Annual Report
A decade of support for the 3Rs
Ten years ago, one of the widest coalitions ever brought together on the topic of alternatives to animal testing led to the creation of the EPAA. Two EU Commissioners, Janez Potočnik and Günther Verheugen, along with industry representatives from many sectors and myself from the European Parliament called for a new kind of alliance to promote alternative methods. Our aim was an integrated collaboration that would pool resources, build a trusted position and act based on cross-sectoral input.

Today, I am pleased to see that mutual trust has been established between both sides of this Public-Private Initiative. EPAA has paved the way for the development, evaluation and acceptance of many methods enhancing predictive safety science. In the meantime, other collaborative initiatives like IMI and SEURAT-1 arose with different goals, means and roots. The next challenge for EPAA is to foster a closer collaboration between those who promote regulatory acceptance of alternative methods and those who fund their implementation.

In its first 10 years EPAA has established itself as a key player in identifying research gaps, sharing knowledge and good practice across sectors and facilitating acceptance. For the next ten years, let us call for a stronger EPAA that will continue the coordinated promotion of alternatives in Europe!

Dagmar Roth-Behrendt
Former MEP, EPAA EP Co-Founder

In ten years, promoting the validation and acceptance of alternatives has shifted from a technical challenge to a priority for the European citizens.

Earlier this year, the European Citizens Initiative “Stop Vivisection” gathered more than 1 million signatures. This illustrates public concerns and echoes the pioneering positions Europe has taken in the promotion of alternatives to animal testing. European institutions, European citizens and European industry are committed to foster together better predictive safety science.

Consumer safety must remain a top priority while keeping in mind the objectives of the 2020 Animal Welfare Strategy and the need to actively promote innovation and research.

As a Member of the European Parliament and Chair of the ENVI Committee, responsible for Environment, Public Health and Food Safety, I want to support the 3Rs goals (Replacement, Reduction and Refinement). Although the European Union currently has a head start in the development and promotion of 3Rs in animal testing, the challenge remains the global acceptance of alternative approaches.

European legislation on Cosmetics has inspired many countries to introduce similar Regulations, but still others require animal testing for cosmetics.

EPAA workshops, such as the one on Harmonization of 3Rs in Biologics, attracted regulators from as far as the USA, Canada, China, Brazil and Japan. This shows that there is willingness for international dialogue on this topic and we very much welcome these initiatives.

Giovanni La Via MEP
Chair of the ENVI Parliamentary Committee
II - Action Programme 2016-2020

Prioritizing actions in promoting 3Rs

Following the principles of the 3Rs declaration signed in 2005, the EPAA partners concluded at the end of 2014 that they wish to continue the mandate of EPAA until at least 2020. In 2015, a comprehensive overview of priorities for all EPAA partners was compiled that constitutes the new action programme for the next 5 years. In doing so, EPAA seeks to support the implementation of Directive 2010/63 on the protection of animals used for scientific purposes while maintaining the balance between safety (of products), animal welfare and scientific innovation as wanted by the regulators and required for the continuity of R&D in Europe.

In the next 5 years, EPAA shall focus on closer co-operation with regulators at global, European and national levels striving to promote international convergence of regulatory safety testing requirements. The unique range of partners in the EPAA projects including industry, regulators and animal welfare groups give it the ability to act as a forum for cross-sector dialogue. The EPAA can reach out to Member States and help provide a coordinated EU voice. Through the involvement of the EU Commission and global companies, EPAA has the potential to liaise with the wider international community. The next Action Programme includes activities related to:

1. Regulatory acceptance and the use of 3Rs
   This section aims to identify and address obstacles to implementation of alternative methods in regulatory decision-making, alternative methods that are currently applied by industry but not accepted by regulators, and reliable and cost-effective alternative methods that could be accessible and applied broadly amongst members of industry. It also provides a science-based platform for knowledge sharing and promotion of cost effective alternative methods which target all 3Rs. Promotion of networking and communication amongst regulators and industry representatives from different sectors to share good practice and knowledge and data sharing recognising intellectual property issues is also vital.

2. International convergence
   Main activities within this section include identifying the hurdles preventing international acceptance and application of the 3Rs approaches, alongside with the promotion of international collaboration to facilitate international convergence and standardisation of new methods and the mutual acceptance of data. Promotion of the necessity, application and use of Integrated Approaches on Testing and Assessment (IATA), is also crucial.

