NATURAL RESOURCES DEFENSE COUNCIL
THE EARTH'S BEST DEFENSE

March 19, 2013

The National Academies
Review the Styrene Assessment in the
NTP 12th ROC (DELS-BEST-12-05)
and
Review of the Formaldehyde Assessment in the
NTP 12th ROC (DELS-BEST-12-04)

Dear Committee Members,

Thank you for taking the time to review the government's styrene and formaldehyde assessments for the 12th Report on Carcinogens (ROC).[1] In June 2011 the prestigious and internationally-respected National Toxicology Program issued the 12th Report on Carcinogens (ROC), a Congressionally mandated public list of agents that are "known" or "reasonably anticipated" to cause cancer in humans.[2] [3]

Here we present comments documenting the political process that has forced these two chemicals to the National Academies (NAS) for review, and show that it is not a process of genuine scientific inquiry, but rather the result of political manipulations by the chemical industry to protect its hazardous chemical products.

Following these comments, please see Appendix 1 on styrene and Appendix 2 on formaldehyde for a scientific review and critique of recent industry-funded reports.

The ROC report listed styrene as "*Reasonably anticipated to be a human carcinogen*" based on limited evidence of carcinogenicity from workplace epidemiologic studies, sufficient evidence of carcinogenicity from studies in experimental animals, and supporting data on mechanisms of carcinogenesis. ROC experts concluded that styrene and its major metabolite, styrene-7,8-oxide (SO) are both mutagenic and clastogenic. Previously, the International Agency for

[1] NTP Report on carcinogens, 12th edn. Research Triangle Park, NC: US Department of Health and Human Services, Public Health Service, National Toxicology Program, National Institute of Environmental Health Sciences, 2011.
[2] http://www.niehs.nih.gov/health/topics/agents/sya-roc/#general05
[3] The 11th Report on Carcinogens was finalized January 2005. Section 301(b)(4) of the Public Health Service Act, as amended, provides that the Secretary, DHHS, shall publish the report biennially.

Research on Cancer (IARC) expert Working Group determined that styrene was a *possible* human carcinogen (Group 2B) in 1994 (Vol 60) and again in 2002 (Vol 82), and that the metabolite SO was *probably* carcinogenic to humans (Group 2A) based on sufficient evidence in animals (IARC, 1994).[4] The recent 12th ROC assessment of styrene is consistent with IARC's expert working group conclusions. Despite undergoing multiple rounds of expert and public review, when the 12th ROC was finally published, the styrene industry immediately filed a lawsuit to have the listing withdrawn. That lawsuit is now ongoing.

There is no question that formaldehyde is dangerous. The chemical is recognized as a carcinogen by EPA, the International Agency on Research on Cancer (IARC) and the National Toxicology Program (NTP), among other authoritative bodies.[5] Although the link between formaldehyde inhalation and cancers of the nose and throat (nasopharyngeal region) has been widely accepted, the chemical industry has waged a battle for more than a decade over whether or not formaldehyde also causes leukemia, and over the cancer potency of formaldehyde (how much formaldehyde causes how much cancer).

Now, the chemical industry is pushing for legislation to prevent the NTP from conducting any work on the next ROC pending the outcome of the NRC review of the styrene listing and the formaldehyde listing – something that was strongly opposed in a letter to Congress signed by over 70 health scientists, including nurses, medical doctors, and retired government scientists.[6] We believe that the ROC styrene and formaldehyde assessments have addressed all the relevant scientific challenges raised by the chemical industry during the public review process, and represent the current scientific state of knowledge. Further, the request for this committee to provide further review is the result of extensive political efforts by the chemical industry to discredit the ROC, and not to improve the science.

Why is the NRC reviewing the styrene and formaldehyde assessments, which have both already undergone years of public and scientific review?

The campaign by the chemical industry to "protect" formaldehyde and styrene from a growing body of scientific evidence that they cause cancer in humans is now more than a decade old.[7] [8] Industry efforts to derail and discredit an EPA IRIS assessment of formaldehyde are directly relevant and responsible for this review of the ROC's listing of styrene and of formaldehyde.

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[4] IARC Monographs on the evaluation of carcinogenic risk of chemicals to humans. Volume 71. Re-evaluation of some organic chemicals, hydrazine and hydrogen peroxide (part 1). Lyon: IARC, 1999.
IARC Monographs on the evaluation of carcinogenic risk of chemicals to humans. Volume 82. Some traditional herbal medicines, some mycotoxins, naphthalene and styrene. Lyon: IARC, 2002.

[5] National Cancer Institute Factsheet. Formaldehyde and Cancer Risk. 11/20/2009. http://www.cancer.gov/cancertopics/factsheet/Risk/formaldehyde

[6] http://switchboard.nrdc.org/blogs/jsass/health_scientists_sign_on_to_t.html
http://blogs.edf.org/nanotechnology/2012/09/05/hands-off-the-report-on-carcinogens/

[7] http://blogs.edf.org/nanotechnology/2011/06/13/acc-resorts-to-smear-tactics-to-defend-its-cash-cows-formaldehyde-and-styrene/

[8] http://switchboard.nrdc.org/blogs/drosenberg/cancer-causing_chemicals_have.html

The condensed recent history on formaldehyde is this: EPA began an effort to update its initial health assessment of formaldehyde in 1998. In 2003, studies from the National Cancer Institute (NCI) and the National Institute of Occupational Safety and Health (NIOSH) reported evidence of an association between workplace exposure to formaldehyde and leukemia.[9] In 2004, U.S. Senator James Inhofe demanded that EPA postpone its revision to the formaldehyde assessment until the agency could take into account industry data developed in response to the workplace studies. The Bush administration agreed.

In 2009 EPA again prepared to issue its revised assessment of formaldehyde. In response, the industry trade group "The Formaldehyde Council" enlisted U.S. Senator David Vitter of Louisiana to place a hold on the Obama Administration's nominee to be the head of EPA's Office of Research and Development (which is where the IRIS program that did the formaldehyde assessment is located) until EPA Administrator Lisa Jackson agreed to send EPA's draft assessment of formaldehyde to the National Academy of Sciences (NAS) for review.[10] The EPA Administrator ultimately agreed to make the referral, which further delayed the agency from moving forward on the assessment – already underway for a decade - for an additional two years.[11]

In April 2011, the NAS released its report on EPA's IRIS assessment of formaldehyde. Although the report was critical of some aspects of EPA's draft assessment, including its length, organization, and clarity, it did not dispute the central findings of EPA that there is strong evidence to support formaldehyde being a cause of nasopharyngeal cancer and some evidence, including from studies of people exposed in workplace settings, for formaldehyde being a cause of myeloid leukemia.

