IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

STYRENE INFORMATION AND RESEARCH CENTER, INC., **801 North Quincy Street** **Arlington, VA 22203, and** **DART CONTAINER CORPORATION,** **50 Hogsback Road** **Mason, MI 48854,** **Plaintiffs,** **v.** **KATHLEEN SEBELIUS,** **Secretary,** **U.S. Department of Health and Human Services** **200 Independence Avenue, S.W.** **Washington, DC 20201, and** **UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES** **200 Independence Avenue, S.W.** **Washington, DC 20201,** **Defendants.**	)	**Civil Action No._____**

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

Plaintiffs Styrene Information and Research Center, Inc., on behalf of itself and its member companies, and Dart Container Corporation (collectively, "Plaintiffs"), by their undersigned counsel, for their complaint against Kathleen Sebelius and the United States Department of Health and Human Services ("HHS"), allege as follows:

NATURE OF THE CASE

1. This is an action for declaratory and injunctive relief to require HHS to withdraw the 12th Annual Report on Carcinogens ("RoC") as it relates to the chemical styrene, based on HHS' failure to comply with applicable law and its own procedures, that, in turn, makes the RoC listing of styrene fatally flawed because it is arbitrary, capricious, an abuse of discretion and not in accordance with the law. The RoC listing of styrene is contrary to the weight of scientific evidence and opinion and is based primarily on improper and unreviewed information and manipulation of data which further demonstrates that it is arbitrary, capricious, an abuse of discretion and not in accordance with law.

THE PARTIES

2. The Styrene Information and Research Center, Inc. ("SIRC") was formed in 1987 as the principal focal point for public information and research on styrene. SIRC is a non-profit organization consisting of voting member companies involved in the manufacturing or processing of styrene, and associate member companies that fabricate styrene-based products. Collectively, SIRC's membership represents approximately 95% of the North American styrene industry. SIRC serves as a liaison between industry, federal and state governments, and international agencies on health-related issues involving styrene. SIRC is headquartered in Arlington, Virginia. SIRC has been actively involved in the National Toxicology Program ("NTP") process for the 12th RoC through the submission of written comments and public testimony and through correspondence and other communications with NTP and HHS.

3. Plaintiff Dart Container Corporation ("Dart") is an international manufacturer of a broad range of quality single-use products for the foodservice, retail/consumer, and food

packaging industries and is the world's largest manufacturer of foam cups. Dart utilizes polystyrene, which is manufactured from styrene, in its products.

4. Defendant Kathleen Sebelius is the Secretary of HHS. Her office is located at 200 Independence Avenue, S.W., Washington, DC 20201. Secretary Sebelius is responsible for supervising the activities of HHS and is the person responsible for issuing the 12th RoC. She is being sued in her official capacity.

5. Defendant HHS is the federal agency charged with the administration of the 12th RoC and that issued the regulations, guidance documents, public notices and correspondence that are the subject of review in this matter.

JURISDICTION AND VENUE

6. This Court has subject matter jurisdiction over this matter pursuant to 28 U.S.C. § 1331 because the causes of action arise under the laws of the United States: 5 U.S.C. §§ 701-706, known commonly as the Administrative Procedure Act ("APA"); the Declaratory Judgment Act, 28 U.S.C. §§ 2201-2202; and the due process clause of the Fifth Amendment of the Constitution of the United States.

7. The Court has authority to grant declaratory and injunctive relief pursuant to 28 U.S.C. §§ 2201-02 and the provisions of the APA, 5 U.S.C. §§ 701-06.

8. Venue is appropriate in this judicial district pursuant to 28 U.S.C. § 1391(e)(1) because defendants Kathleen Sebelius and HHS reside in this district for venue purposes and because a substantial portion of the acts and omissions giving rise to this lawsuit occurred in this judicial district.

THE INFORMATION QUALITY ACT

9. The Information Quality Act ("IQA"), 44 U.S.C. § 3516 note (2000), and implementing guidelines issued by the Office of Management and Budget ("OMB"), *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies*, 67 Fed. Reg. 8452 (Feb. 22, 2002), the HHS, HHS, *Guidelines for Ensuring the Quality of Information Disseminated to the Public*[1], and the National Institutes of Health ("NIH"), NIH, *Guidelines for Ensuring the Quality of Information Disseminated to the Public*[2], apply to the 12th RoC because it is information disseminated by a federal agency. It must meet requirements of objectivity and utility. The IQA requires that influential scientific information disseminated by a government agency be of appropriate "quality," which encompasses utility, objectivity and integrity. The 12th RoC is subject to the most demanding requirements of OMB's, HHS's and NIH's IQA Guidelines because it is "influential scientific information" that "present[s] information on health effects." Among other things, NTP is required to incorporate a "high degree of transparency about the data and methods to facilitate the reproducibility of such information by qualified third parties." *See* OMB's Government-wide Data Quality Act Guidelines, 67 Fed. Reg. 8452 (Feb. 22, 2002).

