

INTRODUCTION

Research is the foundation of scientific advancement. However, these advancements have also brought to the fore various ethical concerns surrounding the treatment of research subjects. As the pursuit of knowledge pushes the boundaries of innovation in health, behavioural, and biological sciences, the protection of human and animal subjects remains a moral and regulatory imperative. In human research, ethical issues revolve around safeguarding autonomy, obtaining informed consent, ensuring beneficence, and protecting vulnerable populations such as children, prisoners, and individuals with diminished decision-making capacity¹. The codification of ethical standards for human research has evolved historically, particularly after the revelations of egregious human rights violations during World War II². The ethical standards of human research gained prominence following the Nuremberg tribunal, which exposed Nazi war crimes, including vicious human subject experiments without consent or regard for well-being³. In response, the Nuremberg Code was established, emphasizing that research involving humans is only permissible if the results are beneficial to society, the participants voluntarily consent and retain the right to withdraw, and no harm, loss of opportunity, or unnecessary discomfort is inflicted³. Despite its foundational role, the Nuremberg Code did not adequately address research involving vulnerable populations such as children, cognitively impaired individuals, and those unable to provide informed consent⁴. To

bridge this gap, the Declaration of Helsinki, adopted by the World Medical Association in 1964, introduced more comprehensive ethical guidance by allowing the use of legally authorized representatives to consent on behalf of individuals incapable of doing so, while emphasizing the primacy of participant welfare^{5,6}. This Declaration is now widely regarded as the cornerstone of international biomedical research ethics. Building upon these frameworks, the Belmont Report was introduced in 1979 by the U.S. Department of Health, Education, and Welfare, articulating three fundamental principles that underpin modern human research ethics: respect for persons, beneficence, and justice⁷. These principles require researchers to uphold the autonomy of all participants, minimize harm while maximizing benefit, and equitably distribute research risks and outcomes². While these developments have strengthened the ethical infrastructure of human research, modern advancements in biotechnology, artificial intelligence, and genomic editing have introduced complex ethical dilemmas around consent, privacy, and equity, especially in cross-cultural and international research settings⁸.

In parallel, the use of animals in scientific research has played an essential role in the development of medical therapies, vaccine trials, surgical techniques, and toxicity testing^{4,9}. However, it presents a profound ethical paradox: the pursuit of human benefit at the expense of animal suffering¹⁰. Concerns over the moral status of animals, their capacity for pain, and the necessity of their use have prompted the development of

ethical guidelines and the application of the “3Rs” principle: Replacement (using alternatives to animals when possible), Reduction (minimizing the number of animals used), and Refinement (enhancing procedures to reduce suffering)^{4,11}. Despite the widespread acceptance of these principles, their practical application varies significantly across research institutions, and critics argue that utilitarian justifications often override animal welfare considerations¹². Public awareness, bolstered by advocacy from animal rights organizations, has intensified the demand for transparency and the development of non-animal models such as in vitro systems, computer simulations, and organ-on-chip technologies.¹³

Consequently, as research technologies and methodologies continue to evolve, ethical considerations must adapt accordingly, by ensuring that the dignity, rights, and well-being of all research participants (human and animals) remain at the forefront of scientific inquiry. This study therefore critically examines the ethical issues surrounding both human and animal research, analysing historical contexts by examining case studies and the importance of addressing these ethical issues in research, with the ultimate goal of promoting ethically sound, socially responsible, and scientifically rigorous research practices.

MATERIALS AND METHODS

A narrative review of literature from 2015 to 2025 was conducted, focusing on PubMed-indexed, peer-reviewed articles. The review included primary research studies and

systematic reviews related to ethical issues in human and animal research. Studies were identified through the PubMed database using keywords such as "Principles of ethics," "human and animal research," "case studies," and "emerging technologies."

Preference was given to the recent papers to ensure the inclusion of the current findings. Highly cited and robust articles on research ethics were selected for their relevance and impact on the key review. Information from CIOMS International Ethical Guidelines for Health-related Research Involving Humans, The Belmont Report on research ethics, The Nuremberg Code and World Medical Association Declaration of Helsinki were included for expert guidelines. Non-English studies, non-peer-reviewed articles, and papers unrelated to ethical issues in human and animal research were excluded.

