BIOMEDICINSKA ISTRAŽIVANJA
2024;15(2):1–9

UDK: 001.891:614.253
DOI: 10.59137/BII202402451K

Review

Possibilities of violation of ethical principles in industry-sponsored research: analysis, consequences, and prevention measures

Jovan Kulić[1], Dragana Aksentijević[2], Ana Kostović[3], Dejan Krstić[4], Dragana Branović[3], Bojan Joksimović[1], Marija Milić[5], Stefan Mitić[6], Siniša Ristić[1]

[1]University of East Sarajevo, Faculty of Medicine Foča, Republic of Srpska, Bosnia and Herzegovina
[2]Health Center Kosovska Mitrovica, Kosovska Mitrovica, Serbia
[3]Clinical Hospital Center Kosovska Mitrovica, Medical Center in Leposavić, Leposavić, Serbia
[4]Health Center "Donja Gušterica", Lipljan, Serbia
[5]Univerity of Priština, Faculty of Medicine, temporarily settled in Kosovska Mitrovica, Kosovska Mitrovica, Serbia
[6]University Hospital Center "Dr Dragiša Mišović", Belgrade, Serbia

Primljen – Received: 24/06/2024
Prihvaćen – Accepted: 16/12/2024

Corresponding author:
Siniša Ristić, MD, PhD
Studentska 5, 73300 Foča
e-mail: risticsinisa@yahoo.com

Summary

The growing trend of securing private industry funding for biomedical research, particularly from pharmaceutical and medical device companies, has raised significant ethical concerns. Since the 1980s, private industry has become the primary funder of biomedical research, surpassing government funding in the U.S. and other developed countries. This shift introduces potential ethical violations, including hidden conflicts of interest, data manipulation, disregard for ethical guidelines, non-disclosure of negative results, and compromised research independence. These issues can undermine research integrity, compromise patient safety, and erode public trust in scientific findings. Effective measures to prevent ethical violations include strengthening transparency, enhancing research independence, promoting ethical education, and reinforcing regulatory frameworks. By fostering open dialogue, implementing stringent disclosure requirements, and ensuring independent oversight, participants can uphold ethical standards in sponsored research. Addressing these challenges is essential to maintaining the credibility of biomedical research, protecting participant rights, and ensuring that research outcomes reliably contribute to evidence-based medicine and public health.

Keywords: biomedical research, ethics, industry-sponsored research

Introduction

In recent years, an increasing number of researchers have sought funding for scientific studies from private industries, primarily pharmaceutical companies or those involved in medical equipment production [1–4]. This trend of funding medical studies began in the 1980s, when it was observed that most medical research conducted in the United States was funded by private companies [1, 5]. Over the next decade, private industry surpassed the U.S. government to become the largest

funder of biomedical research, a trend that has continued and become even more pronounced today [1–5]. This same trend has been noted in other developed countries, where more than 80% of clinical research is financed by private industries or sponsors [1–5].

International documents like the Declaration of Helsinki and the International Guidelines for Biomedical Research Involving Humans still lack a clear definition of a sponsor and sponsor's duties. The World Health Organization provided the first definition of the sponsor in biomedical research in 1995, stating that the sponsor is an individual, company, institution, or organization taking the responsibility for initiating, managing, and/or financing clinical research [6]. This definition has evolved over time. In the latest version of this definition, found in Regulation (EU) No 536/2014 of the European Parliament on clinical trials of medicinal products for human use, the term "financing" was replaced with "establishing or arranging financing." This change implies that the budget can come either directly from the sponsor or from another external source (non-commercial research) [6, 7].

