IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

STYRENE INFORMATION AND RESEARCH CENTER, INC., *et al.*,	)	
Plaintiffs,	)	
v.	)	**Civil Action No. 1:11-cv-01079-RBW**
KATHLEEN SEBELIUS, *et al.*,	)	
Defendants.	)	

MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT OF PLAINTIFFS' MOTION FOR A PRELIMINARY INJUNCTION

Pursuant to Federal Rule of Civil Procedure 65(a), Plaintiffs Styrene Information and Research Center ("SIRC") and Dart Container Corporation, by their undersigned counsel, submit this memorandum of points and authorities in support of their Motion for a Preliminary Injunction.

PRELIMINARY STATEMENT

The Report on Carcinogens ("RoC") is mandated by Congress. 42 U.S.C. § 241(b)(4)(A). According to the statute, the Secretary of HHS shall publish a biennial report that contains, in relevant part, "a list of all substances (i) which either are known to be carcinogens or may reasonably be anticipated to be carcinogens and (ii) to which a significant number of persons residing in the United States are exposed." *Id.* Under the statutory scheme, substances that have only suggestive evidence of carcinogenicity should not be listed at all, that is, HHS has not been directed to list "possible" or "suspected" carcinogens.

Defendant United States Department of Health and Human Services ("HHS"), through its National Toxicology Program ("NTP"), has identified the chemical styrene as "reasonably anticipated to be a human carcinogen" in its Report on Carcinogens, Twelfth Edition (2011) ("RoC"), based on a process that violated its statutory authority, procedures and policies, and inappropriately and illegally relied on the creation of *ad hoc* science.[1] Plaintiffs will be irreparably harmed if HHS' characterization of styrene on the RoC is allowed to stand because products made with styrene will face prompt and extensive deselection in the market. Because HHS has acted illegally it must be ordered to withdraw from publication the RoC with regard to styrene.

HHS is authorized to list substances in the RoC when it concludes that they are known or reasonably anticipated to be a human carcinogen, but evidence regarding styrene does not meet these criteria. This is reflected in a conclusion recently reached by HHS' Agency for Toxic Substances and Disease Registry ("ATSDR") and two international bodies. Indeed, no other governmental organization has reached the conclusion reached by NTP, despite relying on essentially the same body of scientific work. These differing conclusions are not merely a matter of scientific perspective or interpretation; they embody the procedural and policy errors in HHS' approach to its review of styrene.

HHS adopted procedures and policies requiring that decisions to include substances in the RoC be based on publicly-available and peer-reviewed scientific papers. "Peer review is one of the important procedures used to ensure that the quality of published information meets the

[1] The Secretary of HHS has delegated to NTP responsibility for preparing the RoC. RoC at 4. NTP is housed within the National Institute of Environmental Health Sciences ("NIEHS") at the National Institutes of Health ("NIH"). The Director of NIEHS/NIH serves as the director of NTP. *See* http://ntp.niehs.nih.gov/?objectid=720163E9-BDB7-CEBA-FB0157221EB4375F.

standards of the scientific and technical community. It is a form of deliberation involving an exchange of judgments about the appropriateness of methods and the strength of the author's inferences." Office of Management and Budget, Final Information Quality Bulletin for Peer Review, 70 Fed. Reg. 2664, 2665 (Jan. 14, 2005). HHS references this OMB Bulletin in the RoC. RoC at 7, *available at* http://ntp.niehs.nih.gov/ntp/roc/twelfth/roc12.pdf.

HHS has admitted to relying on *ad hoc* reanalyses of two papers when such reanalyses had been neither published nor peer-reviewed. In one instance, in an attempt to demonstrate a link between styrene and cancer in the test animals from a 1979 National Cancer Institute ("NCI") study ("1979 NCI Study"), HHS simply substituted data from a different laboratory's set of control animals in disregard of the conclusions of both the study authors and the peer reviewers of the original study, and despite the fact that original 1979 NCI Study conclusions had been accepted for 30 years without challenge.

Second, NTP reanalyzed the data from a published study on workers in the rubber industry to reach a conclusion of a potential link between human exposure to styrene and cancer although no such conclusion was reached by the study authors or original peer reviewers of that study. Indeed, the study's lead author objected to NTP's reanalysis and conclusions in a written submission to HHS.

Third, despite NTP's interpretation of its statutory mandate as requiring it to rely on "all relevant evidence," NTP has consistently identified, and relied only upon, information "that supports the listing." It was only through these *ad hoc* creations and one-sided interpretations that NTP could justify reaching a conclusion on the carcinogenicity of styrene that is different from the conclusion reached in November 2010 by ATSDR. NTP's failure to follow its own

procedures is arbitrary and capricious, and its decision to list styrene on the RoC is an *ultra vires* act that must be enjoined.

HHS claims that the RoC complies with the Information Quality Act, 44 U.S.C. § 3516 note, because it "was prepared following procedures that maximized the quality, objectivity, utility, and integrity of the information contained in the report." RoC at 7. But the arbitrary, capricious and contrary to law nature of HHS' action fundamentally is demonstrated by its disregard for the twin standards of objectivity and utility by generating a document that does not rely on the best available science, presents an inaccurate and unreliable characterization of styrene's carcinogenic potential, and fails to document or properly publish its new studies. HHS also violated the IQA's standard of utility by publishing a document that deprives the public of making an informed judgment about the carcinogenicity of styrene.

If HHS is not enjoined from publishing the styrene provisions of the RoC, Plaintiffs will be irreparably harmed by the adverse impact to the styrene industry caused by the chemical's inclusion on the RoC for the first time that improperly identifies styrene as reasonably anticipated to be a human carcinogen. This will lead to swift deselection of products made from styrene. This deselection is expressly encouraged by HHS when it states in the RoC that "[i]t is reasonable and prudent to accept that *reducing exposure for any reason, particularly to substances shown to be carcinogenic* in experimental animals, will decrease the incidence of cancer in humans." RoC at 6 (emphasis added). HHS' numerous violations of the law have resulted in a flawed conclusion about the carcinogenicity of styrene and injunctive relief is demonstrably warranted.

FACTUAL BACKGROUND

I. STYRENE AND RELATED PRODUCTS

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. *See* RoC at 387; Declaration of Michael Levy ("Levy Declaration") at ¶ 4, attached hereto as Exhibit 1; Declaration of John Schweitzer ("Schweitzer Declaration") at ¶ 3, attached hereto as Exhibit 2. Styrene is used in a wide variety of everyday goods, including foodservice containers, agricultural shipping and storage containers, bicycle helmets, refrigerators, microwave ovens, computers, televisions, trucks, cars, boats and carpets and other home furniture. RoC at 387; Levy Declaration, Exhibit 1, at ¶ 4. Derived from petroleum and natural gas by-products, styrene helps create products that are strong, lightweight, corrosion resistant, flexible and easy to clean. Schweitzer Declaration, Exhibit 3, at ¶ 2. 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 strawberries, beef and spices such as cinnamon, as well as being naturally produced in processing foods, such as wine, cheese and roasted coffee. D.H. Steel, *et al.*, "Determination of styrene in selected foods," J. Agric. Food Chem. 42:1661-65 (1994); R.R. Miller, *et al.*, "Styrene production, use and human exposure," Crit. Rev. Toxicol. 24 (suppl. 1):S1-S10 (1994); RoC at 387.

