

# Animal Research Ethics: Challenges and Proposed Answers

## Some Results of an International Retreat Week

Tatiana Hetzel, Karla Alex, Katharina Braun, Samuel Camenzind, Sara Capas Peneda, Rita Dodaro, Svea Jörgensen, Hannes Kahress, Erich Linder, Eva Reihls, Felicitas Selter, Vini Tiwari, Zorana Todorovic, Marcel Mertz

### Areas of Ethical Challenge in Animal Research

<b>Approaching the Moral Conflict (Freedom of Research vs. Non-Harming of Animals)</b>	
<b>Best Practice Standards?</b> <ul style="list-style-type: none"> <li>➤ Different public stances on animal research in different countries</li> <li>➤ Different scientific cultures and stances within the sciences</li> </ul>	<b>Ethics Committees (Project Reviews)?</b> <ul style="list-style-type: none"> <li>➤ Different composition and modi operandi depending on the country [1]</li> <li>➤ Appropriate expertise not guaranteed</li> <li>➤ Lacking evidence of HBA and 3R enforcement [2]</li> <li>➤ Social and professional roles influence deliberation strongly [3]</li> <li>➤ Conflicts of interests when deciding upon project applications of colleagues [4]</li> <li>➤ Focus on technical questions [5, 6]</li> </ul>
<b>Standardized Explicit Method?</b> <ul style="list-style-type: none"> <li>➤ Not available, esp. not across countries</li> </ul>	
<b>Tools of Deliberation: Shortcomings in HBA and 3R</b>	
<b>Harm-Benefit Analysis (HBA): An "Impossible" Tool?</b>	
<b>Evaluation of HBA in Reviews of Project Applications?</b> <ul style="list-style-type: none"> <li>➤ Lacking standard for carrying out HBA [7, 8]</li> <li>➤ Rejections are hardly justifiable, thus most applications are approved</li> </ul>	<b>Overlooked Uncertainties?</b> <ul style="list-style-type: none"> <li>➤ Lacking acknowledgment of uncertainties and risks in HBA [2]</li> <li>➤ Researchers have almost no control over ultimate benefits, which creates incentive to fabricate stories [9, 10]</li> <li>➤ Retrospective assessments of harm rarely done although assessing harms and benefits accurately beforehand is challenging [11]</li> <li>➤ Questionable whether objective comparison of different benefits and harms for different animals is possible [13, 14]</li> </ul>
<b>Overemphasis on HBA?</b> <ul style="list-style-type: none"> <li>➤ Treated as the cornerstone of ethical review process by law and regulating authorities</li> <li>➤ Moral residual remains even if HBA would give a clear result [12]</li> </ul>	
<b>Limits of the 3R Principle (Replace, Reduce, Refine)</b>	
<b>... In Theory</b> <ul style="list-style-type: none"> <li>➤ 3R is silent regarding: the question of general justification, how to balance animal harms with/against human ends</li> <li>➤ Strictly connected to pathocentric ethics and anthropocentrism</li> </ul>	<b>... In Practice</b> <ul style="list-style-type: none"> <li>➤ Insufficient knowledge: 3R sometimes confused with each other [2], might be prioritized in the wrong order [15]</li> <li>➤ Carries the risk of welfare washing [16]</li> </ul>
<b>Quality of Science</b>	
<b>Choice Between Animal or Animal-Free Method?</b> <ul style="list-style-type: none"> <li>➤ Best practice standards not always the deciding factor</li> <li>➤ Social factors like tradition, accessibility of alternative methods as another possible influence [20]</li> </ul>	<b>Translation and Reproducibility?</b> <ul style="list-style-type: none"> <li>➤ Doubtable benefit and justification for research on non-human animals when translational significances are low or unclear [17, 18]</li> <li>➤ Reproducibility Crisis and Publication Bias lead to higher usage of animals than needed [19]</li> <li>➤ Overestimation of benefits when a study is poorly designed or reported [9]</li> </ul>

