EPAA - CEFIC LRI JOINT WORKSHOP SKIN SENSITIZATION ROUNDTABLE

flash

Helsinki, Finland, February 4th 2013

SKIN SENSITISATION – MOVING FORWARD WITH NON-ANIMAL TESTING STRATEGIES

The third in a series of CEFIC-LRI/EPAA workshops on skin sensitization was hosted in Helsinki by the European Chemicals Agency (ECHA) on February 4th 2013. More than 50 participants, of whom the majority were from regulatory agencies, considered the issues associated with the use of non-animal test data in hazard identification and classification. Topics included use of such data from alternative methods both before and after formal validation, as well as continuing the thinking from the previous workshop regarding how the information can be used in Weight of Evidence (WoE) and hazard/risk assessment approaches.

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. Active validation of three in vitro methods is entering its final stages in the EURL-ECVAM. These methods cover three key stages in the Adverse Outcome Pathway (AOP) for skin sensitization, namely protein reactivity, keratinocyte activation, and dendritic cell responses. These methods will be included in the OECD work plan for the test guidelines programme for 2013.

"It is essential for both industry and regulators to prepare for this revolution in skin sensitization prediction"

Accordingly, it is essential for industry and the regulatory community both to prepare for this revolution in skin sensitization prediction, as well as to continue to give active feedback on the challenges that it will present. In addition, it remains important for industry to receive input from regulators concerning the prerequisites necessary for ITS to be accepted for registration of chemicals.

The first half of the workshop was devoted to platform presentations from industry and regulators detailing current practice in the prediction of skin sensitization potentials, new concepts and the validation of non-animal testing methods, and the strategies for hazard/risk assessment without animal testing. This material generated some discussion, but its primary purpose was to set the scene for the second part of the workshop, involving two break-out groups and a roundtable discussion. These activities were focused on four key questions:

1. What are regulatory requirements for the acceptance of non-animal test methods under REACH? (e.g. as WoE; as a stand alone method; as part of a testing strategy)

2. What would regulators see as necessary requirements for non-animal test methods or ITS for skin sensitisation that would help them to take regulatory decisions in a confident way?

3. Until non-animal approaches become available at a regulatory level (i.e. OECD), what is needed in the interim for facilitating regulatory decision making on the basis of existing non-animal ITS?

a. Can strategies be accepted already? (e.g. if published in peer reviewed journals; do the methods need to have been submitted to ECVAM, what is needed to allow the prediction of non-sensitizers)).
b. What can be used prior to OECD guideline publication? (e.g. what is required; what is needed after publication; are legal adjustments to current regulation/annexes needed)?

4. What can industry and others do to facilitate acceptance procedures?

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The responses to these questions were interesting, partly for their content, but also for the high level of consensus between industry and regulatory participants. For example, participants expected that the in vitro alternatives likely to be available in the relatively near future would only provide an adequate replacement for the in vivo methods when deployed in an ITS. They also recognised that the limitations on any ITS using in vitro methods would mean that the ITS should not be overly rigid and should be presented in the form of a weight of evidence argument concerning substance classification.

Flexibility in the ITS might be required for instance because of the applicability domain limitations associated with in vitro methods due to e.g. metabolism, solubility, etc. Importantly, submission of data/information should be presented in sufficient detail that the ITS and/or weight of evidence argument can be seen to be scientifically robust – something that the regulatory representatives noted as lacking in a number of current submissions (although not necessarily for this toxicology endpoint!). As one group put it, "make the regulators feel confident!".

" In vitro data can be acceptable in many cases, including with ITS "

It was confirmed that in vitro data, including within an ITS, can in many cases already be acceptable in submissions. Indeed, it is encouraged, given the 2018 deadline (and with the high number of substances and tight testing schedules involved) for lower tonnage substances that dossiers including non-animal and/or ITS strategies be submitted, the earlier the better. Such submissions help to build experience, highlight challenges and encourage exchange between industry and regulators, as well as informing those responsible for validation and the development of a formal ITS of issues that need to be addressed.

On the key question of what can industry and others do to facilitate acceptance, the responses of the groups were more varied, but nevertheless contained core themes of openly sharing information, including by peer-reviewed publication, of continuing dialogue and of the preparation of guidance documentation, e.g. on use of human data and applicability domains. In this respect, industry volunteered to organise an informal follow-up small scale discussion to investigate pragmatic solutions and make interim recommendations. **This has already been set up for the end of April in Brussels with the key stakeholders.**

Perhaps the most significant aspect of this workshop is it paved the way for, and perhaps even set the model for, future collaborations between CEFIC-LRI, EPAA, ECHA and the national authorities in charge of implementing alternative approaches to animal testing. The positive atmosphere of the event and the valuable progress made, was surprising to some, but in reality a necessity for the prompt adoption of skin sensitization in vitro alternatives that can deliver the same degree of human health protection currently afforded by the in vivo methods. Thus, it is felt that this Skin Sensitization training workshop was a breakthrough in international collaboration on 3Rs which will promote their adoption and use in regulatory toxicology.

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.

Further information is available on www.epaa.eu.com

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.

Further information is available on http://www.cefic-lri.org/

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