Dr Ruth Lunn,
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19th October 2008

Subject: Unjustified classification of styrene under NTP's 12th Report on carcinogens

Dear Dr. Lunn,

I am writing to you on behalf of the Styrenic Steering Committee and Styrene Producers Association, affiliated to the European Chemicals Industry Council[1] concerning the National Toxicology Program's (NTP) Report on Carcinogens Expert Panel recommendation that styrene be listed as "reasonably anticipated to be a human carcinogen" in the NTP's 12th Report on Carcinogens (RoC).

The RoC recommendation came as a surprise especially as an extensive and thorough Risk Assessment of styrene undertaken in the European Union concluded that styrene does not cause cancer in humans. We have added the section detailing this conclusion at the end of this letter together with a link to the complete RAR[2].

The EU Risk Assessment Report is based on a 10 year scientific review and was confirmed by the European Union Technical Committee for Classification and Labelling in 2007 which agreed that styrene does not have to be classified for carcinogenicity. This conclusion was also agreed upon by EU TCNES[3].

Although the classification criteria of the EU and NTP do not exactly correspond to each other, both are so similar that the different conclusions between the NTP proposal and the non-classification in the EU will severely cause confusion within the industry, international regulatory community and the general public. Harmonisation is fundamental and actually totally in line with the implementation of the GHS aiming at ensuring a common basis and above all, avoiding, market uncertainty.

In the light of the above, we would like to request a re-evaluation of the recent RoC recommendation on styrene. We remain at your disposal to provide you with any scientific information at EU level you may require for this re-evaluation.

In anticipation of your reply on this matter,

Yours sincerely,

Dr. Oliver Sloan osl@cefic.be
Director Styrenics Chain, European Chemical Industry Council, CEFIC
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[1] CEFIC - http://www.styrenemonomer.org

[2] Styrene risk assessment report: as prepared by the United Kingdom Health and Safety Executive
http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/DRAFT/R034_0001_0711_env_hh.pdf

[3] Technical Committee for New and Existing Chemicals. This Committee is in charge of the implementation of the EU Regulation 793/93 on Existing Substances and is composed by scientific experts of each of the 27 EU Member States

Extract from Styrene Risk Assessment Report (Human Health section, page 275)

(Note: Permission to include this extract has been given by the United Kingdom Health and Safety Executive government department, the author of the RAR)

4.1.2.8.3 Summary of carcinogenicity

In relation to human studies, several cohort and case-control studies covering workers exposed to styrene are available. In large, well-conducted studies, cancer mortality was investigated in the GRP industry with relatively high exposure to styrene and no significant exposures to other chemicals. In these studies, and in studies in styrene production workers, 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.

The carcinogenic potential of styrene has been explored in rats and mice, using the inhalation and oral routes of exposure. A carcinogenic effect of styrene towards the lung is evident in the mouse. This has been shown in a well-conducted lifetime inhalation study in CD1 mice at exposure concentrations of ≥ 20 ppm styrene and, somewhat less convincingly, in an oral study in mice of the B6C3F1 strain. The inhalation study, which included extensive histopathological examination, showed that the tumours (prevalently adenomas) were preceded by cytotoxicity characterised by early Clara cell toxicity followed by progressive bronchiolar epithelial hyperplasia and bronchiolar-alveolar hyperplasia.

In the rat, styrene has not exhibited any clear evidence of carcinogenic potential by the inhalation or oral route. In individual studies there have been isolated findings of statistically significantly higher incidences of various particular tumour types in particular groups of styrene-treated animals, compared with the in-study controls. However, the findings have been within historical background ranges, not reproducible between studies, in some cases have not shown an upward trend with increasing dose, and have not been associated with evidence of underlying styrene-induced changes at the site in question.