In response to the NAS review of formaldehyde, Assistant Administrator Paul Anastas (whose nomination was held up by Senator Vitter) announced EPA's intent to follow the recommendations made by the NAS, both for the formaldehyde assessment itself, as well as future chemical assessments. Dr. Anastas proposed additional changes including the formation of a new standing peer-review panel of its Science Advisory Board, to review IRIS assessments.

Last October 2012 the chemical industry and its Congressional allies renewed its attack on science with a proposed Bill (HR6564) targeting the structure and function of the EPA Science

[9] NCI. National Toxicology Program. Bioassay of Styrene for Possible Carcinogenicity (CAS No.100-42-5). Natl Toxicol Program Tech Rep Ser. 1979;185:1-107.

[10] Sapien J. How Senator Vitter Battled the EPA Over Formaldehyde's Link to Cancer. Why is formaldehyde still listed by the EPA as a probable rather than a known carcinogen, despite major scientific research linking it to leukemia and other forms of cancer? Scientific American, April 16, 2010. Available at http://www.scientificamerican.com/article.cfm?id=vitter-formaldehyde-epa

[11] Sass JB, Rosenberg DR. The Delay Game: How the Chemical Industry Ducks. Regulation of the Most Toxic Substances. A report of the Natural Resources Defense Council (NRDC). October 2011. Available at http://www.nrdc.org/health/thedelaygame.asp

Senate confirms deputy administrator, research chief. Sara Goodman, E&E reporter. Published: Monday, January 4, 2010

Advisory Board (SAB) that would favor participation by industry scientists (for example, by stating that people with direct financial conflicts should not be excluded), while excluding independent scientists (for example, by limiting participation of scientists with government funding). The bill was strongly opposed in letters to Congress by public interest groups and prominent scientists including Deans of several Schools of Public Health, and the Executive Director of the American Public Health Association.[12]

Nevertheless, the chemical industry and its Congressional allies have seized upon the NAS formaldehyde report and used it ever since to support its claim that the IRIS program lacks credibility and cannot be trusted to competently assess the health effects of chemicals.[13,14]

When the House Appropriations Committee finalized its appropriations bill for EPA in July 2011 a rider was included that required EPA to send three of its IRIS assessments to the NAS for review. However, although the bill was briefly debated on the floor of the House, it was pulled by House leaders before the IRIS rider could be debated or an amendment to strike it from the legislation could be put to a vote. The Senate never considered or debated an IRIS provision. A modified version of the House rider was ultimately included in the Omnibus Spending bill in December 2011, requiring EPA to send three IRIS assessments to the NAS for review.[15] After the rider was enacted, the scope of the NAS review was further revised to instead be a panel conducting a broad overview of the IRIS program, and a panel to review the IRIS program's draft assessment of inorganic arsenic.[16]

The other target of chemical industry's efforts is the National Toxicology Program (NTP), which is under the jurisdiction of the Department of Health and Human Services (HHS).[17] The 12th ROC was released in July, 2011. In August, the American Chemistry Council (ACC) met with the White House Office of Management and Budget (OMB) to ask for greater White House control over both the EPA IRIS program and the NTP - in other words, greater political control over scientific assessments of chemical industry products. [18] The chemical industry also went to

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[12] http://switchboard.nrdc.org/blogs/jsass/hr6564_-_the_house_republican.html
http://blogs.edf.org/nanotechnology/2012/12/07/scientists-push-back-against-a-bill-that-would-pervert-the-whole-concept-of-conflict-of-interest/

[13] EPA Faulted Over IRIS, Peer Review Reforms. Inside EPA. Posted: February 21, 2013

[14] Letter from Senators Vitter, Crapo, and Inhofe to EPA Acting Administrator Perciasepe and Dr. Olden. February 20, 2013

[15] Democrats pleased with EPA provisions in omnibus. Jeremy P. Jacobs, E&E reporter. Published: Friday, December 16, 2011

[16] Guidance for and Review of EPA's IRIS Toxicological Assessment of Inorganic Arsenic. DELS-BEST-12-01

[17] http://switchboard.nrdc.org/blogs/drosenberg/cancer-causing_chemicals_have_1.html

[18] CPG. Small Businesses, Public Health, and Scientific Integrity: Whose Interests Does the Office of Advocacy at the Small Business Administration Serve? A report of the Center for Progressive Government. January, 2013. Available at: http://www.foreffectivegov.org/files/regs/office-of-advocacy-report.pdf
CPR. Distorting the Interests of Small Business: How the Small Business Administration Office of Advocacy's Politicization of Small Business Concerns Undermines Public Health and Safety. A report of the Center for Progressive Reform. White Paper #1302. January 2013. Available at:
http://www.progressivereform.org/articles/SBA_Office_of_Advocacy_1302.pdf

Congress to build support for legislation to force the Report on Carcinogens listing of formaldehyde and styrene to be reviewed by the NAS.

The House Science Committee held a hearing last year (April 2012) on the ROC and styrene that was framed around the industry talking points, and that included representatives of global chemical manufacturing companies claiming to be representing small business interests. The title of the Hearing was, "*How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs*". [19] The industry speakers spent their time trying to discredit the ROC process and chemical assessments.

Most significantly, two letters signed by a bipartisan collection of Senators were sent to HHS Secretary Kathleen Sebelius, urging her to refer the Report on Carcinogens to the NAS for review.[20] The Congressional letters are primarily based on two assertions, both false. First, the letters posit that that the NTP relied on EPA's draft assessment of formaldehyde. In fact, the NTP assessment was conducted independently of EPA – a point the NTP made clear in its addendum to the Report's formaldehyde listing.[21] Second, the letters suggest that the NAS criticisms of EPA's formaldehyde assessment by implication also "raise questions" about the NTP's assessment. This is also false, since the two assessments are independent of each other and the NAS did not review the NTP's listing of formaldehyde (or styrene), and those listings had not been published when the NAS conducted its review of EPA's IRIS assessment of formaldehyde. One of the letters went so far as to suggest that the NAS' criticism of EPA's formaldehyde assessment somehow discredited the NTP's listing of styrene.

One of the Congressional letters was written by Senator Richard Shelby (R-AL) and Mark Warner (D-VA). The Shelby/Warner letter was blatantly inaccurate in its assertions, which are almost identical to styrene industry talking points.[22] The Shelby/Warner letter says that the NTP finding regarding styrene is "contrary" to two recent assessments: a report "conducted by the European Union" and a study by a "'blue ribbon' panel of epidemiologists." The EU report is actually a draft Risk Assessment Report prepared by the U.K. which failed peer review by the EU's Scientific Committee on Environmental Risk, and was never finalized.[23] The "blue ribbon" panel report is a styrene industry funded review article of existing scientific literature that was reviewed by the NTP.[24] Both the rejected draft U.K. Report and the industry-sponsored review article reject the link between styrene and cancer, and are featured on the industry's webpage, "YouKnowStyrene.Org".