THE FEDERAL ADVISORY COMMITTEE ACT

10. The Federal Advisory Committee Act ("FACA"), 5 U.S.C. App. 2, governs the behavior of federal advisory committees. FACA applies to groups that are "established or utilized . . . in the interest of obtaining advice or recommendation for . . . one or more agencies or officers of the Federal Government." *Id.* at § 3(2). FACA requires that the records, reports, transcripts, minutes, appendixes, working papers, drafts, studies, agenda, or other documents that

[1] Available at http://www.hhs.gov/infoquality/part1.html.

[2] Available at http://aspe.hhs.gov/infoquality/Guidelines/NIHinfo2.shtml.

were made available to or prepared for or by each advisory committee be available to the public. Additionally, detailed minutes of each meeting of each advisory committee must be kept that include a record of the persons present, a complete and accurate description of matters discussed and conclusions reached. FACA also requires that an advisory committee be "fairly balanced in terms of the points of view represented and the functions to be performed by the advisory committee."

FACTUAL BACKGROUND

Styrene

11. Styrene is a clear, colorless liquid that is a component of materials used to make thousands of everyday products for home, school, work and play. Styrene is used in a wide variety of everyday goods from food containers, utensils, furniture and packaging materials to cars, boats, computers, and video games. Derived from petroleum and natural gas by-products, styrene helps create thousands of products with a wide range of performance attributes—strength, flexibility, insulation and lightweight—representing a vital part of the U.S. economy and contributing to quality of life. The styrene used in these products is manufactured synthetically in petrochemical plants. However, styrene also occurs naturally in the environment and is present at low levels in common foods, such as coffee, strawberries, and cinnamon.

12. Styrene is approved by the United States Food and Drug Administration as a flavoring additive. *See* 21 C.F.R. § 172.515. Styrene is used as a flavoring additive in food such as baked goods, frozen dairy products, soft candy, and gelatins and puddings.

The Report on Carcinogens - Generally

13. The Report on Carcinogens ("RoC") is mandated by Congress which stipulated that the Secretary of HHS publish a biennial report that contains, in relevant part, a list of all substances (i) which either are known to be carcinogens in humans or may reasonably be anticipated to be human carcinogens and (ii) to which a significant number of persons residing in the United States are exposed. *See* 42 U.S.C. § 241(b)(4)(A).

14. Under the statutory scheme, substances that have only suggestive evidence of carcinogenicity should not be listed at all. NTP has not been directed to list "possible" or "suspected" carcinogens. *See id.* The mandate from Congress to NTP was clear on this point:

> [T]he 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 grounds for designating a substance as a putative carcinogen."

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 CONG. REC. H38657 (1978) (statement of Rep. Rogers).

15. HHS maintains that conclusions regarding carcinogenicity in humans or experimental animals in the RoC 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 is 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.[3]

16. The Secretary of HHS has delegated responsibility for preparing the RoC to NTP. *See e.g.*, 72 Fed. Reg. 18999 (Apr. 16, 2007).

17. NTP is located administratively at the National Institute of Environmental Health Sciences ("NIEHS") of NIH. The Director of NIEHS/NIH serves as NTP's director.

Current Classifications of Styrene by HHS and Other Governmental Agencies

18. The Agency for Toxic Substances and Disease Registry ("ATSDR") is an operating division of HHS. ATSDR is part of the Centers for Disease Control and Prevention ("CDC"), an agency of the Public Health Service, which, in turn, is an agency of HHS. The Director of the CDC is also the administrator of ATSDR.

19. According to its website, "ATSDR is directed by congressional mandate to perform specific functions concerning the effect on public health of hazardous substances in the environment. These functions include . . . health consultations concerning specific hazardous substances, health surveillance and registries, . . ., applied research in support of public health assessments, information development and dissemination, and education and training concerning hazardous substances." http://www.atsdr.cdc.gov/about/index.html. ATSDR ensures "that our research and our services are based on sound science and meet real public needs to achieve our public health goals." http://www.atsdr.cdc.gov/about/mission_vision_goals.html.

[3] *See* NTP "Listing Criteria," http://ntp.niehs.nih.gov/index.cfm?objectid=03C9CE38-E5CD-EE56-D21B94351DBC8FC3.

