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Brazilian guidelines for biorepositories and biobanks of human biological material[☆]

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A B S T R A C T

Objective: To characterize the participatory and democratic creation of the Brazilian guidelines for biorepositories and biobanks of human biological material with the purpose of research based on the ethical principles of human dignity, autonomy, beneficence, justice, and precaution.

Methods: An interdisciplinary work group was constituted to prepare the document, considering the following criteria: experience in biobank operation, regional representation, type of stored biological material, and bioethics specialists. Members of the National Health Surveillance Agency (Agência Nacional de Vigilância Sanitária – Anvisa), also participated due to their regulatory competence. Members from the National Commission on Ethics in Research (Comissão Nacional de Ética em Pesquisa – Conep) participated as the social control organization.

Results: The document, based on ethical, legal, and technical guidelines, presents the concepts, activities, purposes, and differences between biorepositories and biobanks; forms of consent on the part of the subject; in addition to other aspects permeated by concerns regarding the appropriate use of information. The Brazilian guidelines for biorepository and biobank of human biological material with the purpose of research contains 39 articles, which are distributed in five chapters.

Conclusion: The importance of legislation arises from the ethical concern, considering morals and taking into account the legal aspects, which translate into a document that does not end in itself. The dynamics of science always leads to changes in paradigms, which can go beyond the existing laws.

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Diretrizes nacionais para biorrepositório e biobanco de material biológico humano

R E S U M O

Palavras-chave:

Bioética
Biobancos
Biorrepositório
Diretrizes

Objetivo: Caracterizar a construção participativa e democrática das Diretrizes Nacionais para Biorrepositório e Biobanco de Material Biológico Humano com Finalidade de Pesquisa, baseada nos princípios éticos da dignidade humana, da autonomia, da beneficência, da justiça e da precaução.

Métodos: Para a elaboração do documento formou-se um grupo de trabalho interdisciplinar considerando os seguintes critérios: experiência na operacionalização de biobancos, representatividade regional, tipo de material biológico acondicionado e especialistas em bioética. Participaram, também, membros da Agência Nacional de Vigilância Sanitária – Anvisa, pela competência regulatória e da Comissão Nacional de Ética em Pesquisa – Conep, enquanto controle social.

Resultados: O documento, baseado nos preceitos éticos, legais e técnicos, apresenta os conceitos, as atividades, finalidades e diferenças entre biorrepositórios e biobancos, as formas de consentimento do sujeito, além de outros aspectos permeados pela preocupação do uso adequado da informação. As Diretrizes Nacionais para Biorrepositório e Biobanco de Material Biológico Humano com Finalidade de Pesquisa contém 39 artigos, dispostos em cinco capítulos.

Conclusão: A importância de uma regulamentação surge da reflexão ética, considerando a moral, e tendo como norteador os aspectos legais, os quais se traduzem em um documento que não se esgota em si mesmo. A dinamicidade da ciência sempre nos remete à mudança de paradigmas, que podem ir além das legislações existentes.

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Introduction

The biorepositories and biobanks of human biological material – body fluids, cells, tissues, intracellular substances, and DNA – and associated information, have become an important resource for biomedical research, and the development of diagnostic and therapeutic procedures.¹ For a long time, the storage of human biological material was carried out by researchers in research institutes and hospitals, mainly in the departments of pathology, being mostly performed in a disorderly manner and without associating information of related clinical data.

A worldwide concern has been the establishment of a coordinated network of biobanks that respect the ethical, legal, and technical guidelines of the member countries. In international discussions, the need and the importance of feasible cooperation between local institutions and between institutions from different countries has been observed, as well as the need for the organization of recommendations regarding language patterns, forms of communication, bioinformatics system, and specific terminology for the designation of human biological materials.

