naphthalene Council
Jack Waggener	URS Corporation
Tim Brown	Consumer Specialty Products Association
Robert Collette	Institute of Shortening and Edible Oils
Todd Stedeford	EPA
Charles Franklin	Akin Gump Strauss Hauer & Feld
Joanne Thelmo	American Cleaning Institute
Phil Moffat	Verdent Law
Martha Manapese	Keller Heckman and Heckman
Danielle Jones	OMB
Lester Facey	EPA
Mara Kinter	Specialty Graphic Imaging Association

This list reflects participants from the May 5 and July 29, 2011, and March 16, 2012 roundtables. An attendance list for the June 22, 2011 meeting could not be located. Advocacy does not have the ability to identify the roughly 10 to 30 people who participated in each roundtable by telephone.

Question 1(B):

Please provide a description of what steps were taken by the independent Office of Advocacy to "look into" the 12th RoC, and how the office determined that there would be an "impact on small business."

Answer 1(B):

As described in the answer to Question 1(A), Advocacy determines impacts by meeting and speaking with the small businesses and their industry representatives that are directly impacted, or expect to be directly impacted, by government rulemaking and other regulatory activities.

Advocacy performs this outreach in a number of ways. One of the most significant methods is through roundtables. Advocacy held three roundtables devoted to federal government science processes. Advocacy estimates in total about 80 people were involved in the RoC-related roundtables. Please see the answer to question 4(C) for more information.

Advocacy also reaches out to trade associations and directly to small businesses through email, telephone calls, and in-person meetings. Small businesses and trade associations also will contact the office to discuss issues impacting their firms.

Advocacy was not contacted by a single small business or small-business representative who was in support of the RoC process.

Question 2:

We heard at the hearing that not all small businesses view the Office of Advocacy's intervention on the 12th RoC to be in their interests—in fact, it appears that for the green chemistry segment of the chemicals market, the Office's actions may be counter-productive. Please describe in detail the steps taken by the Office to determine that an intervention in this case was, on net, in the interests of America's small business.

Answer 2:

Advocacy does not believe that its comments on the 12th RoC were counterproductive for the green-chemistry segment of the chemicals market. Advocacy strives to act as the voice of all small businesses and also takes the public interest into account. All businesses benefit from robust and accurate scientific determinations.

Further, during the witness testimony of Ms. Ally La Tourelle, the representative of a green chemistry small business, Ms. La Tourelle twice mentioned that the "ongoing reporting of carcinogens has a negligible impact on competition" in the 21st century.

Question 3:

You argued that NIEHS/NTP "can do a weight-of-evidence analysis during the [RoC] process, looking more completely at the contradictory data as well as the data that supports the listing." Does the Office of Advocacy routinely use a similar analytical approach to determine when to intervene on a regulatory or, as in this case, non-regulatory matter so that the net effects for American small businesses are positive? If not, why not?

Answer 3:

Scientists employ the weight-of-evidence analysis to review multiple studies that have conflicting scientific outcomes. A weight-of-evidence analysis cannot be applied to regulatory analyses. Therefore, Advocacy does not base its decisions on a weight-of-evidence analysis. Advocacy does rely on scientists to make such determinations, however. Advocacy agrees with the National Academy of Sciences that the weight-of-evidence approach is more appropriate to use in hazard assessments than other approaches, such as the "strength of evidence" approach employed by NTP.

Question 4:

If the Office does not have a method for determining that an advocacy position of the Office would be a net benefit to small businesses:

A) How does the Office determine when to intervene and on what side?

B) What evidence is collected by the Office?

C) What notifications are made to the public or to other sectors of industry regarding the Office's development of a position?

D) What transparency steps does the Office take to inform the public and other small businesses that it is considering taking a position, and then the communications and other means used to express that position?

Question 4(A):

How does the Office determine when to intervene and on what side?

Answer 4(A):

Advocacy's authorizing statute requires the office to serve as a focal point for concerns about the policies and activities of federal agencies that affect small businesses, and to represent the views and interests of small businesses before the federal agencies whose policies and activities may affect small business.

Advocacy routinely comments on federal agencies' regulations and on federal activities that are not regulations. For example, within the last two years Advocacy has commented on issues related to the length of time it takes the Food and Drug Administration to approve new and innovative medical devices for introduction into the marketplace, reports issued by the Administrative Conference of the United States on potential changes to the regulatory process, and issues presented by the Financial Accounting Standards Board.

Question 4(B):

What evidence is collected by the Office?

Answer 4(B):

Advocacy identifies small-business concerns by speaking directly with stakeholders. For several decades, Advocacy has solicited input from small businesses, the public and federal agencies in the formulation of public policy. Advocacy also reviews the relevant documents from federal agencies and the public. Advocacy strives to act as a voice for all small business.

Advocacy looks for evidence of a direct economic impact of a regulation, policy or program on small businesses. For example, from meeting and speaking with small businesses, Advocacy learned that the direct economic impacts for styrene-related small businesses included difficulty finding and keeping employees as well as higher insurance premiums. Additionally, Advocacy reviewed many documents from the styrene proceeding, most of which are cited in the November 2011 letter. Please see our answer to question 6(C) for a list of these documents. As stated in the answer to Question 1, Advocacy staffers met with styrene users on November 16, 2011, and representatives for styrene users on January 20, 2012.

Advocacy staff also attended via teleconference the RoC Review Process listening session on November 29, 2011 and the NTP's Board of Scientific Counselor's meeting on December 15, 2011.

Advocacy staff also attended a March 22, 2012 workshop on Capitol Hill focused on how the federal government uses scientific data to make hazard and exposure assessments for certain chemicals and other substances, and the regulatory and non-regulatory impacts of these assessments on the marketplace.

Finally, Advocacy also had contacts with HHS and NTP regarding both the formaldehyde and styrene RoC determinations.

Question 4(C):

What notifications are made to the public or to other sectors of industry regarding the Office's development of a position?

Answer 4(C):

Advocacy held three roundtables devoted to RoC or related science process issues. Often, the appropriate federal agency attends Advocacy's public roundtables.

In this instance, Advocacy invited the NTP to participate at a roundtable in July 28, 2011, and NTP declined.

Advocacy also had several email exchanges and oral conversations with NTP and HHS during 2011. In preparation for the recent hearing, NTP Congressional staff met with Advocacy staff.

Question 4(D):

What transparency steps does the Office take to inform the public and other small businesses that it is considering taking a position, and then the communications and other means used to express that position?

Answer 4(D):

Advocacy's comment letters are public. They are available on the Advocacy website. The comment letters also are distributed to the more than 12,000 recipients on the Advocacy regulatory listserv.

Also, Advocacy annually submits its report on the Regulatory Flexibility Act (RFA), which details the office's regulatory activities, to Congress. To view electronic copies of Advocacy's RFA Annual Reports from FY 2001 to FY 2011, please visit the Advocacy website at http://www.sba.gov/advocacy/823/4798.

Finally, Advocacy seeks input from small-business stakeholders through roundtables and meetings when an agency's proposed rule, policy, or program has a potential to impact small businesses.

Question 5:

In response to a question about impacts from the RoC on your workplace, you responded that:

> *"a new listing to the RoC would require changes to manufacturers' safety data sheets."*

It is true that listing as a "known" or "reasonably anticipated" carcinogen does require language in Manufacturers Safety Data Sheets (MSDS) reflecting this listing. However, staff have reviewed numerous MSDS materials available through a simple Google search. Almost invariably, those sheets - some going back to 1990 - already discuss the possibility that Styrene could be a carcinogen. There is also ample scope for a firm to directly address their views on the weight of evidence regarding the science.

A) Was your office aware that most MSDS's on Styrene already discuss the carcinogenicity of styrene (particularly since the IARC "possible" carcinogen determination)?

B) Was your office aware that firms are allowed to directly address their views on the weight-of-evidence in their MSDS's in ways that can minimize concerns among workers in their business?

C) Did your office make any effort to determine whether there were already existing carcinogens (such as formaldehyde, for example) in these same workplaces the presence of which would undercut concerns that workers and neighbors may suddenly be worried about the health consequences of working or living near the company?

Question 5(A):

Was your office aware that most MSDS's on Styrene already discuss the carcinogenicity of styrene (particularly since the IARC "possible" carcinogen determination)?

Answer 5(A):

Based on the views of small businesses, Advocacy believes that there is an important distinction between a "possible carcinogen," the International Agency for Research on Cancer (IARC) designation, and a RoC listing of "reasonably anticipated" to be a carcinogen. This is particularly the case when the available evidence suggests the risk of human cancer is limited. Advocacy was aware that the IARC listing of "possible carcinogen" already was required.

Question 5(B):

Was your office aware that firms are allowed to directly address their views on the weight-of-evidence in their MSDS's in ways that can minimize concerns among workers in their business?

Answer 5(B):

Advocacy does not believe that a Safety Data Sheet is an effective mechanism for assuaging the public about potentially alarming language regarding the NTP designation.

Question 5(C):

Did your office make any effort to determine whether there were already existing carcinogens (such as formaldehyde, for example) in these same workplaces the presence of which would undercut concerns that workers and neighbors may suddenly be worried about the health consequences of working or living near the company?

Answer 5(C):

Advocacy does not believe that concerns about other chemicals assuage concerns about styrene that are not warranted by the evidence.

Question 6:

In response to a question regarding the similarity between your Office's criticism of the 12th RoC and that of representatives of the styrene industry, you stated:

> *"I am not as familiar with the, all of the criticisms of the styrene industry. They were among the small businesses who did come to our office to suggest that there were problems with the 12th RoC."*
>
> *In response to a follow-up question that stated, "So your testimony today, your criticisms have come to you from the styrene industry. Is that correct?"*
>
> *In response, you replied: "In part. Yes."*

Question 6(A):

Are there any contacts, from small businesses, other-sized businesses, associations, firms or think tanks that are not listed in response to Question 1 above that informed your Office's position on the 12th RoC?

Answer 6(A):

No.

Question 6(B):

If the answer to 6A is "yes," please provide a complete accounting of those contacts in the same format as requested in Question 1 above

Answer 6(B):

N/A

Question 6(C):

Please make clear all sources of information the Office relied upon in developing its position on the 12th RoC as reflected in the letter from Chief Counsel Sargeant to Secretary Sebellius and the Office's testimony.

Answer 6(C):

1. The original requirement for this report was established in November 1978 by the Community Mental Health Center Act, Amendments, Section 262, Public Law 95-622, Part E (pp. 3435-3436). An amendment in 1993 (42 US Code 241) substituted a biennial report for an annual report in the introductory provisions.

2. U.S. Department of Health and Human Services, National Toxicology Program, http://ntp.niehs.nih.gov/?objectid=72016262-BDB7-CEBA-FA60E922B18C2540.
3. Office of Technology Assessment, *Identifying and Regulating Carcinogens,* Washington, D.C.: U.S. Government Printing Office, 1987.
4. U.S. Department of Health and Human Services, National Toxicology Program, http://ntp.niehs.nih.gov/?objectid=3756DE0C-FA7A-404B-3F72194C30ABD961.
5. National Toxicology Program (NTP) Final Process for Preparation of the Report on Carcinogens (RoC), 77 Fed. Reg. 1707 (Jan. 11, 2012), *available at* http://ntp.niehs.nih.gov/NTP/PressCtr/FRN/2012/77FRN7ROC20120111.pdf.
6. U.S. Department of Health and Human Services, National Toxicology Program, http://ntp.niehs.nih.gov/?objectid=C3265922-AFC1-098A-6BDE6B05F18DE4AC.
7. Request for Public Comment on Nominations and Call for Additional Nominations to the Report on Carcinogens, 77 Fed. Reg. 2728 (Jan. 19, 2012), *available at* http://www.gpo.gov/fdsys/pkg/FR-2012-01-19/pdf/2012-875.pdf.
8. Consolidated Appropriations Act, 2012 of 2011, Pub. L. No. 112-74.
9. National Toxicology Program, U.S. Department of Health and Human Services, Report on Carcinogens, Twelfth Edition (2011).
10. Lorenz R. Rhomberg, Principal, Gradient Principal Environmental Consultants, Comments to the National Toxicology Program, Report on Carcinogens, Twelfth Edition Proposed Review Process (Nov. 29, 2011), *available at* http://ntp.niehs.nih.gov/NTP/About_NTP/BSC/2011/December/PublicComm/Rhomberg20111202.pdf.
11. Safe Drinking Water and Toxic Enforcement Act of 1986, 1986 Cal. Stat. *available at* http://oehha.ca.gov/prop65/law/pdf_zip/P65LAW72003.pdf.
12. Exec. Order No. 13,563, 76 Fed. Reg. 32,088 (Jan. 18, 2011), *available at* http://www.gpo.gov/fdsys/pkg/FR-2011-01-21/pdf/2011-1385.pdf.
13. Memorandum for the Heads of Executive Departments and Agencies on Scientific Integrity, 1 PUB. PAPERS 1013 (Mar. 9, 2009), *available at* http://www.whitehouse.gov/the_press_office/Memorandum-for-the-Heads-of-Executive-Departments-and-Agencies-3-9-09/.
14. Proposed National Toxicology Program (NTP) Review Process for the Report on Carcinogens: Request for Public Comment and Listening Session, 76 Fed. Reg. 67,200 (Oct. 31, 2011), *available at* http://ntp.niehs.nih.gov/ntp/PressCtr/FRN/2011/76FRN210ROC20111031.pdf.
15. C. Richard Titus, Executive Vice President, Kitchen Cabinet Manufacturers Association, Presentation to Small Business Administration, Office of Advocacy Roundtable: Formaldehyde in the 12th Report on Carcinogens (Jul. 28, 2011).
16. European Chemicals Agency, European Union Risk Assessment Report: Styrene (2008), *available at* http://echa.europa.eu/doc/trd_substances/styrene/rar/trd_rar_uk_styrene.pdf.
17. Boffetta *et al*, *Epidemiologic Studies of Styrene and Cancer: A Review of the Literature*, 51 J Occup Environ Med. 1275, 1275-87 (2009).
18. Letter from Elizabeth Delzell, Researcher, University of Alabama, to Barbara Shane, Executive Secretary, Board of Scientific Counselors, National Toxicology Program (Feb. 5, 2009), *available at* http://www.box.net/shared/static/slm4m8tp7a.pdf.
19. International Agency for Research on Cancer [IARC], World Health Organization [WHO], *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Some*

Traditional Herbal Medicines, Some Mycotoxins, Naphthalene and Styrene, (2002), *available at* http://monographs.iarc.fr/ENG/Monographs/vol82/mono82-9.pdf.
20. Press Release, Jack Snyder, Executive Director, Styrene Information and Research Center, Styrene Industry Will Contest Vigorously the Unwarranted listing of Styrene in 12th Report on Carcinogens (Jun. 10, 2011), *available at* http://www.styrene.org/news/pdfs/06-10-11-statement-ntp-listing.pdf.
21. National Academy of Sciences, National Research Council, Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde (Apr. 8, 2011), *available at* http://www.nap.edu/catalog.php?record_id=13142#toc.
22. Richard B. Belzer, The Report on Carcinogens: What Went Wrong; What can be Done to Fix It 1 (Jan. 2012), *available at* http://www.rbbelzer.com/uploads/7/1/7/4/7174353/111103_regcheck_working_paper_on_roc.pdf.
23. National Toxicology Program, Department of Health and Human Services, NTP Report on Carcinogens Review Process Schematic (Nov. 11, 2011), *available at* http://ntp.niehs.hin.gov/images/12thprocess-large.jpg.
24. Bergeson & Campbell PC, NTP Proposes to Revise RoC Review Process (Nov. 1, 2011), *available at* http://www.lawbc.com/tsca/memoranda-2011-51-mobile.html.
25. Letter from Jack Snyder, Executive Director, Styrene Research and Information Center & John Schweitzer, Senior Director – Government Affairs, American Composites Manufacturers Association to the Kathleen Sebelius, Secretary, U.S. Department of Health and Human Services (May 24, 2011), *available at* http://www.styrene.org/news/pdfs/05-24-11-letter-to-HHS.pdf.
26. Letter from Cal Dooley, President and CEO, American Chemistry Council, to David Lane, Assistant to the President and Counselor to the White House Chief of Staff and Cass Sunstein, Administrator, Office of Information and Regulatory Affairs, Office of Management and Budget (Sep. 21, 2011).
27. National Toxicology Program, Department of Health and Human Services, Proposed Review Process for the Report on Carcinogens (Nov. 16, 2011).

Question 7:

Your office was created to be a voice in government for small businesses that did not have the resources of larger companies to push their concerns before the government. How does your office verify that companies contacting your office for help are truly "small?"

Answer 7:

Advocacy uses the "Table of Small Business Size Standards" established by the Small Business Administration to determine whether businesses contacting the office for help are indeed small business. Since, under the size standards, small businesses constitute 99 percent of all businesses, in most cases, it is generally unnecessary to verify the exact size of a business. When this is an issue, Advocacy verifies with the affected company by requesting the number of employees or sales. This commonly occurs when the office must verify the small-business status for Small Business Advocacy Panel proceedings at the Environmental Protection Agency, Occupational Safety and Health Administration, or Consumer Financial Protection Bureau.

The Dow Chemical Company
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USA

June 21, 2012

John Serrano
Research Assistant
Committee on Science, Space, and Technology
Subcommittee on Investigations and Oversight
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John.Serrano@mail.house.gov

Re: Response to *Questions For The Record, "How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"*

Dear Mr. Serrano:

Thank you for your Email of May 23, 2012, in which you asked for a response to twelve questions regarding my April 25, 2012, testimony before the U.S. House of Representatives Committee on Science, Space, and Technology, Subcommittee on Investigations & Oversight and Committee on Small Business, Subcommittee on Healthcare and Technology.

As indicated in both my oral and written testimony, I participated in this hearing as a representative of the Styrene Information and Research Center (SIRC), of which my employer (The Dow Chemical Company) is a founding member. Similarly, my answers to the *Questions For The Record* are also respectfully submitted on behalf of SIRC.

The industry I represent appreciates the opportunity to provide our perspective on the Report on Carcinogens.

Best regards,

James S. Bus, PhD, DABT, ATS
JSBus@dow.com

1. **What value does the *RoC* provide – in other words, in what way is the *RoC's* contribution to science or the public's understanding of substance hazards unique?**

Given the significant concerns regarding the *Report on Carcinogens (RoC)* outlined in my public testimony,[1] the *RoC* as currently implemented provides little if any unique contribution to understanding potential cancer hazards. The *RoC* is largely redundant to significantly more robust and transparent cancer evaluations that have emerged since the original Congressional commissioning of the *RoC* in 1978, *e.g.*, those implemented by the U.S. Environmental Protection Agency (EPA). Although the *RoC* deserves credit for providing useful information in its early years, it has not kept pace with advances in evidence-based evaluation processes designed to produce scientifically credible and transparent cancer reviews.

The *Congressional Record* indicates that it was Congress' intent that the *RoC* was to only identify serious carcinogenic concerns. This is made clear in the Joint House-Senate Comparative Summary:

> *"...the phrase 'suspected carcinogens' [was replaced] with 'substances... reasonably anticipated to be carcinogens', in order to make it absolutely clear in the statute that there must be reasonable ground for designating a substance as a putative carcinogen."*[2]

Indeed, the final Congressional language departed from earlier proposals that would have expansively listed substances as "suspect" carcinogens based on much looser criteria, such as "sound theoretical grounds."[3]

The *RoC* was not intended to list substances as carcinogens that fell short of being "a putative carcinogen." Accordingly, the *RoC* only called for listing substances that met criteria for "putative" carcinogens, namely substances that were:

- "Known to be a human carcinogen" or
- "Reasonably anticipated to be a human carcinogen."

Classification based on looser criteria, such as "sound theoretical grounds," was not intended.

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[1] Written Testimony provided to the U.S. House of Representatives' Committee on Science, Space & Technology, Subcommittee on Investigations & Oversight and Committee on Small Business, Subcommittee on Health Care & Technology, Joint Hearing: "How the *Report on Carcinogens* Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs," James S. Bus, PhD, DABT, ATS; The Dow Chemical Company, April 25, 2012, http://science.house.gov/sites/republicans.science.house.gov/files/documents/hearings/HHRG-112-SY21-WState-JBus-20120425.pdf.

[2] Joint House-Senate Comparative Summary and Explanation of Title II of H.R. 12460 and H.R. 12347, as Reported by the Committee on Interstate and Foreign Commerce, the Senate Bill, S. 2450, and the House Amendment in the Nature of a Substitute. *124 Congressional Record H38657* (1978) (statement of Rep. Rogers).

[3] *124 Congressional Record H34938* (1978) (statement of Rep. Rogers).

NTP's recently published 12th *RoC* includes a large number of substances as "reasonably anticipated" carcinogens for which the scientific evidence is far more "theoretical" than "putative." Indeed, I believe that such substances, including styrene, should not be classified as they currently are in the *RoC* because the evidence supporting a cancer hazard falls short of what Congress intended.

In its current form, the *RoC* at best can be said to be similar to an initial screening tool which provides only a very preliminary and non-definitive indication of the potential for a substance to be considered to be a carcinogen. In contrast, the hazard and risk assessment approaches taken by a number of other Federal agencies (US EPA, FDA, ATSDR, etc.) incorporated more current, transparent, rigorous and sophisticated evidence-based assessment principles as the science of chemical risk and hazard assessment matured. Unfortunately, however, over this same period of time, the *RoC* has remained largely static; its simplistic assessment process lacks scientific rigor and clarity in a world where highly sophisticated research and risk/hazard assessment methods are now available.

The disparity between the *RoC* and other cancer assessments is demonstrated in a straightforward way. The entire process for *RoC* assessments is documented in just four pages of discussion and one process diagram,[4] whereas the U.S. Environmental Protection Agency's "Guidelines for Carcinogen Risk Assessment" includes 166 pages. The EPA clearly details the steps for how data must be identified, assessed, documented, weighed and transparently vetted.[5]

For substances such as styrene, which have robust, high quality scientific databases, the *RoC* process as currently practiced is not able to provide a useful indicator of actual hazards to the American public, and can, through scientifically unjustified listings, create public and worker safety concerns where none are warranted by the science.

2. Can you please explain how people can be exposed to styrene through natural substances like cinnamon, versus a manufactured container made of Styrofoam?

Styrene is a naturally occurring constituent of some foods – for example, strawberries, coffee, beef, nuts, beer and cinnamon.[6] In fact, styrene was first detected and isolated from a natural source in 1839 – the benzoin resin of the Turkish sweetgum tree (*Liquidambar orientalis*) – before being synthetically produced.[7] Regardless of source of exposure, either natural or synthetic, the

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[4] *Process for Preparation of the Report on Carcinogens*, 11 Jan 2012, http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.

[5] *Guidelines for Carcinogen Risk Assessment*, Risk Assessment Forum, United States Environmental Protection Agency, 166 pages, 2005, http://www.epa.gov/raf/publications/pdfs/CANCER_GUIDELINES_FINAL_3-25-05.PDF.

[6] NTP-CERHR Expert Panel Report on the Reproductive and Developmental Toxicity of Styrene," Appendix 2, Table 5, p. 11-7, June 2005, http://ntp.niehs.nih.gov/ntp/ohat/styrene/Styrene_final.pdf.

[7] Wünsch, J.R., "Polystyrene: synthesis, production and applications," *Rapra Review Reports*, p. 6, v. 10, no. 4, 2000.

potential human health risks of chemicals like styrene must consider the "dose" which people consume. Thus, for polystyrene food and beverage containers, the Food and Drug Administration has robust analytical and risk review processes for assuring that the "dose" of any chemicals potentially leaching from food and beverage containers do not present human health risks to consumers.

3. Do you believe the process Dr. Birnbaum described at the hearing would lead to an accurate characterization of the cancer potential for substances?

No. As Dr. Bimbaum stated in her testimony before the Joint Committee, "[the *RoC*] is not a risk assessment document."[8]

The process described by Dr. Birnbaum includes only the very most basic and fundamental components of a screening assessment for a carcinogenic hazard and is seriously out-of-date (see answer to Question 1). NTP's *RoC* process does not adequately document or provide for the necessary transparency and scientific robustness that is core to state-of-art evidence-based reviews, and which is critically necessary in order for NTP to reach its classification listing decisions. Additionally, the *RoC* process lacks the detailed checks and balances that are standard in current hazard assessment processes.

In her testimony, Dr. Birnbaum also stated:

> "The listing criteria specify the level of evidence that must be met in order for a substance to be listed in the Report in either category. For a substance to be listed in the *known* category, there must be sufficient evidence from studies in humans that indicates a causal relationship between exposure to the substance and human cancer. In brief, for a substance to be listed in the *reasonably anticipated* category, the level of evidence can be based on one of three scenarios:
>
> 1) Limited evidence of carcinogenicity from studies in humans or
> 2) Sufficient evidence of carcinogenicity from studies in experimental animals or
> 3) Evidence that a substance is a member of a class of substances already listed in the Report or that it causes biological effects known to lead to the development of cancer in humans"[9] (emphasis in original).
>
> The conclusion to list a substance in the Report is based upon scientific judgment with NTP giving consideration to all relevant data and to input from the advisory groups and the public."

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[8] Testimony Before the Science, Space, & Technology Committee's Subcommittee on Investigations and Oversight and the Small Business Committee's Subcommittee on Healthcare and Technology , United States House of Representatives, *The Report on Carcinogens*, Statement of Linda Birnbaum, Ph.D., D.A.B.T., A.T.S., Director, National Institute of Environmental Health Sciences, National Institutes of Health, and Director, National Toxicology Program U.S. Department of Health and Human Services, 25 Apr 2010, p. 2, http://science.house.gov/sites/republicans.science.house.gov/files/documents/hearings/HHRG-112-SY21-WState-LBirnbaum-20120425.pdf.

[9] *Ibid.*, p. 4.

What Dr. Birnbaum did not state was that this essentially is the extent of the public details about how NTP considers data – NTP's entire written *RoC* process provides little more detail than did Dr. Birnbaum's own statement to the Joint Committees. There simply is no definition to quantify even simplistically how data are weighed – again, in dramatic contrast to the level of scientific scrutiny required by EPA.

The recently updated NTP process states "The *RoC Monograph* has ... a cancer evaluation component that reviews all information that may bear on a decision, assesses its quality and sufficiency for reaching a listing decision...", "...with consideration of all inputs to its development ..." (this includes all public comments), and will seek "external scientific input, as needed."[10] However, the fact is that the way NTP will do this is not adequately detailed, thus leaving most steps of the evaluation process to the Agency's discretion, and largely absent any verification by independently-commissioned external peer reviewers.

The NTP process, both for the 12th *RoC* and as newly updated, simply does not provide for, or document, a complete, transparent, and externally validated review of the full database on a substance, and thus leaves NTP's process open to deficiencies, inaccuracies and biases, given that the process fundamentally is completely internal to NTP. This is neither an appropriate, nor a scientifically valid approach for a Federal government agency to conduct critical assessments or make its classification determinations.

4. **Regarding styrene, if you believe NTP mischaracterized its listing in the 12th *RoC*, could you tell us specifically how they got it wrong?**

Yes. At various stages during the12th *RoC* review, several industry representatives, including myself, provided testimony and written comments to NTP regarding concerns about NTP's proposed *RoC* listing of styrene. NTP was advised that an evidence-based review of the science did not meet the minimum requirements for listing styrene as "reasonably anticipated to be a human carcinogen." The testimony and comments also indicated that industry did not believe that NTP accurately applied its own guidelines in listing styrene.[11] This information can be found in NTP's public record for its review of styrene.[12]

This failure to meet even NTP's minimum requirements is in large part due to the fact that NTP placed significant emphasis in its listing justification on studies for both human and animal evidence where NTP chose to conclude that certain published studies supported cancer findings that the authors had not reported.

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[10] *Process for Preparation of the Report on Carcinogens*, 11 Jan 2012; pp. 2-3, 4 & 5, http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.

[11] "Meeting Presentations – Feb. 24, 2009 BSC, *Report on Carcinogens (RoC)*: Peer Review of Draft Substance Profiles, Draft Substance Profile on Styrene," http://ntp.niehs.nih.gov/index.cfm?objectid=576ED5D4-F1F6-975E-771445374E536BE4.

[12] See 12th *RoC* public comment docket with SIRC and other comments: http://ntp.niehs.nih.gov/index.cfm?objectid=20A477F2-F1F6-975E-7472FC6B0DA56D9C#styrene.

For two of the key styrene studies which NTP used to meet its criteria of "sufficient" evidence in animals and "limited" evidence in humans, the primary conclusions of published scientific papers were upgraded (altered) by NTP – studies that, as published, did not fulfill criteria necessary to justify a "reasonably anticipated" listing were re-interpreted by NTP so as to support that classification.

- Epidemiology (human) study –.the data reinterpretation for this study was utilized even after the original author of the study protested to NTP in writing.[13] Furthermore, Dr. Birnbaum has stated that the reanalysis was based on information received "over the phone" without any additional documentation.[14]
- Animal cancer data assessment – NTP revised the findings of a National Cancer Institute (NCI) study by relying on a reanalysis of historical control data; an action that directly violated NTP's own published recommendations against such substitution and manipulation of historical control data.[15] Further, had NTP not upgraded the NCI study, it would not have been able to cite findings in studies by two routes of exposure, which was the basis for concluding there was "sufficient" evidence in animals.

The fact that NTP changed the original study findings to support its classification decision is not reflected in NTP's documentation on styrene – and yet NTP cited them as fundamental to the styrene listing.

Dr. Birnbaum did not acknowledge these facts in characterizing NTP's styrene assessment in her testimony to Congress. And while reassessment of published data is not, in principle, scientifically inappropriate, these reassessments were done absent any substantive external peer review, which is.

As NTP staff themselves have acknowledged, NTP relies on a "strength of the evidence" assessment approach.[16] Simply put, this means that they seek to identify studies that suggest a potential cancer effect without regard to other information or factors that might call these "positive" results into question. When studies that do not show an effect ("negative" findings) are identified, their findings are basically ignored. In today's modern risk and hazard assessments, this approach is at best simply a screening process that is most commonly used to exclude substances, which do not require further study. In the greater scientific community, however, such outdated screening approaches have been replaced with the hypothesis-based "weight of the evidence" approach, which considers and weighs together all available data.