3. New scientific research needs
   Main activities are focused around identifying knowledge gaps in the fields of regulatory toxicology by engaging the scientific community across sectors (via the Project Platform, workshops or consultations). The research needs for developing and optimising alternative methods through relevant programmes and calls for proposals of the European Commission and other research funding institutions shall be identified and communicated.

4. Dissemination and Communication
   Recognition of 3Rs research and good practice shall be increased via acknowledging and promoting laboratory scientists’ contribution to the 3Rs with special focus on refinement. The network shall be extended and the involvement shall be sought through young scientists and scientists from areas not directly related to biosciences to increase knowledge and leverage understanding of the 3Rs within the scientific community. Access to information and opportunities to connect regulators and the regulated, alternative method developers and those who are in charge of validation of alternative approaches should be significantly improved.

The programme is available on the EPAA website.
III - Project Platform: Activities updates

The Project Platform unites the former EPAA Platform on Science and Platform on 3Rs in Regulation. Under its supervision, EPAA Partners and associates work on prioritising, promoting and implementing the application of the 3Rs. They also work to facilitate the validation, acceptance and implementation of 3R alternatives in European regulatory testing and decision making. In 2015, EPAA has been working on the following 7 projects:

a. Optimised strategies for assessing Skin sensitisation
b. Vaccines consistency approach
c. Acute Toxicity
d. User-friendly in vitro/in vivo exposure predictor
e. Biologicals
f. Advancing 3Rs in Regulatory Toxicology
g. Stem Cells

a. Optimised strategies for assessing Skin Sensitisation

Facilitating the adoption of non-animal integrated approaches

In recent years, great emphasis is placed on the need to establish non-animal test methods that reflect key biological events in the adverse outcome pathway (AOP) associated with skin sensitisation as published by OECD in 2012.

This is because skin sensitisation remains an important endpoint in safety evaluation of chemicals that must be assessed under the current chemical legislation in Europe (REACH: 1907/2006). Other legislation including the EU Cosmetics Regulation (1223/2009) also require assessments of skin sensitisation potential, whilst since March 2013 animal testing of cosmetic ingredients marketed in Europe has been prohibited. Therefore, the assessment of skin sensitisation potential of substances without animal testing has been at the centre of efforts in the recent years.

Two validated non-animal tests are now accepted as OECD Test Guidelines (a third one will be adopted soon) and this has triggered the need for agreed approaches to the use of the data generated using these tests for regulatory decision-making. In order to help address this challenge, the EPAA organised a skin sensitisation workshop in collaboration with Cefic LRI and Cosmetics Europe on 23-24 April 2015. The workshop was the fourth organised on this topic by EPAA and Cefic in the last years. It was hosted by ECHA in Helsinki and attended by experts from national competent authorities, ECHA, OECD, EC and industry.

The participants considered the introduction of new integrated non-animal skin sensitisation strategies, critically assessed their use for hazard classification in the regulatory context, and discussed several case studies regarding hazard, potency and weight of evidence for different chemical classes. Ongoing efforts directed towards the Integrated Approaches to Testing and Assessment (IATA)¹ were assessed by examining the case studies involving non-animal methods in testing strategies and discussed some of the challenges that these presented. Important conclusions from the workshop were the need for greater clarity in the definition of applicability domains and that no single method but a tiered strategy based on the AOP for skin sensitisation may help to better characterise the skin sensitisation potential. Other key issues identified included the feasibility of using the new approaches by SMEs, especially when operating through CROs, monitoring uptake in regulatory filings and ECHA acceptance.

The press release and Flash Report from the workshop are available online (http://cefic-lri.org/wp-content/uploads/2014/03/Joint-WS-Skin-Sensitisation-Alternatives-2015-Flash-report.pdf). The full report from the workshop was published in the peer-reviewed journal Regulatory Toxicology & Pharmacology earlier this year².

The current focus and goal of the skin sensitisation project is to share information about existing IATA for regulatory decisions on skin sensitisation for hazard classification in time for REACH 2018. ECHA has prepared a new draft guidance which is currently in consultation by a Partner Expert Group (PEG) in which Cefic and other industry sectors also participate; this guidance is expected to be published in 2016.