20. On or about November 30, 2010, ATSDR issued a Toxicological Profile For Styrene, a peer-reviewed document ("ATSDR Report"). *See* 75 Fed. Reg. 74,053 (Nov. 30, 2010); *see also*, http://www.atsdr.cdc.gov/ToxProfiles/TP.asp?id=421&tid=74#bookmark01 According to the ATSDR Report, the toxicological profile

> Succinctly characterizes the toxicologic and adverse health effects information for the hazardous substances described here. Each peer-reviewed profile identifies and reviews the key literature that describes a hazardous substance's toxicologic properties. Other pertinent literature is also presented, but is described in less detail than the key studies.

Id. at Foreward. According to ATSDR, the profile "reflects ATSDR's assessment of all relevant toxicologic testing and information that has been peer-reviewed." *Id.* The profile was reviewed by staffs of the CDC and other federal scientists. Finally, the profile was peer-reviewed by a nongovernmental panel and was made available for public review." *Id.*

21. ATSDR concluded that "[t]aken together, the animal and human data indicate that styrene may possibly be a weak human carcinogen." *Id.* at 133. This peer-reviewed finding by an HHS agency can, at most, be characterized as a possible carcinogen evaluation. As reflected in ATSDR's Cancer Policy Framework, a possible carcinogen classification does not support the inclusion of styrene in the RoC as reasonably anticipated to be a human carcinogen. *See* ATSDR Cancer Policy Framework, Appendix A (1993), available at http://www.atsdr.cdc.gov/cancer.html (website page reviewed and updated by ASTDR on June 25, 2001).

22. In 2002, the International Agency for Research on Cancer ("IARC"), part of the World Health Organization, evaluated the carcinogenicity of styrene. *See* IARC Monograph 82, http://monographs.iarc.fr/ENG/Monographs/vol82/index.php. Styrene was considered *possibly carcinogenic to humans* (Group 2B) out of four possible categories.[4] Again, HHS, through ATSDR,

[4] The four groups are identified in Exhibit 1, attached.

has demonstrated that this IARC classification would not result in the inclusion of styrene in the RoC. *See* ATSDR Cancer Policy Framework, Appendix A (1993), *supra.*

23. In June 2008, the United Kingdom published the draft European Union ("EU") Risk Assessment Report on Styrene ("RAR") and submitted it to the European Chemicals Agency ("ECHA"). The RAR was agreed to by the EU's Technical Committee for New and Existing Substances in 2008 and underwent independent peer review by the EU's Scientific Committee on Health and Environmental Risks.[5] The RAR found that:

> In relation to human studies, several cohort and case-control studies covering workers exposed to styrene are available. In large, well-conducted studies, cancer mortality was investigated in the GRP [glass-reinforced plastic] industry with relatively high exposure to styrene and no significant exposures to other chemicals. In these studies, and in studies in styrene production workers, there was no clear and consistent evidence for a causal link between specific cancer mortality and exposure to styrene. The increased risks for lymphatic and haematopoietic neoplasms observed in some of these studies are generally small, statistically unstable and often based on subgroup analyses. These findings are not very robust and the possibility that the observations are the results of chance, bias or confounding by other occupational exposures cannot be ruled out. In the styrene-butadiene rubber industry, several studies have pointed to an increased risk of cancer of the lymphatic and haematopoietic systems. However, detailed analysis of these data, together with the general toxicological picture for styrene and butadiene (see butadiene EU RAR), suggests that where increases are due to occupational exposure, it is butadiene, not styrene, that is the more likely causative agent. In conclusion, based on human studies, there is no clear and consistent evidence for a causal link between specific cancer mortality and exposure to styrene.
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[5] The RAR was never formally "finalized" because the legislation under which it was published was repealed and replaced by REACH (Registration, Evaluation and Authorisation of Chemicals). However, an Annex XV Restriction document was developed for styrene under REACH. The Annex XV report does not re-evaluate any conclusions about the hazardous properties of styrene set out in the RAR. The Annex XV report stated that it "will not revisit any other conclusions made in the RAR."

> There is no evidence from extensive epidemiological investigations that long term exposure to styrene has produced lung damage or lung cancer in humans. Hence, overall, the weight of evidence appears to indicate that the consequences of long term exposure to styrene in mouse lung cannot be replicated in the human situation at relevant levels of exposure.

Id. at 271-72. These findings would not result in the inclusion of styrene in the RoC.

24. The scientific literature upon which these evaluations were based is essentially the same literature reviewed by NTP in conducting its assessment of styrene.

