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Report from George Cruzan, PhD on proposed Bill 127

The proposed County of Maui Ordinance (Bill 127(2016)), states in Section 1 “polystyrene has significant negative impacts on the environment, contributes to the potential death of marine animals and avian populations through ingestion, and is a suspected human carcinogen.” The last phrase is not correct. Polystyrene is not a suspected carcinogen, nor should it be confused with styrene.

1. Credentials

George Cruzan, PhD. BA in chemistry 1965 The King’s College. PhD in biochemistry 1969 Purdue University. Professional toxicologist 1976 to present (41 years), Diplomate of American Board of Toxicology 1980-2015. President of ToxWorks (toxicology consulting firm) 1995 to present (22 years).

Studying health and environmental effects of styrene and leading \$20 million research program, 1989 to present (28 years)

2. Polystyrene

Polystyrene is a polymer synthesized by connecting many molecules of styrene together, and should not be confused with the styrene. Styrene is a liquid; polystyrene is a solid. Although the names sound familiar and may be confusing, styrene and polystyrene are different and have completely different properties. Styrene is reactive; polystyrene is inert. In other words, polystyrene does not have the properties of styrene. This is true of all polymers; they are different from the monomer they are synthesized from. A common example is the difference between sugar and wood. Sugar is a monomer with distinct properties. Join many sugar molecule together and you get cellulose, the main polymer in wood.

Thus the health effects of polystyrene should be based on polystyrene, not on styrene. There are no adverse health effects on humans from polystyrene.

Polystyrene contains some residual unreacted styrene. Typical products contain less than 300 ppm. Thus a typical foam cup, weighing 1.6 grams, will contain less than 0.5 milligram (mg) styrene trapped within the polymer.

2. Sources of Styrene Exposure

Styrene is everywhere in minute amounts. Ambient air always contains styrene from automobile exhaust, cigarette smoke, wood smoke, plant emissions. Average concentration is about 4 microgram (ug)/ cubic meter (m³). Typical human breathing is 20 m³/day. Therefore, normal inhalation of ambient styrene from air is 80 ug/day (4 ug/m³ * 20 m³/day).

Styrene is naturally present in several foods. It has been measured in foods that have not had contact with polystyrene containers. It is present in the highest concentration in coffee, cinnamon, beer and nuts. Based on average consumption, it is estimated that the average person ingests 9 ug styrene per day from naturally occurring styrene in their food.

There is a small amount of unreacted styrene within polystyrene; some of this may migrate into food in the container. The residual styrene will migrate from areas of higher concentration to lower areas of concentration. The only styrene that can migrate into food or drink is the styrene that is at the interior surface of the cup. As this styrene migrates from the surface of the cup into the food or drink, additional molecules of styrene migrate to the surface and then into the food. About half of the unreacted styrene will migrate over time to the inside surface and half to the outside surface.

The results of a 2013 study show that the maximum amount of styrene that could migrate from polystyrene food-contact packaging is calculated to be 6.6 micrograms (about 1 millionth of a teaspoon) per person per day. As mentioned above, several foods (e.g., coffee, cinnamon) naturally contain styrene; the average consumption of styrene from natural food sources is about 9 ug/day. The FDA's acceptable daily intake of styrene is calculated to be 90,000 micrograms per person per day. This demonstrates a safety factor of more than four orders of magnitude (10,000 times). Link: <https://plasticfoodservicefacts.com/main/Safety/Safety-of-PS-Foodservice-Products>

Total styrene migration from all PS foam food service products results in ingestion of 4 ug/day styrene.

Total styrene exposure averages about 96 ug/day.

3. Health Effects of Styrene

Fiberglass workers have highest exposures, especially in the past. Exposure greater than 50 ppm for 8 hrs. may cause headaches, or slowed reaction time. Exposures greater than 30 ppm 8 hr./day for more than 10 years may cause a slight reduction in hearing.

