EPAA 2008 PROGRESS REPORT

The European Partnership
for Alternative Approaches to Animal Testing

EPAA 2008 PROGRESS REPORT
CONTENTS

1. EXECUTIVE SUMMARY

The European Partnership for Alternative Approaches to Animal Testing (EPAA) is a joint initiative from the European Commission, European industry associations and individual companies from seven sectors. It was launched in November 2005 to promote modern alternative approaches in the field of safety testing.

Evaluation of safety is the legitimate precondition that society - and science - imposes on products that are placed on the market, administered to patients, or released into the environment. Regulatory requirements currently imply the use of animals for many of the tests on human and veterinary medicines, food additives, consumer products, agricultural and industrial chemicals and biological substances. The objective is to generate the necessary safety data to undertake risk assessments that effectively protect human and animal health and the environment.

The work of EPAA is focused on the development and implementation of new approaches that can replace, reduce, or refine the use of animals in such tests - a concept collectively known as "the 3Rs".

EPAA continues to grow as it conducts this work. Two further companies joined during the year, bringing its corporate membership to 37. Seven sector associations are also partners, representing chemicals, pharmaceuticals, cosmetics, biotechnology, veterinary medicines, soaps and detergents, and crop protection products. Five Directorates-General of the European Commission are also partners: Enterprise and Industry; Research; Health and Consumer Protection; Environment; and the Joint Research Centre, with its European Centre for the Validation of Alternative Methods (ECVAM).

EPAA is very much a partnership. With its broad membership, it constitutes a platform where every party brings sectoral or institutional experience to the search for better procedures and processes. This makes it possible to identify good practice, and - crucially, as this year has demonstrated - to reapply it, within and across sectors. Because EPAA embraces both the “regulators” and the “regulated”, it can bring the two perspectives together, and help to create new solutions through joint public/private collaboration.

For the development of strategic direction and the implementation of its Action Programme, EPAA benefits from discussion with the Mirror Group, i.e. independent experts from academia, animal interest groups and other stakeholders. Experts from several NGOs and other stakeholder groups also take an active part in EPAA activities.

In this way EPAA offers a win-win situation to all collaborating partners - and the best chance of making real advances both in tests and in the testing regime, ensuring high levels of safety while helping replace, reduce, or refine the use of animals.

A mid-term revision to EPAA's Action Programme at the beginning of 2008 clarified the tasks of each of its working groups, reinforcing the potential for cross-sector reapplication, cross-fertilisation and synergy among them, and re-focusing their activities on tangible outcomes.

The lead theme for EPAA in 2008 is "Research into 3Rs". Research has been promoted particularly through a workshop in April 2008 on new perspectives on safety, which has developed recommendations for further follow-up. The outcome will also help to inform future calls for proposals that the EU will issue under its new framework research programme, FP7, and will help define new fields of investment.

There were several notable achievements during the year in terms of reapplication - where the same testing approach, the same regulatory practice or the same techniques successful in one sector can be redeployed in other sectors. EPAA efforts to reapply regulatory practices are further demonstrated by the work that it has commenced on applying to other sectors the experience of the pharmaceutical sector in reducing acute toxicity testing, and another project on *in vitro* metabolism - one of the most difficult areas, but also with great potential for reapplication and collaboration. The evolving EPAA databases of in-house methods and ongoing research projects also provide valuable information for reapplication and have served as a basis for beginning the activities on *in vitro* metabolism. Investigating the applicability to other sectors of an extended one-generation approach developed for crop protection was an important milestone.

Work continued on finding ways to overcome the identified barriers to validation. A new framework for collaboration with ECVAM has been established, particularly through a May 2008 workshop with ECVAM. In particular, during this workshop input was provided on the rationalisation of test submissions. Recommendations have been developed on peer review and will be presented to the ECVAM Scientific Advisory Committee, ESAC. The work on 'barriers to validation' represented a genuinely collaborative activity of EPAA, with industry, and the European Commission all working together to characterise the issues in a constructive search for solutions.

EPAA and its partners have acted to promote faster and more efficient regulatory acceptance. There has been some initial scoping on the creation of a single information portal, which is an attempt to fill gaps in information that potentially impede the uptake of 3Rs methods. Work has also advanced on developing a regulatory module in validation. Procedures for regulatory acceptance have been reshaped at EU level. And more generally, there has been a consistent attempt to find ways to involve regulators at all stages right from the validation process, including at international level.