The RoC Process at NTP

25. Under NTP's procedural framework, the preparation of the RoC consists of the following steps:

a. The nomination of substances by NTP for review, public comment, and finalization of the list of substances for review.

b. The publication of a draft background document for each substance followed by an opportunity for public comment.

c. Review of the draft background document by an expert panel.

d. Publication of a panel report, which contains both the panel's views on the draft background document together with a listing recommendation.

e. Opportunity for comment on the expert panel report.

f. Finalization of the draft background document based on the expert panel's report and any public comments.

g. Preparation and opportunity for comment on a draft substance profile that is, in essence, a chapter in the RoC containing an abbreviated discussion of the substance's toxicology and listing status.

h. Preparation of the draft Report on Carcinogen by NTP, and

i. Final approval by the Secretary of HHS.[6]

[6] *See* http://ntp.niehs.nih.gov/images/12thProcess-large.jpg.

26. It is NTP's policy that the scientific evidence cited in support of the NTP's policy decision must come from publicly available, peer-reviewed sources. According to NTP's Background Document on Styrene, the information in a Background Document's sections discussing to Human Cancer Studies, Studies of Cancers in Experimental Animals and Other Relevant Data "must come from publicly available, peer-reviewed sources. . . . For each study cited in the background document from the peer-reviewed literature, information on funding sources (if available) and the authors' affiliations are provided in the reference section. Final Report on Carcinogens Background Document for Styrene ("Final Background Document"), at i (Sept. 29, 2008), *available at* http://ntp.niehs.nih.gov/files/Styrene_Background_Document_%289-29-08%29F%5B1%5D.pdf.

27. Peer review of "influential scientific information" that is disseminated by the federal government is required under the OMB's "Final Information Quality Bulletin for Peer Review."[7] The more important scientific assessments disseminated by the federal government require "more intensive" peer review. *Id.* at 2.

28. According to OMB, peer review 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.
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> 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 the methods for the hypotheses being tested, the extent to which the

[7] *See* http://www.whitehouse.gov/sites/default/files/omb/memoranda/fy2005/m05-03.pdf.

> conclusions follow from the analysis, and the strengths and limitations of the overall product.

Id. at p. 3-4. Nowhere does OMB include the re-analysis of data as part of the peer review process.

Development of the 12th ROC Relating to Styrene

29. On May 19, 2004, NTP announced the nomination of styrene for consideration for the 12th RoC with a 60-day comment period. 69 Fed. Reg. 28940 (May 19, 2004); *see also*, 69 Fed. Reg. 62276 (Oct. 25, 2004).

30. On October 18, 2005, NTP solicited public comments on an updated list of nominations proposed for review in the 12th RoC, including styrene. 70 Fed. Reg. 60548-53 (Oct. 18, 2005).

31. On April 16, 2007, NTP announced in the Federal Register that it had added two "important elements in the RoC review process." For the 12th RoC, the review process would include: "(1) the public peer review of draft background documents by ad hoc scientific expert panels and (2) the public peer review of draft substance profiles by the NTP Board of Scientific Counselors." 72 Fed. Reg. 18999 (Apr. 16, 2007). NTP further stated that it would prepare a response to public comments for the 12th RoC on a "trial basis." *Id.*

32. On May 9, 2007, NTP published a request for nominations of Scientific Experts ("Expert Panel") to "serve on expert panels" as part of the review process for the 12th RoC identified in its earlier Federal Register notice. 72 Fed. Reg. 26394 (May 9, 2007). As noted by NTP, "[t]he NTP will convene an ad hoc expert panel to peer review the draft background document at a public meeting and make a recommendation to the NTP on the candidate substance's listing status for the RoC." *Id.*

33. On May 20, 2008, NTP announced the availability of the draft Background Document for Styrene. 73 Fed. Reg. 29,139 (May 20, 2008). NTP solicited public comments on the draft by July 7. NTP further announced that the Styrene Expert Panel would be meeting on July 21-22, 2008.

34. In the Draft Background document, NTP concluded that workers in the reinforced plastics industry were the most relevant study population for epidemiology studies of styrene exposure rather than workers in the synthetic rubber industry. Draft Background Document at 133 (May 22, 2008).

