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Supersede The Traditional Animal Experiments: An Exploration of Ethical, Welfare and Alternative Methods

Supersede The Traditional Animal Experiments: An Exploration On Ethical, Welfare And Alternative Methods

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➤ **Abstract:**

From long ago since the fifth century BC, there have been reports of scientific trials involving Animals, but their use has come more frequent since the nineteenth century. Animal weal would also comprise only stress reduction, beast suffering not being taken into account for numerous times. In 1824, the first beast protection society, the Society for the protection and secure the life of the under test animals, was established in England that's principal aim was animal's consolation and their otiosity. In 1959, Russell and Burch described the principle of the “3 Rs” – Replace, Reduce, upgrade – for exploration using Animals. This principle recommended substituting conscious living invertebrates with phylogenetically further primitive life forms, similar as the further degenerate metazoan microorganisms and endoparasites, or with motorized simulations. The reduction principle advised that exploration and procedures should be carried out with as many creatures as possible, while the refinement principle suggested that the ways used should drop their pain and torture at all stages of the study. In Brazil, Law No. 11,794/ 08, modified and bring a limitation on the use of animals in scientific experiments. ‘Chapter IV’ of the Arouca Law describes the conditions for parentage and using these creatures in tutoring and scientific exploration, similar as the use of sedation, analgesia or anesthesia in any trial that may beget pain or torture. It also recommends performing euthanasia whenever the trial is terminated or at any of its phases when there's violent suffering of the beast. The Arouca Law created Brazil's National Council for the Control of Animal Experimentation as a necessary condition for the accreditation of tutoring and exploration institutions that use animals in scientific trials. The purpose of using creatures in tutoring is to illustrate or carry out procedures that are formerly known, unlike their use in exploration, which is aimed at contributing to developing new medicines or treatments, in addition to clarifying certain natural marvels. Numerous advances in health lores were possible thanks to scientific trials conducted on creatures. However, conduct from non-governmental associations (NGOs) towards guarding and conserving creatures are still iterative. Some scientists argue that the prophetic value of this type of

exploration is frequently low and may lead to prejudiced or squishy results, which would affect in gratuitous suffering to the creatures and clinically inapplicable data. It can thus be stated that the practice of beast trial is considered a wide exertion in the scientific terrain. nonetheless, it has provoked public responses, and this practice has been intensively batted both in society and academic institutions. Our study was aimed at bearing a narrative review on ethics and weal in beast trial, as well as agitating indispensable styles to its use.

Keywords: Humanity, Diagnosis of diseases, Alternative methods, Ethics.

1. Introduction:

In a present day involved the animals in scientific experiments is an ethical dilemma. Humanity has been using creatures formerly for a long time, originally for food, for transport and as companion[1]. From the ancient Greece where Aristotle and Hippocrates laid down their knowledge on structure and function of the mortal body in their separate 'Historia Animalium' and 'Corpus Hippocraticum', substantially grounded on deconstructions in creatures, animals are being used for experiment and development of new drugs. Galen (130 – 201 announcement), croaker of the Roman emperor Marcus Aurelius, performed physiological trials on gormandizers, monkeys and tykes, which handed a base for medical practices also in the centuries later.[2]

After Galen, experimental wisdom stopped till the morning of the Renaissance when Vesalius took up the empirical approach, starting with anatomical studies. latterly on, physiological studies were also performed. With the Cartesian gospel in the 17th century, trials on creatures could be performed without great moral problems. The French champion Rene Descartes (1596 – 1650) stated that living systems could be understood on pure mechanical principles. The difference between man and animal is that man has a mind, which is a prerequisite for mindfulness and accordingly for the capability of feeling pain. animals can't suppose and are more like machines.[3]

Animal trials is a debating issue for a long time because of torture, pain and death of beast during scientific trial.[2] Colourful rules and regulations have been made to bring out a limitation to avoid the unwanted pain of the experimental animals. E.g. In 1824, a early commission was established to avoid brutality at animals in the way of experiment. Later, in 1876, the United Kingdom enacted legislation aimed at reducing animal cruelty. It came into actuality in India in 1960 which are generally known as the forestalling of atrocity to Animal act 1960.[6]

