



Summary Record

MEETING OF EUROPEAN 3Rs CENTRES

21-22 April 2015

The meeting of European 3Rs centres was organised and hosted by EURL ECVAM at the Joint Research Centre (Ispra, Italy). The outcome of the discussions are summarised below and structured by the topics covered.

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1. Topics of Common Interest for Closer Collaboration

Each 3Rs centre introduced itself by describing its organisation and activities in advancing the Reduction, Replacement and Refinement (3Rs) of animal use for scientific purposes. This then helped participants to identify topics of common interest that could be further explored as a basis

for closer collaboration. The topics identified are as follows, ranked according to their importance/interest:

1. Identification of priorities to reduce animal use in biomedical research (incl. addressing concerns related to the increasing use of transgenic animals)
2. Communication and dissemination
3. Promoting the use of alternative methods/models as biotechnological resources (incl. characterisation and standardisation)
4. Education and training
5. Validation towards regulatory acceptance (incl. EU-NETVAL)
6. Research funding provided by 3Rs centres

A presentation was also given by S. Louhimies (DG ENV) on aspects of Directive 2010/63 including project evaluation. Topics 1, 2 and 4 were subsequently discussed in detail. In addition, other (cross-cutting) topics were covered to varying degrees, namely, (i) 3R-metrics; (ii) Networking between 3Rs centres; and (iii) the role of 3Rs centres in project evaluation (Directive 2010/63).

2. Reducing Animal Use in Biomedical Research

The participants acknowledged the fact that the proportion of animals used for scientific purposes in the EU is highest in academia for biomedical research (nearly 50%). There are also increasing concerns about the possible suffering of transgenic animals bred as disease models. The participants identified four main priorities for reduction of animal use in biomedical research:

Priority #1: More systematic and effective critical assessment of animal-based studies. This assessment should include historical as well as newly acquired mechanistic information provided by animal-free testing approaches. This information is to guide proper animal model selection or development, will ensure that animal studies are only conducted when really necessary, and are designed and carried out appropriately. It could also aid in better comparison of animal and non-animal based studies where appropriate.

Priority #2: Improve communication about all aspects of the 3Rs (see section 3) including the development of ambitious education and training programmes (see section 4). There are considerable resources and extensive knowledge that can be better used to replace, reduce and refine experimentation on animals. However it is believed that for the most part, project proposers and project evaluators are not sufficiently informed about alternative approaches leading to the approval of questionable studies. A thorough analysis needs to be conducted of the degree of awareness of the various actors and the findings should then be used to develop improved communication, education and training initiatives/programmes.

Priority #3: Understand and describe organisational and institutional obstacles to the 3Rs. This will help to explain and make evident the reasons for any absence of a well-embedded 3Rs-culture in an organisation and any lack of supporting processes for efficient and effective implementation of alternative approaches. It will help constructively and critically challenge the use of animal studies while promoting the 3Rs as central in delivering holistic solutions to research and testing needs in

the long-term. Systematically identifying and removing obstacles to the 3Rs will foster their uptake and increase impact and interest.

Priority #4: Facilitate more extensive input from 3Rs centres in the project evaluation process. This includes providing expert advice (or suggestions of experts that should be consulted) on the availability of alternative methods and approaches and advising funding bodies on the appropriateness of research proposals in light of adherence to the 3Rs.

3. Communication and Dissemination

Participants emphasised that communication and dissemination are key for promoting the 3Rs and that they should be expanded and strengthened to target four target groups/levels: (1) political; (2) academia & research; (3) regulatory authorities and (4) the public.

(1) At the political level, suitably targeted and tailored communication should influence political opinion about how alternative methods are not only ethically desirable but are also beneficial for society for many socio-economic reasons.

(2) At the level of academia and research, communication style and tools should capture the intellectual curiosity of scientists and trigger their interest in the 3Rs and stimulate them to develop and using alternative approaches. This should be supported by appropriate training and education programmes;

(3) At the level of regulatory authorities, the aim should be to make them aware of the existence and utility of alternative approaches, encouraging a stronger 3Rs culture and commitment in this community. An ambition would be to get more participation of regulatory bodies in demonstrating the scientific value and trustworthiness of 3Rs approaches.

