Check for updates

*Workshop Report*

# The Istanbul Workshop organised by the 'IMPROVE' COST Action Ethics Crossover Group

Alternatives to Laboratory Animals
2025, Vol. 53(4) 232–235
© The Author(s) 2025
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/02611929251345074
journals.sagepub.com/home/atl
Sage

**Augusto Vitale[1], Simone Pollo[2], Nikos Kostomitsopoulos[3], Aurélie Thomas[4], Gamze Kaya[5], Kaan Bicici[6] and Yesim Isil Ulman[7]**

**Abstract**

The overall aim of the 'Improving the Quality of Biomedical Science with 3Rs Concepts' (IMPROVE) COST Action (CA21139) is to establish an interdisciplinary network dedicated to refining, harmonising and promoting the adoption of the Three Rs concepts, to enhance the quality of biomedical research. The 'IMPROVE' COST Action has assembled an Ethics Crossover Group composed of volunteer members from each of IMPROVE's four established Working Groups: 'Quality and translatability of science', 'Implementation', 'Dissemination' and 'Education'. This report relates to a two-day workshop, held in Acibadem University in Istanbul on 2–3 September 2024. The workshop was organised by the Ethics Crossover Group in line with the aims and the scope of the 'IMPROVE' COST Action, to address the ethical dimension of research and experiments on laboratory animals.

**Keywords**

3Rs, animal experimentation, NAMs, ONE Health, research ethics, Three Rs principles, xenotransplantation

## Introduction

This report provides information on the Istanbul Workshop, held within the scope of the 'Improving the Quality of Biomedical Science with 3Rs Concepts' (IMPROVE) COST Action (CA21139) to address the ethical dimension of research and experiments on laboratory animals. The overall aim of the 'IMPROVE' COST Action is to establish an interdisciplinary network dedicated to refining, harmonising and promoting the adoption of the Three Rs concepts, to enhance the quality of biomedical research.[1] The 'IMPROVE' COST Action has assembled an Ethics Crossover Group, composed of volunteer members from each of the four established Working Groups in the COST Action (namely, 'Quality and translatability of science', 'Implementation', 'Dissemination' and 'Education'). The aims of the Ethics Crossover Group are:

- to interpret *replacement*, *reduction* and *refinement* (the Three Rs),[2] in view of the current scientific literature;
- to clarify the terminology regarding animal research, alternatives, non-animal models and the Three Rs; [3] and
- to explore the One Health[4] approach in view of ethical principles and in relation to animal research (including veterinary clinical and basic research), interlinking human health, animal welfare and environmental sustainability.

In line with IMPROVE's aims and scope, the Ethics Crossover Group tackles different ethical issues related to the work carried out by the four Working Groups.6 For instance, the Ethics Crossover Group recently published a new interpretation of the Three Rs principles that was agreed on by the members of the IMPROVE COST Action.[5] As part

[1]Center for Behavioural Science and Mental Health, Istituto Superiore di Sanità, Rome, Italy
[2]Department of Philosophy, Sapienza Universita di Roma, Rome, Italy
[3]Laboratory Animal Facility, Biomedical Research Foundation of the Academy of Athens, Athens, Greece
[4]Animal Sciences & Technology, Clinical Pharmacology and Safety Sciences, R&D, AstraZeneca, Cambridge, UK
[5]Bioethics MSc Programme, Acibadem University, Istanbul, Turkey
[6]Biophysics MSc Programme, Acibadem University, Istanbul, Turkey
[7]History of Medicine and Ethics Department, School of Medicine & Bioethics, Acibadem University, Istanbul, Turkey

**Corresponding author:**
Augusto Vitale, Center for Behavioural Science and Mental Health, Istituto Superiore di Sanità, Viale Regina Elena 299, Rome 00161, Italy.
Email: augustovitale083@gmail.com

of these activities, a two-day workshop on the ethical issues associated with animal research was also organised by the Ethics Crossover Group. This workshop was held in Acibadem University in Istanbul (Turkey), on 2–3 September 2024.[6]