2. Reasons behind choosing animal model:

There are reasons for their use in several studies, similar as those probing mortal conditions and in toxin tests. In addition, creatures are used as an asset to tutoring health professionals and training their surgical chops.[8] Investigators should know the particular traits of the species they intend to use, similar as its physiology, experimental stages, reproductive characteristics, specific behaviours and nutritive requirements. In practice, when actually conducting trials, choosing the applicable beast model is done grounded on how easy the

husbandry practices and running of the beast species are, rather than experimental design or beast natural applicability.[9]

Rodents, especially rats and mice, are among the most generally used creatures in scientific exploration.[4] In the United States alone, 26 million mice and rats are used per time, which makes up to 96 to 98 of all beast testing.[10] Rats are most applicable for work involving shock, sepsis, rotundity, peritonitis, cancer, gastric ulcers, intestinal operations, the mononuclear phagocytic system, spleen, crack mending and organ transplantations. Mice, in turn, are more suited to studying megacolon and becks, as well as shock, sepsis, rotundity and cancer, as preliminarily mentioned.[4]

Pigs are commonly utilized in research involving the liver, stomach, and organ transplantation, while rabbits are more appropriate for studies focused on immunology, shock, inflammation, colitis, vascular procedures, and transplant research. Dogs fell into desuetude, substantially due to the exertion of NGOs engaged in guarding the species. still, their use was common in tutoring surgical fashion and studying shock, malabsorption, colitis, pancreatitis, hepatic and splenic operations, as well as transplantations.[29] Therefore, choosing an animal for laboratory use depends on the scientific exploration. There are some creatures whose inheritable lineage makes them prone to certain conditions, similar as diabetes mellitus or high blood pressure, and thus are ideal choices for testing medicines and/or procedures when studying similar conditions.[30]

It's of utmost significance to know the microbiological standard of laboratory animals, given that it not only affects people, but can also impact the results of the trials.[32] Studies have been using an adding number of specific pathogen-free (SPF) animals, that is, animals which are free of specific microorganisms and spongers. In order to gain this type of aseptic status, it's essential that creatures be conserved and kept in settings that are defended by strict aseptic walls and constantly covered, since numerous rodent infections are subclinical.[11]

3. Why should we do explore alternatives of animals model in experimental studies:

Using animals in experimental studies is an ethical dilemma. According to CPCSEA, IAEC, OECD guidelines it is pretty clear that all are promoting human care animals used in research and testing.[37] All are looking for reducing pain and sacrificing them during experiments. It is the questions of ethical liability of humanity. There have several reasons as describing below to do explore alternatives of animals in experimental studies.[18]

3.1. Animals often do not accurately replicate the complexity of many human diseases:

To diagnosis human diseases accurately, using animals as a model is severely limited. This is very true when it comes to diseases of the nervous system, cardiovascular system, in the case of diagnosis and treat diuretics, hypertensive disorder etc.[20] Numerous fundamental differences exist between the brains of humans and the experimental animals most commonly used monkey.[21] These include the relative proportions of neuronal types, their laminar distribution, gene expression biographies, and morphology.[45]

These differences are critical when trying to answer questions about the causes of conditions that are simply mortal[47]. Unlike humans, monkeys do not typically develop neurological conditions such as Alzheimer's, Parkinson's, Huntington's disease, or many other disorders that are primarily seen in humans. This means scientists must essay to instinctively induce these diseases in animals to model them for experimental purposes[50].

