A CROSS SECTOR WORKSHOP
THE LOCAL LYMPH NODE ASSAY AND BEYOND
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The European Partnership for Alternative Approaches to Animal Testing

A SUCCESSFULL WORKSHOP GATHERING EXPERTS FROM MANY SECTORS

This follow up meeting to the CEFIC/LRI workshop held in 2010, was held on September 19th and 20th in Brussels and was hosted by the EPAA and Cefic/LRI. 50 expert participants from industry, academia and regulatory agencies heard some 25 high level presentations and associated discussions. The workshop reviewed experience with in silico and in vitro approaches to skin sensitisation, as well as the currently used animal methods, particularly post-validation experience with the local lymph node assay (LLNA). Key topics discussed also included how information can be best used in weight of evidence and risk assessment concepts.

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Key themes of the meeting were the current use of the LLNA, a reduction and refinement alternative, including its non-radioactive variants in regulatory toxicology across sectors, namely for cosmetic ingredients, general chemicals, agrochemicals and pharmaceuticals and how to integrate non-animal testing method strategies into integrated testing strategies for sensitization testing.

Despite use of the LLNA differing in various industry sectors, there were a number of issues that were shared in common. These included limitations of test methods and their outcomes, the awareness of when the result, e.g. in a LLNA, was likely to be incorrect, and how this information could be addressed in a regulatory setting. The use of LLNA data as a gold standard in the development of non-animal hazard identification alternatives was discussed. Furthermore, the assembly of a gold standard skin sensitiser potency dataset remains to be completed, since for progressing truly useful alternatives it is an essential requirement. A weight of evidence assessment based on available pertinent information from all information - which can involve the use of non-animal test methods - was considered most relevant for the this purpose. A number of integrated testing strategies and “toolbox” approaches were presented.

Currently, the LLNA is the only method that can give an estimate on the potency of a sensitiser to be used in risk assessment. It was discussed how to advance the use of non-animal methods from yes/no answers useful in hazard identification towards their use in hazard identification and risk assessment. Finally (although many other issues were raised), the general questions on formal validation, including accelerating the process, the acceptance by regulatory bodies, and post-validation processes, were prominently discussed. The LLNA, being one of the first ever validated alternative, provides a useful learning experience.

Validation can never hope to cover every possible challenge that a new assay may face once it is subjected to the diverse world of toxicological chemistry. Combinations of methods may at least partly help to address this issue. No test is, or will be, perfect, which immediately begs the question of how toxicologists and regulators can learn from the expanding body of knowledge with an assay or combinations thereof. A willingness for industry to publish the experience in peer reviewed journals is critical to this, but so is the willingness of regulators to listen and to learn, and having learned to use the knowledge gained to apply regulations appropriately. This matter remains a substantive challenge, one that is bound to increase as the move to in vitro and in silico models takes place, a time that, at least for skin sensitisation, may be only a very few years away.

A detailed report summarizing the scientific outcome of the workshop and recommendations for future developments in skin sensitisation testing will follow in due course.

CONTACT

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