The main objective of the Istanbul Workshop was to reflect on the ethical dimension of animal experiments in the age of emerging technologies such as New Approach Methodologies (NAMs), fuelling new awareness of animal welfare in the context of such approaches.[7] The novelty of the Workshop was that the organisers worked hard to get the audience actively involved, beyond the usual presentation of talks and related discussions. This was achieved by prompting debate, encouraging and facilitating brainstorming, and promoting interactions. A total of 47 participants were present (40 in person and seven online), from a number of European countries (UK, Germany, Italy, Portugal, Luxembourg, Austria, Greece, Estonia, Kosovo, Bosnia Herzegovina, North Macedonia, Moldova, Serbia and Turkey). The participants had varied professional backgrounds — for example, biomedical researchers, health professionals, veterinarians, philosophers, social scientists, scholars and bioethicists. The attendees had the opportunity to interact and enrich the scientific programme, which included keynote lectures, Q&A sessions and Working Group exercises.

## Outline of the workshop format

The Workshop programme consisted of three invited keynote speakers, as well as discussion groups and panel meetings. Each discussion group comprised between eight and nine members, who were asked to discuss the questions raised by each invited speaker. Each group nominated a rapporteur who presented the outcome of the group's discussion to the audience, in an attempt to promote further debate.

### *First keynote lecture*

The first keynote lecture '*Does moral reflection improve the quality of biomedical research?*' was given by Prof. Simone Pollo, from La Sapienza University in Rome (Italy). The talk explored the relationship between moral reflection and the quality of biomedical research, addressing the question in the title. The central thesis is that scientific research is not value-neutral but deeply intertwined with moral considerations, particularly in democratic societies where science contributes to advancing democratic principles such as equality, justice and freedom. By examining the historical and conceptual ties between science and democracy, the talk highlighted how modern science — with its egalitarian and progressive method — has shaped the concept of liberal democracy and contributed to its affirmation.

Then the talk focused on the ethical challenges posed by biomedical research involving animals, emphasising the growing recognition of the moral and legal status of non-human animals within democratic societies. Animal experimentation is a classic example of the intersection of scientific practices with democratic values. This requires a dual-level moral reflection — both institutional and individual. On the institutional level, public deliberation and regulatory processes must address ethical conflicts, while on the personal level, researchers must critically evaluate their protocols and practices to ensure alignment with democratic values.[8] Emphasis was given to the role of moral reflection in resolving conflicts between advancing knowledge and protecting animal welfare, proposing that such reflection could improve research quality by fostering transparency, ethical accountability and societal trust.

At the end of the lecture, four key questions were raised to trigger further discussion on the democratic integration of moral considerations into biomedical research practices. These questions, which are shown below, address the promotion of democratic values through research, public engagement and the participatory evaluation of ethical trade-offs:

1. How do biomedical research practices promote outcomes and values that are conducive to a democratic environment?
2. How can a democratic discussion on the ethical problems of research (relating to the aims of the research itself and the protection of the animals involved) be achieved in laboratory real-life?
3. How can the democratic participation of the lay, non-specialist, public in biomedical research practices be promoted?
4. In the regulation of animal research, a harm–benefit assessment is essential. In a democratic society, who is responsible for defining these harms and benefits, and who should participate in the evaluation procedures?

### *Second keynote lecture*

The title of the second keynote lecture, '*Ethical dilemmas in the use of animals as human organ donors*', was presented by Dr Nikolaos Kostomitsopoulos from the Biomedical Research Foundation of the Academy of Athens, Greece. The aim of the presentation was to promote discussion between the participants of the Workshop in relation to the use of animals as organ donors for humans. Due to the serious lack of human organ donors, an alternative solution for some individuals could be the use of animals as organ donors.[9] However, a number of questions are raised in relation to this practice: Do we really need xeno-transplantation? Does transplantation change our definition of human? Are we breaking the laws of nature? Are we

breaking religious laws? Do we need life extension at any cost? What are the psychological and biological effects of xenotransplantation on recipients? What are the implications for society and future generations? What are the effects on animals and on the environment? Do we care about animal suffering and animal genetic manipulation? Are there any alternative methods which could be used instead of animals?