4. Impotent translation results to ineffective treatments:

The degree of restatement for neurological diseases is so poor that the National seminars of lores, Engineering, and Medicine concluded that “Advances ingenetics and other new technologies are beginning to bring forth new molecular targets and identify new biomarkers”, and that these are “Openings to accelerate early stages of medicine development for nervous system diseases in the absence of beast models that reflect complaint and prognosticate efficacy”.[51] This statement is bolstered by the proliferation of numerous mortal- grounded druthers to the use of monkeys and other creatures, performing in further effective and ethical wisdom.[52]

Alternative methods are those methods or anything from certain to partial removal of live animals in testing and research or development and implemented methods of testing which get off the use of live animals.[53][54] There so many alternative methods are available to use instead of animal which are described as follows:

4.1 Advanced and Innovative Human-Based Technologies Should Replace Animal Testing:

The emergence of human stem cell-based technologies—particularly human brain organoids—has significantly advanced the study of brain function within the framework of personalized medicine. These models provide insights into neurological disorders that reflect the full genetic and ethnic diversity of the human population, offering advantages that animal models such as monkeys and mice cannot match.[56] Alongside techniques like live human brain imaging, transcriptomic analyses, and detailed examination of post-mortem human brain tissue, these human-specific approaches present a far more accurate path toward uncovering the root causes of neurological diseases.[57]

Highlighting the shift toward these innovative methods, the U.S. National Institutes of Health (NIH) announced on February 1, 2024, that it will give precedence to the development and implementation of New Approach Methodologies (NAMs) over traditional animal testing.[58] This policy change follows the FDA Modernization Act 2.0, which authorizes the U.S. Food and Drug Administration to consider data derived from human cell-based models instead of mandating animal-based testing for new drug approvals.[59]

As a result, the use of rodents and non-human primates is no longer at the forefront of neurological research in the 21st century.[60] Human-relevant brain models have emerged as

essential tools in advancing our understanding of neuropsychiatric disorders and developing effective therapeutic interventions.[61]

4.2 CAL (Computer Assisted Learning):

CAL is an interactive computer assisted learning program without involvement of real experimental tools. CAL is a good alternative to live animal trials. It helps the scholars to understand generalities of medicine conduct, ADR and their choice. It is an important study instrument equally acceptable to students & faculty.[62]

- CAL had better problem solving attitude & the cost was much less than the traditional laboratory practices.[63]

4.3 Two software are currently used in INDIA:

Ex-Pharm: Ex-Pharma is a computer-assisted learning (CAL) software designed to simulate animal experiments in the field of pharmacology. It includes a range of modules that illustrate the effects of drugs on various physiological systems in animals.[64]

X-cology: It offers video demonstrations that guide users through essential laboratory techniques, such as the isolation and mounting of animal tissues. The platform also includes an interactive screen interface that allows learners to explore how different drugs affect these isolated tissues, enhancing understanding through virtual experimentation.[64]

5. Investigators' ethics:

The role of scientists and professionals conducting research using animals is changing with the advancement of modern technology and knowledge. Today, animals are considered to have a perception of pain, memory, suffering, and survival instincts that are largely equivalent to humans. In light of this realization, the responsibility of researchers has become even more important—they must ensure that ethical standards are maintained in every study conducted on animals and that there is no evidence of any abuse.[65]

Many invasive experiments have shown that animals are not relieved of pain—which is worrisome.[53] Therefore, there must be a clear and binding law that will ensure the design, methods, and care of animals for research. In particular, when it is intended to achieve scientific results through animal experiments, the research must be properly planned from an ethical perspective. It is important to determine the number of animals in a rational manner so as to avoid unnecessary suffering.[66]

Every researcher should conduct every experiment with conscience, so as not to cause injustice to animals and to minimize their suffering as much as possible. Universities, where

future researchers are being trained, should seriously consider limiting or banning the use of animal research.[67]

Scientists should use their knowledge and experience to explain to the public why animal research is still relevant and when it is acceptable. At the same time, research institutions also have a responsibility to raise public awareness and maintain transparency. Not only the results of the research, but also the research methods and aspects of animal care should be presented to the public.[67]

6. Final consideration:

Animals have been used in research and education, and have made important contributions, especially in the health sciences. Many important discoveries have been made possible by relying on animals, such as the development of new drugs and medical procedures and the elucidation of some of the complex mysteries of nature. Nevertheless, many organizations and activists working on animal rights and welfare are still active, who are vocal against cruelty and unethical behaviour in animal research.[69]