35. The Draft Background Document did not include consideration of a peer-reviewed paper by Dr. Delzell and colleagues, "An Updated Study of Mortality Among North American Synthetic Rubber Industry Workers," *Health Effects Institute Research Report Number 132*, (2006), relating to workers in the synthetic rubber industry. According to the study, workers in the synthetic rubber industry were exposed to three significant chemicals: 1,3-butadiene ("BD"), styrene and dimethyldithiocarbamate ("DMDTC"). After controlling for effects of BD, the authors found no consistent exposure-response relation between styrene and all leukemias, chronic myelogenous leukemia, or chronic lymphocytic leukemia (CLL). According to the authors, the data from this study indicate that employment in the synthetic rubber industry is related causally to leukemia. The authors further found uncertainty remains about the specific agent or agents responsible for that association. According to the authors, the carcinogenic mechanisms through which BD, styrene, or DMDTC could cause leukemia in humans have not been established and epidemiologic support for a leukemogenic role is limited for these agents. While the study reported an association between styrene exposure and non-Hodgkin Lymphoma

(NHL), relative risks were not statistically different from unexposed persons. Dr. Delzell has characterized the results for styrene and NHL as "unconvincing."[8]

36. According to a Commentary on the Delzell paper published by the Heath Effects Institute Health Review Committee, "the current analysis does not provide evidence that styrene is a leukemogen which is consistent with the results of another study of styrene-exposed workers in the boatbuilding industry. (Ruder et al 2004)." *Id.* at 70.

37. On July 21-22, 2008, the Styrene Expert Panel met for the purpose of conducting a "peer review" of the Draft Background Document on Styrene and to recommend whether styrene should be included in the 12th RoC, and, if so, at what level.

38. The Expert Panel did not conduct a peer-review and did not act consistent with the OMB's "Final Information Quality Bulletin for Peer Review" (Dec. 16, 2004). Rather, the Expert Panel rejected conclusions of the NTP Draft Background Document, developed "new" information, and invented its own analysis. This included a new statistical analysis of Dr. Delzell's 2006 paper, a study not considered in the Draft Background Document before the Expert Panel. The Expert Panel also modified a 1979 NCI study by substituting new data from a different set of animals for a control group and then creating another new analysis. Based on these new analyses, the Expert Panel recommended that styrene be listed in the 12th RoC as "reasonably anticipated to be a human carcinogen" based on "limited" evidence in human data and "sufficient" evidence in animal data.

39. Participation in the Expert Panel by Dr. Genevieve Matanoski presented an appearance of both bias and conflict of interest. The appearance of bias arises from being asked to peer review the significance of her own work. *See, e.g.*, Draft Background Document at pages

[8] *See* ¶ 52 and n.9, *infra.*

94-96 and 104. The conflict of interest arose because Dr. Matanoski was critical of conclusions reached in a study by Dr. Delzell, et al. (2006). Dr. Delzell's study was a follow-up on an earlier 1987 study that Dr. Matanoski initially conducted but for which she was not hired to update. Dr. Matanoski explained her re-analysis of Dr. Delzell's data when she stated: "[i]f you recombine the groups as we've done in looking at the tables we've recombined these that say have five groups into three groups you find a nice monotonic linear exposure. So it has to do with grouping to some extent." The Expert Panel then concluded, based on a facially biased and conflicted review using newly derived data that the re-interpreted Delzell paper supported an association between non-Hodgkin Lymphoma (NHL) and styrene contrary to the peer-reviewed conclusion of Dr. Delzell and her colleagues. This relationship between styrene and NHL was subsequently incorporated by HHS in the Substance Profile for styrene.[9]

40. The new analysis of Dr. Delzell's study is undocumented. As Samuel Wilson, Acting Director of NTP stated in a letter to John Tickle dated October 1, 2008, (page 2, paragraph 3): "No new analyses of the results from any epidemiology studies were presented as part of this process." This is in violation of the IQA: nothing showing the recombined groups appears in either the Background Document or the Expert Panel materials and the analysis was not produced in response to a request submitted by SIRC under the Freedom of Information Act, 5 U.S.C. § 552. HHS NIH NIEHS FOI Case No. 35461.

41. The newly created analysis developed by the Expert Panel did not constitute peer-review of the NTP Draft. Furthermore, the reanalysis itself has not been peer reviewed. The Expert Panel cannot peer review its own work and no other expert panel was convened to conduct that function.

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[9] *See* ¶ 54, *infra*.

42. The new analysis by the Expert Panel is not "from the peer-reviewed literature" as required by NTP policy and practice.

43. The Expert Panel also modified a 1979 National Cancer Institute animal study titled "Bioassay of Styrene for Possible Carcinogenicity" (*Technical Report Series No. 185*, 1979) ("1979 NCI Study"), and, using new data outside of the 1979 NCI Study, reached conclusions different from the authors of that paper.

44. In 1979 NCI Study orally dosed Fischer 344 rats and B6C3F1 mice with styrene. *Id.* at vii, 8-9. NCI stated in the report's summary that "no convincing evidence for the carcinogenicity of the compound was obtained in Fischer 344 rats or B6C3F1 mice of either sex." *Id.* at viii. According to the summary,

> In male mice, there was a significant positive association between styrene dosage and the incidences of a combination of adenomas and carcinomas of the lung. This finding was supported by the high dose to control Fisher exact comparison. However, the variation of the incidence of these neoplasms in historical control male mice at this laboratory does not permit a firm conclusion of carcinogenicity. There was no significant difference between tumor incidence at any other site in male mice, or at any site in rats or female mice, when dosed groups were compared to vehicle controls.