Biomedical research is crucial for advancing medical knowledge and improving patient care. However, the involvement of external sponsors, such as pharmaceutical companies, medical device manufacturers, and private foundations, introduces ethical complexities. These sponsors provide essential funding and resources but can also create conflicts of interest, where financial or commercial interests may influence research design, data interpretation, and publication of decisions [8]. The influence of industry funding on the research agenda means shaping research priorities in line with commercial interests rather than realistic public health needs, focusing on profitable treatments rather than preventive measures. It has also been noted that industry-funded research is more likely to produce results favorable to the sponsor, but also that industry sponsorship directs research toward specific topics benefiting the sponsor's products or services, and that may influence public health policy in ways which may not be in the best interests of public health [9].

This revision aligns with efforts to limit the ethical issues arising from research sponsorship by private industries and to highlight the importance of non-commercial research, which is conducted without pharmaceutical industry involvement and often relies on external funding from foundations or charitable organizations. These sources include universities, hospitals, scientific organizations, non-profit institutions, patient organizations, or individual researchers [6].

Ethics in sponsor-funded medical research is a critical concern, particularly in low- and middle-income countries (LMICs), where socio-economic vulnerabilities and systemic inequities often exacerbate ethical challenges. These regions face unique issues requiring careful attention in the broader discussion on sponsored research ethics [10].

Potential violations of ethical principles in sponsored research

Hidden conflicts of interest

One significant ethical challenge in sponsored biomedical research is the presence of hidden conflicts of interest. Researchers might prioritize sponsor interests over scientific objectivity, leading to selective reporting of data, biased interpretation of results, and suppression of unfavorable findings [11, 12]. These practices can distort the evidence base, undermine research integrity, and compromise patient safety. Industry-sponsored studies are more likely to produce outcomes favorable to sponsors, raising concerns about the transparency and independence of research findings [13].

Ethics in sponsor-funded medical research is the major concern, particularly in low- and middle-income countries (LMICs), where unique challenges and vulnerabilities create

ethical dilemmas. In these regions, limited access to healthcare and poor living conditions makes research participants more susceptible to financial incentives, which may encourage them to participate in studies that they otherwise might not [10].

Non-disclosure of negative results

The selective publication of positive results while withholding negative or inconclusive findings is a pervasive issue in sponsored biomedical research [14]. Sponsors may exert pressure on researchers to prioritize favorable outcomes, leading to publication bias and distorting the overall evidence base [15]. This practice not only skews the scientific literature but also impedes evidence-based decision-making in clinical practice and public health policy [16]. To address non-disclosure of negative results, regulatory bodies and academic institutions should promote the mandatory registration of clinical trials, transparent reporting of study outcomes, and dissemination of all study findings, regardless of the direction or statistical significance of results [15, 16]. Open science initiatives, such as data-sharing platforms and journals prioritizing reproducibility and transparency, are crucial for mitigating publication bias and promoting scientific rigor [16].

Data manipulation is another critical ethical concern in sponsored research. Researchers might feel compelled to alter data or analytical methods to achieve desired results, compromising the validity and reproducibility of findings [15, 16]. Industry-sponsored studies have been shown to selectively report outcomes favoring the sponsor's products or interventions, contributing to publication bias and distorting the overall evidence base [17]. Poor health literacy and a lack of understanding about research protocols can result in participants not fully comprehending the risks, benefits, or the purpose of the study. This raises concerns about the informed consent process, which may be difficult to navigate in such circumstances.

Disregard for ethical guidelines

Sponsored research can sometimes lead to the disregard for established ethical guidelines, such as those outlined in the Declaration of Helsinki and Institutional Review Board (IRB) protocols [18]. Pressures to meet sponsor expectations may result in inadequate protection of participants' rights, insufficient informed consent processes, and inadequate risk assessment [19, 8]. Another significant issue in these settings is the weak regulatory framework. In many LMICs, insufficient regulations or the lack of enforcement allow sponsors to bypass stringent ethical guidelines that would typically be required in high-income countries. This creates a double standard, exacerbating inequities and leading to the exploitation of vulnerable populations. Ethical violations in research conduct not only jeopardize participant welfare but also undermine the credibility of research findings and institutional reputations [20]. Adhering to stringent ethical standards, including independent ethical review and oversight, is essential to ensuring participant safety and maintaining public trust in biomedical research [21].