[19] http://science.house.gov/hearing/committee-science-space-technology-subcommittee-investigations-oversight-and-committee-small

[20] Links to letters are here: http://switchboard.nrdc.org/blogs/drosenberg/cancer-causing_chemicals_have_1.html

[21] http://ntp.niehs.nih.gov/ntp/roc/twelfth/Addendum.pdf

[22] http://youknowstyrene.org/health-and-safety/expert-science-reviews/

[23] "European Risk Assessment Report, Styrene," Draft for publication, June 2008, United Kingdom. Available at: http://youknowstyrene.org/health-and-safety/expert-science-reviews/source/

[24] Boffetta P, Adami HO, Cole P, Trichopoulos D, Mandel JS. Epidemiologic studies of styrene and cancer: a review of the literature. J Occup Environ Med. 2009 Nov;51(11):1275-87.

When the final Omnibus spending bill was released at the end of 2011, the rider requiring the NAS to review the ROC's listings of formaldehyde and styrene was included, without ever having been subject to congressional debate, notice to the public or opportunity for public comment, or vote on the content of the rider.[25] This is darkly ironic given the industry's professed love of process, transparency and opportunity for public comment.

In summary, this NRC Committee does not arise from a process of genuine scientific inquiry, but rather from a political process that has been co-opted by the profit motivations of chemical manufacturing corporations that do not represent the interests of the public, small businesses, communities, labor, environmental health experts, or families affected by unsafe exposure to styrene or formaldehyde.

Response to general industry criticisms of the RoC process

The chemical manufacturers and their experts-for-hire have leveled some specific criticisms about the ROC[26] addressed below:

1) *The chemical industry alleges that the ROC only considers the studies that find a link with cancer, rather than the overall 'weight of evidence,' which would also consider studies that fail to identify a cancer link.*

The chemical industry is wrong on this point. The industry is conflating the final, brief, written cancer summaries with the process that leads up to those summaries. When NTP is putting together the ROC they review all publicly available studies, including information on production and use of the chemical, physical properties, human exposure, toxicokinetics, cancer in humans, cancer in experimental animals, mechanistic studies, and other relevant studies.[27] Once there is agreement that a chemical is a carcinogen and should be listed in the ROC, the final summaries are fairly short – just a few pages - and emphasize the most informative and highest quality science that supports the final listing decision. Including every possible study in the final write-up on a chemical would make the report overly long and unreadable for most people (a criticism that has been levied against EPA IRIS Reviews by Committees of the National Academies).

2) *The chemical industry says that the ROC should not rely on cancer data from animal or epidemiologic studies if the mechanism for how that chemical causes cancer cannot be fully explained.*

The fact is that understanding *how* a chemical leads to cancer often comes much later than the evidence that it does so. But when there is scientific evidence showing a statistically significant

[25] http://blogs.edf.org/nanotechnology/2012/09/05/hands-off-the-report-on-carcinogens/
[26] Public comments to the NTP Board of Scientific Counselors, December 15, 2011. http://ntp.niehs.nih.gov/?objectid=13BBADB8-AFDA-7523-3C14A341F04C9BBC
[27] http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf

causal link between an exposure and an adverse effect, science accepts that evidence even without a full mechanistic explanation. For example, science still cannot fully explain exactly how lead damages kid's brains, but we know it does and we banned lead from house paint in 1978 and from gasoline in 1986. Congress banned PCB's long before scientists understood how they caused cancer. Since then we've learned more about the mechanism, but if we'd waited then many more kids would have had permanent lead-induced brain damage and more people would have had PCB-related cancer. Science is still exploring the mechanism of how smoking causes cancer, but we no longer allow smoking in most public places. In fact, we now know that the tobacco industry hid evidence for decades that cigarette smoking caused premature death, that tobacco was addictive, and that its own health research was a sham.[28] [29] The chemical industry's proposition that no conclusion can be reached about a chemical's hazard and no regulation should take place until we fully understand the mechanism of action is a self-interested effort – based upon the precedent of the tobacco industry's historic efforts to disregard evidence, delay regulations, and deny harm.

In conclusion, the ROC process is a model for how to summarize the state-of-the-science on chemicals and cancer. It lays all the information out for public scrutiny and comment, evaluates the quality of the data, and says exactly how it will come to a decision to list or not to list the chemical under review. The effort by the chemical industry to attack the ROC and tie its process up in knots is part of its larger goal of defending its toxic products by silencing the evidence of harm.

Conclusion

Although scientific debate may continue regarding the attributable risks that either butadiene alone, styrene alone, or both together contribute to the burden of cancer, there is agreement among experts that both pose cancer risks, and therefore meaningful reductions in exposure to both solvents are urgently needed.[30] [31] In fact, the American Conference of Governmental Industrial Hygienists (ACGIH) (which is not a governmental agency and includes many industry members) over the past few decades has recommended significant reductions in occupational exposure limits for these two chemicals, from 5000 to 2 ppm for butadiene and from 400 to 20 ppm for styrene.[32] The ROC is a public report of the Department of Human Health Services, and

[28] Cummings MK, Brown A, O'Connor R. The cigarette controversy. Cancer Epidemiol Biomarkers Prev. 2007 June;16:1070

[29] Glantz SA, Barnes DE, Bero LA, Hanauer P, Slade J. Looking through a keyhole at the tobacco industry: the Brown and Williamson documents. JAMA 1995;274:219–24

Glantz SA, Slade J, Bero LA, Hanauer P, Barnes DE. The cigarette papers. Berkeley (CA): University of California Press; 1996.

[30] Tomatis L. The IARC monographs program: changing attitudes towards public health. Int J Occup Environ Health 2002. 8144–152.152.

[31] Straif K, Baan R, Cogliano V. Butadiene or styrene or butadiene and styrene or else? Occup Environ Med. 2006 Mar;63(3):157-8.

[32] American Conference of Governmental Industrial Hygienists Documentation of the threshold limit values and biological exposure indices. Cincinnati, OH: ACGIH, 2004.

as such has an obligation to represent the scientific consensus of public health experts, not of those defending profitable industrial products.

NAS reviews of chemical assessments are costly – about a million dollars on average – and they can impose additional and unnecessary delay on updating of health protections for air, drinking water, and contaminated soil. In addition, in instances when they are ordered by Congress at the behest of the regulated industry, without any public notice or opportunity for discussion or debate as a tactic to delay or reverse unwanted negative conclusions by non-industry scientists than they are a misuse of public funds, and of the NAS itself.