Regarding the ethical aspects, informed consent calls into question whether recontact is needed for each research, or just the initial consent; recontact and information provision to the individual; feedback of research results to trial participants; and who is in charge of their interpretation

and distribution, in addition to matters of privacy and confidentiality of data through information system security policies.^{2,3} Regarding the technical aspects, working organization is crucial, as well as the phases of collection, processing, storage, distribution and disposal of human biological material, and financial aspects involved in both the initial development – facilities and infrastructure – and subsequent maintenance.⁴ Concerning the legal issues, the intellectual property (patents, copyrights) of the biological material and sharing policies of information and stored materials, at both national and international level, must be considered.

This organization process is interdisciplinary, relying on the participation of many individuals from the natural sciences and humanities fields, such as health professionals, philosophers, sociologists, bioethicists, systems analysts, managers, among others, who must have great responsibility regarding the confidentiality of the biological material⁵ and the protection of the individual.

To date, Brazil does not have an ordinary law regarding research involving humans, nor a specific law concerning the storage and use of human biological material in research. However, there is a legislative basis in the Constitution of 1988⁵ - in Article 199, which provides for the disposition of conditions and requirements for the elimination of human samples for research purposes, among others, highlighting the aspect of the prohibition of any kind of

commercialization. The Civil Code and other legislation on related matters also provide a legislative basis, such as the Law 11.105/05 (Biosafety Act), which establishes safety standards and control mechanisms for activities involving genetically modified organisms and their derivatives, and the use of embryonic stem cells; the RDC⁶ 23/11 – Agência Nacional de Vigilância Sanitária (Anvisa), which regulates with technical standards for the operation of cell and germinative tissue banks;⁷ and the Resolution CNS 347/05, which regulated the use of human biological material in the context of research projects,⁸ which can be considered a regulatory and historic milestone for research in this field of knowledge.

The nonexistence of the law weakens the control of the National Health Council and of the Federal Government on research activities involving human subjects when performed by removing human biological material. In this sense, the new Brazilian normative documents, CNS Resolution 441 of 2011,⁹ which revokes the CNS Resolution 347 of 2005, and the Decree of the Brazilian Ministry of Health presented here, are of great importance for the regulation of this issue, especially when considering the implementation and operation of the new Brazilian biobanks for research purposes.

The present article aims to characterize the participatory and democratic creation of the Decree of the Brazilian Ministry of Health that establishes the Brazilian guidelines for biorepositories and biobanks of human biological material with research purpose,¹⁰ based on the ethical principles of human dignity, autonomy, beneficence, justice, and precaution.

History of the creation of the Brazilian Guidelines

Considering the international scenario on the organization of biobanks, which intensified during the end of 2008, and considering the appeal from the national scientific community, the Brazilian Ministry of Health decided to organize and, in January 2009, the Department of Science and Technology, through the Coordination of Research Ethics and Bioethics, began assessing the theme and prioritized as one of its actions, the need for national guidelines to regulate the storage and use of human biological material in research, especially considering the need to establish and operate appropriate biobanks in the country.

The identification of Brazilian institutions that had biobanks was crucial for the development of this study. During this mapping, it was observed that most institutions only had biorepositories. The National Institute of Cancer (Instituto Nacional do Câncer – INCA) and the Hospital AC Camargo maintained properly established biobanks.

When preparing the document, an interdisciplinary work group was constituted considering the following criteria: experience in biobank operation, regional representation, type of stored biological material, and bioethics specialists. Members of the National Health

Surveillance Agency – Anvisa, due to their regulatory competence, also participated, as well as members from the National Commission on Ethics in Research (Comissão Nacional de Ética em Pesquisa – Conep), as the social control organization.

Concomitantly, the Brazilian Ministry of Health and the Conep were represented in national and international discussion forums that addressed the issue of biobanks. Participation in these meetings showed that Brazil was in the same state-of-the-art as other countries, and consolidated aspects that should be addressed in this document.