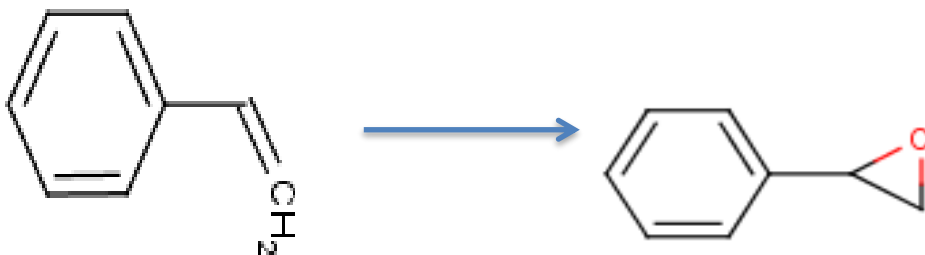
US National Toxicology Program lists styrene as reasonably anticipated to be a human carcinogen in Report on Carcinogens (ROC). This is based on suggestive increases in cancer among highly exposed reinforced plastics workers and on increased lung tumors in mice exposed to styrene for 2 years.

The causes of deaths in most of the cohorts (or groups) of reinforced plastics workers have been updated since the ROC in 2011. The further evaluations of these workers do not support a conclusion that styrene induces cancer in these workers. Furthermore, even if there were evidence of cancer in these workers, it would not imply a cancer hazard from residual styrene in polystyrene. Exposure of these workers is 500,000 fold higher than exposure from polystyrene products.

Recent research, since the evaluation by the NTP, has demonstrated that styrene-induced lung tumors in mice is caused by specific metabolism of styrene in mouse lung, which does not occur to a significant extent in rats or humans.

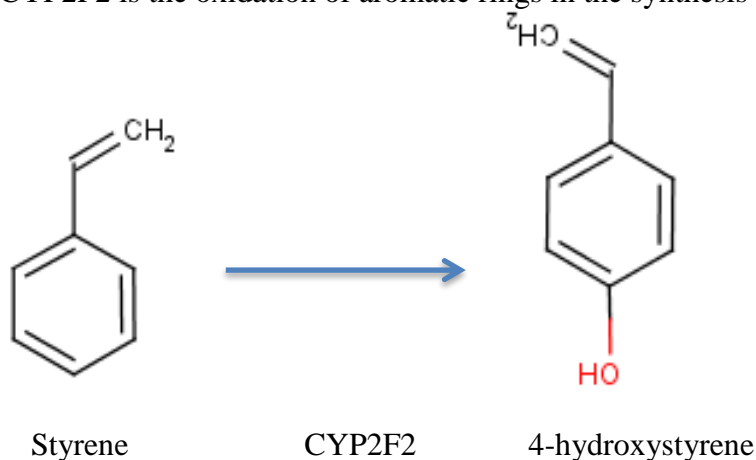
An enzyme CYP2F2 is present in high concentration in mouse lungs. In genetically modified mice that do not produce CYP2F2, styrene has no effect in the lung (Cruzan et al., 2012, 2017). In a recently completed study, 78% of normal mice (that produce CYP2F2) exposed for their lifetime to a very high concentration of styrene had neoplastic or pre-neoplastic lung alterations (Cruzan et al., 2017). There were no neoplastic or pre-neoplastic alterations in CYP2F2-deficient mice from lifetime exposure to a very high concentration to styrene (Cruzan et al., 2017). Furthermore, assessment of gene expression clearly demonstrated that these alterations were not caused by any genotoxic reactions (Andersen et al., 2017). Rats and humans have much lower levels of CYP2F2 in the lung and do not have any lung toxicity from styrene.

Metabolism of styrene by CYP2F2 causes the formation of different metabolites than normal styrene metabolism. Styrene metabolism in rats and humans is mainly by CYP2E1, which produces styrene-7,8-oxide. It has been postulated that any toxic or neoplastic effects of styrene are caused by styrene-7,8-oxide. A recent study demonstrates that styrene-7,8-oxide has no effect on mouse lung unless it is metabolized further by CYP2F2 (Cruzan et al., 2012); i.e., in the absence of CYP2F2, styrene-7,8-oxide has no effect on mouse lung.



