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Ihre Nachricht

Ihr Zeichen

Unser Zeichen

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14 May 2013

RE: *Public Comment Submitted by the CEFIC Phenol & Acetone Producers Sector Group: Draft NTP RoC monograph on Cumene*

Dear Dr. Lunn,

The CEFIC Phenol & Acetone Producers Sector Group would like to submit a list of references, relevant to the carcinogenicity of Cumene.

The list of references is based on the Chemical Safety Report that has been submitted for Cumene to meet the European regulatory requirements under REACH.

The reference list is in large parts based on the references used for the European Risk Assessment report for Cumene (2001). New data include the 2009 NTP study on the carcinogenicity of Cumene.

The Chemical Safety Report discusses all available data and, after dissemination of the REACH registration dossier, we can share that the conclusions are as follows:

Based on criteria set by NTP it was concluded by the authors that Cumene showed clear evidence of carcinogenicity based on adenoma of nose and adenoma or carcinoma of the kidney (male rats only).

The male rat kidney toxicity and resulting tumours fit the alpha-2u-globulin mode of action (MOA). This MOA does not occur in humans and, therefore, these tumours are not relevant for human risk assessment.

The effects observed in the respiratory epithelium are mediated by cytotoxicity and regenerative hyperplasia. The cytotoxicity is derived from species specific metabolic activation via CYP2F4 in rats.

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Species differences observed between mouse and rat are likely contributed to different enzymatic metabolism by CYP2F2 in mouse and CYP2F4 in rat. The human CYP2F1 is much less prevalent in these tissues and is much less effective at metabolizing these compounds than either 2F2 or 2F4.

Therefore, this mode of action is of low relevance for humans, and the relevance for human health risk assessment should be considered with care.

Cumene is a natural component of fuels. The vast majority of general population exposure to cumene is attributable to mobile and point source emissions from fuels, primarily gasoline. The animal toxicity and carcinogenicity of wholly-vaporized gasoline have been extensively studied. The draft monograph does not consider any of the fuel toxicity evidence, which indicates a substantially lower concern for a potential human cancer hazard.

In comparison with the big number of individuals exposed to fuel vapours the number of workers in the cumene, phenol and acetone plants is extremely small. In such plants cumene is handled in close systems, and the exposures are very limited (usually < 1 ppm in the air at the workplace, in the wastewater and in the offgas of the phenol/acetone plants). Worldwide more than 98 % of the produced cumene is used for the phenol/acetone manufacture.

Therefore we think that the proposed listing of cumene in the US National Toxicology Program 13th edition of the Report on Carcinogens (RoC) as "Reasonably anticipated to be a human carcinogen" is unwarranted.

Kind regards.

[Redacted]

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Encl.

Cumene-References

Cumene - References

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