The first meeting of the working group resulted in an initial proposal that was discussed and improved in subsequent meetings, in addition to contributions from the National Health Council (Conselho Nacional de Saúde – CNS) and Conep. This proposal was reviewed internally at Decit with the participation of legal counsel of the Brazilian Ministry of Health, resulting in the text that was published in the Official Gazette (Diário Oficial da União – DOU) on April 12, 2010, and presented for public consultation in May, 2010. This consultation resulted in 229 contributions that were compiled and analyzed during the final draft of the document.⁵

It should be noted that all technical policy guidelines issued by the Brazilian Ministry of Health are extensively discussed with the three branches of government and civil society representatives, such as managers, service providers, researchers, health professionals, and user representatives, thus resulting in an agreement that was democratic and egalitarian.

The creation of the National Guidelines

When developing the guidelines, national and international provisions were considered, such as laws, declarations, regulations, resolutions, and scientific production related to the theme. Recognizing the different competencies of research institutions in Brazil, and that many health institutions have repositories of human biological material, the document refers to biorepositories and biobanks.

Thus, the guidelines aim to establish the principles and standards to be used when establishing and operating biobanks and biorepositories of human biological material for research purposes, as well as the information related to the samples that comprise them, and to ensure ethical and legal standards of the procedures regarding their use. These guidelines are governed by the bioethical principles of human dignity, autonomy, beneficence, justice, and precaution. The bioethical principles were crucial for the creation of the guidelines, as it is known that they promote not only the building of standards but also awareness of ethical values, and that they can influence, directly or indirectly, the formulation of health policies.¹¹

The document discusses the conceptual aspects, activities, goals, and differences between biorepositories and biobanks; consent forms; the rights of the research

subjects; and other aspects permeated by concerns on the appropriate use of information. The Decree of the Ministry of Health number 2201 from September 14, 2011, which established the Brazilian guidelines for biorepositories and biobanks of human biological material with research purpose, was published in the DOU on September 15, 2011; it contains 39 articles, which are divided in five chapters and arranged as follows:

Chapter I: On general dispositions

Chapter II: On consent

Chapter III: On the research subject's rights

Chapter IV: On biorepositories and biobanks

Section I – On general dispositions

Section II - On biorepositories

Section III - On biobanks

Chapter V: On final dispositions

The first chapter is preceded by considerations that include the Constitution of the Federative Republic of Brazil, the mainstay of the principle of human dignity and fundamental rights to life, liberty, and physical and moral integrity; the Civil Code; the principles of the Brazilian Unified Health System (Sistema Único de Saúde – SUS), particularly the preservation of the autonomy of individuals in defense of their physical and moral integrity, equality of health care without prejudices or privileges of any kind, and the right of the assisted persons to have information about their health; the provisions stated in international documents such as the Nuremberg Code, the Universal Declaration of Human Rights, the Declaration of Helsinki, the International Ethical Guidelines for Biomedical Research Involving Human Subjects (CIOMS/WHO), the Universal Declaration on Bioethics and Human Rights, the Universal Declaration on the Human Genome and Human Rights, and the International Declaration on Human Genetic Data and Recommendations of the World Health Organization on Common Minimum Technical Standards and Protocols for Biological Resource Centers (WHO/IARC); the Brazilian laws, particularly Law No. 9.279/96, which regulates the rights and obligations related to industrial property, and Law #11.105/05 which concerns biosafety; the National Health Council Resolutions pertaining to the subject; Resolution #358/05 of the National Environment Council; and Resolution #306/04 of Anvisa's Collegiate Board that are relevant to the topic.

In accordance with Chapter I of the Decree, article 3,a biobank is an organized collection of human biological material and associated information collected and stored for research purposes, in accordance with pre-defined ethical and operational regulations or technical standards; the stored material is under institutional responsibility and management, with non-profit objectives.

In biobanks, the human biological material belongs to the research subject, and its safekeeping and management is the responsibility of the institution, with indefinite storage time, i.e., as long as the material is viable, requiring quality control to ensure the reliability of the material to be used in biological research.

To establish a biobank, it is necessary to submit a development protocol that will be analyzed by the institutional research ethics committee (REC) or one indicated by Conep and, when approved, it will be compulsorily evaluated by Conep.

