



The Styrene Information & Research Center

August 26, 2004

Dorothy Shimer
Research Division
Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Re: Styrene References in "Indoor Air Pollution in California" Report

Dear Ms. Shimer:

The Styrene Information and Research Center, Inc¹ (SIRC) appreciates the opportunity to comment on the California Air Resources Board (CARB) Draft Report, *Indoor Air Pollution in California* ("Report"), released in June 2004. We appreciate CARB's extension of this comment period through August 27, 2004. SIRC specifically would like to offer comment on the characterization of styrene in the Report, and the references used to support styrene's inclusion.

SIRC compliments the CARB on producing a thoughtful, well-compiled, Report to the Legislature, which brings together a considerable body of information on the nature of indoor air pollution.

In the interest of ensuring that the Report is based on the most current and accurate information available, we are providing comments that would help to more correctly characterize the health effects of styrene, based on more recent assessments and research data than are cited in the Report, as well as the way styrene is characterized as a potential component of indoor air. In light of these more current data, we also address the level of attention and priority that styrene should receive in the report and any subsequent legislation.

¹ The Styrene Information and Research Center's (SIRC's) mission is to evaluate existing data on potential health effects of styrene, and develop additional data where it is needed. SIRC has gained recognition as a reliable source of information on styrene and helping ensure that regulatory decisions are based on sound science. For more information, visit <http://www.styrene.org>.

Specific changes that we suggest to the Report are as follows.

A. Change Heading for Third Column in Tables ES-1 (p.3) and 2.1 (p.28) from “Potential Health Effects” TO “ONE OR MORE OF THESE CHEMICALS HAS BEEN SHOWN TO CAUSE THESE POTENTIAL HEALTH EFFECTS”

We agree that styrene, as an organic chemical and solvent, can cause nasal irritation and affect coordination at high exposure levels. However, SIRC does not believe that styrene can be accurately characterized as being a potential cancer-causing agent, or as causing liver, kidney or brain effects.

Although SIRC appreciates the CARB’s need to streamline the characterization of groups of chemicals, it does not appear to serve the public’s best interest to place a chemical in a table that suggests it may cause any of numerous potential health effects. SIRC believes that the California public would be more effectively informed by providing current, accurate information on the health effects of individual chemicals, which permits a more effective interpretation of potential concern from indoor air exposure. At the very least, this should include an appropriate characterization that not all chemicals grouped together in a table cause all the potential effects noted.

More appropriately, SIRC does not believe that it is productive to associate styrene with many of the health effects suggested by these two tables. We do not feel that, based on careful assessment of the data, an appropriate characterization of styrene’s potential health effects has been indicated. For the CARB’s reference, APPENDIX A to this letter provides a brief assessment of the animal and human data relative to carcinogenic potential, while APPENDIX B is a brief assessment of the data on liver, kidney or brain effects.

B. Delete Reference to Styrene as a Potential Cause of Respiratory Effects (p.31)

In the Report, styrene is cited as being associated with occupational asthma and respiratory infections in newborns (Delfino et al., 2003). SIRC has assessed the Delfino review and believes that the linkage between styrene and respiratory effects is not relevant to indoor air concentrations of styrene. An extensive literature search found a total of four cases of asthma reported to be caused by occupational exposure to styrene during the period of 1970 to 2004. Four cases out of the hundreds of thousands of styrene-exposed workers worldwide indicate that styrene-induced occupational asthma is not a significant workplace problem. Secondly, occupational exposures to styrene are 200,000-fold higher than the indoor air concentrations reported in the Report, or in other reports, and are thus not relevant to health effects from indoor air. Thirdly, Delfino et al. specifically examined the association of a number of indoor air pollutants with children’s asthma; they reported no association of styrene with asthma (Delfino et al., J. Exp. Anal. Environ. Epidem. 13: 348-363, 2003; Delfino et al., Env. Health Perspect. 110 (suppl 4): 573-589 (2002)).