This review is categorized into sections of the importance of addressing ethical issues in research, major ethical issues in human and animal research in relation to the principles of ethics, illustration of case studies and ethical issues in emerging technologies.

RESULTS AND DISCUSSION

Importance of Addressing Ethical Issues in Research

Research involving human and animal subjects is integral to advancing scientific knowledge, improving healthcare, and informing policy. However, pursuing such knowledge must be grounded in ethical principles to ensure that the rights, dignity, and welfare of participants (human or animal) are safeguarded throughout the research process. Addressing ethical issues

in research is essential for legal compliance and maintaining public trust, ensuring scientific integrity, and protecting the vulnerable.¹⁴

Ethical practices such as rigorous peer review, transparent methodology, and adherence to established protocols ensure that research findings are reliable and valid¹⁵. When studies are conducted ethically, they are less likely to be marred by biases, fabrications, or errors that could compromise credibility. For instance, ethical standards demand accurate data reporting and full disclosure of any potential conflicts of interest, which directly contribute to the integrity and trustworthiness of research findings^{15,16}.

Also, ethical research practices often align with broader societal values and needs, leading to outcomes that are not only scientifically significant but also socially beneficial¹⁴. By respecting principles like justice and beneficence, researchers ensure that their work with human subjects contributes positively to society¹⁷. For example, ethical guidelines in medical research emphasize the need to balance scientific advancement with patient welfare, ensuring that new treatments are both effective and safe. This balance is crucial in addressing pressing societal health concerns while safeguarding individual rights and well-being.

Furthermore, the relationship between the public and the scientific community is heavily reliant on trust, which is fostered through consistent ethical conduct in research¹⁴. When the public perceives that researchers are committed to ethical standards, it reinforces their confidence in

the scientific process and its outcomes. Ethical research practices demonstrate a respect for societal norms and values, reinforcing the perception that science serves the public good¹⁶.

Therefore, ethical issues in human and animal research are not peripheral concerns but central pillars of responsible scientific practice. Addressing them ensures the protection of subjects, upholds human dignity and animal welfare, promotes credible science, and fosters societal benefit.

Major Ethical Issues in Human Research

The most salient ethical principles that govern human subject research are: Beneficence (the obligation to do good), non-maleficence (the duty to avoid causing harm), fidelity and trust within the fiduciary investigator-participant relationship, respect for personal dignity, autonomy (encompassing informed, voluntary, and competent decision-making), and privacy, particularly the protection of personal and sensitive data¹⁸.

These principles are enshrined in international codes and guidelines such as the Nuremberg Code (1947)^{3,19}, the Declaration of Helsinki (1964, and subsequent revisions)²⁰, and the Belmont Report (1979)^{7,21}.

Informed Consent

Participants involved in a research study must be adequately informed about the study's nature and associated risks and must voluntarily agree to participate by giving informed consent. It is essential that all participants receive detailed information regarding the study's objectives,

methodology, potential benefits and harms, as well as any existing conflicts of interest.^{22,23} They must also be made aware of their right to decline participation or to withdraw at any stage without any consequences.¹⁶ In situations where an individual is not capable of giving informed consent, a legally authorized representative should provide consent on their behalf.²² However, Avasthi *et al.*²⁴ argued that if no such representative is available and the research must begin immediately, the study may proceed without prior consent, provided that the justification for this is documented in the research protocol and approved by an ethics review board. They further stated that consent from a legal representative should be sought at the earliest opportunity to allow continued participation in the study.

Privacy and Confidentiality

In the context of clinical research, privacy refers to an individual's ability to control the disclosure of personal details related to their health status, emotions, and social relationships to researchers.²⁵ Confidentiality involves safeguarding the participant's private data and limiting when and how that information can be accessed or shared with others.²⁶ Visual data such as X-rays, ultrasound scans, pathology slides, or internal body images do not violate confidentiality, provided that any identifying information is removed and the data is anonymized beforehand.²³

Beneficence

In the realm of human research, the principle of beneficence refers to the ethical obligation of researchers to prioritize the

well-being of research participants by maximizing possible benefits and minimizing potential harms.²⁷ This principle mandates a proactive approach that researchers are not only required to avoid causing harm but are also expected to promote the welfare of participants throughout the study.²⁶ Beneficence supports moral duties such as defending the rights of individuals, preventing harm, assisting vulnerable populations, and contributing positively to human welfare.²⁸

In the research setting, this involves designing studies that have the potential for meaningful scientific advancement while ensuring participants are not exploited or subjected to unnecessary risks. Furthermore, researchers often owe a duty to society due to the public support for education and scientific infrastructure, making the ethical application of beneficence not only an altruistic responsibility but also a form of social reciprocity.²⁷ This principle becomes particularly relevant when conducting clinical trials where the direct therapeutic benefit to participants may be uncertain but the potential societal gain is high.