(4) At the level of the public, communication should focus on conveying in simple terms (e.g. through practical examples or success stories) the importance of alternative approaches in improving human health and protecting the environment protection, in addition to addressing ethical concerns. Communication to the public needs to be more innovative to generate excitement and encourage more widespread engagement.

To achieve these objectives, the 3Rs centres identified several possibilities:

(a) Sharing intellectual resources and ways to advertise them to end-users. For instance, facilitating ready access to information and databases for researchers, evaluators and regulators;

(b) Coordinating communication at the European scale. This could be done through a dedicated communication-network of contact points in 3Rs centres. The network could ensure exchange, prior-notification, synchronisation and syndication of communication items while adapting style, content and anchoring to achieve maximum local impact.

(c) Amplifying news items about 3Rs issues across geographical regions and sectors. More optimal use of social media tools will be essential to reach a wide audience and maximise impact;

(d) Emphasising the economic and scientific merits of alternative methods in addition to their ethical value. This includes new business/market opportunities, job creation, supporting innovation in research and product development, increasing trade and exports, and better health and safety for humans and the environment.

(e) Giving guidance to test developers for improving the readiness and quality of candidate methods that could enter the validation process. Communicating expectations and good practice on regarding the design, execution and reporting of validation studies would also be of value since it would increase the amount and effectiveness of validation efforts and help to expedite the peer-review and regulatory acceptance process.

4. Education and Training

The participants considered education and training on the 3Rs and alternative approaches as being an essential element in creating strong 3Rs culture and practice within the research community. They recognised that although a number of 3Rs centres and many academic institutions have developed courses and course materials, there is a clear need to properly map education and training programmes already available or under development across the EU and beyond, to facilitate sharing and to stimulate joint initiatives. Education and training courses/materials need to be tailored and offered at various levels, including under-graduates, post-graduate students, as well as of professionals.

Apart from providing comprehensive training on alternative methods, attention should also be given to teaching best practice on the design and conducting of animal studies when necessary, to ensure that the results generated are reliable and relevant and do not lead to inconclusive outcomes, retesting, or unnecessary animal use and suffering.

The feasibility and relevance of using alternative methods for assessing human health effects and studying disease should be conveyed to students and researchers. This should highlight that extrapolation from *in vitro* to human and human to *in vitro* can be made, particularly by employing the right computational/modelling tools. Finally, students and professionals should be made aware of the advantages of being knowledgeable and skilled in alternative methods in terms of job prospects and career development opportunities to provide further incentive for them to focus their interest on the 3Rs.

5. 3R-Metrics

The discussion on 3R-metrics was structured following three main questions:

Why? Why are metrics important, and why do we need them?

The participants deemed that the metrics should:

- Demonstrate the impact of 3Rs policies and 3Rs approaches
- Demonstrate the uptake of alternative approaches and monitor how widely they are used in different areas
- Justify and trigger funding for 3Rs research and development

- Show the economic benefits of 3Rs policies and approaches
- Illustrate the financial incentives to do 3Rs research
- Illustrate the financial burden of animal research (e.g. high costs of animal husbandry)

- Prioritise areas where 3Rs efforts should be reinforced
- Monitor performance of 3Rs related projects
- Influence policy making to gain more 3Rs support
- Communicate key information on 3Rs to stakeholders
- Inform on best practices in studies
- Show the scientific value and the robustness of alternative approaches
- Demonstrate the utilisation of alternative approaches in regulatory decision making
- Be a tool to trigger changes in regulation to opt for alternative solutions
- Demonstrate the strengths and limitations of both in vivo and in vitro methods in a transparent and objective way to enhance confidence and build trust
- Identify areas where animals are mostly used
- Quantify the amount of teaching on 3Rs
- Measuring the number, type and source of training courses available
- Listing and explaining (if possible) successes and failures realised with alternative approaches

What? What type of 3R-metrics do we need? What metrics have already been used?

- A metric could be either qualitative or quantitative (e.g. the "3Rs index initiative" in NL is a qualitative tool that investigates the uptake of the 3Rs)
- Metrics should allow for analysis of geographical distribution where relevant
- Metrics related to economics aspects of 3Rs would be useful
- Indicators of level of investment in 3Rs related activities
- Metrics that show the level of (social) media interest in and coverage of 3Rs topics
- Metrics to show degree of professional/public interest (e.g. newsletter subscriptions)
- Time spent by people reading papers/material with a 3Rs aspect
- Metrics on successes and failures

How? How can we identify the relevant data to calculate a 3R-metric? What are the relevant sources of data and how can we collect and gather them?