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[13] Letter from Dr. E. Delzell, University of Alabama to Dr. B. Shane, NTP, .5 Feb 2009, http://ntp.niehs.nih.gov/files/20090205Delzell.pdf.

[14] Question 6, letter of John Shadegg and Rick Boucher, Congressmen, to Linda Birnbaum, Director of NTP, 22 Oct 2010, quoting Dr. Bimbaum from her July 29, 2010 meeting with the Congressmen.

[15] See minutes of February 24, 2009 Board of Scientific Counselors meeting, pp.19-20, comments of Dr. Jeffrey Charles: http://ntp.niehs.nih.gov/?objectid=720164F2-BDB7-CEBA-F5C6A2E21851F0C4&#20090224, and public comments by Dr. Charles from same meeting: http://ntp.niehs.nih.gov/index.cfm?objectid=576ED5D4-F1F6-975E-771445374E536BE4.

[16] "Peer Review of Draft Substance Profiles for the 12th *Report on Carcinogens*," slide 6 of presentation by Mary S. Wolfe of NTP to the NTP Board of Scientific Counselors Meeting, 24 Feb 2009, http://ntp.niehs.nih.gov/files/Wolfe20090224.pdf.

The body of scientific data on styrene is one of the largest and most comprehensive of any industrial chemical, and while there are several studies that suggest possible effects in laboratory animals – for example, exposure to styrene clearly resulted in mostly benign lung tumors in laboratory mice – the preponderance of the data shows that exposure to styrene does not result in carcinogenic effects in laboratory rats or in people, and state-of-the-art research using genetically-engineered mice strongly indicates that the specific physiology of the mouse results in a species-specific susceptibility to lung tumors. Additionally, as the physiology of other species, including rats and humans, is different from that of mice, these effects are not relevant to a human cancer concern.[17] Further, initial human studies suggesting some level of effects are inconsistent, and the findings were not replicated following more detailed examination. Using a weight of evidence approach in reviewing the collective database, the European Union and Denmark both recently concluded[18,19] that styrene is not a human carcinogen concern – certainly a profound difference in conclusions from NTP's "reasonably anticipated," yet based on the most current and rigorous assessment principles.

5. **You have said that the Board of Scientific Counselors (BSC) is no longer required to peer review the *RoC* listing recommendations. But didn't the BSC agree with this change in the process at their December 15, 2011 meeting? Won't the peer review now be done by specialized panels that will have the required expertise on them for the review instead of the BSC, which has a much broader membership? Isn't the new process actually an improvement compared to the old process?**

The updated *RoC* process indicates that NTP can choose to seek outside review at its own discretion – *i.e.*, NTP will be able to determine if and when it feels some sort of external check is required – or not. NTP's use of meaningful peer review has steadily diminished over time. In the past, the BSC was asked to formally vote on proposed listings. Indeed, in the few instances where the decision was made not to list a substance in the *RoC*, each time it was the result of the BSC vetoing recommendations of the NTP staff.[20] For the 12th *RoC*, NTP revised its process and removed the formal vote by the BSC, using the BSC only to provide comment. The process now leaves any consultation with the BSC beyond an initial conceptual review and, later in the process, "present[ing] information" to the BSC regarding substances being reviewed entirely to NTP's discretion.

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[17] Goodman, J.E., Rhomberg, L., "Why Styrene Should Not Be Classified as a Human Carcinogen And Does Not Belong in the NTP's 12th *Report on Carcinogens*," *Daily Environment Report*, BNA, 12 Mar 2012, http://www.gradientcorp.com/alerts/pdf/Styrene.pdf.

[18] "European Risk Assessment Report, Styrene," Draft for publication, June 2008, United Kingdom, available at http://echa.europa.eu/documents/10162/13630/trd_rar_uk_styrene_en.rtf .

[19] Danish Environmental Protection Agency, "Proposal for Harmonised Classification and Labelling" for styrene, p. 50 and p. 52, 2011, http://echa.europa.eu/documents/10162/13626/clh_report_styrene_en.pdf.

[20] *12th Report on Carcinogens, Appendix C*, http://ntp.niehs.nih.gov/ntp/roc/twelfth/roc12.pdf, p. 470 (lists these substances); the outcomes of the BSC deliberations can be found by reviewing the documents related to each review (available on request from NTP).

Indeed, it is unfortunate the BSC itself failed to appreciate the key role it should legitimately play, and that removing the BSC from any formal review responsibility eliminates a critical check and balance to assuring the overall scientific quality of NTP *RoC* listing evaluations – and even more so in those situations in which NTP has made it's own discretionary decision not to employ any external peer review. Comprehensive external peer review is fundamental to validating scientific conclusions; a credible scientific journal does not publish an article that has not been externally vetted by persons with related expertise, and any reviewer comments addressed by the author. NTP does not require this of its own conclusions.

As to the BSC's review of the new *RoC* process, this again goes to the very broad way that NTP has defined its *RoC* process: the process contains the core steps for a cancer hazard screening assessment, but does not include the necessary detailed documentation as to how those steps are undertaken. As noted in my following comments (see response to Question 11) on the nature of expert panel operations, coupled with the fact the panel members place great faith in the NTP staff that it has provided adequate background information, it is not surprising that the BSC did not have serious objections to the new process. The core steps of a hazard screening assessment were there, and the assumption was that NTP would appropriately implement them. As stakeholders discovered with the 12th *RoC* process, however, the devil is in the details – or in the *RoC*'s case, the lack thereof.

6. **Do you think that the *Report on Carcinogens* serves to advance public health? Are ordinary Americans given useful information they can actually use to reduce their risk of disease?**

No. At present, the *RoC* may provide "information," but it lacks any public context regarding its relevancy to human health, and the "reasonably anticipated" classification simply promotes fear in the absence of an evidence-based risk context. In fact, the way NTP approaches the *RoC* today is counter to the original Congressional intent, as discussed in my response to Question 1.

Because NTP does not employ the accepted standard for hazard assessment embraced by the wider scientific community – and indeed other regulatory agencies globally – the public health value of its conclusions is questionable at best and, in the case of styrene, has created concern about the safety of styrene and styrenics products where more thorough assessments have shown none exists. Styrenics products are ubiquitous in our society, and provide vast public benefits in medicine, safety, energy, transportation and communications. For NTP to brand styrene as "reasonably anticipated to cause cancer," when the process it used to reach that conclusion is outside the scientific norm and its transparency has been seriously questioned (to the point of Congress directing HHS to contract the National Academy of Science to review the *RoC* styrene listing), means that the average American has not been well-served by NTP's listing.

In Dr. Birnbaum's testimony on April 25, she said "A listing in the Report indicates a potential hazard for cancer, but does not estimate cancer risks that individuals may

face when encountering listed substances in their daily lives."[21] Because the *RoC* is a hazard assessment, and does not consider exposure factors, it does not provide the benefits of a full risk assessment – which in turn would provide a far more informed basis for helping the public make informed risk management decisions. The *RoC*, instead, plants the seeds of a concern while simultaneously suggesting that no actual health risk may exist for consumer applications. Two statements made by different NTP officials following the release of the 12th RoC illustrate this:

- "Simply avoid using products containing these substances if you are uncomfortable with the risk" – Dr. John Bucher, NTP Associate Director.[22]
- "Let me put your mind at ease right away about Styrofoam..." "In finished products, certainly styrene is not an issue." Exposure to [styrene] from riding in a boat "is infinitesimal," – Dr. Linda Birnbaum, NTP Director.[23]

This "information" only serves to infer health concerns where none may exist.

7. When does NTP respond to public comment during the process? What is the effect of this on the scientific quality of the assessment of a substance?

Consistent with its process description for the 12th *RoC*, NTP did not produce written responses to public comments on nominated substances until after Secretary Sibelius had approved the *RoC* and it was published.[24] Such a delayed response to public comment significantly compromises not only the public's ability to point out deficiencies in the NTP responses, but even more importantly, fails to provide external peer review panels any opportunity to judge the scientific merits of NTP responses to externally-provided critiques of its analyses. NTP's "Response to Issues Raised in the Public Comments" did not address the serious challenges to its conclusions that were raised in public comments to the record during the 12th *RoC*, and thus the public comment process for the 12th *RoC* had little or no actual impact on the *RoC* assessment process. Since NTP was not required to transparently or adequately address challenges to its conclusions, or to acknowledge valid conflicting scientific hypotheses, the opinions of outside scientists had little chance of having an impact on *RoC* listings, making the *RoC* process very misleading – it looks like it is open and transparent on the surface, but in practice is in fact quite the opposite.

For the new 13th *RoC* process, NTP no longer will respond to public comments at all.[25] While NTP insists that its *RoC* process now includes even more opportunities for public "input" than it did in the past, and that NTP will "consider" such comments, again this requires Congress, stakeholders, and the public simply to assume that

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[21] Birnbaum testimony, 25 Apr 2012, p. 2, *op. cit.*

[22] Dr. John Bucher, as quoted in "8 'New' Cancer Causes U.S. Adds 8 Chemicals -- Some Common – to Carcinogen List," *Web*MD *Health News*, D.J. DeNoon, 10 Jun 2011, http://www.webmd.com/cancer/news/20110610/8-new-cancer-causes.

[23] Dr. Linda Birnbaum, as quoted in "Weighing Cancer Risks, From Cellphones To Coffee," The Associated Press, *National Public Radio*, 15 Jun 2011.

[24] *NTP Response to Issues Raised in the Public Comments for Candidate Substances for the 12th Report on Carcinogens*, National Toxicology Program, 50 pages, 2011, http://ntp.niehs.nih.gov/ntp/roc/twelfth/2011/ResponsePublicComments2011.pdf.

[25] NTP Board of Scientific Counselors Meeting, 15 Dec 2011, statement of Dr. John Bucher, at 6:15 minutes of the recording, available at https://www.box.com/shared/static/ea274f5a6547994936ac.wma.

public "input" will be given more than a cursory review and have the potential to actually impact the outcome of NTP's review. The public comment process now has become a black box, as NTP will no longer provide any way for the public to evaluate how NTP used its input. For NTP not to transparently and thoroughly define the need to respond to any alternative hypotheses that may be presented in the comments, nor to address fundamental challenges to the integrity of the process NTP uses, reduces the *RoC* to an almost completely discretionary policy document – NTP may claim it has "checked all the boxes" in its simplistic *RoC* process, but there will be no documentation of how well – or how fairly – that is done.

8. **How do you believe the public comment process could be improved, and what would the impact of an improved public comment process be on the *Report on Carcinogens*?**

NTP needs to implement a state-of-the-art, evidence-based review process for the *RoC*. I believe that the NTP would significantly benefit from a detailed NAS review of its *RoC* process that focuses on the alignment of the *RoC* process with the principles outlined by the NAS in Chapter 7 of the NAS review on the IRIS formaldehyde report.[26]

Relative to public comments, this should include NTP defining a clear and thorough process for vetting outside comments, that would provide opportunity for direct discussion – not mere submission – of conflicting theories, in a transparent and well-documented forum, and would require NTP to systematically address all public comments and provide justification as to why – or why not – NTP chose to reflect the valid input of external scientists.

While the process used for the 12th *RoC* provided opportunities for the public to submit written comments, and make oral presentations, NTP's engagement of these comments was perfunctory at best; written comments were "made available" to reviewers, and oral comments were entertained, but never discussed, due at least in part to very tight panel meeting agendas. And, in the case of the BSC, oral comments were presented immediately prior to BSC members being asked to deliver previously prepared statements on the data based only on NTP's input (which did not include a discussion of conflicting information provided through public comments). Public comment opportunities should involve direct discussion of any conflicting opinions, with engagement by all reviewing parties, and those contradicting theories need to be transparently included in the overall NTP assessment and documentation, in order for the Congress, regulators and the public to have the complete story on a substance.

9. **If NTP comes up with even one study that shows that styrene is a possible carcinogen, why do they need to look for more studies before warning the American public so that they can protect themselves?**

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[26] *Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde*, Board on Environmental Studies and Toxicology, National Research Council of the National Academies, 189 pages, 2011, National Academies Press, Washington, D.C., http://www.nap.edu/catalog/13142.html.

The *Congressional Record* makes it clear that it was Congress' intent that the *RoC* was to "*...make it absolutely clear ... that there must be reasonable ground for designating a substance as a putative carcinogen.*"[27]

Therefore, the purpose of the *RoC* is not simply to inform the public if NTP identifies "even one study" that seems to indicate a concern; rather, the purpose is to determine the "reasonable ground" upon which a substance should or should not be designated as a "putative carcinogen."

As noted in the answer to Question 4, the standard for the scientific community is to adopt an evidence-based, or "weight" of the evidence, approach in making such determinations. Instead of following this method, NTP has embraced a "strength" of the evidence approach for the *RoC*.

A simple scenario involving a substance with ten scientific studies may be helpful in understanding what this approach implies. Assuming that one of these ten studies is positive (*i.e.*, suggests a cancer effect) and nine are negative (*i.e.*, do not suggest a cancer effect), a strength of evidence review would use that one study as evidence of a cancer concern and the nine negative studies would be dismissed.

Conversely, hazard assessors now recognize the need to balance that one positive study against the nine negative ones, in what is termed an evidence-based review. For example the assessors will ask questions, such as:

- Is the effect a trend?
- Is it replicated in similar studies?
- What was the relative scientific quality of the research process and the data on which the findings were based?

For weight of evidence assessments where there is only limited, and perhaps inconsistent, evidence of an effect, countered by substantial evidence of no effect, equal credence must be given to the negative studies to determine if the positive effect(s) is valid, or if perhaps the finding is an anomaly that can be validly explained as not applicable to the overall hazard assessment.

Further, as noted previously, in the case of styrene, if NTP had not itself "upgraded" the conclusions of published authors – and absent any meaningful external peer review – it simply would not have been able to cite enough scientific data to meet its own screening threshold for "limited" human data or "sufficient" animal data (the *RoC* listing criteria require that NTP finds the data meet either the "limited" human data or "sufficient" animal data thresholds). Such a clear lack of transparency and checks-and-balances is antithetical to sound hazard assessment practices – both scientific and governmental – as cited by the NAS.

Given that other recent and far more rigorous styrene reviews came to distinctly opposing conclusions for styrene, for NTP essentially to resort to creating new

[27] *124 Congressional Record H38657* (1978) (statement of Rep. Rogers), *op cit.*

analyses absent any external check process, and then use those new "findings" to justify its listing, does not seem to serve the American public's interests in any way.

10. You have argued that NTP did not address public comments during the course of their assessment. But didn't they put them up on the Internet for everyone to see?

Indeed, NTP did produce cursory responses to public comments at the time the 12th *RoC* was published (see response to Question 7). Thus, although NTP publicly posted external comments, the lack of any timely written NTP response to those posted comments significantly compromises not only the public's, but also external peer review panels' ability, to judge the adequacy of NTP's reaction to potentially important scientific controversies raised in those comments. By publicly responding to external comments only after final and formal completion of *RoC* listings, the purpose of public comment, to identify controversies important to listing decision deliberations, is largely abrogated.

Importantly, simply posting public comment on the Internet also is not an adequate means to assuring scientific controversies will be appropriately considered, and particularly so if adequate *time* is not allotted for consideration by external review panels. Again using the example of styrene, the public comment period officially closed only 4 working days before the meeting of the "Interagency Scientific Review Group."[28] Such a brief interlude between the close of the public comment period and the interagency review session virtually assured that the public comments would not be able to be adequately incorporated into the review, and clearly suggests NTP does not view public comment as an important opportunity to seek input and critique of their evaluations.

In addition, the styrene industry submitted a Request for Correction to NTP of its Styrene Background Document under the Information Quality Act that consisted of over 100 pages of direct challenges to deficiencies in the document and mischaracterizations of the data.[29] After taking over one year to respond to the Request for Correction, NTP acknowledged only about a dozen minor editorial corrections and dismissed the remaining scientific challenges essentially based on the assertion that NTP had "followed its process" and did not need to acknowledge these fundamental scientific deficiencies cited by stakeholders. The NTP's response to SIRC noted "The NTP identified several edits to the Background Document that will be made by issuing 'Erratum and Addendum to the Final Report on Carcinogens Background Document for Styrene.'"[30,31]

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[28] The Public Comment period for written comments closed on October 23, 2008 (*Federal Register*, v. 173, no., 174, p. 52059, 8 Sep 2008, http://ntp.niehs.nih.gov/files/73_FR_174_Styrene.pdf); the Interagency Scientific Review Group met on October 29, 2008.

[29] Letter from Jack Snyder, Styrene Information & Research Center to John Burklow, National Institutes of Health, "Re: Request for Correction of Information under the Information Quality Act," 101 pages, 26 Oct 2009, http://aspe.hhs.gov/infoQuality/request&response/36a.pdf.

[30] Letter to Jack Snyder from John R. Bucher, 23 Dec 2010, p. 23, http://aspe.hhs.gov/infoquality/request&response/36b7.pdf.

[31] Erratum and Addendum to the Final Report on Carcinogens Background Document for Styrene, http://ntp.niehs.nih.gov/NTP/roc/twelfth/2010/FinalBDs/StyreneErratumAddendum.pdf.

Accordingly, it is clear that NTP believes it has met its need to seek public comment purely by soliciting comments and posting them in a publicly available on-line docket. NTP does not seem to believe – as the new *RoC* process clearly reveals – that stakeholder input needs to be transparently addressed.

11. Peer reviewers are experienced academics and they know how to use the Internet – don't the public scientists get to present their views directly to the peer reviewers themselves, and isn't this the best way of making sure that their comments get heard correctly?

Having served on the NTP's BSC, the National Academy of Sciences, and other such external advisory panels, I unfortunately am aware that such bodies often do not fully utilize public comment as a productive means to identify scientific controversies or other issues associated with technical documents developed by government scientists. Although there are many reasons for this, one recurrent and key reason is that, as noted in the response to Question 10, detailed public comments are often not made available to external peer reviewers in a timeframe suitable for their effective incorporation into their peer review deliberations. In addition, since scientific controversies identified in written comments submitted by the public address often address complex technical issues, for example as was the case with styrene, it is entirely unreasonable that an appropriate understanding of the controversies can be effectively communicated to academic peer reviewers within a timeframe of a 7 minute oral presentation (as was mandated for individual oral public comment for the 12th *RoC* by NTP)[32]. Such communication challenges are further complicated by the fact that NTP, by its own process requirements and as noted above, remains totally silent on its position on the merits of public comments. Finally, NTP peer review panels have no standing charge question requiring them to evaluate and respond to issues raised in external public comment, which further promotes relegation of such comments to often at best a background focus of individual peer reviewers' attention.

12. You have said that NTP does not address public comments, but didn't NTP write a long document that responded to the public comments submitted during the 12th *RoC*?

See above responses to Questions 7, 8 and 10 regarding NTP's approach to providing a response to public comments. As required by the 12th *RoC* process, NTP's response to public comment was only offered after final publication of the *RoC* listing. The timing of these delayed, after-the-fact, responses essentially means that if external stakeholders maintain that NTP written responses are unresponsive to controversies or errors raised in previous public comment, the only recourse to resolve such concerns is to nominate a controversial listing for delisting. The formal NTP delisting process can take several years for implementation and resolution, during which time the listed compound is burdened with a cancer listing that may be scientifically unwarranted.

[32] *Federal Register*, v. 73, no. 98, p. 29140, 23 May 2008, http://www.gpo.gov/fdsys/pkg/FR-2008-05-20/pdf/E8-11192.pdf.

Finally, as previously cited, it is important to note that under the newly revised process for the 13th *RoC*, NTP is *never* required to offer any responses to public comment, further ensuring that such controversies will only be magnified in the future.

U.S. House of Representatives

Committee on Science, Space, and Technology
Subcommittee on Investigations & Oversight
and
Committee on Small Business
Subcommittee on Healthcare and Technology

QUESTIONS FOR THE RECORD

"How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"

Wednesday, April 25, 2012

Dr. Faye Grimsley, Associate Professor,
Tulane School of Public Health and Tropical Medicine,
Department of Global environmental Health Sciences

Questions submitted by Dr. Paul Broun, Chairman, House Science, Space and Technology, Subcommittee on Investigations & Oversight and Rep. Renee Ellmers, Chairwoman, House Small Business Subcommittee on Healthcare and Technology

1) Have you personally been involved in the process used to determine whether substances should be listed in the Report on Carcinogens?

   No I have not

2) How do you use the information provided in the Report on Carcinogens?

   In various ways, primarily to determine risk and toxicity for chemicals in the workplace and community settings. The RoC is a great reference for conducting literature searches to see what type of research studies have been conducted for a specific agent.

3) The RoC statute directs NTP to include substances in the report that are "known" or "reasonably anticipated" human carcinogens.
   A) "Known" is a pretty high standard in science. Presumably it does not mean 100% certainty. As a scientist, what do you consider to be the minimum probability needed in order to designate a substance as a "known" human carcinogen? There is not a straight forward answer to this question; it depends upon the agent and data that is available to make decision whether or not it is known or reasonably anticipated. If data used to make determination is reliable and consistent, more confidence is placed with the designation in the known category.

B) What about a "reasonably anticipated" human carcinogen? What is the minimum probability necessary in order to designate a substance as "reasonably anticipated" to cause cancer? Again, as stated above it depends on the data that is available to base ones decision for the designation. For example, the preferred type of data comes from epidemiological studies in defined human populations which are not always available.

4) Following up on the previous question, how should an employer explain what NTP means when they say that a substance is "known" or "reasonably anticipated" to be a human carcinogen?
   A) As an industrial hygienist, do you find the terminology confusing?

      For a particular agent that is known to be a carcinogen, data indicates that it can cause cancer in humans. For reasonably anticipated, less data is available to support that it causes cancer in humans, but it has been shown to be associated with cancer in animals.

      As an industrial hygienist I do not find the terminology confusing.

5) In your written testimony you list eight federal agencies and organizations that produce hazard assessment information for substances.
   A) Do you believe that businesses and the public may be confused by so many agencies and organizations producing this information? No, since most businesses have health and safety personnel to explain the role of various agencies and the information provided. Many community members now have access to non-profit environmental organizations and groups who have provided details of various agencies and types of hazard assessment information that is available.
   B) Do you rely on one agency or organization's assessments more than another? It depends on the situation. If the chemical is not listed by one agency, one would typically search for hazard information from another agency. If the chemical has consistent hazard information from many sources the better. For workplace situations, OSHA, NIOSH, ACGIH, IARC and NTP are preferred and relied upon the most. Sometimes for environmental situations that involves the public ATSDR, EPA, IARC, NTP, ACGIH are preferred.
   C) If yes, which agency or organization do you rely on most heavily and why? Same as above in B. In the United States, recognized authorities most often used by occupational health safety professionals for workplace hazard and toxicity information are OSHA, ACGIH, AIHA, and NIOSH.
   D) If not, how do you reconcile the information provided by the various agencies and organizations? As an industrial hygienist we are trained to use professional judgment. You look at the information provided and determine the best approach to recognize, evaluate, and control the hazard.
   E) Do you believe that the general public or small businesses have the expertise to reconcile the information being produced by the eight federal agencies and organizations that you listed in your testimony? No in most cases they do not. I

believe Ms. Webster, from the small business, Monroe Industries, indicated she had to seek this type of expertise from an outside consultant.

6) The Report on Carcinogens identifies the exposure limits set by federal agencies, but it does not assess whether the exposure limits are decreasing the risk to public health from the listed substances, as is congressionally mandated. Do you believe the public would benefit from knowing whether exposure limits are reducing adverse health effects? Yes as a scientist I believe it would be advantageous to be able to measure and explain if to what extent exposure limits prevent adverse health effects.

7) In the context of evaluating scientific studies, please explain the difference between a strength-of-evidence approach versus a weight-of-evidence approach?
   A) Which of these approaches best describes the method employed by NTP in listing substances in the RoC? I have prepared a synopsis of the carcinogen review processes used by IARC and NTP in a separate document. Briefly, various methods are used to determine strength of evidence and weight of evidence. Typically, experts with various backgrounds are convened to review and determine the strength of the evidence (specific indicator—presence of tumors in animals for a specific chemical or agent, etc.), which in some cases is a part of the overall process of determining the weight of the evidence (broad --all types of evidence included, tumors, animal data, human data, etc.). NTP uses both approaches, the strength of evidence (review of specific information) and the weight of evidence (review and weighting of all evidence).

National Toxicology Program Report on Carcinogens Review Process
Strength of Evidence and Weight of Evidence-Testimony Addendum

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Tulane University School of Public Health and Tropical Medicine

May 8, 2012

In response to the question/issue, (can you address the controversy of strength of the evidence and weight of the evidence?) raised by Mr. McNerney in the Subcommittee on Healthcare and Technology Joint Hearing with Committee on Science, Space, & Technology Subcommittee on Investigations & Oversight on "How the Report on Carcinogens uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs", A brief overview of the topic and examples are provided.

As indicated in the hearing April 25, 2012, the review process for determining if an agent should be listed and categorized as carcinogenic can vary by agencies and organizations. Most include looking at the strength and weight of evidence at some stage of the review process. Experts with various backgrounds and experiences are selected to serve on panels and working groups that evaluate available data for evidence of carcinogenicity. Panels and groups use scientific and qualitative judgment when evaluating evidence for or against carcinogenicity. Topics or agents are selected based on different criteria, including if there is evidence for human exposure and if there is some evidence or suspicion of carcinogenicity. The following is a summary of the International Agency for Research on Cancer (IARC) and the National Toxicology Program (NTP) classifications as examples of strength and weight of evidence. Note: for reference and clarification, strength of evidence is usually associated with relevance of information to a specific indicator, such as number of tumors produced in animals. Whereas, weight of evidence includes all types of evidence, positive and negative, mechanistic and non-mechanistic, in vivo and in vitro, in addition to human and animal studies.[1] In an article that gives an overview of the role of weight of evidence (WOE) in regulatory science, Krimsky states that the trend has been to move from strength of evidence to a broader weight of evidence approach. [2]

IARC Review -Strength of Evidence: After reviewing quality and summary of relevant epidemiological studies of cancer, a judgment is made concerning the strength of evidence that the agent is carcinogenic for humans. When making this judgment, several criteria are deliberated for causality.

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[1] Willhite C., "Weight-of-Evidence versus Strength-of-Evidence in Toxicologic Hazard Identification: Di(2-Ethylhexyl)Phthalate(DEHP)," Toxicology 160(2001): 219-226.

[2] Krimsky S., " The Weight of Evidence in Policy and Law," American Journal of Public Health Vol 95, No.S1: S129-S136.

Based on the degree of relative risk (e.g., a large risk would indicate strong association and small a weak association), causality is determined. Replicated studies of similar design and findings of association, lead to stronger evidence. Studies that are judged to be high quality are given more weight than those judged to be less sound because of methodological issues. If an exposure response relationship exist (e.g., increased exposure leads to increased disease or reduced exposure leads to less disease), this is considered to be strong evidence. Although, if exposure response relationship is not present this does not necessarily mean a causal relationship does not exist. Experts also consider if the agent acts on multiple or specific organs, the more specificity the better case for causality and strength of evidence. Ideal studies for strong evidence inclusion are randomized control, but these types of studies rarely exist for data evaluation. If studies with little or no association for exposure and cancer are reviewed, judgment can be made if there is a lack of evidence for carcinogenicity.
If adequate human data is not available, then data from experimental animal studies with sufficient evidence of carcinogenicity and relevance should be considered. Other data related to genotoxicity of the agent is also considered.

Degree of evidence is classified by IARC by using the following circumstances: 1) Sufficient evidence of carcinogenicity- positive relationship exist in which chance, bias, and confounding could be ruled out with reasonable confidence; 2) – Limited evidence of carcinogenicity- a positive association observed, but chance, bias or confounding could not be ruled out with confidence; 3) Inadequate evidence of carcinogenicity – available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association, or no data on cancer in humans are available; 4) Evidence suggesting lack of carcinogenicity - several studies consistently do not show a positive association between any observed exposure to agent and any studied cancer. Degree of evidence for experimental animal studies and other relevant laboratory studies are judged and classified in a similar manner as outlined.

Overall evaluation by the expert panel or working group consists of looking at all data as a whole and final decisions for categories/groups of carcinogenicity (e.g., carcinogenic to humans, carcinogenic to animals, probably not carcinogenic to humans, etc.) are made based on scientific judgment and reflection on the strength of the evidence from human and animal studies. IARC Categories: Group 1- Carcinogenic to humans; Group 2A- Probably carcinogenic to humans; Group 2B- Possibly carcinogenic to humans; Group 3-Unclassifiable as to carcinogenicity in humans; and Group 4- Probably not carcinogenic to humans.[3] (IARC 2006).

NTP Review –Strength of Evidence: The listing criteria outlined and described in the National Toxicology Program (NTP) Report on Carcinogens (RoC) is used to evaluate the scientific evidence on a

[3] IARC Monographs on the Evaluation of Carcinogenic Risks to Humans (Preamble) Volume 88 (2006) Formaldehyde, 2-Butoxyethanol and 1-*tert*-Butoxypropan-2-ol

substance to determine whether or not to list as carcinogenic. A candidate substance can be on the list as: known, reasonably anticipated, or not included and placed in the category of do not list. Listing is based on strength of the evidence. There are specific standards that the body of scientific evidence must meet to reach a listing determination. Conclusion is based on scientific judgment with consideration of all relevant information.[4]

According to the NTP, the Report on Carcinogens review process includes a scientific review of candidate substances. The scientific review process consists of three major steps: (1) preparation of the draft background document, (2) review by an expert panel at a public meeting, and (3) internal review by two independent federal committees. Expert panels are convened for each candidate substance. The expert panel is charged with peer reviewing the background document and applying the RoC listing criteria (see below for more detail) to the relevant scientific evidence and to make a recommendation regarding the listing status for a candidate substance and to provide scientific justification for that recommendation. The background document includes the following data for each candidate substance, chemical, physical, biological properties of the substance; a scientific rationale for review; human exposure data; human cancer studies; experimental animal studies; and other relevant mechanistic and scientific information such as absorption, distribution, excretion, and metabolism, genetic damage and related effects, mechanistic studies, toxicity, and carcinogenicity and mutagenicity of structural analogues. Studies in both humans and experimental animals are used to evaluate whether substances are potentially carcinogenic in humans. Other studies may be considered to determine possible carcinogen mechanisms, as well. The strongest evidence for establishing a relationship between exposure and cancer in humans comes from epidemiological studies in defined human populations. [5] The listing criteria used in the RoC review process are described as following:

1. Known to be Human Carcinogens: There is sufficient evidence of carcinogenicity from studies in humans,* which indicates a causal relationship between exposure to the agent, substance or mixture and human cancer.