Styrene CYP2E1 Styrene-7,8-oxide

CYP2F2 cause oxidation of the aromatic ring of styrene, producing 4-hydroxystyrene, 3,4-dihydroxystyrene, and 4-hydroxystyrene-7,8-oxide. 4-Hydroxystyrene was toxic to mouse lungs at a 50-fold lower dose than styrene-7,8-oxide following 2 weeks of exposure (Cruzan et al., 2005). Ring oxidation of styrene by CYP2F2 could be expected because the normal function of CYP2F2 is the oxidation of aromatic rings in the synthesis of Coenzyme Q.



Summary of the mode of action

	Mouse	Rat
Lung tumors in mice, not in rats	Supporting	Supporting
Lung toxicity in mice, not in rats	Supporting	Supporting
Toxicity and metabolism in Club (Clara) cells in mice, not rats	Supporting	Supporting
Lung toxicity from 4HS in mice, not rats	Supporting	Supporting
Elimination of lung toxicity from styrene and SO in CYP2F2-KO mice	Supporting	
80% reduction on ring-oxidized metabolites in CYP2F2-KO mice	Supporting	
Lower level of CYP2F4 in rats does not produce toxicity		Supporting
Greater lung toxicity in mice from 4HS than from SO	Supporting	
Limited toxicity from 4HS in 2F2-KO mice	Supporting	
3- or 4-methylstyrene do not cause lung tumors in mice	Supporting	
Enhanced expression of cell cycle genes in WT mice	Supporting	
No enhanced gene expression from styrene in KO mice	Supporting	

Inconsistent and questionable increases in cancer deaths among workers with very high exposures to styrene do not imply a cancer hazard from residual styrene in polystyrene products because the exposures are 500,000 fold lower. Increased tumors in mice are not indicative of human cancer risk from styrene because the effects in mouse lung are

caused by metabolism of styrene by CYP2F2, which does not occur in rats or humans to a biologically meaningful extent.

4. Risk Assessment

Exposure of reinforced plastics workers has been 2,000,000 ug/day over many years. A microgram (ug) is 1 millionth of a gram, about 1/4 millionth of a teaspoon.

Total styrene naturally in food results in ingestion of 9 ug/day styrene. Total styrene migration from all PS foam food service products results in ingestion of 4 ug/day styrene (about 1 millionth of a teaspoon). Inhaled styrene from ambient air results in intake of 80 ug/day styrene. The total styrene intake is about 96 ug/day. Banning PS foam products would reduce that by less than 5%.

US EPA acceptable exposure is 20,000 ug/day. Exposure from PS foam is less than 4 ug/day. 5000 fold safety factor.

Dr. Linda Birnbaum, Ph.D., Director, U.S. National Toxicology Program was quoted widely in [Associated Press](#) reports in June 2011: "Let me put your mind at ease right away about polystyrene foam*" ... [the levels of styrene from polystyrene containers] "are hundreds if not thousands of times lower than have occurred in the occupational setting...In finished products, certainly styrene is not an issue." *Source: news reports of Associated Press story, June 2011*

John Bucher, associate director of the National Toxicology Program, was quoted in [Associated Press](#) reports in August 2011: "The risks, in my estimation, from polystyrene are not very great," he said. "It's not worth being concerned about."
Source: news reports of Associated Press story, August 2011

U.S. National Institutes of Environmental Health Sciences (NIEHS)

[NIEHS](#) in June 2011 noted: "Styrene should not be confused with polystyrene (foam)*. Although styrene, a liquid, is used to make polystyrene, which is a solid plastic, we do not believe that people are at risk from using polystyrene products."
Source: NIEHS web site

The amount of styrene migrating from PS foam foodservice products is so small that there is no measurable risk. Styrene from foam is not a health issue. In conclusion, no government agencies consider polystyrene to be a carcinogen, nor to pose any health risk.