SCIENTIFIC CONTRIBUTION

JUNE 2022

Formacare scientific contribution to the consultation on the IRIS Risk Assessment of US EPA on formaldehyde

Formacare, the sector group of the European Chemical Industry Council (Cefic), representing key European producers of formaldehyde and derivatives, welcomes the opportunity to provide comments to the draft IRIS Risk Assessment of US EPA on formaldehyde.

We are concerned about the draft IRIS Risk Assessment as it is not consistent with the scientific and regulatory conclusions on formaldehyde in the European Union. This contribution aims to highlight some data which we would like to bring to your attention[1].

About formaldehyde

Formaldehyde is a very versatile building block. It is used in a wide variety of applications in the construction, automotive and furniture industries. Given formaldehyde's excellent adhesive and binding properties, the majority of formaldehyde produced in the EU is made into resins. These are essential to produce, for instance, wood-based panels and particle boards used in construction and furniture making.

European Union regulations for formaldehyde

Formaldehyde is a very well-known chemical. It is one of the first that having registered under the EU REACH regulation (EC) No 1907/2006 and benefits from decades of extensive scientific research.

Formaldehyde is already highly regulated: consumer and worker safety are ensured in the European Union via harmonised classifications under the (EC) No 1272/2008 Regulation, existing and forthcoming REACH restrictions and the implementation of an EU-wide Binding Occupational Exposure Limit (BOEL). This BOEL is based on the evaluation of the European Scientific Committee on Occupational Exposure Levels (SCOEL) which derived an occupational exposure limit (OEL) of 0.3 ppm TWA and a short-term exposure limit (STEL) of 0.6 ppm. The opinion of the SCOEL was joint to this submission.

An important prerequisite for the derivation of these exposure limits was the categorization as a so-called group C carcinogen, i.e. a genotoxic carcinogen with a mode-of-action based threshold. For all relevant steps of local carcinogenesis, clear No-Observed-Adverse-Effect-Concentrations (NOAECs) could be identified (cf. page 9 of the joint SCOEL document):

> *"Experimental studies support that the local carcinogenesis at the portal-of-entry is pivotal. In the sensitive rat species, the apparent LOAEC was 6 ppm, and the apparent*

[1] This data was previously shared with the European Chemicals Agency (ECHA) in 2020 as part of the public consultation for the purpose of a restriction on formaldehyde and formaldehyde releasers in articles under the REACH Regulation (EC) No 1907/2006. This procedure is still ongoing.

NOAEC was 2 ppm for nasal cancer. Experimentally, the histopathological NOAEC for nasal effects of FA in rats and monkeys is 1 ppm and the NOAEC for regenerative cell replication is 2 ppm. At these NOAECs, the FA-DNA adducts were less in monkeys than in rats as was the relationship of exogenous/endogenous DNA adducts, which is in line with the assumption that humans should be a less sensitive species. The new studies confirm that local FA-DNA adducts show a highly non-linear relationship with external FA exposures. At ⩽ 2 ppm FA, the FA DNA-adducts induced by external exposures comprise a minor portion of the total FA-DNA adducts, which were driven mainly by internal (naturally generated) FA. This is supported by considerations on toxicokinetics, concluding that the intracellular FA concentration increases only slightly, and the intracellular glutathione concentration decreases only slightly in this range and that the homeostasis within the epithelial cells would not be affected. Therefore, the apparent NOAEC of 1 ppm can be considered a mode-of-action based NOAEC for carcinogenic effects at the portal-of-entry."

Formacare views on the IRIS Risk Assessment of US EPA

In the IRIS Risk Assessment, calculated unit risk estimates were in the range of 6.4 x 10^{-6} and 3.4 x 10^{-5} per µg/m^3 for the respective cancer types and reference concentrations (RfCs) for non-cancer health effects were derived in the order of 0.001-0.01 mg/m^3. It is worth noting that, as given in the WHO indoor guidance documentation from 2010[2] and updated in 2017[3], the formaldehyde concentration in exhaled air from humans is just in the same range: "*Human exhaled air contains formaldehyde in concentration in the order of 0.001–0.01 mg/m^3, with an average value of about 0.005 mg/m^3"*. Formacare would recommend putting the unit risk estimates and RfCs for the respective diseases in perspective with the respective prevalence considering actual exposures. This could avoid that the assessment misses capturing the possible risk from formaldehyde exposure in indoor environments and at the workplace.

Our conclusion

Formacare is deeply concerned about the discrepancy between the ongoing assessment of the US EPA and the latest scientific and regulatory conclusions on formaldehyde in the EU. Given the implications of the EPA draft assessment for many stakeholders including beyond the USA, and considering the available data from a broader perspective, we hope that our contribution will effectively support a final sound evaluation of the risks from formaldehyde. We finally and respectfully call on the US EPA to consider including Formacare's scientific input into the final IRIS Risk Assessment on formaldehyde.

[2] https://www.euro.who.int/__data/assets/pdf_file/0009/128169/e94535.pdf
[3] https://link.springer.com/content/pdf/10.1007/s00204-016-1733-8.pdf

Formacare remains at the disposal of the US EPA for any further discussions in the context of the ongoing work, with the ultimate goal of promoting science-based, health-protective international regulations for formaldehyde.

About Formaldehyde
Formaldehyde is a naturally occurring chemical widely produced for applications such as glues for wood panels, coatings for paints, lubricants, high-end plastics, etc. The formaldehyde value chain provides direct jobs to 30,000 people in Europe, with as many as 1,7 million jobs in downstream sectors being supported by formaldehyde applications.

About Formacare
Formacare is the formaldehyde sector group of the European Chemical Industry Council (Cefic) representing key European producers of formaldehyde, aminoplast glues and polyols. Made up of representatives from large chemical and manufacturing companies across Europe, Formacare promotes the safe use and manufacturing of formaldehyde in accordance with the strictest health, safety and environmental regulations.

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