Delfino also cites Diez et al. (Diez et al., Int. J. Hyg. Environ. Health 203: 23-28 (2000)), that styrene exposure was associated with increased respiratory infections in children. It should be noted that these were not healthy children. They were either very low birth weight (1500 -2500g, 3 lb, 5 oz – 5 lb, 8 oz), or whose cord blood had high levels of IgE (i.e. abnormal immune response).

C. Delete the Last Four Chemicals from Table 2.4 (p.32)

Table 2.4 is titled “Common Carcinogenic Indoor Air Pollutants.” This conveys a certainty that they cause cancer in humans, yet the last four chemicals on the list are either “under consideration” or “not classifiable.” To improve the credibility of this report, these four chemicals should be removed from table 2.4 and references in Table 2.1 and ES-1 should be deleted.

The inclusion of styrene in Table 2.4 as a “Carcinogenic Air Pollutant” is misleading. As the CARB correctly states, styrene’s carcinogenic potential currently is “under consideration” by the U.S. Environmental Protection Agency (USEPA), for its Integrated Risk Information System (IRIS) program. However, the suggestion that styrene’s USEPA classification is a “possible human carcinogen” is both premature and inaccurate, since the IRIS office has not issued even a draft IRIS review for styrene, which would then need to undergo scientific peer review. Also, when an IRIS determination is issued, any classification of styrene by USEPA likely will be characterized using a newer USEPA classification scheme that no longer uses the term “possible carcinogen,” and will be accompanied by a narrative description of how their conclusion is reached. Thus, inferring that styrene is a “possible carcinogen” is both premature and unlikely to reflect any potential USEPA classification category.

SIRC also would urge the CARB to consider the following comments, addressing whether styrene is fundamentally an appropriate candidate for inclusion in the Report.

D. Reconsider Inclusion of VOC’s in the Report Based on Prioritization Considerations

According the CARB, all VOC's that it considered (benzene, chloroform, formaldehyde, methylene chloride, paradichlorobenzene, perchloroethylene, phthalates, styrene, etc.) collectively account for roughly 2% of total indoor air costs and impacts (pp. 10, 85 & 90). From a priority-setting perspective, if all VOC’s constitute only 2% of the impact, focusing on any one VOC will address less then 1% of the overall issue. The state’s own estimate clearly points to focusing its resources in other areas.²

² SIRC supports the comments filed by the American Chemistry Council (ACC) in response to the draft report. Our suggestion of reconsidering the inclusion of VOC's is not intended to conflict with the ACC's critique of the use of the term VOC's and their collective treatment in the report.

E. Indoor Exposures to Styrene Should not be a Focus of Any Additional Control Efforts

The levels of exposure to styrene in indoor air are very low and no further control efforts to reduce them further are warranted. Sources of styrene in ambient air include principally industrial activity and motor vehicle exhaust. Indoor sources of styrene other than tobacco smoke are either natural in origin or are currently minimized through manufacturing processes. With regard to natural sources, styrene is a component of raw agricultural commodities, such as strawberries, wheat, peanuts, beef, and spices. There is evidence suggesting that styrene is a metabolite of microbiological processes that occur in wines, beer, grains, and cheeses. Pine and other evergreen trees also emit styrene.

With regard to manufactured products that are part of the food pathway, migration and diffusion studies demonstrate that exposure to styrene migration from food contact materials is limited. A 1999 study on the migration of styrene monomer from food-contact packaging to food estimated that the total dietary intake from polystyrene food-contact polymers would be 9 µg/day. Styrene concentration in indoor air has been measured in various regions of the country. Median concentrations of styrene in indoor air have been measured at 0.4 - 3.6 micrograms per cubic meter (mg/m³) (0.093 to 0.845 ppb).³

Styrenic materials may be part of some carpet systems, and styrene may be emitted by the rubber backing found on new carpets. However, as CARB noted in the draft report, the Carpet and Rug Institute (CRI) has developed indoor air quality programs to minimize the potential of emissions from new carpet installations (Report at p.106). The test procedures follow an approved methodology recognized by the USEPA and found in an ASTM standard (ASTM D-5116). Products meeting the emission criteria are allowed to display a label that signifies that the testing criteria have been met. For carpet, the allowable emission factor for styrene for a carpet sample is 0.4 mg/m². In carpet cushion, the allowable emission factor for total volatile organic compounds (TVOC) is 1.00 mg/m². In carpet floor covering adhesives, the criterion for TVOC emissions is 10.0 mg/m²/hr. New carpet emissions are typically not a factor within 96 hours after installation.⁴ The CRI label is on more than 70% of new carpets.⁵