EPAA makes the best use of synergy in combining its efforts - for instance in the projects on *in vitro* metabolism or on acute toxicity. It demonstrates improved collaboration in areas such as validation. And it shows that it is turned face-on to the future with endpoint-based integrated testing strategies, with its alertness to different ways of validating/assessing/reviewing alternative approaches, and with its determination to reinforce its data bases - including the ambition to build on all EU framework programme research projects.

The provision of truly innovative approaches that will allow the safe development of new products without recourse to animal studies is amongst the great scientific challenges, and is promoted as such by EPAA. Research and development of new knowledge and understanding of biological events is required to develop new methods and approaches, and this is a long process, which can extend over many years. The lack of full replacement for animal testing is not due to an investment deficit, but rather the lack of adequate science. Despite the advances in computer modelling and in alternative methods such as the use of cell cultures, the development of diseases or physiological processes cannot always be sufficiently studied with these techniques. But the fact that achieving that goal fully is beyond the current horizon does not make the challenge any less intriguing, or any less worthwhile.

EPAA is the manifestation of these continuing efforts. This progress report offers some further detail on what is still very much work in progress in the search for and implementation of techniques of replacement, reduction and refinement. The research conducted and the conferences organised are examples of the steps towards realising the longer-term goal.

EPAA itself is not, of course, the principal agent for the application of new methodologies. It focuses the theory and suggests ways for improving the development, validation and acceptance. The generation of alternative approaches and their practical application are dependent on the ingenuity, investment and innovative capacity of organisations conducting research and testing. And even when promising alternative tests are developed, they must await validation and acceptance by the regulatory authorities. What gives EPAA its particular significance in this process is that its membership unites so many of these different elements - and therefore increases the chances of stimulating progress and seeing it put into effect.

Where EPAA partners cannot bring a solution, they suggest a roadmap that could lead to one, and identify stakeholders for implementation and follow-up.

More detailed information is available on www.epaa.eu.com.

2. HIGHLIGHTS OF EPAA WORK DURING THE YEAR

The lead theme for 2008 was **research**. The revised Action Programme and activities undertaken placed more emphasis on **reapplication** of solutions across sectors. Among the numerous initiatives taken by EPAA in its second full year of operation, we highlight below the activities which have had the greatest impact on understanding and prospects for alternative approaches.

NEW PERSPECTIVES ON SAFETY

Hazard characterisation is one of the most challenging questions in safety testing generally, and specifically for alternative approaches to the use of animals. The main topic for one of EPAA's working groups during 2008 has been assessing the potential of exogenous chemicals or proteins to elicit adverse effects, as revealed by chronic repeat dose systemic toxicity testing.

The April 2008 workshop on “New Perspectives on Safety” brought together eminent scientists from different disciplines to advise on the research needed to enable future hazard identification without the use of animal testing. Under the moderation of the Editor-in-Chief of Nature magazine, constructive discussions were held on questions raised by EPAA and stakeholders. The meeting identified areas of complementary science which have the capacity to revolutionise the science of safety assessment. The key success factor will be engagement of the wider science community through legitimisation of alternatives research.

The workshop objectives were:

- To identify truly novel 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 confer greater legitimacy on alternative research among the scientific community.
- To engage a wider segment of the research community in consideration of the ways in which new developments in science and technology can be exploited for improved safety assessment.

The participants agreed there is a case for reconsidering the science base for regulatory testing in the field of repeat dose systemic toxicity. They felt the time is right to harness the

substantial achievements in biology and chemistry during the last ten years, putting the discoveries and technological advances to use in the development of alternative approaches. The opportunity exists to re-invigorate alternatives research.

Funding was recommended particularly at the nexus of the disciplines of toxicology, biology chemistry and mathematics. The workshop also identified opportunities in computational chemistry, in mathematical modelling, in stem cell biology and in the potential of various 'omics' technologies, which could each be developed in tandem with systems biology and bio-engineering.

Innovation can play its part in refinement and reduction as well as in the longer-term prospect of replacement. The meeting urged consideration of approaches using lower organisms linked with highly targeted transgenic animals. Recommendations for the future included subject-focused workshops and steps to ensure greater access and compatibility to databases.

The provision of truly innovative approaches to testing that will allow the safe development of new products without recourse to animal experiments is amongst the great scientific challenges. The current remoteness of this goal is an incentive to action rather than a discouragement.