¹ According to EURL ECVAM, IATA is a structured approach used for hazard identification (potential), hazard characterisation (potency) and/or safety assessment (potential/potency and exposure) of a chemical or group of chemicals, which strategically integrates and weights all relevant data to inform regulatory decision regarding potential hazard and/or risk.

b. Vaccines Consistency Approach

Replacement of animal-based batch release tests

The consistency approach is based upon thorough characterization of the vaccine during manufacture and the principle that the quality of subsequent batches is guaranteed by the strict application of a quality system and of a consistent production of batches identical to reference lots of known potency and safety. The consistency approach is already used for recently registered vaccines whereas many older vaccines continue to rely on tests in laboratory animals for confirming the quality of each batch. The EPAA Vaccines Consistency Approach project initially spread over 4 work streams: Human and Veterinary Rabies vaccines, DTaP vaccines (Diphtheria, Tetanus and acellular Pertussis) and Clostridial vaccines. With regard to Veterinary rabies vaccines and DTaP vaccines no activities have been launched under the EPAA umbrella, since there is a lot of work going on at individual company or institution level and further research activities have been included into the IMI2 proposal. Meanwhile, significant progress has been achieved with the two other projects:

Clostridial Vaccines: Work is focused on Cl. septicum and on the replacement of toxicity and antigenicity testing in mice by cell line-based assays. A validation study (BSP130) with 11 participants conducted under the joint aegis of EPAA and EDQM (Council of Europe) has been completed.

The results of the study were discussed with the participating laboratories at the “EPAA-EDQM workshop on Clostridium septicum vaccines project BSP 130” (15-16th September 2015 at Egmond aan Zee, the Netherlands). The results show that the in vitro assays are repeatable and reproducible and that there is excellent overall concordance with the mouse tests. However, the in vitro assays were not fully optimised and the findings directly relate only to Cl. septicum antigens. Further work is necessary to fully validate the in vitro assays and subsequently incorporate them into the European Pharmacopoeia monographs. Discussion with the European Pharmacopoeia group of experts responsible for veterinary vaccines (15V) on inclusion of the in vitro methods into the relevant monographs has started in October 2015. It is expected that the final report of the collaborative study will be finalised by the end of 2015 and the corresponding scientific paper will be subsequently prepared.

EPAA and EDQM (Council of Europe) are currently discussing a possible continuation of the project by the conduct of a collaborative study with optimised in vitro assays.

Human Rabies Vaccines: The overall aim is to replace the current in vivo potency test (NIH, mice intracranial challenge test) for human rabies vaccines with in vitro antigen quantification using ELISA technology. A pre-collaborative study involving five laboratories to evaluate three ELISAs and to select the most appropriate ELISA has been completed.

A workshop was held on 10-11th May 2015 to discuss the results, to agree on the chosen ELISA characteristics and to define the next steps. Participants included representatives of EDQM, regulatory bodies, manufacturers and participating laboratories, and WHO.

Next steps:

(i) A paper is being drafted to publish the results of the pre-collaborative study and selection of the agreed ELISA method.

(ii) Evaluate whether or not the agreed ELISA method is applicable to rabies vaccine strains less frequently used for vaccine production; i.e. other than the three included in the pre-collaborative study.

(iii) Based on the endorsement of the group on the protocol, a proposal for a BSP collaborative study will be drafted and submitted to EDQM. The BSP collaborative study should evaluate the transferability and reproducibility of the ELISA method across a larger number of laboratories and a panel of vaccines representative of the global market.

Presentation of the data on the suitability of the agree ELISA method for multiple rabies vaccine strains and a proposal for a collaborative study to BSP are expected by June 2016. Key issues currently being addressed are the availability of vaccines samples from different manufacturers and funding of this preparatory work for a BSP study.

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1 An article summarising the activities and progress of the project has just been published (De Mattia F et al., 2015. The Vaccines Consistency Approach Project: An EPAA initiative. Pharmeuropa Bio&SN, May 2015, 30-56).
c. Acute Toxicity

Replacement of death as an end-point and waiving of the dermal route

Whilst acute toxicity testing is no longer needed in the pharmaceutical sector and is banned in cosmetics, evaluation of acute toxicity is still required for chemicals and agrochemicals in order to establish their overall hazard profile and classification, labelling and packaging (CLP) requirements that are relevant for human safety, for example, in emergency situations.