2. Reasonably Anticipated to be Human Carcinogens: There is limited evidence of carcinogenicity from studies in humans,* which indicates that causal interpretation is credible but that alternative explanations such as chance, bias or confounding factors could not adequately be excluded;

or There is sufficient evidence of carcinogenicity from studies in experimental animals which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors: (1)

[4] Wolfe, National Toxicology Program (NTP) Board of Scientific Counselor (BSC) Meeting, February 24, 2009: http://ntp.niehs.nih.gov/files/Wolfe20090224.pdf

[5] National Toxicology Program (NTP), Report on Carcinogens, Twelfth Edition, June 11, 2011.

In multiple species, or at multiple tissue sites, or (2) by multiple routes of exposure, or (3) to an unusual degree with regard to incidence, site or type of tumor or age at onset;

or There is less than sufficient evidence of carcinogenicity in humans or laboratory animals, however; the agent, substance or mixture belongs to a well -defined, structurally-related class of substances whose members are listed in a previous Report on Carcinogens as either a known to be human carcinogen, or reasonably anticipated to be human carcinogen or there is convincing relevant information that the agent acts through mechanisms indicating it would likely cause cancer in humans.

Conclusions regarding carcinogenicity in humans or experimental animals are based on scientific judgment, with consideration given to all relevant information. Relevant information includes, but is not limited to dose response, route of exposure, chemical structure, metabolism, pharmacokinetics, sensitive sub populations, genetic effects, or other data relating to mechanism of action or factors that may be unique to a given substance. For example, there may be substances for which there is evidence of carcinogenicity in laboratory animals but there are compelling data indicating that the agent acts through mechanisms which do not operate in humans and would therefore not reasonably be anticipated to cause cancer in humans.[6]

*This evidence can include traditional cancer epidemiology studies, data from clinical studies, and/or data derived from the study of tissues or cells from humans exposed to the substance in question that can be useful for evaluating whether a relevant cancer mechanism is operating in people.

Summary:

Some of the controversy related to assessing and interpreting scientific evidence is associated with various methods used and full disclosure of how these methods are used in making policy decisions. It is noted in published literature that several problems are associated with weight of evidence concepts and methods, most notably, multiple definitions and uses, different kinds of weights, and another concern is the role of judgment which is emphasized in many approaches to risk assessment.[7]

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[6] -[Federal Register Volume 64, Number 63 (Friday, April 2, 1999)]
[Notices] [Pages 15983-15984] From the Federal Register Online via the Government Printing Office [www.gpo.gov] [FR Doc No: 99-8098] ; http://www.gpo.gov/fdsys/pkg/FR-1999-04-02/html/99-8098.htm

[7] Weed DL., "Weight of Evidence: A Review of Concept and Methods," Risk Analysis, Vol. 25, No.6, 2005.

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Committee on Small Business
Subcommittee on Healthcare and Technology

QUESTIONS FOR THE RECORD

"How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"

Wednesday, April 25, 2012

Ms. Bonnie Webster, Vice President
Monroe Industries, Inc.

Questions submitted by Dr. Paul Broun, Chairman, House Science, Space and Technology, Subcommittee on Investigations & Oversight and Rep. Renee Ellmers, Chairwoman, House Small Business Subcommittee on Healthcare and Technology

1) By listing styrene in the Report on Carcinogens, NTP has put you in the position of having to explain what "reasonably anticipated" means to your employees. How would you explain to an employee or plant neighbor what NTP really means when they say that styrene is a "reasonably anticipated" carcinogen?

   If my neighbors or employees come to me asking about the NTP and reasonable anticipated carcinogen.... how would I handle that..... It would for sure open up a can of potential worms, but I would be honest with my views. I would share with them all the efforts our company has taken to reduce Styrene exposure. I would answer all of their questions to the best of my ability. I would probably also ask them to call a chemist and have a frank discussion with them as well.

2) Are you holding off on hiring employees?

   Are we holding off on hiring employees? YES, Until this is resolved, I am holding idle..... I am not expanding and I am hoping we can maintain the business we have until I know for sure if my costs are going to skyrocket out of control.

3) Are you holding off on reinvesting money in your business?

   Are we holding off on reinvesting into the business? We continue to invest in good and newer equipment if it means betterment to the employees. However we are

holding off putting on an addition until we know more about our operating expenditures. Workers Comp/Business Ins. I can't stay in business if I can't offer a competitive price product. Would you pay more for cultured marble than Corian? Probably not, and that's basically what would happen.

Question submitted by Rep. Brad Miller

1) In response to a question regarding insurance companies dropping coverage of small businesses that use styrene in their business you indicated there was one company that had been mentioned in a conference call. You mentioned that one participant in that call was Mr. John Schweitzer.
   A. Can you identify who John Schweitzer is and how we might contact him?

John Scheitzer is available at 703-525-0511 (office) his office is located at 3033 Wilson Blvd, Suite 420 Arlington.

   B. Do you have any further information regarding the company that had lost their coverage?

Please see attachment about the company that lost their coverage.

I hope I have answered all of your questions. I would also like to add, that back several weeks, we had a NYS DEC officer in our plant and he took a reading of our Styrene, at the heaviest part of the day. Our reading was 27PPM. Since 2008, business has not been the same. It is a struggle with all the ups and downs of this economy.

Regards,
Bonnie Webster

Statement of Teri Schenk, Global Composites

Energy and Commerce Roundtable on "Business Impacts of IRIS"

March 22, 2012

1. My name is Teri Schenk. I manage regulatory compliance for Global Composites, a small company in Elkhart, Indiana that employs 266 people. We use styrene-polyester resin and glass fiber to make component parts for the RV and motorhome industry such as front caps, rear caps and the large sidewall panels and roofs. We also make septic tank covers. I also do environmental consulting for a number of other small companies.

2. President Obama has twice visited Elkhart to talk about the high unemployment there. In 2010, the composites industry employed more than 15,000 people in Indiana. It's certainly smaller than that today, because of the depressed state of the RV and housing industries.

3. Small companies, especially those that use chemicals as we do, depend on Federal and state agencies to help us protect employees and community members. Because we comply with OSHA regulations, with EPA's air emission control rule for composite manufacturing, and with our state-issued air permit, we know we provide the appropriate safeguards and protections.

4. However, I am here today to tell you that Federal scientific statements are stopping businesses in my industry from hiring, are putting current jobs at risk, and are preventing our nation's young people from being trained for jobs in our industry.

5. A styrene cancer classification in the Report on Carcinogens less than a year ago is causing real problems. EPA is also reviewing styrene for an update to IRIS. As you probably know, the National Academy of Sciences has been very critical about the scientific validity of some of the IRIS assessments, so we are very concerned.

6. As a small company we can't survive regulations and health warnings that are based on outdated science, on shortcuts, or on undisclosed and non-transparent policy decisions biased in favor of an exceedingly high level of precaution. Our competitors in Mexico, China, Canada, South America and Japan don't face these barriers. Even Denmark, and other countries in the EU, welcome composites manufacturing, because they recently looked carefully at the styrene data and determined that it's not a carcinogen.

7. Let me tell you what Global and other composite manufacturers have found since the RoC styrene listing last June:

    a. Rising costs – A Google search of "styrene toxic tort" returns a list of many law firms that now claim to specialize in "styrene injury suits"; styrene was not a business opportunity for these law firms a year ago. Not surprisingly, many composite manufacturers report they are having trouble obtaining liability and workers comp insurance, and that the rates are much higher when they do find a carrier. My clients report increases of 18-25%. I spoke to a representative of one carrier and they clearly feel we are likely to face toxic tort cases because of the RoC styrene listing. One of my clients was dropped by their workers comp carrier and were told they are too much of a risk for claims.

    b. Lost job opportunities – A recent upturn in business has allowed us to expand production and start hiring people for the first time in a long time. But now we are seeing something brand new, and it's especially troubling given the high unemployment rate in our area. Like all manufacturers, we carefully train new hires on hazards, precautions, and safety procedures. As required under the OSHA Hazard Communication Standard, the safety data sheets for the styrene-based resin were recently updated to show the RoC cancer listing. Many new hires, after they have been through introductory training and reviewing the information on safety data sheets, just disappear. Of the 93 people we hired in the last three months, only 51 are still working. We are

careful to offer a very competitive package of pay and benefits, so that's definitely not the issue.

c. We are currently working with a high school that is working with the design of automobiles for better gas mileage. They compete in huge competitions and come in and out of our plants to learn the composite manufacturing processes. Recently, we have been told that those local programs might go away because one of the school nurses has seen the recently posted RoC information and feels the students could be at risk.

d. I've heard from composite manufacturers that their local vocational schools, which have been a good source of trained workers, are concerned about the liability of working with the styrene-based resins and are discontinuing the training programs.

e. I've heard from other companies that uncertainty about the regulatory and legal situation for styrene is causing them to delay investment in new production capacity. I think it's fair to say that there are many Americans today who would have jobs if the RoC was not misinforming people about styrene safety.

f. Unnecessary public concern – A receptionist, who works in the office of one of my clients, has chronic asthma. On a recent doctors visit, she was told she should quit her job because of "dangerous chemicals" – even though she's both had asthma and worked in this company for a long time. This is another indication of a growing general misperception about the safety of our raw materials.

g. Many business owners and employees, and families of employees, are confused about styrene safety. The RoC styrene listing contradicts many other recent expert assessments. And the RoC program itself confusingly says, "Listing of a chemical in the RoC does not mean that exposed people will actually get cancer".

h. Safety is harder – As I mentioned, OSHA's Hazard Communications Standard requires a reference to the RoC listing on the labels of the drums of styrene-polyester resin we use, and many of the drums we've received now have these updated labels. But I understand that the RoC reference will not be required under OSHA's updated HCS, released in final form by OSHA on March 20. So now the labels will have to be revised again to remove the RoC reference.

i. The confusion is making it harder to keep our employees focused on real safety issues such as flammability, using protective measures like respirators and safety glasses, etc.

j. Permitting obstacles – One of my clients has a nearby resident who tried to get the state to cancel the company's operating permit, because the resident feels chemicals are contaminating his food when he barbecues outside.

k. Many state air pollution regulatory programs will look at the RoC listing and set styrene ground-level exposure limits based on a presumption of carcinogenicity, and this will make it impossible for composite manufacturers to get or renew operating permits.

l. Most composite manufacturers are required under the Clean Air Act to post a public notice every 5 years when they renew their operating permits. In many cases, plant neighbors will find a reference to the RoC listing on the Internet and will incorrectly but understandably believe that the permits should not be renewed.

8. Our industry is trying to repeal the RoC styrene listing. Recently available data add even more strength to the conclusion that styrene does not pose a cancer risk. In the meantime, all the bad industry impacts I just described would be even worse if EPA issues an IRIS cancer listing for styrene.

9. Americans will continue to demand styrene-based composite products. For example, composite ballistic panels saved the lives of many American soldiers in

Iraq and Afghanistan, and composite fuel storage tanks are the only proven technology to prevent groundwater contamination at gas stations. We'll just have to move 250,000 composite industry jobs out of the U.S. and make these and thousands of other important and useful products in other countries.

10. Since we are officially talking about IRIS here, let me tell you a particular concern. According to a recent National Academy of Science report, EPA often does not follow its own official guidelines and rarely bases its decisions on a robust "mode-of-action" analysis. If this continues, EPA is likely to base a cancer classification for styrene on animal data, even though experts widely agree a mode-of-action analysis reveals that the styrene tests with animals are not relevant to humans.

11. IRIS and RoC have hidden in the shadows, pretending only to be harmless input to public health agencies. They have been largely unsupervised by the Congress, unreachable by the courts, and not even carefully supervised by the senior officials in their respective agencies. Yet, their actions have every bit as much an impact as regulations, which in contrast are subject to the Administrative Procedure Act, are held accountable for responding to public comments, are scrutinized by the Congress, and can be challenged appropriately in Court.

12. Our industry association is proposing modest commonsense reforms, which could be enacted legislatively or administratively, and which would dramatically improve the scientific quality of the IRIS and RoC programs. We feel our suggested reforms could also serve as a model for improving the quality of Federal science in other areas.

13. Thank you very much for the opportunity to provide these comments.

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Congressmen ask for review of styrene safety

By Mike Verespej
November 9, 2011
PLASTICS NEWS STAFF

WASHINGTON (Nov. 9, 4 p.m. ET) – Fifty members of the U.S. House of Representatives have sent a letter to the White House, asking for a National Academy of Sciences review of the chemical styrene.

The letter, sent Nov. 9 to White House Chief of Staff William Daley, comes six weeks after 21 companies from the American Composites Manufacturers Association sent a similar letter to Daley, saying that without a review by NAS of the safety of styrene their companies and the thousands of workers they employ are in jeopardy.

Styrene has been classified as a human carcinogen by the Department of Health and Human Services' National Toxicity Program.

ACMA members, largely boat builders and composite manufacturers, said in their letter Sept. 26 that, "left unchallenged," the listing of styrene as a carcinogen would "have the long-term effect of moving manufacturing jobs to Mexico, China, France or one of the many other countries that have not taken such an obviously misleading position regarding styrene."

The 12 Democrats and 38 Republicans who signed the Congressional letter told Daley that their request for an NAS study "is driven by the conflict of authorities both within and outside of the federal government regarding the health effects of styrene, and [the] public confusion that has occurred as a result of the listing June 10th of styrene as a 'reasonably anticipated to be a human carcinogen.'"

"A definite styrene carcinogenicity assessment from the .... NAS would ... allow the administration to base its regulatory decisions and hazard identification on the best available information," said the letter, which urged the White House to have NAS conduct "an independent and rigorous review of the potential health effects" of styrene.

"The hundreds of thousands of American workers whose jobs depend on styrene are indebted to Congressmen [Donald] Manzullo and [Tim] Ryan for their steadfast leadership in trying to correct an unfortunate ruling based on bad science," said Tom Dobbins, the chief staff executive of ACMA and Jack Snyder, executive director of the Styrene Information and Research Center, in a joint statement.

Several privately held second-generation family companies already are experiencing the fallout from the federal government's classification of styrene as a human carcinogen.

Some are experiencing higher workers' compensation costs, others are delaying investments because of the uncertainty, and many have a deep concern and belief that it will force companies to move their manufacturing outside of the U.S., killing the domestic composites industry.

For example, Lori Miles-Luchak, president of Portland-based Miles Fiberglass and Composites, said that when the company's workers' compensation insurance came up for renewal this year, they were dropped by their insurance carrier and ended up paying virtually twice as much annually—$144,000 compared to the previous $73,000.

"I do believe it was the NTP listing because the letter said we hadn't done styrene testing," said Miles-Luchak, who is also president of ACMA. "This is quite concerning. It may be our industry today, but who will it be next?"

Additionally, in an economy where unemployment remains above nine percent, the classification of styrene as

a carcinogen by the federal government has caused some composite manufacturers to delay investments.

"We are reluctant to make investments" because of the uncertainty, said Steve Linneman, president of RL Industries, Inc., West Chester, Ohio. "We employ 81 and I see the potential to bring on another 40 people" if the uncertainty can be cleared.

Bonnie Webster, vice president of sales and marketing at Monroe Industries Inc. in Avon, N.Y., agreed.

"We had a really good year and are in need of an addition," she said. "But we are not willing to make an investment because of the uncertainty."

Another composites manufacturer that completed a $1 million investment earlier this year added that his company wouldn't be making that investment today. "Had I known this [ruling] was coming, I would have stopped all investment until clarity was back in the marketplace," said Wayne Spidahl, general manager at the Grand Forks, N.D., plant of Nordic Fiberglass Inc., which is based in Warren, Minn.

Still, he said that "we employ over 100 and have the potential to increase that by over 50 percent in the next two years as the economy improves."

However, the long-term outlook is gloomier.

"As this thing unfolds, and if nothing changes, it will force us to look" to manufacture elsewhere, said Spidahl. "If the classification of styrene stays in its current form, it will kill the industry [in the United States]. There won't be any industry left. I don't think there is any doubt about it. All of it is going to go to Mexico because we won't be able to operate" in the United States.

In addition to the requests from the 50 members of the House of Representatives and the ACMA for an NAS review, the SIRC has asked the U.S. District Court for the District of Columbia for a summary judgment to vacate the ruling. But that court action is expected to drag on until at least late March.

SIRC has also created a website, www.youknowstyrene.org, to educate consumers and communities about the health and safety of styrene, and how many jobs in the U.S. are styrene-related.

According to the SIRC website, more than 5,000 manufacturing plants in the U.S. produce or fabricate styrene products and employ about 90,000 material workers. SIRC said that as many as 750,000 jobs in the U.S. are related to the production, fabrication, installation or sales of these goods.

Styrene is used to manufacture products ranging from recreational boats to residential bathtubs and showers, building insulation and medical products, pollution control equipment to non-rusting highway bridges, and ballistic shields for the military.

As the plastic polystyrene, it is also used for food packaging. However, the Food and Drug Administration has approved the use of PS for food packaging.

Across the globe, Health Canada concluded in 1994 that styrene is nontoxic and does not need to be regulated. Similarly, scientists in the European Union have said styrene should not be classified, labeled or regulated as a carcinogen.

But for U.S. composite manufacturers, it is quite a different story right now.

"The cancer warnings are out there and will remain out there until HHS changes its mind," said John Schweitzer, head of legislative affairs for ACMA. "Even if it is scientifically incorrect, if people are concerned about the cancer issues, I think all the manufacturing jobs [related to composites manufacturing] are at stake."

[redacted]

NOTICE OF NONRENEWAL OF INSURANCE

Named Insured & Mailing Address:

MILES FIBERGLASS & COMPOSITES INC
8855 SE OTTY RD
PORTLAND OR 97086

Producer: 700148

[redacted]

Policy No.: 52WEZX9545
Type of Policy: WORKERS' COMPENSATION
Date of Expiration: 07/01/2011; 12:01 A.M. Local Time at the mailing address of the Named Insured.

We will not renew this policy when it expires. Your insurance will cease on the Expiration Date shown above.

The reason for nonrenewal is due to a recent Hartford loss control we are non renewing the account for the following: the long term exposure to styrene which has likely exceeded the permissible expected limit for quite sometime and can have an adverse long term health effect.

Named Insured

MILES FIBERGLASS & COMPOSITES INC
8855 SE OTTY RD
PORTLAND OR 97086

Date Mailed:
22nd day of April, 2011

Kristine R Azar

KRISTINE AZAR

ORCN26NONE APP

10/17/99
MFC performed 8 hr. TWA styrene testing at both facilities via test badges
Otty Rd. well below the 100ppm threshold
OC one readings was slightly raised
* MFC installed an additional pusher fan in the lay up area where there seem to be a problem.

01/04/00
MFC asked SAIF to performed 8 hr. TWA styrene testing at both facilities via test badges
OC all results were below 100ppm threshold
Otty Rd. all results were below 100ppm threshold with the exception of one which was 104ppm. Considering the +/- error rate this puts us even closer.

10/13/00
MFC performed 8 hr. TWA styrene testing at both facilities via test badges.
OC all results were below 100ppm threshold and most below the 50ppm
Otty Rd. all results were below well 100 and the 50ppm

10/15/01
MFC performed 8 hr. TWA styrene testing at the OC facilities via test badges.
All results were below the targeted 50ppm.

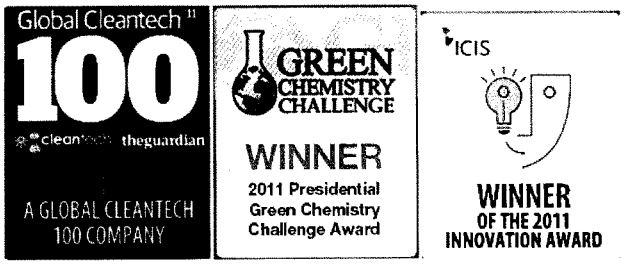
1/29/03
MFC performed 8 hr. TWA styrene testing at the Otty Rd. facilities via test badges.
All results were below the 100ppm and a few were below the 50ppm.

11/21/06
MFC performed 8 hr. TWA styrene testing at OC and Otty Rd. facilities via test badges.
OC results were below the 100ppm and one under the 50ppm
Otty Rd. results were at 100ppm or below.

07/20/07
OSHA Inspection conducted no violations found with the exception of safety minutes were not posted. No fine given.

11/27/07
Health consultation with OR-OSHA for the SHARP program. OSHA performed 8 hr. TWA styrene test performed at both locations.
OC and Otty Rd. no workers were exposed over the targeted 50 ppm. and no safety violations were found.

BioAmber
CHEMISTRY



U.S. House of Representatives

Committee on Science, Space, and Technology
Subcommittee on Investigations & Oversight
and
Committee on Small Business
Subcommittee on Healthcare and Technology

QUESTIONS FOR THE RECORD

"How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"

Tuesday, June 5th, 2012

Ms. Ally LaTourelle, Esp.,
Vice President of Governmental Affairs,
BioAmber, Inc.

BioAmber CHEMISTRY

Questions submitted by Dr. Paul Broun, Chairman, House Science, Space and Technology, Subcommittee on Investigations & Oversight and Rep. Renee Ellmers, Chairwoman, House Small Business Subcommittee on Healthcare and Technology

1) According to BioAmber's Form S-1 Securities Exchange Commission (SEC) filing for its $150 million initial public offering, BioAmber is building manufacturing facilities in Ontario, Canada and Thailand. It also notes that BioAmber is considering building a facility in Brazil or the United States.
   a) What factors led to BioAmber building manufacturing facilities ***outside*** the United States?

Answer 1 (a) *Site selection factors in Canada.*

The primary consideration in selecting Sarnia, Ontario was an additional $35.0 million in 0% interest and low-interest loans and governmental grants that have been committed, subject to our meeting certain milestones, by various governmental authorities in Canada. Other factors considered are outlined in the answer to question 2.

Background: *The first facility we plan to build in cooperation with Mitsui will be located in a bio-industrial park in Sarnia, Ontario. We expect to start construction of this facility in 2012 and to commence production in 2013 with an initial capacity of approximately 17,000 metric tons of bio-succinic acid per year. Completion of this initial phase of the Sarnia facility is expected to cost approximately $78.0 million, which will be met by capital contributions of $30.1 million and $12.9 million from us and from Mitsui, respectively.*

   b) Did BioAmber consider the regulatory or corporate tax structure in Ontario, Canada in making the decision to locate the bio-succinic acid plant in Sarnia, Ontario?

Answer: 1 (b) (part 1) *Regulatory considerations during site selection.*

Yes, BioAmber considered regulatory structure but this was not a primary consideration. BioAmber is subject to all chemical industry regulations pursuant to the jurisdiction where the chemicals are manufactured, transported, and sold world wide. As any chemical company, any failure by us or our industry partners to comply with applicable regulatory rules and regulations could harm our reputation as well as our business, financial condition and operating results.

Background: *BioAmber supports chemical regulation and current regulatory reforms, even if the expense for our company is increased by future changes. For example, in 2009, the Environmental Protection Agency announced its "Essential Principles for Reform of Chemicals Management Legislation" and in April 2011, the Safe Chemicals Act of 2011 was introduced in Congress. This bill would amend TSCA to be more like REACH and require safety testing of all industrial chemicals and could result in the need to disclose confidential business information relating to chemical safety.*

We are in support of this and other legislative and regulatory changes, despite a rise in our costs, because these changes will provide increased harmonization of chemical regulations globally, decrease regulatory uncertainty, increase transparency of chemical ingredients and product formulations that mitigate our risk when entering partnerships. Increased regulation and transparency will provide the EPA with tools necessary for adequate safety assessment of existing and future chemical production and increase consumer awareness to make safer,

healthier choices when purchasing products. This position supports long term success rather than short term quarterly profit gains.

***Answer 1 (b) (part 2)** Tax structure considerations during site selection.*

Yes, BioAmber also considered the corporate tax structure in Ontario, Canada. The Federal Corporate tax rate in Canada was deemed comparable to the corporate rate in U.S. in the analysis. However, the final site in the U.S. had a favorable State tax structure. That state charges no corporate tax. The Canadian Government incentives trumpted any tax advantages at the state level in the U.S.

***Background:** In general, the company calculates its income tax charge on the basis of the tax laws enacted at the balance sheet date in the countries where the Company and its subsidiaries operate and generate taxable income. Management periodically evaluates positions taken in tax returns with respect to situations in which applicable tax regulation is subject to interpretation. It establishes provisions where appropriate on the basis of amounts expected to be paid to the tax authorities.*

Income taxes on the consolidated statements of operations consist of state, federal and foreign jurisdictions income taxes related to the Company and its subsidiaries. Income taxes are provided for the tax effects of transactions reported in the financial statements and consist of taxes currently due plus deferred taxes related to temporary differences arising from assets and liabilities whose basis are different for financial reporting and income tax purposes.

Deferred taxes are provided using the asset and liability method whereby deferred tax assets are recognized for deductible temporary differences and net operating loss, and deferred tax liabilities are recognized for taxable temporary differences. Temporary differences are the differences between reported amounts of assets and liabilities and their tax basis. Deferred tax assets and liabilities are adjusted for the effects of changes in tax laws and rates on the date of enactment. A valuation allowance is provided to reduce net deferred tax assets to an amount that is more likely than not to be realized. The amount of the valuation allowance is based on the Company's best estimate of the recoverability of its deferred tax assets.

c) How many jobs has BioAmber created in the United States and how many jobs has BioAmber created outside of the United States?

***Answer: 1) c.** BioAmber jobs created outside the US.*

As of May 29th 2012, BioAmber employs 114 people. This includes full-time employees, consultants, and full-time equivalents. 17 full-time employees are based outside of the U.S.

d) Please list the number of employees BioAmber employs in each country. How many jobs will be created at the new Sarnia facility?

***Answer 1) d.** BioAmber employees by country.*

BioAmber has 48 full-time employees: 31 in the U.S., 11 in Canada, and 6 in Europe. We also have 46 full-time equivalents through our research and development collaborations and toll manufacturing agreement.

In addition to direct employment, BioAmber's plant in Ontario will create more than 40 jobs. Below is a breakdown of the positions and payrates.

BioAmber CHEMISTRY

Job Classification	Number of Employees	Base Rate ($/hr)	Multiplier for Benefits	Hours Worked per Year	Annual Wage & Benefits
Plant Manager	1	$79	1.3	1,920	$197,184
Operations Mgr	1	$60	1.3	1,920	$149,760
Services Mgr	1	$45	1.3	1,920	$112,320
Logistics Mgr	1	$45	1.3	1,920	$112,320
Chief Engineer	1	$60	1.3	1,920	$149,760
Shift Supv	5	$30	1.3	1,920	$374,400
Operators	15	$20	1.3	1,920	$748,800
Maintenance	5	$20	1.3	1,920	$249,600
Analytical	2	$30	1.3	1,920	$149,760
Administrative	3	$20	1.3	1,920	$149,760

***Background**: As background to give an indication as to rate of job growth in this sector, six months ago, in December 31, 2011, BioAmber employed 78 people. This included 28 full time employees and 46 full-time equivalents through our various collaboration arrangements. Of these employees, 10 research and development, 6 sales and marketing, 10 general and administrative activities and 2 operations activities. Eight employees are based in Canada, 17 are based in the United States and the remaining three employees are located in Europe. Of our full-time equivalents, we engage eight full-time equivalents in a consulting capacity, 21 full-time equivalents through our research and development collaborations with third parties, and 17 full-time equivalents through our toll manufacturing agreement with ARD. We also employ other temporary staff across the organization to augment support for our employees.*

2) What factors would lead BioAmber to build a manufacturing facility ***in*** the United States?

***Answer 2)** Site selection factors in the US.*

Since last June 2011, when the BioAmber US site selection lost out to Canada, there have been several legislative proposals in both the House and Senate which, if enacted, are "game changing" for companies that want to locate in the US. Any one of these three proposals enacted by Congress and signed into law within the next year would be enough incentive, in and of itself, for BioAmber to build a plant in the US.

1. *Passage of Farm Bill Legislation that includes Senator Lugar Rural Energy Initiative language including renewable chemicals provisions. This legislation would open up the §9003 Biorefinery Assistance program to renewable chemicals and bioproduct manufacturing.*
2. *Passage of the Bi-partisan supported Renewable Chemicals Production Tax Credit H.R. 4953 introduced by Congressmen Pascrell and Bilbray. This is a limited term tax credit to offset current tax advantages to petrochemical producers.*
3. *Passage of the Make It in Amercia Tax Credit Act, S. 1764, introduced by Senator Stabinow and supported by the US Chamber of Commerce, that would give a tax credit to companies that expand, re-equip, or build new factories in the U.S*

***Background:** After a first site feasibility screening, the determinative factor is financing. The availability and cost of capital (interest rate that determines the ongoing*

debt burden during operations) to build the infrastructure for a commercial scale biobased chemical production plant is the primary factor for site selection. If not for the financing, the project does not exist.

In addition, BioAmber considered multiple factors when deciding to build its first commercial scale biobased succinic acid manufacturing facility. We undertook a site selection analysis that surveyed over 100 sites across North America. The first screening of logistics, infrastructure and operating costs determined sites which, when financed, would benefit the project's long term operating costs. We ranked the North American sites according to logistical considerations such as the proximity to feedstock processing, developed infrastructure, rail spur at the site itself, shipping container storage, intermodal transport. We also considered infrastructure support such as electrical capacity, wastewater treatment capacity, steam capacity, and operating cost factors such as competitive long term utility pricing, skilled workforce availability (training costs), available labor and community support.

In the US, we looked at Municipal, State, and Federal Tax Incentives, commercial loan availability, Federal Loan Guarantee availability, and Federal, State and Local Grants. Here is an exerpt from my letter to the local economic development corporation giving explanation as to why we were not locating in their town. The local, municipal and state offices all worked tirelessly for BioAmber in hopes of landing the project.