Id. at vii.

45. The Draft Background Document did not question NCI's findings. Draft NTP Report at 171.

46. The Expert Panel, however, substituted a different set of data for animal controls for those originally used in the NCI study and, based on this new and non-peer reviewed approach, the Expert Panel concluded that there was "sufficient evidence" of a link between styrene and tumors in the mice. Styrene Expert Panel Report, Part B at 3.

47. HHS's ATSDR report did not include any such re-examination and neither did the EU Draft Report or IARC.

48. The new data and statistical analysis created by the Expert Panel did not constitute peer-review of the NTP Draft. Furthermore, the new analysis has not been peer reviewed. The Expert Panel cannot peer review its own work and no other expert panel was convened to conduct that function.

49. The new data and statistical analysis created by the Expert Panel did not constitute a "publicly available peer reviewed" source as required by NTP policy and procedure. As NTP Director Linda Birnbaum stated in a September 9, 2010, letter to Congressman Rick Boucher, the NTP process seeks to "assess the body of scientific evidence on styrene" and "must come from publicly available, peer-reviewed sources."

50. On September 8, 2008, NTP "invited" public comment on the recommendation from the Expert Panel "on the listing status for styrene in the 12th RoC and the scientific justification for the recommendation." 73 Fed. Reg. 52059-60 (Sept. 8, 2008). According to the notice, the Expert Panel Report (Part B) would be available for public comment on September 3, 2008. *Id.* Comments were to be submitted by October 23, 2008.

51. Both Part A and Part B of the Expert Panel report were signed and finalized on August 26, 2008. Further, on September 29, 2008, before the close of the comment period on the Expert Panel Report recommendations, NTP finalized the Draft Background Document and published its Final Background Document. *Available at* http://ntp.niehs.nih.gov/files/Styrene_Background_Document_(9-29-08)F[1].pdf. According to the Final Background Document, the previous Draft Background Document was "finalized based on the peer-review recommendations of the expert panel and public comments received

on the draft document." Final Background Document at i. The Final Background Document relied upon the Draft Background Document. NTP's finalization of the Background Document during the comment period was arbitrary, capricious, and contrary to law.

52. On October 10, 2008, Dr. Delzell submitted her Comments on the RoC Background Document for Styrene and Related Documents to SIRC, which, in turn, submitted them to NTP during the previously announced comment period. Dr. Delzell disagreed with the Expert Panel's re-analysis of her peer-reviewed paper and explained that the original conclusions reached by the study authors, including herself, were correct.[10]

53. According to the NTP process, after the Background Document is completed, NTP drafts a Substance Profile for each substance. The Substance Profiles are short documents setting out NTP's classification of the substance and information about Carcinogenicity, Properties, Use, Production, Exposure, Regulations and Guidelines. The compiled Substance Profiles constitute the RoC.

54. On December 22, 2008, NTP announced the availability of the draft Substance Profile for styrene and that the NTP Board of Scientific Counselors ("NTP BSC") would be meeting on February 24, 2009. 73 Fed. Reg. 78364-5 (Dec. 22, 2008). According to the announcement, the NTP BSC is a federally-chartered, external advisory group that provides primary scientific oversight to NTP and evaluates the scientific merit of NTP's intramural and collaborative programs. *Id.*

55. The NTP BSC was told by NTP to "[d]etermine whether the scientific information cited in the draft substance profile for a candidate substance is technically correct,

[10] Dr. Delzell's comments can be found as "attachment a" to the October 23, 2008, submittal by Jack Snyder available at http://ntp.niehs.nih.gov/index.cfm?objectid=20A477F2-F1F6-975E-7472FC6B0DA56D9C#styrene

clearly stated, and supports the NTP's preliminary policy decision regarding its listing in the RoC." The NTP BSC was not asked to comment on NTP's decision relating to the classification of styrene. Summary Minutes of February 24, 2009, NTP Board of Scientific Counselors at 6. The NTP BSC was not asked to peer-review the Expert Panels' analysis of either the Delzell paper or the reanalysis of the 1979 NCI Report.