In this context, the 3Rs principle—replacement, reduction, and refinement—is considered an important advance in animal welfare.[67] However, simply reducing the number of animals is not enough; if the quality and purpose of the research are not clear, the usefulness of the research will be lost. The aim of this principle is to use models or methods that reduce the dependence on animals, but in reality, it is still difficult to imagine alternatives to animals in some complex research.[72]

Before starting a research, the researcher should gain detailed knowledge of the relevant animal species and develop a specific research plan, so as to avoid unnecessary animal use. It is also the ethical responsibility of the researcher to ensure proper shelter and care for animals, and to protect them from pain, suffering, and emotional distress. Environmental enrichment, such as providing proper food, shelter, and psychological stimulation, helps to maintain the well-being of animals.[71] The mental and physical state of the animal can affect the results of the research, so it is important to consider these aspects if credibility is to be maintained. Research ethics must be ensured and alternative methods of animal use—such as in vitro research, cadaveric studies, or computer simulations—should always be encouraged, wherever possible.[73]

7. Conclusion:

The use of animals in education and research still poses many problems.[72] However, it cannot be denied that many important medicines and vaccines have been discovered through these studies and will continue to be discovered in the future, which are essential for human health. However, animals are sentient beings, so their use must be limited and only in necessary cases.[74] Researchers have a responsibility to ensure the well-being of animals

used in laboratories and to avoid any kind of pain and suffering. In addition, emphasis should be placed on using alternative methods whenever possible. When animals need to be killed for the purpose of testing, it should be done in a way that ensures their quick and painless death—by stopping blood circulation and stopping brain function.[75]

➤ **References:**

1. Sonali K, et al. Alternatives to animal testing: A review. *Saudi Pharm J.* 2015;23(3):215-332.
2. Arora T, et al. Substitute of animals in drug research: An approach towards fulfillment of 4R's. *Indian J pharm sci.*2011;73(1):1-6
3. Miziara ID, Magalhaes ATM, Santos MA, Gomes EF, Oliveira RA. Research ethics in animal models. *Braz J Otorhinolaryngol.* 2012; 78(2):128-31.
4. Petroianu A. Aspectos eticos na pesquisa em animais. *Acta Cir Bras.* 1996 MES; 11(3):157-64.
5. BRASIL. Lei n 11.794 de 8 de outubro de 2008. Procedimentos para o uso científico de animais. *Diario Oficial da Uniao;* 196; Seção 1.
6. Trez TA. Caracterização do uso de animais no ensino a partir da percepção de estudantes de ciencias biologicas e da saúde. *Hist Cienc Saude.* 2015; 22(3):863-80.
7. Singh VP, Pratap K, Sinha J, Desiraju K, Bahal D, Kukreti R. Critical evaluation of challenges and future use of animals in experimentation for biomedical research. *Int J Immunopathol Pharmacol.* 2016; 29(4):551-61.
8. Kehind EO. They see a rat, we seek a cure for diseases: the current status of animal experimentation in medical practice. *Med Princ Pract.* 2013; 22(Suppl 1):52-61.
9. Knop LB, Maria DA. Metodos substitutivos e a experimentação animal: um enfoque inovador. *RESBCAL.* 2016; 4(2):101-14.
10. Batalha E. Uso de animais em pesquisa abrange desafios eticos e compromisso com novas tecnologias. *Radis.* 2017; 174.
11. Muller CA, Ramos S, Saisse AO, Almosny NRP. Videocameras em bioterios de experimentação: importante ferramenta no controle da contaminação ambiental na microbiota de camundongos. *Arq Bras Med Vet Zootec.* 2015; 67(3):689-97.
12. Weber EM, Dallaire JA, Gaskill BN, Pritchett-Corning KR, Garner JP. Aggression in group-housed laboratory mice: why can't we solve the problem? *LabAnimal.* 2017; 46(4):157-61.
13. Guidelines for the Use of Animals. Guidelines for the treatment of animals in behavioural research and teaching. *Anim Behav.* 2017; 123:1-9.
14. Neves SMP, Prates FM, Rodrigues LD, Santos RA, Fontes RS, Santana RO. Manual de cuidados e procedimentos com animais de laboratorio do Bioterio de Produção e Experimentação da FCF-IQ/USP. São Paulo: FCF-IQ/USP; 2013.
15. Iki Y, Ito T, Kudo K, Noda M, Kanehira M, Sueta T, et al. Animal ethics and welfare education in wet-lab training can foster residents' ethical values toward life. *Exp Anim.* 2017. doi: 10.1538/expanim.17-0026.
16. Conselho Federal de Medicina Veterinária. Guia Brasileiro de Boas Praticas para Eutanasia em Animais. Brasilia: Comissao de Etica, Bioetica e Bem- Estar Animal/CFMV; 2013.
17. Baldelli I, Massaro A, Penco S, Bassi AM, Patuzzo S, Ciliberti R. Conscientious objection to animal experimentation in Italian universities. *Animals.* 2017; 7(24):1-8.
18. Andrade GM, Lopes HDP, Felicio SJO, Carmo VM, Matos EP. Experience report on teaching surgical technique without animal use. *Acta Cir Bras.* 2015; 30(5):371-5.
19. Joffe AR, Bara M, Anton N, Nobis N. The ethics of animal research: a survey of the public and scientists in North America. *BMC Medical Ethics.* 2016; 17:17.
20. Mayir B, Dogan U, Bilecik T, Yardımcı EC, Çakır T, Aslaner A, et al. Why scientists perform animal experiments, scientific or personal aim? *Ulus Cerrahi Derg.* 2016; 32(4):256-60.