The next steps include follow-up on scientific conclusions, possible input for future funding programmes, and communication through a peer reviewed commentary. An EPAA working group is following up the workshop to ensure that all the research opportunities raised are properly addressed, in particular within FP7.

More information: http://ec.europa.eu/enterprise/epaa/wg_2.htm

PROMOTING 3RS RESEARCH TO YOUNG SCIENTISTS

In 2008 EPAA supported the *ecopa* (European Consensus Platform for Alternatives) Science Initiative (eSI workshop), held on October 16-19, near Alicante, Spain. The workshop is organised bi-annually by *ecopa* in order to attract the interest of young scientists, promote 3Rs in basic research and inject promising new ideas, mainly from academia, into the existing scientific pool. This year, the workshop addressed scientific and technological progress in the pharmaceutical and cosmetic fields with regard to 3Rs.

IN VITRO METABOLISM AND THE EPAA DATA BASES

The information needed to assess substances is at the heart of a workshop on in-vitro metabolism organised by EPAA for November 24-25, which could ultimately lead to developments in replacement. This has been designed to involve a carefully defined selection of regulators in an evaluation process. EPAA is focusing on overcoming the limited ability of most *in vitro* methods to metabolise xenobiotics. Evaluation of methodologies available through the EPAA's evolving databases has revealed deficiencies in the ability to account for metabolism among existing alternative approaches, and a potential lack of ongoing research projects addressing this need. EPAA is therefore examining the definition of further research needs, and elucidating the integration of metabolic competence into *in vitro* test systems to make them more predictive for toxicity assessment.

The objective of the workshop is to identify research needs for *in vitro* toxico-kinetics and metabolism in the context of methods and risk assessment strategies. At the same time it will

look at *in vitro* approaches to systemic toxicity and hazard identification for target organs, and the steps required to build in regulatory acceptance. It will review

(i) Developments (publications, workshops, industry findings) that have taken place in the past five years in the field of metabolism and ADME-derived toxicity,
(ii) Activities and results in recent and upcoming framework programmes,
(iii) Regulators' views of how the topic of metabolism could be addressed with in-vitro alternatives,
(iv) Current use of alternative approaches to metabolism and ADME-derived toxicity in industry,
(v) Research support policies from the different stakeholders.

A core team has been formed, and evaluation initiated of current activities and data gaps.

Further information: http://ec.europa.eu/enterprise/epaa/wg2_20081124-25_invitation.pdf

EXTENDED ONE-GENERATION STUDY

Transferring successful approaches from one sector to another is a deliberate strategy EPAA is championing. In 2008 it has devoted attention particularly to whether a valuable alternative test developed for agrochemicals by the ILSI/HESI project on agricultural chemical safety assessment (ACSA) could also be applied to other sectors such as industrial chemicals. Feasibility of the ACSA extended one-generation study protocol is currently being evaluated.

The ACSA testing proposal was designed in the context of an intelligent testing strategy for the evaluation of agrochemicals aimed at addressing the inefficient development of data, much of which is not used in the final risk assessment. It is a scientifically robust approach to reduce and refine the studies required for registration of agrochemicals. One of the core elements is an extended one-generation reproductive toxicity study to replace the classical two-generation study (OECD 416).

An EPAA workshop organised in 2006 concluded that the extended one-generation study could, in principle, be applicable to safety testing under REACH. However, it was also agreed that the complex ACSA protocol would have to be modified in order to meet the current requirements for industrial chemical safety testing.

Since the extended one-generation study addresses far more endpoints than currently required for chemical risk assessment, the ACSA test protocol for use under REACH needs modifying to design reliable triggering and/or waiving criteria for the components of the protocol as modules. A task force of the European Centre for Ecotoxicology and Toxicology of Chemicals has developed these criteria (ECETOC Doc. No. 45, 2008). A subsequent workshop jointly convened by ECETOC and ECVAM in April 2008 discussed these criteria, their relevance, and possible validation needs with invited representatives of industry, academia, and the regulatory community.

Studies on model compounds, based on the ACSA protocol, have been initiated by industry partners (BASF, Bayer CropScience, Dow Agroscience, and Syngenta) of EPAA. It is expected that results from these feasibility studies will be available towards the end of 2008.

The next steps include the evaluation of the outcomes of these feasibility studies, and in-depth discussion with regulators concerning the validity of the one-generation study vs. the value of the second generation in the OECD 416 study. An OECD working group will develop a draft guideline for an extended one-generation study.