Nonmaleficence

The principle of nonmaleficence, which translates to "do no harm," holds a central place in the ethical framework governing research involving human participants.²⁹ This principle underlies several moral imperatives, including refraining from causing unnecessary pain, injury, or distress; avoiding exploitation; and ensuring that participants are not deprived of fundamental rights or resources.²⁹

In practice, non-maleficence obliges researchers to conduct rigorous risk-benefit analyses before initiating a study. For example, invasive procedures, drug trials, or experimental interventions must be justified by the potential scientific or therapeutic benefits and must undergo scrutiny by institutional review boards or ethics committees. Especially in sensitive areas such as end-of-life research, mental health, or vulnerable populations (e.g., children), researchers must ensure that participation does not result in more harm than benefit.¹⁶ Moreover, in cases where research involves foreseeable but unintended side effects (e.g., distress caused by recalling traumatic events during interviews), protocols must be in place to mitigate harm and offer appropriate support services.²⁹ The concept of double effect, where an intervention intended for good also has a secondary, unintended negative consequence, must be ethically justified and carefully monitored within the study's ethical framework.²⁹

Autonomy

Autonomy is a foundational principle in human research ethics, grounded in the idea that individuals possess inherent worth and the right to make decisions about their own lives and bodies (Florijn, 2022).³⁰ Respecting autonomy means that participants should be fully informed about the nature of the research, its risks and benefits, and their rights, including the right to withdraw at any time without penalty.²⁹ This is operationalized through mechanisms like informed consent and confidentiality. However, Resnik¹⁶ argued that autonomy must be balanced against other ethical

principles. For example, if an individual's autonomous choice poses significant harm to others, or if a person lacks decision-making capacity (due to age, cognitive impairment, or mental illness), the principle of autonomy may be limited. In such cases, consent must be obtained from a legally authorized representative, and additional safeguards must be applied to protect participant rights.¹⁶

Also, critiques of the autonomy principle suggest that it may be overly individualistic and fail to account for relational autonomy, which considers how personal decisions are shaped by social contexts such as culture, family, religion, and gender.³¹ In many non-Western societies, collective decision-making processes may be more culturally appropriate than individual consent, particularly in decisions involving serious medical interventions or genetic research.²⁹ Additionally, the practice of paternalism, where researchers or medical professionals make decisions on behalf of participants for their perceived benefit continues to raise ethical debates.³² While rooted in the principle of beneficence, paternalism can undermine autonomy if not carefully justified. Given the evolving landscape of global health, increased literacy, and patient rights movements, it is essential to reassess these dynamics through ethical research and culturally sensitive engagement strategies.³² In line with respecting autonomy, researchers are ethically bound to disclose all necessary information to participants in a manner that is understandable and culturally appropriate. This includes providing details about the study's aims, duration, procedures,

potential risks, benefits, and alternative options.

Case Studies Illustrating Some of these Ethical Issues

The Nazi Medical Crimes and the Nuremberg Trials

The exposure of unethical human experimentation by Nazi physicians during World War II marked a turning point in research ethics.³ In Nazi concentration camps, German doctors conducted brutal and non-consensual experiments including freezing, high-altitude tests, and deliberate infection with diseases often leading to severe suffering or death. Alongside these, over 350,000 German citizens were forcibly sterilized under Nazi eugenic laws aimed at racial purification.^{33,34} This led to the creation of the Nuremberg Code (1947),^{7,19} which established key ethical principles for human research, most notably the necessity of voluntary informed consent and the obligation to avoid unnecessary harm. These events laid the foundation for modern research ethics and reinforced the need for strong oversight mechanisms such as institutional review boards.⁴

The Pfizer Trovan Study in Nigeria (1996)

