Alliance for Biomedical Research in Europe

BioMed Alliance Position Statement in support of the *EU Directive on Animal Research (2010/63/EU)*

European researchers call for the intensification of efforts to develop and adopt alternative approaches, while ensuring a viable context for the pursuit of animal experimentation when it is unavoidable.

Background

Animal experimentation is defined as the use of non-human animals for scientific research. Animal testing regulations, which permit and control such investigations, vary worldwide. In the European Union, *Directive 2010/63/EU on the protection of animals used for scientific purposes* replaced the EEC Directive of 1986[1], thus strengthening legislation by improving the welfare of those animals that still needed to be used, as well as affirming the principles of the Three Rs, (Replacement, Reduction and Refinement of the use of animals) in EU legislation. Moreover, this new Directive 2010/63/EU makes obligatory the application of scientifically valid alternative approaches where they exist, and establishes mechanisms to speed up their development, validation and uptake.

Executive Summary

In March 2015, the 'Stop Vivisection Citizens' Initiative' asked the European Commission to repeal Directive 2010/63/EU and put forward a new proposal aimed at eliminating animal testing based on the belief that animal models are not predictive of human outcomes. The BioMed Alliance agrees that the timing is right for the consideration of the utility of non-animal approaches in the biosciences. It is true that for many therapeutic areas in medicine there is a lack of predictive preclinical models, i.e. cell- and animal-based assays, and this also contributes to the dearth of effective drugs in most company pipelines**. However, the BioMed Alliance emphasises and reiterates[2] that animal models *have been and continue to be instrumental and indispensable:***

- ***in understanding the causes and development of diseases,***
- ***in identifying new targets for therapies and***
- ***in testing the safety of therapeutic interventions.***

[1] Council Directive 86/609/EEC of 24 November 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes

[2] See BioMed Alliance statement of 5 June 2015: http://www.biomedeurope.org/images/animal-research/BioMed_Alliance_welcomes_European_Commission_reply_to_Stop_Vivisection.pdf

Biomedical research using animal models has led to breakthroughs in all medical specialties and therapeutic areas and undoubtedly animals have been and remain a valuable model in biomedical research.

As a strong supporter of science and animal welfare, and in the light of the forthcoming review of Directive 2010//63/EU in 2017, **the BioMed Alliance fully supports the European Commission Communication response to the ECI Stop Vivisection of 3rd June 2015, and concurs in particular with *"the continued need for Directive 201/63/EU"*.**

The BioMed Alliance agrees with the European Commission that focus and effort needs to now be much more strongly directed to ensuring the Directive's proper implementation and enforcement across all EU Member States. This would go a long way in ensuring more harmonised and equal protection of animals across Europe, rather than 'exporting' the problem outside the borders of the European Union, which would mean even less control and legal certainty with regard to animal protection and welfare.

About BioMed Alliance:

The Alliance for Biomedical Research in Europe (BioMed Alliance, http://www.biomedeurope.org) is the result of a unique initiative of leading European medical societies that together include more than 400,000 researchers and health professionals. The BioMed Alliance was created in 2010 to gather strength across different disciplines and areas in biomedical and health research at European level.

BioMed Alliance's members:

European Association for the Study of Diabetes (EASD), European Association for the Study of the Liver (EASL), European Association of Nuclear Medicine (EANM), European Atherosclerosis Society (EAS), European CanCer Organisation (ECCO), European College of Neuropsychopharmacology (ECNP), Federation of European Biochemical Societies (FEBS), European Federation of Immunological Societies (EFIS), European Academy of Neurology (EAN), European Hematology Association (EHA), European League Against Rheumatism, (EULAR), European Respiratory Society (ERS), European Society for Paediatric Research (ESPR), European Society of Anaesthesiology (ESA), European Society of Cardiology (ESC), European Society of Human Reproduction and Embryology (ESHRE), United European Gastroenterology (UEG), European Academy for Allergy and Clinical Immunology (EAACI), European Society of Pathology (ESP), European Society of Endocrinology (ESE), European Organisation for Research and Treatment of Cancer (EORTC), European Society for Molecular Imaging (ESMI), European Association for the Study of Obesity (EASO), The European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN).

[3] First described by W. M. S. Russell and R. L. Burch

BioMed Alliance Position Statement

Biomedical research aims to understand fundamental mechanisms of health and disease with the ultimate goal of improving the well-being of mankind, by providing new medical treatments and diagnostic options, and also by increasing awareness of the importance of lifestyle. This is reflected in the missions of many of the member associations of the Biomed Alliance.

Animal models have been, and continue to be, indispensable to the study of the multifaceted interactions of different complex systems and tissues with a view to understanding and treating disease-related dysfunctions. However, there is growing public concern that biomedical research is too extensively based on animal testing and this is to the detriment of animal welfare.

In view of the forthcoming review of the EU Directive on animal research, the BioMed Alliance and its members believe that the following issues should be carefully considered and taken into account:

1. Ethics of animal experiments in biomedical research

The BioMed Alliance strongly supports that animal experiments for the development of new medical and veterinary options must adhere to general ethical concepts and with the principles of the *Three R's*[3].