The animal welfare benefits delivered by this project include both refinement and a reduction in the number of animals used (more than 40% compared to the two-generation study).

More information:

- http://staging.idweaver.com/ECETOC/Documents/20081009163922-WR_12.pdf
- http://ec.europa.eu/enterprise/epaa/wg_2.htm

ACUTE TOXICITY

Another example of EPAA's work in reapplying approaches from one sector to another is the work on acute toxicity testing. This form of testing currently consumes a large number of animals. Despite significant progress in refinement developed in different sectors, the studies are still associated with substantial adverse effects. In addition, they provide only limited data compared to other animal studies, mainly to estimate likely lethal dose levels needed for classification and labelling purposes for chemicals and agrochemicals. Consequently, the practice has been frequently criticized on both scientific and ethical grounds.

A review of the scientific drivers carried out in the pharmaceutical sector in collaboration with the UK Centre for 3Rs (NC3Rs) led to a successful challenge to the requirement for acute toxicity testing in the assessment of safety for humans in the development of new medicines, and a reduction in animals used. The review revealed that acute toxicity data are:

- Extremely limited with regard to the parameters examined, concentrating on minimum lethal and maximum non-lethal doses.
- Do not provide information on the nature of toxic effects, which are better evaluated in other routine studies
- Are not, in practice, used to set doses in the first human clinical trials or in human safety assessment because other routine studies provide more informative data.

The sharing of best practice led to a reduction of studies carried out. A revision of international guidelines (under the International Conference on Harmonisation) is now ongoing, with eventual waiving of acute toxicity testing likely.

This may lead to questions for other sectors and is an opportunity for EPAA to conduct a proactive analysis of regulatory and scientific drivers across sectors and to make recommendations on what is possible or not in different sectors. Because acute toxicity tests are conducted in most sectors, they are an ideal subject for cross-sectoral analysis and sharing of best practice with the aim of identifying opportunities for application of the 3Rs.

Based on experience in the pharmaceutical sector, a project team of EPAA members and additional stakeholders is now examining on a cross-sectoral basis the need for acute toxicity studies where only very limited value is obtained. Where the acute toxicity test cannot be waived, the collaboration may lead to improved study designs with direct 3Rs benefit. A meeting in May reviewed the drivers in each sector, and some areas for 3Rs opportunity were subsequently agreed - notably, to review whether data will support challenging the current requirement for more than one route of administration for classification purposes (e.g. oral, inhalation, dermal).

The next steps will include a follow up analysis by ECVAM of the data available with the New Chemicals database, with additional data supplied from the group members to ensure all sectors are covered. Further meetings will follow up on the areas identified for data sharing/analysis, including eventually a workshop and publication of recommendations. This could possibly result in a significant reduction in animal numbers in these tests.

More information:

- http://ec.europa.eu/enterprise/epaa/wg4_acute_tox_for_cross_sector.pps
- http://ec.europa.eu/enterprise/epaa/ann_conf_2007/posters/az_acute_tox_parliament_final_poster.pdf

OVERCOMING BARRIERS TO VALIDATION

A workshop organised in Ispra in May 2008 by ECVAM and industry members of EPAA opened the way to optimising administrative procedures with the validation path. Aspects such as the peer review process, test submission, and availability of reference in vivo data were discussed. Processes were assessed and recommendations made to streamline and shorten some administrative procedures (taking into account the ongoing work already undertaken at ECVAM).

Consequently, an opportunity has opened up to tackle in a similarly collaborative fashion the challenges of validating and promoting the acceptance of alternative approaches for complex endpoints that require integrated testing strategies.

Among the key recommendations were:

- Transparency (unique entry point and clear timings) and the systematic application of identical procedures for all submissions for validation should be enhanced;
- A case study: a new two-step submission process should be tested on three partial replacement methods for skin sensitisation in order to establish realistic timelines, necessary SOPs and regulatory relevance;
- Criteria for admitting a method for a validation study will be defined and disclosed. Such criteria, it was agreed, will include regulatory relevance, such as the need to formally validate a method in order to accept its use in the regulatory context;
- The selection of test substances for validation studies should not include proprietary substances and data. Stakeholders should be involved in the test /substance selection at an early stage of the validation study.
- Adjustments should be made to the peer-review process, such as broadening the pool of experts, allocating specific resources in ECVAM to follow the process, and organizing virtual work methods between ESAC meetings (twice per year);
- Other validation centres such as ICCVAM or JaCVAM should be consulted at an early stage. This might facilitate their involvement in the validation study and promote regulatory acceptance in other regions.

