



Styrene Information and Research Center (SIRC)

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**Styrene Information and Research Center Briefing Paper:
New Research Findings Show Mouse Tumors Are Not Relevant for Human Risk
Assessment; Styrene Does not Belong in NTP *Report on Carcinogens***

Preliminary findings from new research clearly show that data from toxicity tests with laboratory animals for the versatile, widely used chemical styrene do not support a conclusion that it is a human carcinogen, and undermine the basis for a proposed cancer classification for styrene by the U.S. National Toxicology Program (NTP).

These findings directly rebut the NTP's current recommendation to list styrene as "reasonably anticipated to be a human carcinogen" in its upcoming (12th) *Report on Carcinogens (RoC)*, which is expected to be published within the next several months.

The cutting-edge research -- supported by the Styrene Information and Research Center (SIRC) -- uses customized "knock-out" mice (i.e., mice bred to have a specific gene removed) to test whether or not mouse lung toxicity and, ultimately, tumors observed following inhalation of styrene in previously conducted research are relevant for human risk assessment¹.

Dr. Xinxin Ding of the State University of New York-Albany has received funding from the National Institute of Environmental Health Sciences (NIEHS) to develop mice in which key metabolizing enzymes in the lung are "knocked out." SIRC provided supplemental funding to Dr. Ding to create mice bred with the CYP2F2 gene² removed specifically to test styrene toxicity in the lung. Dr. Ding's research relies on techniques that won the Nobel Prize in Medicine³ in 2007. The NTP is part of NIEHS.

Scientific studies over many years have shown that normal mice develop lung tumors from styrene exposure, while humans and rats do not. The prior research also suggested that a particular type of gene in normal mice produces high levels of an enzyme in mouse lung tissue that could be responsible for its unique sensitivity to styrene lung toxicity and subsequent lung

¹ A briefing paper on "Styrene's Mode of Action" -- how it acts within and upon an organism to produce effects -- is available on the Styrene Information and Research Center Web site, www.styrene.org.

² See the "Styrene's Mode of Action" briefing paper, available at www.styrene.org, for further information on the CYP2F2 gene.

³ Mario R. Capecchi, Sir Martin J. Evans, Oliver Smithies "for their discoveries of principles for introducing specific gene modifications in mice by the use of embryonic stem cells."

tumors. The corresponding genes in humans and rats produce much lower levels of this enzyme in the lung.

The early findings from this new and ongoing research, indicating no styrene toxicity in the lungs of the “knock-out” mice, have been provided to NIEHS/NTP Director Dr. Linda Birnbaum and Health and Human Services (HHS) Secretary Kathleen Sebelius. They also have been submitted⁴ for presentation at the 2011 Society of Toxicology meeting.

The NTP is moving to include styrene as “reasonably anticipated to be a human carcinogen” in the 12th *Report on Carcinogens* based partly on increased lung tumors in mice found in earlier studies. This latest research in the “knock-out” mouse model demonstrates that styrene lung toxicity in mice is totally dependent on metabolism associated with a particular enzyme. Rats and very likely humans are not susceptible to styrene lung effects because they have much lower levels of this enzyme in their lungs.

Clearly, the early findings from this important research significantly lessen the scientific justification for NTP to include styrene in its 12th *Report on Carcinogens*.

This ongoing scientific investigation also demonstrates how taxpayers’ money dedicated to this type of NIEHS-funded research can be leveraged from a practical standpoint – by using customized mice to inform critical decisions on the human health relevance of animal toxicity responses.

Styrene-based materials, including polystyrene, ABS, styrene-butadiene rubber, styrene-butadiene latex and styrene composites are used to make a wide variety of useful products⁵ that extend the life of transportation infrastructure; increase fuel efficiency; protect our troops; produce “green” energy; increase consumer safety; prevent pollution; save lives, and improve sports. The U.S. styrene industry represents some half-million workers at thousands of small and large businesses across all 50 states.

-- SIRC --

⁴ “Initial CYP2F2 Knock-Out Mouse Exposure Study Findings” abstract available upon request.

⁵ More information can be found in the SIRC booklet *Styrene: Bringing Peace of Mind and Quality to Life* and in “Questions and Answers about Styrene,” both of which are available on the SIRC Website, www.styrene.org.