EUROPEAN COMMISSION
JOINT RESEARCH CENTRE
Health, Consumers and Reference Materials
Chemical Safety and Alternative Methods Unit
EU Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM)

Summary Record

PARERE Meeting

8th November 2016, Ispra, Italy

The meeting of the members of the PARERE network started in the morning of 8th November 2016. All presentations and documents are available on CIRCABC.

Opening of the meeting and welcome

EURL ECVAM opened the meeting with a discussion on the current state of the network in the Member States (MS). The role of PARERE is to ensure that there is continuing engagement from the relevant players throughout the validation and adoption process of methods and approaches. Members represent a variety of sectors and EURL ECVAM recognises the importance of this for communicating with the regulatory and scientific communities to ensure continual engagement in the validation process. EURL ECVAM emphasised the importance of identifying the key players within the relevant networks in a Member State in order to increase the dialogue and to bring solutions to potential problems. Several members mentioned that there is a continuing need to try to engage a variety of experts and stakeholders in order to get feedback. The interest from relevant scientific and regulatory groups varies from MS to MS and this poses some problems to individual PARERE members. Additionally, identifying contact points is not always easy. As such, EURL ECVAM will provide PARERE with a list of committees for each legislation/regulatory area outlining their roles.

Update on the Nordic PARERE initiative and feedback from PARERE on the establishment of the network in their Member States

A brief discussion took place regarding the establishment of an initiative by the Nordic PARERE members to engage the competent authorities for a variety of sectors. The initiative aimed to bring regulators from similar countries together to improve the quality of consultations. The response has been positive from some areas, but others require more effort to engage.

EURL ECVAM took this opportunity to ask PARERE how we could enhance our information flow, using this network to channel information to the right places. It was agreed that there needs to be more active communication and EURL ECVAM will look at how it can send regular updates with hyperlinks to news items to PARERE members so that they can disseminate this within their networks.

Consultation of PARERE on the EDITOX test method submission

EURL ECVAM outlined the principles of the method that had been submitted to EURL ECVAM in 2016. EDITOX is an *in vitro* cell-based method to assess the risk for chemical compounds to induce psychiatric adverse side effects (depression, suicide). It consists of the quantitative analysis of RNA editing modifications of the serotonin receptor 2C (5-HT2cR) induced by pharmaceutical compounds. The EDITOX assay entered the EURL ECVAM validation process at the stage of the pre-submission in June 2016. The consultation of PARERE on this method ran until the 20th of January 2017.

Consultation of PARERE on the bioaccessability method

In September 2016, ECHA established an Expert Group on bioelution to advise on the use of bioelution assays in a regulatory context (with CLP as the main focus). The bioelution test method measures the release of a metal ion into 0.07 N hydrochloric acid which is proposed to serve as simulated physiological fluid (i.e. simulated gastric fluid). The bioaccessibility is the fraction of the substance that dissolves under these conditions and is potentially available for absorption into systemic circulation. This method proposes to generate bioaccessible metal ion data for the oral route of exposure, which is relevant to systemic effects of metal-containing materials. However, it is not a toxicity test. PARERE members gave feedback during the meeting which resulted in EURL ECVAM revising the questions of the consultation, which ran until the 20th of January 2017.

A proposal for a Guidance Document on the characterisation of *in vitro* human hepatic metabolic clearance methods

There is increasing demand (from researchers, test method developers, regulators, end-users) to integrate kinetics information in chemical risk assessment. This is based on the fact that exposure to a chemical does not automatically mean that all of the dose will be bioavailable and therefore able to cause a specific toxicity. Hence the knowledge of the chemical's human kinetics can assist to better design toxicity tests (both *in vivo* and *in vitro*) and interpret toxicological findings. With a view to enhancing the use of human *in vitro* methods for hepatic metabolic clearance in chemical hazard and risk assessment, a new project proposal on an OECD Guidance Document (GD) will be submitted to the OECD in order to characterise *in vitro* hepatic metabolic clearance methods and to facilitate method comparison and the evaluation of their performance. The Guidance Document will therefore aid clearance method developers and end-user to characterise and report the salient attributes of different methods to facilitate method comparison and increase confidence in their use to support chemical risk assessment.

New project proposal to the OECD to develop a Performance-Based Test Guideline on Defined Approaches for skin sensitisation testing

The project proposal for the development of a Performance-Based Test Guideline (PBTG) for skin sensitisation was outlined by EURL ECVAM. The PBTG would include Defined Approaches (DA) and possibly individual test methods which have been shown to provide comparable information to the Local Lymph Node Assay (LLNA) for hazard identification or hazard characterisation purposes. The project would be led by EC, US and Canada with the support from all other ICATM partners. Assessment criteria for defined approaches will be established following systematic evaluation of the uncertainty of LLNA reference data (in terms of reproducibility and relevance to humans). Defined

approaches can be evaluated against these assessment criteria and in the light of the systematic review of the LLNA data. Defined approaches/individual methods meeting the criteria would be annexed to the PBTG and information generated with these defined approaches/methods would be covered by Mutual Acceptance of Data (MAD) and would have equal footing with information obtained with the animal-based method.

Follow-up:

Following the discussions which took place during the meeting, the following was agreed:

- EURL ECVAM will provide PARERE members with a list of relevant committees which they could consider contacting.
- A one page leaflet detailing the roles and responsibilities of the PARERE network will be created so that PARERE can use this to inform third parties.
- EURL ECVAM will also consider packaging information and news items for PARERE members in an email newsletter which can then be forwarded to their networks.

Annex I – Agenda

PARERE Meeting

JRC Ispra, 8th November 2016

Building 101, Room 1302

9:00-9:15	Opening of the meeting and welcome
9:15-10.15	Update on the Nordic PARERE initiative Feedback from PARERE on the establishment of the network in their Member States
10:15-10:45	*Coffee Break*
10:45-12:30	Consultation of PARERE on the EDITOX test method submission *Francesca Pistollato, EURL ECVAM* Consultation of PARERE on the bioaccessability method *Pilar Prieto-Peraita, EURL ECVAM* A proposal for a Guidance Document on the characterisation of *in vitro* human hepatic metabolic clearance methods *Alfonso Lostia, EURL ECVAM* New project proposal to the OECD to develop a Performance-Based Test Guideline on Defined Approaches for skin sensitisation testing *Silvia Casati, EURL ECVAM*
12:30-13:00	AOB
13:00-14:00	*Lunch*

Joint PARERE-ESTAF meeting starts at 14:00.