56. NTP did not adhere to Congressional direction or its own stated process in preparing the RoC by failing to weigh all relevant information for and against listing. At the June 21, 2010, meeting of the NTP BSC called to review several draft profiles for the RoC, Dr. Gloria Jahnke of NIEHS/NTP stated that NTP had not included a particular relevant study because "I'm not recording negative data here; I am recording data that supports our call. So that's why you didn't see it."[11]

57. At the NTP BSC meeting on February 24, 2009, at which styrene was considered, Dr. Mary Wolfe gave an overview of the RoC process before the NTP BSC turned to the individual draft substance profiles, including styrene. Dr. Wolfe, referring to a Power Point slide, stated:

> Here I show you the criteria they've [Expert Panel] used to evaluate the body of science on a substance and determine whether or not to list it and if they decide to list it whether we would list it as a known human carcinogen or a reasonably anticipated human carcinogen, or if the evidence is not sufficient we would not list. Each listing determination is based on the *strength of the evidence*. There's standards that the body of scientific evidence must meet to be put into the categories. In addition, conclusions regarding the carcinogenicity are based on scientific judgment with consideration given to all relevant information.

[11] Meeting materials are available at http://ntp.niehs.nih.gov/?objectid=720164F2-BDB7-CEBA-F5C6A2E21851F0C4&#20090224. NTP makes recordings of the meeting available to the public and this statement was transcribed from the NTP recording.

(emphasis added). In fact, the phrase "strength of the evidence" appeared in the PowerPoint slide from which Dr. Wolfe was speaking at the time.

58. In scientific terms, a "strength of evidence" review only considers the data supporting a carcinogen classification, not the contrary data. In contrast, a "weight of evidence" review considers and balances all the available data. Thus, while NTP may state that it considers all relevant information, relevant is defined as only that data supporting a listing.

59. The actions of the NTP staff in conducting only a "strength of evidence" review, and the NTP BSC's doing the same, is contrary to the language of the authorizing statute as well as NTP's own pledge that it will make listing determinations "with consideration given to all relevant information." Therefore, NTP's actions were arbitrary and capricious and contrary to law.

60. Although certain members of the NTP BSC raised questions about the draft Substance Profile for Styrene, the Board took no vote and issued no report documenting any review of the Draft Substance Profile. The only documentation of the BSC's "peer review" is the minutes of its public meeting.

61. According to the NTP schematic of the RoC process, after the peer review of the Draft Substance Profiles, NTP prepares a draft RoC. The draft RoC is then submitted first to the Director, NTP and then to the Secretary, HHS to transmit to Congress and the public. *See* http://ntp.niehs.nih.gov/images/12thProcess-large.jpg.

Relevant Published Research since the Review of the Draft Substance Profile

62. On October 22, 2009, SIRC provided NTP with a copy of a paper titled "Mouse specific lung tumors from CYP2F2-mediated cytotoxic metabolism: An endpoint/toxic response where data from multiple chemicals converge to support a mode of action" that had been

published in *Regulatory Toxicology & Pharmacology*, Vol. 55, Pp. 205-218 (Nov. 2009), a peer-reviewed journal. The authors document the extensive evidence for styrene's non-genotoxic mode of action in causing lung tumors in mice thereby calling into question the genotoxicologic information relied upon by the Expert Panel to support its recommendation.

63. SIRC was informed by the Director of NTP that NTP would consider any peer-reviewed paper published prior to NTP's transmittal of the Draft 12th RoC to the Secretary of HHS. Linda Birnbaum, NTP, letter of July 2, 2009, to Jack Snyder, SIRC.

64. In November 2009, Boffetta, *et al.*, published a paper titled Epidemiologic Studies of Styrene and Cancer: A Review of the Literature in the *Journal of Occupational & Environmental Medicine*, a peer-reviewed journal.[12] The authors stated that they "found no consistent increased risk of any cancer among workers exposed to styrene" and concluded that "the available epidemiologic evidence does not support a causal relationship between styrene exposure and any type of human cancer." A copy of this paper was provided to NTP.

SIRC's Pending Information Quality Act Request for Correction

65. On October 26, 2009, SIRC submitted a Request for Correction under the Information Quality Act to NIH seeking corrections to the Final Background Document for Styrene. This 100-page document contained: (a) detailed descriptions of the portions of the Background Document that require correction, (b) the specific reasons why those portions do

[12] The authors were Paoloa Boffetta, MD, MPH (International Agency for Research on Cancer, Lyon, France; Vanderbilt University, Nashville, Tennessee); Hans Olov Adami, MD, PhD(Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts); Philip Cole, MD, DrPH (School of Public Health, University of Alabama, Birmingham, Alabama); Dimitrious Trichopoulos, MD, PhD (Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts); and Jack Mandel, PhD, MPH.(Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario). While this panel's review was funded by SIRC, SIRC completely distanced itself from the development, conduct, and conclusions of the Panel and saw the conclusions for the first time on the same day as did NTP.

not comply with IQA requirements, (c) suggested recommendations for revising the Background Document, and (d) an explanation of how the Background Document affected and will affect SIRC and its members. Despite its stated policy of responding to IQA correction requests in 60 days, NTP did not respond until December 23, 2010.