> *"The proposed site in Watertown, South Dakota, provided an excellent opportunity for the location of a large-scale biobased manufacturing project. Proximity to rail, truck, feedstock supply, electrical capacity, wastewater management capacity, skilled labor, as well as offerings of infrastructure improvements and local financial incentives are all factors that distinguished Watertown from over 110 sites reviewed in 11 different states in the U.S. Watertown ultimately emerged as one of the top 2 sites in North America.*
>
> *In addition, the Focus Watertown team provided the integral connection to the community, lenders, council members and local businesses during the process. The BioAmber team is especially grateful for the personal efforts of Focus Watertown President, Craig Atkins. Craig in particular remained tireless in his efforts to innovate and develop creative financial mechanisms from which to drive benefit to the BioAmber project. His willingness to remain flexible, innovative and exhaustive in the search for the right financial incentives was critical to the financing in this extremely difficult economic climate.*
>
> *However, even as Focus Watertown provided a superb site and exemplary local financial incentives, a lack of U.S. Federal incentive programming and a negative lending*

environment trumped the collective efforts of all. In June, 2011, the BioAmber Board of Directors voted to move forward and locate at a site in Ontario, Canada.

Currently in the U.S., post economic crisis financing of a large-scale infrastructure project that is not eligible for specific Federal programming requires the convergence of a multitude of financial mechanisms. In the case of South Dakota, the BioAmber Succinic Acid Plant project finance structure included: commercial lending, government loan guarantees, corporate loan guarantees, a state taxable bond offering, interim construction lending, state loans and grants, state and local tax incentives as well as local lending. Despite the best efforts of all parties, the sheer volume of required components and issues within each of the moving financing parts ultimately proved to be too difficult to overcome in aggregate.

In contrast, the Ontario province and Canadian Federal government has offered the BioAmber project over $35M in no interest or low-interest loans and grants directly. Once the company successfully hurdled competitive application processes, BioAmber was assured of loan offerings that do not involve lead lenders, Federal loan guarantees, or interim construction lending, and are disbursed directly from the governments, as the project is under way.

As a U.S. company based in the Midwest, it was a difficult decision to locate the project in Canada. However, this decision ensures that BioAmber will develop the first commercial scale production of succinic acid in step with a fast growing renewable chemical industry. We continue to push the industry forward and hope to incentivize by example future investing in renewable chemical projects and plants in the U.S. and worldwide."

3) In BioAmber's Form S-1 SEC filing for its $150 million initial public offering, it is noted that "[failure] to obtain regulatory approvals or permits in a timely fashion could adversely affect our operations."

   a) How costly would a failure to obtain a regulatory approval or permit be to BioAmber?

Answer 3) a. *Costs if failure to obtain regulatory approvals.*

Our business currently has all necessary operating approvals material to our current operations, and we are well into the process of obtaining and maintaining numerous

Canadian regulatory approvals and permits in order to build and operate our planned manufacturing facility in Sarnia, Ontario.

The construction and operation of our production plants will require obtaining permits and other approvals in various jurisdictions. For example, the production plant in Sarnia, Ontario, Canada will require Certificates of Approval from the Ministry of Environment, an Environmental Assessment under the Canadian Environmental Assessment Act, and planning, construction, building, occupancy and fire permits from the City of Sarnia. Similar requirements are anticipated to apply in other countries where production plants are or may be planned.

Certainly, compliance with applicable regulatory rules and regulations can be costly and time consuming. ***BioAmber has the resources and funding to accommodate these costs****. In addition, new laws, new regulations, new interpretations of existing laws or regulations, future governmental enforcement of environmental laws or other developments could result in significant expenditures. This is especially true with the existing regulatory environment for the chemical industry.*

In most ***cases it is not the regulations themselves that prevent enough investment capital to offset the cost, but the effects of the continued regulatory uncertainty.*** *A discord of global chemical regulation with different standards in different global markets has increased overall risk to the development of new technologies. Because of the increased costs associated with compliance of differing systems, private capital has hesitated to invest in green chemicals that inherently reduce energy consumption and increase product safety.* ***Chemical non-regulation in the U.S. has been especially harmful*** *to both consumers and workers by preventing innovation developments and commercialization for high performance materials that have a better carbon footprint, and sequester C02 in the process as in bio succinic acid.*

In the case of the U.S., the obvious absence of regulation has given more than 60,000 chemicals grandfathered in under the Toxic Chemicals Safety Act a distinct advantage in the market place by crafting a place for products without toxicity testing.

Background:

Regulations for the Chemical Industry:

In the United States:

1. Occupational Safety and Health Act and analogous state laws and regulations govern the protection of the health and safety of employees.

2. Clean Air Act and analogous state laws and regulations impose obligations related to emissions of air pollutants, including greenhouse gases.

3. CERCLA (Comprehensive Environmental Response, Compensation, and Liability Act) and analogous state laws and regulations govern the clean-up of hazardous substances.

4. Water Pollution Control Act, also known as the Clean Water Act, and analogous state laws and regulations govern discharges into waters.

5. Toxic Substances Control Act, or TSCA, and analogous state laws and regulations impose requirements on the production, importation, use and disposal of chemicals and genetically modified microorganisms.

In Canada,

6. Similar regulatory programs exist under the Canadian Environmental Protection Act (CEPA 1999). In particular, a regulatory program similar to TSCA requires that Environment Canada approve the manufacture of any chemical not already included on the Domestic Substances List (DSL).

In the European Union:

7. REACH (Registration, Evaluation, Authorization, and Restriction of Chemical Substances). Under REACH, we are required to register our products with the European Commission.

More on the effects of an unregulated chemical industry.

The Economic Benefits of a Green Chemical Industry in the United States Report by James Heintz and Robert Pollin states, "The outdated TSCA regulates many of the chemicals used in industrial production and consumer products. However, under TSCA, the ability of the Environmental Protection Agency (EPA) to oversee the development and marketing of chemicals is constrained. The EPA is required to demonstrate that products are harmful before regulating them. Moreover, TSCA grandfathered in about 62,000 chemicals which were in use prior to 1979. The end result is that the information available on chemicals is limited or non-existent and many remain virtually unregulated. A failure to reform TSCA has a number of implications for the future of the U.S. chemical industry and the U.S. economy:

1. U.S. regulatory framework lags far behind other countries and regions, such as the European Union and
Canada, with consequences for access to important markets.
2. TSCA fails to address the problem that significant costs associated with hazardous chemicals are being imposed on consumers and downstream users.
3. Consumers, investors, workers, and businesses have inadequate information on chemical products, limiting their ability to make informed decisions and creating market failures.
4. TSCA perpetuates perverse incentives that hamstring innovation and cause producers
to favor existing chemicals rather than investing in safer alternatives

b) Could a failure to obtain a regulatory approval or permit significantly impact BioAmber's financial condition?

Answer 3) b. Financial impact if failure to obtain regulatory approvals

In the event that we fail to ultimately obtain all necessary permits, we may be forced to delay operations of the facility and the receipt of related revenues or abandon the project altogether and lose the benefit of any development costs already incurred, which would have an adverse effect on our results of operations.

4) How much money does BioAmber spend on an annual basis to comply with regulations?
   a) Do you have staff that works on regulatory compliance issues? If so, how many employees work on regulatory compliance issues and how much of their time is spent on regulatory compliance issues?

BioAmber CHEMISTRY

Answer 4) a.

BioAmber has a full time VP Compliance and Regulatory Affairs, Dr. Laurent Bernier, plus an additional employee working part time on compliance and regulations. We expect the amount of time spent in this area to increase by 35% in 2011.

Cash spent on regulatory affairs in 2011 (USD)

Supplier	Total
Staff salary	113,785.78
Staff Salary – Part Time	24,503.58
ECHA	23,632.00
Travels	23,633.00
Acera Consult	10,963.93
Cantox Health Sciences Inc.	4,045.72
OPTIMUM INC.	8,262.91
BIOTECANADA	626.58
GESTION SOLTIS INC.	35,840.78
Eco-Mundo	12,995.95
	258,290.23

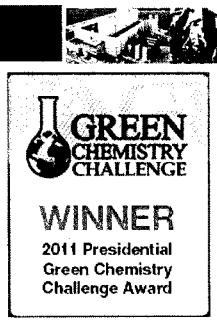
5) Please provide toxicology studies supporting the safety of the primary raw materials and finished products you described at the hearing. Please include all data supporting assessment of eye and skin irritation, sensitization, acute toxicity, subchronic and chronic toxicity (including animal bioassays), genetic toxicology, developmental toxicology, reproductive toxicology (including multi-generation studies). Please include any epidemiology data evaluating human health effects. Please include any evaluations of any of these products by regulatory agencies and/or other federal institutions such as the National Toxicology Program. Documentation of toxicology studies, supporting safety of the primary raw materials and finished products.

i) **SUCCINIC ACID**

(1) USDA BioPreferred product status. BioAmber was one of the first companies to have a chemical intermediate awarded the USDA Certified Biobased Product Label.

USDA CERTIFIED BIOBASED PRODUCT PRODUCT 97%

(2) 2011 EPA Presidential Green Chemistry Award - The Office of Chemical Safety and Pollution Prevention of the EPA awarded BioAmber the Presidential Green Chemistry Award, 2011. The Presidential Green Chemistry Challenge recognizes chemical technologies that incorporate the principles of green chemistry into chemical design, manufacture,



and use. For the purposes of the program, green chemistry is defined as the use of chemistry for source reduction. Source reduction prevents the formation of any hazardous substance in any chemical product or process. Source reduction is the highest tier of the risk management hierarchy as described in the Pollution Prevention Act of 1990 (PPA). It is preferable to recycling, treatment, or disposal. The term "source reduction" includes any practice which: (i) reduces the amount of any hazardous substance, and (ii) reduces the hazards to public health and the environment

Included within PDF document:

(3) **BioAmber Company Profile**: description of portfolio of renewable chemicals
(4) **Material Safety Data Sheet (MSDS) Succinic Acid 2. Hazards Identification, 11. Toxicological Information**
(5) **Generally Recognized As Safe (GRAS) status document** from the Food and Drug Administration (FDA). Succinic acid is in the CODEX ALIMENTARIUS as a safe food additive, mostly used for food preservation and as a flavoring agent.
(6) **European Registration Evaluation Authorization and Restriction of Chemical substances (REACh, EC 1907/2006)** [1] **Submission Report** – UD309022-56.
(7) **ASTM-D6866-11 Report of Biobased Content Analysis** from ISO-17025 Accredited Testing Laboratory

ii) **mPBS** – High performance material and product made from succinic acid
(1) **FDA Food Contact Compliant** - Keller and Heckman opinion letter

(2) **General Manager, Amberworks JV Matrix** TSCA (USA Chemical Inventory)--We are fully compliant. All components listed.
(3) REACH (Europe Chemical Inventory)—we are compliant. All components are listed.

	TSCA	FDA*	REACH
AW 2400	Compliant - all components are listed	Compliant with FDA regualtions under the "Housewares Exemption"	Compliant - all required components are listed
AW 3000	Compliant - all components are listed	Compliant with FDA regualtions under the "Housewares Exemption"	Compliant - all components are listed
837 01 01 (AP7)	Compliant - all components are listed	Compliant with FDA regualtions under the "Housewares Exemption"	Compliant - all components are listed

(4) EU Food Contact—all components are listed.

6) Would your company benefit in any way from efforts to promote public fear of substances currently in the marketplace?

Answer 6. *No benefit to company from promotion of public fear in the marketplace.*

[1] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32006R1907:EN:NOT

No. Promotion of public fear of substances currently in the marketplace will not benefit BioAmber. However, providing consumers and investors with accurate information regarding chemical production and the risks associated with specific chemicals may begin to correct the unfair advantage that unregulated incumbent chemical companies have enjoyed since the industry's inception.

Consumers and investment analysts that have access to documents like the Report on Carcinogens are better informed at purchase, more likely to identify material risks in a company such as increased insurance rates. With increased transparency, consumers will be able to avoid products which contain chemicals that are suspected to increase health risks, thus adopting a prudent standard of care with regard to their own health. Analysts will be able to identify which companies are more at risk than others and value shares accordingly.

A better informed marketplace will spur innovations that benefit society, the environment and our citizens according to the needs of the people. If we are to believe that the we should "let the market decide" what innovation or product succeeds, then we must provide the marketplace with the appropriate information to make that decision.

7) Would overly cautious interpretation of scientific literature that prompt listings in government assessment reports increase demand for your products?

Answer 7. *No increase in demand for products with overly cautious interpretation of scientific literature.*

No. An overly cautious interpretation of scientific literature may cause a "chilling effect" on larger chemical company partners to invest in new alternatives and innovative product materials. Our market research shows that some chemical company executives fear consumers will question their existing products if the company promote or produces new "non-toxic" alternatives. This could diminish high performance application development and hinder the natural growth of adoption in the incumbent industry.

Overly cautious consumers could may simply stop buying plastic and chemical products because of confusion over chemical names and formulations. Lack of government regulation based on comprehensive information from chemical companies only compounds existing fears that consumers remain unprotected. Over cautious interpretation of scientific literature would by the same reasoning quell investment in Green Chemistry.

BioAmber remains confident that readily available accurate information and adequate chemical safety regulation by the US government harmonized with REACh will be a net positive for companies, consumers and government alike. Unfortunately, the market remains uninformed, unprotected and underinvested.

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September 2, 2010

Via Electronic and U.S. Mail

Mr. Ray Balee
President
Sinoven Biopolymers, Inc.
1895 Page Place
Malvern, Pennsylvania 19355

Re: FDA Status of Sinoven Biopolymer's Modified Polybutylene Succinate Product When Used in Food Contact Applications; Our File No. SI14398-01

Dear Mr. Balee:

The purpose of this letter is to respond to your request for our opinion regarding the status, under the laws and regulations administered by the U.S. Food and Drug Administration (FDA), of Sinoven Biopolymers' modified polybutylene succinate (mPBS) product for use in certain food-contact applications. More specifically, we understand that Sinoven's mPBS product is intended for use in the construction of disposable tableware, to include items such as cups, cup lidding, dishware, utensils, stirrers, straws, *etc.* Based on the information that you have provided us, including molecular weight and residual data, we have no hesitation in concluding that Sinoven's mPBS product may be used as intended in the construction of disposable tableware, and that such use may properly be said to comply fully with the Federal Food, Drug, and Cosmetic Act (the Act) and all applicable food additive regulations.

We trust that you will find this letter to be fully responsive to your request for our opinion. Should you have any further questions, or if we may be of assistance in any other way, please do not hesitate to contact us.

Cordially yours,

Pamela L. Langhorn

BIOAMBER S.A.S.

Foundation
- 2008

Branches
- Wholesale to customers in bioplastics and renewable chemicals
- Polyurethanes
- Cosmetics, Coatings & Resins
- Plasticizers
- Deicers
- Lubricants
- Solvents
- Food & Flavours

Key bio-based products
- Biosuccinic Acid
- Bio-based 1,4 BDO
- mPBS
- Phthalate-free Plasticizers
- PLA/mPBS blends
- C6 chemicals

BioAmber
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Company Profile

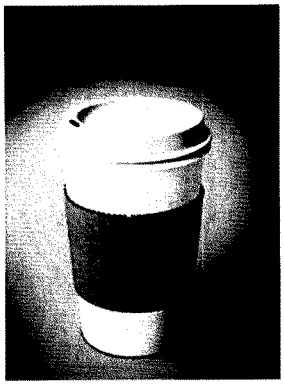
BioAmber is a next generation chemicals company whose business model of open innovation and partnerships is bringing cost-effective performance materials to market and driving customer innovation in a broad range of applications. Its proprietary technology platform combines industrial biotechnology, an innovative purification process and chemical catalysis to convert renewable feedstocks into chemicals for use in a wide variety of everyday products.

BioAmber is a private, US company with a global presence, based in Minnesota, USA. In addition to its European plant, the only commercial scale plant for biobased succinic acid today, BioAmber is building the world's largest commercial plant for biosuccinic acid in North America (Sarnia, Ontario), together with Mitsui & Co. The Sarnia plant will produce both biosuccinic acid and biobased 1,4 Butanediol (BDO).

Portfolio of Renewable Chemicals

BioAmber offers a portfolio of renewable chemicals based on succinic acid and other C4 chemicals, including 1,4-butanediol (BDO) and esters of succinic acid, as well as a new biopolymer platform based on the modified polybutylene succinate biopolymer (mPBS). mPBS is biodegradable and will be >50% renewable with biobased succinic acid and 100% renewable with biobased 1,4-BDO. mPBS can be used at higher heat distortion temperatures, has better strength and stiffness, and drop-in processability for extrusion and injection moulding.

BioAmber will also use mPBS in a new family of compounded PLA/mPBS resin grades thanks to its joint venture with NatureWorks, which is already offering samples of developmental grades for thermoforming and injection moulding processes. This new family is designed for food service ware applications, expanding the PLA property range in terms of flexibility, toughness, heat resistance and drop-in processability on existing manufacturing equipment. BioAmber is also developing a C6 Platform that will provide biobased adipic acid, bio-caprolactam and bio-HMDA.



mPBS

BioAmber produces modified polybutylene succinate (mPBS), a biodegradable polymer with high heat resistance that feels and performs like high-impact polystyrene, polypropylene or PVC. Use of BioAmber biosuccinc acid in mPBS offers a biopolymer that is not only degradable but also partially renewable. As BioAmber's biobased 1,4 Bio-BDO becomes available, mPBS will be 100% renewable.

Compounded PLA/mPBS

Through BioAmber's joint venture with NatureWorks, a new family of developmental PLA/mPBS compounded resins have been developed for food service ware applications. Based on market interest, further formulated PLA/mPBS solutions will be developed.

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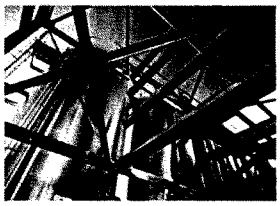
Link to Agrobiobase

Plasticisers
The market is moving to replace phthalates with alternative plasticisers where possible, especially in sensitive applications such as children's products. BioAmber has partnered with Lanxess, a leader in specialty non-phthalate plasticisers to develop a new family of biobased succinate plasticizers.

Polyurethanes
BioAmber's biosuccinic acid can be used to replace petroleum based dibasic acids used in polyester polyols for more environmentally friendly polyurethanes that offer performance benefits in specific applications.

Resins and Coatings
Biosuccinic acid can be used to replace adipic acid in polyester coating resins, powder coatings and unsaturated polyester resins (UPR) to provide environmentally-friendly coatings with a lower carbon footprint.



Cosmetics and Personal Care
BioAmber's biosuccinic acid and its esters can be used in wide range of personal care applications; for example, as natural surfactants and emollients.

Deicers
BioAmber's patented biobased succinate salts derived from biosuccinic acid offer environmentally-sound deicing solutions with enhanced corrosion protection.

Foods and Flavours
Succinic acid is used in food applications as a pH regulator and a flavouring agent, among other functionalities. BioAmber's biosuccinic acid offers food and flavours companies a natural alternative to petroleum-derived succinic for enhancing food naturally.

Lubricants
Biosuccinic esters are environmentally-friendly solutions for the lubricants market as base oils and additives in industrial lubricants and metal-working fluids, with improved flowability in cold temperatures and better prevention of oxidation and corrosion.

Solvents
Succinate esters have demonstrated performance in solvents; BioAmber's biosuccinc acid can be used to provide biobased, non-VOC, non-toxic solvents that substitute conventional solvents.

Contact

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France
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www.bio-amber.com

Contact person

Wladimir Moraes
Wladimir.Moraes@bio-amber.com

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September 2, 2010

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Cordially yours,

Pamela L. Langhorn

BioAmber
CHEMISTRY INSPIRED BY NATURE

Version 5
Revision Date 11/03/2010

MATERIAL SAFETY DATA SHEET

CHEMICAL PRODUCT FOR INDUSTRIAL USE

According to Regulation EC No 1907/2006 of the European Parliament and of the Council of 18 December 2006 (REACh).

SUCCINIC ACID

1. PRODUCT AND COMPANY IDENTIFICATION

Product name :	SUCCINIC ACID
Chemical name :	SUCCINIC ACID
Company :	Bioamber S.A.S. Route de Pomacle F-51110 Bazancourt, France
Telephone :	+33 3 26 89 48 90
Emergency Phone # :	+33 6 75 72 88 87
Email :	patrick.piot@bio-amber.com
MSDS Contact :	Patrick Piot

2. HAZARDS IDENTIFICATION

Classification Regulation	**Classification, Symbols, R Phrases, S Phrases, Signal Words, Hazard Statements, and Precautionary Statements**
According to Regulation (EC) 1272/2008	Skin irritation (category 2) Serious eye damage (category 1) Xi: Irritant R Phrases: R36/37/38, R41 S Phrases: S26, S36/37/39 
According to Directive 67/548/CEE	Skin and respiratory irritation. May cause serious eye damage.
GHS	Pictogram:  Signal word: Danger Hazard statements: H315, H318, H335 Precautionary statements: P261, P280, P305 + P351 + P338
OSHA Hazards	Irritant
HMIS Classification	Health hazard: 2 Flammability: 0 Physical hazards: 0
NFPA Rating	Health hazard: 2 Fire: 0 Reactivity Hazard: 0
WHMIS Classification	Class D2B (eye irritation) 

Most Important Hazards : May be harmful if inhaled. Causes respiratory tract irritation. May be harmful if swallowed. May be harmful if absorbed through skin. May cause skin irritation. Causes eye irritation.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Synonyms : Butanedioic acid
Formula : C4H6O4
Molecular Weight : 118.09 g/mol

CAS-No	EC-No	Index-No	Classification	Concentration
Succinic Acid				
110-15-6	203-740-4	---	Skin Irrit. 2; Eye Dam. 1; STOT SE 3; H315, H318, H335 Xi, R36/37/38 – R41	90%-100%

4. FIRST AID MEASURES

General advice
Consult a physician. Show this safety data sheet to the doctor in attendance. Move out of dangerous area.

If inhaled
If breathed in, move person into fresh air. If not breathing give artificial respiration Consult a physician.

In case of skin contact
Wash off with soap and plenty of water. Consult a physician.

In case of eye contact
Rinse thoroughly with plenty of water for at least 15 minutes and consult a physician.

If swallowed
Never give anything by mouth to an unconscious person. Rinse mouth with water. Consult a physician.

5. FIRE-FIGHTING MEASURES

Flash point No data available
Flammable Limits in Air
Lower (LFL): No data available
Upper (UFL): No data available
Suitable extinguishing media
Use water spray, alcohol-resistant foam, dry chemical or carbon dioxide.

Fire-Fighting Instructions
Promptly isolate the scene by removing all persons from the vicinity of the incident if there is a fire. No action shall be taken involving any personal risk or without suitable training.
Special protective equipment for fire-fighters
Wear self contained breathing apparatus for firefighting if necessary.
Hazardous Combustion Products
Hazardous decomposition products formed under fire conditions. - Carbon oxides.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions
Use personal protective equipment. Avoid dust formation. Avoid breathing dust. Ensure adequate ventilation.
Environmental precautions
Do not let product enter drains.
Methods and materials for containment and cleaning up
Pick up and arrange disposal without creating dust. Keep in suitable, closed containers for disposal.

7. HANDLING AND STORAGE

Precautions for safe handling
Avoid contact with skin and eyes. Avoid formation of dust and aerosols. Provide appropriate exhaust ventilation at places where dust is formed. Normal measures for preventive fire protection.
Conditions for safe storage
Keep container tightly closed in a dry and well-ventilated place.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Contains no substances with occupational exposure limit values.
Exposure Limit
ACGIH: Not established
OSHA: Not established
Engineering Measures:
No special ventilation requirements. Good general ventilation should be sufficient to control worker exposure to airborne contaminants.
Personal protective equipment
Respiratory protection
Where risk assessment shows air-purifying respirators are appropriate use a dust mask type N95 (US) or type P3 (EN 143) respirator. Use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU).
Hand protection
Handle with gloves.
Eye protection
Safety glasses with side-shields conforming to EN166.
Skin and body protection
Choose body protection according to the amount and concentration of the dangerous substance at the work place.
Hygiene measures
Handle in accordance with good industrial hygiene and safety practice. Wash hands before breaks and at the end of workday.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance	
Powder	
Color white	
Odor/Odor threshold	Odorless
Safety data	
pH (1% in water)	2.4 – 2.8
Melting point	184 - 192°C
Boiling point	No data available
Decomposition temperature	No data available

Auto-ignition temperature	No data available
Explosion properties	
– Sensitivity to mechanical impact	No data available
– Sensitivity to static discharge	No data available
Density/Specific gravity	No data available
Evaporation rate	No data available
Coefficient of water/oil distribution	No data available
Vapor pressure	No data available
Vapor density	No data available
Kst, Pmax	Kst = 51 bar.m/s - Pmax = 7,4 bar
Min. Flammability Energy	> 1 000 mJ
Min. Flammability Temp. (cloud)	620°C
Water solubility	Moderately soluble

10. STABILITY AND REACTIVITY

Chemical stability
Stable under recommended storage conditions.
Conditions to avoid
No data available.
Materials to avoid
Bases, Oxidizing agents, Reducing agents.
Hazardous decomposition products
Hazardous decomposition products formed under fire conditions. - Carbon oxides.
Hazardous polymerization
Under normal conditions of storage and use, hazardous polymerization will not occur.

11. TOXICOLOGICAL INFORMATION

Routes of Entry
Inhalation, ingestion, and dermal and eye contact.
Acute toxicity

Chemical Name/CAS No.	Route & Species	Value
Succinic acid/ 110-15-6	Oral (Rat)	LD50 = 2,260 mg/kg

Skin corrosion/irritation
Causes skin irritation.
Serious eye damage/eye irritation
Eyes – rabbit - Severe eye irritation.
Respiratory or skin sensitization
No data available.
Germ cell mutagenicity
Genotoxicity in vitro - Human - fibroblast.
DNA inhibition.
Carcinogenicity

IARC:	No component of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.
ACGIH:	No component of this product present at levels greater than or equal to 0.1% is identified as a carcinogen or potential carcinogen by ACGIH.
NTP:	No component of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.
OSHA:	No component of this product present at levels greater than or equal to 0.1% is identified as a carcinogen or potential carcinogen by OSHA.

Reproductive toxicity
No data available.
Teratogenicity/Embryotoxicity

No data available.
Specific target organ toxicity - single exposure (GHS)
Inhalation - May cause respiratory irritation.
Specific target organ toxicity - repeated exposure (GHS)
No data available.
Aspiration hazard
No data available.
Toxicologically synergistic materials
No data available.
Potential health effects
Inhalation May be harmful if inhaled. Causes respiratory tract irritation.
Ingestion May be harmful if swallowed.
Skin May be harmful if absorbed through skin. Causes skin irritation.
Eyes Causes eye irritation.

12. ECOLOGICAL INFORMATION

Toxicity
Not available.
Persistence and degradability
Not available.
Bioaccumulative potential
Not available.
Mobility in soil
Not available.
PBT and vPvB assessment
Not available.
Other adverse effects
Not available.

13. DISPOSAL CONSIDERATIONS

Product
Observe all federal, state, and local environmental regulations. Contact a licensed professional waste disposal service to dispose of this material.
Contaminated packaging
Dispose of as unused product.

14. TRANSPORT INFORMATION

Regulation	Proper Shipping Name	UN Number	Hazard Class	PG
DOT (US)	Not regulated	---	---	---
TDG (Canada):	Not regulated	---	---	---
IMDG (International - Maritime):	Not regulated	---	---	---
IATA	Not regulated	---	---	---

15. REGULATORY INFORMATION

Country	Regulatory Information
Succinic Acid	
EU	According to **Regulation EC No 1907/2006** of the European Parliament and of the **Council of 18 December 2006 (REACh)**. **Substance classifying** According to Regulation (EC) 1272/2008 Skin irritation (category 2) Serious eye damage (category 1)  **Xi** **Irritant** **R Phrases** **R36/37/38** Irritating to eyes, respiratory system and skin **R41** Risk of serious damage to eyes **S Phrases** **S26** In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. **S36/37/39** Wear suitable protective clothing, gloves and eye/face protection. **According to Directive 67/548/CEE** Skin and respiratory irritation. May cause serious eye damage.
GHS	Pictogram  Signal word Danger Hazard statement(s) H315 Causes skin irritation. H318 Causes serious eye damage. H335 May cause respiratory irritation. Precautionary statement(s) P261 Avoid breathing dust/fume/gas/mist/vapours/spray. P280 Wear protective gloves/eye protection/face protection. P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
US	**OSHA Hazards** Irritant **SARA 302 Components** SARA 302: No chemicals in this material are subject to the reporting requirements of SARA Title III, Section 302. **SARA 313 Components** SARA 313: This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313. **SARA 311/312 Hazards** Acute Health Hazard **Massachusetts Right To Know Components** No components are subject to the Massachusetts Right to Know Act. **Pennsylvania Right To Know Components** Succinic acid CAS-No. 110-15-6 Revision Date

	New Jersey Right To Know Components Succinic acid CAS-No. 110-15-6 Revision Date **California Prop. 65 Components** This product does not contain any chemicals known to State of California to cause cancer, birth defects, or any other reproductive harm.
Canada	**WHMIS** Class D2B (Eye irritation)  **DSL Status** All components of this product are on the Canadian DSL list. This product has been classified in accordance with the hazard criteria of the *Controlled Products Regulations* and the MSDS contains all the information required by the *Controlled Products Regulations*.

16. OTHER INFORMATION

The above information is believed to be correct but does not purport to be all inclusive and shall be used only as a guide. The information in this document is based on the present state of our knowledge and is applicable to the product with regard to appropriate safety precautions. It does not represent any guarantee of the properties of the product. Bioamber shall not be held liable for any damage resulting from handling or from contact with the above product.