21. Kehinde EO. They see a rat, we seek a cure for diseases: the current status of animal experimentation in medical practice. *Med Princ Pract.* 2013; 22(Suppl - 1):52-61.
22. Bennett AJ, Ringach DL. Animal research in neuroscience: a duty to engage. *Neuron.* 2016; 92(3):653-7.
23. Balls M, Combes R. Animal experimentation and alternatives: revealed preferences. *Altern Lab Anim.* 2017; 45(1):1-3.
24. Pasupuleti MK, Molahally SS, Salwaji S. Ethical guidelines, animal profile, various animal models used in periodontal research with alternatives and future perspectives. *J Indian Soc Periodontol.* 2016; 20(4):360-8.
25. Zoupa M, Machera K. Zebrafish as an alternative vertebrate model for investigating developmental toxicity—The Triadimefon Example. *Int J Mol Sci.* 2017; 18(4):817.
26. Ramalli Jr EL, Ho W, Alves M, Rocha EM. Progress in animal experimentation ethics: a case study from a Brazilian medical school and from the international medical literature. *Acta Cir Bras.* 2012; 27(9):659-63.
27. Abubakar AA, Noordin MM, Azmi TI, Kaka U, Loqman MY. The use of rats and mice as animal models in ex vivo bone growth and development studies. *Bone Joint Res.* 2016; 5(12):610-8.
28. Brito CVB, Soares RHFC, Botelho NM. Analgesia de animais de laboratorio: responsabilidade dos comites de etica e obrigaçao dos pesquisadores. *Rev Bioet.* 2016; 24(3):528-31.
29. Yang NB, Pan XJ, Cheng JJ, Lin JQ, Zhu JY. Ethical Inspection about laboratory animals. *Zhongguo Ying Yong Sheng Li Xue Za Zhi.* 2015; 31(6):504-7.
30. Singh VP, Pratap K, Sinha J, Desiraju K, Bahal D, Kukreti R. Critical evaluation of challenges and future use of animals in experimentation for biomedical research. *Int J Immunopathol Pharmacol.* 2016; 29(4):551-61.
31. Tanner R, McShane H. Replacing, reducing and refining the use of animals in tuberculosis vaccine research. *ALTEX.* 2017; 34(1):157-66.
32. Cassar S, Adatto I, Freeman JL, Gamse JT, Iturria I, Lawrence C, Muriana A, Peterson RT, Van Cruchten S, Zon LI. Use of zebrafish in drug discovery toxicology. *Chemical research in toxicology.* 2019 Oct 18;33(1):95-118.
33. Flecknell P. Replacement, reduction, refinement. *ALTEX-Alternatives to animal experimentation.* 2002 May 1;19(2):73-8.
34. Sneddon LU, Halsey LG, Bury NR. Considering aspects of the 3Rs principles within experimental animal biology. *Journal of Experimental Biology.* 2017 Sep 1;220(17):3007-16.
35. Kirk RG. Recovering the principles of humane experimental technique: the 3Rs and the human essence of animal research. *Science, technology, & human values.* 2018 Jul;43(4):622-48.
36. Tannenbaum J, Bennett BT. Russell and Burch's 3Rs then and now: the need for clarity in definition and purpose. *Journal of the American association for laboratory animal science.* 2015 Mar 1;54(2):120-32.
37. Eggel M, Würbel H. Internal consistency and compatibility of the 3Rs and 3Vs principles for project evaluation of animal research. *Laboratory animals.* 2021 Jun;55(3):233-43.
38. Tornqvist E, Annas A, Granath B, Jalkestén E, Cotgreave I, Oberg M. Strategic focus on 3R principles reveals major reductions in the use of animals in pharmaceutical toxicity testing. *PLoS one.* 2014 Jul 23;9(7):e101638.
39. Franco NH, Olsson IA. Scientists and the 3Rs: attitudes to animal use in biomedical research and the effect of mandatory training in laboratory animal science. *Laboratory animals.* 2014 Jan;48(1):50-60.
40. Franco NH, Sandøe P, Olsson IA. Researchers' attitudes to the 3Rs—An upturned hierarchy?. *PLoS One.* 2018 Aug 15;13(8):e0200895.
41. Franco NH. Animal experiments in biomedical research: a historical perspective. *Animals.* 2013 Mar 19;3(1):238-73.
42. Guerrini A. *Experimenting with humans and animals: from Galen to animal rights.* JHU Press; 2003 Jul 2.

