interface
comunicação, saúde, educação
https://www.interface.org.br
eISSN 1807-5762

Editorial

The Ethical Crisis of Clinical Research in Brazil: Law 14.874/2024 and the Flexibilization of Brazilian Regulations for Participant Protection

A crise ética da pesquisa clínica no Brasil: Lei 14.874/2024 e a flexibilizações das normativas brasileiras de proteção dos participantes

La crisis ética de la investigación clínica en Brasil: Ley 14.874/2024 y la Flexibilización de las Normativas Brasileñas de Protección de los Participantes

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Clinical research is an essential field for the advancement of medical science and the development of new treatments. However, the globalization of clinical trials has caused controversy, especially regarding the integrity of the data collected and possible violations of participants' rights[1-3]. Lobbying in Brazil by the international biopharmaceutical industry ("Big Pharma") is strong and has led to the relaxation of regulations protecting participants, raising serious ethical concerns. With the recent enactment of Law 14.874/2024[4] it is imperative to discuss how these regulatory changes affect research ethics and the need for policies that prioritize the protection of participants and national sovereignty.

Hellmann F, Guedert JM. The Ethical Crisis of Clinical Research in Brazil: Law 14.874/2024 and the Flexibilization of Brazilian Regulations for Participant Protection. Interface (Botucatu). 2024; 28: e240246
https://doi.org/10.1590/interface.240271

Brazil as a destination for multinational clinical research

Brazil is an ideal location for multinational clinical trials: a very diverse population; large hospitals concentrated in populous regions, facilitating recruitment and leading to lower costs; a large number of untreated people outside of clinical trials; a strong physician-patient relationship; qualified professionals and stable health regulations[3,5]. Other reasons for international pharmaceutical companies to carry out experiments on human beings are the large Brazilian market and the possibility of institutional purchase by the Brazilian National Health System (SUS) and the judicialization of health, which forces governments to buy new and expensive drugs, even when there are cheaper equivalent alternatives[6,7].

Inequalities and social impacts of clinical research in Brazil

There are no ethical regulations to guarantee that all social strata are represented in pharmaceutical research. In practice, there is a predominance of research participants from socially vulnerable populations. In recruiting these participants, poor access to health services becomes an opportunity to take part in clinical trials[2]. In this way, companies capitalize on illness and vulnerability, particularly among marginalized populations, notably blacks and the poor, with practices that regulate life and expose people to the risk of death. This reveals an interdependence between biopolitics and necropolitics in the context of health and, in Brazil, reflects the dynamics of power and exploitation that characterize the contemporary pharmaceutical industry[2].

The implementation of international clinical drug trials in Latin America, including Brazil, lack robust social value, provide financial benefits primarily to large pharmaceutical corporations, and result in the marketing of drugs with questionable safety[3,8,9]. Only a small percentage of new pharmaceutical products add therapeutic value[8]. Most are developed to maximize profits, such as the so-called *me-too drugs* launched to secure a market. There is no guarantee that products tested in the country will be registered there, and there is no requirement that they be sold at affordable prices[10]. Only 60% of new drugs approved by the Food and Drug Administration (FDA) and tested in Latin America are registered in the host countries, most of them at exorbitant prices[10].

When Big Pharma studies are carried out in public institutions, public money subsidizes private pharmaceutical research, with the SUS providing human and physical resources and bearing the costs of treating adverse events. Latin American researchers, including Brazilians, are often not valorised, acting as research assistants, recruiters and data collectors rather than as independent scientists and research collaborators[11]. In addition, neglected diseases in Brazil are not adequately investigated due to low public investment in research[12] and researchers being oriented towards more lucrative projects for the pharmaceutical industry[11].

Influence of Big Pharma and political lobbying

The pharmaceutical industry knows that its economic success depends on political decisions and lobbies hard to influence public policies and regulations. The aim is to facilitate clinical trials, approval of new drugs and expansion of use, prioritizing profits over public health. This lobbying includes electoral donations, payment for travel and other benefits, and the practice of "revolving doors", where former public officials are hired by the industry and vice versa[13]. For example, Interfarma (the Pharmaceutical Research Industry Association) – which represents 56 foreign laboratories and is responsible for 80% of reference drug sales and 33% of generic drugs in Brazil – has sponsored international trips for Brazilian parliamentarians[13]. These strategies influence both Congress, with the formation of the "Medicines Caucus", and the Executive, shaping the decisions of regulatory agencies and ministries to pass laws and regulations that favour the sector.