Styrene is a $28-billion dollar industry, comprising hundreds of companies with thousands of facilities throughout the country. Declaration of John O. Snyder ("Snyder Declaration") at ¶ 8, attached hereto as Exhibit 3. The industry produces nearly 12 billion pounds of styrene annually. RoC at 387. Nearly 450,000 workers throughout the country

depend on the styrenics industry for their livelihood. Snyder Declaration, Exhibit 3, at ¶ 8. This includes 128,000 workers who are employed in monomer, polymer, and fabrication facilities, 158,000 workers who are employed in supplier industries that provide goods and services to the styrenics industry, and 157,000 workers who are supported by the personal expenditures of the direct and indirect workers. *Id.*

II. EVALUATIONS OF STYRENE BY OTHER GOVERNMENTAL ENTITIES

Styrene is approved by the United States Food and Drug Administration as a flavoring additive to food and is widely used in food packaging. *See* 21 C.F.R. § 172.515; RoC at 387.

United States and European government agencies have reviewed the carcinogenicity of styrene, including the Agency for Toxic Substances and Disease Registry ("ATSDR"), an agency of HHS; the International Agency for Research on Cancer ("IARC"); and the government of the United Kingdom on behalf of the EU. These reviews found no causal link between styrene and cancer in humans. They concluded that styrene was not carcinogenic to humans or, at most, is a possible human carcinogen, but the evidence they identified, by their own characterization, is weak. These reviews conflict with the HHS RoC listing of styrene as "reasonably anticipated to be a human carcinogen." The scientific literature upon which these evaluations were based is essentially the same literature reviewed by NTP in conducting its assessment of styrene for the RoC.

ATSDR is a public health agency of HHS. *See* http://www.atsdr.cdc.gov. ATSDR is part of the Centers for Disease Control and Prevention ("CDC"). CDC describes itself as "one of the major operating components" of HHS. *See* http://www.cdc.gov/about/organization/cio.htm.

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. On the issue of accountability, 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.

On November 30, 2010, ATSDR published a notice of availability for an updated Toxicological Profile For Styrene ("ATSDR Toxicological Profile"), which is a peer-reviewed document. *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 Toxicological Profile, the toxicological profile "[s]uccinctly 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 Foreword. 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.*

The ATSDR Toxicological Profile 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. Thus, this ATSDR conclusion does not support any RoC listing.

IARC, part of the World Health Organization, evaluated the potential carcinogenicity of styrene in 1978, 1987, 1994, and 2002. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans* Volume 82 at 437 (2002), *available at* http://monographs.iarc.fr/ENG/Monographs/vol82/index.php. IARC first classified styrene as "possibly carcinogenic" in 1987. *See* Supplement No. 7, Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42 at pages 345-47 (1987), *available at* http://monographs.iarc.fr/ENG/Monographs/supplements.php. Through subsequent reviews, this classification has remained unchanged. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans* at 437.

Like HHS, IARC classifies the carcinogenic potential of substances based on an assessment of the sufficiency of the scientific information from peer-reviewed publications using a tiered classification system. Of four possible categories, styrene has been consistently classified by IARC as possibly carcinogenic to humans (Group 2B) beginning with the 1987

review.[2] The evidentiary basis for a Group 2B classification is not sufficient to support listing styrene in the RoC as reasonably anticipated to be a human carcinogen. This is reflected in HHS' failure to list styrene on the RoC between 1987 and 2011, and explained by ATSDR's Cancer Policy Framework. Only IARC Group 1 or Group 2A support a listing on the RoC.[3] ATSDR equates IARC's Group 2A (probably carcinogenic to humans) with NTP's "reasonably

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[2] The four IARC categories are:

Group 1 - Carcinogenic to humans
Group 2A - Probably carcinogenic to humans
Group 2B - Possibly carcinogenic to humans
Group 3 - Not classifiable
Group 4 - Probably not carcinogenic to humans

[3] This is demonstrated by Table 1, shown below, which comprises Appendix A to ATSDR's Cancer Policy Framework, *available at* http://www.atsdr.cdc.gov/cancer.html.

Table 1. Classification of carcinogens

EPA	IARC	NTP	OSHA
(Group A) Human Carcinogen	(Group 1) Carcinogenic to Humans	Human Carcinogen	Category I
(Group B1, B2) Probable Human Carcinogen	(Group 2A) Probably Carcinogenic to Humans	Reasonably Anticipated to be a Carcinogen	Category II
(Group C) Possible Human Carcinogen	(Group 2B) Possibly Carcinogenic to Humans		
(Group D) Not Classifiable as to Human Carcinogenicity	(Group3) Not Classifiable as to Human Carcinogenicity		
(Group E) Evidence of Non-Carcinogenicity for Humans			

anticipated to be a carcinogen." IARC's Group 2B (possibly carcinogenic to humans), which includes styrene, does not meet the sufficiency of evidence necessary for listing. A similar comparison of IARC and NTP was recently made by the National Research Council of the National Academy of Sciences.[4] The Department of Labor, through the Occupational Safety and Health Administration, also differentiates between the IARC 2A and 2B categories.[5]

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.[6] The RAR found that:

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[4] The National Research Council of the National Academy of Sciences concurs with ATSDR's conclusions as set out in this table. NAS in its 2011 Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde stated that "[a]lthough the term 'likely' can have a probabilistic connotation in other contexts, its use as a weight of evidence descriptor does not correspond with quantifiable probability of whether the chemical is carcinogenic. This is because the data that support cancer assessments generally are not suitable for numerical calculations of the probability that an agent is a carcinogen. Other health agencies have expressed a comparable weight of evidence using terms such as 'Reasonably Anticipated to Be a Human Carcinogen' (NTP) or 'Probably Carcinogenic to Humans' (International Agency for Research on Cancer)." Appendix B at 134, *available at* http://books.nap.edu/openbook.php?record_id=13142&page=134.

[5] The Occupational Safety and Health Administration's Hazard Communication Standard ("HCS") differentiates obligations based on IARC 2A and 2B classifications. *See* 29 C.F.R. § 1910.1200. Under the HCS Inspection Procedures, an IARC 2B classification triggers MSDS requirements but not labeling requirements. However, a substance's inclusion at any level on the RoC triggers MSDS and labeling requirements. *See* OSHA Directive Number: CPL 02-02-038, Inspection Procedures for the Hazard Communication Standard (1998), *available at* http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_id=1551&p_table=DIRECTIVES (Table A1).

[6] 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

> 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.

Id. at 271-72.

