Online workshop on the scientific feasibility of exposure-based adaptations in the regulatory setting

Workshop Report No. 37

EUROPEAN CENTRE FOR ECOTOXICOLOGY AND TOXICOLOGY OF CHEMICALS

Online workshop on the scientific feasibility of exposure-based adaptations in the regulatory setting

Workshop Report No. 37

Brussels, November 2020

ISSN-2078-7219-037 (online)

ECETOC Workshop Report No. 37

European Centre for Ecotoxicology and Toxicology of Chemicals
2 Avenue E. Van Nieuwenhuyse (Bte 8), B-1160 Brussels, Belgium.

DISCLAIMER: The representatives of the European Commission, ECHA and national competent Authorities expressed no view or position on the scientific matters discussed during the breakout sessions, hence their participation cannot be taken as agreement/disagreement to the views and positions expressed during the breakout sessions.

Online workshop on the scientific feasibility of exposure-based adaptations in the regulatory setting

CONTENTS

INTRODUCTION

Throughout global chemical management regulatory programmes there is an underlying concept of using exposure potential to prioritise and determine the data needed to support a risk assessment. This allows focusing on those substances which pose the greatest potential risk. The EU REACH regulation is no exception to this, incorporating several exposure-based approaches to set and modify the data required to register a substance, for example, the use of annual tonnage to determine what data are required to support a registration. However, as currently written the EU REACH legal text severely limits the possibility to use a more adequate exposure metric and risk- based approaches to adapt the default data requirements for human health and the environment. The ECETOC Exposure based adaptation taskforce was established to assess the current approaches for utilising exposure-based adaptations approaches under REACH and devise how it could be done in a scientifically robust manner, laying out what criteria should be met for exposure and toxicity data as well as how to document the case. Complementary to this, Concawe has run a project to evaluate whether and what exposure-based adaptation approaches could be practically applied to complex petroleum substances, as a case study.

Leveraging the learnings and recommendations from both project teams, this workshop provided a platform for scientific and regulatory discussions with the aim to review the concept of exposure-based adaptation as a mean to reduce unnecessary animal testing, assess potential barriers and pitfalls, and formulate acceptance criteria for exposure and toxicity data expected in exposure-based adaptation.

The workshop was split into three main sessions: setting the scene for the regulatory basis for and experience with exposure based adaptations; providing the analysis of the existing provisions for exposure based adaptations; providing a proposal for modifying the 'Risk-based' exposure based adaptation and breakout groups to discuss the proposal`. The aims of the workshop were:

- To reach a common understanding on how to make the best use of an exposure-based approach without compromising the core goals of REACH, namely protection of human health and the environment.

- To exchange ideas to feed further into the REACH Annex XI amendment proposal document for regulators and provide a platform for discussion.

The workshop was attended by 67 participants, with a mix of regulators, industry, academia and NGOs.

The outcome of the workshop will be part of a consolidated into ECETOC technical report which will form the basis for future scientific and advocacy work relating to the use and improvement of exposure-based adaptations (EBA).

PRESENTATION SUMMARIES

Representatives from the European Commission (DG GROW), European Chemicals Agency (ECHA) and RIVM (Dutch National Institute for Public Health and the Environment) provided the regulatory backdrop to the use of exposure-based adaptations and the experience with REACH registrations making use of these adaptations. To date, although exposure-based adaptations (column 2 and Annex XI) have been used in approximately 15% of evaluated dossiers, the success rate is very low, particularly for Annex XI, 3.2(a) adaptations where the risk assessment approach has been used. This low rate of success was echoed by RIVM.

An industry perspective on the use of exposure-based adaptations highlighted the challenge with ambiguous terminology within the REACH legal text and explored the potential to use a threshold of toxicological concern (TTC) approach to aid in defining 'low' or 'negligible' exposure conditions.

The ECETOC taskforce presented on their work to analyse the existing REACH provisions for exposure-based adaptations from a human health hazard and exposure assessment perspective. Some of the key issues with the current provisions were highlighted. Following this a proposal on how to modify the existing approach for using a risk-assessment driven exposure-based adaptation was presented, and this formed the basis for the subsequent breakout group discussions.

Prior to the breakout group discussions, there was a look to the future with a presentation by ECETOC giving an overview of a new Transformational Program being designed. This aims to explore how to move away from the current 'tonnage-based testing annex' driven assessment to an exposure-led chemical safety assessment, integrating different sources of information, including "new approach methodologies" (NAMs), in an objective way to provide sufficient weight of evidence to make risk assessments with confidence.

