

Response to Morfeld (2013): commentary to Gebel 2012: a quantitative review should apply meta-analytical methods

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Dear Editor,

I am thankful for the possibility to clarify several points raised in a commentary from Morfeld (2013). Morfeld expresses a general concern with respect to the fact that formal requirements for a meta-analysis were not adequately taken into account in Gebel (2012). It should be noted that the evaluations made are nowhere in the paper called meta-analysis. In the evaluation performed in Gebel (2012), original experimental data have been assembled and compared. It was not intended that existing formal requirements of a meta-analysis should be met. The aim of the present evaluation was to stick to the underlying original experimental data as close as possible and to keep statistical calculations to a minimum. Thus, the reader has the possibility to follow the line of evaluations performed and can follow the conclusions drawn from the original data. It can be recollected from the summarized original data that the carcinogenic potency difference in rat inhalation studies comparing GBP nanomaterials and GBP micromaterials is low. The main conclusions are based on simple descriptive statistics of original data. This could further be substantiated by re-running an analysis according to requirements of meta-analyses with the data presented, but there is no stringent necessity to follow this line.

There may be misunderstandings by Morfeld (2013) on how calculations have been performed in Gebel (2012). For

instance, significance tests (e.g., the *U* test) were not performed on derived statistics but from collected single experimental observations (i.e., tumor rates in a dose group in a carcinogenicity study related to the respective exposure metrics). As a consequence, statistical variability of the input data has been taken into account and not been ignored as Morfeld (2013) states.

Morfeld criticizes that ‘the chosen statistical procedures are inappropriate and may lead to unreliable findings’ and refers to an epidemiological textbook (Rothman et al. 2008). It is unclear which specific inappropriateness is meant. Moreover, the performed evaluation is not a combined reanalysis of epidemiological studies but an evaluation of collected original data of experimental studies.

It is correct that the lung burden data were not copied into table 1 in Gebel (2012) as Morfeld (2013) recognizes. It was not possible to include all used original data used in all calculations in table 1. For instance, also the weekly exposure durations used in the long-term studies which were necessary to derive the cumulative exposures are also not contained in table 1. All these data are contained in the original publications included in the analysis and are available. The point by Morfeld to request a definition for cumulative lung burden is not understood. It is explained in the paper which data have been used for the metrics cumulative lung burden. It is given in the second last paragraph of the methods chapter that the lung burden data after 12-month exposure were used as cumulative dose metrics, that is, the cumulative lung burden in this case. Thus, the requested information is already contained and explained.

Taken together, the results obtained in Gebel (2012) could be further supported by additional analyses proposed by Morfeld (2013). However, a relevant change of the results presented is neither expected nor likely.

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