The ATSDR Toxicological Profile, the IARC classification, and the EU Risk Assessment Report conflict with and do not support the inclusion of styrene in the RoC as a substance reasonably anticipated to be a human carcinogen. These contrary determinations demonstrate that the procedural errors made by HHS in preparing the RoC with regard to styrene were outcome determinative, arbitrary, capricious, an abuse of discretion, and *ultra vires*.

III. REPORT ON CARCINOGENS

A. The Regulatory Framework

The Report on Carcinogens ("RoC") is mandated by Congress. 42 U.S.C. § 241(b)(4)(A). According to the statute, the Secretary of HHS shall publish a biennial report that contains, in relevant part, "a list of all substances (i) which either are known to be carcinogens or may reasonably be anticipated to be carcinogens and (ii) to which a significant number of

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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."

persons residing in the United States are exposed." *Id.* Under the statutory scheme, substances that have only suggestive evidence of carcinogenicity should not be listed at all. That is, HHS has not been directed to list "possible" or "suspected" carcinogens. *See id.*

The mandate from Congress to HHS was clear on this point: "the phrase 'suspected carcinogens' [was replaced] with 'substances . . . reasonably anticipated to be carcinogens,' in order to make it absolutely clear in the statute that there must be reasonable 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).

HHS states that conclusions in the RoC "regarding carcinogenicity in humans or experimental animals are based on scientific judgment, with consideration given to all relevant information." RoC at 4; *see also* NTP "Listing Criteria," *available at* http://ntp.niehs.nih.gov/index.cfm?objectid=03C9CE38-E5CD-EE56-D21B94351DBC8FC3. The plain language of HHS' policy correctly interpreted Congress' mandate, but HHS failed to follow that policy.

B. Development of the Report on Carcinogens Generally

The preparation of the 12th RoC consisted 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 an expert panel report, which was supposed to contain the panel's peer review of the draft background document and 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 RoC by NTP; and,

i. Final approval of the RoC by the Secretary of HHS.

RoC at 8-10.

Under NTP policy, the information in a background document's sections discussing human cancer studies, studies of cancers in experimental animals, and other relevant data "must come from publicly available, peer-reviewed sources. . . . [In addition, f]or 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 (Sept. 29, 2008) at i, *available at* http://ntp.niehs.nih.gov/files/Styrene_Background_Document_%289-29-08%29F%5B1%5D.pdf; RoC at 8. 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."

The more important scientific assessments disseminated by the federal government require "more intensive" peer review. 70 Fed. Reg. 2664, 2665.

IV. DEVELOPMENT OF THE 12TH REPORT ON CARCINOGENS RELATING TO STYRENE

A. Nomination of Styrene and Announcement of NTP's Procedures

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). 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).

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 an ad hoc scientific expert panel 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.*

On May 9, 2007, NTP published a request for nominations of Scientific Experts to "serve on expert panels" as part of the review process for the 12th RoC. 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.*

B. The Background Document on Styrene, the Expert Panel Review, and *Ad Hoc* Science

On May 20, 2008, NTP announced the availability of the Draft Background Document for Styrene. Availability of the Draft Background Document for Styrene, 73 Fed. Reg. 29,139, 2,9139-40 (May 20, 2008). NTP solicited public comments on the draft by July 7, 2008. *Id*. NTP further announced that the Styrene Expert Panel would be meeting on July 21-22, 2008. *Id.*

The Draft Background Document did not consider the 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) ("Delzell Paper"), relating to workers in the synthetic rubber industry. According to the Delzell Paper, 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. According to the paper's authors, the data from this study indicate that employment in the synthetic rubber industry is related causally to leukemia; however, 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 that of unexposed persons. Dr. Delzell has characterized the results for styrene and NHL as "unconvincing." 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.

According to a Commentary on the Delzell Paper published by the Health 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. Health Effects Institute Research Report Number 132 at 70 (2006). This is consistent with the approach taken in the EU Risk Assessment.[7]

On July 21-22, 2008, the NTP Styrene Expert Panel ("Expert Panel") met for the purpose of conducting a "peer review" of the Draft Background Document on Styrene and to recommend whether, and at what level, styrene should be included in the 12th RoC. NTP added this Expert Panel step for the 12th RoC process, doing so "to enhance the scientific development of the report and address guidance in the Office of Management and Budget's 'Final Information Quality Bulletin for Peer Review' (OMB 2004)." RoC at 4. 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. [8]

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[7] The RAR at 271-72 states:

> 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.

[8] OMB, "Final Information Quality Bulletin for Peer Review" (Dec. 16, 2004) at 3-4. The OMB Guidelines further state:

The Expert Panel, however, did not conduct a peer review of the Draft Background Document and did not conform to the OMB Guidelines. Rather, the Expert Panel rejected conclusions of the Draft Background Document, developed "new" information, and invented its own data comparisons and conclusions.

In the Draft Background Document, NTP concluded that workers in the reinforced plastics industry—rather than workers in the synthetic rubber industry—were the most relevant study population for epidemiology studies of styrene exposure. Draft Background Document at 133. But the Expert Panel rejected this conclusion. Instead, the Expert Panel added a discussion of the Delzell Paper, which paper had not been considered by NTP in the first instance, and developed a new statistical analysis of the data reported in the paper that had not been considered by Dr. Delzell and her colleagues in their own publication and had not otherwise been published in the scientific literature. Additionally, the Expert Panel created a new study by combining data from a 1979 NCI mouse study and data about the control-group animals from a different mouse study and then using this comparison as the basis for a new analysis that allegedly made a new finding of an effect in the NCI-tested animals. Based on these new studies or analyses, the Expert Panel recommended that styrene be listed in the 12th RoC as "reasonably anticipated to

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

be a human carcinogen," based on "limited" evidence in human data and "sufficient" evidence in animal data. *See* Expert Panel Report, Part B – "Recommendation for listing status for 'styrene.'"

Further, participation in the Expert Panel by Dr. Genevieve Matanoski violated the OMB Peer Review Bulletin's requirement of independence and presented an appearance of bias. The lack of independence arose from her having been asked to peer review her own work, which the Bulletin flatly prohibits. *See, e.g.*, Draft Background Document at 94-96, 104; 74 Fed. Reg. 2675 ("Peer reviewers shall not have participated in development of the work product."). The appearance of bias arose because the Delzell Paper was an update of an earlier 1987 study that Dr. Matanoski initially conducted but was not hired to update. In addition, Dr. Matanoski is referenced as the primary author of five studies upon which the Background Document rests. Background Document at 423-24 (references 311-15).

