Correspondence to the Editor Re: Implementing systematic review techniques in chemical risk assessment: Challenges, opportunities and recommendations

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We have read the series of articles in the special issue "Systematic review methods for advancing chemical risk assessment" with great interest. Whaley et al. (2016) provided a comprehensive synthesis on opportunities, challenges and recommendations for applying systematic review (SR) techniques in chemical risk assessment (CRA). Some guidance for SR implementation in CRA has been mentioned by Rooney et al. (2016). As demonstration applying SR and meta-analysis to evaluate health risk of low-frequency magnetic and electrical field (Golbach et al., 2016) and organophosphate pesticide exposure (Ross et al., 2016) has been presented.

Although systematic review and meta-analysis is a systematic, rigorous and transparent method to provide research evidence relevant to a specific question with minimized error and bias, the result of this method may not provide the endpoint required for a CRA. The pooled estimates of a meta-analysis can address the question on what is the risk of a specific health effect in relation to the presence of an exposure (i.e. relative risk, how much will risk increase when there is a unit of exposure increase). Whereas, the endpoint of a CRA needs to addresses the question on how much risk of a specific health effect is due to exposure to an agent at a specific dose. For instance, the policy and decision makers need to know how much risk of adverse health effect occurs at the 5th percentile of exposure to substance, so they can decide actions for risk management to protect the population. In order to get this endpoint, the quantitative dose-response measures (NOEAL, LOEL, ADI, Reference Dose, etc.) need to be combined with exposure assessment to characterize risk. Nevertheless, as mentioned by Whaley et al. (2016), SR methods do not include assessment of dose-response and have not been applied to the exposure assessment component of a CRA yet. Therefore, we would like to add some points as additional contributions to the work of Whaley et al. (2016) as below:

- Systematic review (SR) and meta-regression (MR) methods may be more suitable than pooled estimates of meta-analysis in assessing dose-response using animal and

epidemiological data, since a meta-regression model (linear or non-linear) can be used to quantify the measures of dose-response assessment. For example, NOAEL can be calculated from the meta-regression model as the dose when relative risk equals 1, where the dependent variable is relative risk and main independent variable is dose obtained from animal and epidemiological studies;

- Systematic review and meta-regression should also be considered in exposure assessment of a CRA for two reasons. First, SR and MR can enhance the sample size of exposure measurements from different sources and evaluate the heterogeneity of these measurements. Second, MR can quantify the exposure levels while taking into account of potential confounding factors (e.g. sample size of exposure monitoring, average age of participants, etc.);

- The instructions for using SR methods in probabilistic health risk assessment (PHRA) should be added in the previous guidance, since this guidance has not been mentioned in previous documents. PHRA uses distributions of value rather than single values as traditional risk assessment, so PHRA has added value since it incorporates variability into risk estimation (WHO, 2011). MR may be ideal methods for PHRA because it presents dose-response and exposure as regression lines of distributions.

References

Golbach et al., 2016, Calcium homeostasis and low-frequency magnetic and electric field exposure: a systematic review and meta-analysis of in vitro studies. Environ. Int., 92-93 (2016), pp. 695-706

Rooney et al., 2016, How credible are the study results? Evaluating and applying internal validity tools to literature-based assessments of environmental health hazards. Environ. Int., 92-93 (2016), pp. 617-629

Ross et al., 2016, Reflections on the process of using systematic review techniques to evaluate the literature regarding the neurotoxicity of low level exposure to organophosphate pesticides. Environ. Int., 92-93 (2016), pp. 569-573

Whaley et al., 2016, Implementing systematic review techniques in chemical risk assessment: challenges, opportunities and recommendations. Environ. Int., 92-93 (2016), pp. 556-564

Who, 2011, Generic Risk Assessment Model for Indoor and Outdoor Space Spraying of Insecticides. WHO/HTM/NTD/WHOPES/2010.6 (2011). In WHO website: www.who.int.