The development protocol is the document that defines the creation and operation of a biobank, its managers, and its fundamental aspects, such as the informed consent to be used; the information related to the subject and to the samples; and the steps of collection, processing, storing, distributing, and disposing of human biological material. It must be accompanied by the Internal Regulations for Biobanks, which includes the characteristics, purpose, organizational structure and *modus operandi* of each biobank, and by the institutional disclaimer, which is a statement of technical and financial responsibility for the creation and maintenance of the biobank, as provided in the Brazilian Ministry of Health Decree.

Regarding the biorepository, it is a collection of human biological material, collected and stored during the performance of a specific research project, according to regulations or pre-defined technical, ethical, and operational standards, under institutional responsibility and researcher management, for non-commercial use.

Human biological material stored in a biorepository is also the property of the research subject, whereas the institution and its researchers are in charge of its management; the storage period should be in accordance with the chronogram of the corresponding research, and should meet the current standards of the CNS.

The biorepositories and biobanks should adopt a set of practices, equipment and facilities aimed at preventing, minimizing, or eliminating risks inherent to research activities, with goals of human health, preservation of the environment, and quality of results.

According to Chapter II of the Decree, the subject's consent to the collection, storage, and use of human biological material in a biobank is necessarily formalized through the informed consent (IC). This document should contain two options, mutually exclusive, regarding the use of stored material for every study, for purposes of the expressed and individual decision on the part of the subject: the need for a new consent, or new consent waiver.

Thus, the individuals' right to choose to give their consent regarding future use of their biological material stored in biobanks is explained and ensured, in projects approved by the national system of ethical assessment of research in human subjects at the same time that the individuals give their authorization for collection and storage, exempting new contacts for obtaining and clarifying the consent. Conversely, the subject's right to be informed about the purpose of the use of the samples stored at each approved research remains, if it is his/her will, and he/she

can decide whether or not to give consent, after contact and presentation of his/hers IC. In this situation, if the subject refuses to give consent to the use of the material, the sample cannot be used against his/her will, preserving the individual's interests and decision. In the particular case in which the subject cannot be found, even if he/she opted for new contact and consent for each research, upon presentation of reasonable justifications by the researcher, the REC may or may not authorize the use of the stored sample.

Regarding the IC for the use of human biological samples in a biorepository, it must be specific for each research, as recommended by the resolutions of the CNS.

In Chapter III of this document, the rights of the research subjects have to be detailed and must appear in the IC, such as: free access to information associated with the stored human biological material; free access to information obtained or generated from the human biological material used; free access to genetic information obtained or generated from the human biological material used, including those that imply risks for non-preventable diseases or familial risks; free access to genetic counseling, if applicable; anonymity in any form of release of the information or results associated with the human biological material used; withdrawal of consent at any time; designation of persons who may have access to their genetic information in the event of death or disabling condition; and access to information on storage purposes, including those responsible for it, the risks and potential benefits, guarantee of quality and integrity of storage, as well as measures to ensure privacy and confidentiality.

Regarding the feedback of research results to participants expressed in Article 4, paragraph 3 of the Decree, and the right to free access to genetic counseling in Chapter III, Article 8, section IV, it must be emphasized that the Brazilian position on this issue is to ensure, through a normative document, that the participant has the right to decide whether or not to be informed about research results, depending on the manifestation of his will, and to receive genetic counseling, when the results of research show known and consistent clinical implications during the course of a research project.

Throughout Chapter IV, on biorepositories and biobanks, in addition to the general provisions relating to both, the differences between them are described; for instance, regarding the management, time of storage, and disposal of human biological material. In Section III of this Chapter, it is noted that biobanks should be accredited in the REC/Conep system, and will be subject to inspection by the health authorities.

According to Chapter V of the said Decree, biobanks established from the date of its publication onward should be created in accordance with it, and those previously established should comply within one year. Compliance with the standards contained in this decree shall be subject to review and approval by REC/Conep system. Moreover, CNS resolutions on human biological material shall be considered.