Against this background of potential bias, Dr. Matanoski proceeded to reject the conclusions of the study authors and the peer reviewers of the Delzell Paper. Dr. Matanoski described this when she described the new analysis of that paper at the Expert Panel meeting: "[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." Transcript of July 21-22, 2008, Meeting of the NTP Styrene Expert Panel at Part 25. Based on this facially-biased review using newly-created but unwritten data that departed from the Delzell Paper conclusions, the Expert Panel then found an association between styrene and non-Hodgkin Lymphoma ("NHL"), an association that the peer-reviewed conclusion of Dr. Delzell and her colleagues found was "unconvincing." This

relationship between styrene and NHL was subsequently incorporated by HHS in the draft and final Substance Profiles for styrene, but was not in the peer-reviewed literature. RoC at 384; 73 Fed. Reg. 78,364 (Dec. 22. 2008)(notice of availability of draft Substance Profile).[9]

The creation a new study by manipulating the tabular data in the Delzell Paper is undocumented and in violation of the Information Quality Act; nothing showing the recombined groups appears in either the Background Document or the Expert Panel materials and the analysis was not provided by NTP in response to a request submitted by SIRC under the Freedom of Information Act. HHS NIH NIEHS FOI Case No. 35461.

The new studies developed by the Expert Panel did not constitute peer-review of the NTP Draft. Furthermore, the re-analysis itself has not been peer reviewed. The Expert Panel cannot, by definition, peer review its own work, and no other expert panel was convened to perform that function. Also, the new analysis by the Expert Panel is not "from the peer-reviewed literature" as required by NTP policy.

The Expert Panel also developed a new study by comparing data from a 1979 National Cancer Institute ("NCI") animal study titled "Bioassay of Styrene for Possible Carcinogenicity (Technical Report Series No. 185, 1979) ("1979 NCI Study") with new data outside of the 1979 NCI Study. Based on this newly-invented comparison, the Expert Panel reached conclusions different from the authors of that paper. The 1979 NCI Study examined rats and mice for adverse health effects from 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 (emphasis added). The Draft Background Document did

[9] The RoC also cites two studies by Dr. Matanoski. RoC at 389.

not question NCI's findings in discussing the study. Draft Background Document at 171. 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 novel and non-peer reviewed approach proceeded to find "sufficient evidence" of a link between styrene and tumors in the mice. Styrene Expert Panel Report, Part B at 3.

Just as with its reanalysis of the Delzell Paper, the Expert Panel's actions and the subsequent acceptance by HHS was *ultra vires* and contrary to HHS' stated policy. HHS could not properly consider this new study without publication and the scrutiny of scientific peer review. This new data and statistical analysis created by the Expert Panel did not constitute peer-review of the NTP Draft Report. *See* n.3 and discussion, *supra.* The new analysis has not been peer reviewed as the Expert Panel cannot peer review its own work and no other expert panel was convened to conduct that function. Nor did the new data and statistical analysis created by the Expert Panel constitute a "publicly available peer reviewed" source as required by NTP practice and procedure.

On September 8, 2008, NTP "invited" public comment on Part B of the Expert Panel's report, that is, its recommendation "on the listing status for styrene in the 12th RoC and the scientific justification for the recommendation." Request for Public Comments on the RoC Expert Panel's Recommendation on Listing Styrene on the 12th RoC, 73 Fed. Reg. 52,059, 52, 059-60 (Sept. 8, 2008). Comments were due to be submitted by October 23, 2008. Both Part A (the Expert Panel's "peer review" comments on the draft Background Document) and Part B of the Expert Panel Report were signed and finalized on August 26, 2008. *See* Styrene Expert Panel Report, Part B at 4, *available at*

http://ntp.niehs.nih.gov/files/Styrene_Panel_report_B_final_Rdtd.pdf; Styrene Expert Panel Report Part A at 33, *available at* http://ntp.niehs.nih.gov/NTP/ROC/twelfth/2009/Styrene/PanelReportA_BD_final_Rdtd1.pdf.

However, on September 29, 2008, nearly a month before the close of the comment period on the Expert Panel Report recommendations, NTP finalized the Draft Background Document and published its Final Report on Carcinogens Background Document for Styrene ("Final Background Document"). *See* http://ntp.niehs.nih.gov/files/Styrene_Background_Document_(9-29-08)F[1].pdf. According to the Final Background Document, the 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. Although HHS appears to segregate the Background Document development from the Expert Panel's listing recommendation, as show below, the Expert Panel's listing recommendation is based on nothing other then the Background Document that the Expert Panel modified through the creation of new and unreviewed studies of their own making.

C. The Styrene Substance Profile

According to the NTP process, once the Background Document and Expert Panel recommendation are finalized, NTP drafts a substance profile for each substance. The substance profiles are short documents summarizing NTP's classification of the substance and information about carcinogenicity, properties, use, production, exposure, regulations and guidelines. The compiled substance profiles constitute the RoC.

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. Meeting of NTP Board of Scientific Counselors, 73 Fed. Reg. 78,364,

78,364-65 (Dec. 22, 2008). According to the announcement, the NTP BSC is a federally-chartered, external advisory group that provides primary scientific oversight to the NTP and evaluates the scientific merit of NTP's intramural and collaborative programs. *Id.* The NTP BSC was charged with "[d]etermin[ing] whether the scientific information cited in the draft substance profile for a candidate substance is technically correct, clearly stated, and supports the NTP's preliminary policy decision regarding its listing in the RoC." Summary Minutes of February 24, 2009, NTP Board of Scientific Counselors at 6. However, the NTP did not ask the NTP BSC to comment on the policy decision to list a chemical on the RoC. *Id.*

After the peer review of the Draft Substance Profiles, NTP prepares a draft RoC. The draft RoC is then submitted first to the Director of NTP and then to the Secretary of HHS to transmit to Congress and the public.

The 12th Report on Carcinogens was signed by the Secretary of HHS on June 10, 2011.

V. SIRC'S INFORMATION QUALITY ACT REQUEST FOR CORRECTION

The Information Quality Act ("IQA"), 44 U.S.C. § 3516 note, and implementing guidelines issued by OMB,[10] HHS,[11] and NIH[12] apply to the RoC because it is information disseminated by a federal agency. The IQA requires that influential scientific information disseminated by a government agency be of appropriate "quality," which encompasses utility, objectivity and integrity. OMB, Guidelines for Ensuring and Maximizing the Quality,

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[10] Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies, 67 Fed. Reg. 8452 (Feb. 22, 2002),

[11] Guidelines for Ensuring the Quality of Information Disseminated to the Public, *available at* http://aspe.hhs.gov/infoquality/guidelines/part1.shtml

[12] Guidelines for Ensuring the Quality of Information Disseminated to the Public, *available at* http://aspe.hhs.gov/infoquality/guidelines/NIHinfo2.shtml

Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies, 67 Fed. Reg. 8452, 8457 (Feb. 22, 2002).[13] As such, 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." *Id*. at 8457, 8459-60. NTP is also required to incorporate a "high degree of transparency about the data and methods to facilitate the reproducibility of such information by qualified third parties." *Id*. at 8460.

On October 26, 2009, SIRC submitted to NIH a Request for Correction under the IQA 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 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—14 months after SIRC submitted the request. Letter of Dec. 23, 2010, from John R. Bucher, Ph.D., Associate Director, NTP to Jack Snyder, Executive Director, SIRC.