### Answers (What is Needed?)

<b>Harmonization and Internationalization</b>	<ul style="list-style-type: none"> <li>✓ Global public database for animal research</li> <li>✓ Training in 3R, animal ethics and animal-free methods for researchers and ethics committees (AECs)</li> <li>✓ Leave room for variation (e.g. legal requirements) for each country, but define best practice standards and agree on limits to discourage ethics dumping</li> <li>✓ Interdisciplinary research and communication between scientific disciplines, scientific communities</li> <li>✓ Professionalization of ethics committees (vs. unpaid honorary posts)</li> </ul>
<b>Designing the Toolset of an International Animal Research Ethics</b>	<ul style="list-style-type: none"> <li>✓ Development and communication of:                     <ul style="list-style-type: none"> <li>Harmonized explicit methodology for the process of ethical justification / ethical review</li> <li>Harmonized best practice standards</li> <li>HBA: Improved explicit methodology</li> </ul> </li> <li>✓ Role of HBA and 3R should not be overstretched beyond their capabilities</li> <li>✓ Revision of the ethical review process</li> <li>✓ Assessments of ethical and epistemic uncertainties in HBA or its alternatives</li> <li>✓ An ethics of uncertainty in research with animals</li> <li>✓ Acknowledgment that the ethical weighing of harms and benefits is problematic</li> <li>✓ Acknowledgment of moral conflicts between conflicting "oughts"                     <ul style="list-style-type: none"> <li>Development of tools that help to replace animals</li> <li>Dissemination of knowledge</li> <li>Training in alternative methods</li> </ul> </li> </ul>
<b>Encouragements, Obligations and Incentives</b>	<ul style="list-style-type: none"> <li>✓ Replace: focus on                     <ul style="list-style-type: none"> <li>Scientific and ethical standards</li> <li>Designing good experiments</li> <li>Alternative methods, minimizing harm</li> </ul> </li> <li>✓ Refine, Reduce: Improve animal welfare laws to decrease suffering and access to technologies that assess suffering</li> <li>✓ Obligation to pre-register and report all animal research and educational use in a public database, enforced by funding and research organizations</li> <li>✓ Training is key:                     <ul style="list-style-type: none"> <li>Scientific and ethical standards</li> <li>Designing good experiments</li> <li>Alternative methods, minimizing harm</li> </ul> </li> </ul>
<b>Proper Dissemination of Knowledge</b>	<ul style="list-style-type: none"> <li>✓ Painting a more complete picture: negative results need to also be published; journals, research institutions and funders should mandate ARRIVE guidelines [21]</li> <li>✓ Improve Transparency: global public database of animal research projects and their results</li> <li>✓ Combating the Reproducibility Crisis is a strategy to reduce animal experimentation                     <ul style="list-style-type: none"> <li>➔ Epistemic values also benefit animal research ethics</li> </ul> </li> </ul>

### Conclusions

Animal ethics, law and the sciences jointly shape the practices of animal research. In order to understand these systemic interdependencies and to improve the status quo, interdisciplinary approaches are required. Concepts, ideas or data that have been known and discussed for decades can be utilized, for instance by translating them into the language of another relevant discipline (e.g. *Five Freedoms* into legal rights), by applying them where needed (e.g. data on how harm and positive life experiences can be measured in different animals), or by simply disseminating them (better) between scientific fields and communities. During our exchange, it became clear that interdisciplinary efforts furthermore show promise since challenges in the sciences intersect with issues in animal ethics.

