

Understanding research using animals and the alternatives

Report of a meeting hosted by Vicky Ford MEP and Dr Cristian Busoi MEP and chaired by Professor Dermot Kelleher FMedSci, President, Federation of European Academies of Medicine
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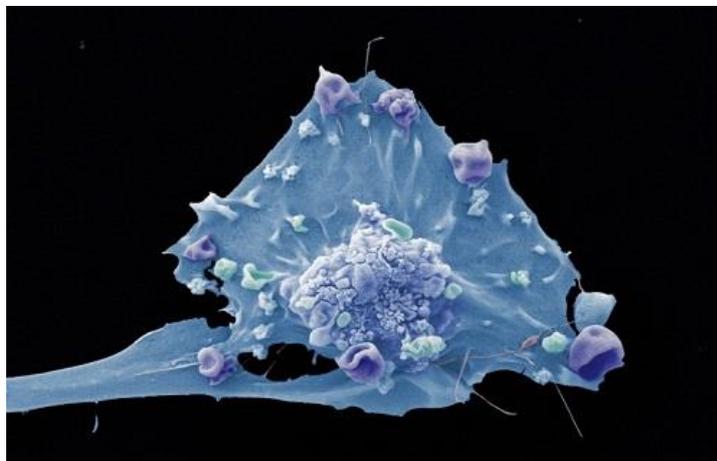


Image: Breast cancer cell, colour-enhanced image of a breast cancer cell.
Anne Weston, LRI, CRUK, Wellcome Images

Key messages

- The European Union (EU) is a world leader in the responsible use of animals in research and promotes what are widely regarded as the highest standards of animal protection in the world. The EU should be proud of this achievement.
- Research using animals continues to be essential for medical progress, from furthering our understanding of human and animal health and disease, to the development of safe and effective therapies for use in both medical and veterinary practice. The scientific community is developing alternative methods to animal models, however, they are not yet able to fully replace the use of animals in research.
- The principles of replacement, reduction and refinement are rightly enshrined in the European Directive 2010/63/EU on the protection of animals used for scientific purposes. To create an environment in which these principles are centre stage necessitates active engagement of the scientific community. Any attempt to compromise the implementation of the Directive would have significant negative consequences on animal welfare and research across the EU.

Background to the European Directive 2010/63/EU ('Directive') and to the 3Rs

- The new Directive on the protection of animals used for scientific purposes was introduced in September 2010 and took full effect from 01 January 2013.
- It was developed over a significant period of time in consultation with many groups, including animal welfare organisations, animal technologists, scientists and industry, and raises and harmonises welfare standards across the EU.
- By harmonising legislation across Member States, the Directive enhances the competitiveness of the EU, thereby ensuring it remains a world leader in biomedical research.
- The Directive provides a framework for the use of animals in research: animals are only allowed to be used in research when the possible scientific, educational, medical or veterinary benefits are compelling, and when there is no alternative method.
- Research under the Directive also needs to be ethically justifiable and should not duplicate results that are already known. It is important to note that the use of animals for testing cosmetic products has been illegal in the EU since 2009.

- At its core, the Directive introduces a requirement to consider the 3Rs when using animals in research. The 3Rs are:
 - Replacement: methods that avoid the use of animals in areas where they otherwise would have been used (for example, computer modelling or *in vitro* methods).
 - Reduction: methods that minimise the number of animals used consistent with scientific objectives.
 - Refinement: methods that minimise pain, suffering, distress or lasting harm and / or improve animal welfare.
- The Directive also underlines the importance of staff training to ensure competence and high levels of animal welfare. A culture of care should be central to all animal facilities and needs to be nurtured.

Animal research

- Research using animals continues to be vital to our understanding of human and animal health and disease. It has contributed to the development of safe and effective therapies for use in both medical and veterinary practice, and plays a key role in improving treatments for the benefit of patients across the world.
- Animals and humans have many similarities, including organs, physiological functions, genes and proteins, metabolism, and pathology. By careful consideration of these similarities, together with known differences, animal models can be developed to mimic human diseases, which can then be analysed to enhance our understanding of diseases and to develop treatments. Animal models are also currently essential for more applied research, such as establishing how drugs interact and potential toxicity.
- Approximately 80% of animals used in research are rodents (mice and rats) and rabbits, with reptiles, amphibians, fish and birds making up the majority of the remaining 20%. Non-human primates (NHPs) represent a small proportion of species used (circa 0.05%) and the Directive bans research using great apes.^{i,ii,iii}
- The approach of using the 3Rs has enhanced the quality of research in the EU and its inclusion in the Directive has been welcomed by the scientific and patient communities.
- Animal research will continue to be essential to make progress in finding therapies in areas of high unmet medical need, including rare diseases, new emerging viral diseases like Ebola, and other diseases for which there are currently no cures, such as cancer, Parkinson's disease, amyotrophic lateral sclerosis and dementia.
- Drugs developed for use in human disease are frequently used to treat disease in veterinary practice.
- While all communities agree that it would be preferable if this research entailed fewer – or even no – animals, currently research involving animals remains essential. Such research should be performed in a careful and humane manner in accordance with the regulations as described in the Directive.