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

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[13] OMB defines "influential" information as that which **"**has a clear and substantial impact on important public policies or private sector decisions." 67 Fed. Reg. 8460. It is clear that NIH regards the RoCs as "influential;" *see* NIH IQA Guidelines, n.12, *supra*, at § V.2.d ("One of our most visible publications is the Report on Carcinogens . . . ."). Finally, in its responses to SIRC's Request for Correction and SIRC's appeal of that request, NIH has never disputed the characterization of the RoC as "influential."

misunderstanding of the objectivity criterion under the IQA, as demonstrated in SIRC's IQA Appeal of February 11, 2011, which was denied in a letter dated June 8, 2011, shortly before the RoC was issued.[14] For the Background Document to comply with the IQA 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 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.

VI. THE IMPACT OF LISTING STYRENE IN THE REPORT ON CARCINOGENS

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 include the following:

The Occupational Safety and Health Administration's ("OSHA") Hazard Communication Standard ("HCS") states that "Chemical manufacturers and importers shall evaluate chemicals produced in their workplaces or imported by them to determine if they are hazardous." 29 C.F.R. § 1910.1200(d)(1). Under the HCS, "[a] chemical is considered to be a carcinogen if: (b) it is listed as a carcinogen or potential carcinogen in the Annual Report on Carcinogens published by the National Toxicology Program." *Id.* at Appendix A to § 1910.1200. 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

[14] Letter from Allen Dearry, Ph.D, Senior Advisor, National Institutes of Health, National Institute of Environmental Health Sciences, to Jack Snyder, Executive Director, Styrene Information and Research Center, Inc. (June 8, 2011), attached hereto as Exhibit 4.

Standard" states that HCS labeling requirements apply to substances that NTP designates as reasonably anticipated to be a human carcinogen.[15] *See* http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_id=1551&p_table=DIRECTIVES (Table A1). NTP is aware of this consequence.[16]

California's Safe Drinking Water and Toxic Enforcement Act of 1986, 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. Cal. Health and Safety Code § 25249.6. 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. *See* Questions & Answers about the RoC, "What does a listing in the RoC mean?," *available at* http://ntp.niehs.nih.gov/index.cfm?objectid=03CA6383-9766-1F64-6637241FE0114FE9.

In fact, NTP's activity leading up to the RoC already has had a negative impact on styrene. In February 2010, the Office of Environmental Health Hazard Assessment ("OEHHA"), California Environmental Protection Agency, published its Draft Public Health Goal for Styrene in Drinking Water. In the Summary of that publication, OEHHA cited the recommendation of the NTP Expert Panel to include styrene in the RoC, demonstrating that NTP's actions are already influencing the decision making of other governmental agencies. Draft Public Health

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[15] Under the HCS Inspection Procedures, IARC's classification of styrene as a 2B substance (possibly carcinogenic to humans) triggers only MSDS requirements. Inclusion on the RoC would trigger MSDS and labeling requirements.

[16] *See* Questions & Answers about the RoC, "What does a listing in the RoC mean?," *available at* http://ntp.niehs.nih.gov/index.cfm?objectid=03CA6383-9766-1F64-6637241FE0114FE9.

Goal for Styrene in Drinking Water at 2, *available at* http://oehha.ca.gov/water/phg/pdf/Styrene020410.pdf.

ARGUMENT

A preliminary injunction is available when a party demonstrates: "(1) a substantial likelihood of success on the merits; (2) that it would suffer irreparable injury if the requested injunction is not granted; (3) that an injunction would not substantially injure other interested parties; and (4) that the public interest would be furthered by the injunction." *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1066 (D.C. Cir. 1998) (citing *City-Fed Financial Corp. v. Office of Thrift Supervision*, 58 F.3d 738, 746 (D.C. Cir. 1995)). *See also Nat'l Treasury Employees Union v. U.S.*, 927 F.2d 1253, 1254 (D.C. Cir. 1991); *Sea Containers, Ltd. v. Stena AB*, 890 F.2d 1205, 1208 (D.C. Cir. 1989); *Wash. Metro. Area Transit Comm'n v. Holiday Tours*, 559 F.2d 841, 943 (D.C. Cir. 1977); *Va. Petroleum Jobbers Ass'n v. Federal Power Comm'n*, 259 F.2d 921, 925 (D.C. Cir. 1958). A plaintiff is not required to prevail under each of these factors; rather, "the factors must be viewed as a continuum, with more of one factor compensating for less of another." *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 27 (D.D.C. 1997). Indeed, "[t]o justify the granting of a stay, a movant need not always establish a high probability of success on the merits. Probability of success is inversely proportional to the degree of irreparable injury evidenced. A stay may be granted with either a high probability of success and some injury, or vice versa." *Cuomo v. NRC*, 772 F.2d 972, 974 (D.C. Cir. 1985). In this case, however, each factor strongly favors the award of injunctive relief.

As shown below, each of these four factors is amply satisfied and the court should issue an injunction.

I. PLAINTIFFS ARE SUBSTANTIALLY LIKELY TO SUCCEEED ON THE MERITS

The Administrative Procedure Act ("APA") permits individuals suffering a legal wrong because of final agency action to seek judicial review thereof. 5 U.S.C. § 702. Our Court of Appeals has held that publication of the RoC constitutes a reviewable final agency action. *Tozzi v. U.S. Dep't of Health and Human Servs.*, 271 F.3d 301, 310 (D.C. Cir. 2001).

The APA authorizes agency action to be struck down for any of three bases that are applicable to NTP's listing of styrene on the 12th RoC. It provides that courts "shall . . . hold unlawful and set aside agency action" that is "in excess of statutory jurisdiction, authority, or limitations, or short of statutory right," 5 U.S.C. § 706(2)(C), taken "without observance of procedure required by law," *id*. § 706(2)(D), or "arbitrary, capricious, an abuse of discretion or otherwise not in accordance with the law." *Id.* § 706(2)(A). As demonstrated below, Plaintiffs are likely to succeed on the merits on all three of these grounds.

A. The Public Health Service Act Does Not Authorize Listing a "Possible Carcinogen" on the Report on Carcinogens

The statute which authorizes the RoC, the Public Health Service Act, instructs the Secretary of HHS to publish reports listing "all substances (i) which either are known to be carcinogens or may reasonably be anticipated to be carcinogens and (ii) to which a significant number of persons residing in the United States are exposed." 42 U.S.C. § 241(b)(4)(A). The statute does not authorize the Secretary to list substances that have only suggestive evidence of carcinogenicity; *i.e.*, that are "possible" or "suspected" carcinogens. "[T]here 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).

The body of peer-reviewed literature that NTP has cited in the RoC is substantially the same body of literature that was reviewed just last year by NTP's sister agency ATSDR. Interpreting the literature in November 2010, ATSDR issued a peer-reviewed Toxicological Profile for Styrene which concludes that styrene "may possibly be a weak human carcinogen." *See* Profile at 133, *available at* http://www.atsdr.cdc.gov/ToxProfiles/TP.asp?id=421&tid=74#bookmark01. ATSDR's conclusion about styrene does not support a conclusion that styrene is reasonably anticipated to be a human carcinogen.