In 1996, during a severe outbreak of cerebrospinal meningitis in Tudun Wada, Kano State, northern Nigeria, an ethically controversial clinical trial was conducted by the multinational pharmaceutical company Pfizer.^{35,36} The epidemic, which primarily affected children, prompted a rapid response from both local and international actors. The

Kano State Government mobilized resources to contain the outbreak, while humanitarian organizations such as Médecins Sans Frontières (MSF) also provided critical medical assistance.³⁷

Amidst the crisis, Pfizer deployed a medical team to conduct a clinical trial of an experimental antibiotic, Trovafloxacin (commercially known as Trovan), a member of the quinolone class.^{35,37} The company aimed to test Trovan's efficacy and safety compared to standard treatments already in use. Pfizer recruited 200 children into the study, assigning them to two treatment arms: one group received oral Trovan, while the control group received Ceftriaxone or Chloramphenicol, both known effective therapies for meningitis.³⁷

The trial was completed within three weeks, having rapidly reached its participant target. However, it drew intense scrutiny and criticism due to serious ethical lapses. Reports indicated that some children died, while others suffered long-term disabilities potentially linked to the experimental drug or the conditions under which the study was conducted.^{37,38}

Several allegations were raised against Pfizer's conduct: Lack of ethical clearance from relevant Nigerian regulatory bodies before initiating the trial. Failure to obtain informed consent from the parents or guardians of the children enrolled, with no clear disclosure that Trovan was an experimental drug. Exploitation of a vulnerable population, taking advantage of the community's poverty, low literacy, and desperation amidst an epidemic. Finally, abandonment of the community after the

study's conclusion, despite the epidemic still being active.³⁷

The controversy culminated in multiple lawsuits against Pfizer in both Nigeria and the United States of America. In 2009, the company reached an out-of-court settlement and paid \$75 million to Kano State and \$175,000 to four families of dead children.³⁷ This case has since become one of the most cited examples of ethical misconduct in international biomedical research, highlighting the dangers of conducting clinical trials in resource-limited settings without stringent ethical safeguards.

The ACTG 076 Trial and the Ethical Controversy of Placebo-Controlled HIV Studies in Developing Countries

In 1994, the AIDS Clinical Trials Group (ACTG) reported the groundbreaking results of its Study 076, which demonstrated that the administration of Zidovudine (AZT) to HIV-positive pregnant women significantly reduced the risk of mother-to-child transmission (MTCT) of HIV.³⁹ Specifically, the regimen consisted of oral AZT during pregnancy, intravenous AZT during labour, and oral AZT administered to the newborn reduced the vertical transmission rate by approximately two-thirds.³⁹ As a result of these findings, this protocol rapidly became the standard of care for HIV-positive pregnant women in the United States of America and Europe.

However, the widespread implementation of the ACTG 076 regimen was deemed financially and logistically infeasible in many low- and middle-income countries, particularly in sub-Saharan Africa, where the burden of HIV was (and remains)

disproportionately high. In response to these challenges, the World Health Organization (WHO) convened a global meeting to explore more affordable and context-appropriate alternatives for the prevention of MTCT in resource-limited settings.⁴⁰

Following this, a number of placebo-controlled clinical trials were initiated across Africa and Asia to assess the effectiveness of short-course AZT regimens or other reduced-cost interventions.^{41,42} These studies aimed to find cheaper options that could be more feasibly implemented in low-income countries. However, their ethical legitimacy became the subject of intense international debate.

Bioethicists and public health advocates raised concerns regarding the moral justification of using a placebo-controlled design in these trials. They argued that, given the established efficacy of the ACTG 076 regimen, the ethical research question should not have been whether cheaper interventions were better than nothing, but rather whether these reduced regimens were comparably effective to the existing standard.^{42,43} From this perspective, an equivalence or non-inferiority study design, using ACTG 076 as the control arm, would have been more appropriate and ethically sound.