A number of concerns were also raised, such as the risk of disease transmission to humans and obtaining informed consent. In fact, the recipients must understand the potential risks involved, including the possibility of contracting new diseases. Additionally, concerns have been raised about genetically modified animals being used for xenotransplantation. The potential long-term health effects have been questioned. It has been argued that extensive research is needed to evaluate the safety and efficacy of xenotransplantation procedures over time.

Closing the presentation, the speaker highlighted the following four areas for potential debate within the discussion groups (one point for each of the groups):

1. Replacement strategies.
2. The use of animals as human organ donors — One Health and One Welfare.
3. Ethical issues raised by the use of animals as human organ donors.
4. Xenotransplantation and the role of the Three Rs centres.

### *Third keynote lecture*

The third keynote lecture, '*Making NAMs (New Approach Methodologies) the ethical solution to animal use*', was presented by Dr Aurélie Thomas, from AstraZeneca in the UK. The phasing-in of NAMs in the pharmaceutical industry is motivated by the need for more predictive models to accelerate the discovery, safety and efficacy assessment of drug candidates ahead of clinical trials. NAMs are human-derived *in vitro* or *in silico* models (e.g. organoids, gene editing and artificial intelligence) that have the potential to reduce or replace animal models as primary proxies for human biology.[10]

Ethical and regulatory frameworks supporting the use of animals in biomedical science follow a utilitarian approach, whereby any inflicted harm is expected to be outweighed by health benefits for the wider population. Despite animal models having played an instrumental role in the life sciences, the translatability of *in vivo* studies has been repeatedly challenged on scientific grounds, therefore questioning the morality of such animal use. While NAMs may alleviate the ethical concerns pertaining to animal use, they also raise significant and new ethical challenges for which there is no established bioethical framework. The aim of this lecture was to present the ethical challenges inherent to NAMs, and outline four crucial dimensions that should be considered when laying the foundations for an ethical framework, namely: i) scientific quality, especially clinical translatability to patient populations; ii) acceptability from the patients, the public and regulatory bodies; iii) equity of drug accessibility; and iv) environmental sustainability. A proposed framework based on these principles would provide proactive bioethical guidance that would evolve alongside NAM development, taking stakeholders needs into account and decreasing the reliance of the pharmaceutical industry on animal use for innovative drug discovery.

Dr Thomas explained that NAMs reduce reliance on animal models by improving clinical translation. She argued that human-derived self-organising cellular models present their own ethical challenges — for example, those associated with biobanking and the use of pluripotent stem cells — that cannot be addressed by a two-way utilitarian harm–benefit analysis. She outlined a framework for the ethical implementation of NAMs in the pharmaceutical industry that would encompass four crucial dimensions listed above, and proposed the following topics for discussion by the groups after the lecture:

1. The societal acceptability of animal use and NAMs across different cultures.
2. Are NAMs likely to boost the use of animal-derived sera/media?
3. The harm–benefit analysis of projects involving both NAMs and animal models.
4. Can environmental sustainability play a role in the ethical implementation of NAMs within the pharmaceutical industry?

## Discussion and conclusions

The Istanbul Workshop provided an interdisciplinary platform for further developing discussions on the ethical dimension of biomedical research and the applicability of the Three R principles (*reduction*, *refinement* and *replacement*). The keynote lectures focused on the role of ethics and democratic values in biomedical research, as well as the ethical considerations associated with xenotransplantation and potential NAMs.