43. Newton DE. The animal experimentation debate: A reference handbook. Bloomsbury Publishing USA; 2013 May 9.
44. Rowan AN. Of mice, models, and men: A critical evaluation of animal research. SUNY Press; 1984.
45. Gordon SG, Kittleson MD. Drugs used in the management of heart disease and cardiac arrhythmias. *Small animal clinical pharmacology*. 2008 Jan 1:380-457.
46. Korner PI. Essential hypertension and its causes: neural and non-neural mechanisms. Oxford University Press; 2007 May 11.
47. Patil P. *Clinical Application of Repertories in the Management of Essential Hypertension* (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)).
48. Taylor RN, Roberts JM, Cunningham GF, Lindheimer MD, editors. *Chesley's hypertensive disorders in pregnancy*. Elsevier; 2014 Aug 28.
49. Selzer A. *Understanding heart disease*. Univ of California Press; 2023 Nov 15.
50. National Institutes of Health. *Guide for the care and use of laboratory animals*. National Academies; 1985.
51. Institute of Laboratory Animal Resources (US). *Committee on Care, Use of Laboratory Animals. Guide for the care and use of laboratory animals*. US Department of Health and Human Services, Public Health Service, National Institutes of Health; 1986.
52. Sikes RS, Animal Care and Use Committee of the American Society of Mammalogists. 2016 Guidelines of the American Society of Mammalogists for the use of wild mammals in research and education. *Journal of mammalogy*. 2016 Jun 9;97(3):663-88.
53. Strahle U, Scholz S, Geisler R, Greiner P, Hollert H, Rastegar S, Schumacher A, Selderslaghs I, Weiss C, Witters H, Braunbeck T. Zebrafish embryos as an alternative to animal experiments—A commentary on the definition of the onset of protected life stages in animal welfare regulations. *Reproductive Toxicology*. 2012 Apr 1;33(2):128-32.
54. Gannon WL, Sikes RS, Animal Care and Use Committee of the American Society of Mammalogists. Guidelines of the American Society of Mammalogists for the use of wild mammals in research. *Journal of Mammalogy*. 2007 Jun 1;88(3):809-23.
55. Lebreton JD, Burnham KP, Clobert J, Anderson DR. Modeling survival and testing biological hypotheses using marked animals: a unified approach with case studies. *Ecological monographs*. 1992 Mar;62(1):67-118.
56. Bennett BT, Brown MJ, Schofield JC. *Essentials for animal research: A primer for research personnel*. US Department of Agriculture, National Agricultural Library; 1990.
57. Du Sert NP, Ahluwalia A, Alam S, Avey MT, Baker M, Browne WJ, Clark A, Cuthill IC, Dirnagl U, Emerson M, Garner P. Reporting animal research: Explanation and elaboration for the ARRIVE guidelines 2.0. *PLoS biology*. 2020 Jul 14;18(7):e3000411.
58. Holt WV. Alternative strategies for the long-term preservation of spermatozoa. *Reproduction, Fertility and Development*. 1997;9(3):309-20.
59. Orlans FB. *The human use of animals: case studies in ethical choice*. Oxford University Press, USA; 1998.
60. Bishop LJ, Nolen AL. *Animals in research and education: Ethical issues*. Kennedy Institute of Ethics Journal. 2001;11(1):91-112.
61. Kiani AK, Pheby D, Henehan G, Brown R, Sieving P, Sykora P, Marks R, Falsini B, Capodicasa N, Miertus S, Lorusso L. Ethical considerations regarding animal experimentation. *Journal of preventive medicine and hygiene*. 2022 Jun;63(2 Suppl 3):E255.
62. KOCAMAN KALKAN K, KEKECOGLU M. Ethical Principles and Rules in Experimental Animal Studies: A Comprehensive Review. *Duzce Medical Journal*. 2024 Jan 2;26.
63. Baumans V. Use of animals in experimental research: an ethical dilemma?. *Gene therapy*. 2004 Oct;11(1):S64-6.
64. Webster J. Ethical and animal welfare considerations in relation to species selection for animal experimentation. *Animals*. 2014 Dec 3;4(4):729-41.