Consequences of violating ethical principles

Loss of trust in the scientific community

Ethical violations in sponsored research can erode public trust in the scientific community, undermining confidence in research findings and academic institutions [22]. When conflicts of interest are not disclosed or managed appropriately, participants, including patients, policymakers, and the public, may perceive research outcomes as biased or influenced by commercial

interests [17]. Restoring trust requires transparency, accountability, and a commitment to upholding ethical standards in research conduct and reporting [13]. The exploitation of participants in LMICs has long-term repercussions, eroding public trust in medical research and potentially deterring future participation. Systemic issues, such as lack of transparency and insufficient oversight, may contribute to harm on a societal level, further entrenching inequities in global healthcare access.

Violation of participants' rights

Ethical violations in sponsored research can result in infringements on participants' rights, including inadequate informed consent processes, failure to protect privacy, and insufficient risk assessment [19]. Participants trust researchers to prioritize their welfare and adhere to ethical principles governing research conduct [8]. Failure to uphold these principles can harm participants and compromise the validity of research outcomes, highlighting the importance of robust ethical oversight and participant protection [21].

Damage to the reputation of researchers and institutions

Ethical lapses in sponsored research can tarnish the reputations of researchers, institutions, and sponsors, resulting in loss of credibility, research funding, and professional opportunities [11]. Academic institutions and funding agencies rely on trust and integrity to foster collaborations and attract research funding [10]. Adherence to ethical standards and transparency in research conduct are essential for safeguarding institutional reputations and maintaining participants confidence in research outcomes [23].

Measures to prevent violations of ethical principles in sponsored research

To prevent violations of ethical principles in sponsored research, participants should implement robust strategies to promote transparency, enhance research independence, and uphold participant welfare. To address data manipulation, researchers and sponsors must adhere to rigorous methodological standards, promote data transparency, and facilitate independent scrutiny of study findings [17]. Transparent reporting practices, pre-registration of study protocols, and open access to data are essential to safeguarding research integrity and ensuring unbiased scientific inquiry. To reduce reliance on sponsor-funded research, governments and international agencies must prioritize funding mechanisms tailored to LMICs. Public-private partnerships and philanthropic contributions could be leveraged to support ethical research initiatives [24].

Strengthening transparency

Transparency in research design, methodology, data collection, and reporting is essential for mitigating conflicts of interest and promoting research integrity [25]. Researchers and sponsors should adhere to rigorous reporting standards, disclose financial and non-financial interests, and provide open access to study protocols and data [26, 15]. The ability to replicate biomedical research findings, as well as rigor in designing and conducting scientific research, are two of the cornerstones of scientific growth [27]. Integrating transparency techniques into research articles can considerably increase the reproducibility of outcomes by independent laboratories [28]. Authors can write manuscripts in a transparent and detailed manner by improving reporting standards through the adoption of comprehensive reporting guidelines and

full disclosure of research methods and results, by sharing data to facilitate replication and secondary analyzes of now publicly available data, by improving peer review with the option of open peer review with disclosure of the identity and comments of reviewers, by promoting the use of registered reports where study protocols are peer-reviewed and pre-approved before research is conducted to reduce publication bias and increase research integrity, and by providing better training and resources for researchers on best practices in research design, data analysis and reporting to foster a culture of rigor and transparency [29].