³ Styrene can be found at low (ppb) levels in raw agricultural commodities, such as strawberries, wheat, peanuts, coffee, and beef. Styrene has been measured at higher levels (approximately 40 ppb) in cinnamon and in certain other foods and beverages. Steele, D.H., et al. Determination of Styrene and Benzene in Selected Foods, Midwest Research Institute (November 2, 1992); Steele, D.H., et al. Determination of Styrene in Selected Foods, J. Agric. Food Chem. 42:1661 (1994); Tang, W., Styrene in Foods and the Resulting Exposure in Humans, Dept. of Food Chemistry and Environmental Toxicology, University of Kaiserslautern (August 1992). The amount of styrene found in four ounces (113 grams) of some common foods include 5.6 µg in strawberries, 40.7 µg in coffee, and 7.1 to 22.6 µg in beer. There is evidence to suggest that styrene is a metabolite of microbiological processes that occur in wines, grains, and cheeses. Id. Due to the flavoring properties of styrene the Food and Drug Administration (FDA) permit it as a food additive. 21 C.F.R. §172.515. The amount of styrene used as a direct food additive is currently unknown, but thought to be limited.

⁴ Cornell University. Facility Planning and Management Notes, Vol. 1, No. 2 (Feb. 1996).

⁵ Herlihy, J. *Carpet — Environmental Manufacture, Installation, and Disposal*, Environmental Design and Construction (1997).

The CARB report correctly identifies tobacco smoke as a major indoor air concern. Styrene is one of more than 3,000 individual components which may be present in trace amounts in tobacco smoke.⁶ The concentration of styrene in cigarette smoke, which appears to vary with the condensation level associated with the cigarette, may range from 0.1 - 1 µg to 10 µg per cigarette.⁷ Indoor air exposures to styrene at levels of 2.2 µg/m³ have been recorded for smokers.⁸ While tobacco smoke in the indoor environment is clearly a matter of concern, as identified in the CARB report, the styrene component of tobacco smoke is clearly not the focus of that concern.

In summary, given the sources of styrene in indoor air, the levels of exposure, and steps that are currently taken in the manufacturing processes for some of the potential sources of concern (e.g., food contact materials and carpet), it is clear that additional efforts to control styrene exposure would be a misallocation of public health resources. **We believe that it is important for the CARB report to place these matters in the proper context so that the simple presence of styrene in the indoor environment is not interpreted by the California Legislature as an indication of unacceptable risk, or as a basis for further action focused on styrene.**

F. Conclusion

SIRC appreciates and supports CARB's draft Report, responding to the requirements of Assembly Bill 1173, and summarizing available information on indoor air pollution.

In the interest of providing the most accurate information that will inform both the Legislature, as well as the citizens of California, SIRC urges that inclusion of styrene in the final Report be based on a thorough assessment of all the available data on potential health effects, as well as the current regulatory status of styrene – especially in regard to the pending carcinogen classification of styrene by the USEPA. Further, SIRC strongly urges that discussion of indoor exposure to styrene be placed in the proper perspective in terms of these potential health effects, the low level of exposure, and the limitations on any possible further reductions in these exposures. We believe that placing styrene exposure in this context will lead to the conclusion that further efforts to control styrene exposures in indoor environments would be a misallocation of public health resources.

We respectfully request your consideration of the comments outlined above. We would be pleased to provide more detailed assessments on the health effects data

⁶ Brooks, et al. *Indoor Air Pollution: An Edifice Complex*, *Clinical Toxicology*, 29, 3:315-374 (1991).