For references and affiliations, see:



#### Contact details

Dr. Marcel Mertz  
Institute for Ethics, History and  
Philosophy of Medicine  
OE 5450  
Carl-Neuberg-Straße 1, 30625 Hannover  
mertz.marcel@mh-hannover.de

SPONSORED BY THE



Federal Ministry  
of Education  
and Research

For more information about the retreat week, see:

[https://www.mhh.de/fileadmin/mhh/geschichte-ethik-philosophie-medizin/downloads/TIVE\\_Retreat\\_Week.pdf](https://www.mhh.de/fileadmin/mhh/geschichte-ethik-philosophie-medizin/downloads/TIVE_Retreat_Week.pdf)



## References

- [1] Schuppli, C. A., Fraser, D. (2007). Factors influencing the effectiveness of research ethics committees. *Journal of Medical Ethics*, 33(5), 294–301. <https://doi.org/10.1136/jme.2005.015057>
- [2] Jörgensen, S., Lindsjö, J., Weber, E. M., Röcklinsberg, H. (2021). Reviewing the Review: A Pilot Study of the Ethical Review Process of Animal Research in Sweden. *Animals*, 11(3), 708. <https://doi.org/10.3390/ani11030708>
- [3] Silverman, J., Lidz, C. W., Clayfield, J., Murray, A., Simon, L. J., Maranda, L. (2017). Factors Influencing IACUC Decision Making: Who Leads the Discussions? *Journal of Empirical Research on Human Research Ethics*, 12(4), 209–216. <https://doi.org/10.1177/1556264617717827>
- [4] Hansen, L. A., Goodman, J. R., Chandna, A. (2012). Analysis of Animal Research Ethics Committee Membership at American Institutions. *Animals*, 2(1), 68–75. <https://doi.org/10.3390/ani2010068>
- [5] Bout, H. J., Van Vlissingen, J. M. F., Karssing, E. D. (2014). Evaluating the ethical acceptability of animal research. *Lab Animal*, 43(11), 411–414. <https://doi.org/10.1038/labana.572>
- [6] Ideland, M. (2009). Different views on ethics: how animal ethics is situated in a committee culture. *Journal of Medical Ethics*, 35(4), 258–261. <https://doi.org/10.1136/jme.2008.026989>
- [7] Brønstad, A., Newcomer, C. E., Decelle, T., Everitt, J. I., Guillen, J., Laber, K. (2016). Current concepts of Harm–Benefit Analysis of Animal Experiments – Report from the AALAS–FELASA Working Group on Harm–Benefit Analysis – Part 1. *Laboratory Animals*, 50(1\_suppl), 1–20. <https://doi.org/10.1177/0023677216642398>
- [8] Gutfreund, Y. (2020). Harm-Benefit Analysis May Not Be the Best Approach to Ensure Minimal Harms and Maximal Benefits of Animal Research—Alternatives Should Be Explored. *Animals*, 10(2), 291. <https://doi.org/10.3390/ani10020291>
- [9] Eggel, M., Grimm, H. (2018). Necessary, but Not Sufficient. The Benefit Concept in the Project Evaluation of Animal Research in the Context of Directive 2010/63/EU. *Animals*, 8(3), 34. <https://doi.org/10.3390/ani8030034>
- [10] Grimm, H., Eggel, M. (2017). White Paper and Colourful Language: Toward a Realistic View of Animal Research. *Alternatives to Laboratory Animals*, 45(2), 101–103. <https://doi.org/10.1177/026119291704500207>
- [11] Pound, P., Nicol, C. J. (2018). Retrospective harm benefit analysis of pre-clinical animal research for six treatment interventions. *PLOS ONE*, 13(3), e0193758. <https://doi.org/10.1371/journal.pone.0193758>
- [12] Linder, E., Grimm, H. (2022). Aspect-seeing in animal research: the absence of justice in the harm-benefit-analysis. *Transforming Food Systems: Ethics, Innovation and Responsibility*. <https://doi.org/10.3920/978-90-8686-939-8>
- [13] Grimm, H. (2015). Turning Apples into Oranges? The Harm-Benefit Analysis and how to Take Ethical Considerations into Account. *Alternatives to Laboratory Animals*, 43(2), P22–P24. <https://doi.org/10.1177/026119291504300211>
- [14] Maisack, C. (2015). Harm-Benefit Analysis According to Directive 2010/63/EU, Article 38: What Does It Mean and How To Realize It? *ALTEX Proceedings*, 4(1), 24–27. <https://doi.org/10.58847/ap.1501>
- [15] Franco, N. H., Sandøe, P., Olsson, I. A. S. (2018). Researchers' attitudes to the 3Rs—An upturned hierarchy? *PLOS ONE*, 13(8), e0200895. <https://doi.org/10.1371/journal.pone.0200895>
- [16] Balls, M., Parascandola, J. (2019). The Emergence and Early Fate of the Three Rs Concept. *Alternatives to Laboratory Animals*. <https://doi.org/10.1177/0261192919896352>
- [17] Neuhaus, C. P. (2022). Threats to Benefits: Assessing Knowledge Production in Nonhuman Models of Human Neuropsychiatric Disorders. *Hastings Center Report*, 52(S2). <https://doi.org/10.1002/hast.1430>
- [18] Pound, P., Ebrahim, S., Sandercock, P., Bracken, M. B., Roberts, I. (2004). Where is the evidence that animal research benefits humans? *BMJ*, 328(7438), 514–517. <https://doi.org/10.1136/bmj.328.7438.514>
- [19] Würbel, H. (2017). More than 3Rs: the importance of scientific validity for harm-benefit analysis of animal research. *Lab Animal*, 46(4), 164–166. <https://doi.org/10.1038/labana.1220>
- [20] Nuffield Council on Bioethics. (2005). The Ethics of Research Involving Animals. 196–199. Retrieved from <https://www.nuffieldbioethics.org/wp-content/uploads/The-ethics-of-research-involving-animals-full-report.pdf>
- [21] Percie Du Sert, N., Hurst, V., Ahluwalia, A., Alam, S., Avey, M. T., Baker, M., . . . Würbel, H. (2020). The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. *PLOS Biology*, 18(7), e3000410. <https://doi.org/10.1371/journal.pbio.3000410>. See also <https://arriveguidelines.org/>