NTP's conclusion that styrene warrants listing on the RoC, when its sister agency ATSDR reached a conclusion that would not support a listing demonstrates the result-oriented capriciousness of the RoC process, a disregard for its statutory mandate, and that the procedural errors lead to an arbitrary and capricious decision to list styrene as reasonably anticipated to be a human carcinogen.

Two international agencies also have evaluated the relevant literature and come to the same conclusion as ATSDR. First, the European Union ("EU") Risk Assessment Report on Styrene ("RAR") submitted to the European Chemicals Agency in June 2008 (and subsequently agreed to by the EU's Technical Committee for New and Existing Substances independently peer reviewed by the EU's Scientific Committee on Health and Environmental Risks) concluded: "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. Second, over the past 24 years, the International Agency for Research on Cancer ("IARC") has consistently classified styrene as "possibly carcinogenic." *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans* Volume 82 at 437 (2002), *available at* http://monographs.iarc.fr/ENG/Monographs/vol82/index.php. ATSDR's Cancer Policy Framework clearly indicates that this IARC conclusion (Group 2B - possibly carcinogenic to humans) does not meeting the NTP classification of "reasonably anticipated" to be a human carcinogen. *See* ATSDR – Cancer Policy Framework, Appendix A, Table 1, *available at* http://www.atsdr.cdc.gov/cancer.html. The National Academy of Sciences agrees.[17]

The conclusions of ATSDR, the EU and IARC that styrene is at best a possible human carcinogen indicate that NTP has acted arbitrarily and capriciously in interpreting the same scientific literature as justifying a "reasonably anticipated" classification. NTP has thus exceeded its statutory authority and the RoC's listing of styrene cannot stand.

B. NTP Violated Its Own Procedural Requirements in Listing Styrene

Federal agencies are "bound by the standards by which [they] profess [their] actions to be judged." *Lopez v. Fed. Aviation Admin.*, 318 F.3d 242, 246 (D.C. Cir. 2003) (citing *SEC v. Chenery Corp.*, 318 U.S. 80, 87-88 (1943)). Thus, agencies "must follow their own rules, even gratuitous procedural rules that limit otherwise discretionary actions." *Steenholdt v. FAA*, 314 F.3d 633 (D.C. Cir. 2003). In the case of an alleged violation of an agency procedure designed

[17] *See* n.4, *supra.* SIRC's references to the ATSDR and IARC reviews are not intended to be an endorsement of those conclusions, with which SIRC has some disagreement. Rather, even if the ATSDR and IARC classifications are assumed to be correct for purposes of argument, NTP's action is unsupported.

to provide the agency with information it needs to reach an informed decision, the complaining party must show that the agency violation caused it to suffer substantial prejudice. *Lopez*, 318 F.3d at 247. However, no special showing is necessary if the agency rule is intend primarily to provide procedural benefits to individuals in the face of otherwise unfettered agency discretion. *Id.*

At several crucial steps in the process of the developing the RoC's listing of styrene, HHS failed to follow its own procedures and policies, thereby fatally compromising the integrity of the process and the legitimacy of its conclusions and rendering the styrene listing invalid as taken "without observance of procedure required by law." 5 U.S.C. § 706(2)(D).

First, the Expert Panel did not conduct a peer review of the studies behind the Draft Background Report as required by NTP procedure. Rather, the Expert Panel rejected the substantive conclusions of the Background Report, developed new information, and invented its own science. The Background Report did not even consider the Delzell Paper. The Expert Panel took it up spontaneously and then developed a new but undocumented analysis of that study's data in an attempt to support a conclusion that styrene has human carcinogenic properties. The Delzell Paper concluded the opposite—that there was no clear relationship between styrene and cancer—as Dr. Delzell herself stated to NTP. Similarly, after thirty years of global acceptance of the study authors' peer-reviewed conclusions, the Expert Panel combined some data from the 1979 NCI Study with new data from a different set of animals for a control group, creating a new study in an attempt to support a finding of human carcinogenicity. As with the Delzell Paper, the 1979 NCI Study concluded that there was no firm conclusion of styrene carcinogenicity. This activity was beyond the authority and purpose of the Expert Panel as constituted by HHS.

These new analyses by the Expert Panel do not constitute peer review. Furthermore, the Expert Panel's new analyses have not been published in the public literature and have not been peer reviewed. Under NTP's procedures, these new analyses cannot be relied upon to support the RoC. The Expert Panel cannot peer review its own work, and no other body was convened to peer review its work product.

Next, HHS finalized the Draft Background Document nearly a month before the end of the public comment period on the Expert Panel's recommendations regarding the appropriate cancer classification of styrene and the scientific justification for that listing status. The Expert Panel's recommendations resulted in NTP dramatically reshaping the Background Document to conform to those recommendations. Public comments on the Expert Panel's report could—and should—have directly impacted the final form of the Background Report. But HHS precluded that possibility when it shortcut the process and finalized the Background Report almost a month before the end of the public comment period on the Expert Panel report.[18]

Third, NTP did not weigh all evidence relating to styrene to make a sound and reasoned determination of its carcinogenicity based on the science, as required by NTP's own

[18] In response to SIRC's IQA request for correction, NTP argued that it had not sought comment on the Expert Panel's peer review comments on the draft Background Document (Part A of its report), but only on Part B (the Expert Panel's proposed cancer classification and scientific justification therefore). It may be, as a matter of procedural formality, that "conclusions reached by the expert panel and reported in the Expert Panel Report, Part B, are independent of the Background Document." NTP Response at 6. In reality, however, that statement is demonstrably false. The conclusions set out in the Expert Panel's scientific justification for listing are woven throughout the Expert Panel's peer review comments, which are self-evidently constructed to maximize apparent support for those conclusions. This can be readily seen by comparing the two at any corresponding points. Compare, for example, the discussion of Delzell *et al.* in Part B of the report (p. 2) with the discussion in Part A (pp. 8 & 12).

interpretation of its statutory mandate under the Public Health Service Act. NTP has stated that its obligation is to make determinations "based on scientific judgment, with consideration given to all relevant information." NTP "Listing Criteria," *available at* http://ntp.niehs.nih.gov/INDEX4244_2.HTM?objectid=47B37760-F1F6-975E-7C15022B9C93B5A6. Relevant information includes negative information.[19] The record reveals, however, that NTP consistently ignored evidence that conflicted with that conclusion. For example, in June 2010, Dr. Gloria Jahnke of NIEHS/NTP stated that NTP has not included a particular relevant study in the Background Document because the document did not support listing styrene on the RoC: "I'm not recording negative data here; I am recording data that supports our call. So that's why you didn't see it."[20] Additionally, the Board of Scientific Counselors, a body designed to ensure scientific credibility, stated at its February 24, 2009, meeting that styrene was included on the RoC based on the "strength of the evidence" in support of its inclusion. A "strength of the evidence" review only considers data in support of a carcinogenicity classification.[21] Finally, NTP's Response to Comments document states baldly: "The substance profile is a concise summary of the scientific evidence *that supports the listing*

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[19] "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 that do not operate in humans and would therefore not reasonably be anticipated to cause cancer in humans." NTP "Listing Criteria," *available at* http://ntp.niehs.nih.gov/INDEX4244_2.HTM?objectid=47B37760-F1F6-975E-7C15022B9C93B5A6.