Generally speaking, the NAS should be allowed to focus on larger scientific issues of the day, not diverted by Congress on behalf of the chemical industry and put in the position of micromanaging every EPA assessment of chemicals that industry doesn't like. Disparaging and delaying health assessments of chemicals does not make them any safer. People still get cancers, birth defects, learning disabilities, and other diseases from harmful exposures to some toxic chemicals. Industry's efforts to challenge negative assessments of styrene, formaldehyde and other chemicals by attacking the integrity and credibility of non-industry scientists and enlisting the NAS to provide cover and ensure delay may be politically savvy and profitable, but its success comes at the expense of public health and an unbiased scientific method.

Thank you for the opportunity to present these comments.

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(see Appendix 1 on styrene, and Appendix 2 on formaldehyde, below)

APPENDIX 1 – STYRENE SCIENCE

Response to the styrene industry substantive points

Limited evidence of carcinogenicity from workplace epidemiologic studies

Studies of workers in the reinforced-plastics industry or the styrene-butadiene rubber industry were reviewed by the ROC staff. Studies of workers in the reinforced plastics industry had the highest styrene exposures, and fewer confounding exposures to other workplace carcinogens, notably butadiene (a known human carcinogen), but tended to have shorter employment periods. In contrast, workers in the styrene-butadiene industry studies had lower exposure levels but longer follow-up times, and co-exposure to butadiene which is known to cause leukemia cancers in humans.

Two large cohort studies of reinforced-plastics industrial workers (Kolstad et al, 1994, 1995) were considered most informative by NTP.[33] [34] For the styrene-butadiene workers, NTP relied primarily on a large multi-plant cohort mortality study of US and Canadian male workers[35] [36] which encompassed workers from previously published cohorts.[37]

Industry argues that the epidemiology studies show no consistent increased incidence or mortality from any specific cancer type.[38] The truth is that styrene-exposed workers in both the reinforced plastics and the styrene-butadiene industry studies showed increased risks of leukemia, lymphoma, or all lymphohematopoietic cancers (Kogevinas et al 1994; Delzell et al 2006). A nested case-control study of styrene-butadiene rubber workers reported multiple myeloma, lymphosarcoma, and all lymphomas associated with exposure to styrene.[39] A large epidemiology study across six European countries of cancer among workers ever-exposed occupationally to solvents reported a significant upward trend for B-cell non-Hodgkin's

[33] Kogevinas M, Ferro G, Andersen A, Bellander T, Biocca M, Coggon D, Gennaro V, Hutchings S, Kolstad H, Lundberg I, et al. Cancer mortality in a historical cohort study of workers exposed to styrene. Scand J Work Environ Health. 1994 Aug;20(4):251-61.

[34] Kolstad HA, Ebbehøj N, Bonde JP, Lynge E, Albin M. [Health effects following occupational styrene exposure in the reinforced plastics industry]. Ugeskr Laeger. 2012 Jan 30;174(5):267-70. Danish.

[35] Delzell E, Sathiakumar N, Graff J, Macaluso M, Maldonado G, Matthews R; Health Effects Institute. An updated study of mortality among North American synthetic rubber industry workers. Res Rep Health Eff Inst. 2006 Aug;(132):1-63; discussion 65-74.

[36] Graff JJ, Sathiakumar N, Macaluso M, Maldonado G, Matthews R, Delzell E. Chemical exposures in the synthetic rubber industry and lymphohematopoietic cancer mortality. J Occup Environ Med. 2005 Sep;47(9):916-32.

[37] Matanoski G, Francis M, Correa-Villaseñor A, Elliott E, Santos-Burgoa C, Schwartz L. Cancer epidemiology among styrene-butadiene rubber workers. IARC Sci Publ. 1993;(127):363-74.

[38] Rhomberg LR, Goodman JE, Prueitt RL. The Weight of Evidence Does Not Support the Listing of Styrene as "Reasonably Anticipated to be a Human Carcinogen" in NTP's Twelfth Report on Carcinogens. Hum Ecol Risk Assess. 2013 Jan;19(1):4-27.

[39] Matanoski G, Elliott E, Tao X, Francis M, Correa-Villasenor A, Santos-Burgoa C. Lymphohematopoietic cancers and butadiene and styrene exposure in synthetic rubber manufacture. Ann N Y Acad Sci. 1997 Dec 26;837:157-69.

Lymphoma and styrene (OR=1.6, 95% CI= 1.1-2.3).[40] These studies, taken together, provide evidence which the ROC determined to be "limited" supporting the carcinogenicity of styrene.

Although the specific type of lymphohematopoietic cancers varies across styrene-exposed cohorts, this has been reported for other epoxide-forming chemicals including butadiene and ethylene oxide, suggesting that inconsistency of cancer endpoint is to be expected for carcinogens like styrene. In addition, the ROC notes that it is likely that different studies may have grouped or classified the type of lymphohematopoietic cancers differently, and that death certificates may have misclassified the type as well, making it to necessary consider the risk of elevated lymphohematopoietic cancers as a group together.

Dow Chemical authors recently published a follow up study of cancer among workers in the reinforced plastics industry by Collins and colleagues (2013).[41] The study is a follow up to a 1990 and 1994 analysis of the same cohort (ROC 2011).[42] Workers were exposed to an average of 28 ppm styrene for an average duration of 4.3 years. The authors report an excess of death from all cancers combined, and an elevated risk of kidney (SMR=1.18, 95%CI=0.83-1.62) and bladder cancer (1.25, 0.87-1.74). The authors attribute this to smoking, without any supporting evidence. In fact, since the study reports a negative trend between cumulative exposure and lung cancer, and since no effect was detected for nonmalignant respiratory disease, then the positive trend for kidney cancer (with a significant increase in the highest exposure group) cannot be attributed to confounding from cigarette smoking. A similar argument holds for the positive association for pancreatic cancer. The attempt by the Dow authors to blame smoking for the observed excess risk of cancer is pure speculation, when in fact the cancer findings are supported by some previous workplaces studies that have reported elevations in kidney cancer and other cancers. (Kogevinas et al 1994; Kolstad et al 1995)

Workplace studies also point to risk of esophageal and pancreatic cancers among styrene-workers in the reinforced plastics industry, something noted in the earlier IARC reviews and the 12th ROC assessment, which provides additional support for a causal link between styrene and cancer, including the earlier report by Wong et al (1994) of this cohort that the current Dow study reports on (Ruder et al 2004; Wong et al 1994; ROC 2011).[43] Both the recent Dow study[44] and the earlier European multi-plant cohort reported that the elevated pancreatic cancer risk was associated with increasing cumulative exposure (Kogevinas et al 1993, 1994; ROC 2011), making the Dow study consistent with other scientific reports.