Instead, the use of a placebo arm reframed the question to: "Are these cheaper interventions better than nothing?" effectively denying participants in the control group access to a proven life-saving treatment.⁴⁰ Critics argued that such a trial design would have been unacceptable in developed countries, where withholding AZT would be considered unethical, and

therefore its implementation in the Global South reflected a double standard and ethical imperialism.⁴⁴

As a result of these placebo-controlled trials, numerous neonates were denied access to AZT, which could have significantly reduced their risk of contracting HIV.⁴⁰ Ethicists contended that this violated the principle of beneficence and justice, as these children were effectively sacrificed in the pursuit of cost-effective research, despite the existence of a known effective treatment.⁴³

Ethical Issues in Clinical Trials and Drug Development

Clinical trials are essential in the drug development process, as they ascertain the safety, efficacy and suitability of pharmaceutical product for mass production.²³ Due to an ever-evolving regulatory landscape, pharmaceutical companies are under increasing pressure to ensure that clinical trials are conducted in line with ethical best practices. Those who work in clinical trials are tasked with working out a drug's optimal dosage, efficacy, and safety while adhering to the latest guidelines and regulations, recognising the need for clinical trials which balance ethics and efficiency. A failure to uphold ethical standards can result in inaccurate results, harm to patients, and an undermining of public trust.^{23,24} To prevent these damaging outcomes, it is imperative for pharmaceutical companies to adhere to these key ethical considerations in clinical trials and drug development

Informed Consent: Participants in clinical trials must be fully informed about the

potential risks and benefits of the study, and their consent must be freely given.²³

Vulnerable Populations: Special considerations are required when including vulnerable populations, such as children or the terminally ill, in clinical trials

Equitable Subject Selection: Participant selection must be fair and inclusive, ensuring that the burdens and benefits of research are distributed equitably.

Monitoring and Safety: Rigorous monitoring procedures are essential to identify and address any adverse events or safety concerns that arise during clinical trials.

Post-Trial Access: Ethical guidelines address the issue of providing participants with continued access to successful experimental treatments after a trial has ended.

Emerging Technologies and Ethical issues

The rapid advancement of emerging technologies in biomedical and scientific research has brought about transformative possibilities but also introduced significant ethical challenges. For instance, innovations such as gene editing, artificial intelligence (AI), and neurotechnology offer powerful tools for improving health and human capabilities. However, their development and application raise complex questions about human rights, societal values, and the boundaries of ethical research.^{45,46} Some of the ethical issues associated with these emerging technologies include:

Gene Editing: The development of gene editing technology raises ethical issues about the potential for misuse, the impact on human genetic diversity, and the creation of

"designer babies" with enhanced or modified traits.^{45,47}

Artificial Intelligence: Use of AI in research raises questions about algorithmic bias, privacy, and the potential for AI-driven decision-making that may have unintended consequences on vulnerable populations (Belenguer, 2022).⁴⁸

Neurotechnology: Advances in neurotechnology, such as brain-computer interfaces and neural implants, raise ethical issues about the potential for manipulation of the human mind, privacy violations, and the impact on personal autonomy.⁴⁶

Ethical issues in animal research

Animal model-based research started in the 5th century BC and has increased since the 19th century.⁴⁹ Most institutions for medical research around the world use non-human animals as experimental subjects because they play an important part in the chain of research evidence and as such are used to decide which interventions are taken forward in clinical trials.⁵⁰ Among the several animal species, rats, mice and purpose-bred birds comprise almost 90% of the animals that are used for research purpose.⁵⁰ The World Health Organization estimates that 25% of 57 million deaths per annum that occur globally are caused by microbes.⁵¹ Zoonotic diseases constitute more than 60% of all known infectious diseases, with humans serving as the primary reservoir for only 3% of them.⁵² The efficacy of therapeutic interventions in zoonoses is believed to be similar across species and it is prudent to demand scientifically valid evidence of efficacy of an obligation in animal experiments for

newer drugs that are applicable to multiple species including humans.⁵²

There is an increased tendency with stringent ethical obligations towards limiting the number of animals used in experiments while at the same time ensuring that the replication of previous research is reduced. Around 50 to 100 million vertebrate animals are used worldwide annually for research and experiments to increase the understanding of the functioning of both the human and animal body (Asokanet *al.*, 2012).⁵²

The 4Rs (Replacement, Reduction, Refinement and responsibility for the experimental animal) of humane animal experimentation are widely considered to be the guiding principles for the use of animals in research.⁵³

Reduction: this refers to methods that enable researchers to obtain comparable levels of information from fewer animals or to obtain more information from the same numbers of animals.⁴

Refinement: involves improvements in procedure that minimize the harmful effects of the proposed experiments on the animals involved, such as reducing pain, distress and suffering in a manner that leads to a general improvement in animal welfare.⁵³ This can be achieved by improving the living conditions for research animals, proper training of people handling animals, application of anesthesia and analgesia when required and the need for euthanasia of the animals at the end of the experiment to curtail their suffering.

