The European Partnership for Alternative Approaches to Animal Testing

Alternative Test Methods Session

of the 5th Meeting of Chairs and Secretariats of EU Commission and Agency Scientific Committees and Panels involved in Risk Assessment. Brussels 19 November 2009

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EPAA Principles and Values

- Science based improvement in implementation of 3Rs
- Consensus based approach between industry and authorities
- Pragmatic mechanisms and a workable structure
- Dialogue and transparency towards stakeholders and interested parties in particular through a Mirror Group
- Commitment of partners to act in a coherent and consistent way

Main areas of EPAA activities

- How to get the best out of Research
- Assessment of relevance legal requirements and implementation
- Streamlining Validation and Acceptance
- Improving Information and Dissemination

Some representative EPAA projects

- EPAA databases for in house methods and publicly funded R&D projects
- **Evaluate opportunities across all sectors for an extended one-generation study for reproductive toxicity**
- Framework for cooperation on validation
- Regulatory acceptance
- **Paving the way towards new perspectives on safety**
- In vitro metabolism test systems as essential part of ITS for long term toxicities
- **Acute toxicity testing across sectors**
- EPAA annual lead themes, e.g. 2009 Dissemination
- **New initiatives, e.g. Validation of ITS**, vaccines, weight of evidence

ACSA extended one-generation study

Developed in the crop-protection context.

Status of feasibility evaluation for chemicals:

- Evaluation by four EPAA member companies: 2 are currently finalizing their studies / evaluations
- An OECD draft guideline is open for comments,including triggering criteria, however there is some reluctance to accept it without assessment of all cohorts.
- EPAA will support a workshop with ECPA in 2010 to disseminate the latest results to the stakeholders

Acute toxicity

- The requirement for acute toxicity within the pharmaceutical sector has been successfully challenged
- EPAA is reviewing drivers for this test to identify 3Rs opportunities for all sectors

Status

- Publication on drivers for acute tox testing across sectors in 2009
- Opportunities for waiving one of the three routes of administration
  - **Two separate but complementary retrospective data analyses conducted by ECVAM/HSI and the UK NC3Rs**
  - **EPAA Workshop with regulators to discuss findings in early 2010**

New perspectives on safety

- Workshop in 2008:
  - To identify truly novel non-animal approaches for the characterization of the potential hazards of chemicals and drugs.
  - To develop a view of which areas of science and technology should be exploited to create new approaches to safety assessment, and of which activities may inform and shape the forward research agenda.
  - To invest in alternatives research a greater legitimacy among the scientific community.

New perspectives on safety
Next steps

1. Progress with 2 specific outputs from the New Perspectives on Safety workshop
   - Computational chemistry and toxicology – case study: liver
   - Stem cells
2. Engage scientists from international groups previously unconnected with 'alternatives' in the scientific challenges we face
3. Consider how these two themes could align with overall challenge of assessing chronic repeat dose systemic toxicity without the use of animal testing

   The Commission /Colipa Joint Intitiative (FP7 call – 50Mios €) is already building on the EPAA initiative.

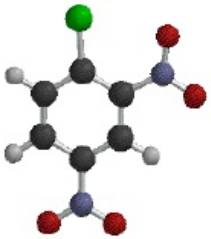
COLIPA
THE EUROPEAN COSMETICS ASSOCIATION

Skin Sensitisation Risk Assessment

Risk ?

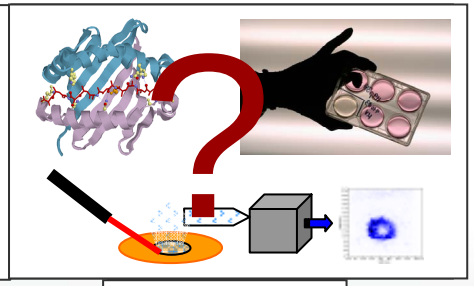
Hazard

Exposure



Historical

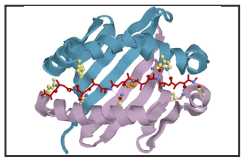
In Silico



In Vitro

X

How can we characterise sensitiser potency without animal testing?

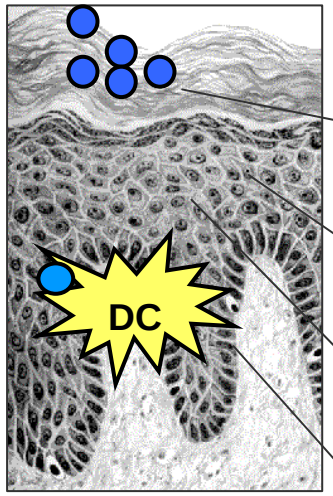


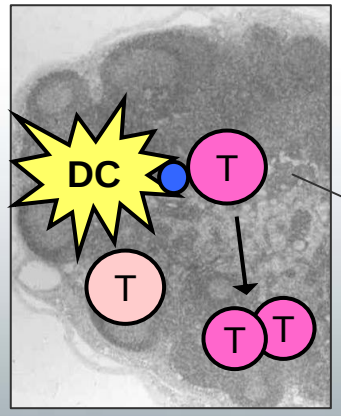
- Identify the key parameters involved in skin sensitisation induction

- Develop non-animal test methods that aim to model each key parameters

- Integrate data from different test methods to predict sensitiser potency information

Testing strategies for the prediction of skin sensitisation potency information





Exposure & Bioavailability

Skin innate immune response

Protein Reactivity

DC Activation

T cell response

A future approach to measuring relative skin sensitising potency: a proposal

Ian R. Jowsey, David A. Basketter, Carl Westmoreland and Ian Kimber

Skin Sensitisation

The Acquisition of Skin Sensitisation

Jowsey et al. 2006. *J. App. Toxicol*. **26**. 341-350.

Evaluating *in vitro* test methods for Skin Sensitisation

- Three *in vitro* test methods accepted for ECVAM phase III pre-validation:
  - Direct Peptide Reactivity Assay (DPRA)
  - Human Cell Line Activation Test (h-CLAT)
  - Myeloid U937 Skin Sensitisation Test (MUSST)

- Each test had previously undergone in-house and interlaboratory evaluation to:
  - Optimise and fix protocol
  - Evaluate protocol transferability
  - Characterise accuracy of prediction
  - Define applicability domain

Integrated Testing Strategies in the regulatory context

- Two workshops: November 2008 and October 2009
- Objectives
  - Discuss to which extent the existing validation principles are applicable to validation of testing strategies (based on selected case studies)
  - Develop a draft approach for validation of ITS and apply it to the selected case studies
- Status
  - Agreement on the assessment of the building blocks which will be integrated via a testing strategy
  - Is there added value in validation of a testing strategy?
  - Recommendation for a 3rd EPAA Workshop – Q2 2010 – Regulatory Acceptance of Testing Strategies

Why is Dissemination Important for the Partnership?

- Dissemination of information about existing replacement, reduction and refinement methods is one of the conditions for
  - better implementation of 3Rs and
  - better acceptance by regulatory authorities.

Conclusions

- Provide appropriate answers to regulatory & safety requirements, bringing together advanced scientific approaches and the 3Rs
- Help the dialogue between industry, academia and regulators in order to facilitate the international implementation of these approaches
- Improve our efficiency by adapting our working processes and facilitating interactions with our stakeholders with the help of the Mirror Group.