

Science in dialogue

The future of Life Science research in Europe – how animal and non-animal approaches can contribute

25 October 2022

EVENT REPORT

Hosted by

**Allianz der
Wissenschaftsorganisationen**

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Innovation drives reductions in animal research, but essential uses remain

Applying the 3Rs (replace, reduce, refine) when using animals in research and testing is required by European Union legislation, and is a guiding principle in the legal and ethical framework for academic and private-sector research across the region. Both animal and non-animal methods are being used, each with their benefits and limitations depending on the research question at hand. Researchers are bound to choose the best model systems and strive for continuous improvement. In that quest, science is making significant advances in developing non-animal methods. However, each advance brings a new appreciation of the limitations of each individual model. It shows that, for the foreseeable future, animal models will remain essential in order to understand the function of complex biological systems and diseases, and to allow the development of new treatments.

This view was apparent at a *Science in dialogue* meeting held in October 2022 to discuss how animal and non-animal approaches can contribute to the future of life science research in Europe. Hosted and supported by a range of renowned research organisations¹, the meeting was specifically addressed to delegates from the European Parliament, the European Commission and other interested European institutions. The event aimed to contribute high-level scientific expertise to ongoing general debates on animal and non-animal research methods, and to specific discussions on the European Parliament's "*resolution on plans and actions to accelerate the transition to innovation without use of animals in research, regulatory testing and education*". The event built on the results of a STOA workshop on the use of animals for scientific research in Europe, held in June.

Developments in alternatives: potential and limitations

The meeting heard about several developments that are contributing to the reduction and replacement of animal procedures, using cell culture and sophisticated computing methods.

In toxicology, great efforts are currently being made to advance non-animal methods. Computing methods are under development that apply machine learning to data from clinical trials and epidemiology to help reliably predict the toxicity of new small molecules. Sophisticated computing and cell culture methods are key to make progress towards the vision of risk and safety assessment procedures based on human data, the meeting heard. Progress is less advanced when it comes to biological therapeutics, an increasingly important class of medicines, where alternatives to animal studies are at a very early stage of development.

¹ The event was hosted by the French National Alliance for Life Sciences and Health (AVIESAN), the Alliance of Science Organizations in Germany, the Netherlands Organization for Health Research and Development (ZonMw) and the Dutch Research Council (NWO). It was endorsed by Science Europe, the All European Academies (ALLEA), the League of European Research Universities (LERU), and the European Animal Research Association (EARA).



At a more complex level, it is, for instance, possible to use cell culture to grow human brain tissue in the laboratory in a way that reproduces some of the organ's natural structural complexity. This includes the relationships between different kinds of cells in the brain, and some of the connections that form in the early stages of development. Work with these organoids can increase basic knowledge about brain development, and allow factors that disturb this process to be studied.

However, these tissues are not suited to study late phases of brain development and do not reproduce brain functions in fully developed human or animal brains and, ultimately, complex functions such as consciousness. This limits how far these organoids can go in replacing animal studies, which are still necessary if researchers need to relate brain structure and signalling with cognition and behaviour, or to test potential therapies before it is ethically acceptable to move on to human studies.

Organoids have also been produced for tissues in the kidney, heart and eye, with similar limitations regarding structure and function, and a similar need for complementary animal studies in certain kinds of research and therapy development. As a future perspective, high potential is seen in the use of in vitro models derived from patient tissue for personalised medicine. However, the development of such models has proved challenging and they will require considerable work in order to fulfil their promise.

A continuing need to use animals is also foreseen when studying immunity and immune protection, as was evident during the COVID-19 pandemic. Animal studies were essential for the ultrafast development of vaccines and antiviral drugs. The immune system is so complex that it cannot be modelled on a computer or reproduced in the lab, and only challenge experiments with a given pathogen allow a proof-of-principle of the antiviral effect of new vaccine candidates or drugs. The pandemic also highlighted the importance of basic research involving animals, which laid the foundations for a rapid response decades before it was needed.

Progress is driven by the combination of complementary animal and non-animal research methods

Discussion at the meeting focused on the need for a combination of alternatives and animal studies in order to achieve a thorough understanding of complex biological functions, continuing improvements in human healthcare and the development of new treatments. While much can be done with alternative methods, animal studies remain necessary if human studies are to take place safely and ethically.

For any individual scientific question, it is important that researchers carefully choose the most appropriate models in order to provide the most robust answers. This should be done transparently, with complete openness about the benefits and limitations of both animal and non-animal models. Any limitations should be addressed by improving the models in use and



developing new model systems. Whatever the situation, researchers should not promise more than their methods can deliver.

Several speakers commented that the complementarity between animal and non-animal methods made it difficult to identify the impact of alternatives with respect to the 3Rs. In the case of organoids, for example, it is hard to say whether they fully replace animal experiments, allow their reduction, or rather bring complementary information to the table. The collection of more detailed data on animal studies could help in this respect, going beyond the official statistics that presently count only the total procedures carried out on each species. With more detailed monitoring data, it would be possible to identify successes and potential for future progress.

The discussion also considered steps that could be taken to accelerate the reduction of animal use and the implementation of non-animal models as set out in EU legislation.

Progress could be enhanced, it was suggested, by further encouraging researchers to look beyond familiar methods and consider if newly emerging non-animal methods might yield equally or even more robust results. Awareness of the options available could be further raised by enhanced education and training. Resources should also be made available to cover the additional costs of developing and implementing new or improved alternatives to animal methods.

It was also noted that work to develop new 3Rs methods and techniques requires greater support and recognition in the academic reward systems, so that it becomes a flourishing research field in its own right. Similarly, greater credit should be given to work on validating non-animal methods for use in safety and risk assessment.

Summarising the discussion, the experts emphasised the need to continue animal-based research in an ethical fashion in parallel to promoting innovation for the development of alternative approaches, and supporting the implementation and accessibility of non-animal methods for broader use. The value of basic research should be recognised as essential for any innovation, with its impact on translation often only realised in the long run. The importance of the complementarity of methods should be acknowledged, both for scientific progress and, eventually, human and animal well-being, and should be openly communicated to the public. This includes sustained support for animal research.

The experts warned that research involving animals should not be allowed to move to other countries, especially those where legislation is more permissive. Further restricting animal research in European countries will, de facto, force it to move elsewhere, making Europe highly dependent on other nations for the development of innovative medical treatments. This, in turn, would severely threaten the European biomedical industry and therefore Europe's economy.

Finally, the experts called for the participation of the scientific community in the debates about how to advance the 3Rs in the context of the overarching aim to safeguard beneficial conditions for scientific and technological progress in Europe.

Expert scientists contributing to the event

- **Johannes BECKERS**, Institute of Experimental Genetics, Helmholtz Munich;
- **Herwig GRIMM**, Unit of Ethics and Human-Animal Studies, University of Veterinary Medicine, Vienna and Medical University, Vienna and University Vienna;
- **Juliette LEGLER**, Division of Toxicology at the Institute for Risk Assessment Sciences, Utrecht University;
- **Serge PICAUD**, Vision Institute, Sorbonne Université-INSERM-CNRS, Paris;
- **Alessandra PIERANI**, Institute of Psychiatry and Neuroscience of Paris and Imagine Institute, CNRS-INSERM-Université Paris Cité;
- **Jan Bas PRINS**, Biological Research Facility, the Francis Crick Institute and Leiden University;
- **Ulrike PROTZER**, Institute of Virology, Technical University Munich and Helmholtz Munich.

Link to event webpage

https://www.zonmw.nl/index.php?id=11559&no_cache=1

Contact to host organisations

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January 2023

The Event was endorsed by

