# Towards Innovation in Life Sciences: Are EU scientific policies aligned with scientific evidence?

Luísa Bastos, Animals in Science Programme Leader, Eurogroup for Animals, Brussels

Every year, more than 12 million animals are used in research, testing and education in the EU.[1] The number of animals used for this purpose is still not decreasing despite the steady EU investment on alternatives to animals in science and the EU commitment to fully replace the use of animals in these areas.[2]

The growing scientific evidence showing the need for more human-relevant science to significantly improve healthcare is also not producing an impact on the reported numbers. In the past decades, systematic reviews of animal studies have consistently shown the poor scientific value of this practice.[3-11] Today we know that animal experimentation has failed to contribute to the development of new treatments for diseases like cancer[12] and alzheimer.[13] It has failed to predict toxicity of substances in humans,[14] and even understand crucial properties of drugs.[15] A new Directive for the protection of animals used for scientific purposes was adopted in 2010, but the conformity checks of the national transpositions are still taking place. The first review of this Directive showed that one possible consequence of its implementation may be that those using animals feel increasingly justified in doing so. Additionally, the concept and practice of the 3Rs - replacement, reduction and refinement – seems stagnated.[16,17]

One aspect of the Directive 2010/63/EU on the protection of animals used for scientific purposes is that it gives the minimum standards that need to be adopted by animal breeders, sellers and users when keeping or using animals for scientific purposes. Although the goal of this Directive is the harmonisation of the internal market, it does provide some flexibility on how Member States implement it.

For example, Member States have implemented project evaluation and authorisation processes in diverse ways. In two extremes, some center the processes in a national competent authority, others leave the responsibilities to the institutions proposing the project. However, looking deeper into who are the people responsible for evaluating project applications, it is clear that, in the majority of cases, the evaluation of the animal-based project is conducted mainly by individuals with a link to animal experimentation.

The probable partiality of project evaluators may be one element that is hindering innovation in life sciences. Without a comprehensive assessment of applications by experts in other scientific practices, the evaluation is not fully addressing the first R of the 3Rs - replacement; Without the assessment by target professionals as clinicians, the evaluation is not addressing the feasibility of a potential benefit of the project results. Besides guaranteeing a project evaluation based on the best application of historical knowledge of scientific impact and the 3R principles, a holistic scientific policy needs to guarantee the education and resources to empower scientists to move towards non-animal science. EU and national scientific policies need to take into consideration scientific evidence, political goals, and the current paradigm.

Innovation-leading scientists have a recurrent complaint: they have limited support to continue their research. However, under the EU Directive 2010/63, the European Commission and Member States have the responsibility to foster the development, validation and uptake of alternative approaches (article 47). Scientific policies can channel their support to prioritise a shift towards human-relevant and non-animal science, while at the same time discouraging animal-based research. Priority areas include fields where other methods either exist (e.g. medical and veterinary education and training), are being explored in parallel (e.g. orga transplantation), or can be developed without major technological challenges (e.g. education and training in laboratory animal science).

Progress in other areas where the contribution of animal studies has not been assessed can be initially tackled by Thematic Reviews as foreseen in article 58 of Directive 2010/63/EU. Besides analysing the applicability, stage of development, and potential of non-animal approaches in a specific scientific area, an independent and consensual Thematic Review should ideally lead to a strategy to phase out the use of animals in the specified area of research, education or testing.

In conclusion, although the political commitment and scientific innovation have been showing the possibilities to move towards non-animal science, concrete policies that can effectively shift scientific development into a different direction are still too slim to hold visible results for science, human health, and animal welfare.

**References :**

1.European Commission, DG Environment. EU Member States national statistical reports (2014 and onward), http://ec.europa.eu/environment/chemicals/lab_animals/member_states_stats_reports_en.htm.

2.Council, E. European Commission (2010) Directive 2010/63/Eu on the protection of animals used for scientific purposes. Ispra, Italy: Institute for Health and Consumer Protection (2010).

3.Lindl, T., Voelkel, M. & Kolar, R. [Animal experiments in biomedical research. An evaluation of the clinical relevance of approved animal experimental projects]. ALTEX 22, 143–151 (2005).

4.Perel, P. et al. Comparison of treatment effects between animal experiments and clinical trials: systematic review. BMJ 334, 197–197 (2007).

5.Roberts, I. Does animal experimentation inform human healthcare? Observations from a systematic review of international animal experiments on fluid resuscitation. BMJ 324, 474–476 (2002).

6.Corpet, D. E. & Pierre, F. How good are rodent models of carcinogenesis in predicting efficacy in humans? A systematic review and meta-analysis of colon chemoprevention in rats, mice and men. European Journal of Cancer 41, 1911–1922 (2005).

7.Martić-Kehl, M. I., Wernery, J., Folkers, G. & Schubiger, P. A. Quality of Animal Experiments in Anti-Angiogenic Cancer Drug Development – A Systematic Review. PLOS ONE 10, e0137235 (2015).

8.Banwell, V., Sena, E. S. & Macleod, M. R. Systematic Review and Stratified Meta-analysis of the Efficacy of Interleukin-1 Receptor Antagonist in Animal Models of Stroke. Journal of Stroke and Cerebrovascular Diseases 18, 269–276 (2009).

9.Knight, A. Systematic reviews of animal experiments demonstrate poor contributions toward human healthcare. Rev Recent Clin Trials 3, 89–96 (2008).

10.Knight, A. Systematic reviews of animal experiments demonstrate poor human clinical and toxicological utility. Altern Lab Anim 35, 641–659 (2007).

11.Lucas, C., Criens-Poublon, L. J., Cockrell, C. T. & de Haan, R. J. Wound Healing in Cell Studies and Animal Model Experiments by Low Level Laser Therapy; Were Clinical Studies Justified? A Systematic Review. Lasers in Medical Science 17, 110–134 (2002).

12.Gura, T. CANCER MODELS: Systems for Identifying New Drugs Are Often Faulty. Science 278, 1041–1042 (1997).

13.Cummings, J. L., Morstorf, T. & Zhong, K. Alzheimer's disease drug-development pipeline: few candidates, frequent failures. Alzheimer's Research & Therapy 6, 37 (2014).

14.Ennever, F. K., Noonan, T. J. & Rosenkranz, H. S. The predictivity of animal bioassays and short-term genotoxicity tests for carcinogenicity and non-carcinogenicity to humans. Mutagenesis 2, 73–78 (1987).
15.Lin, J. H. Species similarities and differences in pharmacokinetics. Drug Metab. Dispos. 23, 1008–1021 (1995).

16.European Commission. COMMISSION STAFF WORKING DOCUMENT Accompanying the document REPORT FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL, THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE AND THE COMMITTEE OF THE REGIONS In accordance with Article 58 of Directive 2010/63/EU on the protection of animals used for scientific purposes. (2017).

17.European Commission. REPORT FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL, THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE AND THE COMMITTEE OF THE REGIONS in accordance with Article 58 of Directive 2010/63/EU on the protection of animals used for scientific purposes. (2017).

# Notes