- Many different metrics could be derived from the published literature (e.g. by elaborating statistics on PubMed articles/contents/comments).
- Metrics could be derived from information about events, conferences, and seminars that have a 3Rs relevance, for example by analysing programmes, abstracts and so on. Use a voting system before and after meetings or courses to quantify the impact of information on the 3Rs on participants or students
- Usage-statistics from web-based 3Rs resources such as databases
- Using/combining different indicators (including those from non-3Rs fields)

It was agreed that this topic should be followed up since it has relevance for all centres.

Action 1: EURL ECVAM will format/edit the input gathered on 3R-metrics at the meeting and distribute this to all participants with the intention of elaborating this topic further with interested parties.

6. Role of 3Rs Centres in Project Evaluation

It was suggested during the meeting that 3Rs centres could play an important (advisory) role in project evaluations, which are conducted in Member States following the provisions of Directive 2010/63. The expertise of 3Rs centres (and experts recommended by them) could be better exploited at different stages by different actors, including upstream and downstream of the project evaluation process itself. Therefore 3Rs centres could be more widely consulted by investigators during project conception; by project evaluation committees and competent authorities during project evaluation; and by National Committees and National Contact Points for the Directive on an ad hoc basis. It was also recognised that 3Rs centres could also participate more in (1) advising funding agencies on the appropriateness of studies proposed in project proposal from a 3Rs perspective and (2) in severity assessment which is mandatory during any project evaluation process.

7. Networking between 3Rs Centres

A clear desire was expressed by meeting participants to explore possibilities for cooperation between 3Rs centres on a variety of different topics and at a number of different levels, from the more political to the technical. It was acknowledged that although each centre has its own unique profile, priorities and context/situation, there were obvious opportunities to work more closely together in some areas for mutual benefit. Initial attention could be focused on; (1) elaborating further the topics and issues where more coordinated/collective action would be of common benefit (2) explore the possibility of devising and adopting a coherent/common strategy of communicating to key target groups for which improved communication is a priority; and (3) seek mutual support during promotional events and/or campaigns, especially those targeting the public.

Action 2: 3Rs centres to propose communication contact points (i.e. names and contact details) within their organisation. EURL ECVAM to create and distribute a list of the proposed communication contact points to the 3Rs centres. These colleagues will be included in the "Communication & Dissemination" Working Group by default (unless requested otherwise).

It was noted that some 3Rs centres hold legal mandates while others don't. Although those holding a legal mandate are interested in networking between centres, they indicated that they need to be attentive to any potential conflicts of interest.

The participants considered the meeting to be a very useful forum for exchanging information and building collaboration and suggested that more meetings be held in the future if possible, perhaps on an annual basis. It was recognised that other (new) 3Rs centres not present may be interested to join future meetings.

Action 3: EURL ECVAM to consider hosting another meeting of this type during 2016 and to consider updating the participant list depending on suggestions from 3Rs centres.

It was agreed to establish a number of informal Work Groups (WGs) to bring together representatives from 3Rs centres interested in possible collaboration on specific topics. The WGs are expected to essentially organise themselves and decide what possible activities to pursue together and how to interact. Each group should nominate a contact point to allow for general communication between WGs (and 3Rs centres). Getting each WG up and running will depend on group members taking initiative to organise some initial exchanges.

The initial topics proposed for possible WGs are;

1. Reducing animal use in biomedical research
2. Communication and dissemination
3. Promoting alternative methods/models as biotechnological resources
4. Education and training
5. Validation towards regulatory acceptance
6. Research funding provided by 3Rs centres
7. Role of 3Rs centres in project evaluation
8. 3R-metrics

Action 4: EURL ECVAM will request 3Rs centres to indicate which WGs they would like to participate in, who they want to nominate as members (incl. contact details), and an indication of any particular idea or initiative that they would like to discuss within the WG.

The participants agreed to share their slide presentations (PDF) with the understanding that they were not intended for public dissemination and any specific content would not be used without prior consent from the relevant party/parties.

Action 5: EURL ECVAM to gather the slide presentations and make them available to all participants.

Prepared by EURL ECVAM.