The REACH standard information requirements for the endpoint of acute toxicity (REACH Annex VIII, point 8.5) currently requires testing via two routes for substances in the tonnage band at 10t and higher, unless the second route can be waived based on exposure consideration.

Based on technical progress and recently established 3Rs “best practices” for acute toxicity testing adopted in the EU biocides and plant protection data requirements, the EPAA Acute toxicity technical expert group and the Humane Society International submitted proposals to the European regulators, in 2012, recommending to waive acute toxicity testing via the dermal route for substances which are non-toxic via the oral route. The aim is to improve animal welfare and facilitate reduction in animal use for meeting information requirements under REACH. The proposals are being considered at the level of Competent Authorities for REACH and CLP (CARACAL) and it is expected that they will be adopted soon.

The EPAA project has identified opportunities to waive acute animal testing requirements completely or, where this is not possible, to refine the decision-making steps or assessment strategies to minimise suffering of test animals. Recommendations on a 3Rs-based classification & labelling decision framework to include replacement of death as an endpoint have been drafted. Additional evidence in support of this framework is being developed through data mining of acute oral toxicity studies in collaboration with the UK National Centre for the 3Rs (NC3Rs) and the UK Chemicals Regulation Directorate. Data from previously filed acute toxicity studies are collected and will be analysed to confirm that clinical signs (evident toxicity) are an appropriate alternative to death as an endpoint. The findings will be considered in the overall framework document.

In 2015, the data mining exercise has been further progressed, although delays were encountered in the selection and accessibility of the data.

In addition, further to a request from ECHA, industry members of EPAA shared experience on Acute Toxicity assessment for REACH purposes based on feedback received mainly from cosmetic and chemical companies. Discussions with ECHA are ongoing to ensure relevance of project outputs to ECHA guidance for acute toxicity and classification of chemicals which will be updated in 2016.
d. User-friendly in vitro/in vivo exposure predictor

A user-friendly web-based tool for exposure prediction

Building on earlier work, such as workshops, review papers and research supported by EPAA and its partners in the area of ADME (Absorption, Distribution, Metabolism and Excretion), an EPAA-funded project was initiated in June 2014 at the Health and Safety Laboratory (HSL, UK). The aim of this project is to expand HSL’s existing PBTK model equation generator to a user-friendly, free-to-use, web-based, open-source tool that would enable exposure predictions (from in vitro to in vivo and from in vivo to in vitro). Exposure needs to be assessed before conducting risk assessment of chemicals, pharmaceuticals and other products to which people are exposed. The tool will eventually be made freely available online.

In this project, in vitro measurements of concentration-response relationships are used to identify where prolonged or excessive perturbations of biochemical pathways are likely to cause adverse health effects. A wide range of in vitro, in silico and in chemico generated data are compiled in physiologically-based toxicokinetic (PBTK) models.

The first tasks aimed to build a more user-friendly version starting of the computational model originally built by HSL were completed as planned in the first half of 2015 and the preliminary prototype version of the “downloadable app” was delivered and assessed by the EPAA Technical Advisory Team, to which also CEFIC LRI and ECETOC representatives participate, in July 2015. Further steps include performing a global sensitivity analysis, Markov Chain Monte Carlo (MCMC) sampling and entering of anatomical, physiological and biochemical parameter ranges in the system. The project is expected to be completed by December 2015.

By enabling across sector sharing of knowledge and experience, the EPAA has facilitated the optimisation and application of this innovative approach to industry’s needs. In addition to the interest expressed by the chemical sector, pharma companies from the American 3Rs Lead group of IQ are interested in testing the tool later on. This is an example of the synergies developed between EPAA and its partners as research ideas or approaches incubated in EPAA have been brought into larger research programmes (e.g. Cefic LRI, IMI-2, SEURAT-1) or tested for application in different sectors.

