



Centers for Disease Control
and Prevention (CDC)
Atlanta, GA 30333

December 9, 2011

Mr. Jack Snyder
Executive Director
Styrene Information and Research Center
801 N. Quincy Street – Suite 700
Arlington, Virginia 22203

Dear Mr. Snyder:

The Agency for Toxic Substances and Disease Registry (ATSDR) is responding to the February 13, 2011 Information Quality Request for Correction regarding ATSDR's Toxicological Profile for Styrene ("Profile") that you submitted on behalf of the Styrene Information and Research Center, Inc. (SIRC). You have asked for additional studies to be included in the Styrene Toxicological Profile, which you contend support conclusions that conflict with those of ATSDR in the Profile related to the carcinogenicity of styrene. You also contend that some of the information in the Profile is not supported by the scientific literature and does not meet ATSDR's information quality assurance of "objectivity" and "utility." The response below describes the intent of the Styrene Toxicological Profile and our responses to your requests that specific peer review studies be cited.

As stated in the Foreword of all toxicological profiles, "The ATSDR toxicological profile succinctly characterizes the toxicologic and adverse health effects information for these toxic substances described therein. Each peer-reviewed profile identifies and reviews the key literature that describes a substance's toxicologic properties. Other pertinent literature is also presented, but is described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced." ATSDR does not classify substances as to their carcinogenicity. The toxicological profiles provide a non-exhaustive summary of relevant cancer literature and classification from various sources.

The Styrene Profile was reviewed and posted for public comment in 2007. In the final Profile issued in November 2010, following an established practice for development of toxicological profiles,¹ we considered relevant studies through 2009 and stated that HHS had not yet "evaluated the carcinogenic potential of styrene." After the publication of the Styrene Toxicological Profile, the Department of Health and Human Service (DHHS) published the Report on Carcinogens, Twelfth Edition classifying styrene as "reasonably anticipated to be a human carcinogen." In response, ATSDR issued an Addendum to the

¹ http://www.atsdr.cdc.gov/toxprofiles/guidance/profile_development_guidance.pdf

Styrene Profile² dated September 12, 2011, stating that ATSDR and the National Center for Environmental Health were included in the National Toxicology Program (NTP) deliberations on styrene carcinogenicity and agree with the NTP in its classification of styrene. The conclusions in the Styrene Toxicological Profile are also consistent with those of the International Agency for Research on Cancer (IARC).

You requested that specific studies be added to the Styrene Toxicological Profile. Our rationale for not including them in the Profile is discussed below.

Boffetta et al. (2009). The Boffetta et al. paper reference is a review of literature on epidemiologic studies of styrene and cancers. The primary studies by Kogevinas et al. (1994), Ruder (2004), and Wong et al. (2004) reviewed by Boffetta et al. were already discussed in the Styrene Toxicological Profile. ATSDR chose to review the primary references, rather than rely on the review article by Boffetta et al.

Cruzan et al. (2009). Cruzan et al. (2009) reference was not cited in the Styrene Toxicological Profile. As the profiles are not intended to be exhaustive, the Cruzan et al. (2009) paper was not cited in the Styrene Profile because the pertinent information related to styrene provided by this study was included in Cruzan et al. (2002) publication and was already cited in the Profile. The 2009 Cruzan article had additional information on other chemicals but no additional relevant information on styrene.

Carlson papers. You commented that many of Dr. Carlson's papers were not cited in the Styrene Toxicological Profile. These papers reported on characterization of P450 isoenzyme CYP2E2 in metabolism of styrene to styrene oxide and 4-vinylphenol, a minor metabolite of styrene. Such information was already included in the Profile (page 117). Again, the profiles are not intended to be exhaustive and all-inclusive documents; the Carlson papers cited by the requestor were not included in the Styrene Toxicological Profile because they did not substantively add to information already in the Profile from other sources.

EU Risk Assessment Report. The EU Risk Assessment Report on Styrene was not included in the Styrene Toxicological Profile because it was, as you acknowledge, in draft, meaning that the scientific contents of the document or even its conclusions may change.

CONCLUSION:

ATSDR believes that information provided in the Styrene Toxicological Profile satisfies the ATSDR's information quality guidelines 3 with respect to "objectivity" and "utility."

According to the OMB Guidelines,⁴ "[i]f the results have been subjected to formal,

² <http://www.atsdr.cdc.gov/toxprofiles/profilesaddenda.asp>

³ <http://aspe.hhs.gov/infoquality/guidelines/cdcinfo2.shtml> and <http://www.cdc.gov/maso/qualitycontrol/Guidelines.htm>

⁴ http://www.whitehouse.gov/omb/fedreg_final_information_quality_guidelines

independent, external peer review, the information can generally be presumed to be of acceptable objectivity.” The Styrene Profile presents information on peer-reviewed studies with both positive and negative findings in an accurate, reliable and unbiased manner. The profile reflects ATSDR’s assessment of relevant toxicological testing and information that has been peer-reviewed. Staff of the Centers for Disease Control and Prevention and other Federal scientists have also reviewed the profile. The Styrene Toxicological Profile was peer-reviewed by a nongovernmental panel and was also made available for public review. Additionally, ATSDR believes that the “utility” criterion is satisfied. The Toxicological Profile is useful to the reader. It is a public resource document that provides information from published, publicly available information on styrene including use, production, exposure, health and toxicology information, analytic methods, and regulations and guidelines, and is available in both electronic and printed formats. As noted above, no changes to the Profile will be made as a result of your information quality correction request.

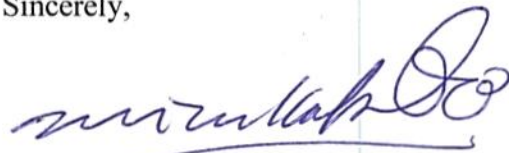
If you wish to appeal this response to your request for correction, you may submit a written appeal (Request for Reconsideration) or electronic request for reconsideration within 30 days of receipt of our response. The appeal must state the reasons why the agency response is insufficient or inadequate. You must attach a copy of your original request and the agency's response to it. Also, clearly mark the appeal with the words, "Information Quality Appeal" and send the appeal:

Mail:

Centers for Disease Control and Prevention
Management Analysis and Services Office
1600 Clifton Road, N.E., Mailstop E-11
Atlanta, Georgia 30333 or

Fax: 404-929-2781 or Electronic-Mail: InfoQuality@cdc.gov

Sincerely,



Vikas Kapil, DO, MPH, FACOEM
Chief Medical Officer and Associate
Director for Science, National Center
for Environmental Health, and
Agency for Toxic Substance and
Disease Registry