All animal experimentation should be conducted according to the requirements as reflected in the 3R principles (3Rs), which demand the Refinement, Reduction and Replacement of animal experiments, including those included in the current EU directive 2010/63/EU on animal research. To this end, experiments using live animal models to improve medical and veterinary options should be:

- Necessary and suitable in order to obtain the required insight and information
- Designed to maximise the benefit for the patient
- Designed to minimise the harm inflicted on animals
- Designed to generate maximal achievable safety before testing in humans or target animal species
- Not replaceable by existing experiments that do not use animals

[3] First described by W. M. S. Russell and R. L. Burch

2. Cross-sectoral and collaborative framework to develop more sophisticated models and alternative approaches

Notwithstanding their contribution to the considerable insight into pathways linked to various aspects of diseases, as the knowledge of the complexity of disease grows, there is an increased recognition within the research community that animal models are not always sophisticated enough. **This requires a move towards a model of greater collaboration among all actors involved in biomedical research e.g. academia, funding agencies, industry, clinicians, publishers.**

The BioMed Alliance calls for a collaborative European approach among all stakeholders to:

- **develop incentives to replace the simple duplication of testing by controlled reproducibility approaches,**
- **implement open data and open access schemes,**
- **emphasise the importance of the publication of negative results**
- **shift the focus from quantitative parameters to research quality and relevance in academic evaluation and promotion schemes.**

The BioMed Alliance is convinced that this approach would be much more effective and sustainable than would an increase in regulatory restrictions. It would draw upon the inherent creativity in the scientific community and the strong desire of both young and senior researchers to combine high ethical standards of research with personal academic success.

3. Emerging alternative approaches in translational biomedical research

Alternative and innovative approaches are increasingly becoming available and allow the replacement of animal experiments. However, it is crucial that they comply with the same rigorous scientific standards as do approaches involving animals.

These ***R***eplace options do not render animal experiments completely unnecessary, but they can reduce the territory of scientific questions that can only be addressed by approaches based on genetically modified laboratory animals. In the scientific environment, they are however, in competition with well-established approaches involving animal research. This competition pertains to many different aspects of biomedical research, including funding and publication.

Major new approaches include:

- Use of (human) induced pluripotent stem cells (iPS)
- Gene editing of such cells allowing, for example, targeted alteration of their cellular genetic and epigenetic properties in order to simulate specific diseases or treatments
- Cultivation of organoids or artificial tissues *in vitro* ('human on a chip') based on increased understanding and proficiency in *in vitro* constructs involving different cell types and functions
- *In silico* models ranging from the simulation of molecular interactions to multiscale representations of normal or diseased physiological systems
- Advanced imaging techniques for the analysis of human tissue samples.

[3] First described by W. M. S. Russell and R. L. Burch

At the present time, alternative methods in biomedical research still have only a very small fraction of funding compared to that for research using animal models. Moreover, top level publication platforms frequently require research results to have been tested in an animal model, often essential for understanding the basic mechanisms and pathogenesis of health and disease. This is a partially self-repeating cycle in the current research framework; low funding for the development and application of alternative approaches leads to less impressive experimental results and achievements which, in turn, reinforce the need to include animals in biomedical research projects.

Given the above, the BioMed Alliance would welcome greater collaborative efforts from all stakeholders and policy makers in the development of alternative approaches. It is an ethical requirement for all stakeholders in biomedical research to support the development and validation of such approaches. To do so would entail that alternative methods were tested using the same rigorous standards that apply to animal models, thus ensuring they can be safely used to replace animal-based approaches. Further, it will be necessary to develop standardisation and easy access of tissue cultures and biobanks for alternative studies. This will require a proactive attitude by the entire scientific community, including individual researchers, research organisations, and international associations including those represented in the Biomed Alliance and funding agencies, as well as on the political level.

4. The scientific and policy framework

As a strong supporter of science and animal welfare, and in the light of the forthcoming review of Directive 2010//63/EU in 2017, **the BioMed Alliance fully supports the European Commission Communication response to the ECI Stop Vivisection of 3rd June 2015, and concurs in particular with *"the continued need for Directive 201/63/EU"*. The BioMed Alliance agrees with the European Commission that focus and effort needs to now be much more strongly directed to ensuring the Directive's proper implementation and enforcement across all EU Member States.**

The Biomed Alliance urges the scientific community, funding agencies and policy makers to support the development, validation and use of alternative approaches through targeted incentives in both biomedical and veterinary research. We call for a speedy increase in the availability, use and acceptance of alternative and innovative approaches in biomedical and veterinary research. This could be achieved through bold measures to be taken by the European Commission and national or, international funding agencies. Such an initiative could, for instance, take the form of specific calls for funding or quotas as well as the further development of international repositories and databases of research protocols and methods related to alternatives.

[3] First described by W. M. S. Russell and R. L. Burch