The follow-up work has already started at ECVAM: the dialogue on simplifying the structure and content of test submissions should result in a final document in the form of a user-friendly electronic submission. Partnership recommendations about the peer review process will be discussed with the ECVAM Scientific Advisory Committee in November. Based on the templates developed in collaboration with ECVAM, an early call for data is about to be launched for the skin sensitisation projects to provide input to the substance selection process, which would be carried out later with a view to launching the scientific validation work.

While not all implementation steps depend directly on the members of the partnership, the EPAA will encourage follow-up and monitor progress and barriers.

Remaining recommendations will be addressed in the course of 2008 and 2009.

The need for validation or other types of assessment, including testing strategies for regulatory purposes, will be examined further.

More information:
http://ec.europa.eu/enterprise/epaa/wg_5_3.htm

3. FOLLOW UP TO EPAA 2007 CONFERENCE: REGULATORY ACCEPTANCE

A number of activities are currently implemented by EPAA that address recommendations of the 2007 Conference. In addition to activities carried out by EPAA, attention is also drawn to other current activities independent of the EPAA framework, which were either presented in the 2007 Conference or will have a significant impact on the areas it highlighted, in particular on streamlining acceptance and regulatory drivers.

INFORMATION TO REGULATORS

Information to regulators was considered as the key condition for regulatory involvement. Measures contemplated by EPAA include:

- the work on a single portal for information on alternative approaches relevant for regulatory testing, to be hosted by ECVAM.
- the mechanisms for information to regulators from different sectors about the validation process (for evaluation of regulatory relevance)
- reapplication of experience gained through bilateral dialogue and scientific advice on 3Rs issues within sectors or across sectors ("one stop shop").

STREAMLINING ACCEPTANCE

Speeding up regulatory acceptance procedures was one of the main issues of discussion between the European Parliament and the European Commission during the debate on test methods for REACH. A number of measures will be implemented to speed up the acceptance process, including assessment of regulatory relevance, a web-based tracking mechanism for alternative methods, and close monitoring of the OECD process (along with opportunities for streamlining it).

REGULATORY DRIVERS

Work on a new regulatory framework on plant protection products is continuing at EU level, between the European Parliament, the Council and the Commission. Final adoption is foreseen for the first half of 2009. This framework will introduce strict rules on the 3Rs, including mechanisms to avoid unnecessary duplication of tests.

INTERNATIONAL COOPERATION

Alternatives to animal testing have become a priority in international discussions. Given the stringent timelines for the phase-out of animal testing for cosmetics in Europe, the European Commission, the US Food and Drug Administration, Health Canada and the Ministry of Health, Labour and Welfare in Japan are working together within the framework of the "International Cooperation on Cosmetic Regulation" (ICCR) and have created a working

group to enhance cooperation in replacing, reducing, and refining animal testing. As a result, the International Cooperation on Alternative Test Methods (ICATM) was created including validation bodies from EU, US, Japan and Canada, which will also address other sectors, such as chemicals.

Regulatory acceptance at international level beyond the EU is necessary, but will need more time, because of differences in regulatory incentives or in procedure. The enhanced international dialogue has deepened mutual understanding and willingness to adopt 3R approaches, and cooperation with regulators from other regions is starting already at the level of validation.

CASE STUDIES

Industry members of EPAA provided a number of additional data to allow the US ICCVAM to finalise and publish their report on the evaluation of the **Local Lymph Node Assay** in 2008. Final ICCVAM recommendations are expected before the end of 2008. On that basis, EPAA and its partners will examine how the assay can be further promoted for regulatory acceptance.

The European Pharmacopoeia Commission and its group of experts have published (20.3 of Pharmeuropa July 2008) a draft-general chapter on methods concerning monocyte-activation tests with the ultimate aim of regulatory acceptance of possible alternative ***in vitro* pyrogenicity tests** as discussed in the 2007 Conference. Furthermore ICCVAM is still evaluating the five alternative *in vitro* pyrogenicity tests (raising the prospect of possible acceptance beyond Europe).