U.S. Food & Drug Administration

Database of Select Committee on GRAS Substances (SCOGS) Reviews

Succinic acid

Return to Listing[5]

Report No.:	53
Type of Conclusion:	1
ID Code:	110-15-6
Year:	1975
CFR Section:	184.1091
SCOGS Opinion:	Succinic acid occurs widely as a natural constituent of the plants and animals which are commonly used for human food. As one of the intermediary metabolites in the citric acid cycle, it may participate in the net synthesis of glucose and other sugars and fatty acids normally present in plant and animal tissue. At the level succinic acid occurs naturally in foods, there is no evidence that it is hazardous to man or animals. Moreover, experimental animals tolarate succinic acid in amounts equivalent to several g per kg of body weight. By contrast, a reasonable average daily intake of succinic acid added to foods is estimated to be less than 0.01 mg per day, a dosage that is orders of magnitude less than that required to elicit toxic signs in experimental animals. There have been few scientific studies designed to explore possible untoward effects of succinic acid. However, the normal role of succinic acid as an intermediary metabolite in living organisms including man, is persuasive in favor of its safety. Based on these considerations, the Select Committee concludes that: There is no evidence in the available information on succinic acid that demonstrates, or suggests reasonable ground to suspect, a hazard to the public when it is used at levels that are now current or that might reasonably be expected in the future.

Links on this page:

1. http://www.addthis.com/bookmark.php?u508=true&v=152&username=fdamain
2. http://www.addthis.com/bookmark.php
3. http://www.fda.gov/default.htm
4. http://www.fda.gov/Food/FoodIngredientsPackaging/GenerallyRecognizedasSafeGRAS/GRASSubstancesSCOGSDatabase/default.htm
5. /scripts/fcn/fcnNavigation.cfm?filter=succinic&sortColumn=36%28%25%JAH%2152ED0%21AP%2C%2C1M%2F5Q9Q%2CF%40++%0D%0A&rpt=scogsListing&displayAll=false#339

Page Last Updated: 10/31/2006

Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

Submission Report - UD309022-56

Dossier type: Registration
Submission number: UD309022-56
Reference date: 26/03/2012
Reference number: 01-2119896114-34-0001
Submission date: 17/04/2012
Current state: Complete

Tonnage band: Over 1000 tonnes/year
On-site isolated intermediates tonnage band: -
Transported isolated intermediates tonnage band: -
Is phase in: Yes
Joint submission name: JS_SA_203-740-4
Purchase order: -
Fee waiver: No
Dossier file name: Update_succinic acid_2.i5z

Substance name: [203-740-4] succinic acid

Remark:

Dossier UUID : IUC5-c6da609a-1135-4166-ad16-02e8f404bdc7
Dossier creator: -

Name given by the dossier creator: Update_succinic acid
Submitting legal entity: ARD
Submitting legal entity UUID: ECHA-faf760b4-3719-4121-933c-c7393cf20e36

Is the submission an update?: Yes
Last submission number: XP305063-27

Further to a request/decision from regulatory body: No
Spontaneous Update: Yes

Joint submission: Yes
Company Size: Large
Invoice contact name: DARGELOS MARIANNE
Declaration: No
Number of study summaries/robust study summaries: -
List of study summaries/robust study summaries: -

Submission Report - UD309022-56

Justification(s) for the above confidentiality claim(s): -

Lead completeness check: Succeeded

No.	Task	Remark	Result
1.	Virus check	-	Succeeded
2.	File format validation	-	Succeeded
3.	Check XML structure	-	Succeeded
4.	Enforce Rules	-	Succeeded
5.	Store Dossier	-	Succeeded
6.	Create Substance Identity	-	Succeeded
7.	Assign MSCAs	-	Succeeded
8.	Technical Completeness Check	-	Succeeded
9.	Pay Submission Fee	-	Succeeded
10.	Overall Completeness Check	-	Succeeded
11.	Issue Reference Number	-	Succeeded
12.	End of Pipeline Activities	-	Succeeded
13.	Data Dissemination	-	Skipped
14.	Trigger WorkFlow	-	Succeeded

ISO-17025 Accredited Testing Laboratory

PJLA ISO/IEC 17025:2005 Testing Accreditation# 59423

Beta Analytic Inc.
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www.betalabservices.com

Report of Biobased Content Analysis using ASTM-D6866-11

Submitter: BioAmber Inc.

Submitter Label: Crystalline Succinic Acid (USDA Application# 1803)

Laboratory Number: Beta-311521

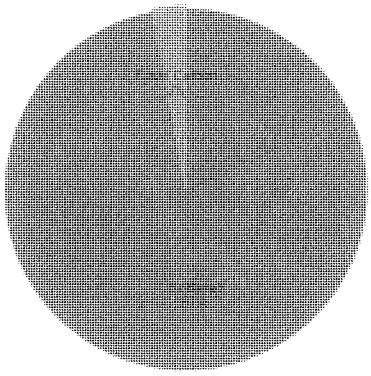
Material: Biobased Solid

Date Received: December 06, 2011

Date Reported: December 11, 2011

Mean Biobased Result : 97 % *

Proportions Biobased vs. Fossil Based indicated by 14C content



* ASTM-D6866 cites precision on The Mean Biobased Result as +/- 3% (absolute). This is the most conservative estimate of error in the measurement of complex biobased containing solids and liquids based on empirical results. Real precision for readily combustible and homogenous materials (e.g. gasoline) and especially samples recieved as CO_2 (e.g. flue gas or CEMS exhaust) can be as low as +/- 0.5-2%. The result only applies to the analyzed material. Fluctuations in carbon content within a batch of product, gasoline or flue gas must be determined separately (e.g. averaged measurements of multiple solids or liquids, and single measurement of the combination of gas aliquots collected over time). The accuracy of the result as it applies to the analyzed product, fuel, or flue gas relies upon all the carbon in the analyzed material originating from either recently respired atmospheric carbon dioxide (within the last decade) or fossil carbon (more than 50,000 years old). "Percent biobased" specifically relates % renewable (or fossil) carbon to total carbon, not to total mass or molecular weight. Mean Biobased estimates greater than 100% are assigned a value of 100% for simplification.

BETA

ISO-17025 Accredited Testing Laboratory

PJLA ISO/IEC 17025:2005 Testing Accreditation# 59423

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info@betalabservices.com
www.betalabservices.com

Explanation of Results

Biobased Analysis using ASTM-D6866-11, April 2011

The application of ASTM-D6866 to derive a "Biobased content" is built on the same concepts as radiocarbon dating, but without use of the age equations. It is done by deriving a ratio of the amount of radiocarbon (14C) in an unknown sample to that of a modern reference standard. This ratio is calculated as a percentage with the units "pMC" (percent modern carbon). If the material being analyzed is a mixture of present day radiocarbon and fossil carbon (containing no radiocarbon), then the pMC value obtained correlates directly to the amount of biomass derived carbon in the sample.

The modern reference standard used in radiocarbon dating is a NIST (National Institute of Standards and Technology) standard with a known radiocarbon content equivalent approximately to the year AD 1950. AD 1950 was chosen since it represented a time prior to thermo-nuclear weapons testing which introduced large emounts of excess radiocarbon into the atmosphere with each explosion (termed "bomb carbon"). This was a logical point in time to use as a reference for archaeologists and geologists. For an archaeologist or geologist using radiocarbon dates, AD 1950 equals "zero years old". It also represents 100 pMC.

"Bomb carbon" in the atmosphere reached almost twice normal levels in 1963 at the peak of testing and prior to the treaty halting the testing. Its distribution within the atmosphere has been approximated since its appearance, showing values that are greater than 100 pMC for plants and animals living since AD 1950. It has gradually decreased over time with today's value being near 105 pMC. This means that a fresh biomass material such as corn, sugar cane or soybeans would give a radiocarbon signature near 105 pMC.

Combining fossil carbon with present day carbon into a material will result in a dilution of the present day pMC content. By presuming ~105 pMC represents present day biomass materials and 0 pMC represents petroleum derivatives, the measured pMC value for that material will reflect the proportions of the two component types. For example, a material derived 100% from present day soybeans would give a radiocarbon signature near 105 pMC. But if it was diluted with 50% petroleum carbon, it would give a radiocarbon signature near 53 pMC.

The "biobased content" of a material is reported as a percent value relating total renewable organic carbon to total organic carbon. The final result is calculated by multiplying the pMC value measured for the material by 0.95 (to adjust for bomb carbon effect). The final value is cited as the MEAN BIOBASED RESULT and assumes all the components within the analyzed material were either present day living (within the last decade) or fossil in origin.

The results provided in this report are uniquely applicable to the analyzed material and are reported using the designated labeling provided with the sample. Although analytical precision is typically 0.1 to 0.5 pMC, empirical data has demonstrated that indeterminant errors can introduce uncertainty to 2 to 3 pMC. As such, ASTM-D6866 cites an uncertainty of +/- 3 % (absolute) on each result. Remember the results only relate carbon source, not mass source. A reported percentage does not represent to the total mass of fossil vs. renewable components present. Only the amount of renewable carbon vs fossil carbon present is indicated.

U.S. House of Representatives

Committee on Science, Space, and Technology
Subcommittee on Investigations & Oversight
and
Committee on Small Business
Subcommittee on Healthcare and Technology

QUESTIONS FOR THE RECORD

"How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"

Wednesday, April 25, 2012

Mr. John Barker, Corporate Manager,
Environmental Affairs, Safety and Loss Prevention,
Strongwell Corporation

Questions submitted by Dr. Paul Broun, Chairman, House Science, Space and Technology, Subcommittee on Investigations & Oversight and Rep. Renee Ellmers, Chairwoman, House Small Business Subcommittee on Healthcare and Technology

1) In your testimony you stated that "there is no reasonable replacement" for styrene. Can you elaborate on that statement?

   Answer: Polyester resin with styrene accounts for 95% of Strongwell's production, has a cost of $.88 per pound and is about one third of our raw material cost. Phenolic resin contains no styrene, has a cost of $1.25 per pound, has poorer physical characteristics, has special processing concerns and an employee exposure level which is $1/10^{th}$ that of styrene, making it difficult for employees to work with. Epoxy resin contains no styrene but is prohibitively expensive at $2.30 per pound. Other available resin systems are usually for specialty applications at significantly higher costs.

2) I understand that Strongwell has competitors overseas. If you are forced to increase your products' prices due to new regulations, or the need to use a substance other than styrene, are you concerned that you may lose business to your overseas competitors?

   Answer: If Strongwell were forced use a substance other than styrene we would in most cases use an epoxy system. Our Chinese and Indian competitors already have the advantage of low labor costs and few requirements to comply with stringent environmental and safety regulations. Replacing styrene with another resin system would increase our total raw materials cost to a level 75% higher material costs than our Asian competitors. We simply could not compete with that kind of advantage.

Questions submitted by Rep. Brad Miller

1) You promised at the hearing to provide the Styrene MSDS sheets used by Strongwell—one from before the 12th RoC and one from after. Subsequent to the hearing, you sent two MSDSs to staff via email (see attached MSDS documents for reference). Are these two MSDS's the sheets actually relied on by Strongwell as a reference for staff?

   Strongwell maintains MSDSs from each source of material in use. These MSDSs are available at any time to any employee. Both of these MSDSs are in use.

2) You indicated that the listing of styrene as a "reasonably anticipated" carcinogen "distracts our employees from the real concerns that they should be dealing with on a day-to-day basis, wearing the proper protective equipment, being concerned about the physical hazards they work with, and they are distracted because of the concern about getting cancer from styrene that the NTP has said is reasonably anticipated to be a carcinogen."
   A) Since styrene has been listed for over a decade by IARC as a "possible" carcinogen, and that is to appear on MSDS's, what has changed in the day-to-day work environment for your workforce?

      Answer: Our concern is for our employees' safety. Our excellent safety record is in large part due to our employees' safety awareness. We believe the attention of our employees has shifted from an awareness of legitimate safety issues to an unwarranted and unnecessary fear of getting cancer. This certainly has the potential to have a negative effect on safety.

   B) How do you educate your workers about the health dangers of styrene, and other toxic substances used in your workplaces?

      Answer: Initial new hire training, annual refresher training and training anytime process changes or work requirements warrant.

   C) Please list all other chemicals used by your company that had been listed by April 25, 2012 in either the Report on Carcinogens or the IARC as carcinogens (known, reasonably anticipated, proven, probable or possible).

      Answer: Styrene, antimony trioxide, formaldehyde

3) In response to a question about firms losing their insurance coverage, you indicated you were aware of one company that had lost such coverage. Have you been able to identify that company, or others, that have lost their coverage due to styrene's listing as a "reasonably anticipated" carcinogen in the 12th Report on Carcinogens?

Answer: Please see attachment "Notice of Nonrenewal of Insurance" to Miles Fiberglass and Composites denying coverage, and attached summary of studies showing that the styrene exposure limit was NOT exceeded contrary to the insurance carrier's claim.

Also please see the attached statement of Teri Schenk, Global Composites, submitted for a March 22 Energy and Commerce Committee roundtable on "Business Impacts of IRIS" and the attached Plastics News article.

4) In response to a question about whether Strongwell Corporation participated in the public comment process of the 12th RoC, you indicated that the company had. Then Congresswoman Ellmers asked, "Can you tell us whether or not your comments were responded to by the NTP?" You responded, "Our comments, as far as I know, were not responded to." Congresswomen Ellmers then highlighted that your response seemed to undercut a claim she assigned to Dr. Birnbaum that all comments were responded to.

Staff found a letter from Mr. John Tickle, the President of the Strongwell Corporation, dated May 19, 2009 to Dr. Linda Birnbaum, that directly discusses the NTP and styrene. That letter is attached to these questions. The letter does not provide new scientific information about the health effects of exposure to styrene, but instead emphasizes the potential economic harm of a listing. Since the comment period was intended to gather scientific information that would be relevant to the NTP process, it is hard to know what sort of response Strongwell expected.

However, on May 27, 2009, Dr. Birnbaum sent a response (also attached) thanking you for your comments and inviting the submission of "any peer-reviewed, publicly available publications for our consideration in this evaluation."

A) Did Strongwell make any additional submission as part of the record on the 12th RoC review of styrene? If yes, please provide a copy for the record.

Answer: Clearly the receipt of Mr. Tickle's letter was acknowledged; however, there was no substantive response. Mr. Tickle and Mr. Kreysler expressed specific concerns, to which Dr. Birnbaum replied with complete non-sequiturs, ignoring completely the content of the letter. Mr. Tickle's letter had nothing to do with the comment period, and what was expected was for NTP to acknowledge these concerns and consider changing its approach to avoid the unwarranted negative impacts on the industry.

B) If an additional submission was made, please double check that no response was received from NIEHS as you implied during the hearing.

Regarding further Strongwell submissions to NTP, on behalf of Strongwell, SIRC submitted scientific information to NTP, to which NTP responded only after the RoC was finalized, and even then the responses were again not substantive.

Please see the attached SIRC IQA Request for Correction which provides more information about NTP ignoring scientific information.

C) Whether or not an additional submission was made, the company's May 2009 submission was responded to. Please explain why the Corporate Manager of Environmental Affairs was unaware that Dr. Birnbaum had written back to your company in May of 2009, creating the false impression that NIEHS had ignored your company's submission.

Answer: Again there were no substantive responses.

Attachments

Questions submitted by Rep. Brad Miller

1) You promised at the hearing to provide the Styrene MSDS sheets used by Strongwell—one from before the 12th RoC and one from after. Subsequent to the hearing, you sent two MSDSs to staff via email (see attached MSDS documents for reference). Are these two MSDS's the sheets actually relied on by Strongwell as a reference for staff?

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      Answer: Our concern is for our employee's safety. Our excellent safety record is in large part due to our employee's safety awareness. Any unnecessary distraction from that awareness such as an unwarranted fear of getting cancer has the potential to affect safety.

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      Answer: Initial new hire training, annual refresher training and training anytime process changes or work requirements warrant.

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Answer: Please see attachment "Notice of Nonrenewal of Insurance" to Miles Fiberglass and Composites denying coverage, and attached summary of studies showing that the styrene exposure limit was NOT exceeded contrary to the insurance carrier's claim.

Also please see the attached statement of Teri Schenk, Global Composites, submitted for a March 22 Energy and Commerce Committee roundtable on "Business Impacts of IRIS" and the attached Plastics News article.

Additionally, during the hearing of Wednesday, April 25, 2012, a statement was made by Mr. Barker that requires clarification/amendment. The following statement appears in the transcript on page 78, lines 1761-1766: "Because we self-insure, styrene, or Strongwell has had to place a significant amount of money into reserves to protect ourselves against potential liability lawsuits. The money that we must reserve for liability purposes could be used for investment and job creation and expansion if it weren't for this listing."

Strongwell does indeed self-insure and we are understandably concerned over the possibility of styrene litigation. However, we would like to amend the record to indicate that a reserve account for styrene litigation has not yet been set-up. It should be noted though that should Strongwell become a target of a styrene lawsuit and it becomes necessary to establish one, it may reduce the money we can invest in capital improvements and expansion.

4) In response to a question about whether Strongwell Corporation participated in the public comment process of the 12th RoC, you indicated that the company had. Then Congresswoman Ellmers asked, "Can you tell us whether or not your comments were responded to by the NTP?" You responded, "Our comments, as far as I know, were not responded to." Congresswomen Ellmers then highlighted that your response seemed to undercut a claim she assigned to Dr. Birnbaum that all comments were responded to.

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   However, on May 27, 2009, Dr. Birnbaum sent a response (also attached) thanking you for your comments and inviting the submission of "any peer-reviewed, publicly available publications for our consideration in this evaluation."

   A) Did Strongwell make any additional submission as part of the record on the 12th RoC review of styrene? If yes, please provide a copy for the record.

Styrene Information and Research Center (SIRC)
601 N. Quincy Street, Suite 700, Arlington, VA 22203-1730
Phone: 703-875-0736 Website: www.styrene.org

February 11, 2011

Via email to InfoQuality@od.nih.gov

John T. Burklow
Associate Director for Communications
Office of the Director
National Institutes of Health
Building 1, Room 344
9000 Rockville Pike
Bethesda, MD 20892

Re: Information Quality Act Appeal – Styrene Background Document [1]

Dear Mr. Burklow:

This appeal by the Styrene Information and Research Center, Inc. (SIRC) is being submitted under the Information Quality Act (IQA)[2] and implementing guidelines issued by the Office of Management and Budget (OMB),[3] the U.S. Department of Health and Human Services (HHS)[4] and the National Institutes of Health (NIH).[5] SIRC filed its Request for Correction (RFC) of the Final Report on Carcinogens Background Document for Styrene on October 26, 2009, and the National Toxicology Program (NTP) provided a response dated December 23, 2010 (NTP's Response) which SIRC received on January 14, 2011.[6]

[1] SIRC is not aware of any NIH tracking number being assigned to its original Request for Correction.

[2] Pub. L. No. 106-554, § 515, 114 Stat. 2763A-153 to 2763A-154, 44 U.S.C. § 3516 note (2000).

[3] *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies*, 67 Fed. Reg. 8452 (Feb. 22, 2002).

[4] HHS, *Guidelines for Ensuring the Quality of Information Disseminated to the Public*, available at http://www.hhs.gov/infoquality/part1.html.

[5] NIH, *Guidelines for Ensuring the Quality of Information Disseminated to the Public*, available at http://aspe.hhs.gov/infoquality/Guidelines/NIHinfo2.shtml.

[6] NTP's response was received by SIRC via Federal Express delivery on January 14, 2011. Consistent with the NIH procedures regarding appeals, copies of both SIRC's RFC and NTP's response are attached. They are: letter of October 26, 2009, from Jack Snyder, Executive Director, SIRC to John Burklow, Associate Director for Communications, Office of the Director, NIH; and letter of December 23, 2010, from John R. Bucher, Associate Director, NTP to Jack Snyder, Executive Director, SIRC.

In response to SIRC's RFC, NTP's Response does acknowledge the need to make roughly a dozen corrections to the Background Document and provides some additional clarifications. While these are appreciated, the bulk of NTP's Response consists of formulaic statements to the effect that NTP followed its procedures, and thus the Background Document must be correct. Consistent with the IQA, SIRC's RFC principally addressed the substantive science issues raised by the Background Document. In contrast, NTP's Response studiously avoids the substance of the science and reiterates procedural conclusions like "the Background Document follows the standard format" (p. 5) and "NTP has chosen to accept the advice of the RoC expert panel" (p. 7).

NTP's Response reflects a fundamental misunderstanding of the objectivity criterion under the IQA, as we demonstrate with the examples that appear below. For the Background Document to comply with that criterion, it must be "accurate [and] reliable," contain "the best available . . . science," and present that information in a "complete and unbiased manner . . . within the proper context." It currently does not. The Background Document also violates the "utility" criterion of the IQA because it does not enable a reader to make an informed judgment about the carcinogenicity of styrene.

Finally, NTP fails to rebut the single procedural argument that SIRC *did* make in its RFC – that NTP finalized the Background Document before the close of the public comment period on the Expert Panel's draft report. Those comments were invited to address the Panel's scientific justification for listing styrene, a justification that is based on and inseparable as a factual matter from the manipulations and characterizations of the data that the Expert Panel introduced into the final Background Document through its review comments on the draft, which NTP adopted across the board. We recognize that NTP's procedural approach attempts to sever the Background Document from the Panel's scientific justification, but we view these as interdependent. Thus the Background Document was finalized before NTP had even received all of the public comments on what became fundamental (and problematic) elements of the final Background Document.

The balance of this appeal explains the foregoing assertions and demonstrates how NTP failed to comply with the requirements of the IQA in crafting its reply and why NIH should grant SIRC's appeal and revise the Background Document – and the Substance Profile based on it – accordingly. Because this appeal and the Background Document it addresses are so fundamental to HHS' final listing decision regarding styrene, NTP should not include any decision about styrene in the 12th *Report on Carcinogens (RoC)* until these corrections and associated changes are made in the Draft Profile on styrene.

I. THE IQA REQUIREMENTS OF OBJECTIVITY AND UTILITY

Congress enacted the IQA to ensure and maximize the "quality, objectivity, utility and integrity of information . . . disseminated by Federal agencies" like NIH.[7]

[7] Pub. L. No. 106-554, *supra* note 2, at § 515(a).

"Objectivity" is centrally relevant in cases of scientific health assessments such as the Report on Carcinogens (RoC). "Objectivity" means that information must be *accurate, reliable* and *unbiased*.[8] Moreover, "influential" scientific information like the RoC that bears on assessment of health risks must be based on "*the best available . . . science . . . conducted in accordance with sound and objective scientific practices*."[9] Science that is not the best available, or that is generated by practices that are chosen to produce a given effect, is not objective. NTP's Response fails to rebut (or even address, in some cases) the RFC's demonstration that the Background Document, in many places, is not objective in this respect.

Objectivity must also be reflected in the way that information is presented. To be objective, information must be presented in an *accurate, clear, complete* and *unbiased* manner, which includes presentation in the proper context.[10] In particular, the Background Document is a prime example of a case in which, "in disseminating . . . information to the public, other information must also be disseminated in order to ensure an accurate, clear, complete and unbiased presentation."[11] Influential scientific information bearing on assessing health risks – like the Background Document – must present "each significant uncertainty identified in the process" and "peer-reviewed studies . . . that fail to support any estimate of risk."[12] Again, NTP's Response does not rebut SIRC's demonstration in the RFC that the Background Document fails this aspect of the objectivity criterion in many instances.

Finally, the IQA also aims to ensure the "utility" of information that comes from Federal agencies. "Utility" is equally as important as objectivity and requires that information, as it is presented, be useful to its intended users, including the public.[13] SIRC's RFC demonstrated that the Background Document is not useful because it does not allow a reader to make a reliable judgment about the carcinogenicity of styrene due to NTP's failure to report valid alternative interpretations of fundamental scientific studies. NTP's Response does not overcome that showing.

II. NTP'S RESPONSE DEMONSTRATES THAT IT FUNDAMENTALLY MISUNDERSTANDS THE REQUIREMENTS OF THE OBJECTIVITY AND UTILITY CRITERIA

To satisfy the objectivity and utility criteria, the Background Document generally should:

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[8] 67 Fed. Reg. 8549 (emphasis added).

[9] *Id.* at 8457 (emphasis added).

[10] *Id.* at 8459 (emphasis added).

[11] *Id.*

[12] *Id.* at 8457-58.

[13] *Id.* at 8459; *cf.* 44 U.S.C. § 3504(e)(1)(B) (2006).

(1) Inventory all the relevant, peer-reviewed literature on a particular point; and
(2) Present the methodologies and findings of those studies in an accurate and complete manner, which includes discussing their strengths, limitations and data to the extent they may be relevant to plausible scientific interpretations.[14]

There is probably no dispute among the parties on these steps (although, as shown below, NTP did not always follow them). And so far as it goes, NTP's "standard format" of describing data could accomplish these functions.[15] But no matter how hard NTP strives to characterize the function of a Background Document as a ministerial, descriptive summary of studies, it cannot escape several complexities forced on it by the requirements of objectivity and utility – and merely asserting that it "follow[ed] the standard format" is insufficient to dismiss these inherent challenges.

Below we describe four ways in which the Background Document violates the demands of the objectivity and utility requirements, in each case noting one or more examples. Each of those examples is then explained at greater length.

- **Omission of Analysis of Study Results by the Original Author**
  The views of the relevant scientific community on a particular study are certainly relevant to whether it, or conclusions drawn from it, are "reliable" or represent the "best available . . . science." This is most certainly the case when the principal author of a published study offers interpretations that contradict those in the Background Document. A complete discussion of the study must at least note the fact of this disagreement.
    - Specifically, NTP failed to acknowledge that the principal investigator in Delzell et al. (2006) flatly disagreed with the Expert Panel's characterization of her findings, a characterization that NTP incorporated into the final Background Document.

- **Reliance on a Study Hampered by Methodological Limitations**
  At some point, the methodological limitations of a study may render its findings unreliable, or at least far less reliable than other studies not so limited. It is not sufficient for the Background Document to note the limitations of a study but then to present the resulting data as if they were equally significant as other, more reliable results – especially when these findings, *without* a necessary qualifier about their limitations,

[14] We stress that we are not suggesting that the Background Document needs to contain interpretations. Rather, it should summarize studies so that readers can make informed judgments when more then one plausible interpretation of the data is possible. However, as we note below, in several instances NTP crafted the Background Document to promote a particular interpretation of the data, while ignoring other plausible interpretations without providing any justification for doing so.

[15] *See, e.g.*, NTP's characterization on page 4 of NTP's Response: "The NTP would like point out that the Background Document for styrene follows a standard format for reporting the human cancer studies. In general, the approach was to describe the study population(s), exposure assessment, and methods of statistical analysis, and to extensively report the findings including results for the overall population and any subgroups."

become part of the scientific justification for listing. Such a presentation almost assures that judgments based on the Background Document will fail to reflect the best available science and will be unreliable.

- Specifically, NTP relied on results from Kolstad et al. (1995, 1994) that were not statistically significant to support a finding of an effect.

- **Unexplained Departure from Standard NTP Practice**
  Multiple times in the Background Document, NTP departs from standard NTP practices without acknowledging that departure. Where NTP departs from a standard practice, such as its use of historical controls, the IQA requirement for "sound and objective scientific practice" obliges NTP to:
  - Note the prior policy;
  - Provide a justification for departing from the policy, including whether the departure is a special exception based on particular data, or instead a program-wide decision prompted by the evolving state of scientific understanding; and
  - Inform the public whether NTP will be applying this new position uniformly in the future.

  NTP must follow this process not only to satisfy the IQA, but also to comply with general principles of administrative law and due process.
  - Specifically, NTP used a new historical control analysis to evaluate NCI (1979a), which departs from NTP's practice of not engaging in additional analyses of historical controls;
  - NTP relied on Huff et al. (1984), even though NTP has not typically combined the particular tumor types in question for over two decades; and
  - NTP relied on results that were not statistically significant in Kolstad et al. (1995, 1994) to support a finding of an effect.

- **Omission of Contextual Information Regarding the State of the Science**
  By definition, studies based on hypothesis testing are premised on one of several competing theories about causation. In some cases, each of those theories may be supported by roughly equivalent bodies of work and enjoy comparable support within the scientific community. In other cases, however, the weight of evidence is strongly toward one hypothesis and away from others. Thus, the state of the science provides essential context and must be addressed for the presentation of information to be considered complete and accurate. For example, a discussion on the possible reasons for the variety of finch beaks observed in the Galapagos would not be expected to explain even-handedly that natural selection and "intelligent design" were two alternative explanations. Rather, the discussion must provide the context that, based on the published literature, creationism was a less plausible interpretation of the data.[16] A report would certainly not be "biased" if it did so; to the contrary, it would be biased and misleading if it did not.

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[16] *See, e.g.*, National Research Council, SCIENCE, EVOLUTION, AND CREATIONISM (2008), available at http://www.nap.edu/catalog.php?record_id=11876&utm_medium=etmail&utm_source=National%20Academies%20Press&utm_campaign=NAP+mail+eblast+1.21.11+-+Readers+Choice+Final&utm_content=customer&utm_term=.

- Specifically, NTP relied on Huff et al. (1984), even though the statistical approach of combining tumors in the study was shown to be erroneous a few years after completion of the study; and
- NTP failed to acknowledge the conclusion in Boffetta et al. (2009) that is contrary to the conclusion of the Background Document regarding the characterization of lymphohematopoietic malignancies.

As noted above, simply stating that NTP has followed its standard format does not explain how NTP has grappled with and resolved these unavoidable issues. Nor does the objectivity requirement allow NTP to justify its actions by simply stating that they "were consistent with the Expert Panel." NTP sometimes accepts and sometimes rejects the suggestions of expert panels, as is clear from the disparate treatment of expert panel recommendations regarding substances being reviewed for inclusion in the 12th RoC.[17] In all cases, the IQA and the Administrative Procedure Act (APA) require NTP to give adequate reasons for its choices. NTP's actions must be based on a rational interpretation of underlying data, which must be generated, analyzed and presented objectively. When that analysis is unsound and unreliable and its presentation is biased and incomplete, the resulting characterization can become arbitrary and capricious under the APA – as has occurred here.

SIRC does not dispute that it is difficult to craft a textual summary that accurately and completely characterizes a collection of studies in light of the scientific context in which they are situated. But that is NTP's obligation under the IQA. As the following examples show, the styrene Background Document does not meet those obligations, despite what NTP's Response says in its defense.