Representatives of Big Pharma and Contract Research Organizations(CROs) have argued that changes to ethical research standards would make Brazil "more attractive" for international multi-centre studies[14]. This claim is misleading, as clinical trials take place at the final stage of development, while innovation and the granting of patents take place at the beginning of the process. Furthermore, Brazil's innovative performance in the pharmaceutical sector is mediocre, reflecting the country's lack of incentives for innovation in line with health priorities[14].

The population faces difficulties in accessing medicines due to economic policies subordinated to predatory capitalist logic. It is therefore fallacious to claim that the clinical trials carried out by international pharmaceutical companies in Brazil guarantee access to cutting-edge technologies for the Brazilian people. These studies are not treatments; they are experiments to evaluate an intervention that is not always (even only rarely) beneficial to the participants (especially in the early phases 1-2 of trials). Many receive a placebo without fully understanding this possibility, and in the event that a drug is approved and marketed, the there is no guarantee of post-study access to a potentially beneficial pharmaceutical product developed through research in their bodies[9].

Law 14.874/2024: ethics sacrificed for profit

The historical configuration of research ethics in Brazil combines subjects, factors and political struggles, and understanding this requires considering the role of social movements in the ethical regulation of clinical trials[15], which began in the late 1980s (CNS Resolution 01/1988) and was consolidated with the creation of the CEP/Conep System (current Brazilian Research Ethics System) (CNS Resolution 196/1996). The recent Law 14.874/2024[4] makes ethical standards more flexible, and we argue, prioritizes corporate profits over participant safety. Originating as PL 200/2015 in the Senate, under the tutelage of Interfarma and Aliança Pesquisa Clínica Brasil, the bill was modified in the House as PL 7082/17, and then returned to the Senate as PL 6.007/2023[16] where it was approved and finally sanctioned by President Lula on May 28, 2024[4].

Although all versions of the Law were heavily criticized[14,17-19] and numerous organizations called for several vetoes, the President vetoed only two points of the law on the grounds that they were unconstitutional and contrary to the public interest. The first required the Public Prosecutor's Office to be notified of the participation of Indigenous peoples in research, which violated the principle of equality and suggested that they should be protected by the state, a condition that has already been overcome by legislation. The second limited the continuity of care and the free supply of a drug to five years after its commercial availability in the country[4]. This loss of access to the medication after five years has a negative impact on the health (and the rights) of participants and jeopardizes the development of ethical clinical research. However, other problems related to post-study access remain, such as the sponsor and the researcher, not the treating physician, indicating the need to maintain the therapy, based on established criteria, including the severity of the disease and the availability of satisfactory local therapeutic alternatives for treatment. It is understood that post-study access should be guaranteed to all research participants who have benefited from the intervention and to those in the placebo group, for as long as necessary and beneficial[20]. In Brazil, dispensation of the tested drug is ensured by Anvisa's (Brazilian Health Surveillance Agency) Post-Trial Supply Program[21].

End of the CEP/Conep System

The new law[4] ignores the historical trajectory of the National Health Council (CNS) in the regulation of research ethics and decrees the end of the Research Ethics Committee (REC)/Conep system which, despite its weaknesses, has almost 900 RECs spread across the country and more than 16,000 people directly involved, most of them voluntarily, focused on protecting research participants. One of its greatest attributes was social control, but even in a government supported by entities representing social movements, the pharmaceutical lobby tramples on public rights and interests and puts the health of clinical research participants at risk. Although public debate on the need for social control of research has not been as sustained as we would like[22], this control should be maintained.

Law 14.874/2024[4] replaces Conep with the National Research Ethics Body, coordinated by a technical area within the Ministry of Health, with its composition and regulations to be defined in a future regulation. This represents the extinction of social control of the ethics of human research and a step backwards in ethical governance. The original bill was restricted to clinical research. The approved law extended this scope to all areas of research, to be defined by resolution. This expansion accentuates the problem of ethical evaluation of research in the Social Sciences and Humanities and may result in a lack of adequacy and understanding of their specificities.