BREAKOUT SESSION

The breakout session allowed discussion of the ECETOC TF proposal to for a risk assessment driven exposure-based adaptation. The discussion in each group was built around 4 statements. The key findings from the discussions are collated below.

Exposure assessment: There should be no a-priori limitation on the uses and extent of exposure when using an exposure-based adaptation.

There was a general consensus that limiting use of EBA to where there was no or 'no significant' exposure presents an unnecessary barrier. It was also agreed that terminology such as 'no significant exposure' is interpreted differently by different stakeholders, adding to the challenge of using an EBA. "No significant" implies exposure is below a certain level, which should be determined accurately incorporating the uncertainty from lacking higher tier animal data. In other words, there should be a hazard benchmark to compare the estimated exposurew with to be able to judge on its (in)significance.

In principle all types of uses could be evaluated as part of an EBA recognising that for some uses (for example consumer) there is greater uncertainty in the exposure assessment which must be addressed. Information on uses and exposure scenarios should also reflect the 'real' situation as much as possible. One consistent concern from the regulatory perspective is the accuracy, reliability and completeness of use information relative to the real-world situation. All actors in the supply chain must work closely together to ensure all uses are covered in order to improve acceptance of EBA.

To better characterise exposure, a proposal was made to classify 'real-world' exposures into different categories, 1 (higher exposure) to 4 (low exposure). This could be combined with tonnage band to provide a more refined approach to characterise exposure when determining what studies would be needed. This would move away from EBA towards a more exposure-based platform for supporting chemical management.

DNEL Derivation: There should be no restriction on which type of study data to use for deriving a DNEL when using exposure-based adaptation. In the absence of DNEL data for it is acceptable to use a TTC approach

It was generally agreed that use of studies such as the 28-day repeated dose study and the OECD 422 combined repeated dose/reproductive toxicity study could serve as a starting point for setting a DNEL when using an EBA. However, it was acknowledged that such studies address fewer endpoints than higher tier studies such as the 90-day study, and have limited coverage of the developmental endpoints. To address this, additional data-driven assessment factors could be a solution. The use of such factors must be employed with caution since lower tonnage band registrations which do not require higher tier human health studies are not required to consider any additional uncertainty relating to the coverage of toxicity endpoints. It is evident that in setting higher data requirements for higher tonnage level registrations, the greater expectation for data leads to greater uncertainty when higher tier studies are waived. Finding a better way to link data needs to actual

exposures versus a more arbitrary metric such as tonnage band should help address the above perception of uncertainty.

All breakout groups felt the TTC approach as an alternative to a DNEL when using a risk-based EBA would have limited use as TTC values are very low. The TTC may still have use in defining a benchmark for 'no significant' exposure.

Risk assessment – Uncertainty: It is not necessary to mandate exposure be 'well below the DNEL'. Uncertainty can be addressed when deriving the DNEL.

It was noted that by requiring exposure to be well below the DNEL when using an EBA, there is an assumption that the risk assessment should be more rigorous (conservative) than required as part of a standard chemical safety assessment (CSA). Meaning that, to adapt a higher tier data requirement, simply demonstrating 'safe use' with an RCR <1 is considered insufficient since, in principle, this could lead to a situation where adapting higher tier data requirements becomes the default and performing studies the exception. Here, the term "safe use (advice)" and the associated RCR<1 rule might have been misconceived. While for CSA derivation of safe use advice implies identification of specific operational conditions and risk management measures (RMMs) needed to control exposure below the DNEL, for the EBA type of assessments exposure scenarios should reflect **actual/existing RMMs already in place (commensurate with identified hazards based on available tox data) ; introduction of any additional RMMs to bring the RCRs below the specifically derived DNEL is discouraged.** Hence, EBA aim to (a) verify the *status quo* safe use for the substance based on the current hazard and exposure knowledge and (b) confirm no changes to existing RMMs are necessary even when compared to the lower DNEL that incorporates the uncertainty from omitting the study.

When considering the idea of 'well below the DNEL', it is implied that in addition to the uncertainty associated with the hazard characterisation, there is additional uncertainty in the exposure assessment that must also be accounted for – together this was designated as 'compound uncertainty'. It was recognised the widely acceptable practice of application of a suitable assessment factor to address uncertainty when deriving the DNEL could make the requirement to have exposure 'well below' the DNEL redundant. Alternatively, one suggestion was that rather than including an additional assessment factor, a definition for 'well below' could be established. The example was given of using a benchmark of 1/10th of the OEL when occupational hygienists control to 'well-below' the OEL.

Potential roadblocks: What roadblocks do we foresee in the use of the risk-based exposure adaptation as proposed in the workshop and how can these be resolved/addressed?