III. Specific Examples

A. NCI Oral Study (failure to explain departures from standard NTP practice)

In the final Background Document, NTP developed and used a new historical control analysis to evaluate the NCI (1979a) study, in which NCI had concluded that its mouse tumor data were within the historical control range and provided no more than suggestive evidence of cancer. SIRC proposed that NTP delete the new analysis as "not reflect[ing] sound and objective scientific practice." SIRC cited the following as evidence "suggest[ing] an attempt to bias the interpretation of the NCI study to support a preferred hypothesis."

[17] *See, e.g.*, NTP's determinations regarding glass fibers. The Expert Panel Report Part B: Recommendation for Listing Status, and the Scientific Justification for the Recommendation for Glass Fibers states: "by a vote of 8 yes/0 no that glass wool fibers . . . should not be classified either as known to be a human carcinogen or reasonably anticipated to be a human carcinogen." (Available at http://ntp.niehs.nih.gov/Ntp/roc/twelfth/2009/june/GWF_PartB.pdf.) NTP's draft substance profile for glass fibers proposes to classify as reasonably anticipated to be a human carcinogen. If the simple statement that NTP elected to follow an expert panel's recommendation is sufficient justification for a cancer classification, than the simple statement that NTP did *not* follow a recommendation should suffice to *invalidate* the resulting classification. If an expert panel's recommendation is not to be dispositive, then additional explanation is always required, and citing a recommendation is not a sufficient basis for the agency's action.

- NTP's new historical control analysis used animals from a laboratory different than that used in NCI (1979a). NTP justified this action as being required to obtain a sufficient number of controls for studies that used corn oil as the vehicle for administration of the test substance. The Background Document failed to note, however, that NCI's own earlier analysis of control data from NTP studies had concluded that: (i) use of corn oil had no impact on the incidence of lung tumors; and (ii) historical controls for mouse tumor studies should be drawn only from studies conducted by the same laboratory because there are different rates of lung tumors in controls from different laboratories.[18]
- NTP failed to address its departure from its traditional practice of not engaging in additional analyses of historical controls, or to explain why this is the sole study among the hundreds referenced in the Background Document for which it chose this unusual approach.

NTP offers two reasons for its departure from the norm (p. 12). First, NTP argues that its new analysis of historical controls is clearly presented, so that the reader should not confuse these with the data in the original study; and it "has chosen to follow the advice of the RoC expert panel." As to the first response, potential confusion was never SIRC's complaint; SIRC wanted the new analysis removed altogether as being "not valid."

NTP's second response is that it "has chosen to follow the advice of the RoC expert panel." As discussed above, however, mere citation to the Expert Panel does not take the place of explaining why NTP changed its scientific position regarding (i) the effect of a corn oil vehicle for administration of the test substance, and the (ii) appropriateness of mixing controls from different labs, or why NTP was justified in changing its practice regarding historical controls in this case but no others. As to the corn oil issue, NTP's own analysis of the NTP historical control database (Haseman et al., 1985) concluded that use of corn oil vehicle in the NCI study specifically *did not* impact lung tumor incidence in B6C3F1 mice in NCI-NTP carcinogenesis bioassays. NTP thus failed to justify why its novel historical control analysis using corn oil historical controls was a scientifically necessary alternative approach in the face of the authors' own published conclusions. Remarkably, the Background Document does not even reference Haseman et al. (1985), despite that fact that the lead author was listed as a contributing consultant on the Background Document (page iii).[19]

As to the issue of mixing controls, NTP also has published its position that, because of significant inter-laboratory variability in the incidence of background mouse lung tumors, historical control tumor analyses for this endpoint should be restricted to tumor incidences

[18] These issues and comparison with NCI (1979b) and Ponomarkov (1978) are discussed on pages 51-55 of SIRC's initial Request for Correction.

[19] References demonstrating standard NTP practice: Haseman JK, Huff, J, Boorman, GA. 1984. Use of historical control data in carcinogenicity studies in rodents. *Toxicologic Pathology* 12: 126-135; Haseman JK, Huff JE, Rao GN, Arnold JE, Boorman GA, McConnell EE. 1985. Neoplasms observed in untreated and corn oil gavage control groups of F344 rats and (C57Bl/6N x C3H/HeN)F1 (B6C3F1) mice. JNCI. 75: 975-984.

observed within the same testing laboratory (Haseman et al. 1984). The basis for this concern is specifically evident in the NTP Background Document analysis: the lung tumor incidence in control animals in the laboratory conducting the NCI bioassay was 3-fold higher than the control incidence in the laboratory selected for the NTP analysis – a point that SIRC made in its RFC (p. 55). Again, despite NTP's own opposing recommendations for use of such historical data, no justification was provided in the Background Document for alternative use of inter-laboratory historical control data.[20]

Objectivity requires that NTP give reasoned explanations for deviations from established practice like the use of new historical control analysis in the Background Document, particularly since NTP's novel analysis was key to supporting its conclusion that the animal tumorigenicity data justified the proposed "reasonably anticipated as a human carcinogen" RoC listing. NTP fails to provide sound and reliable justification for this substantial deviation.[21] Thus the portion of the Background Document containing this analysis continues to violate the objectivity requirement of the IQA and must be corrected. NTP's decision to engage in new historical control analysis is also arbitrary and capricious under the APA, and cannot be used as the basis for listing styrene as a reasonably anticipated human carcinogen.

B. Delzell et al. (2006) (failure to include analysis of study results by the original author)

The final Background Document contains an extended and substantial discussion of studies of styrene-butadiene rubber (SBR) industry workers by Delzell et al. (2006). NTP re-interpreted Delzell et al. to assert an association even though the authors themselves did not conclude that styrene caused cancer. It did so largely at the direction of the Expert Panel, which asserted that there is increased risk of Non-Hodgkin lymphoma (NHL), and NHL combined with chronic lymphocytic leukemia (CLL), caused by styrene and not by butadiene in the SBR cohort:

> In the Delzell study there was an exposure-response relationship for NHL and NHL plus chronic lymphocytic leukemia (CLL) that was not attenuated by control for butadiene and

[20] See, e.g., Keenan C, Elmore S, Francke-Carroll S, Kemp R, Kerlin R, Peddada S, Pletcher J, Rinke M, Schmidt SP, Taylor I, and Wolf DC. 2009. Best Practices for Use of Historical Control Data of Proliferative Rodent Lesions. Toxicologic Pathology 37: 679-693. The authors of this paper, including representatives of NTP, NIEHS, FDA, and USEPA, recommended consensus principles to guide the use of historical control data from chronic rodent bioassays. Their first consensus principle is that the "current control group is the most relevant comparator for determining treatment-related effects in a study." In preparing the Background Document, NTP departed from these consensus principles without adequate explanation.

[21] In developing a new analysis or interpretation of the original study using additional data, NTP also departed from its policy stating that it only relies on peer-reviewed studies in preparing the Background Document. The new analysis should have first been published in a peer review journal. That process would have provided the necessary scientific scrutiny and comparison with consensus practices. NTP has never done this. Ironically, Boffetta et al., which NTP declines to reference, is a peer-reviewed publication critically discounting the Expert Panel's conclusions, as discussed below.

> only mildly attenuated by control for dimethyldithio-carbamate (DMDTC) (which may not have been appropriate to control for).[22]

Dr. Delzell reviewed the Expert Panel report and the final Background Document, and her comments were submitted to NTP. In response to the foregoing quote, she said flatly:

> To the extent that the above statement implies that the epidemiologic results for NHL from the two studies constitute strong evidence of a causal relation with styrene, I do not agree. Results for styrene and NHL from both studies are unconvincing . . . . As the Background document points out frequently, the papers and report on the UAB study did not include any statistical tests of exposure-response trends for styrene and NHL or NHL/CLL.
>
> In the case of styrene and NHL, such supportive epidemiologic evidence is not sufficient for a conclusion of causality. The epidemiologic studies, including the UAB study, are, at best, weakly supportive. The Background document downplays the fact that studies of reinforced plastics industry workers do not provide clear support for a causal relationship between styrene and NHL, citing exposure misclassification, short follow-up, large proportions of short-term employees, etc., as explanations. However, reinforced plastics industry workers on average experienced styrene exposure concentrations much higher than those in the synthetic rubber industry. Even short-term workers in the reinforced plastics industry could have had cumulative styrene exposures similar to, or above, the median cumulative exposure of 17 ppm-years estimated for all styrene-exposed decedents (or the median of 30 ppm-years among NHL decedents) in the UAB study (Delzell et al., 2006). Thus, the lack of a clear association between styrene and NHL in the studies of reinforced plastics industry workers is an important shortfall of the evidence for the hypothesis that styrene causes NHL.[23]

Thus the author of a key publication in the Background Document directly disagrees with NTP's characterization of the publication's conclusion. However, the Background Document makes no reference to the author's disagreement.[24] Such a stunning omission signals a failure to present the relevant science accurately and objectively. The motives for this omission are inevitably called into question, moreover, by NTP's additional failure to discuss Boffetta et al. (2009), which was provided to NTP before SIRC filed its RFC. Boffetta et al. (2009) also included an evaluation of Delzell et al. (2006) and, like Dr. Delzell, concluded that styrene was not causally associated with the cancers claimed in the Background Document. *See* Part III.E below.

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[22] Scientific Justification, at 2.

[23] Comments of Dr. Delzell, included as Attachment A to SIRC's comments on the draft Expert Panel Report (Oct. 23, 2008), available at http://ntp.niehs.nih.gov/index.cfm?objectid=20A477F2-F1F6-975E-7472FC6B0DA56D9C#styrene.

[24] Conceivably NTP will respond that this is because it finalized the Background Document before the close of the comment period for the Expert Panel's report. This is precisely why that sequence of events was so illogical and detrimental to the quality of the final Background Document. *See* Part IV below.

C. Huff et al. (1984) (failure to provide contextual information regarding the state of the science, and failure to acknowledge departure from standard NTP practice)

NTP's response with regard to Huff et al. (1984) is the mirror image of its response to NCI (1979a). Regarding NCI (1979a), NTP departs from the study authors' conclusions and its own standard practice to support an interpretation. With regard to Huff, et al. (1984), NTP supports the study author's finding of an effect despite the fact that the statistical approach of combining tumors taken in Huff et al. (1984) was shown to be erroneous a few years later and, as a result, NTP has not typically combined the particular tumor types in question for over two decades.[25]

In its RFC, SIRC noted (p. 56) that combining various types of mammary tumors as done in Huff et al. (1984) is not appropriate because fibroadenomas are not related to adenocarcinomas. McConnell et al. (1986)[26] demonstrated that mammary fibroadenomas should not be combined with malignant mammary tumors unless a continuum has been demonstrated within a given study. No such continuum was demonstrated in the Beliles et al. (1985) drinking water study that Huff et al. (1984) was reanalyzing. Therefore, combining them does not represent "sound . . . and objective scientific practice" and is misleading. SIRC thus requested that discussions of Huff et al. (1984) or such combinations of tumors be removed from the Background Document.

NTP responds (p. 13) that no changes are needed to the discussion on Huff et al. (1984) in the Background Document because the text in question "all refers to factual information from Huff (1984)." Again, this was never the criticism posed by SIRC. The discussion of Huff et al. (1984) is misleading because it presents an approach to combining tumors that has since been discredited. NTP should delete any reference to Huff et al. (1984) in the Background Document; if it retains references to the study, NTP must explain why it is departing from standard practice, and how inclusion of Huff et al. (1984) constitutes sound and objective scientific practice in light of the findings of McConnell et al. (1986).

D. Kolstad et al. (1995, 1994) (relying on a study hampered by methodological limitations, and failure to acknowledge departure from standard NTP practice)

The serious methodological flaws with Kolstad et al. (1995, 1994) prompted the EU to characterize the study's estimate of the number of exposed workers as "highly questionable," particularly because the assessment of which workers had "high" or "low" exposures was regarded as unreliable. In line with the EU's conclusion that Kolstad presented "no evidence [of] an increased cancer risk," SIRC explained that the *accurate* summary of Kolstad is that, "[b]ased on this methodology and data, it is not reasonable to conclude that this study provides evidence of increased cancer from styrene exposure." NTP rejected SIRC's request for correction because "the Background Document does not draw conclusions relative to the study's findings," and NTP declined to include "SIRC's interpretation of the study's findings" (NTP's Response, page 5).

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[25] McConnell E.E., *Solleveld H.A., Swenberg J.A., Boorman G.A. Guidelines for Combining Neoplasms for Evaluation of Rodent Carcinogenesis Studies* J. Nat'l Cancer Inst. 76: 283-289 (1986).

[26] *Id.*

Instead, the Background Document simply acknowledges "a methodological limitation of this study" and then proceeds to present data from Kolstad, most of which showed nonsignificant increases for cancer (*see esp.* pp. 95-96). That description of the study is then repeated in NTP's draft Substance Profile, which cites Kolstad et al. (1995, 1994) in support of an effect.[27]

OMB's IQA Guidelines state: "[I]t is clear that agencies should not disseminate substantive information that does not meet a basic level of quality."[28] In the case of RoC Background Documents, meeting that level of quality requires "us[ing] the best available . . . science," reflecting "sound and objective scientific practices," and being "reliable."[29] NTP faces a challenge. It must either:

- Omit studies that are as flawed methodologically as Kolstad et al. (1995, 1994);
- "[D]raw conclusions" about their reliability; or
- Ensure that it does not allow methodologically limited data to shed its limitations and emerge unqualified in shorter or more influential documents.

But NTP cannot leave the matter as it stands now.

As noted above, most of the increases that Kolstad et al. (1995, 1994) described were not statistically significant. As with its flawed use of Huff et al. (1984), NTP's inclusion of data that are not statistically significant and suffered from recognized methodologic limitations to support a finding of an effect also departs from generally accepted scientific norms. NTP does not address this fundamental issue; thus the references to nonstatistically significant and methodologically limited data should be removed or validated in some substantial (and presumably highly qualified) fashion.

E. Improper Characterization of Lymphohematopoietic Malignancies (failure to provide contextual information regarding the state of the science)

SIRC requested that NTP revise a statement in the Background Document relating to the characterization of lymphohematopoietic malignancies in the styrene monomer/polymer industries to be consistent with Boffetta et al. (2009). Again, NTP responded that the statement in the Background Document is correct and that it would not include SIRC's "interpretation of the studies' findings . . . ." (NTP's Response, p. 8). However, SIRC was not asking NTP to include SIRC's opinion or interpretation. Rather, SIRC was asking NTP to incorporate a direct quote from Boffetta et al. (2009) reflecting those authors' conclusion upon reviewing the same four studies that the Background Document presents on the topic: "In the styrene monomer and polymer industries, studies of styrene production workers, while limited by small size, *do not provide evidence for a causal association between styrene exposure and cancer, including lymphohematopoietic malignancies*" (emphasis added).

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[27] Draft Substance Profile at 2-4.

[28] 67 Fed. Reg. 8452.

[29] *Id.* at 8457, 8457 and 8459, respectively.

The Background Document must present "each significant uncertainty identified in the process" of assessing the risk of styrene. The IQA requires NTP to discuss "peer-reviewed studies . . . that fail to support any estimate of risk."[30] NTP's Response itself captures the profound uncertainties that remain to this day regarding the different interpretations that can be drawn from the human studies. NTP's Response states (p. 8):

> SIRC requests specific revisions to the statement in the Background Document on page 192, "[i]n the styrene monomer and polymer industries, the risk of lymphohematopoietic malignancies was also increased in most of the studies (as well as the total number of observed cases across studies), but these workers might also have been exposed to benzene," to be consistent with Boffetta et al. (2009), "[i]n the styrene monomer and polymer industries, studies of styrene production workers, while limited by small size, do not provide evidence for a causal association between styrene exposure and cancer, including lymphohematopoietic malignancies."

Yet the Background Document conceals this uncertainty by omitting any reference to Boffetta et al. (2009).[31]

Even more troubling than this omission, however, is NTP's insistence that "[t]he information given on page 192" does not require correction. The statement on page 192 ("the risk of lymphohematopoietic malignancies was also increased in most of the studies") is clearly not an accurate characterization of the four studies summarized in Table 3-8 (pp. 171-72). As that table shows, only one of the four studies (Hodgson and Jones) found a statistically significant increase in any LH cancers ("all LH," both by standard incidence ratio and standard mortality ratio). As Boffetta et al. (2009) explained, there was no trend among these by length of service. All the other findings among the four studies were not statistically significant and almost completely offsetting:

- Hodgson and Jones: 3 (+), 3(-)
- Bond: 6 (+), 5(-)
- Nicholson: 1(+), 2 (-)
- Frentzel, Beyme et al. [none]

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[30] *Id.* at 8457-58.

[31] SIRC submitted Boffetta et al. in a letter dated December 16, 2008, available at http://ntp.niehs.nih.gov/index.cfm?objectid=20A477F2-F1F6-975E-7472FC6B0DA56D9C#styrene. While this was after the close of the comment period on the draft Expert Panel report, SIRC had repeatedly advised NTP that the Boffetta et al. Blue Ribbon Panel's work was in progress and had requested an extension of the comment period to accommodate submission of its manuscript. NTP denied SIRC's request for an extension. In any event, NTP has a continuing obligation to maintain the quality of the Background Document, particularly while the 12th RoC is still in development. *See* 67 Fed. Reg. 8459 (Feb. 22, 2002) (OMB IQA Guidelines) ("Agencies shall treat information quality as integral to every step of an agency's development of information, including creation, collection, maintenance and dissemination . . . . The agency's administrative [correction] mechanisms . . . shall apply . . . regardless of when the agency first disseminated the information.").

It is simply wrong to describe this random scatter of data as showing that "the risk . . . was . . . increased in most of the studies."

NTP's Response notes that the Background Document does not express an opinion concerning a particular listing status in the Report on Carcinogens. While it is true that NTP does not explicitly express an opinion in the Background Document, NTP's selective presentation of data and published conclusions clearly conveys a variety of toxicological and epidemiological conclusions. As a result, the tailored Background Document can more readily be cited in NTP's draft Substance Profile in support of the overt statement of those same conclusions. Failing to acknowledge a contrary and scientifically credible conclusion in the published, peer-reviewed literature is an inaccuracy in the final Background Document. Also, as noted above regarding Delzell, NTP failed to address that the Background Document relied on a non-peer reviewed and non-published novel evaluation of Delzell developed by the Expert Panel and directly contrary to the published findings of Boffetta et al. Unless the full range of science is presented completely and accurately, the reader is left with the inaccurate impression that only those conclusions presented by NTP are viable.

IV. NTP FINALIZED THE BACKGROUND DOCUMENT BEFORE REVIEWING PUBLIC COMMENTS ON RELEVANT ISSUES

In its RFC, SIRC explained that:

- NTP finalized the Background Document after it had received the Expert Panel's draft report but before the deadline for submission of public comments on the draft; and
- NTP adopted essentially every recommendation of the Expert Panel, making significant changes in the final Background Document that rendered it even less objective and useful within the meaning of the IQA.

Thus, by the time NTP had received comments explaining the problems with the Expert Panel's draft report, the damage was done: the Background Document had been revised to incorporate those problems, which in turn have been carried into the draft Substance Profile. SIRC pointed out that this improper procedure undermined the normal presumption of objectivity that attaches to a peer-reviewed document – but obviously, this procedure is also inherently illogical (and thus arbitrary and capricious).[32]

In response, NTP repeatedly insists that the Expert Panel's peer review comments on the draft Background Document were Part A of its report, and that NTP had not sought comment on Part A, but only on Part B (the Expert Panel's proposed cancer classification and scientific justification therefore). It may be, as a matter of procedural formality, that "conclusions reached

[32] *See, e.g.*, Illinois Public Telecommunications Ass'n v. FCC, 117 F.3d 555, 566 (D.C. Cir. 1997) ("The Commission's failure to provide an explanation for this seemingly illogical decision is arbitrary and capricious.").

by the expert panel and reported in the Expert Panel Report, Part B, are independent of the Background Document" (Response at 6). In reality, however, that statement is demonstrably false. The conclusions set out in the Expert Panel's scientific justification for listing are woven throughout the Panel's peer review comments, which are self-evidently constructed to maximize apparent support for those conclusions. This can be readily seen by comparing the two at any corresponding points. Compare, for example, the two documents on the significance of Delzell et al. (2006):

Scientific Justification (p. 2):

> The strongest evidence for cancer in humans is the association between styrene exposure and non-Hodgkin lymphoma (NHL). This evidence comes from the Delzell et al. (2006) analysis in the styrene-butadiene industry and the Kogevinas (1994a) study in the reinforced plastics industry. In the Delzell study there was an exposure-response relationship for NHL and NHL plus chronic lymphocytic leukemia (CLL) that was not attenuated by control for butadiene and only mildly attenuated by control for dimethyldithiocarbamate (DMDTC) (which may not have been appropriate to control for). It is very unlikely that such a strong exposure-response trend could be due to chance, bias, or confounding.

Peer Review Comments:

> The Delzell et al. 2006 report also analyzes leukemia, NHL and NHL-CLL data for three-chemical exposures, butadiene, styrene, and DMDTC. Both butadiene and styrene in single-agent models are associated with significantly increased risks for all leukemias in the two highest exposed groups and both show a dose response (although no trend information is provided). When both of these chemicals are in the model, both chemicals show increases in RR with increasing dose, but when DMDTC is added to the model as reported by Graff et al. 2005, the styrene risk disappears. Using a different exposure measure [in Table 12], namely number of styrene peaks, styrene in the single chemical model has RR values for all leukemia that are slightly higher than those of butadiene alone (except at the highest quartile). Both styrene and butadiene are associated with significant excesses of all leukemias at the highest quartile for number of peak exposures. Both have apparent positive dose responses for each chemical. Using a two-chemical model, an increasing frequency of peak styrene exposures in relation to the risk of all leukemias is associated with higher RR values for styrene than butadiene. The RRs remain significant only for styrene at high peak doses. The higher risks for styrene compared with butadiene remain even in the three-chemical (styrene+butadiene+DMDTC) model.[33]
>
> Add results for CLL and NHL combined and for NHL alone that are described in Delzell et al. 2006 (See Part A: Additional Information above). These studies found an exposure-response relationship with cumulative exposure to styrene for CLL and NHL combined or NHL alone that was not attenuated when butadiene was added to the model. These results should also be added to Section 3.8 (Summary for selected cancer sites).[34]

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[33] Part A at 8.

[34] *Id.* at 12.

As is obvious, therefore:

- The Expert Panel's peer review comments embodied the same judgments as its scientific justification;
- By incorporating those comments into the final Background Document, NTP produced a document that more consistently supported those judgments; and
- By finalizing the Background Document before it received public comments on the draft Expert Report, NTP ensured the comments would not have any effect on the Background Document.

We acknowledge that NTP has previously taken the position that, because the Expert Panel is an independent advisory committee operating under the Federal Advisory Committee Act (FACA), its reports are not agency disseminations subject to the IQA. Regardless, it is clear that when NTP incorporates recommendations of the Expert Panel into the Background Document in a way that at least "reasonably suggests that the agency agrees with the information, this appearance of having the information represent agency views makes agency dissemination of the information subject to th[e IQA] guidelines."[35] Accordingly, NTP should reopen the Background Document and revise it in light of the comments filed on the draft Expert Report. NTP should also change the process of soliciting comments described above for the 13th and future RoCs.

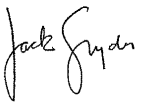
V. CONCLUSION

For the above-stated reasons, which highlight only a few of the flaws in NTP's Response, the Background Document of September 29, 2008, does not conform to the requirements of the Information Quality Act, must be withdrawn and, if reissued, corrected. Similarly, all subsequent NTP documents based on the flawed Background Document – in particular, the draft substance profile issued in December 2008 – should be withdrawn and, if reissued, revised consistent with the corrected Background Document.

[35] 67 Fed. Reg. at 8454.

SIRC and its members would welcome the opportunity to meet and discuss these issues or provide clarifications to assist the review and correction of the Background Document. Please do not hesitate to contact me for any further information.

Sincerely,



Jack Snyder
Executive Director
Styrene Information & Research Center, Inc,
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Jack_Snyder@styrene.org

cc: John R. Bucher, Ph.D., Associate Director, NTP
Peter de la Cruz, Keller and Heckman LLP
James W. Conrad, Jr., Conrad Law & Policy Counsel

Enclosures: SIRC IQA Request for Correction (October 26, 2009)
NTP's Response (December 23, 2010)

Answer: Clearly the receipt of Mr. Tickle's letter was acknowledged, however, there was no substantive response. Mr. Tickle and Mr. Kreysler expressed specific concerns, to which Dr. Birnbaum replied with complete non-sequiturs, ignoring completely the content of the letter. Mr. Tickle's letter had nothing to do with the comment period, and what was expected was NTP to acknowledge the concerns and consider changing their approach to avoid the unwarranted negative impacts on the industry.

B) If an additional submission was made, please double check that no response was received from NIEHS as you implied during the hearing.

Regarding further Strongwell submissions to NTP, on behalf of Strongwell, SIRC submitted scientific information to NTP, to which NTP responded only after the RoC was finalized, and even then the responses were again not substantive. Please see the attached SIRC IQA Request for Correction which provides more information about NTP ignoring scientific information.

C) Whether or not an additional submission was made, the company's May 2009 submission was responded to. Please explain why the Corporate Manager of Environmental Affairs was unaware that Dr. Birnbaum had written back to your company in May of 2009, creating the false impression that NIEHS had ignored your company's submission.

Answer: Again there were no substantive responses.

Attachments

REGULATORY
CHECKBOOK

June 2, 2012

Responses of

Dr. Richard B. Belzer

to

Questions for the Record

on the Hearing

"How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"

Wednesday, April 25, 2012

QUESTIONS SUBMITTED BY DR. PAUL BROUN, CHAIRMAN, HOUSE SCIENCE, SPACE AND TECHNOLOGY, SUBCOMMITTEE ON INVESTIGATIONS & OVERSIGHT AND REP. RENEE ELLMERS, CHAIRWOMAN, HOUSE SMALL BUSINESS SUBCOMMITTEE ON HEALTHCARE AND TECHNOLOGY

1) How is the RoC's contribution to science or the public's understanding of substance hazards unique?

Based on my research, there appears to be nothing unique about the RoC's contributions to science. To prepare the RoC, the NTP performs no original research and conducts no original studies. While the NTP's substance profiles are peer reviewed, this is a captive procedure controlled by the authors. There is no peer review procedure in the world of scholarship that allows authors to control the selection of peer reviewers, dictate their charge, and choose whether to accept or reject their work.

Substantively, the RoC appears to be duplicative of other federal programs that perform hazard (but not risk) assessment, such as EPA's IRIS program and ATSDR's toxicological profile program. When the cancer assessment program of the International Agency for the Research on Cancer (IARC) is taken into account, the RoC is almost wholly redundant.

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To be sure, the EPA and ATSDR programs have similar defects. Each performs only "hazard" assessments (for carcinogens) and "safety" assessments (for non-carcinogens). A hazard assessment alone has little or no value for informing public and private decision making. A safety assessment is exactly what it sounds like: it tells the public what constant dose or exposure the agencies' scientists think is "safe." However, because "safe" cannot be defined scientifically, all safety assessments are policy decisions analogous to NTP listing decisions.

The other programs differ from the RoC, and are at least in principle potentially superior to it, because they produce more information. EPA and IARC, for example, have their own classification systems that provide for more than two categories. EPA and ATSDR also determine "unit cancer risk" estimates. These could be valuable if they objectively characterized average risk to an exposed population. Unfortunately, they do not.

First, unit risk estimates are almost always extrapolated from very high to very low doses using linear no-threshold (LNT) models. These models are preferred by agency scientists precisely because they tend to overstate estimated cancer risk. Second, unit risk estimates are obtained by using upper-bound predictions from these LNT models. The likelihood that they overstate cancer risk, even if all other modeling assumptions are correct, is 20 to 1. Third, they often are based on the assumption that humans are at least as susceptible to chemical carcinogenesis as the most sensitive rodent species tested in a laboratory. Because this is possible but highly unlikely, it is another source of upward bias in the estimation of unit cancer risks.

All three of these non-scientific assumptions is motivated by a highly precautionary, risk-averse view about what the government's risk management policies ought to be. And this is why hazard assessment—whether performed by EPA, ATSDR, or the NTP—is so highly controversial. What's going on is not risk assessment; it's policy making behind a façade of science.

The RoC is unique in one important respect. It is highly influenced, if not controlled by, something called the NTP Executive Committee, which consists of the Consumer Product Safety Commission, the Department of Defense, the Environmental Protection Agency, the Food and Drug Administration, the National Cancer Institute, the National Center for Environmental Health/Agency for

Toxic Substances and Disease Registry, the National Institute of Environmental Health Sciences, the National Institute for Occupational Safety and Health, and the Occupational Safety and Health Administration. Thus, it is not clear whether listing decisions are made by NTP Director Linda Birnbaum or by a politically complex interagency process. (Of the nine members, five are subordinate to the Secretary of Health and Human Services.)

Nothing about the procedures, discussions, actions or recommendations of the NTP Executive Committee is ever disclosed. This is highly peculiar if the RoC is a scientific compendium; after all, if it's "just science," then there is no policy making going on and nothing pre-decisional to legitimately keep from the public.

2) How does a weight-of-evidence assessment differ from what NTP does in the RoC?

The RoC program appears to use a strength-of-evidence framework, meaning that the only evidence that the NTP considers is evidence supporting listing. This has been alleged many times over the years, and it is verified by carefully reading the new procedures NTP intends to follow for the 13th edition.[1] The nomination process considers only "relevant data [that] support[s] the [NTP's] rationale" for listing, and the initial peer review considers only evidence that supports listing. The revised process identifies no role for negative or equivocal data.

Further, as I explained in my testimony, the NTP's listing criteria also provide no role for the consideration of negative or equivocal data.[2] The criteria speak only of the "evidence of carcinogenicity" (emphasis added) and they establish a non-scientific, wholly policy-driven process for deciding whether this evidence is "sufficient" or "limited."

In her testimony, Dr. Birnbaum asserted that NTP determinations are "based on scientific judgment with consideration of all relevant research data and input from advisory groups and the

[1] National Toxicology Program, 2012. *Process for Preparation of the Report on Carcinogens,* http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.