The participants delved into these topics and explored their contribution toward improving scientific quality and promoting animal welfare. In particular, they identified a range of ethical implications associated with the development and implementation of NAMs that would need to be addressed before a reduction in the current reliance on animal models could be effected. Furthermore, the potential for environmental sustainability and ethical compatibility of these methodologies was also discussed.

## Outcomes from the workshop

In summary, the interdisciplinary discussions at the workshop resulted in a number of recommendations, from both an ethical viewpoint and a scientific perspective, that could be utilised by the biomedical community when making significant decisions. Among these recommendations, the following stand out:

1. There is a need to establish new ethical deliberations that balance animal welfare and the advancement of knowledge.
2. Transparent discussion mechanisms that encourage democratic participation should be implemented.
3. Further research is needed on the effectiveness and acceptability of NAMs.
4. Informed consent and ethical accountability should be standardised.
5. There is a need to continue to balance animal welfare and the advancement of knowledge, focusing of particular case studies.
6. A transparent framework that takes into account, and tries to balance, scientific research involving animals, human health requirements, ethical compatibility and environmental sustainability, is essential in a democratic, pluralistic society.

### Acknowledgements

We are grateful to the 'IMPROVE' COST Action led by Prof. Winfried Neuhaus and Prof. Arti Devi Ahluwalia for providing us with a platform to discuss the ethics of animal research. We are thankful to both in-person and online participants, and to the moderators of the working groups of the Istanbul Workshop for helping to achieve this multidisciplinary platform of ideas exchange on animal science. Last but not least, we thank Acibadem University for its support.

### Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Funding

The authors disclosed receipt of the following financial support for the research, authorship and/or publication of this article: This article is based upon work from COST Action CA21139, 'Improving the Quality of Biomedical Science with 3Rs Concepts (IMPROVE), supported by COST (European Cooperation in Science and Technology).

### ORCID iD

Augusto Vitale https://orcid.org/0000-0001-8078-3831

### References

1. COST. *CA21139 — 3Rs concepts to improve the quality of biomedical science (IMPROVE)*. https://www.cost.eu/actions/CA21139/ (accessed 3 April 2025).
2. European Commission. *Animals used for scientific purposes*. https://wayback.archive-it.org/org-1495/20230304151254mp_/https:/ec.europa.eu/environment/chemicals/lab_animals/3r/alternative_en.htm (accessed 20 February 2025).
3. European Commission. *Directive 2010/63/EU* of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes. *Off J Euro Union* 2010; L276, 20.10.2010: 33–79.
4. World Health Organization. *One health*. https://www.who.int/health-topics/one-health#tab=tab_1 (accessed 3 April 2025).
5. Lauwereyns J, Bajramovic J, Bert B, et al. Toward a common interpretation of the 3Rs principles in animal research. *Lab Anim* 2024; 53: 347–350.
6. Acibadem University. *CA 21139 COST Action IMPROVE Ethics X-over Group Istanbul Workshop*. https://www.acibadem.edu.tr/en/news/ca-21139-cost-action-improve-ethics-x-over-group-istanbul-workshop (2024, accessed 3 April 2025).
7. Ulman YI, Ulus IH, Ozpinar A, et al. Preliminary notes for ethical conduct of animal experimentation with special reference to studies in Turkey. *Kafkas Universitesi Veteriner Fakultesi Dergisi* 2011; 17: 1051–1056.
8. Pollo S and Vitale A. Invertebrates and humans: Science, ethics, and policy. In: Carere C and Mather J (eds). *The welfare of invertebrate animals. Animal Welfare*, Vol 18. Cham: Springer, 2019, pp. 7–22.
9. Lelovas PP, Kostomitsopoulos NG and Xanthos TT. A comparative anatomic and physiologic overview of the porcine heart. *J Am Assoc Lab Anim Sci* 2014; 53: 432–438.
10. Stresser DM, Kopec AK, Hewitt P, et al. Towards *in vitro* models for reducing or replacing the use of animals in drug testing. *Nat Biomed Eng* 2024; 8: 930–935.