There was a clear message that increased use of EBA would make assessment of compliance by ECHA and member states more difficult. This is particularly an issue given the concerns about existing dossier quality. If the criteria and requirements for EBA are to be changed, it should not lead to a greater burden on the regulatory community.

Increased use of EBA and a subsequent reduction in generation of higher tier studies could impact the effectiveness of classification and labelling and subsequent default risk management measures (if they are to be based on C&L/Hazard only). However, in principle, if EBA has been properly applied, then the performance of higher tier studies would not result in a need to increase the risk management measures.

To improve the utility of EBA, particularly the risk-based EBA, there must be a change to the REACH legal text as well as improvements in the guidance and clarification of vague terminology. In addition to this, improvements in exposure information and ways to express exposure in a more robust manner (e.g. exposure categories) would help address concerns about the robustness of EBA. Finally, a change in mindset is needed regarding the reliance on animal intensive, higher-tier studies. Rather than continue to mandate the need for these studies to address concerns, can we not consider how NAMs could be employed instead?

CLOSE OF THE WORKSHOP

The main points from the breakout groups were reviewed and discussed. The workshop was brought to a close with a presentation from the EPAA about their activities which include a further look into the use of EBA and other alternative risk-assessment approaches which aim at reducing wherever possible the requirement for new animal studies as part of chemical management programs.

APPENDIX A: WORKSHOP PROGRAMME

Programme		
09.30-09.50	Introduction	Olivier de Matos (ECETOC) Nick Ball (DOW), on behalf of ECETOC EBW TF
09.50-10.20	What is an exposure-based adaptation approach and where does it fit into a chemical management framework? ▪ Regulatory perspective in EU ▪ Practical perspective on EBA under REACH	Workshop moderator: Erik Van Miert (Solvay) Peter Baricic (DG GROW) David Bell (ECHA)
10.20-10.45	Challenges faced currently with implementation of exposure-based adaptations under REACH and barriers to the use of exposure-based adaptations ▪ MS perspective ▪ Industry perspective	Emiel Rorije (RIVM) Stefan Hahn (Fraunhofer ITEM /Concawe)
10.45-11.00	**Break**	
11.00-11.15	Review of the Human Health hazard assessment	Nick Ball (DOW), on behalf of ECETOC EBW TF
11.15-11.45	Review of the Exposure assessment	Tatsiana Dudzina (Exxonmobil), on behalf of ECETOC EBW TF
11.45-12.45	**Break**	
12.45-13.10	Proposal for Risk-based approach to EBA	Harrie Buist (TNO), on behalf of ECETOC EBW TF
13.10 – 13.20	ECETOC Transformational program (TP)	John Doe, on behalf of ECETOC TP
13.20 – 13.30	**Break**	
13.30-14.30	Breakout groups to review Risk-based approach to EBA	Moderators: Ilse Tuinman (Shell), ECETOC EBW TF member Tatsiana Dudzina (Exxonmobil), ECETOC EBW TF member Nick Ball (DOW), ECETOC EBW TF member
14.30-15.00	**Break**	
15.00-16.00	Closing session – Review output of Breakout sessions and Wrap up	Erik Van Miert (Solvay), ECETOC EBW TF member. Nick Ball (DOW), ECETOC EBW TF member. Ilse Tuinman (Shell), ECETOC EBW TF member Tatsiana Dudzina (Exxonmobil), ECETOC EBW TF member Irene Manou (EPAA)

APPENDIX B: ORGANISING COMMITTEE

Nick Ball (**Task Force Chair**)	Dow - CH
Tanya Dudzina	Exxon Mobil – BE
Franz Lamplmair	DG GROW - BE
Irene Manou	EPAA - BE
Erik Van Miert (Steward)	Solvay - BE
Marilena Trantallidi	Concawe – BE
Zvonimir Zvonar	EPAA – BE
Olivier de Matos	ECETOC – BE
Andreea Cuciureanu	ECETOC – BE
Francesca Uguccioni	ECETOC – BE
Virginie van der Steeg	ECETOC - BE

ECETOC PUBLISHED REPORTS

The full catalogue of ECETOC publications can be found on the ECETOC website:
http://www.ecetoc.org/publications

Responsible Editor:
Mr Olivier de Matos
ECETOC AISBL
Rue Belliard 40
B-1040 Brussels, Belgium
VAT: BE 0418344469
www.ecetoc.org
D-2021-3001-259

Since 1978 ECETOC, is a collaborative space for leading scientists from industry, academia and governments to develop and promote practical, trusted and sustainable solutions to scientific challenges which are valuable to industry, as well as to the regulatory community and society in general.