66. Although NTP recognized the need to make roughly a dozen corrections to the Background Document, and to provide some additional clarifications, it responded to the majority of SIRC's comments with formulaic statements to the effect that it had followed its procedures and thus the Background Document must be correct. NTP's Response reflected a fundamental misunderstanding of the objectivity criterion under the IQA, as demonstrated in SIRC's Information Quality Act Appeal of February 11, 2011, which is pending. 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. NTP failed to respond to the substantive scientific issues raised by SIRC, and NTP's failure was arbitrary, capricious and contrary to law.

The Impact of the Report – Triggering Other Regulatory Requirements

67. NTP acknowledges that the listing of a substance in the RoC may prompt regulatory agencies to consider limiting exposures or uses of a substance. Examples of such actions noted by NTP would include the following:

a. The OSHA Hazard communication standard states that "Chemical manufacturers and importers shall evaluate chemicals produced in their workplaces or imported by them to determine if they are hazardous. . . and that

chemical manufacturers, importers and employers evaluating chemicals shall treat the NTP Annual RoC as a source establishing that a chemical is a carcinogen or potential carcinogen for hazard communication purposes." Written hazard communications required of employers for carcinogens include labels and other forms of warning, material safety data sheets, and employee information and training. In particular, OSHA's 1998 Directive entitled "Inspection Procedures for the Hazard Communication Standard" would likely require changes to product container labels if NTP designates styrene as reasonably anticipated to be a human carcinogen.

b. California's Safe Drinking Water and Toxic Enforcement Act of 1986 [citation], also known as Proposition 65, requires "clear and reasonable warnings" for "knowing and intentional exposures" to chemicals that have been placed on the Proposition 65 list of substances known to cause cancer or reproductive toxicity. The NTP has been designated as authoritative in the area of carcinogenicity, and, chemicals identified in the RoC may be placed on the Proposition 65 list and influence the labeling of certain products containing such substances nationwide.

Questions and Answers about the RoC, "What does a listing in the RoC mean?," http://ntp.niehs.nih.gov/index.cfm?objectid=03CA6383-9766-1F64-6637241FE0114FE9.

68. In February 2010, the Office of Environmental Health Hazard Assessment, California Environmental Protection Agency published its Draft Public Health Goal for Styrene in Drinking Water. In the summary of that publication, OEHHA cited, with approval, the

recommendation of the "NTP expert panel," showing that NTP's actions are already influencing the decision making of other governmental agencies.

69. On information and belief, the draft 12th RoC has been transmitted to Defendant Sebelius and was signed on June 10, 2011.

FIRST CLAIM FOR RELIEF

70. Plaintiffs incorporate Paragraphs 1- 63 as if fully set forth herein.

71. NTP's failure to follow its own procedures, announced in the Federal Register, violates the Administrative Procedure Act.

SECOND CLAIM FOR RELIEF

72. Plaintiffs incorporate Paragraphs 1-63 as if fully set forth herein.

73. HHS's actions in creating and reviewing the 12th RoC have contravened the Public Health Service Act, and thus are not in accordance with law.

THIRD CLAIM FOR RELIEF

74. Plaintiffs incorporate Paragraphs 1-67 as if fully set forth herein.

75. HHS's actions in creating and reviewing the 12th RoC have been arbitrary and capricious, an abuse of discretion and not in accordance with law.

FOURTH CLAIM FOR RELIEF

76. Plaintiffs incorporate Paragraphs 1-63 as if fully set forth herein.

77. HHS's actions in extending for over a year the deadline for response to SIRC's IQA correction constitutes a constructive denial of that request, in violation of the IQA.

RELIEF REQUESTED

WHEREFORE, Plaintiffs demand judgment against Defendants Kathleen Sebelius and HHS as follows:

1. DECLARING that HHS and its Secretary have not complied with their own policies and procedures in the preparation of the 12th RoC as it relates to styrene;

2. DECLARING that the decision to include styrene in the 12th RoC is arbitrary, capricious, an abuse of discretion and not in accordance with law;

3. PRELIMINARILY, AND PERMANENTLY, ENJOINING Defendants from including styrene in the 12th RoC; and

4. GRANTING such other and further relief as this Court deems appropriate, including but not limited to reasonable attorneys' fees.

Dated: June 10, 2011

Respectfully submitted,

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