“The user-friendly tool will eventually be made freely available online”
e. Biologicals

International convergence of 3Rs in Biologicals

Art. 13 of the EU Directive 2010/63 on the protection of animals used for scientific purposes requires the use of alternative methods to animal testing always where they are recognised by the EU legislation. For global industries it is therefore important that where regional divergences of regulatory testing requirements exist, a convergence is facilitated to enhance application of 3Rs.

Most regulatory testing divergences (animal vs. non-animal tests or test waivers) occur in the field of biological products leading to unnecessary duplication of testing that impacts on the one hand animal welfare (excessive use of animals) and on the other hand the manufacturers. It increases the development costs, is ethically unsound, and may delay patient access to essential vaccines and medicines. Against this background, the EPAA Biologicals project brought together representatives of European and international stakeholders to analyse existing differences in regulatory safety and potency testing requirements for human and veterinary vaccines as well as other biologicals (e.g. blood products, monoclonal antibodies, etc.) between the EU and other regions, identify areas that would benefit from a specific coordinated action at a global level and jointly design most effective pathways towards international convergence in the application and acceptance of 3Rs methods.

EPAA hosted an international workshop gathering 46 participants from industry as well as European and overseas regulators on 15-16th September 2015 entitled “Modern science for better quality control of medicinal products: Towards global harmonization of 3Rs in biologicals” to discuss four case studies and on this basis, to understand the reasons and barriers why differences exist in regulations. The workshop defined concrete actions required to progress internationally harmonised translation and uptake of 3Rs into regulatory practice. Key opportunity identified to reduce animal use was the deletion of the obsolete general safety tests for vaccines that are still a legal requirement in some geographies. The participants agreed that these tests do not have any scientific justification anymore and developed a plan to delete this testing requirement.

Participants agreed that building the confidence of all relevant regulatory authorities in the new non-animal methods is key to promote their global acceptance. The WHO and the OIE are key players in pursuing this task since all national authorities are required to make communications to these organizations. From the European perspective, all initiatives should further take into account ongoing 3Rs-relevant work at the EDQM and the EMA via its joint expert group on the application of the 3Rs in regulatory testing (JEG 3Rs).

Also after uptake of a new method, e.g. in the respective pharmacopoeia monographs, further initiatives may be necessary to provide evidence to individual authorities that the new method is indeed able to detect inconsistent batches. Industry is the key player in furthering the use of the new methods, even more so since, e.g. in Europe, the Official Medicines Control Laboratories that assist national authorities during vaccine lot release are obliged to use the same tests as the marketing authorization holders. To ensure adequate control, the new methodologies have to capture the key quality parameters that are essential for safety assessment. There was consensus that the consistency approach is key for promoting the regulatory acceptance of new assays.

Finally, also financial incentives were addressed as supplementary tools to promote the validation and use of new, non-animal test methods on the manufacturer’s side. For instance, in Germany and in the United Kingdom charges are reduced, when batch release tests are based on non-animal methods. While it was confirmed that such measures would contribute to alleviate the economic hurdle to validate new product-specific methods, the need for global harmonization of testing requirements was recognized as core element in promoting the 3Rs principle in the area of vaccine quality control.

Striving for global harmonization was seen as a combined evolutionary process during which the regulators in charge of animal testing, the regulators in charge of assessing the vaccines and the manufacturers engage in continuous collaborative discussions.

A comprehensive report will be available in December 2015 and the project team aims at submitting its conclusions for publication in a peer-reviewed journal.
f. Advancing the 3Rs in Regulatory Toxicology

Waiving of two-year carcinogenicity studies

Building on the outcome of an earlier review and workshop held by EPAA, this project is being progressed since mid 2013. It aims at collecting scientific evidence through an extended database that would convince regulators to accept waiving of the 2-year carcinogenicity study on rats. This study forms part of the regulatory package for pharmaceuticals, additives and chemicals (mainly agrochemicals) and it entails the use of large number of animals, high costs and time. The rodent carcinogenicity study relevance for human safety has been questioned since long, but thus far it remains the default choice.

The overall objective is to identify opportunities for improving the science supporting the regulatory testing of medicines and chemicals and to achieve Reduction when assessing carcinogenicity.