⁷ Baggett, M.S., et al. *Quantitative Determination of Semivolatile Compounds of Cigarette Smoke*, *J. Chromatogr.* 97:79-82 (1974); Byrd, G.D. et al. *Isotope Dilution Gas Chromatography-Mass Spectrometry in the Determination of Benzene, Toluene, Styrene, and Acrylonitrile in Mainstream Cigarette Smoke*, *J. Chromatogr.* 503:359-368 (1990); Dmitriev, M.T. et al. *Hygienic Evaluation of Organic Substances in Tobacco Smoke*, *Gig. Sanit.* 8:7-11 (1983); Grob, K. *Gas Chromatography of Cigarette Smoke*, Ch. III: Separation of the Overlap Region of Gas and Particulate Phase by Capillary Columns, *J. Gas Chromatogr.* 3:52-56 (1965);

⁸ Byrd, G.D. et al. *Isotope Dilution Gas Chromatography-Mass Spectrometry in the Determination of Benzene, Toluene, Styrene, and Acrylonitrile in Mainstream Cigarette Smoke*, *J. Chromatogr.* 503:359-368 (1990); Higgins, C.E. et al. *Application of Tenax Trapping to Analysis of Gas Phase Organic Compounds in Ultra-Low Tar Cigarette Smoke*, *J. Assoc. Off. Anal. Chem.* 66:1074-1083 (1983).

summarized in Appendices A and B, and would welcome the opportunity to discuss these data with you and your CARB associates, should you have questions or require more information.

Very truly yours,

A handwritten signature in black ink, appearing to read "John O. Snyder". The signature is fluid and cursive, with the first name "John" and last name "Snyder" clearly legible.

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The document delivered electronically.

Attachments:
Appendix A
Appendix B

APPENDIX A

ASSESSMENT OF HUMAN AND ANIMAL DATA RELATIVE TO POTENTIAL CARCINOGENICITY OF STYRENE

Animal Data - In regard to styrene's potential carcinogenicity, the animal data provide only limited evidence of carcinogenicity based upon:

- The clear lack of carcinogenicity in rats, as supported by numerous studies in which rats were given styrene by a variety of routes, and
- Findings of only lung tumors in mice, particularly when exposed by inhalation.

Extensive mode of action data indicate that the mouse lung tumors are the result of cytotoxicity caused by *in situ* metabolism of styrene and are not relevant for human risk assessment. Fairly strong evidence indicates that ring-oxidized products of styrene are responsible for the cytotoxicity and styrene-7,8-oxide plays a minor role, if any. These ring-oxidized products are generated by CYP2F2 in the mouse lung. In contrast, the metabolism of styrene, including ring oxidation, in the human lung is extremely low and no activity of the human CYP2F1 to styrene has been detected. This provides further evidence that the mouse lung tumors are not relevant for human risk assessment.

Human Data – There are eight published epidemiological studies of workers in the reinforced plastics, composites, and styrene-butadiene rubber plants exposed to styrene, which are assessed as follows:

1. Monomer, polymer and styrene-butadiene rubber (SBR) manufacture - In the U.S. study (Ott et al., 1980, Bond et al., 1992), the authors reported that the risk among workers in high-exposure groups was unremarkable, and there was no pattern of risk with regard to year of first exposure or latency. Therefore, this does *not* indicate an association of styrene with increased cancer.

In a second study, Hodgson and Jones (1985) reported a significant increase in lymphoma (not leukemia) among 622 workers involved in the production of styrene monomer, polymerization and manufacture of finished products. However, workers were exposed to many other chemicals in addition to styrene. Significantly, no measure of styrene exposure was taken and no attempt was made to determine if the increase was “associated with styrene exposure.”

In the SBR cohort, most recently studied by Delzell and coworkers, IARC correctly reports that increased leukemia was more strongly correlated with butadiene exposure than styrene exposure, but concludes that concomitant exposures to styrene and butadiene “makes it difficult to disentangle the effects of these two exposures.” However, regarding leukemia, Delzell and coworkers (2001) concluded:

“After further adjusting each agent-specific set of RRs [Relative Risks] for the other two agents, a positive but imprecise relation remained for BD [butadiene]

and DMDTTC [dimethyldithiocarbamate] but not for STY [styrene]. . . . BD and DMDTTC, but not STY, were positively associated with leukemia in multivariate analyses. The independent effect of each agent was difficult to evaluate because of correlations with other agents and imprecision.”

