

SKIN SENSITIZATION ALTERNATIVES

EPAA-Cefic LRI-Cosmetics Europe Joint Workshop



Helsinki, Finland, April 23-24th 2015

Joint cross-sector workshop on Alternatives for Skin sensitization testing and assessment

The next in a series of CEFIC-LRI/EPAA/Cosmetics Europe workshops on skin sensitization was again hosted in Helsinki by the European Chemicals Agency (ECHA) on April 23rd/24th 2015. Approximately 60 participants, of whom the majority were from ECHA and EU member state regulatory agencies, considered the issues associated with the use of non-animal test data in hazard identification and classification, including for potency sub-categorisation. The overall objectives of the event were to undertake a critical assessment of how in vitro skin sensitisation data can be used in a weight of evidence approach to enable a defensible classification decision on a substance. In addition, key strengths and limitations, plus future needs were actively addressed.

At the last workshop, just 2 years ago it was noted that in "this area of toxicology, it is very likely that integrated testing strategies (ITS) which are based on in vitro methods will at least partially replace in vivo methods for skin sensitization within just 2-3 years". That probability is now a reality. The formal validation of two in vitro methods which address two key events in the adverse outcome pathway (AOP) for skin sensitization, i.e. protein reactivity and, keratinocyte activation have been translated into OECD Guide-

lines; a further method, addressing the third key event of the AOP, dendritic cell activation, the human cell line activation test (h-CLAT) has been validated by EURL-ECVAM and has a draft guideline under awaiting OECD approval. Accordingly, it is essential for industry and the regulatory community to co-operate so that the progress from validation, through acceptance to practical use can be expedited.

On April 23rd, the workshop heard platform presentations from industry and regulators detailing current status of in vitro methods regarding the prediction of skin sensitization hazard, the potential for sensitisation potency assessment and approaches to the integrated assessment of data from multiple methods. This material was given a practical spin by the presentation of 6 individual case studies. These explored individual substances, specific ITS/IATA (integrated approaches to testing and assessment) strategies and the challenges faced by those undertaking and/or reviewing the data.

On April 24th, the second part of the workshop, three break-out groups addressed key questions, these being followed by an open workshop discussion. One focus

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The Workshop, hosted by ECHA, in Helsinki

was on the question of how to integrate data from multiple assays, balancing harmonisation of approach for regulatory use with a need for some flexibility. The second group considered questions on the use of the methods for hazard identification, asking what level of uncertainty of prediction was acceptable. It was then noted that on current evidence, the prediction of skin sensitisation potential in humans appears to be more accurate from in vitro tests than from existing animal tests.

However, it was recognised/concluded that, given the limitations and availability of the data, all of the information, including animal tests and studies of humans would need considered to establish the best predictor for humans. The third group extended this challenge to reflect on whether and to what extent the potency of an identified sensitiser could be predicted by in vitro methods. A key discussion point asked whether a sufficient body of human evidence exists to give reassurance that the predictions have merit?

The overall output from the break out groups coalesced into a few key points and recommendations. These can be summarised best by reflecting that we now have non-animal testing tools that represent the first three Key Events (KE) of the AOP. With two already having become official OECD Test Guidelines and a third enticingly close to that position (the Direct Peptide Reactivity Assay for KE1, Keratinosens for KE2 and h-CLAT for KE3), the switch from a primary requirement for LLNA data to a requirement for in vitro evidence is an imminent reality for those substances which fit within their applicability domain. ECHA is in the process of updating its guidance documents to reflect what registrants need to provide if data from combinations of these tests are to be used to meet regulatory requirements of the REACH Regulation.

So what is still needed? First and foremost perhaps is that submissions must be adequately argued in the sense of providing a solid scientific foundation for decisions based on the outputs of these methods, taking into account any other contributions to the weight of evidence (the most obvious being knowledge from chemical structure). Particularly, where data is discordant, an adequate rationale to explain this must form part of the dossier. Helping to provide confidence for all will be clarity in the matters

of applicability domains and any uncertainties associated with the assays and gathering and sharing experience of their use. It has to be recognised that IATAs are not yet in a mature phase, such that the workshop contained much active debate on several aspects.

Nevertheless, there was broad consensus that a simple and transparent stepwise process involving the validated methods was an opportunity now waiting to be seized. There was also strong feeling that the approach should not be so rigidly defined that assay variations and alternative tests for the KEs were locked out,

nor that it should preclude more complex IATAs being used within industries for their own purposes.

Perhaps on a final note, all were reminded that the ultimate goal is a high level of protection of human health, and thus it will be the experience of people that will ultimately be the final arbiter of whether toxicological predictions are, or are not, correct. None of the existing assays are perfect; the in vitro methods should not be expected to be so either, but by use of these methods and all other relevant information, including clinical feedback, we have the opportunity to continue to improve.

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Participating Organisations

AirLiquide/SEPPIC
BASF
Beiersdorf
British Health & Safety Executive
BUAV/ECEAE
CAAT EU
Cefic LRI
Chemical Watch
Clariant
Danish MSC member
ECHA
EPAA
European Commission DG JRC/EURL ECVAM
European Commission, DG ENV
European Commission, DG GROW
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KAO Corp.
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Merck KGaA
OECD
Polish Bureau for Chemical Substances - Department for Risk Assessment
Procter & Gamble
Rhodia / Solvay
RIVM
Romanian Chemical Department - National Environmental Protection Agency,
Shiseido
Symrise



Panel Discussion

About EPAA

EPAA is a Public-Private Partnership across seven industry sectors and between European Commission and Industry stakeholders. Launched in 2005, it gathers 36 companies, 7 European trade federations and 5 Directorates-General of the European Commission.

About LRI

Launched 15 years ago, the Long-Range Research Initiative (LRI) is one of the major voluntary initiatives of the European chemical industry to support its competitiveness and innovation potential. LRI aims to identify and fill gaps in our understanding of the hazards posed by chemicals and to improve the methods available for assessing the associated risks.

LRI sponsors high quality research, published in peer-reviewed journals, and seeks to provide sound scientific advice on which industry and regulatory bodies will draw to respond more quickly and accurately to the public's concerns.

About Cosmetics Europe

Cosmetics Europe is the European trade association representing the interests of the cosmetics industry. Its membership consists of 27 national associations of the EU Member States and beyond, 16 major international companies, four supporting association members, four supporting corporate members and four correspondent members associated members. Cosmetics Europe represents more than 4,000 companies throughout the EU via the active representation of its member national associations.

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