Protection against conflicts of interest in the pharmaceutical market depends on social control and proper ethical evaluation, which are essential if clinical research is to have social and scientific value.

Changes in RECs

The new law establishes that the REC must be made up of "members from the medical, scientific and non-scientific fields", but does not state the need to have professionals who understand applied ethics, such as bioethicists, or even lawyers, pharmacists, pharmacologists, and other professionals. Furthermore, it only requires one representative of research participants, regardless of the total number of members (VII Article 7)[4]. This may be insufficient to guarantee adequate representation.

The law establishes that the ethical analysis of multi-centre research will be carried out by a single REC, preferably the one linked to the centre coordinating the research, which will issue the opinion and notify the other participating RECs. High-risk clinical trials require independent, impartial ethical evaluation and experienced, ethically-supported reviewers. Allowing only one REC, linked to the researcher's institution; to carry out the ethical analysis could compromise the independence of this evaluation. It is recommended that RECs of participating centres evaluate research protocols to assess their local viability, ensuring trained staff and available care resources for the protection of participants and adequate response to adverse effects and minimization of harm.

The law also changes the requirement for research reports, which will now be annual instead of biannual, as recommended by CNS Resolution 466/12. This reduces the frequency with which information is monitored and updated, affecting transparency and the ability to respond quickly to problems that arise during studies. Another problem is the issuing of opinions by RECs, which can approve, disapprove or suspend research for safety reasons (§ 4 Article 14).[4]Article 14 does not provide for the possibility of issuing pending opinions requesting adjustments.

Questions about the Protection of Research Participants

Another worrying aspect is the permission to pay healthy individuals taking part in phase I clinical trials or bioequivalence studies. This issue, also present in CNS Resolution 466/12[23] ignores the constitutional principle of the dignity of the human person, which prohibits the commercialization of the human body or its parts. The possibility of financial gain for participating in research is especially worrying in the Brazilian context, where social vulnerability is prevalent.

Article 23 of Law 14.874/2024[4] guarantees that the participant will be compensated for any damage suffered during the research and will receive the necessary health care. However, the law does not clearly specify who is responsible for compensation, which can lead to uncertainty and difficulties in enforcing this right.

Regarding the storage of research data and the sending of biological material abroad, strict regulation is essential to protect the rights of participants and national sovereignty. However, the approved law compromises these rights by allowing the material, once outside the country, to be governed by foreign legislation that may not offer the same level of protection, with the possibility of its patenting and commercialization, putting national sovereignty over genetic and biological resources at risk.

A call for ethics in Brazilian clinical research

Clinical research in Brazil must be conducted ethically, fairly, transparently and for the benefit of society as a whole. The loosening of standards for the protection of participants in favour of commercial interests is an unacceptable step backwards, and especially detrimental to vulnerable populations. The protection of vulnerable groups is not sufficiently addressed in the new law. There are no penalties for researchers and sponsors who violate ethical standards.

It is essential that the new "National System for Ethics in Research with Human Beings" considers social control, works in line with Anvisa and is adequately funded to fulfil its mandate. Part of this funding could come from the collection of fees by the Federal Treasury (and not by the RECs) for the ethical evaluation of commercial clinical research protocols.

It is necessary to establish a clinical research system that promotes innovation in an ethical and sustainable way, benefiting public health and the country's scientific development. In addition, robust government programs will be needed to stimulate studies on neglected diseases and populations historically deprived of safe therapies, such as pediatrics, since the industry is not interested in them due to the greater risk (and thus increased oversight) and low profit margin.

The ethical crisis in clinical research in Brazil requires an urgent response. To this end, the Executive Branch urgently needs to work on regulating Law 14.874/2024, with the aim of reducing the damage caused and enhancing the protection of clinical research participants and national sovereignty.

Authors' contribution

Both authors actively participated in all stages of preparing the manuscript.

Acknowledgments

Thanks to Bryn Williams-Jones for proofreading and translating into English.

Conflict of interest

Both authors have no conflict of interest to declare.

Editor
Antonio Pithon Cyrino
Associated editor
Manoela de Carvalho

Translator
Bryn Williams-Jones

Submitted on
05/22/24
Approved on
06/05/24

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