Thus, although workers were often exposed to both butadiene and styrene, the authors indicate that when butadiene exposure was considered, styrene was not a factor in leukemia.

Accordingly, the collective studies do *not* provide evidence of increased cancer risk from styrene.

2. Reinforced plastics manufacture - A National Institute for Occupational Safety and Health study by Okun *et al.*, (1985), showed no increase in lymphatic or hematopoietic cancer. This study has since been updated by the addition of 21 years of follow-up (Ruder *et al.*, 2004). While it is still the smallest of the three independent studies (5201 workers), it has the longest follow-up (average 26 years). There still was no increase in lymphatic or hematopoietic cancers.

The other U.S. cohort study (Wong, 1990, Wong *et al.*, 1994) showed no excess in lymphatic or hematopoietic cancers relative to time since first exposure, duration of exposure or cumulative exposure. Wong performed two proportional hazard analyses: one with only cumulative exposure and one with cumulative exposure and length of exposure. The result of both models was the same. Thus, this study of 15,826 workers with an average of 19.5 years follow-up provides *no* evidence of styrene-related cancer increase.

A multicentric European study by Kogevinas *et al.* (1994) study reported no increased cancer when compared to the relevant country statistics, reported that the risk of lymphatic and hematopoietic neoplasms was increased based on internal comparisons among exposed workers after more than 20 years since their first exposure to styrene, and increased with increasing intensity of exposure, but not with increasing cumulative exposure to styrene. In 2002, the International Agency for Research on Cancer (IARC) dismissed the lack of increase based on cumulative exposure (normal metric) because they considered the estimations of cumulative exposure to be unreliable. However, because of the way average level of exposure (“intensity”) was calculated, if the duration of exposure was unreliable, then the average level of exposure was also unreliable.

The increases in the Kogevinas study are almost entirely contributed by the Danish sub-cohort, which was drawn from the Kolstad *et al.* (1994) study. The Danish sub-cohort contributed 49% of the overall lymphatic and hematopoietic cancers and 59% of the leukemias, while contributing only 39% of the cohort members and 32% of the person-years. Because the Epidemiology Subgroup at the 2002 IARC Working group on styrene stated that the Kolstad study was the

key positive study to justify upgrading the classification of the human data from “insufficient” to “limited,” a careful review of this study is clearly warranted. In this cohort there was no attempt to ascertain if any of the cases of cancer were among the minority of workers who were involved in lamination processes, which might be expected to involve styrene exposure, versus those not involved in any aspect of reinforced plastics manufacture. Furthermore, there are a number of issues of concern to consider with respect to cohort assembly, employment duration, exposure definition and relationships of cancers to styrene exposure. While Kolstad et al. (1994) found a significant excess of leukemia among workers hired before 1970 when a 10-year lag time was applied, this phenomenon was only observed among short-term workers (less than one year employment) with uncertain and undocumented exposure to styrene.

References

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APPENDIX B

ASSESSMENT OF STYRENE'S POTENTIAL TO CAUSE LIVER, KIDNEY, OR BRAIN DAMAGE EFFECTS

Acute high doses of styrene may cause liver damage in mice; this is either lethal in a few days or the mice recover. In rats, much higher doses cause increased liver weight, but not liver damage. In humans, effects on some blood enzymes or chemicals indicative of liver damage have been inconsistently reported; some studies have reported effects, while others have reported the same endpoints to be normal. Effects on kidney have not been found in any of the subchronic or chronic studies of styrene. In addition, kidney toxicity is not reported in workers exposed to styrene. Likewise, brain damage has not been found in any of the subchronic or chronic studies of styrene in rats or mice. Furthermore, there is no evidence of brain damage in humans exposed to styrene. High concentrations of styrene induce acute symptoms of intoxication, but these dissipate when exposure ceases and no permanent effects are seen.

Based on the available data, SIRC does not believe that styrene can be accurately characterized as being a potential cause of liver, kidney, or brain damage.