

EPAA 2011 ANNUAL CONFERENCE

flash



The European Partnership
for Alternative Approaches to Animal Testing

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INTEGRATED TESTING STRATEGIES AND THEIR IMPACT ON THE IMPLEMENTATION OF 3Rs

At six years old the EPAA is no longer a novelty. But if the concept of reducing, refining and replacing the use of animals in scientific and industrial testing (the "3Rs") is increasingly understood and applauded, the hard graft of translating ambitions and visions into workable animal-free tests that regulators will approve remains challenging. And yet solid progress is being made, as shown by a number of reports and contributions to the EPAA's seventh annual meeting, held in the European Commission's Charlemagne Building Brussels on 9 November.

The theme of the meeting was Integrated Testing Strategies, or ITS for short – essentially, the idea that the combination of a number of different (non-animal and animal) approaches may result sufficient for appropriate risk assessment in comparison with traditional individual tests. One of great attractions of such an approach is that it allows the use of batteries of tests, approaches and methods that on their own might not be powerful enough to convince regulators to waive tests on animals. But whilst ITS are these days commonly used in industry for internal decision making purposes, much work still needs to be done as far as acceptance by regulatory risk assessors is concerned.

Opening the meeting on behalf of the European Commission, DG Environment, Susanna Louhimies said the EPAA's initial focus was on developing alternative methods and one-to-one replacement of animal tests. Now, she said, "We have turned our attention towards innovation and the use of new science in risk assessment." This approach of placing more emphasis on reduction and refinement and on Integrated Testing Strategies could produce many more results than the traditional way of applying the 3Rs. It would also open up possibilities for further cooperation with other stakeholders, including regulators, and even other regions.

She described the EPAA as a "unique and voluntary partnership", one that brings ideas, knowledge and creativity together with great success. It is part of an overall approach, and EPAA work is reinforced by a continuity in action under the EU's own competencies. Therefore, "There is no better way for industry and the Commission to work together towards accelerating the development, validation and acceptance of all possible alternative approaches," she said. Louhimies was followed by industry representative Thomas Foerster, Corporate Vice-President R&D Cosmetics for Henkel, the company that will provide next year's EPAA Co-Chair. Foerster described

the regulatory challenges for companies working at the global level, and the potential for cooperation in 3Rs and Risk Assessment. He qualified the EPAA as "an outstanding platform for collaboration, discovery, alignment", and pointed to a number of impressive successes in reducing the number of animals used in regulatory testing in the European Union. On the other hand, he said, the total replacement of animal tests will not be feasible in the near future. However, in his view the EPAA provides a strategic tool to promote the 3Rs globally based on excellent science.

“EPAA is an outstanding platform for collaboration, discovery and alignment.”

Dr T. Förster

Joachim Kreysa, of ECVAM, stressed the role of innovation, implemented through dialog, research and information. "We need innovation that takes findings from scientific research and translates them into test methods that are reliable, relevant, useful and affordable", he said. And there is a further requirement: "If we are to introduce new methods as alternatives into the area of regulatory compliance, we need to prove added value." This is where validation comes in: it is, he said, a very useful way of promoting the use of functional, valid methods.

Gianni Dal Negro, Worldwide Director Animal Research Responsibility from GSK and EPAA's current industry co-chair, outlined the main achievements of the EPAA over the past year. These included progress on an EPAA project around the "consistency approach" in vaccine production, a project relevant to the EPAA because of its significant impact on the use of animals and the use of the EPAA as a platform between regulators, academia and



G. Dal Negro, co-chair of the EPAA Steering Committee, presenting the main achievements of EPAA in 2011

industry. As Coenrad Hendriksen from the EPAA Vaccines Project Committee explained, the consistency approach starts from the assumption that if each batch is produced with the same starting material and with a standardised process, then instead of having to test each batch in series, one just has to show that the following batches are consistent with the first ones. If adopted widely, this approach would have a dramatic impact on the use of animals, as batch testing of vaccines is one of the largest single users of animals for testing purposes. The project is looking for a mixture of quick wins (achieving 3Rs benefits with existing techniques and the current regulatory frameworks) and what Coenraad Hendriksen called "hard wins", which would require new research and new regulatory frameworks but offer much more important benefits. As ever, timescales are an issue.

The EPAA's ability to stimulate practical progress was demonstrated by a talk by Dr. Felix Spöler, the recipient of the Platform's Science Award in 2010. His project for an integrated replacement for the animal-based Draize eye irritation test attracted great interest. For Dr Spöler, the value of the EPAA Award also lies in the improved access to regulators and industry, allowing to finalise work on an innovative test method and bringing it closer to validation and practical use.

Reporting on the EPAA's ITS Workshop in Brussels on 26 September, Gianni Dal Negro called for greater integration of effort between European public-private partnerships working on ITS (in particular more discussion between scientific advisory boards), more discussion between funding bodies, and for common routes of publication to make it easier for everyone to find and share relevant new information.

EPAA work on ITS should be seen in a wider context of science, innovation in risk assessment and global developments.

Wolfgang Dekant, from the Institut für Toxicologie at the University of Würzburg, looked at the new challenges for risk assessment. Dekant is part of a European Commission Scientific Committees' working group that was asked to carry out a comprehensive review of risk assessment pro-

cedures and to prioritise areas for further research. Based on the preliminary report (final report will be published in 2012) one relevant avenue could be the exposure-driven approach. "If you don't have a lot of exposure there is often no problem," said Dekant. Hence the growing interest in the concept of threshold of toxicological concern (also known as TTC), the establishment of a human exposure threshold value for a chemical, below which there would be no appreciable risk to health.

