CEFIC Long-range Research Initiative
Request for Proposals (RfP)

Title and Code Number:
LRI B19: Extrapolating the Applicability of Worker Exposure Measurement Data

Background

A properly conducted exposure assessment is a necessary foundation for soundly based risk assessments. For efficiency reasons the existing approaches include lower Tier assessment with tools such as the ECETOC Targeted Risk Assessment (TRA), requiring limited resources but producing conservative estimates, and higher Tier assessment with more complex models requiring many more inputs such as the LRI-funded Advanced REACH Tool (ART). In the ideal case the assessments are based on actual measurements of exposures of the population of interest (such as those of workers, consumers or the general population), but for many exposure scenarios, such data are either scarce or lacking altogether. In such instances, exposure assessors must rely on estimating exposures using models or by reference to data that might exist for analogous substances or situations. Unfortunately, while there is general agreement that measured data are preferred to modelled estimates of exposure and that good advice exists on how different models should be applied to estimate human exposures, there is a paucity of advice, let alone consensus, on the circumstances where analogous data might be introduced and applied to such exposure assessments. The consequence of this is twofold; 1- it hinders the ability to use existing measurement data to improve exposure estimates, as there is considerable uncertainty concerning whether the use of any existing data will be considered acceptable or not, and 2- because the utility of measured data is seen as limited, this serves as a disincentive to collect and share exposure information beyond the specific situation in which it has been obtained.

The situation that characterizes exposure information should be contrasted with that now being implemented for hazard assessments. Here, processes have been developed and established that enable data from various sources (such as test data for a substance, as well as data available for similar substances) to be combined to improve the veracity of the hazard assessment. These processes consist of various elements, notably an ability to categorise the quality of the available information and then to combine this in a structured and transparent manner, especially where analogous data are used to fill (or 'read across') any gaps where actual test data are lacking and accounting for the quality of the available information.

These approaches to hazard assessment potentially serve as a useful starting point for the development of any comparable approach for exposure assessment. However, perhaps unlike the approaches established for hazard assessment, any approach developed for exposure assessment also needs to account for the situations in which it is intended to be applied (the 'domain' of its application). Generally, hazard assessment is undertaken with a single question in mind: to what extent does the substance present a particular hazard or not? But in exposure assessment, there is likely to be more inherent variability in the data and the assessor must also address factors dependent on the target population and use conditions (for example, the extent to which data on the exposures associated with the use of any substance might also be applied to other uses or substances is likely to be a function not just of the chemical but also the use

conditions and the population) Put simply, how might data be identified that are potentially relevant for the EA being undertaken and to what extent does their quality affect their interpretation?

Development of robust criteria that extends application of exposure measurements obtained for a specific substance(s) and use conditions to other substances under similar use conditions, will be a step change for exposure science. It will provide a scientific, credible basis for extending existing data to inform exposure potential for similar use scenarios where measured data may be lacking. Given the wide range of potential substances and use scenarios that exist, methods that maximize use of available data for both estimating exposure and benchmarking exposure model predictions are critical.

Although a general scheme is lacking, in recent years, proposals have been made for the 'read across' of certain types of exposure information (for example for nanomaterials in defined workplace settings [see Hristozov et al, 2012]). Frameworks have also been proposed that enable exposure considerations to be accounted for in the integration of human experience data in hazard assessment using weight of evidence approaches (ECETOC, 2009; Adami et al, 2011; Lavelle et al, 2012). It is hoped that these developments will provide good foundations and insight for an approach which would be generalizable across worker populations. It is not the intention at this stage to develop an approach for all human population types..

Objectives

The purpose of this project is to develop criteria and examples (case studies) that can be applied to evaluate if exposure measurements for a given substance(s) and use scenario(s) might be reasonably representative for another substance used in the same or similar manner, as well as for the same substance in other use scenarios. This project is looking to develop a pragmatic and agreed process by which existing exposure measurement data on chemical substances (that have been obtained experimentally as opposed to modelled estimates) can be reliably incorporated into those worker exposure assessments that are typically undertaken in support of chemicals regulations. It is anticipated that the process may also be applicable to other settings where an understanding of the magnitude of worker exposures is critical (e.g. occupational hygiene, epidemiology), but in the first instance it is driven by the needs of the European REACH regulation. The project is therefore likely to consist of a number of elements that, together, deliver a structured framework which will enable exposure assessors (and those stakeholders with an interest in the exposure assessment) to consistently and transparently use available workplace exposure data on chemicals to improve the reliability of other assessments with less extensive supporting measurement data.