## Authors and their Affiliations (all authors in alphabetical order except first and last author)

Tatiana Hetzel, Institute for Ethics, History and Philosophy of Medicine, Hannover Medical School, Germany  
Karla Alex, Section for Translational Medical Ethics, NCT Heidelberg, Heidelberg University Hospital (Heidelberg University, Medical Faculty), Germany  
Katharina Braun, Department of Law, Freie Universität Berlin, Germany  
Samuel Camenzind, PhD, Department of Philosophy, University of Vienna, Austria  
Sara Capas Peneda, IMVM, i3S – Institute for Research and Innovation in Health, University of Porto, Portugal / School of Medicine and Biomedical Sciences, University of Porto, Portugal  
Rita Dodaro, MA, Department of Philosophy and Humanities, Freie Universität Berlin / Humanities Department, University of Calabria, Cosenza, Italy  
Dr. PH Hannes Kahrass, Institute for Ethics, History and Philosophy of Medicine, Hannover Medical School, Germany  
Svea Jörgensen, MA, Section of Ethology and Animal Welfare, Department of Animal Environment and Health, Swedish University of Agricultural Studies, Uppsala, Sweden  
Erich Linder, MA, Doctoral School of Philosophy, University of Vienna, Austria / Messerli Research Institute, University of Veterinary Medicine, Vienna, Austria  
Eva Reihls, MSc, Karl Chiari Lab for Orthopaedic Biology, Department of Orthopedics and Trauma Surgery, Medical University of Vienna, Austria  
Felicitas Selter, Institute for Ethics, History and Philosophy of Medicine, Hannover Medical School, Germany  
Vini Tiwari, MSc, Institute of Neuronal Cell Biology, Technical University Munich / German Center for Neurodegenerative Diseases, Munich / Graduate School of Systemic Neurosciences, Ludwig-Maximilians-Universität, Munich, Germany  
Zorana Todorović, PhD, Faculty of Philosophy, University of Belgrade, Serbia  
Dr. phil. Marcel Mertz, Institute for Ethics, History and Philosophy of Medicine, Hannover Medical School, Germany