With so many speakers talking about the importance of a global approach to the 3Rs, it was fitting that Janice Soreth, from the European office of the US Food and Drug Administration introduced FDA's policy on alternative approaches in risk assessment and current FDA initiatives. She declared her enthusiasm for collaboration with the EPAA, and said the FDA was eager to support, promote and collaborate in order to allow for the basic research and the new opportunities it affords.

“US FDA is eager to support, promote and collaborate in order to allow research and the new opportunities it affords.”

Dr J. Soreth

As coordinator of the big EU Research Framework project OSIRIS, looking at optimised strategies for ITS in human and environmental toxicology, Gerrit Schüürmann from the Helmholtz Centre for Environmental Research in

Leipzig, Germany, was ideally placed to give the conference an overview of EU research on alternative approaches. The 31-partner, 14-country project has recently closed, and its conclusions are currently being written up. OSIRIS has developed five ITS schemes for REACH testing, which are freely available in a webtool (<http://osiris.simple.com>).

The original idea of looking for one non-animal test to replace an animal one has given way to a new paradigm: one in vivo test being replaced by a number of non-animal tests. As Schüürmann pointed out, that creates not just new possibilities, but new complexities as well. It also tends to lead to greater emphasis on the reduction of animal use, rather than purely replacement. "This isn't bad news; it's good news if we refine, reduce and replace," he said. "We shouldn't wait until everything is perfect."

Vera Rogiers, Head of the Department of Toxicology at the Vrije Universiteit Brussel and a member of the EPAA's Mirror Group, was keen in her summing up to stress the full range of innovation in the 3Rs – not just in "omics"



The afternoon panel : «ITS and their impact on the 3Rs» (left to right : G.Schüürmann, W. Dekant, G.Dal Negro, J.Kreysa, J. Soreth (standing) & C.Brekelmans)



Conclusions were presented by EPAA Mirror Group Member Vera Rogiers (standing) & Elke Anklam, Director of IHCP.

but also in cell culture and in situ monitoring as well as in systems biology and pathway analysis. But she warned that with so many different tools involved in risk assessment, "we have to make sure that people don't misunderstand us".

Referring to the presentation about

OSIRIS, giving results from the front line of a European project, she said that as there are the tools, there is a task for the EPAA to facilitate their application. She took encouragement from the interest the regulators were showing in ITS. "We should not forget that we want a well defined regulatory acceptance process." ITS could be "the key player" in the paradigm shift from pathology-based toxicology to pathway-based risk assessment.

The EPAA is indeed an excellent tool for international cooperation, Rogiers affirmed. But it's hard to have an international discussion when Europe is internally inconsistent in how it approaches the 3Rs – just replacement in cosmetics, all three Rs in REACH and in pharma. First, said Rogiers, we need harmonisation in Europe.

Finally, Rogiers asked for a renewed political commitment to the EPAA. "We have to be alert" she said. "If you want to change something, you need the attendance, visibility and support of the highest levels in both Commission and Industry."

In her concluding remarks, Elke Anklam, Director of the Institute for Health and Consumer Protection at the European Commission's Joint Research Centre, that hosts ECVAM, stressed the importance of innovation. If we are to protect human health and the environment, we need to advance ITS and reduce animal testing, she said. "The emphasis has to be on providing methods that support decisions on safety assessment better than the current in vivo ones" she added.

Activities need to be clearly targeted, and the ITS approach is clearly the right way forward, but there is still a lack of true integration that needs further work. However, it's not just about integration: we need to be strategic in our scientific goals – short, mid and long term. And once the goals are set, we need to invest properly in the science, she said.

Finally, also Prof. Anklam presented the view that Commission and industry have to reflect how to improve the way the EPAA operates.

The key messages to emerge from the conference were:

>>>The EPAA is a successful platform, increasingly acknowledged at the global level, and with increasing interest from academia, regulators and NGOs; however, at six years old it needs to examine closely ways to increase its performance and innovation potential, in particular by a renewed political commitment at the highest levels.

>>>The original idea of looking for one non-animal test to replace an animal one has given way to a new paradigm: one in vivo test being replaced by a number of non-animal tests, opening the way for better cooperation at the international level.

>>>International cooperation should enable global acceptance by regulators of ITS in testing and assessment; rapid and effective validation is a key part of rising to the innovation challenge.

>>>There should be greater integration among public-private partnerships and research programmes looking at ITS, in particular at the European level.

>>>Because ITS methods require expert judgement, more attention must be given to education in toxicology and safety assessment.

The presentations at the conference, including the progress report with the EPAA's achievements over the past year, can be seen online at www.epaa.eu.com

EPAA AWARDS

The Poster Award, carrying a prize of €1,500 was given to Dr Monica Batke et al. of the Fraunhofer Institute for Toxicology and Experimental Medicine, Hanover, Germany, for her group's poster on "ITS RepDose: A functional Integrated Testing Strategy for the endpoint repeated dose toxicity".

The Recognition Award, reserved for posters from industry, went to John Doe and his colleagues from Parker Doe, UK, for their poster "Moving from Data Requirements to Knowledge Requirements".

This year, the EPAA Steering Committee has decided not to grant the EPAA Communication Award.

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