[20] Meeting materials are available at http://ntp.niehs.nih.gov/INDEX8D14_2.HTM?objectid=720164F2-BDB7-CEBA-F5C6A2E21851F0C4#2010.

[21] *Id*.

and is not intended to be a comprehensive review."[22]

Given their concerted efforts to create new (but undocumented) analyses of existing data, and to ignore (indeed, to suppress by not discussing) relevant information that was presented to them, it is not an exaggeration to regard the actions of NTP and its advisory bodies as approaching the 12th RoC with the intention of listing styrene, and then shaping the underlying documents to support that conclusion. These procedural manipulations—which NTP expressly refused to address in its Response to Comments document[23]—invalidate the document as it concerns styrene.

HHS' failure to follow its internal procedures throughout the RoC process should be reviewable without a showing of substantial prejudice by Plaintiffs. The procedural rules in place were designed to limit HHS and NTP's discretion in selecting and including substances on the RoC. Given the massive economic impact that styrene's listing will have on the industry, *see* Levy Declaration, Exhibit 1, at ¶¶ 7-13, and Schweitzer Declaration, Exhibit 2, at ¶¶ 7-12, it is reasonable to conclude that the procedures established to guide the development of the RoC are intended to benefit individuals from the very arbitrary decision-making that HHS and NTP exercised in including styrene on the RoC. Plaintiffs can also show substantial prejudice, however. As discussed in Part A, above, ATSDR, the EU and IARC have all concluded that styrene is at best a possible human carcinogen. This is a standard lower than any level on the RoC and these conclusions do not support a listing of styrene on the RoC. But for NTP's admitted result-oriented approach to styrene's inclusion on the RoC, which engendered

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[22] *See* NTP Response to Issues Raised in the Public Comments for Candidate Substances for the *12th Report on Carcinogens* (2011) at 43 (emphasis added), *available at* http://ntp.niehs.nih.gov/ntp/roc/twelfth/2011/ResponsePublicComments2011.pdf#page=36.

[23] *See id.* at 34.

reanalyses of academic papers, "new" science, a faulty peer review of the Background Document, and the shortcutting of the public-comment period, styrene very likely would not have been included on the RoC. These violations have substantially prejudiced Plaintiffs in a clear and direct manner and constitute arbitrary and capricious agency action that is contrary to law.

C. NTP Has Violated the Information Quality Act by Failing to Adhere to the Act's Objectivity and Utility Requirements

The Information Quality Act ("IQA"), 44 U.S.C. § 3516 note, requires that information disseminated by federal agencies meet the IQA's twin standards of objectivity and utility. The 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 "involves analysis of risks to human health." 67 Fed. Reg. 8460. To be objective, the RoC must be "accurate, reliable and unbiased," *id.* at 8549, and based on "the best available . . . science . . . conducted in accordance with sound and objective scientific practices." *Id*. at 8457. It must also incorporate a "high degree of transparency about the data and methods to facilitate the reproducibility of such information by qualified third parties." *Id.* at 8460. Objectivity must also be reflected in the way that information is presented: to be objective, information must be presented in an accurate, clear, complete and unbiased manner, which includes presentation in the proper context. *Id.* at 8459. Influential scientific information bearing on assessing health risks—like the RoC—must present "each significant uncertainty identified in the process" and "peer-reviewed studies . . . that fail to support any estimate of risk." *Id.* at 8457-58. Finally, the IQA also aims to ensure the "utility" of information; *i.e.*, that it be useful to its intended users, including the public. *Id.* at 8459; *cf.* 44 U.S.C. § 3504(e)(1)(B).

NTP failed in its duties under the IQA in several ways, each of which is further evidence that HHS' action was arbitrary and capricious and not in accordance with the law under 5 U.S.C. § 706(2)(A). Science that is not the best available, or that is generated by practices that are chosen to produce a given effect, is not objective. As just discussed, NTP approached styrene in a result-oriented manner, intent on including it in the RoC. NTP actively chose not to consider all relevant evidence, but instead highlighted positive findings and omitted significant negative findings and conclusions. The RoC's statements about the carcinogenicity of styrene in humans or rodents are not accurate or reliable, given the improper ways in which they were derived. Nor are they presented in an unbiased way.

Additionally, the expert panel's undocumented re-analysis of the Delzell paper violates the IQA's requirement of transparency. 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 FOIA. HHS NIH NIEHS FOI Case No. 35461.

Finally, the Background Document violates the "utility" criterion of the IQA because it does not enable a reader to make an informed judgment about the carcinogenicity of styrene. Rather, the reader and the public are left with a misleading conclusion that will lead to misinformed decisions. Already the public is being warned not to use any products made from styrene.

Plaintiffs do not seek to enforce the IQA. Rather, Plaintiffs assert that NTP's failure to fulfill its IQA obligations, obligations that have been recognized by NIH (NTP's parent agency) and embraced by HHS as embodied in the RoC, further demonstrates that NTP was acting

arbitrarily and capriciously when it listed styrene in the RoC. Had NTP fulfilled its IQA obligations, this listing likely would not have happened. Thus, NTP's failure to comply with the IQA is further evidence that the RoC is arbitrary, capricious or otherwise not in accordance with the law.

II. PLAINTIFFS WILL SUFFER IRREPARABLE HARM WITHOUT INJUNCTIVE RELIEF

The immediate impacts of styrene's inclusion on the RoC will irreparably harm Plaintiffs and other manufacturers and users of styrene. After a substance is listed as carcinogenic, the process of deselection as a suitable material begins, making it difficult or impossible to regain its reputation among purchasers and consumers. Levy Declaration, Exhibit 1, at ¶¶ 7-13; Schweitzer Declaration, Exhibit 2, at ¶¶ 8-12. The reaction in the marketplace is further fueled by regulatory changes that the RoC fuels.

NTP acknowledges that the listing of a substance in the RoC may prompt state and federal regulatory agencies to consider limiting exposures or uses of a substance. For example, NTP notes that under California's Proposition 65, any substance listed in the RoC must carry a "clear and reasonable warnings" about carcinogenicity. Questions & Answers about the RoC, "What does a listing in the RoC mean?", *available at* http://ntp.niehs.nih.gov/index.cfm?objectid=03CA6383-9766-1F64-6637241FE0114FE9.

