Version 2 Asbestos 02102019

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

Members of the Quality committee: Anne Mette Zenner Boisen (Miljøstyrelsen); Anoop Kumar Sharma (DTU Fødevareinstituttet); Mette Lausten Hansen (Arbejdsmedicin AUH); Jesper Bo Nielsen (Institut for Sundhedstjenesteforskning SDU); Vivi Schlünssen (NFA)

This report is based on a meeting 4th September 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: Niels Hadrup, Anne Thoustrup Saber, Nicklas Raun Jacobsen and Ulla Vogel. Asbestos. Scientific basis for setting a health-based occupational exposure limit. The National Research Centre for the Working Environment (NFA) 2019.

Overall evaluation of the report

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

The structure of the report is a bit challenging to follow, and the committee recommend for future reports to follow the structure used in e.g. the previous report on diesel exhaust particles. Specifically we suggest to move section 7.8 – 8 so they appear before the conclusion.

Some of the scanned tables in the report include reference numbers from original studies not corresponding to the reference list in the current report (for example Table 8 and 12). These reference numbers should be removed.

The suggested OEL for asbestos is mainly based on results from a previous risk assessment from the Netherlands (DECOS 2010). Similar results were seen in a French risk assessment (Afsset 2009). This approach makes excellent use of previous work, and the quality committee support the use of earlier high quality work from other countries. It would have been a tremendous work to base the Danish OEL on the original evidence only, but would have offered a possibility for an independent evaluation. In the Danish report recent key studies are also included. There is an important paper from 2017 (Olsson 2017) the committee suggest also to add. Furthermore there is a recent paper from Denmark on mesothelioma (Dalsgaard 2019) we also recommend to include in the report.

The literature search for the report was supported by research librarians, 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.

Asbestos are silicate minerals encompassing 6 different silicates, of which one, chrysotile has a serpentine (leaf like) structure and the other 5 have an amphibole structure (a chain-like crystalline structure). There is evidence from studies on humans that both serpentine and amphibole structured asbestos can cause cancer (IARC 1212), even though it is quite evident that serpentine asbestos is a less potent carcinogen for especially mesothelioma.

The authors focus on studies and reports dealing with occupational exposure by inhalation, and the committee supports that decision, as inhalation is the major route of exposure for asbestos.

The suggested health-based OEL is based on human data from epidemiological studies, but the authors also assessed asbestos hazard based on experimental animal studies in order to support the human data. The committee supports the use of epidemiological data as the best suited data for setting a health based OEL for asbestos, and we will not further evaluate the hazard assessed from animal studies. Of note, data from animal studies provided substantially higher asbestos levels for excess lung cancer risk level compared to the estimations based on the epidemiological data.

The authors regard carcinogenicity as the critical adverse effects. Interstitial lung disease caused by asbestos (asbestosis, one of more pneumoconiosis) involving inflammation and fibrotic changes is important, but the authors assessed that asbestosis does not represent the critical effect endpoint for hazard assessment due to a likely threshold mechanism of action for asbestosis in contrast to non-threshold mechanism for cancer. This judgement is supported by the committee.

For completeness the report also includes a section on asbestosis which is highly supported by the committee. Asbestosis is described based on a review and a few originals studies. The report would have benefitted from a more systematic approach to the literature with a special focus on existing dose response studies on asbestosis. As an example Loomis et al also published valuable data on asbestosis from the North Carolina asbestos textile workers cohort (Loomis et al 2009). Furthermore the statement about the unofficial lower limit for recognition of asbestosis (25 fibre years) is not relevant and the committee suggest to remove this information from the report.

There is a stronger mechanistic evidence from in vitro studies than in vivo studies for a genotoxic mode of action in inducing the carcinogenic effect of asbestos, but in vitro studies are only sporadically mentioned (section 7.6.3). The author's state that the value of in vitro studies is questionable, which is not supported by the committee. Se for example Huang 2011. The reported positive in vivo studies for genotoxicity are after intratracheal instillation, intraperitoneal injection and oral exposure. There is no genotoxic evidence after the exposure route inhalation. The committee suggests that this should be stated in the report. We suggest to include a more elaborate description (1/2 – 1 page) summarizing the evidence from in vitro studies, including aneugenicity. In Huang et al. 2011 human data for genotoxicity is also provided.

In figure 5, the committee suggests to add Margin of Exposure (MOE) in the box starting with Numerical risk assessment and to add BMDL in the box starting with NOAEL. Both a NOAEL value and a BMDL value can be used to set a health based exposure limit.

One of the studies included in DECOS evaluation (Gustavsson 2002) separates out with a substantial steeper dose-response relation compared to other include studies. The committee suggest the authors to reflect of possible reasons for this difference.

It would be useful with more details about the Inserm model used in the French risk assessment report (Afssat 2008).

Setting an occupational exposure limit for Asbestos

The committee supports the decision to use the epidemiological data to derive an OEL for asbestos.

The authors use Danish life time risk of developing lung cancer (0-74 years): 4.9% for men and 4.5% for women.

The authors recommends that DECOS' K_L values are used for setting the OEL and suggest using the most conservative value for amphiboles, for lung cancer and mesothelioma combined.

Based on the assumption that the vast majority of workers in Denmark are only exposed to chrysotile, and based on the assumption that the level of amphibole contamination in chrysotile in Denmark is similar as the amphibole contamination in studies on chrysotile included in the DECOS K_L values, the committee suggest to use the DECOS recommendation for chrysotile for lung cancer and mesothelioma combined as the relevant measure (0.05 fibres/ml for 1/1000 excess cancer risk, table 23). Based on the numbers for prevalence of lung cancer in Denmark more cases are expected in Denmark, and we want to take this into account in the estimate. We suggest to use the ratio in table 24 between The Danish calculations and DECOS own results for lung cancer and asbestos in general (0.03/0.055). We therefore suggest to use 0.05 * (0.03/0.055) = 0.027 fibres/ml for 1/1000 excess cancer risk.

The quality committee therefore suggest the expected excess lung cancer risk in relation to occupational exposure to asbestos is 1:1 000 at 0.027 fibres/ml, 1:10 000 at 0.0027 fibres/ml, and 1:100 000 at 0.00027 fibres/ml.

References

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