Research into alternatives and the 3Rs

- Alternative methods, including cell culture systems and computer models, are progressing, however they are not yet able to fully replace the use of animals in research, particularly for the study of complex multi-organ diseases such as cancer, diabetes and heart disease.
- The scientific community is central in the development of alternatives and in driving these forward. Key examples are the research projects funded by the UK's NC3Rs aimed at developing alternative methods.^{iv} By focussing on the 3Rs, the Directive ensures that the scientific community is even more proactive in this area.
- Animal studies are often complementary to alternative approaches and many studies use a combination of both non-animal and animal models to provide maximal information.
- Scientists also recognise that animal models have limitations, which they hope to address by developing alternative methods.
- Research into better animal welfare is clearly important for ethical reasons, but also to improve the robustness and reproducibility of studies that can be confounded by pain and distress.
- Implementation of the 3Rs has potential to bring economic benefit by saving time, money and animals, thereby enabling treatments to reach patients more rapidly.

Future directions

- Ensuring appropriate implementation of the Directive across the EU is an imperative. The Commission is monitoring progress and will carry out close follow up with Member States in the near future. Guidance

documents issued by the Commission in different Member State languages should help with the application of the Directive.^v The national Competent Authorities also have an important role to play in ensuring the Directive is appropriately implemented. As part of normal process, a review of the Directive has been scheduled for 2017.

- As part of the Directive, from November 2015 Member States will have to submit statistical information on the use of animals in research to the Commission and make this publicly available. These figures will have to be carefully analysed as they are based on different criteria to those used previously. Due to progress in science, for example the use of genetically-altered animals, the numbers of animals used in research may actually increase in the future, although not as much as they would have done without measures stemming from application of the 3Rs. Additionally, statistics used to detect 3Rs progress must take a large number of variables into account.
- Scientists, patients, welfare groups and legislators will need to work together to create an optimal environment for research that responds to patients' needs, while ensuring high standards for animal welfare are met. Dialogue between the different parties will be essential to inform debates and decision-making.
- The EU scientific community should embrace opportunities for debate and increased communication with multiple stakeholders to encourage open conversation about animal research and disperse any misunderstandings or misconceptions in this area.

Meeting information

- On 20 January 2015, MEPs Vicky Ford and Cristian Busoi hosted a meeting to explore the reasons why, and ways in which, animals are used in scientific, medical and veterinary research in the EU, and the importance of the principles of replacement, reduction and refinement (the '3Rs') and their application in research. This report is a summary of the meeting's discussions.
- The meeting was convened by the Association of Medical Research Charities ([AMRC](#)), the European Animal Research Association ([EARA](#)), the European Federation of Pharmaceutical Industries and Associations ([EFPIA](#)), [EGAN](#) - Patients Network for Medical Research and Health, the Federation of European Academies of Medicine ([FEAM](#)), the Federation of European Neuroscience Societies ([FENS](#)), [Science Europe's Medical Sciences Committee](#), [Science Europe's Life Environmental and Geo Sciences Committee](#) and the [Wellcome Trust](#). The meeting was chaired by Professor Dermot Kelleher FMedSci, President, FEAM.

Acknowledgments

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ⁱ Report from the Commission to the Council and the European Parliament (2013). *Seventh Report on the Statistics on the Number of Animals used for Experimental and other Scientific Purposes in the Member States of the European Union*. <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52013DC0859&from=EN>

ⁱⁱ A proportion of NHP research is for toxicology studies that are required to meet regulatory demands for marketing authorisation.

ⁱⁱⁱ The use of great apes has been banned by the Directive 2010/63/EU, unless a "Member State has justifiable grounds for believing that action is essential for the preservation of the species or in relation to an unexpected outbreak of a life-threatening or debilitating clinical condition in human beings." No great apes have been used in the EU since 1999.

^{iv} <http://www.nc3rs.org.uk/>

^v The European Commission has published guidance documents on the Directive and its implementation covering: the severity assessment framework; EU education and training framework; project evaluation and retrospective assessment; animal welfare bodies and national committees; and inspections and enforcement. The guidelines have been developed by an expert working group comprised of experts from Member States, academia, industry and non-governmental organisations, and have been endorsed by national contact points (*i.e.* competent authority representatives from Member States).