Enhancing research independence

Protecting research independence requires clear separation of research objectives from sponsor interests [10]. Institutions should diversify funding sources, establish conflict of interest policies, and empower researchers to conduct unbiased research [12]. Ensuring academic freedom and fostering a culture of scientific integrity are critical for upholding the autonomy and credibility of research outcomes [30]. The importance of maintaining independence in research is significant because it ensures the reliability of research results serving the general public good. In addition to advocating for increased transparency in research funding and accountability mechanisms, it is essential to establish strong governance structures that will oversee research activities and ensure that they are conducted ethically and independently. It is necessary to strive to promote and encourage greater public investment in global health research in order to reduce reliance on industry or politically motivated funding, but also to encourage collaborative and inclusive research practices with stakeholders from diverse backgrounds, as well as advocating for policies that protect the integrity of research developing globally effective health interventions [31].

Promoting ethical education

Comprehensive ethical training and professional development programs are essential for researchers, sponsors, and institutional review board members [21]. Ethical education should emphasize the importance of informed consent, data integrity, and responsible conduct of research [8]. Case-based learning and ethical decision-making frameworks can enhance awareness of ethical dilemmas and equip participants with the tools to navigate complex research environments [26].

Strengthening regulatory mechanisms

Robust regulatory frameworks, including institutional review boards and research ethics committees, are crucial for overseeing sponsored research and ensuring compliance with ethical guidelines [21]. Addressing hidden conflicts of interest requires robust disclosure policies, independent oversight, and measures to mitigate undue influence on research outcomes [13]. Regulatory bodies should enforce ethical standards, monitor research conduct, and impose sanctions for non-compliance [19]. Independent oversight and auditing of research practices promote accountability and protect participant rights in biomedical research [8].

Encouraging open dialogue and collaboration

Fostering open communication among researchers, sponsors, regulators, and the broader scientific community promotes transparency and ethical accountability [26]. Collaboration across disciplines and institutions facilitates knowledge sharing, promotes best practices in research conduct, and strengthens the collective commitment to ethical standards [11]. Transparent partnerships and collaborative research

efforts are essential for advancing scientific knowledge and addressing global health challenges [12].

Implementing disclosure and reporting requirements

Comprehensive disclosure policies require researchers to disclose financial relationships, potential conflicts of interest, and contributions to study design and data analysis [30]. Journals and funding agencies should enforce reporting guidelines that prioritize transparency and reproducibility in research publications [16]. Transparent reporting of study outcomes, including negative or inconclusive results, contributes to a more accurate evidence base and informs evidence-based decision-making in clinical practice and public health policy [15]. To mitigate conflicts of interest and uphold research independence, institutions should adopt stringent disclosure policies, require researchers to declare financial and non-financial interests, and establish clear guidelines for managing conflicts of interest [12, 25].

Promoting independent oversight and auditing

Independent oversight and auditing of sponsored research activities are critical for identifying and addressing ethical violations [8]. Regulatory bodies, institutional review boards, and ethics committees should conduct regular audits to monitor compliance with ethical guidelines and safeguard participants' rights [19]. Auditing research practices and enforcing ethical standards uphold the credibility and reliability of biomedical research and ensure that research outcomes benefit society as a whole [13].

Conclusion

Sponsored biomedical research is vital for advancing medical knowledge and improving patient care. However, the integration of external sponsorship introduces ethical challenges requiring vigilance and proactive measures. By promoting transparency, enhancing research independence, and upholding ethical standards, participants can mitigate conflicts of interest, safeguard participants' rights, and maintain public trust in biomedical research. Ethical violations can undermine the credibility of scientific findings, harm participant welfare, and damage institutional reputations. Addressing these challenges requires a collective commitment to ethical integrity, accountability, and responsible conduct of research. Addressing the ethical challenges of sponsor-funded medical research requires a nuanced approach that prioritizes equity, transparency, and sustainability. By recognizing the vulnerabilities of LMICs and implementing strategies to mitigate these risks, the global research community can uphold the highest ethical standards. Upholding ethical standards is not only a regulatory imperative but a moral obligation to ensure that biomedical research contributes reliably to evidence-based medicine and benefits society as a whole.

Funding source. The authors received no specific funding for this work.

Ethical approval. This article does not contain any studies with human participants performed by any of the authors.