Proposition 65, California Health and Safety Code §§ 25249.5 *et seq.*, requires the Governor of California to publish a list (updated annually) of chemicals "known to the State of California to cause cancer, birth defects or other reproductive harm." One of the mechanisms by which a chemical may be added to the Proposition 65 list is if an "authoritative body" formally identifies a chemical as causing cancer or reproductive toxicity. California Health and Safety

Code § 25249.8(b). NTP is an authoritative body for purposes of formally identifying chemicals known to the State of California to cause cancer. *See* Cal. Code Regs. tit. 22, § 12306(m)(3). Thus, a listing in the RoC prompts a near-automatic listing under Proposition 65. In addition to enforcement by California authorities, private rights of action can be brought by "any person in the public interest." California Health and Safety Code §§ 2549.7(c)-(d). As noted previously, California has already moved to regulate styrene based on the NTP Expert Panel's work.

Furthermore, inclusion of styrene in the RoC will open a Pandora's Box for the styrene industry that would be impossible to undo. The impacts include massive economic losses through de-selection of products containing styrene and loss of goodwill through stigmatization of styrene as a cancer-causing agent. Schweitzer Declaration, Exhibit 2, at ¶ 8. The adverse effects to Plaintiffs and the styrene industry stemming from a listing are not possible to quantify, rendering the harm not compensable and therefore irreparable. Not least in the calculus would be immense loss of goodwill to the styrene industry and to purveyors of styrene-based products such as Dart and other SIRC members and the corresponding de-selection by would-be purchasers of styrene-containing products. Levy Declaration, Exhibit 1, at ¶¶ 8-9. Indeed, the listing of styrene on the RoC was immediately known and has been widely disseminated throughout the trade media and trade press.[24] It will precipitate immediate deselection of

[24] A few examples of media coverage follow, which include major outlets as well as blogs and business media:

Gardiner Harris, "U.S. Weighs Cancer Risk of Styrene and Formaldehyde," N.Y. Times, June 10, 2011, *available at* http://www.nytimes.com/2011/06/11/health/11carcinogen.html?_r=1

Gardiner Harris, *Government Says 2 Common Materials Pose Risk of Cancer*, N.Y. Times, June 10, 2011, *available at* http://www.nytimes.com/2011/06/11/health/11cancer.html?hp

styrenics from a portion of the market who will not wait for warnings to appear. *Id.* at ¶ 9. Given the $28 billion market for styrene, Snyder Declaration, Exhibit 3, at ¶ 8, even a 10% decline in sales translates into a $2.8 billion loss. These events, flowing as they would from a faulty and illegal process, would work an irreparable harm on Plaintiffs.

Moreover, the government is immune from damage suits, so, even if calculable, Plaintiffs' losses stemming from styrene's listing on the RoC are not compensable. *See Woerner v. U.S. Small Business Admin.*, 739 F.Supp. 641, 650 (D.D.C. June 15, 1990); *Wisconsin v. Stockbridge-Munsee Cmty.*, 67 F.Supp.2d 990, 1019-20 (E.D. Wis. 1999); *Glendale Neighborhood Ass'n v. Greensboro Housing Auth.*, 901 F.Supp. 996, 1002 (M.D.N.C. 1995). Plaintiffs will thus suffer irreparable harm without injunctive relief.

Rob Stein, *Formaldehyde, styrene among substances deemed carcinogens or likely to cause cancer*, Washington Post, June 10, 2011, *available at* http://www.washingtonpost.com/national/formaldehyde-styrene-among-substances-deemed-carcinogens-or-likely-to-cause-cancer/2011/06/10/AG1K3LPH_story.html?hpid=z3

Two main components of coffee cups and carry out containers identified as cancer-causing agents, N.Y. Daily News, June 12, 2011, *available at* http://www.nydailynews.com/lifestyle/health/2011/06/12/2011-06-12_two_main_components_of_coffee_cups_and_carry_out_containers_identified_as_cancer.html.

Jeffrey Young, *Food-Container chemical Added to Carcinogens*, Bloomberg, June 10, 2011, *available at* http://www.bloomberg.com/news/2011-06-10/eight-agents-including-formaldehyde-added-to-list-of-carcinogens.html

Jenifer Goodwin, *Chemical Found in Foam Cups a Possible Carcinogen*, U.S. News & World Report, June 10, 2011, *available at* http://health.usnews.com/health-news/family-health/cancer/articles/2011/06/10/chemical-found-in-foam-cups-a-possible-carcinogen

CNN Wire Staff, *US lists 8 common substances as potential cancer risks*, CNN Health, June 13, 2011, *available at* http://www.cnn.com/2011/HEALTH/06/11/us.carcinogens/

III. THERE IS NO COGNIZABLE HARM TO OTHERS

HHS will suffer no cognizable harm if an injunction is imposed ordering withdrawal of the styrene component of the RoC. Nor will the public be harmed by an injunction. An injunction ordering withdrawal of styrene from the RoC would merely remove styrene from the RoC while NTP is free to follow the proper procedures to evaluate styrene for inclusion on the RoC. The public actually is at greater risk based on actions taken in response to the listing, given the invalidity of that listing. Importantly, none of the original peer-reviewed literature studies on which the RoC relied would be affected by an injunction. Nor would any of the other official positions taken by federal or state government agencies be called into question. Rather, the credibility of ATSDR's classification of styrene would be restored. Thus, the public would continue to have access to an extensive body of accurate, reliable, useful information about styrene and its health effects.

IV. THE PUBLIC INTEREST STRONGLY FAVORS GRANTING INJUNCTIVE RELIEF

As a general matter, "there is a strong public interest in meticulous compliance with law by public officials." *Fund for Animals v. Espy*, 814 F. Supp. 142, 152 (D.D.C. 1993). The public interest is served by requiring an agency to follow federal law and its own procedures when taking actions that affect the public interest. This maxim is particularly forceful when the action contemplated deals with matters that directly and profoundly affect issues of public health and welfare.

Additionally, the risk of harm to the public and the national economy from disseminating faulty and highly prejudicial information about styrene outweighs any benefit to be gained by

allowing the RoC to stand. Styrene is a key component of many daily products that we take for granted, including bicycle helmets, refrigerators, microwave ovens, food-service containers, produce and dairy containers, computers, televisions, carpets and furniture. Levy Declaration, Exhibit 1, at ¶ 4; Schweitzer Declaration, Exhibit 2, at ¶ 3. Consumers who avoid these products for mistaken reasons may be exposed unnecessarily to greater risks, as well as greater costs. Snyder Declaration, Exhibit 3, at ¶ 6.

CONCLUSION

For the reasons stated above, Plaintiffs respectfully requests the issuance of a preliminary injunction ordering Defendants to withdraw publication of the RoC as it relates to styrene until the conclusion of the underlying litigation.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on June 16, 2011, a copy of the foregoing was filed with the Court's CM.ECF software and served via the same of Defendants' counsel of record.

/s/ Robert A. Sheffield
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