The project is funded by EPAA and is carried out by the University of Wageningen in collaboration with the Medicines Evaluation Board (The Netherlands). Data from sub-chronic toxicity and carcinogenicity studies of pharmaceutical compounds have been collected and analysed in order to extend the dataset of Sistare et al (2011). The larger dataset is expected to confirm the earlier hypothesis of these authors that the absence of specific histopathological findings that can be considered risk factors for the development of tumours in rats from 3 and 6-month rat sub-chronic toxicity studies together with negative findings in certain other short-term in vitro and in vivo (genotoxicity) studies may provide sufficient information to predict the rat carcinogenicity outcome, which may prevent the need for a 2-year rat carcinogenicity study (Sistare et al., 2011).

In 2015 the researchers completed the dataset compilation of 364 compounds. These included True Negative, True Positive, False Positive and False Negative compounds based on histopathology results. The data has been stored in the open access ToxRef database in an anonymised way. The histopathology data have been integrated with pharmacological properties of the compounds. A peer-reviewed publication with the conclusions from the extended database will be delivered in the following months (Q1 2016).

On the basis of the publication, a team from EPAA and EFPIA’s Preclinical Development Committee is expected to develop an ICH concept paper in 2016 and agree concrete next steps for talking to the regulators.


“In vitro and in vivo (genotoxicity) studies may provide sufficient data to prevent the need for a 2-year rat carcinogenicity study”
Purpose of this project was to explore the opportunities that stem cells could play in developing novel approaches for the potential hazard characterisation of chemicals and drugs. The identification of gaps in fundamental research on stem cells finally leading to appropriate stem cell derived in vitro models and testing strategies was the top priority for EPAA as well as the selection of cell types of interest for screening and mode of action investigation. This was regarded as a cross-sector project with promising long-term 3Rs benefits. EPAA teams worked on both fundamental research aspects and international collaboration bringing together Stem Cells research consortia.

Indeed, the first working group on ‘Fundamental research on stem cells’ and the associated external stem cells experts identified recommendations for further research that were published in Stem Cells and Development, 2015¹ and stimulated their inclusion into various proposals for scientific research calls (Horizon 2020 etc.).

In late 2014, the second group on “Stem Cells Communication” co-organized an international Stem Cells Forum with the University of Liverpool, UK. The report is under preparation and will be made available online at a later stage. While the Stem Cells Forum proved its attractiveness with overseas participation from US, Canadian and European regulators, it was difficult to maintain activities in Europe on the industry side.

Therefore, in the light of other ongoing activities and research carried out outside EPAA, primarily in the pharmaceutical sector, both stem cells workgroups do not anticipate further activities for the time being, especially since stem cells do not seem to be ready for use in the regulatory context in the medium term. Consequently, the EPAA Steering Committee recommended ceasing Stem Cells activities, reallocating resources for other EPAA cross-sector projects.


“Recommendations from fundamental research experts on stem cells helped defining various proposals for scientific research calls (H2020, etc.)”
IV - Communication and Dissemination Initiatives

Publications in peer-reviewed journals

In 2015, EPAA published 5 peer-reviewed articles summarizing the conclusion of its projects, workshops and scientific recommendations:


Scientific workshops in 2015

In 2015, the EPAA partners organised 4 scientific workshops focusing respectively on:

- EPAA-Cefic LRI-Cosmetics Europe Joint cross-sector workshop on Alternatives for Skin sensitisation testing and assessment, Helsinki, Finland, 23-24 April 2015


- EPAA-EDQM workshop: Clostridial Vaccines workshop BSP 130, Egmond Aan Zee, the Netherlands, 15-16 September 2015

- EPAA Workshop: Modern science for better quality control of medicinal products ‘Towards global harmonization of 3Rs in biologicals, Egmond Aan Zee, the Netherlands, 15-16 September 2015
International conferences

This year, EPAA was represented at the following conferences:

- **EUSAAT 2015** (European Society for Alternatives to Animal Testing) 20-23 September, Linz, Austria
- **EUROTOX 2015**: 51st Congress of the European Societies of Toxicology Bridging Sciences for Safety, 13 - 16 September 2015, Porto, Portugal
- **International Alliance for Biological Standardization (IABS)**, 16-18 September, Egmond aan Zee, the Netherlands

Implementing Alternatives: Video tutorials on Alternatives

In association with the Institute for In Vitro Sciences, EPAA sponsored the development of video trainings on implementation of alternatives methods. In 2015, videos were published on the Bovine Corneal Opacity & Permeability Assay (BCOP) in English, Portuguese and Chinese. These videos are available for free on YouTube’s DG Growth channel.