Replacement: refers to approaches that replace or avoid the use of experimental animals altogether.⁴ These approaches

involve use of in silico methods/computerized techniques/software and in vitro methods like cell and tissue culture testing, as well as relative replacement methods by use of invertebrates like nematode worms, fruit flies and microorganisms in place of vertebrates and higher animals.⁵⁰

Responsibility: refers to concerns around promoting animal welfare by improvements in experimental animals' social life, development of advanced scientific methods.⁵³ Thereby objectively determining sentience, consciousness, experience of pain and intelligence in the animal kingdom, as well as effective involvement in the professionalization of the public discussion on animal ethics⁵⁰

Sample Size

Welfare remains a notable issue in animal experiments. Some disciplines use group sizes of 6 or 8 animals regardless of the type of experiment or number of groups. This same number is also conventionally appropriate in pilot or exploratory studies but not in factorial experimental designs or designs with more than 2–3 treatment groups. There is motive to reduce the number of animals that undergo experiment or are sacrificed and yet not compromise scientific validity.

Translation to Human Trials

Another issue is whether the evidence from a reduction in animal experiments be carried forward to human trials.⁵⁰ A systematic review of 6 interventions by Perel *et al.*,⁵⁴ concluded that agreement between animal studies and clinical studies varied and there are limitations to effective translation of

results from animal to human trial. The possible reasons are bias, random error, the failure of animal models to adequately represent human disease, the non-availability of suitable animal models, clinical heterogeneity and inadequate sample sizes.⁵⁴

Inconclusive Result

Another issue is if it is ethical to carry out human trials based on the uncertain or inconclusive results of animal experiments. There are still inconclusive clinical recommendations even with many systematic reviews that have been done on RCT. This has led to exposure of patients to unnecessary risk, wasting of scarce resources and experimental animals, and even suffering the animals unnecessarily.

Equity

It is unethical to subject healthy human volunteers to risk in the absence of precise and scientifically valid results from animal experiments.⁵² While designing animal experiments the consideration of ethics should not just be limited to the animals alone but also to multiple species to whom the results are then taken forward to.⁵⁰ There should be “shared risks” between humans and animals concerning zoonoses thus promoting better cooperation and collaboration between human and animal health professionals to identify and reduce such risks.⁵²

CONCLUSION

Ethical issues in human and animal research represent a cornerstone of responsible scientific practice. As this study has

demonstrated, the pursuit of scientific advancement must never compromise the dignity, autonomy, or welfare of human and animal subjects. Historically, unethical research practices, such as those conducted during the Nazi era or in the Pfizer Trovan trial in Nigeria, underscore the devastating consequences of neglecting ethical safeguards. These events have led to the development of key international ethical codes and principles such as the Nuremberg Code, the Declaration of Helsinki, and the Belmont Report, that now serve as global standards in research ethics.

Therefore, for human research, the study revealed that fundamental principles such as informed consent, beneficence, nonmaleficence, autonomy, and justice are indispensable in guiding researchers toward practices that respect human rights and minimize harm. The study also emphasized that privacy and confidentiality are not only ethical obligations but critical to maintaining public trust in research.

In animal research, the 4Rs (Replacement, Reduction, Refinement, and Responsibility) offer a framework for minimizing animal suffering while ensuring the scientific validity of experiments. However, ethical challenges persist, including concerns about inconclusive results, limited translation to human trials, and equitable risk distribution between humans and animals, especially in the context of zoonotic diseases.

Emerging technologies such as gene editing, artificial intelligence, and neurotechnology further complicate the ethical landscape, raising novel questions about consent, bias, autonomy, and long-term societal impact. These technologies must be navigated with

caution and a renewed commitment to ethical principles that safeguard both individual rights and collective welfare.

Ultimately, ethical issues surrounding human and animal research must be an ongoing process as new technologies and research methods emerge. Also, addressing the ethical challenges in research requires a collaborative effort of researchers, ethicists, policymakers, and the broader community.

Therefore, by maintaining ethical principles and practices, the scientific community can continue to push the boundaries of knowledge while upholding the fundamental rights and wellbeing of both human and animal participants.

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