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[40] Cocco P, t'Mannetje A, Fadda D, Melis M, Becker N, de Sanjosé S, Foretova L, Mareckova J, Staines A, Kleefeld S, Maynadié M, Nieters A, Brennan P, Boffetta P. Occupational exposure to solvents and risk of lymphoma subtypes: results from the Epilymph case-control study. Occup Environ Med. 2010 May;67(5):341-7.

[41] Collins JJ, Bodner KM, Bus JS. Cancer mortality of workers exposed to styrene in the u.s. Reinforced plastics and composite industry. Epidemiology. 2013 Mar;24(2):195-203.

[42] Wong O, Trent LS, Whorton MD. An updated cohort mortality study of workers exposed to styrene in the reinforced plastics and composites industry. Occup Environ Med. 1994 Jun;51(6):386-96.

[43] Huff J, Infante PF. Styrene exposure and risk of cancer. Mutagenesis. 2011 Sep;26(5):583-4.

[44] Collins JJ, Bodner KM, Bus JS. Cancer mortality of workers exposed to styrene in the u.s. Reinforced plastics and composite industry. Epidemiology. 2013 Mar;24(2):195-203.

It is odd that the Dow study failed to report on whether or not esophageal cancers were elevated, because deaths from this type of cancer were elevated in the earlier study of the same cohort (SMR = 1.92, 95% CI = 1.05 to 3.22; 14 exposed deaths; Wong et al 1994). Dow authors report on all digestive cancer and peritoneum (which includes esophageal cancer), but do not break out the esophageal cancers in their report. This should have been identified separately, since it is a cancer of interest, and was elevated in previous reports on the same cohort.

Overall, the Dow study is consistent with previous reports of elevated cancer, including cancer risks reported in the previous study of the same cohort. (Collins et al 2013; Wong et al 1994) Thus, contrary to the Dow author's conclusions, this new update provides some modest support for carcinogenicity of styrene.

The overall epidemiologic evidence was considered "limited" by the ROC, consistent with the previous IARC reviews – a classification that is well supported by existing epidemiologic studies.

Sufficient evidence of styrene carcinogenicity from studies in experimental animals

In addition to contributing evidence from workplace epidemiologic studies, the animal bioassay studies provide sufficient evidence for the carcinogenicity of styrene based on observed tumors from multiple studies of mice exposed by both inhalation (CD-1 mice)[45] and oral gavage (B6C3F1 mice; NCI 1979) to styrene over two years, and from early-life exposures (O20 mice).[46] The studies showed an increase in lung tumors in male and female mice from inhalation, in male mice from oral gavage, and in both sexes from early-life exposures.

The inhalation studies reported a statistically significant increase in benign lung tumors and in the combined incidence of benign and malignant tumors (adenomas and carcinomas) after 2 years of vapor exposure (20, 40, 80, or 160 ppm styrene) for 6 hours per day, 5 days per week. This study, sponsored by the styrene industry, provides strong evidence for the carcinogenicity of styrene. In the male gavaged mice the combined incidence of benign and malignant tumors was statistically significant and showed a positive dose-response trend (NCI 1979). These two studies were considered the most robust and reliable among the available animal studies.

The early life exposure experiment reported lung tumors in both male and female mice from a single dose administered to the pregnant dam on gestational day 17 (a few days before birth) followed by high-dose oral gavage to the pups once per week from weaning onward (1,350 mg/kg). (Ponomarkov and Tomatis, 1978) The authors reported a significant increase in early onset combined benign and malignant lung tumors as early as 16 weeks after weaning, but

[45] Cruzan G, Cushman JR, Andrews LS, Granville GC, Johnson KA, Bevan C, Hardy CJ,Coombs DW, Mullins PA, Brown WR. Chronic toxicity/oncogenicity study of styrene in CD-1 mice by inhalation exposure for 104 weeks. J Appl Toxicol. 2001 May-Jun;21(3):185-98.

[46] Ponomarkov V, Tomatis L. Effects of long-term oral administration of styrene to mice and rats. Scand J Work Environ Health. 1978;4 Suppl 2:127-35.

noted that lower doses did not produce an increased incidence of tumors. The authors report this as "weak evidence of the carcinogenicity of styrene in one of the two strains of mice tested, when it is given at a high dose level" and the ROC considered it supportive evidence.

Other supportive evidence of carcinogenicity from animal studies included elevated mammary-gland tumors in female Sprague-Dawley® (SD) rats exposed to styrene-contaminated drinking water or by inhalation, although lung tumors were not observed, and an industry-sponsored study failed to find mammary-gland tumors in the same strain of rat. However, the induction of lung tumors in mice but not rats has been demonstrated for other carcinogenic epoxide-forming chemicals besides styrene, such as vinyl chloride, butadiene, and ethylene oxide (see ROC profiles for those chemicals), suggesting that this may be an expected outcome for cancer-causing chemicals related to styrene.

The overall evidence from animal studies was considered "sufficient' by the ROC, consistent with the previous IARC reviews.

Supporting data on mechanisms of carcinogenesis

The styrene industry-sponsored scientists concede that styrene causes lung tumors in mice, but because it does not produce lung tumors in rats the industry scientists argue that it would also not produce lung tumors in humans. Humans are like rats, but not like mice. The simplified version of the argument goes like this: In mice lungs Cyp2f2 is the predominant enzyme (protein) that catalyzes the conversion of styrene to cancer-causing styrene oxide. In human lungs, the equivalent enzyme, CYP2F1, is less efficient at catalyzing this reaction than mice, and therefore humans won't get lung cancer.[47] Rats are somewhere between humans and mice. However, this argument, while logical, is too linear to accurately capture the complexities of the real system.

One of the weaknesses in the industry argument is that it relies on observations from Cyp2f2-knockout mice to argue that the protein is essential for styrene metabolism. But in those KO mice the production of styrene oxide was reduced by half (in lung microsome preparations), but not eliminated, suggesting that other pathways are also significant contributors to the production of styrene oxide.