4. OUTLOOK

Activities undertaken by EPAA are in their majority multiannual projects which will continue throughout 2008-2010. This section outlines new projects for which task forces were established:

- While **integrated testing strategies (ITS)** based on alternative approaches are already used outside the regulatory context, their validation in view of inclusion in regulations (where required) remains a challenge. EPAA will hold a joint workshop with ECVAM and EU regulatory agencies on 19-20 November. The objectives are to reach common definitions and identify the exact nature of the problem, and to decide on follow-up actions to resolve outstanding difficulties.

- The **Global Harmonisation System** (GHS) for classification and labelling of chemicals will have implications for animal testing. While the criteria for classification are defined by animal data, use of weight-of-evidence is strongly encouraged, making use of complex information to come to a conclusion - in the best case without performing new animal studies. This is usually done by an expert on a case-by-case basis. However, acceptance of the criteria for evaluation of *in vitro* and human data to classify substances in the categories defined by GHS is not yet clear. EPAA will explore the potential for an action to harness existing weight-of-evidence approaches and expert judgment across sectors, to maximise the possibilities for avoiding any additional animal testing. A first meeting of

the newly created taskforce for Evidence Based Classification and Labelling for Skin and Eye irritation took place on 17 October 2008.

- **REACH** requirements for data based on volume and exposure are likely to also result in temporary increase in animal testing. However, under REACH several **waiving possibilities** are offered (such as the use of existing information, read-across, grouping, human data and (Q)SAR), and animal testing should be performed only as a last resort. EPAA has defined a monitoring project to check how waivers can be used in practice. Implementation would require involvement of the European Chemicals Agency.

- **Dissemination** was chosen as the lead theme for 2009, an idea supported by the Mirror Group. The definition of characteristics of a single portal would be a key activity in this field. The single portal is meant to address practical issues that will help implementation of methods based on robust scientific evidence and evaluation. Regulators and other stakeholders will be consulted to define needs. Available sources of information such as the database of the Vrije Universiteit Brussel, the Commission's database for ingredients used in cosmetic products or the ECVAM Data Base Service on Alternative Methods (DB-ALM) will be further explored by EPAA. A workshop is being planned on dissemination and implementation, to prepare a programme of activities.

More information about EPAA activities, workshops, documents and governing bodies is available at www.epaa.eu.com

The EPAA Newsletter, providing regular information on the partnership's activities, is now distributed to EPAA partners and a wide range of authorities and otherwise interested parties. To subscribe, contact: entr-epaa@ec.europa.eu

Final 20/10/08

European Commission

DG Enterprise and Industry
DG Research
DG Health and Consumer Protection
DG Environment
DG Joint Research Centre (ECVAM)

Companies

Abbott
Astra Zeneca
Avon
BASF
Bayer
Beiersdorf
Chanel
Colgate-Palmolive
Dow
DSM
Elizabeth Arden
Estée Lauder
Euroderm
Evonik/Degussa
Glaxo SmithKline
Henkel, Phenion
Johnson & Johnson
Kanebo
Kimberly-Clark
L'Oréal
LVMH
Merck
Merck Sharp and Dohme
Novartis
Novo Nordisk
Novozymes
Pfizer
Procter & Gamble
Reckitt Benckiser
Roche (F. Hoffmann-La Roche)
Sanofi-Aventis
Serono
Shiseido
Solvay
StratiCELL
Syngenta
Unilever

Federations

Soaps and detergents (AISE)
Chemicals (CEFIC)
Cosmetics (COLIPA)
Crop protection (ECPA)
Human pharmaceuticals (EFPIA)
Bio-Industries (EuropaBio)
Animal Health (IFAH)

Annex 2: Steering Committee & Working Groups in 2008

- EPAA Steering Committee
  (G. Lalis, DG Enterprise and Industry - B. Garthoff, Bayer)
- Working group on mapping
  (DG Research - Procter & Gamble)
- Working group on research
  (DG Research - BASF)
- Working group on dissemination
  (JRC ECVAM - AstraZeneca)
- Working group on 3Rs in regulatory requirements
  (DG Enterprise and Industry - Henkel)
- Working group on validation and acceptance
  DG Enterprise and Industry - DG JRC ECVAM – EFPIA - L'Oreal)
- Communication Group
  (EFPIA)
- Project team on acute toxicity
  (AstraZeneca)
- Project team on REACH implementation
  (Bayer)
- Project team on Global Harmonisation System & 3Rs
  (AISE)