[2] National Toxicology Program, 2012. *Listing Criteria,* http://ntp.niehs.nih.gov/?objectid=47B37760-F1F6-975E-7C15022B9C93B5A6.

public." But she also stated that substance profiles contain only "the information which supports the determination..." This is identical to a strength-of-evidence framework with the simple proviso that only positive studies will be deemed "relevant," which is exactly what the NTP's nominations process and listing criteria do.

The NTP has never addressed, and Dr. Birnbaum did not discuss in her testimony, how the NTP conducts this review of "all relevant research data." It appears to be a black box. What does the NTP do with "input from advisory groups and the public" when it is not scientific? If listing decisions are scientific, then the only legitimate thing the NTP could do with nonscientific input is to ignore it. This poses a particular problem to the NTP because the advisory committee that performs peer review is directed by its charge to provide policy advice.[3]

It is useful to return to what we know and don't know about the NTP's actual procedures. First, we know that the NTP's listing criteria are inherently non-scientific. To reach a conclusion that a substance is a "known" carcinogen, all the NTP must do is deem the positive evidence from human studies "sufficient," which it has not defined. Thus, proof of "sufficiency" rests on undisclosed policy and political considerations.

Second, we don't know how the NTP evaluates research data. If the NTP takes account of negative and equivocal data in its reviews, it is not reflected in its public description of its process or in the text of its substance profiles. Because it has never published guidelines informing the public concerning how it exercises "scientific" judgment, it is appropriate to infer that the judgments it exercises are not scientific.

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[3] For the 12th RoC, the NTP used BSC review to ratify its policy decisions, not to objectively evaluate the scientific record: "The BSC is charged to determine whether the scientific information cited in the draft substance profile for a candidate substance is technically correct, clearly stated and supports the NTP's policy decision regarding its listing in the RoC" (emphasis added). For the 13th RoC, the role of the BSC is ambiguous and front-loaded to a point in the process when little scientific information is available for review. The manner in which draft substance profiles will be peer reviewed is even more ambiguous, but it continues to focus on the ratification by scientists of NTP policy decisions. See footnote 1, section headed "Public Release of Draft RoC Monograph and Peer Review."

Rigorous weight-of-evidence frameworks, which take account of all data whether positive, negative, or equivocal, have been proposed many times over the years.[4] Federal agencies (including the NTP) resist adopting them. They resist because any credible weight-of-evidence framework would substantially curtail their capacity to make policy decisions behind a façade of science.[5]

There is another crucial point to be made about what the NTP actually does. In the January 2012 revised RoC process, the NTP defined the RoC as

> a Congressionally mandated, biennial document that identifies and discusses agents, substances, mixtures, or exposure circumstances (collectively referred to as "substances") that may pose a hazard to human health by virtue of their carcinogenicity.[6]

This is false, for Congress mandated no such thing. Moreover, nothing in the law authorizes the NTP to list substances "that may pose a hazard to human health by virtue of their carcinogenicity." The law requires the NTP to list substances that are "known" or "reasonably expected" to be human carcinogens. If the NTP were to actually list all substances that may be human carcinogens, the RoC could include thousands of substances, the number dependent only on how much Congress appropriates to the NTP (and its partner agencies) for preparation of the Report.

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[4] For an authoritative report recommending (again) the adoption of weight-of-evidence frameworks, see National Research Council, 2008. *Science and Decisions,* Washington, D.C.: National Academies Press, p. 81: "[Weight-of-evidence] is an example of how [agencies] may benefit from a structured characterization ... of the exact role of a resource-intensive method in supporting the broader goals of public-health and environmental decision-making, which would include, among many other aspects, the use of good scientific practices and consideration of good communication practices. The method would require a more explicit valuation of important attributes of quality in decision support."

[5] The NTP acknowledges that it is engaging in policy making when it characterizes the RoC as a "public health document." See National Toxicology Program, 2011. Report on Carcinogens; 12th Edition, p. 3. In her testimony, NTP Director Dr. Linda Birnbaum used this phrase twice. This is code language for public-health precautionary legislative decision making, something the statute does not authorize the NTP to do.

[6] See footnote 1 (emphasis added).

I regret that I did not flag this in my testimony. At the time, I thought the text quoted above was poorly-written but stray governmental text, likely written by a committee, with no significant import. During the hearing, however, Dr. Birnbaum made very clear that what I had interpreted as merely slopping writing was actually very much intended. She opened my eyes to its true meaning and ramifications.

In her testimony, Dr. Birnbaum used this and similarly incorrect formulations of the NTP's statutory charge several times:

- "By identifying substances that may heighten the risk of cancer, the public is made aware of potentially life-threatening chemicals in our everyday lives."
- "The report lists a wide range of substances, including metals, pesticides, drugs, natural and synthetic chemicals, and biological agents that are considered cancer hazards for people in the United States."
- "A listing in the report indicates a potential hazard for cancer."
- "Reducing exposure to cancer-causing agents is important to public health and the Report on Carcinogens provides important information on substances that might pose a potential cancer risk,..."
- "I think it would be very important that we heard from some of the expert scientists who actually were involved in the conduct of these studies. I think that their expert, unconflicted advice would be very important to understanding the impacts that some of these compounds may have, have the potential to have on human health.
- "The RoC is not a regulatory document. It is a hazard assessment document. It looks at all the information, and I think that is important to state. It looks at all the information, both positive and negative, that is all evaluated and then the information which supports the determination of whether the compound has the potential to cause cancer ... is compiled to make the public health document."
- "Our charge from the Congress is to evaluate the potential for compounds to be a known carcinogen or reasonably anticipated carcinogen."

Besides being false, each of these mischaracterization of the law abandons science as the arbiter of listing determinations. Outside of physics, there is no scientific definition for "potential." Similarly, to say that something "may" happen is to exclude only those events that are infeasible under any imaginable factual circumstance. Dr. Birnbaum has discarded science and replaced it with precautionary policy judgment, something that the law does not permit her to do.

A) What difference does that make when looking at data and studies?

A weight-of-evidence framework would result in many fewer substances being listed. This has to be true because the NTP currently lists any substance that it reviews as long as the positive evidence, considered by itself, is strong enough to be deemed "sufficient."

Under a weight-of-evidence framework, low-quality studies would be given low weight and high-quality studies would be given high weight—regardless of whether they support or contradict the hypothesis of human carcinogenicity. Most importantly, studies that definitively resolve crucial scientific uncertainties—whether in favor or against the hypothesis of carcinogenicity—would be given the greatest weight of all. Indeed, studies of this type would trump almost every other kind of scientific evidence.

Note that a weight-of-evidence framework rewards scientists for conducting high-quality hypothesis tests, and provides an even greater "bang for the buck" for performing studies that resolve crucial scientific uncertainties. Neither reward is possible under the NTP's strength-of-evidence framework. Low-quality studies that appear to support the hypothesis of carcinogenicity are fine. High-quality studies that contradict it are rejected. Studies that resolve crucial scientific uncertainties play no role in listing determinations—unless, that is, they resolve an uncertainty in favor of listing. Thus, the NTP's strength-of-evidence framework actually rewards scientists for conducting low-quality hypothesis tests and studies that merely generate new hypotheses that might be interpreted as suggestive of "potential" cancer risk. The NTP's approach is like a baseball game in which only the home team is allowed to bat and the umpires wear blindfolds.

The NTP's lack of transparency about how it "considers[] all relevant research data," in Dr. Birnbaum's formulation, undermines public confidence that these "considerations" are limited to science.

Occam's Razor argues for defaulting to the simplest explanation in the absence of information: the NTP's listing determinations are wholly controlled by policy considerations. What we do not know is whether these policy decisions are actually made by Dr. Birnbaum or by the NTP Executive Committee.

3) In your working paper on the Report on Carcinogens, you suggest legislative changes to improve the Report on Carcinogens. Do you think legislation is necessary to improve the RoC?

My research shows that the NTP Director has sufficient authority to make the RoC scientifically credible. Because the RoC has been a sustained source of scientific controversy for many years, however, it's clear that NTP Directors past have not been interested in doing so. It is reasonably to infer that they liked the ability to make legislative policy decisions while purporting to be mere scientists.

In her testimony, Dr. Birnbaum made clear that she has no intention of departing from the practices of her predecessors. She did not identify any feature of the RoC that she believed warranted reform. She expressed her support for the process changes announced in January—indeed, they could not have been finalized without it—despite the fact that they received near universal opprobrium from the public. Most troubling, she clearly stated her support for misinterpreting the law to allow the agency to list mere "potential" human carcinogens as if they were "known" or "reasonably anticipated" human carcinogens.

For these reasons, it is up to Congress to act if it wants the RoC to have value as a scientific compendium and to prevent it from continuing to have negative social value. Each of my reform suggestions presumes that Congress intended, and still desires, the RoC to be a valid and reliable scientific compendium. Each proposed reform would make the RoC more scientific, and thus increase its value as a tool for informed public and private decision making.

4) In your testimony, you note that the "NTP completely ignores exposure or dose in making its determinations." Why is it important for exposure or dose to be considered when providing information to the public about substances that have the potential to cause cancer?

The most important reason why the NTP should take exposure into account isn't scientific; it's statutory. The law establishes two thresholds that must be met before a substance may legally be listed. To date, all of the attention has focused on the first one—whether a substance is a "known" or "reasonably anticipated" human carcinogen. As I made amply clear in my monograph, my working paper, and my testimony, these determinations are not scientific. It is ironic that so much energy has been expended on science even though science is largely irrelevant to these determinations.

The second statutory requirement for listing a substance is "a significant number of persons residing in the United States are exposed" to it. In my testimony, I identified the three steps that must be taken to meet this statutory requirement:

- Define "a significant number of persons residing in the United States"
- Define a *de minimis* cancer risk level
- Estimate for each candidate substance the number of persons in the United States exposed above the de minimis cancer risk level

The first two tasks are strictly policy driven; science cannot define a "significant" number of anything, nor can it define a threshold cancer risk below which the public ought not be concerned. But science can objectively estimate the number of persons residing in the United States who are exposed above any specified dose or concentration.

The NTP has performed none of these tasks. Determining which, if any, of the 240 substances listed in RoC are accompanied by this information requires a significant research effort. I have skimmed the 12th RoC for this information and I have yet to find a single substance for which the NTP has taken this statutory text seriously.[7]

[7] An electronic search of the 12th RoC reveals not a single instance in which the statutory text on exposure is even mentioned.

From a public policy perspective, it is obviously important whether many, a few, or virtually no persons residing in the United States are exposed to a bona fide human carcinogen. By ignoring the statutory language, however, the NTP is saying it's not important at all. The only thing that matters is whether there are any conditions—actual, hypothetical, or even imaginary—in which a substance is a "known" or "reasonably anticipated" human carcinogen—or rather, as Dr. Birnbaum has reinterpreted the statutory charge says, whether ta substance "may" be a "potential" human carcinogen.[8]

5) In your testimony, you suggest that substance listings should be sunset to encourage revision. How would that requirement improve the Report on Carcinogens?

The NTP implements the RoC process in a way that is similar to the way people have voted in certain dictatorships: one person, one vote, one time. A substance that is listed is impossible to delisted unless the NTP wants to delist it. NTP considers only positive evidence supporting carcinogenicity; new science refuting this evidence is immaterial. Members of the public may petition for a delisting, but they have no right to compel a review. Even if they had this right, it would be an empty one.[9]

This means the NTP will advance to the listing process only those substances that it (or the NTP Executive Committee) decides to advance. The only substances that advance are substances headed to listing.

My proposal to sunset RoC listings would require the NTP to justify its decisions every several years based on the then-available science. This would not have much public benefit unless the NTP also was required to adopt one or more of the other proposed reforms,

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[8] In addition to the threshold requirement for listing that "a significant number of persons residing in the United States are exposed," the law also requires the NTP to include in each substance profile "information concerning the nature of such exposure and the estimated number of persons exposed to such substances." The NTP does not provide this information.

[9] The RoC Process referenced at footnote 1 notes that the NTP may decide to reject any delisting request, for any reason or no reason at all: "For those nominated substances not selected for evaluation, the NTP notifies the nominators."

such as a weight-of-evidence framework that is transparent, reproducible, and scientific.[10]

6) Your testimony suggests that the National Toxicology Program should be following a rote formula for deciding which chemicals to list. Is there any value to allowing NTP scientists to use their scientific knowledge to make judgments about the data?

The premise of this question is false. There are many alternative weight-of-evidence frameworks around, none of which contains "a rote formula."

In principle, NTP scientists probably ought to be able to "use their scientific knowledge to make judgments about the data." The problem is that they do not disclose how they do this. The public needs full transparency in order to gain the assurance that when NTP scientists exercise judgment, it is scientific judgment only that they are exercising, that they are doing so in ways that the scientific community at large considers reasonable, and that they are exercising scientific judgment in ways that treat similarly situated substances the same way. The NTP's refusal to disclose how its scientists "exercise judgment" convincingly communicates to the public that the judgments its scientists are exercising are policy judgments, not scientific ones, or that their scientific judgments would not be supported by the broader scientific community.

There is a significant limitation on the quality of scientific judgment that NTP scientists could ever exercise. NTP scientists would be the ones most knowledgeable about the science for a particular substance only in rare cases. I suspect, but cannot confirm with evidence, that NTP scientists become less willing to consider alternative scientific views when they are confronted by non-government scientists who have distinguished reputations gained from active research and prolific peer-reviewed publication. In a fair contest, few NTP scientists would be able to hold their own against these scientific stars. But the contest is not a fair one; NTP scientists get to be both contestant and judge, deciding which scientific evidence and arguments prevail. Listing decisions provide unique opportunities to cut the stars in the scientific profession down to size.

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[10] A weight-of-evidence framework that is transparent but policy driven would not be much of an improvement.

Thus, the question is not whether NTP scientists should be allowed to exercise scientific judgment; it is whether they should be allowed to do so secretly, without accountability for the quality of their scientific judgments, and without even a requirement to publicly demonstrate that the judgments they exercise are genuinely scientific.

Historically, the NTP has used its Board of Scientific Counselors to provide the appearance of scientific endorsement of its policy-driven listing decisions. A much better use of the BSC would be to convert it into a body of independent, honest brokers, who arbitrate differences in scientific judgment between the NTP staff and nongovernmental scientists with equivalent or superior experience and expertise. If what NTP scientists are doing is exercising strictly scientific judgment, then they should welcome such a reform because it would validate them when they are correct and generally yield conclusions that are rarely, if ever, scientifically controversial. If the NTP were to reject such a reform, however, it would reinforce the widespread conviction that the discretion NTP wants to preserve is for its scientists (and officials) to make political and policy judgments under the guise of science.

7) You seem to be asking for a great deal of rigor and in-depth analysis for a decision making process that is meant to benefit the public. Are you suggesting that the system be made much more difficult for NTP to publish the RoC?

My reading of NTP publications indicates that it believes its current reviews involve "a great deal of rigor and in-depth analysis for a decision making process that is meant to benefit the public." In her testimony, for example, Dr. Birnbaum characterized them as "thorough" and based on "consideration of all relevant research data." If this accurately characterizes what the NTP now does, the reforms I propose would not make NTP reviews any more burdensome.

If the NTP limited the RoC to science, and began to follow the law, it would be able to publish the RoC with much less controversy. The primary reason why the NTP has been unable to publish the RoC biennially is because its listings are policy decisions, not scientific determinations, and it can be challenging and time-consuming to make it appear as if science is dispositive.

Under a well-designed sunset provision, the NTP might have a much more demanding workload. But this would be true only if the

NTP was bureaucratically or politically determined never to delist substances irrespective of the scientific evidence.

The current RoC has no positive value to the public, and a case can be made that its public value is negative. For substances that are widely agreed by scientists to cause cancer in humans, an NTP listing is neither controversial nor contains any new information. In those cases, the social value of an NTP listing must be zero.

But for substances that, in Dr. Birnbaum's formulation, "may" have the "potential" to be human carcinogens, listings are inherently controversial on legal, scientific, and policy grounds. What's more, these listings mislead the public. When the NTP labels a "potential" human carcinogen as a "reasonably expected" carcinogen, it knowingly disseminates false information. To see why, consider two weather forecasts—one that says weather conditions make a tornado strike a "known" probability, and a second that says weather conditions create the "potential" for a tornado strike. It is critical to seek shelter in response to the first forecast but doing so makes no sense in response to the second.

For unexplained reasons, Dr. Birnbaum believes that it is an ethical practice to mischaracterize substances that "may" pose a "potential" cancer risk as "known" or reasonably anticipated" human carcinogens. Until this deceptive practice is ended, the RoC will continue to have negative social value to the people of the United States.

QUESTIONS SUBMITTED BY REP. PAUL TONKO, RANKING MEMBER, HOUSE SCIENCE, SPACE AND TECHNOLOGY, SUBCOMMITTEE ON ENERGY & ENVIRONMENT

1) You stated in your testimony that:

"In August of 2011, I was asked by the Competitive Enterprise Institute to conduct a short study trying to explain why the RoC had become so intensely controversial. Regulatory Checkbook received an honorarium of $5,000 for a completed published paper... Subsequently, Regulatory Checkbook supplied an additional $5,000 of unrestricted resources."

REGULATORY
CHECKBOOK

This is not a very helpful disclosure of funding as neither Competitive Enterprise Institute nor your Regulatory Checkbook seem to have sources of funding aside from outside contributions or contracts.

A) Please identify the source of the CEI honorarium funds provided by CEI.

I do not know the source of the funds CEI paid to Regulatory Checkbook.

B) If you do not know the source of funds, did you ask CEI regarding the source and the kind of report envisioned?

I did not ask CEI about the source of its funding.

C) If you did not ask about the source of funds, please explain why you did not ask.

In my experience, every research sponsor, whether an individual, a corporation, a union, an advocacy group, a foundation, or a government agency, funds research in order to influence public policy. Thus, independent scholars always have the opportunity to skew their research in ways that appeal to their sponsors. Sometimes skewness is obvious, because even the pretense of objectivity is missing. Other times skewness can be quite subtle, such as when scholars draw inferences that cannot be supported by their research. Sometimes scholars work very hard to prevent being captured by their sponsors, by hewing to strict standards of integrity and objectivity.

But research cannot be skewed in favor of a sponsor if the identify of the sponsor is unknown. Preserving ignorance about the source of funds is the best way for independent scholars to ensure that the integrity and objectivity of their research is not compromised by sponsor interests. For that reason, anonymous sponsorship is the best possible evidence of the absence of sponsor bias.

2) Please identify the source of the $5,000 provided to you by your non-profit corporation, the Regulatory Checkbook.

As I testified, these funds came from unrestricted contributions, which are by definition intermingled. Donors have no control over how they are used. Before expending unrestricted funds, Regulatory Checkbook never seeks donor approval.

The Secretary shall publish a biennial report which contains—

(A) a list of all substances

(i) which either are known to be carcinogens or may reasonably be anticipated to be carcinogens and

(ii) to which a significant number of persons residing in the United States are exposed;

(B) information concerning the nature of such exposure and the estimated number of persons exposed to such substances;

SLIDE 1

There is sufficient evidence of carcinogenicity from studies in humans,* which indicates a causal relationship between exposure to the agent, substance, or mixture, and human cancer.

*This evidence can include traditional cancer epidemiology studies, data from clinical studies, and/or data derived from the study of tissues or cells from humans exposed to the substance in question, which can be useful for evaluating whether a relevant cancer mechanism is operating in humans.

SLIDE 2

There is sufficient evidence of carcinogenicity from studies in humans,* which indicates a causal relationship between exposure to the agent, substance, or mixture, and human cancer.

*This evidence can include traditional cancer epidemiology studies, data from clinical studies, and/or data derived from the study of tissues or cells from humans exposed to the substance in question, which can be useful for evaluating whether a relevant cancer mechanism is operating in humans.

SLIDE 3

There is sufficient evidence of carcinogenicity from studies in humans

SLIDE 4

The Secretary shall publish a biennial report which contains—

(A) a list of all substances

(i) which either are known to be carcinogens or may reasonably be anticipated to be carcinogens and

(ii) to which a significant number of persons residing in the United States are exposed;

(B) information concerning the nature of such exposure and the estimated number of persons exposed to such substances;

SLIDE 5

The Secretary shall publish a biennial report which contains—

(A) a list of all substances

(i) which either are known to be carcinogens or may reasonably be anticipated to be carcinogens and

(ii) **to which a significant number of persons residing in the United States are exposed**;

(B) information concerning the nature of such exposure and the estimated number of persons exposed to such substances;

SLIDE 6

1. Define "a significant number of persons residing in the United States";
2. Define a *de minimis* cancer risk level; and
3. Estimate for each candidate substance the number of persons in
   the United States exposed above the de minimis cancer risk level.

SLIDE 7

Appendix 2

Additional Material for the Record

LETTERS SUBMITTED BY SUBCOMMITTEE CHAIRMAN PAUL BROUN, HOUSE COMMITTEE ON SCIENCE, SPACE AND TECHNOLOGY

CAL DOOLEY
PRESIDENT AND CEO

April 25, 2012

The Honorable Paul Broun
Chairman, Subcommittee on Investigations & Oversight
Committee on Science, Space, & Technology
United States House of Representatives
Washington, D.C. 20515

The Honorable Paul D. Tonko
Ranking Member, Subcommittee on Investigations & Oversight
Committee on Science, Space, & Technology
United States House of Representatives
Washington, D.C. 20515

The Honorable Renee Ellmers
Chairwoman, Subcommittee on Healthcare & Technology
House Committee on Small Business
United States House of Representatives
Washington, D.C. 20515

The Honorable Cedric Richmond
Ranking Member, Subcommittee on Healthcare & Technology
House Committee on Small Business
United States House of Representatives
Washington, D.C. 20515

Dear Chairman Broun, Ranking Member Tonko, Chairwoman Ellmers, and Ranking Member Richmond:

The House Committee on Science, Space, & Technology, Subcommittee on Investigations & Oversight, and the House Committee on Small Business, Subcommittee on Healthcare & Technology are scheduled to hear testimony today from several witnesses concerning the National Toxicology Program's (NTP) Report on Carcinogens (RoC) and its impact on jobs, and the economy. The American Chemistry Council (ACC), a national trade association representing approximately 160 member companies and the business of chemistry which employs nearly 800,000 workers, requests that ACC's perspectives on this important issue be entered into the hearing record.

America's consumers, workers, retailers and manufacturers must have confidence that the government's chemical evaluations are accurate and credible. Indeed, the protection of public health, American innovation and jobs depend on the decisions made in chemical evaluations. We must ensure that those decisions are made on the basis of the highest quality and most reliable science.

Unfortunately, the NTP's Report on Carcinogens (RoC) continues to fall well short of meeting the benchmarks of objectivity, scientific accuracy, and transparency necessary to ensuring high quality, reliable assessments.

Inconsistent Science and Duplicative Programs

ACC has significant concerns with the quality of the RoC evaluation process, as well as the duplicative, inconsistent scientific review processes that exist across multiple agencies and departments. NTP's RoC, EPA's Integrated Risk Information System (IRIS), and the Centers for Disease Controls (CDC) Agency for Toxic Substances and Disease Registry (ATSDR) programs are all housed within different federal departments or agencies. There is considerable overlap in the substances they evaluate, but each program employs different methods for assessing chemical hazards and risks. These overlapping and duplicative programs often produce conflicting conclusions and guidance.

The concurrent evaluation of formaldehyde in EPA's IRIS program and the NTP 12th RoC is a prime example. Just a few weeks after a National Academy of Sciences (NAS) panel concluded that EPA's IRIS program had failed to scientifically justify its conclusion that formaldehyde causes specific types of leukemia, the 12th RoC made the same mistake as EPA, asserting that studies in humans have shown that formaldehyde causes myeloid leukemia.[1] By failing to sufficiently reflect the conclusions of NAS, and by producing a contradictory report, the 12th RoC has created the potential for public confusion and alarm as well as economic harm to the 600,000 Americans employed in industries that depend on the production and use of formaldehyde, all without adequate scientific basis. Although the listing of a substance in the RoC does not constitute a regulation or rulemaking per se, listing determinations often trigger regulatory actions by Federal and State agencies, product deselection, and product liability suits.

It is abundantly clear that federal risk assessment activities are not being coordinated, despite direction and guidance provided by the Administration.[2]

ACC strongly recommends that the Committees carefully consider the relevance and necessity of the RoC. The RoC was a novel approach when Congress authorized it over 30 years ago, but it has been eclipsed by other government programs and the vast array of information available over the Internet. A similar overlap appears to be highly likely for assessments slated to be conducted on the non-cancerous effects of chemicals within the NTP's newly established Office of Health Assessment and Translation. To the extent possible, duplicative and unnecessary chemical evaluation programs should be eliminated, and even those that are specifically mandated by Congress should receive greater scrutiny to confirm their continued value and relevance.

[1] See http://ntp.niehs.nih.ogv/ntp/roc/twelfth/profiles/Formaldehyde.pdf.
[2] See OMB "Final Information Quality Bulletin for Peer Review" and OMB's "Updated Principles for Risk Analysis" (http://www.whitehouse.gov/sites/default/files/omb/memoranda/fy2005/m05-03.pdf; http://www.whitehouse.gov/sites/default/files/omb/assets/regulatory_matters_pdf/m07-24.pdf).

Flawed Process and Procedures

ACC is also concerned about the implications of the largely pro forma manner in which the NTP went about revising portions of the RoC process late last year. On October 31, 2011, NTP published a Federal Register notice seeking stakeholder input on the RoC processes, but allowed only 30 days for submission of written comments. Immediately after the comment period, NTP scheduled discussion of its final revisions by its Board of Scientific Counselors (BOSC) on December 15, 2011, and the agenda specified only half an hour for presentation by NTP, comments by stakeholders, and discussion by the BOSC. ACC objected to the Director of NIEHS regarding this truncated process, and she replied, "While we appreciate the suggestions, we believe that the announced public comment process and timeline provide a reasonable opportunity for interested parties to provide external input, while enabling the NTP to move forward consistent with the RoC's statutory reporting time frame." ACC strongly disagrees that the process was adequate to obtain meaningful input or to obtain the necessary independent review by outside scientists.

With bipartisan support, Congress passed the Consolidated Appropriations Act of 2012, which directed the Department of Health and Human Services to contract with NAS to "conduct a scientific peer review of the 12th Report on Carcinogens determinations related to formaldehyde and styrene. Included in the review should be all relevant, peer-reviewed research related to both formaldehyde and styrene." Despite this explicit Congressional mandate, NTP has yet to contract with the NAS and instead, is immediately moving forward with development of the 13th RoC.

These actions demonstrate the NTP's lack of commitment to improve the data evaluation and weight of evidence procedures of the RoC to meet current standards, including those identified by the NAS in Chapter 7 of the April 2011 NAS formaldehyde scientific peer review report. ACC recommends that the Committees direct the NTP to immediately contract with the NAS to review the 12th RoC styrene and formaldehyde evaluations which led to the listing decisions, and await the report from this NAS review before moving ahead with the 13th RoC. ACC is concerned that unless fundamental and permanent improvements are made, the 13th RoC will suffer from the very same shortcomings that plagued the 12th RoC.

The NTP RoC has reached an important crossroad – unless its policies and practices are revised and significantly improved to meet the highest standards of scientific integrity, transparency, and peer review, flawed assessments will continue to be produced. Continued public confusion, unwarranted alarm, unnecessary product de-selection, and litigation will continue to be the result. Improving the quality of chemical assessments will lead to significant benefits for everyone through better public health decisions based on accurate information and better use of public and private sector resources that can be refocused on promoting American jobs and innovation.

ACC and its members look forward to working with you and the both Committees as discussion around the RoC continues. If we can provide any additional information on ACC's perspectives on this or related topics, please contact me.

Sincerely,

Cal Dooley
President and CEO

April 23, 2012

The Hon. Paul Broun, Chair
Subcommittee on Investigations & Oversight
Science, Space & Technology Committee
U.S. House of Representatives
B-374 Rayburn House Office Building
Washington, DC 20515

The Hon. Paul D. Tonko, Ranking Member
Subcommittee on Investigations & Oversight
Science, Space & Technology Committee
U.S. House of Representatives
394 Ford House Office Building
Washington, DC 20515

The Hon. Renee Ellmers, Chair
Subcommittee on Healthcare & Technology
Small Business Committee
U.S. House of Representatives
2361 Rayburn House Office Building
Washington, DC 20515

The Hon. Cedric Richmond, Ranking Member
Subcommittee on Healthcare & Technology
Small Business Committee
U.S. House of Representatives
B-343C Rayburn House Office Building
Washington, DC 20515

Regarding the April 25th Hearing: How the Report on Carcinogens Uses Science to Meet its Statutory Obligations and its Impact on Small Business Jobs

Dear Chairman Broun, Chairwoman Ellmers, Ranking Member Tonko, and Ranking Member Richmond,

On behalf of the Breast Cancer Fund and our 70,000 members nationwide, I write in strong support of the National Toxicology Program's Report on Carcinogens. The National Toxicology Program (NTP), headquartered at the National Institute of Environmental Health Sciences (NIEHS), produces the Report on Carcinogens to provide science-based information on the health hazards of cancer-causing substances. The information in the Report on Carcinogens serves a wide range of people and needs, providing objective and thorough scientific information that is used across the United States and around the world. We urge the Committee Members to endorse the Report's conclusions and to continue to back, if not expand, this critical public health document moving forward.

The epidemic of cancer in the country has touched all of us. Breast cancer alone accounts for over 230,000 diagnoses and almost 40,000 deaths per year. True prevention is the only way to avoid the devastating impact of a cancer diagnosis on individuals and their families and friends. The Breast Cancer Fund's mission is to prevent breast cancer by identifying and working to eliminate the environmental causes of the disease. As an organization that bases our public education and policy advocacy on a strong foundation of science, we rely heavily on the work of NTP and the Report on Carcinogens to inform ourselves and our members about chemicals that pose health hazards and how to prevent unnecessary exposure to cancer-causing chemicals.