Another weakness is that in the lungs of humans at least a half-dozen proteins may metabolize styrene – CYP2A13, CYP2F1 (equivalent to mouse Cyp2f2 and rat CYP2F4), CYP1A2, CYP2C8, CYP2A6, and CYP2E1. And, CYP2E1 is expressed in human lymphocytes, where it may be active in converting styrene to styrene oxide in those cells. (ROC 2011) In human lungs different

[47] Cruzan G, Bus J, Hotchkiss J, Sura R, Moore C, Yost G, Banton M, Sarang S. Studies of Styrene, Styrene Oxide and 4-Hydroxystyrene Toxicity in CYP2F2 Knockout and CYP2F1 Humanized Mice Support Lack of Human Relevance for Mouse Lung Tumors. Regul Toxicol Pharmacol. 2013 Feb 27.
Cruzan G, Bus J, Hotchkiss J, Harkema J, Banton M, Sarang S. CYP2F2-generated metabolites, not styrene oxide, are a key event mediating the mode of action of styrene-induced mouse lung tumors. Regul Toxicol Pharmacol. 2012 Feb;62(1):214-20.

cytochromes may be active, they are distributed more widely than in rodent lungs, and polymorphisms may play a role in species and tissue differences not accounted for in the experimental data.

Industry also ignores possible genotoxic mechanisms of carcinogenicity, on the basis that the mouse lung tumors likely resulted from cell toxicity (cytotoxicity), not damage to DNA (genotoxicity).[48] However, independent experts have conclude that there is strong evidence for genotoxic effects of styrene, based on workplace epidemiology studies of high exposures (above 10 ppm).[49]

The industry discounts the fact that styrene oxide and styrene oxide-based DNA adducts, single-strand breaks, and chromosomal aberrations have been detected in the blood of styrene-exposed workers by referencing rodent studies, in vitro studies, and extrapolations without supporting data.[50] For example, Rhomberg et al notes that "although SO is directly genotoxic in vitro, oral administration of SO to mice and rats did not lead to systemic tumors…" but it did lead to tumors at the site of contact, the forestomach.[51] The authors emphasize that cell damage also occurred, and state that the observed tumors may have been formed from the cell damage and not from genotoxicity. Then the authors ask us to take a leap of faith, wrapping up the paragraph by stating that this proposed non-genotoxic mechanism may also explain the increased lung tumor incidence in mice after styrene exposure.[52] None of these untested hypotheses and faith-based assumptions poses a credible challenge to the observations in styrene-exposed workers of DNA damage and cancer.

Departure from scientific evidence should be based on observation, not speculation.

[48] Rhomberg LR, Goodman JE, Prueitt RL. The Weight of Evidence Does Not Support the Listing of Styrene as "Reasonably Anticipated to be a Human Carcinogen" in NTP's Twelfth Report on Carcinogens. Hum Ecol Risk Assess. 2013 Jan;19(1):4-27.

[49] Kolstad HA, Ebbehøj N, Bonde JP, Lynge E, Albin M. [Health effects following occupational styrene exposure in the reinforced plastics industry]. Ugeskr Laeger. 2012 Jan 30;174(5):267-70. Danish.

[50] Rhomberg LR, Goodman JE, Prueitt RL. The Weight of Evidence Does Not Support the Listing of Styrene as "Reasonably Anticipated to be a Human Carcinogen" in NTP's Twelfth Report on Carcinogens. Hum Ecol Risk Assess. 2013 Jan;19(1):4-27.

[51] Rhomberg LR, Goodman JE, Prueitt RL. The Weight of Evidence Does Not Support the Listing of Styrene as "Reasonably Anticipated to be a Human Carcinogen" in NTP's Twelfth Report on Carcinogens. Hum Ecol Risk Assess. 2013 Jan;19(1):4-27.

[52] Rhomberg LR, Goodman JE, Prueitt RL. The Weight of Evidence Does Not Support the Listing of Styrene as "Reasonably Anticipated to be a Human Carcinogen" in NTP's Twelfth Report on Carcinogens. Hum Ecol Risk Assess. 2013 Jan;19(1):4-27.

APPENDIX 2 – FORMALDEHYDE POLITICAL INTERFERENCE WITH SCIENTIFIC REVIEW

Formaldehyde is a high volume industrial chemical used primarily to manufacture resins and glues. More than 2 million workers are occupationally exposed in the U.S.[53] The general public is commonly exposed to formaldehyde indoors, where formaldehyde is released into the air from particleboard and plywood.[54] Formaldehyde is also a contaminant of concern outdoors, because it is emitted from vehicles and other sources of fuel combustion, although indoor air levels tend to be about 10-times higher than outdoor air levels.[55] There is no serious question that formaldehyde is dangerous. The chemical is recognized as a carcinogen by EPA, the International Agency on Research on Cancer (IARC, 2009) and the National Toxicology Program (NTP, 2012), among other authoritative bodies, and it can cause burning sensations in the eyes, nose, and throat, wheezing, nausea, and skin irritation. [56]

EPA has been trying to update its formaldehyde assessment, last revised in 1991, since 1998 but has repeatedly stalled and been stymied by industry, other federal agencies, and Congress. It was finally release for public comment June 2, 2010. [57] This assessment finds that there is sufficient evidence that formaldehyde causes cancers of the upper respiratory tracts, as well as leukemia and Hodgkin's lymphoma. The assessment also documents non-cancer health effects from formaldehyde inhalation, including irritation of the eyes, nose, and throat, neurological impairments, reproductive and developmental toxicity, and immune system toxicity.

EPA Integrated Risk Information System (IRIS) staff published its first formaldehyde risk assessment on the IRIS website in 1989, over 20 years ago. At that time a limit for oral exposures was identified, but not inhalation exposures.[58] Shortly after, in 1991, IRIS classified formaldehyde as a probable human carcinogen based on evidence in both humans (cancers of the respiratory tract) and animals (squamous cell carcinomas in rats, mice, hamsters, and monkeys). At that time, IRIS added a risk estimate for cancer from inhalation exposure. [59]

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[53] Zhang et al. 2009. Formaldehyde exposure and leukemia: A new meta-analysis and potential mechanisms. Mutation Research 681: 150-168.

[54] National Cancer Institute Factsheet. Formaldehyde and Cancer Risk. 11/20/2009. http://www.cancer.gov/cancertopics/factsheet/Risk/formaldehyde

[55] U.S. EPA. IRIS Toxicological Review of Formaldehyde-Inhalation Assessment (External Review Draft). U.S. Environmental Protection Agency, Washington, DC, EPA/635/R-10/002A, 2010. http://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=223614

[56] National Cancer Institute Factsheet. Formaldehyde and Cancer Risk. 11/20/2009. http://www.cancer.gov/cancertopics/factsheet/Risk/formaldehyde

[57] U.S. EPA. IRIS Toxicological Review of Formaldehyde-Inhalation Assessment (External Review Draft). U.S. Environmental Protection Agency, Washington, DC, EPA/635/R-10/002A, 2010. http://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=223614

[58] In 1990 EPA set an acceptable oral exposure limit (reference dose, RfD) of 0.2 mg/kg-day based reduced weight gain and cell pathology observed in a 2-year bioassay in rats.