Final considerations

The guidelines issued in this article do not exhaust the complexity of the different aspects involved in the use of biological materials stored in biobanks and biorepositories. The importance of regulations arises from ethical precepts, considering the morality prevailing in the country, and taking into account the legal aspects, which translate into a document that does not end in itself. The dynamics of science always leads to changes in paradigms, which can go beyond the existing laws.

It is expected that the Brazilian Ministry of Health Decree that established the Brazilian guidelines for biorepositories and biobanks of human biological material with the purpose of research will enable the strengthening of ethical and legal standards in studies based on information from biorepositories and biobanks, contributing to the existing quality standards in Brazilian scientific publications. Considering the international context, and specifically that of Latin America, it is noteworthy that Brazil was one of the pioneers in developing a document of this magnitude, with the purpose of research.

The importance of researchers' and institutions' adherence to this document when performing projects that are consistent with the existing standards is emphasized, guaranteeing the continuity of the academic excellence that Brazil has attained in the international scenario.

In parallel, Conep found it was necessary to review and update the CNS Resolution 347/05. Thus, in May 2011, this document was revoked and replaced by CNS Resolution 441/11. Therefore, nationally, there are two complementary documents that govern the subject – the National Health Council Resolution and the Decree of the Ministry of Health.

Conflict of interest

All authors declare to have no conflict of interest.

REFERENCES

1. Godard B, Schmidtke J, Cassiman JJ, Aymé S. Data storage and DNA banking for biomedical research: informed consent, confidentiality, quality issues, ownership, return of benefits. *Eur J Human Genet.* 2003;11(2):88-122.
2. Hansson MG. Ethics and biobanks. *Br J Cancer.* 2009;100: 8-12.
3. Ursin LØ. Biobank research and the right to privacy. *Theor Med Bioeth.* 2008;29:267-285.
4. WHO-IARC. Common minimum technical standards and protocols for biological resource centers dedicated to cancer research. Lyon: WHO; 2007.
5. Brasil. Constituição (1988). Constituição da República Federativa do Brasil: promulgada em 5 de outubro de 1988. Brasília, DF: Senado, 1988.
6. Brasil. Lei de Biossegurança. Lei nº 11.105, de 24 de março de 2005. Brasília, DF, 2005 [cited 2010 Jun 26]. Available from: http://www.planalto.gov.br/ccivil_03/_Ato2004-2006/2005/lei/

- L11105.html
7. Agência Nacional de Vigilância Sanitária. Regulamento técnico para o funcionamento dos bancos de células e tecidos germinativos, RDC nº 23 (27 mai, 2011). [cited 2011 Sept 26]. Available from: <http://e-legis.anvisa.gov.br/leisref/public/showAct.php?id=20954&word=>.
 8. Conselho Nacional de Saúde. Regulamentação do armazenamento e utilização de material biológico humano no âmbito de projetos de pesquisa, Res CNS nº 347 (13 jan, 2005). [cited 2010 Jun 26]. Available from: <http://conselho.saude.gov.br/docs/Reso347.doc>.
 9. Conselho Nacional de Saúde. Resolução nº 441, de 12 de maio de 2011. Diretrizes para análise ética de projetos de pesquisas que envolvam armazenamento de material biológico humano ou uso de material armazenado em pesquisas anteriores. Diário Oficial União. 18 de julho de 2011; Seção 1:60-61. [cited 2011 Aug 2011]. Available from: <http://conselho.saude.gov.br/resolucoes/2011/Reso441.pdf>.
 10. Ministério da Saúde. Portaria nº 2.201, de 14 de setembro de 2011. Diretrizes Nacionais para Biorrepositório e Biobanco de Material Biológico Humano com Finalidade de Pesquisa. Diário Oficial União. 15 de setembro de 2011; Seção 1:40-42. [cited 2011 Sept 2011]. Available from: http://bvsmms.saude.gov.br/bvs/saudelegis/gm/2011/prt2201_14_09_2011.html
 11. Fortes PAC. A equidade no sistema de saúde na visão de bioeticistas. Rev Assoc Med Bras. 2010;56(1):47-50.