Reviewer’s report

Title: Longitudinal Follow-up of Health Effects among Workers Handling Engineered Nanomaterials: A Panel Study

Version: 0 Date: 16 Jul 2019

Reviewer: Michael Riediker

Reviewer's report:

This study investigated the health risk from nanomaterials in populations of nanomaterial workers and unexposed control workers in a prospective follow-up design. A control banding approach is being used to assign relative risk levels to the different sub-populations. This elegantly accounts for the multitude of different nanomaterials in use. The authors assessed a series of physiological and inflammatory health parameters as well as early health response markers. While none of the physiological markers was associated with workplace exposure to nanomaterials, some of the antioxidant markers were changed. This allows the conclusion that the health risk is small. The exposure was able to invoke a mild protective response against oxidative stress but the stress was not strong enough to result in a detectable inflammatory response or any ill-health. Thus, workplace exposures represented by risk levels 1 and 2 seem to be at concentrations that are unlikely to pose any harm to the workers.

Minor essential revisions:

1) It would be useful to discuss the mild antioxidant response to nanomaterial in comparison to other risk factors such as air pollution. Studies in relatively clean countries show that already very low air pollution exposures (from short to long-term) will lead to clear inflammatory responses. No such thing was seen for the nanomaterial workers, which is remarkable. (a side-remark; In follow-up studies, the authors could strengthen this point by assessing air pollution exposure to their population for a more direct comparison).

2) Abstract - Conclusion: The results suggest that the existing workplace exposure levels pose "no elevated health risk" to the workers. This is different than the "absence of a hazard". Rather, the hazardous materials seem to be sufficiently contained. I suggest rephrasing and referring to „no evidence for elevated health risk to the nanomaterials handling workers" rather than „hazard”. I recommend to screen also the remainder of the document to ensure a clear distinction between hazard (the potential to cause harm) and the risk (the possibility of being harmed).

Minor discretionary revisions:

3) The data analysis describes the use of t-test and ANOVA, tests which require approximate normal distribution. It would be helpful if the authors could describe by which means they assessed the distributions before running the tests.
4) There were very few workers in RL3, thus the authors pooled RL2 and RL3. It would be helpful to know if a sensitivity analysis was conducted (i.e. exclude RL3 workers rather than pooling) and what it showed.

5) The conclusion sections makes concluding statements about specific measures to keep workplace exposures low, shown in the supplemental data. As this data seems to be central for the conclusions, it would be nice to move that table to the main manuscript.

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