[59] The 1991 updated IRIS assessment set an estimate of the unit risk of cancer from inhalation exposure at 1.3x10-5 per ug/m^3 based on limited evidence from nine human studies showing site-specific respiratory pre-cancer tissue, and long-term inhalation studies in rats and mice showing nasal cancers. EPA IRIS Formaldehyde Quickview. http://cfpub.epa.gov/ncea/iris/index.cfm?fuseaction=iris.showQuickView&substance_nmbr=0419#carc

In 1998, about a decade after it had first been posted, the IRIS staff began to reassess formaldehyde to update the science. Now, over two decades later, that reassessment has still not been finalized, despite the high health risks it poses, particularly for indoor air quality. [60]

About the same time, the formaldehyde industry developed a mathematical model for toxicity to challenge the exposure limit calculated by IRIS staff in 1991. The cancer risk estimates based upon the industry's model were thousands of times lower (weaker) than the estimate from IRIS staff.[61] At issue was whether or not formaldehyde was a multi-site carcinogen. Although the industry acknowledged the risk of cancers of the upper respiratory tract (nasopharyngeal) associated with formaldehyde, it continued its long-standing denial of risks to other sites, specifically denying bone and blood cancer (leukemia) risks. Therefore the industry model failed to account for the full spectrum of cancer endpoints, whereas the IRIS cancer risk estimate did so, and was therefore higher.

By using the industry model instead of IRIS values, in 2003 the EPA air office issued a proposed rule exempting dozens of plywood facilities from adopting pollution controls for formaldehyde.[62] The rule was adopted in 2004, despite criticism by the Government Accountability Office (GAO) and others. [63] [64] It was eventually overturned by an NRDC court challenge in 2007.[65]

Meanwhile, the science showing harm from formaldehyde just kept getting stronger. In 2003 the National Cancer Institute (NCI) published an update of an epidemiological study of 26 thousand industrial workers showing that workers with high peak and average exposures to formaldehyde have elevated risk levels for myeloid leukemia.[66] The next year, another government study, this time by National Institute of Occupational Safety and Health (NIOSH), reported that a study of over 11,000 garment workers showed an increased risk of leukemia

[60] Risk Policy Report, April 16, 2001.
http://www.insideepa.com/secure/docnum.asp?docnum=2001_3799&f=epa_2001.ask
[61] Risk Policy Report, January 1, 2003. http://www.insideepa.com/secure/docnum.asp?docnum=RISK-10-1-33&f=epa_2001.ask
[62] GAO, 2008. Chemical Assessments: EPAs new assessment process will further limit the productivity and credibility of its Integrated Risk Information System. Testimony before the Subcommittee on Investigations and Oversight, Committee on Science and Technology, House of Representatives. May 21, 2008.
http://s3.amazonaws.com/propublica/assets/formaldehyde/gao_epa_chem_assessments_080521.pdf
[63] The rule was proposed in 2003 and adopted in 2004.
http://www.ucsusa.org/scientific_integrity/abuses_of_science/plywood-plant-pollution.html
[64] GAO, 2008. Chemical Assessments: EPAs new assessment process will further limit the productivity and credibility of its Integrated Risk Information System. Testimony before the Subcommittee on Investigations and Oversight, Committee on Science and Technology, House of Representatives. May 21, 2008.
http://s3.amazonaws.com/propublica/assets/formaldehyde/gao_epa_chem_assessments_080521.pdf
[65] *NRDC v. EPA*, 489 F.3d 1364 (D.C. Cir. June 19, 2007)
[66] Hauptmann M, Lubin JH, Stewart PA, Hayes RB, Blair A. Mortality from lymphohematopoietic malignancies among workers in formaldehyde industries. *Journal of the National Cancer Institute* 2003; 95(21):1615–1623.

associated with long-term exposure.[67] A review of both studies in 2004 by the prestigious International Agency for Research on Cancer (IARC) convinced experts to upgrade the classification of formaldehyde from "probable carcinogen" to "known carcinogen."[68]

In response to the new science, in 2004 industry formed a new coalition called the Formaldehyde Council Inc. (FCI), self-described as representing the leading producers and users of formaldehyde in the U.S. Its website says it "was created principally to address the health effects of formaldehyde through the conduct of research and to communicate the results of the research to federal, state and international agencies".[69] Almost immediately after its formation, scientists sponsored by FCI published a re-analysis of the NCI study to specifically dispute the link between leukemia and formaldehyde.[70]

Later that same year, 2004, Senator James Inhofe demanded that EPA postpone the revisions of the formaldehyde risk assessment. EPA agreed to wait for another NCI study update. [71]

The next summer, 2005, Hurricanes Rita and Katrina devastated the Gulf Coast, triggering a need for temporary housing. The federal government, through FEMA, provided approximately 100,000 trailers to homeless residents in Louisiana and Mississippi. Residents soon begin complaining about respiratory symptoms that were subsequently linked to formaldehyde off-gassing inside the trailers at levels of formaldehyde were high enough to increase the risk of cancer and respiratory illness.[72]

In spring 2008 the GAO released its report, *Chemical Assessments: Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Integrated Risk Information System*, detailing a dismal backlog of unfinished chemical assessments, including formaldehyde.[73] GAO identified factors contributing to the delay, including interference by Senator Inhofe: "In the case of certain controversial chemical assessments, actions by congressional committees and individual members have led EPA to, for example, postpone completion of the IRIS assessment of formaldehyde for years until an update of an

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[67] Pinkerton LE, Hein MJ, Stayner LT. Mortality among a cohort of garment workers exposed to formaldehyde: An update. *Occupational Environmental Medicine* 2004; 61:193–200.

[68] International Agency for Research on Cancer (June 2004). *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 88 (2006): Formaldehyde, 2-Butoxyethanol and 1-tert-Butoxypropan-2-ol*. Retrieved May 4, 2009, from: http://monographs.iarc.fr/ENG/Monographs/vol88/index.php.

