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Short report from Danish Working Environment Authority´s (AT) Occupational exposure limit quality committee. Evaluation of the report: Carbon black: Scientific basis for setting a health-based occupational exposure limit

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This report is based on a meeting 8th April 2019 at AT where the results from the report were discussed after the authors presented the content of the report. The members of the quality committee had the chance to ask questions to the authors.

The Report: Nicklas Raun Jacobsen, Niels Hadrup, Sarah Søs Poulsen, Karin Sørig Hougaard, Anne Thoustrup Saber and Ulla Vogel. Carbon black: Scientific basis for setting a health-based occupational exposure limit. The National Research Centre for the Working Environment (NFA) November 2018. ISBN 978-87-7904-354-1

Overall evaluation of the report

The report reviews data relevant to assessing the hazard of CB nanomaterials (CB NMs) in humans and animals. Furthermore, toxicokinetics and mechanisms of toxicity are reviewed, and core previous risk assessments of CB NMs s are summarized. The scientific basis for setting an occupational exposure limit (OEL) are presented and based on this, the authors suggest a health based OEL for CB NMs.

In general, the report is well written with a clear structure and easy to follow with tables summarizing human and animal studies.

The committee judge the included literature in general to be sufficient and covering. The literature search was performed by a research librarian, and we recommend including details of searched databases and the search strings including dates for covering of the search as an appendix in the report.

Carbon black (CB), CAS number 1333-86-4, is a high volume black solid inorganic and poorly soluble compound produced by controlled incomplete combustion of various carbonaceous gases or liquid products. It is produced by a variety of methods. The authors consider toxicity data from all types of CB NMs. This decision is supported by the committee.

The authors chose to focus on studies dealing with occupational exposure by inhalation, and the committee supports that decision, as inhalation probably is the major route of exposure for CB NM´s.

The authors based the suggested health-based OEL on data from experimental animal studies due to a lack of sufficient epidemiological studies of the needed quality, and the committee supports this decision.

The authors regard inflammation and carcinogenicity as the critical adverse effects, and the committee agree on this decision. It is noted however, that the authors in the risk assessment use a measure where they include both benign and malign tumours in the evaluation of cancer risk, which tends to overestimate the carcinogenic effects of CB NM. The authors based the inclusion of benign tumours on the REACH guidelines stating that: “malignant tumours as well as benign tumours that are suspected of possibly progressing to malignant tumours are taken into account in obtaining the dose-descriptor values” (ECHA, 2012), and the committee supports this decision, but it would be of relevance to consult an expert in pathology to evaluate whether keratinizing cystic squamous-cell tumours are suspected progressing to malignant tumours.

The authors state that there is substantial evidence for both primary and secondary genotoxicity of CB NM, and the committee supports to consider carcinogenicity as a non-threshold effect.

For non-threshold effects, two approaches are used in the report, namely measured lung burden in rats exposed by inhalation, and air concentrations directly. The authors suggest using the first approach and discuss implications of different assumptions with regards to deposition fraction, whereas the committee has a clear preference for using the other approach based on air concentrations.

The authors identified two sub-chronic and one chronic inhalation study in rats as suitable for determining a DNEL for pulmonary inflammation: A 12-month chronic inhalation study in rats (mass concentrations: 0, 2.5, and 6.5 mg/m3), a 13-week sub-chronic inhalation study in mice, rats, and hamsters (0, 1, 7, and 50 mg/m3), and a 13-week sub-chronic inhalation study in rats (0, 1, 7, and 53 mg/m3). For determination of a

non-threshold effect they used a 2-year chronic cancer inhalation study in rats (0 and 12 mg/m3) and a 2-year chronic cancer inhalation study in rats (0, 2.5 and, 6.5 mg/m3).

Setting an occupational exposure limit for CB NM

Inflammation
In setting an occupational exposure limit with inflammation as the critical endpoint the authors used the (NOAEC of 1 mg/m3 which is supported by the committee. Mauderly and co-workers observed effect at the lowest tested mass concentration; resulting in a LOAEC of 2.5 mg/m3 (Mauderly et al., 1994), whereas no effect was observed at 1 and 1.1 mg/m3 in the sub-chronic studies (Driscoll et al 1996; Elder et al 2005)

They corrected the NOAEC value to an 8 hours working day and also took into account the breathing rate for workers at light work: NOAECCorrected = 1 mg/m3 *6 hour/8 hour * 6.7 m3/10 m3 = 0.5 mg/m3. They decided on the following default assessment factors:

Interspecies extrapolation 2.5; Intraspecies interpolation 5; Extrapolation from sub-chronic to chronic: 2

This results in a DNEL for chronic inhalation for pulmonary inflammation of: 20µg/m3.

The quality committee suggest to reduce the Intraspecies interpolation to 2.5 due to no metabolisation of CB NM.

The quality committee therefore recommend a DNEL for pulmonary inflammation of: 40 µg/m3

Cancer
In the final risk estimate the authors used numbers from Heinrich et al 1995, but they found very similar estimates for Mauderly et al 1994. The quality committee recommend using the risk level based on air concentrations directly. This decision is primarily based on the uncertainty with deposition and possible overloading of exposure, which is an issue with the alternative method using lung burden. Otherwise, we agree with the calculations performed. Of note, the calculations are based on both benign and malign tumours and included benign cystic keratinizing squamous cell tumours, a benign tumour of unknown human relevance. The suggested OEL might therefore be based on an overestimation of the risk which ought to be clarified.

The quality committee therefore recommend the expected excess lung cancer risk in relation to occupational exposure to CB NMs is 1:1 000 at 45 µg/m3, 1:10 000 at 4.5 µg/m3 and 1:100 000 at 0.45 µg/m3.

References

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