Conflicts of interest. The authors declare no conflict of interest.

References:

1. Okike K, Kocher MS, Mehlman CT, Bhandari M. Industry-sponsored research. Injury 2008;39(6):666–80.
2. Baird P. Getting it right: industry sponsorship and medical research. CMAJ 2003;168(10):1267–9.
3. Mandal J, Parija SC. Ethics of sponsored research. Trop Parasitol 2014;4(1):2–3.
4. Chopra SS. MSJAMA: Industry funding of clinical trials: benefit or bias? JAMA 2003;290(1):113–4.
5. Hynes V. Cochrane review questions value of industry-funded clinical trials. CMAJ 2013;185(2):E85–6.
6. Ravinetto R, De Nys K, Boelaert M, Diro E, Meintjes G, Adoke Y, et al. Sponsorship in non-commercial clinical trials: definitions, challenges and the role of Good Clinical Practices guidelines. BMC Int Health Hum Rights 2015;15:34.
7. Regulation (EU) No 536/2014 of the European parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC. Official Journal of the European Union. 2014. Available from: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2014.158.01.0001.01.ENG Accessed May 12, 2024
8. Sherlock R, Morrey JD. Ethical issues in biotechnology. Lanham: Rowman & Littlefield; 2002.
9. Fabbri A, Lai A, Grundy Q, Bero LA. The Influence of Industry Sponsorship on the Research Agenda: A Scoping Review. Am J Public Health 2018;108(11):e9–e16.
10. Steinert JI, Nyarige DA, Jacobi M, Kuhnt J, Kaplan L. A systematic review on ethical challenges of 'field' research in low-income and middle-income countries: respect, justice and beneficence for research staff? BMJ Glob Health 2021;6(7):e005380.
11. Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: a systematic review. JAMA 2003;289(4):454–65.
12. Sismondo S. Key opinion leaders and the corruption of medical knowledge: what the Sunshine Act will and won't cast light on. J Law Med Ethics 2013;41(3):635-43.
13. Lexchin J, Bero LA, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. BMJ 2003;326(7400):1167–70.
14. National Ethical Guidelines for Biomedical and Health Research Involving Human Participants. Indian Council of Medical Research; 2017. Available from: https://ethics.ncdirindia.org/asset/pdf/ICMR_National_Ethical_Guidelines.pdf Accessed May 28, 2024
15. Steinman MA, Bero LA, Chren MM, Landefeld CS. Narrative review: the promotion of gabapentin: an analysis of internal industry documents. Ann Intern Med 2006; 145(4):284–93.
16. Chalmers I. Underreporting research is scientific misconduct. JAMA 1990;263(10):1405–8.
17. Fanelli D. "Positive" results increase down the Hierarchy of the Sciences. PLoS One 2010;5(4):e10068.
18. Ioannidis JP, Munafò MR, Fusar-Poli P, Nosek BA, David SP. Publication and other reporting biases in cognitive sciences: detection, prevalence, and prevention. Trends Cogn Sci 2014;18(5):235–41.
19. Chalmers I, Glasziou P. Avoidable waste in the production and reporting of research evidence. Lancet 2009;374(9683):86–9.
20. Bodenheimer T. Uneasy alliance--clinical investigators and the pharmaceutical industry. N Engl J Med 2000;342(20):1539–44.
21. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013;310(20):2191–4.
22. Thompson DF. Understanding financial conflicts of interest. N Engl J Med 1993;329(8):573–6.
23. Monach PA, Branch-Elliman W. Reconsidering 'minimal risk' to expand the repertoire of trials with waiver of informed consent for research. BMJ Open 2021;11(9):e048534.
24. Lescano AG, Cohen CR, Raj T, Rispel L, Garcia PJ, Zunt JR, et al. Strengthening Mentoring in Low- and Middle-Income Countries to Advance Global Health Research: An Overview. Am J Trop Med Hyg 2019;100(1_Suppl):3–8.
25. Wazana A. Physicians and the pharmaceutical industry: is a gift ever just a gift? JAMA 2000;283(3):373–80.