EPAA and IIVS will keep on collaborating on a second video training on the 3T3 NRU Phototoxicity assay, to be released in 2016.

Websites

EPAA revamped its Internet presence, which is now hosted on the website of the Commission’s Directorate-General Internal Market, Industry, Entrepreneurship and SMEs. Please browse the website to find the latest information available about EPAA and its activities (Workshop proceedings, project reports, etc.): [http://ec.europa.eu/growth/sectors/chemicals/epaa/](http://ec.europa.eu/growth/sectors/chemicals/epaa/)

EPAA is also Tweeting: follow us: @EPAA3Rs

3Rs Laboratory Technician / Animal Caretaker Prize 2015

The second EPAA Laboratory Technician Prize has been awarded in 2015. This €3000 prize is bestowed on a laboratory technician/animal caretaker who has demonstrated outstanding achievement in implementing and raising awareness of Replacement, Reduction and Refinement of animal testing. In 2013, the first 3Rs Laboratory Technician Prize was awarded to Jan Bilton of Leeds University.

Laboratory technicians and animal caretakers carry out much of the work using animals for regulatory safety testing purposes and are thus closely involved in efforts to apply refinement strategies in such studies. The purpose of this prize is to acknowledge those actually implementing alternative approaches to animal testing and raise awareness of their role for the day to day application of 3R principles and, in particular, for refinement strategies. Refinement refers to improvements to scientific procedures and husbandry which minimise actual or potential pain, suffering, distress or lasting harm and/or improve animal welfare in situations where the use of animals is unavoidable.

A jury made of representatives from the EPAA Mirror Group, EPAA Commission and Industry partners selected Alexandra Lorenz from TissUse GmbH for her work on “A multi-organ chip for co-culture of organ equivalents for long-term substance testing”.
V - Membership update

As of November 2015, 7 industry umbrella associations, 36 companies and 5 Directorates General of the European Commission are members of EPAA.

Further information is available online at www.epaa.eu.com or http://ec.europa.eu/growth/sectors/chemicals/epaa/partners/index_en.htm
VI- ACRONYMS AND ABBREVIATIONS

3Rs: Replacement, Reduction and Refinement of Animal Testing
3T3 NRU PT: Neutral Red Uptake Photo-toxicity assay using the 3T3 mouse fibroblast cell line
AAT: Alternatives to Animal Testing
AOP: Adverse Outcome Pathway
BCOP: Bovine Corneal Opacity & Permeability Assay
BSP: Biologicals Standardisation Programme
CARACAL: Competent Authorities for REACH and CLP
CEFIC: European Chemical Industry Council
CLP: Classification and Labelling of Products
DG ENV: European Commission Directorate-General for Environment
DG GROW: European Commission Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs
DG JRC: European Commission Directorate-General Joint Research Centre
DG RTD: European Commission Directorate-General for Research and Innovation
DG SANTE: European Commission Directorate-General for Health and Food Safety
EC: European Commission
ECHA: European Chemicals Agency
EDQM: European Directorate for the Quality of Medicines & HealthCare (Council of Europe)
EFPIA: European Federation of Pharmaceutical Industries and Associations
ELISA: Enzyme Linked Immunosorbent Assay
EMA: European Medicines Agency
EP: European Parliament
EPAA: European Partnership for Alternative Approaches to Animal Testing
EURL ECVAM: The European Union Reference Laboratory for Alternatives to Animal Testing
EUROTOX: Association of European Toxicologists and European Societies of Toxicology
EUSAAT: European Society For Alternatives To Animal Testing
IATA: Integrated Approaches to Testing and Assessment
IMI: Innovative Medicines Initiative
ITS: Integrated testing strategies
JEG 3Rs: Joint Expert Group on 3Rs
NC3Rs: National Centre for 3Rs (UK)
OECD: Organisation for Economic Co-operation and Development
OIE: World Organisation for Animal Health
REACH: Registration, Evaluation, Authorisation and Restriction of Chemicals
SEURAT-1: Safety Evaluation Ultimately Replacing Animal Testing
WHO: World Health Organisation
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