[69] Formaldehyde Council website. About FCI. Accessed June 3, 2010. http://www.formaldehyde.org/about/

[70] Marsh GM and Youk AO. Reevaluation of mortality risks from leukemia in the formaldehyde cohort study of the National Cancer Institute. Reg Toxicol Pharm 2004; 40:113-124

[71] Chemical Assessments: Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Integrated Risk Information System. GAO-08-440 March 7, 2008. http://www.gao.gov/products/GAO-08-440

[72] Joaquin Sapien. October 5, 2008. "Why CDC Responded with "Lack of Urgency" to Formaldehyde Warnings. ProPublica. http://www.propublica.org/article/formaldehyde

[73] *Chemical Assessments: Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Integrated Risk Information System*. GAO-08-440 March 7, 2008. http://www.gao.gov/products/GAO-08-440

epidemiological study that had just been released was completed." [74] GAO staff testified in Congress on the years of delay and interference with the IRIS program's attempts to complete its assessment of formaldehyde.[75]

In 2009 the long-awaited NCI study was released. Those federal experts concluded there is significant data linking formaldehyde exposure to leukemia in workers.[76] Workers with high exposures to formaldehyde were found to have a 2.8-fold greater risk of cancer than those with lower exposures. Just a few months later, researchers from NCI and U Cal Berkeley published a study of Chinese workers that found leukemia-specific chromosome changes, strengthening the evidence that formaldehyde can cause leukemia and undercutting the industry claim that NCI's study population was unique.[77]

In the fall of 2009 IARC and the National Toxicology Program (NTP) both conducted rigorous scientific reviews of all relevant data, and not only confirmed previous determinations that formaldehyde causes nasopharyngeal cancer in humans, but went further and linked formaldehyde to leukemia.[78] [79]

The same month that IARC experts concluded that formaldehyde is more carcinogenic than previously thought, Senator David Vitter placed a hold on the Obama Administration nominee to head up the EPA science office (Office of Research and Development), Yale Professor Paul Anastas, until EPA agreed to send its latest draft IRIS assessment to the National Academy of Sciences (NAS) for additional review. EPA objected strongly to this unnecessary delay.

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[74] Chemical Assessments: Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Integrated Risk Information System. GAO-08-440 March 7, 2008. http://www.gao.gov/products/GAO-08-440

[75] GAO, 2008. Chemical Assessments: EPAs new assessment process will further limit the productivity and credibility of its Integrated Risk Information System. Testimony before the Subcommittee on Investigations and Oversight, Committee on Science and Technology, House of Representatives. May 21, 2008. http://s3.amazonaws.com/propublica/assets/formaldehyde/gao_epa_chem_assessments_080521.pdf

[76] Beane Freeman L, Blair A, Lubin JH, et al. Mortality from lymphohematopoietic malignancies among workers in formaldehyde industries: The National Cancer Institute cohort. *Journal of the National Cancer Institute* 2009; 101(10):751–761.

[77] Zhang et al 2009. Meta-analysis of formaldehyde and hematologic cancers in humans. Mutation Research 681: 150-168.

[78] IARC Monographs. A review of human carcinogens - Part F: Chemical agents and related occupations. http://monographs.iarc.fr/ENG/Monographs/vol100fintro/100F-introduction.pdf

[79] RoC meeting results at: http://ntp.niehs.nih.gov/index.cfm?objectid=DFAFC5A1-F1F6-975E-766CD2956416305E The Expert Panel Report Part B (November, 2009) states, "There are four studies (Table 3) that played a key role in this evaluation of the association between formaldehyde exposure and leukemia: a study of mortality from lymphohematopoietic cancers among workers in the U.S. funeral industry (Hauptmann *et al.* 2009); a study of mortality from lymphohematopoietic cancers among U.S. industrial workers employed at 10 formaldehyde-producing or using facilities (the NCI industrial cohort; Beane Freeman *et al.* 2009); a study of British workers employed at six chemical factories (Coggon *et al.* 2003); and a study of workers employed at three facilities in the U.S. garment industry (Pinkerton *et al.* 2004). These four studies are analyses of mortality in populations occupationally exposed to formaldehyde. These studies were judged to be particularly informative because they are relatively large studies that have drawn internal contrasts between workers assessed as having different exposure levels." http://ntp.niehs.nih.gov/ntp/roc/twelfth/2009/November/FA_PartB.pdf

Ironically, Senator Vitter represents Louisiana where thousands of victims say they have suffered health problems from being housed in formaldehyde-contaminated trailers after Hurricane Katrina.[80] In a press release, the industry FCI thanked Sen. Vitter for his interference with the formaldehyde reassessment.[81]

In June 2010 IRIS staff issued in draft form the long-awaited reassessment of formaldehyde, for public comment and review by the NAS. [82] The draft assessment concluded that formaldehyde causes nasopharyngeal (respiratory tract) cancer and, for the first time, links formaldehyde to leukemia. [83] It estimated the cancer risks posed by a full lifetime inhalation exposure to average indoor air formaldehyde levels could be as high as 1 in 1,000 cancers above background, approximately 5-fold more carcinogenic than the 1991 risk estimate still on IRIS. It also linked chronic formaldehyde inhalation to non-cancer health impacts, including lung disease, asthma, reproductive and developmental abnormalities, and impaired immune function.

In April, 2011 the National Academies finalized its review of the EPA formaldehyde assessment.[84] The report confirmed EPA's determination that formaldehyde causes cancer in humans, but recommended that EPA re-write its report to more clearly communicate the scientific reasoning underpinning its assessment, to state its reasoning more concisely, and to separate out leukemia risks from lymphoma risks. Overall, the Academies supported EPA in developing a cancer risk estimate for leukemia, and urged EPA to finalize the assessment as soon as possible.

The 12th ROC was finalized in June, 2011, and included an addendum specifically addressing the National Academies review of EPA's formaldehyde assessment, pointing out that the ROC did not rely on the EPA assessment in any way, and that the Academies was never charged with conducting its own health assessment.[85] [86]

The EPA IRIS formaldehyde draft is now held up – again – with no clear date for it to be finalized.[87]

[80] Risk Policy Report, February 9, 2010. http://www.insideepa.com/secure/docnum.asp?docnum=RISK-17-6-2&f=epa_2001.ask
[81] Formaldehyde Council media release. Senator Vitter, EPA and the National Academy of Sciences. January, 2010. http://www.formaldehyde.org/blog/entry/senator_vitter_epa_and_the_national_academy_of_sciences
[82] Review of EPA's Draft IRIS Assessment of Formaldehyde. DELS-BEST-09-07. Project start date 1/19/2010. Project duration 14 months. http://www8.nationalacademies.org/cp/projectview.aspx?key=49207
[83] EPA timeline and docs here: http://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=223614
[84] http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=13142
[85] http://ntp.niehs.nih.gov/ntp/roc/twelfth/addendum.pdf
[86] http://ntp.niehs.nih.gov/?objectid=03C9AF75-E1BF-FF40-DBA9EC0928DF8B15
[87] http://cfpub.epa.gov/ncea/iristrac/index.cfm?fuseaction=viewChemical.showChemical&sw_id=1031