26. Relman AS. The new medical-industrial complex. N Engl J Med 1980;303(17):963–70.

27. Drazen JM, Curfman GD. Financial associations of authors. N Engl J Med 2002;346(24):1901–2.

28. Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. Cochrane Database Syst Rev 2017;2(2):MR000033.

29. Ott AW, Sol-Church K, Deshpande GM, Knudtson KL, Meyn SM, Mische SM, et al. Rigor, Reproducibility, and Transparency in Shared Research Resources: Follow-Up Survey and Recommendations for Improvements. J Biomol Tech 2022;33(3):3fc1f5fe.fa789303.

30. Prager EM, Chambers KE, Plotkin JL, McArthur DL, Bandrowski AE, Bansal N, et al. Improving transparency and scientific rigor in academic publishing. Brain Behav 2019;9(1):e01141.

31. Bos J. Conflicts of Interest. In: Research Ethics for Students in the Social Sciences. Springer International Publishing, 2020. p. 175–98.

Mogućnost kršenja etičkih principa prilikom sponzorisanja naučnih studija: analiza, posljedice i mjere prevencije

Jovan Kulić[1], Dragana Aksentijević[2], Ana Kostović[3], Dejan Krstić[4], Dragana Branović[3], Bojan Joksimović[1], Marija Milić[5], Siniša Ristić[1]

[1]Univerzitet u Istočnom Sarajevu, Medicinski fakultet Foča, Republika Srpska, Bosna i Hercegovina

[2]Dom zdravlja Kosovska Mitrovica, Kosovska Mitrovica, Kosovo, Srbija

[3]Dom zdravlja Donja Gušterica, Lipljan, Kosovo, Republika Srbija

[4]Kliničko-bolnički centar Kosovska Mitrovica, Dom zdravlja Leposavić, Leposavić, Kosovo, Republika Srbija

[5]Univerzitet u Prištini, Medicinski fakultet, sa privremenim sedištem u Kosovskoj Mitrovici, Kosovska Mitrovica, Kosovo, Republika Srbija

Povećan trend finansiranja biomedicinskih istraživanja od strane privatnog sektora, posebno farmaceutskih kompanija i proizvođača medicinske opreme, izazvao je značajnu zabrinutost i kršenja etičkih normi. Od osamdesetih godina prošlog vijeka, privatni sektor postao je glavni finansijer biomedicinskih istraživanja, nadmašivši državna ulaganja u SAD i drugim razvijenim zemljama. Ovaj pomak otvorio je prostor za potencijalna etička kršenja, uključujući skrivene sukobe interesa, manipulaciju podacima, zanemarivanje etičkih smjernica, neobjavljivanje negativnih rezultata i ugrožavanje nezavisnosti istraživanja. Ovi problemi mogu znatno narušiti integritet istraživanja i istraživača, zatim mogu ugroziti bezbjednost pacijenata i oslabiti povjerenje javnosti u naučna istraživanja. Efikasne mjere za prevenciju etičkih prekršaja uključuju jačanje transparentnosti, unapređenje nezavisnosti istraživanja, promovisanje etičkog obrazovanja i jačanje zakonskih regulativa. Podsticanjem otvorenog dijaloga, implementacijom strogih zahtjeva za objavljivanje i osiguranjem nezavisnog nadzora, zainteresovane strane mogu očuvati etičke standarde u sponzorisanim istraživanjima. Rješavanje ovih izazova je ključ za održavanje kredibiliteta biomedicinskih istraživanja, zaštitu prava učesnika i sigurnost u to da rezultati ovih istraživanja pouzdano doprinose medicini zasnovanoj na dokazima i javnom zdravlju.

Ključne riječi: biomedicinska istraživanja, etika, sponzorisana istraživanja