The Report on Carcinogens, which has been mandated by Congress since 1978, reviews the peer-reviewed science suggesting links between substances and cancer, then summarizes the information and makes it available to government regulators, medical personnel, and the general public. NIEHS scientists have extensive training across a broad range of cancer-related specialties, including breast cancer, and are capable of high-level evaluations of the toxicological and epidemiological studies we rely on to determine safety and hazards. The Report on Carcinogens summarizes the deliberations of many scientists who evaluate the body of scientific

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evidence and come to conclusions regarding the state of the science. These conclusions, which undergo review by scientists outside of NIEHS, form a critical basis for actions in public health and medical practices.

This process is, and must remain, science-based and free from political or economic interference. There is ample opportunity for the public and industry to offer information and input, but the integrity of the report depends on NTP's reliance on the data and the peer review of the report by a panel of external experts. NIEHS is a public health agency, not a regulatory agency. Their mission is to look objectively at the science and provide unbiased information about the risk posed by certain chemicals. This crucial work must continue.

When we are informed about carcinogens in our environment, homes, schools, and workplaces, we are in the best position to protect ourselves, our families, and our communities. The NTP and the Report on Carcinogens provides us with robust and thorough evaluations of carcinogens carried out by an objective scientific agency; it is a public health service that is essential to all of us who care about protecting health and reducing the plague of cancer in our country.

We again urge you and your Subcommittee members to support the work of NTP and of NIEHS as a whole. Our country's health and economic security will be stronger for it.

Sincerely,

Jeanne Rizzo, R.N.
President and CEO

April 23, 2012

To The Honorable Members of the
Subcommittee on Science, Space, & Technology
Subcommittee on Investigations
Subcommittee on Oversight
House Small Business Subcommittee on Healthcare & Technology

Regarding the April 25th Hearing: How the Report on Carcinogens Uses Science to Meet its Statutory Obligations and its Impact on Small business Jobs

My organization, Empire State Consumer Project is focused on the protection of children from hazardous chemicals. We are especially concerned about exposures to carcinogens, which can impose a lifelong burden of health risks. I have worked for over 40 years to protect children and inform the public about hazards, since initially testifying in Washington during the 1970's on health hazards of consumer products. We must know which chemicals are carcinogenic in order to protect the public.

NIEHS provides essential information on chemicals that should be avoided in children's products, home and school materials, and in our communities. Their Report on Carcinogens explains the science and summarizes the information. Many carcinogenic chemicals in the Report on Carcinogens are in products that have historically been used in schools, day care centers, and sold to the public for use in the home. Chemicals such as formaldehyde, which causes leukemia, pose a real and present danger to children in the US and steps are being taken to reduce children's exposures.

Children are especially susceptible to carcinogens, and the consequences of cancer in childhood are especially terrible. In order to prevent exposures to carcinogens we must have complete information. We must have strong and objective scientific information, such as the Report on Carcinogens, to guide our efforts in raising strong healthy children. The work of NIEHS is essential to all of us working in the children's health field. I hope Congress will not only continue to support their work, but increase it so that a broader range of chemicals can be evaluated, and those of us working on children's health issues can provide the best possible information to parents, schools, and others who care for our children.

Sincerely,

Judy Braiman
President
Empire State Consumer Project
50 Landsdowne Lane
Rochester, New York 14618
585-383-1317

April 23, 2012

To the Honorable Members of the Subcommittee on Science, Space & Technology
Subcommittee on Investigations and Subcommittee on Oversight
House Small Business Subcommittee on Healthcare and Technology
The United States House of Representatives
Washington, DC

Regarding the April 25th Hearing: How the Report on Carcinogens Uses Science to Meet its Statutory Obligations and its' Impact on Small Business Jobs

Honorable Representatives,

We are physicians and environmental scientists who write to you about our concern for the continuity of the Report on Carcinogens of the National Toxicology Program. We have learned, to our dismay that your committee is considering limiting or eliminating funding for the ROC because of concerns by industry stakeholders that the ROC places special burdens on them. We believe that limitations placed on the work of the NIEHS and of the National Toxicology Program, that would diminish the scientific integrity and authority of the Report on Carcinogens would be deeply damaging to the medical and scientific community. We also believe that alterations in the authority of the ROC would seriously damage the image of the United States in the eyes of the international scientific community.

The Report on Carcinogens, now in its 12th iteration, forms the only authoritative peer reviewed American view of occupational and environmental carcinogens. It has become a central resource for all of us who work with patients, problems, and consulting issues in occupational and environmental toxicology. It is also regarded as authoritative in scientific work internationally and is widely quoted and relied upon for the public health aspects of occupational and environmental carcinogens. Much of the world's regulatory policy for the prevention of disease and environmental degradation by carcinogens utilizes and refers to the Report on Carcinogens. It is considered a reliable, unbiased and scientifically valid compilation of knowledge about carcinogenic substances. Many physicians, scientists and science based businesses rely upon the Report for up to date, peer reviewed information on the state of the art in carcinogen research and management.

We believe that no reduction should be made to the preparation, publication, and dissemination of the Report on Carcinogens of the National Toxicology Program. This critical function and publication of the National Institute of Environmental Sciences is a major scientific resource provided to the United States medical and scientific community and to the world scientific and medical community. It is vital that the program be continued and if possible, strengthened. This irreplaceable information resource, upon which preventive medical decisions are made every day, cannot be reduced in scope without serious damage to the health and welfare of the people of the United States and of the world.

We hope you will continue support for this program.

Respectfully submitted by the following physicians and medical scientists,

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Colorado School of Public Health
University of Colorado at Denver, Anschutz Medical Campus
Aurora, Colorado
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Michael R. Harbut, MD, MPH, FCCP
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Ellen Silbergeld, PhD
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The Johns Hopkins University
Baltimore, MD

John Bailar, MD
Professor Emeritus, University of Chicago
Scholar in Residence, National Academy of Sciences
Washington, D.C.

Kathleen M. Burns, Ph.D.
Director
Sciencecorps
Lexington, MA

Ronald Melnick, Ph.D.
Ron Melnick, LLC
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David H. Wegman, MD, MSc
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Darius D. Sivin, PhD
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Takoma Park, MD

Devra Davis, Ph.D.
President
EHTRUST

Henry A. Anderson, MD
Adjunct Professor
Department of Population Health
University of Wisconsin School of Medicine and Public Health
Madison, WI 53703

April 24, 2012

To The Honorable Members of the;
Subcommittee on Science, Space, & Technology
Subcommittee on Investigations
Subcommittee on Oversight
House Small Business Subcommittee on Healthcare & Technology

Regarding the April 25th Hearing: How the Report on Carcinogens Uses Science to Meet its Statutory Obligations and its Impact on Small business Jobs

We are Veterans who work with other Veterans from all branches of the military service that were exposed to toxic chemicals during their service. We provide information and assistance to them at no charge, and also provide public information to Veterans through the news media.

Many carcinogenic chemicals in the Report on Carcinogens are found on military bases in the US and overseas. Protection during military service relies on accurate information about the health consequences of chemical exposure. Cancer information is among the most important and necessary in order to minimizing harmful exposure during military service, to the degree possible. This is important for the Armed Services, Service members and Veterans, their families, and for the health of the country.

The strongest federal agency we have to identify cancer-causing chemicals is the National Institute of Environmental Health Sciences (NIEHS). Their cancer listings in the Report on Carcinogens are used to establish protective protocols, and used by medical professionals in their work with Veterans. Full and accurate information is essential. We all know the consequences of burying evidence that chemicals cause cancer. We've been through the Agent Orange tragedy, and the harm from TCE is still unfolding.

Most employers, whether the government or private companies, know that protecting their workers from exposure to carcinogens is good business sense and the humane thing to do. Knowledge of carcinogens allows the military to devise safer processes, provide appropriate protective gear, and reduce the health care costs in the short and long-term.

Those companies that don't want public disclosure of objective cancer information, as NIEHS provides, are trading human lives for profits. That has never been an acceptable way to do business in the United States. And Veterans are frankly offended that a scientist from Dow Chemical, the company responsible for Agent Orange and its continuing legacy of death and disease, is testifying on this issue in our Congress. Their actions are the opposite of what we need in this country.

We condemn efforts to silence or politicize one of the truly objective and politically independent agencies - NIEHS - and hope that Congress will strengthen and support NIEHS in coming years. It is the right thing to do.

Respectfully submitted by Veterans from every United States Military Service Branch.

Robert O'Dowd
U.S. Marine Corps Veteran
Cancer Survivor
Somerdale, New Jersey

Timothy King
U.S. Marine Corps Veteran
Salem, Oregon

James Davis
President and Founder
Veterans for Change
U.S. Navy Veteran
Garden Grove, California

Ernest R. Ramirez
U.S. Marine Corps Veteran
Uniontown, OH

LeAnn Ramirez
U.S. Marine Corps Veteran
Uniontown, OH

Paul Sutton
U.S. Marine Corps Veteran
Ocean View, NJ

Barry Stitts
U.S Navy 1984-2006
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Robert Speakman
USMC
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Robert L. Rohrer
USMC 1956 - 1962
Bermuda Run, NC

Bernard J. Duff
U.S. Army, Cancer Survivor
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Charles Kelley
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Glenn W Sheehan
U.S. Navy
Barrow, Alaska

Eric Karl Jaeger
U.S. Marine Corps
Kansas City, KS

Richard Worst
U.S. Navy
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Major Bill Mimiaga
USMC (Ret)
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MSgt Christine Petersen
USAF (Ret)
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William Shackelford
U.S. Navy
Vietnam Veteran 67-68 & 68-69
Rocky Mount, N.C.

Douglas Arthur Yelmen
U.S. Navy
Lompoc, CA

Chuck Palazzo
USMC
Center Moriches, NY

LETTERS SUBMITTED BY SUBCOMMITTEE CHAIRMAN RENEE ELLMERS, HOUSE COMMITTEE ON SMALL BUSINESS

Advocacy: the voice of small business in government

November 22, 2011

BY ELECTRONIC MAIL

The Honorable Kathleen Sebelius
Secretary of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

RE: Comments on the Department of Health and Human Services, National Toxicology Program's Report on Carcinogens

Dear Secretary Sebelius:

The U.S. Small Business Administration (SBA) Office of Advocacy (Advocacy) submits these comments on the Department of Health and Human Services (HHS), National Toxicology Program's (NTP), Report on Carcinogens (RoC) and on the proposed RoC review process.[1] Advocacy is familiar with the concerns underlying the NTP's decision to review the RoC process as identified by small businesses, including the quality of scientific research and procedural transparency. The efforts of NTP to review the RoC process by inviting public comment are welcomed, however, the proposed review process does not make any substantial or necessary changes.[2] In fact, the NTP's removal of peer review and public comment opportunities in the proposed review document will further hinder the RoC by decreasing the level of transparency.[3]

Advocacy urges the HHS to review and evaluate the RoC's purpose and objectives and to consider whether, if substantial changes cannot be made, the RoC should continue to play a role in the federal government's chemical risk assessment program. Further, the RoC is duplicative of another federal chemical assessment program, the Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS). Advocacy's concern reflects those of small businesses for which a less than robust RoC may have a substantial, negative economic impact.

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[1] Federal Register, Vol. 76, No. 2010, October 31, 2011. Retrieved from http://ntp.niehs.nih.gov/ntp/PressCtr/FRN/2011/76FRN210ROC20111031.pdf.
[2] National Toxicology Program's Proposed Review Process for the Report on Carcinogens available at http://ntp.niehs.nih.gov/?objectid=3756DE0C-FA7A-404B-3F72194C30ABD961.
[3] HHS (2011). Proposed Report on Carcinogens Review Process. U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program, Research Triangle Park, NC. Retrieved from http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/ProposedROCReviewProcess2011.pdf.

Office of Advocacy

Congress established the Office of Advocacy under Pub. L. No. 94-305 to advocate the views of small entities before Federal agencies and Congress. As Advocacy is an independent body within the U.S. Small Business Administration (SBA), the views expressed by Advocacy do not necessarily reflect either the position of the Administration or the SBA.

The RoC Background

The RoC was congressionally mandated in 1978, as part of the Public Health Services Act, in response to Americans' concerns regarding the relationship between their environment and cancer. It was to be a science-based, public health report to identify 'substances' in the environment that may potentially increase the risk of cancer.[4] The biennial publication provides information on cancer studies that support a listing, potential sources of exposure to humans, and current federal regulations to limit exposures. The RoC lists chemicals as either "known to be a human carcinogen" or as "reasonably anticipated to be a human carcinogen."

Notably, on the NTP's website, and in a fact sheet on the 12th RoC published by the NTP, the NTP explains that a listing in the RoC does not "by itself establish that a substance will cause cancer in an individual."[5] Further, the RoC studies were neither designed for, nor intended to inform regulatory decision-making. However, the listings are used by several organizations primarily as substantive guidance documents and to regulate potential human carcinogens. Such organizations include the U.S. Congress, Federal and State agencies including EPA, the Occupational Safety and Health Administration (OSHA), private businesses and unions. Although the RoC was a novel approach when mandated, it overlaps today with other more robust federal chemical assessment programs, such as EPA's IRIS.

Accurate and Reliable Chemical Assessments are Vital for Small Businesses

Small businesses are growing more concerned with the RoC because of the impact that the report may have on their business. The placement of a chemical in a RoC has the potential to substantially stigmatize the chemical post-listing. The stigmatism may lead to substantial adverse economic impacts for small businesses that use that chemical, including de-selection of American products in the marketplace by businesses and consumers, an increase in the likelihood of additional regulations and, an increase in fears of using or buying products manufactured with a labeled chemical.

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[4] U.S. Department of Health and Human Services, National Toxicology Program website. Retrieved from http://ntp.niehs.nih.gov/?objectid=72016262-BDB7-CEBA-FA60E922B18C2540.

[5] U.S. HHS (2011). Fact Sheet on the 12th RoC. U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program, Research Triangle Park, NC, p. 2. Retrieved from http://www.niehs.nih.gov/health/materials/fact_sheet_the_report_on_carcinogens.pdf; *see also* National Toxicology Program website http://www.niehs.nih.gov/news/sya/sya-roc/.

Government agencies should also be aware that technical labels used in the RoC can be misinterpreted and mislead the public about the true nature of risks to health and safety. For example, although the RoC lists chemicals as "reasonably anticipated to be a human carcinogen" or "known to be a human carcinogen," it includes the caveat that "listing of substances in the RoC only indicates a potential hazard and does not establish the exposure conditions that would pose cancer risks to individuals in their daily lives."[6] However, because consumers, businesses and government bodies are likely to be more aware of how the chemical is labeled than the disclaimer that appears in the RoC, and because negative labeling can stigmatize a chemical, an accurate risk characterization is vital.

The call for accurate and consistent risk characterizations based on reliable scientific processes is supported by President Obama's Executive Order 13563 "Improving Regulation and Regulatory Review," issued on January 18, 2011. The E.O. states that the regulatory system "must promote predictability and reduce uncertainty and identify and use the best, most innovative and least burdensome tools for achieving regulatory ends."[7]

The President's 2009 Memorandum on Scientific Integrity states, "Science and the scientific process must inform and guide decisions of my Administration ... The public must be able to trust the science and scientific processes informing public policy decisions."[8] Likewise, small businesses and the public must be able to rely on the scientific integrity and procedures that produce chemical risk characterizations.

Once a substance has been listed in the RoC, the substance may be delisted. However, the process for delisting is a substantial obstacle to having a chemical removed from the RoC. This difficulty is highlighted by the attempt to delist glass wool as "reasonably anticipated to be a human carcinogen" that was listed in the 7th RoC published in 1994. After more than ten years of research, glass wool was nominated for delisting in 2004. However, instead of delisting the substance the NTP modified the substance profile which excluded certain varieties of glass wool that are "not biopersistent" in the lung. In the 12th RoC glass wool does not appear either as a delisted substance or as a listed substance, causing additional confusion. The listing to 'delisting' process for glass wool took more than 20 years.[9]

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[6] U.S. HHS (2011). Report on Carcinogens, Twelfth Edition. U.S. Department of Health and Human Services, Public Health Service, National Toxicological Program, Research Triangle Park, NC, p 3.
[7] Executive Order 13563, Improving Regulation and Regulatory Review (76 Fed. Reg. 32088) (January 18, 2011).
[8] Presidential Memorandum for the Heads of Executive Departments and Agencies on Scientific Integrity. March 9, 2009. Retrieved from http://www.whitehouse.gov/the_press_office/Memorandum-for-the-Heads-of-Executive-Departments-and-Agencies-3-9-09/.
[9] Richard B. Belzer, "The Report on Carcinogens: What Went Wrong; What can be Done to Fix It", Working Paper, Revised October 24, 2011, p. 3. Retrieved from http://www.rbbelzer.com/uploads/7/1/7/4/7174353/111103_regcheck_working_paper_on_roc.pdf.

Small Businesses' Primary Concerns with the Report on Carcinogens are not Addressed in the NTP's Proposed Review Process

Comments made by small businesses since the NTP's June 10, 2011 release of the 12th RoC have highlighted substantive and procedural problems throughout the program. Small businesses' primary concerns with the 12th RoC, and the RoC in general, relate to the quality of scientific analysis, the robustness of the scientific process, including procedures for peer review and public comment procedures, and that the RoC is duplicative of other federal chemical risk assessment programs, particularly the IRIS. The NTP's proposed review process does not improve on these major concerns and will in fact aggravate the existing problems.

RoC's Scientific Analysis and Methods Need Improvement

The 12th RoC included new listings for both styrene and formaldehyde. Small businesses have taken issue with styrene's listing as "reasonably anticipated to be a human carcinogen" and formaldehyde's listing as "known to be a human carcinogen." Styrene is used by thousands of mostly smaller companies in the composites and recreational boat building industries. Formaldehyde is used in numerous products from plywood to embalming fluid and toothpaste.

Substantively, Advocacy is concerned with the quality of scientific analysis undertaken by NTP's researchers in drafting the 12th RoC. The RoC focuses on a selected set of studies and not a weight of evidence assessment. Neither a mode of action analysis nor an understanding of how exposure to a certain chemical leads to cancer are required.[10] It is sufficient for the RoC to show "causality" from human studies defined as a "credible association that cannot be explained by chance, bias, or confounding."[11] However, the RoC only cites data from workers exposed to the highest exposure of formaldehyde[12] and ignores data from negative studies.[13] Because of this, the RoC has been criticized as only undertaking a labeling exercise with almost no value for estimating cancer risk or supporting risk-based decision-making.[14]

Further, the RoC's listing of styrene as a "reasonably anticipated to be a human carcinogen" conflicts with several other studies that have concluded to the contrary. One recent European Union study, a review of the styrene health effects database by scientists, determined that styrene should not be classified or regulated as a carcinogen. [15]

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[10] U.S. HHS (2011). Addendum to the 12th Report on Carcinogens. U.S. Department of Health and Human Services, Public Health Service, National Toxicological Program, Research Triangle Park, NC, p 2. Retrieved from http://ntp.niehs.nih.gov/ntp/roc/twelfth/Addendum.pdf.

[11] *Id.* at 2.

[12] C. Richard Titus, "Formaldehyde in the 12th Report on Carcinogens." Kitchen Cabinet Manufacturers Association. July 2011.

[13] Belzer, *supra* note 9 at 26.

[14] *Id.* at 2.

[15] European Chemicals Agency (2008). European Union Risk Assessment Report: Styrene. Draft for Publication, June 2008, United Kingdom. Retrieved from

A second report in 2009 by a blue ribbon panel of internationally recognized epidemiologists concluded that the, "available epidemiologic evidence does not support a causal relationship between styrene and exposure and any type of human cancer."[16]

The University of Alabama's Dr. Elizabeth Delzell, a styrene researcher, argues that there "is not sufficient science to conclude that styrene causes lymphoma, leukemia or other cancers."[17] Also, the International Agency for Research on Cancer decided to list styrene as a "possible" and not a "probable" carcinogen in a 2002 review.[18] Notably, HHS' own Agency for Toxic Substances and Disease Registry (ATSDR) recently reviewed the same data but instead of finding that styrene was a "reasonably anticipated to be a human carcinogen", found only that styrene "may be a weak carcinogen."[19]

Further, the RoC's listing of formaldehyde as "known to be a human carcinogen" contradicts the National Academy of Sciences' recent independent review of the Draft IRIS Review of Formaldehyde.[20] The NAS found that IRIS' scientific evaluation of formaldehyde did not support its conclusion that formaldehyde caused blood cancers. NTP explained the different hazard characterizations by stating that the NAS critique of the IRIS had 'limited applicability' because the, "NAS document is not an independent hazard assessment."[21]

NTP's proposed review process does not include methods to rectify the RoC's lack of mode of action analysis as well as the understanding of how exposure to chemicals leads to cancer which would lend increased credibility to the RoC.

Peer Review and Public Comment Opportunities are Insufficient

The RoC listings should receive appropriate independent peer review. Advocacy is concerned that the NTP's procedures do not allow for sufficient opportunity for peer review or public comment and are, therefore, insufficiently transparent. Similar concerns

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http://echa.europa.eu/doc/trd_substances/styrene/rar/trd_rar_uk_styrene.pdf; *see also* http://www.box.net/shared/zjv9h7xc6hh66erlmca2.

[16] Boffetta *et al*, "Epidemiologic Studies of Styrene and Cancer: A Review of the Literature", J Occup Environ Med., Vol. 51, N. 11, 1275-1287, November 2009. Retrieved from http://www.box.net/shared/static/mfusvfim1x.pdf.

[17] Letter from Elizabeth Delzell, University of Alabama, to Barbara Shane, Executive Secretary, National Toxicology Program, Board of Scientific Counselors, NIEHS, February 5, 2009, retrieved from http://www.box.net/shared/static/sln4m8tp7a.pdf.

[18] World Health Organization, International Agency for Research on Cancer, "IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Some Traditional Herbal Medicines, Some Mycotoxins, Naphthalene and Styrene", Vol. 82, Lyon: IARC Press, 2002, retrieved from http://monographs.iarc.fr/ENG/Monographs/vol82/mono82-9.pdf.

[19] Styrene Information and Research Center, "Styrene Industry Will Contest Vigorously the Unwarranted listing of Styrene in 12th Report on Carcinogens", Statement by Jack Snyder, Executive Director, June 10, 2011, retrieved from http://www.styrene.org/news/pdfs/06-10-11-statement-ntp-listing.pdf.

[20] NAS. (2011). Review of EPA Formaldehyde April 8 2011 Committee to Review EPA's Draft IRIS Assessment of Formaldehyde. National Academy of Sciences, Washington, D.C.

[21] NTP, *supra* note 10, at 1.

were previously raised following the 11th RoC which prompted the NTP to review and improve its procedures for the 12th RoC review process.

Peer review of the 12th RoC began with an external panel review of the draft background document. The reviewers do not conduct an independent and objective review of the science, but instead are asked to determine whether NTP's policies are supported by its science. The Board of Scientific Counselors (BSC) then undertakes a second scientific peer review. However, for the 12th RoC the BSC was not charged with the review of NTP's decision regarding listing status. Instead, the BSC was asked only to determine, "whether the scientific information cited in the draft substance profile for a candidate substance is technically correct, clearly stated and supports the NTP's policy decision regarding its listing."[22]

Although the NTP procedures provide peer reviewers with access to the scientific data, peer reviewers on the three styrene peer review panels were not informed of the scientific criticisms of NTP's position on styrene.[23] Peer reviewers lack access to, and therefore cannot comment on, public comments and scientific controversies.[24] With the limited time and resources of the peer reviewers, it is difficult for the peer reviewers to review all of the materials and often rely on NTP staff to summarize important information for them. Insufficient opportunity for peer review and public comment decreases transparency and confidence in the NTP process.

Unfortunately, the proposed RoC review process does not bolster opportunity for either peer review or public comment and even takes away from the current opportunities. For example, under the 'Scientific evaluation' phase the new process requires external scientific input only 'as needed'. NTP's explanation for when scientific input is 'needed' is based on "The nature, extent, and complexity of the scientific information on a candidate substance",[25] which does not describe specific circumstances or requirements. Further, this phase only includes one opportunity for public participation, whereas in the 12th RoC this phase included three opportunities. Under the 'Public Release of Draft RoC Monograph and Peer Review' phase, instead of having the NTP BSC peer review the draft, the review may be conducted either by the BSC or an 'ad hoc panel'. There is no explanation of when it is appropriate to choose either the BSC or the ad hoc panel and why this change was made. In the 'HHS Approval and Release' phase the NTP has abandoned the requirement of the NTP to respond to public comments. Advocacy notes that there are additional opportunities for interagency comment early on in the

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[22] Bergeson & Campbell PC, "NTP Proposes to Revise RoC Review Process." November 1, 2011. Retrieved from http://www.lawbc.com/tsca/memoranda-2011-51-mobile.html.
[23] Letter from Jack Snyder, Styrene Research and Information Center & John Schweitzer, American Composites Manufacturers Association to the Hon. Kathleen Sebelius, Secretary, U.S. Department of Health and Human Services, May 24, 2011, retrieved from http://www.styrene.org/news/pdfs/05-24-11-letter-to-HHS.pdf.
[24] Letter from Cal Dooley, American Chemistry Council, to David Lane, Assistant to the President & Cass Sunstein, Administrator, Office of Information and Regulatory Affairs, Office of Management and Budget, September 21, 2011.
[25] NTP, *supra* note 3, p 3.

'Nominations and Selection' and 'Scientific Review' phases, however, interagency review should not take away from the opportunity for the public to comment.

The RoC is Duplicative

Advocacy is concerned about the duplication of work between the RoC and the IRIS. Duplication can lead to inconsistent findings which in turn may increase public uncertainty over the human health and environmental risks. Currently, there is no interagency process to promote uniformity and ensure coordination between agencies with chemical risk assessment responsibilities. Within HHS itself, for example, there are two agencies that duplicate the NTP's hazard assessment objective: the U.S. Food and Drug Administration (FDA) and the ATSDR.

The duplication of federal chemical risk assessment programs is highlighted by the RoC and EPA's IRIS assessments. The IRIS is a human health assessment program that evaluates risk data on effects that may result from exposure to environmental contaminants. The IRIS compiles a database that describes the health effects of substances and contains quantitative and descriptive information on cancer and non-cancer effects. Thus, the IRIS not only duplicates, but exceeds the scientific analyses undertaken by the RoC as the quantitative hazard characterization is not performed by the RoC. The NTP's proposed review process does not address the overlap between the RoC and the IRIS or other federal chemical risk assessments.

Conclusion

Small businesses are concerned that the continued lack of rigorous scientific inquiry and methodology, procedural inadequacies, and the duplication of assessments will have a substantial, negative economic impact on their business. The NTP's proposed review process falls short of making the necessary changes by which to turn the RoC into a transparent and science-based process. If such changes cannot be made HHS should review and evaluate the RoC's purpose and objectives and consider whether the RoC continues to play an important and useful role in the federal government's chemical risk assessment program. If my office can be of any further assistance, please contact me or Sarah Bresolin Silver at (202) 205-6790 or sarah.bresolin@sba.gov.

Sincerely,

/s/

Winslow Sargeant, Ph.D.
Chief Counsel for Advocacy

/s/

Sarah Bresolin Silver
Assistant Chief Counsel

Office of Advocacy

Copy to: The Honorable Cass R. Sunstein, Administrator
Office of Information and Regulatory Affairs
Office of Management and Budget
Dr. John Holdren, Director
Office of Science and Technology Policy
Executive Office of the President
Dr. John Bucher
Associate Director, National Toxicology Program
Director, National Toxicology Program Division
National Institute of Environmental Health Services - National Institutes of Health
Dora L. Hughes, Counselor for Public Health and Science
Office of the Secretary, U.S. Department of Health and Human Services

HK Research CORPORATION

April 18, 2012

Chairwoman, the Honorable Representative Renee Ellmers:
Healthcare and Technology Subcommittee
House Small Business Committee
1533 Longworth House Office Building
Washington DC, 20515

Subjects:
-Unscientifically based regulation and its effect on the composites industry.
-The effect of this improper regulation on Employees and plant Neighbors.

Hearing Title:
"How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs,"

To the Honorable Representative Renee Elmers:

I'm writing to express my appreciation for the hearing your subcommittee will hold on April 25, to investigate science quality problems and business impacts of the HHS National Toxicology Program's *Report on Carcinogens*.

We are a small company supplying styrene-polyester gel coats to composite manufacturers in North Carolina and across the country. The large majority of our customers are small businesses making products such as kitchen and bath components and recreational fiberglass boats.

Styrene has been safely used in our industry for over 50 years. Several recent "weight of evidence" assessments concluded that styrene is not likely to cause cancer in humans (see the list of expert assessments and peer reviewed studies at http://bit.ly/xG8yDW). However, NTP took several shortcuts in reviewing the extensive styrene health effects database and in June, 2011 listed styrene as a "reasonably anticipated" carcinogen in the RoC.

As my colleague Teri Schenk, of Global Composites in Elkhart, Indiana, told a recent House Energy and Commerce Committee roundtable, the styrene RoC listing is attracting the unwarranted attention of personal injury attorneys and as a result insurance carriers are raising the rates for liability insurance for our industry companies, if they are willing to continue coverage at all. Further, the listing in the RoC is understandably causing unfounded concern among our community members and employees, and we believe is contributing to an unusually high level of turnover among new employees.

Because of our safety record we have a very low "mod rate" for our Workman's Comp Insurance. Our company, and I'm sure many other small manufacturers, will lose the exemplary rating simply because the NTP took "shortcuts" in their evaluation of styrene. The change in rating will cause a significant increase in insurance cost caused by a NTP regulation that is not based on sound science.

In addition our employees as well as ourselves are bombarded with training programs since they are now working with "Cancer causing Materials" and since the classification has been liberally reported by the

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HK Research CORPORATION

'Broadcast media' we have received calls from our plant neighbors regarding concerns they may be exposed to cancerous materials.

We, of course have complied with the OSHA Hazardous communication regulations required under the NTP ruling and have updated our Product labels, and over 6,000 product MSDS's at considerable cost in both money and time.

We are hopeful that your hearing will lead to legislative reforms to improve the quality of Federal risk assessment programs such as the RoC. We believe modest commonsense reforms, based on longstanding recommendations of the National Academy of Science and the model offered by empirical science, can lead to the needed improvements in transparency, independent peer review, use of up-to-date assessment methods, and oversight.

Thank you again for the attention of your subcommittee to this very important issue.

Sincerely,

Richard V. Higgins
President
HK Research Corporation

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