65. Harikrishnan VS. Ethical issues in animal experimentation. In Biomedical Product and Materials Evaluation 2022 Jan 1 (pp. 355-372). Woodhead Publishing.
 66. National Institutes of Health. Guide for the care and use of laboratory animals. National Academies; 1985.
 67. Institute of Laboratory Animal Resources (US). Committee on Care, Use of Laboratory Animals. Guide for the care and use of laboratory animals. US Department of Health and Human Services, Public Health Service, National Institutes of Health; 1986.
 68. Sikes RS, Animal Care and Use Committee of the American Society of Mammalogists. 2016 Guidelines of the American Society of Mammalogists for the use of wild mammals in research and education. Journal of mammalogy. 2016 Jun 9;97(3):663-88.
 69. Lebreton JD, Burnham KP, Clobert J, Anderson DR. Modeling survival and testing biological hypotheses using marked animals: a unified approach with case studies. Ecological monographs. 1992 Mar;62(1):67-118.
 70. Strahle U, Scholz S, Geisler R, Greiner P, Hollert H, Rastegar S, Schumacher A, Selderslaghs I, Weiss C, Witters H, Braunbeck T. Zebrafish embryos as an alternative to animal experiments—A commentary on the definition of the onset of protected life stages in animal welfare regulations. Reproductive Toxicology. 2012 Apr 1;33(2):128-32.
 71. Zeman A. A Portrait of the Brain. Yale University Press; 2008.
 72. Quintyn CB. The new eugenics: Modifying biological life in the twenty-first century. Archway Publishing; 2020 Dec 17.
 73. Rooney A. The story of neuroscience. Arcturus Publishing; 2017 Nov 30.
 74. Eagleman D. Livewired: The inside story of the ever-changing brain. Canongate Books; 2020 Aug 27.
 75. Blum D. The monkey wars. Oxford University Press; 1995 Dec 14.
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