Aspects such as how to establish comparable substance properties (i.e., physical chemical properties, physical form) and describing sufficient similarity of use scenarios will need to be elucidated. A scientific rationale will need to be provided to establish criteria for which read across can be applied. It is envisioned that desktop testing of the developed approach will also be undertaken - it should be used at first to develop

exposure predictions for substances/scenarios for which measured data are available, to assess its performance.

It is expected that the project will deliver (but not necessarily be limited to these):

1. A description for what constitutes an adequate measurement data set for use in chemical safety assessment, taking into account how the data relate to toxicological reference values and inherent variability in exposure levels.
2. A scheme for evaluating and classifying worker exposure data types and quality, taking currently available guidance and schemes into account
3. A workshop with stakeholders to identify and assess recent situations/precedents arising from decisions in different areas of EU chemicals regulation e.g. REACH.
4. Activities 1-3 will define the final scope and boundaries of the approach that can be applied to worker EAs intended for use in EU chemicals regulation i.e. improving the confidence of those with higher RCRs and/or reducing the uncertainties associated with those based on limited datasets. It is expected that this step will be supported by a set of demonstration examples for how the proposed scheme would be expected to be applied.
5. Based upon the outcome of the above, a report will be produced with a full description of the approach including supporting documentation; its domain(s) of reliable application; and a library of case studies covering different substance types and use settings.

Scope

CEFIC is seeking to support the development of an approach that is capable of evaluating and categorizing worker exposure measurement data such that, where available, it can potentially be applied outside the specific circumstances in which it was collected. The aim should be on a scheme that will be acceptable in the regulation of current industrial chemicals under REACH, as well as having general utility in workplace risk assessment. No experimental work is foreseen.

This project will need to account for:

- Previous work that has addressed how exposure data quality might be evaluated and classified
- Identification of key determinants to assess the representativeness of an existing data set for other substances (physical chemical property domain, metabolic domains) and other exposure situations (for example, if data are available for a spray use, what are the factors to consider if the exposure adequately represents other spray applications; factors here may need to include such things as characteristics of the use environment, duration, use concentration)
- Identification of quality control measures on data sets.
- A framework describing the process for combining all of these essential elements to maximize the information value of existing exposure data sets through broader extension.
- The need to demonstrate the utility of the proposed approach by its application across a representative range of case studies
- The need to obtain stakeholder review and support for the proposed scheme

Deliverables
The final report shall contain an executive summary (2 pages max), a main part (max. 50 pages) and a detailed bibliography.
It is expected that the findings will be developed into at least one peer reviewed publication, following postering(s) and presentation(s) at suitable scientific conference(s).

Cost and Timing
Start 1 January 2017, duration 18 months.
Budget in the order of €110,000.

Partnering/Co-funding
Applicants should provide an indication of additional partners and funding opportunities that can be appropriately leveraged as part of their proposal. Partners can include, but are not limited to industry, government/regulatory organizations, research institutes, etc. Statements from potential partners should be included in the proposal package.

Fit with LRI objectives/Possible regulatory and policy impact involvements/ Dissemination
Applicants should provide information on the fit of their proposal with LRI objectives and an indication on how and where they could play a role in the regulatory and policy areas. Dissemination plans should also be laid down.

References
Adami HO, Berry SC, Breckenridge CB, Smith LL, Swenberg JA, Trichopoulos D, Weiss NS, Pastoor TP., Toxicology and epidemiology: improving the science with a framework for combining toxicological and epidemiological evidence to establish causal inference. Toxicol Sci. 2011 Aug;122(2):223-34. .

ECETOC, Framework for the Integration of Human and Animal Data in Chemical Risk Assessment, Technical Report No. 104, ECETOC, Brussels, 2009

Danail R. Hristozov, Stefania Gottardo, Marco Cinelli, Panagiotis Isigonis, Alex Zabeoa Andrea Critto, Martie Van Tongeren, Lang Tran & Antonio Marcomini, Application of a quantitative weight of evidence approach for ranking and prioritising occupational exposure scenarios for titanium dioxide and carbon nanomaterials, Nanotoxicology, Volume 8, Issue 2, 2014, pages 117-131

Karlene Lavelle, Robert Schnatter, Kim Travis, Gerard Swaen, Dirk Pallapies, Chris Money, Peter Priem and Henk Vrijhof, 'Framework for Integrating Human and Animal Data in Chemical Risk assessment', (2012) Regulatory Toxicology and Pharmacology 62, 302-312

DEADLINE FOR SUBMISSIONS: 31 August 2016
Please see www.cefic-lri.org for general LRI objectives information, project proposal form and further guidance for grant applications.