Code of Ethics and Good Scientific Practice

IdiPAZ
Instituto de Investigación
Hospital Universitario La Paz

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CONTENT

1. PRESENTATION

The objective of this Guide is to establish an ethical code of conduct for the Institute's staff in the development of their research to ensure its the results while providing IdiPAZ with documentation shared and accepted by all members of the Institute. This document contains the rules of action and ethical principles relating to the research activity carried out, including both the planning and development of such activity as well as its recording and communication.

This Code of Ethics and Good Scientific Practice establishes the ethical and quality criteria that will guide the research activity carried out by the Instituto de Investigación Sanitaria de La Paz (IdiPAZ)/ Fundación de Investigación Biomédica del Hospital Universitario La Paz (FIBHULP).

This code constitutes the commitment adopted by the scientific personnel of the Institute regarding the quality and integrity of research and will be applicable to all research carried out totally or partially at the Institute or by research personnel linked to it.

2. CODE OF GOOD SCIENTIFIC PRACTICE

The IdiPAZ Code of Ethics and Good Practices is substantiated on a series of general principles related to the responsibility of the research activity which the practice of scientific research carried out at the institute will be based on.

These principles are:

- Professionalism and rigor in research practice.
- Intellectual honesty in research development.
- The search for sustainable scientific research.
- Accountability both financially and ethically.

The research carried out by the Institute will comply with the provisions of the applicable ethical and legal norms, bearing in mind that:

- All research involving the participation of individuals, the use of human biological samples or personal data must be reviewed by a Drug Research Ethics Committee (CEIm) as established by the Biomedical Research Act.
- All animal research must be reviewed by an Animal Experimentation Ethics Committee.
- All projects will comply with the applicable legal regulations, both at national and regional level, and will seek the pertinent administrative authorization if necessary.

In order to guarantee the quality of research and the correct execution of all research activities carried out in the Institute's environment, IdiPAZ has the following units, committees and platforms:

- Committee on Drug Research Ethics (CEIm).
- Animal Welfare Bodies (OEBA .
- Internal Scientific Committee.
- Clinical Research and Clinical Trials Unit (UICEC).
- Innovation Support Unit.
- Biobank.
- Biostatistics.
- Experimental surgery: animal facility.
- Documentalist.
- OTRI.
- Internationalization.
- Innovation Support Unit.
- Shared laboratories.
- Sequencing platform.
- Bioinformatics Platform.
- PAIN platform.
- Nutrition, food and health platform.
- Simulation platform.
- Tissue engineering and 3D printing platform (PITI3D).

3. RESEARCHER VALUES

The involvement, training, monitoring and supervision of all the Institute's personnel in good research practices is essential to guarantee the quality and integrity of research practice. The main values that should be present in good research practice are the following:

- Honesty.
- Integrity.
- Transparency.
- Trustworthiness.
- Leadership.
- Cooperation.

4. SUPERVISION, TRAINING AND MENTORING OF RESEARCH PERSONNEL

The supervisors/mentors themselves are expected to advise and supervise the entire research process, including the drafting of hypotheses, methodology, application for funding, data recording, data analysis and evaluation of any ethical issues that may arise.

The training and development of young researchers is a central matter within the Institute's quality and integrity policy. For this reason, the Institute has the duty to ensure the proper direction of research and supervision of any person linked to the Institute for training as a scientific researcher or research assistance technician.

In the field of training new professionals, the directors of research groups and principal researchers are the ones who must advise the members of their teams and provide them with specific guidance and training to develop, design and structure their research activities appropriately and to foster a culture of research integrity.

The personnel in training linked to the Institute will have a person in charge/tutor to ensure the punctual fulfillment of the learning objectives and expectations initially established.

With respect to the training of research personnel, the Institute has developed a unique and integrated Training Plan formembers of the Institute. One of the essential objectives of this plan is to promote training in ethics and good scientific practices.

5. GOOD PRACTICES IN RESEARCH

Development of research projects

Research projects will be devised following a research protocol developed under the responsibility of the lead researcher.

Definition of the research protocol

The research protocol should clearly and precisely express the objectives and the research plan. The content should be sufficiently detailed and complete so that anyone can repeat the research and obtain similar results or evaluate the validity and reliability of the steps of the study.

The basic components or contents that a research protocol should contain are:

- Title.
- Research team (data on researchers and participating institutions).

- Summary.
- Problem statement.
- Background and justification for the need to conduct the study.
- Bibliographic references.
- Hypothesis, general and specific objectives.
- Methodological design (design, subjects, variables, data collection, statistical analysis, limitations of the study).
- Ethical aspects.
- Work plan (chronogram) and distribution of tasks.
- Resources available and necessary and their justification.
- Data management plan, according to the Data Protection Manual.

Research protocols should consider and be sensitive to some relevant differences such as age, gender, ethnicity, etc.

In addition, the research protocol should be clear, simple and written in such a way that its content can be understood by the project evaluators, the researchers, and the technicians involved in its execution. It should be ordered in such a way that the relationship of one phase with the other can be perceived, and its consistency in the context of the document. To this end, it is suggested to present the protocol in interrelated sections, so that there is a common thread in its content.

An additional or complementary research question to an already established project (e.g., in case the use of biological and chemical material resulting from a specific research is foreseen for purposes other than those foreseen in the original protocol) must lead to the drafting of a written modification to the research protocol before proceeding with its execution.

Under no circumstances do we justify the lack of a written protocol or a possible drafting without meeting the most basic standards in research projects of immediate start and/or a simplified protocol that directly involve humans or experimental animals.

It is advisable that all research protocols be independently evaluated by third parties, with the exception of those in which such review is already mandatory and institutionalized (research grant applications and protocols involving animals or humans).

Regulatory requirements

Research projects must respect the fundamental principles established in the Declaration of Helsinki, the Oviedo Convention on Human Rights and Biomedicine and the UNESCO Universal

Declaration on the Human Genome and Human Rights, as well as comply with the requirements established in Spanish legislation in the field of biomedical research (Law 14/2007, of July 3, 2007, on Biomedical Research). Any research protocol that involves the use of institutional computer files or the development of databases with information relating to individuals must comply with Organic Law 3/2018, of 5 December, on the Protection of Personal Data and guarantee of digital rights and the EU General Data Protection Regulation 2016/679.

Documentation, storage and data safe-keeping, records and biological or chemical material resulting from investigations.

Every research protocol should include a specific plan for the collection of data, records and biological or chemical material resulting from the execution of the research, as well as with respect to its safe-keeping and conservation.

The lead researcher and his/her collaborating personnel have the obligation to record each and every detail observed in the research experiments. All information, whatever it may be, must be permanently written down and incorporated into the record books or laboratory notebooks. So much so, that any intermediate or final data must have its correspondence with that of the original documents, as would be the case of the patient's clinical history in clinical trials. Experiments and observations must include the number of people who have participated, as well as the time and circumstances of their performance. No mistakes, as well as negative, unexpected or discordant results should ever be overlooked. Rectifications must be clearly traceable and there must be systematic identification of the person making the corrections.

The lead researcher must foresee the different aids that will be required for a correct custody and conservation of the different documentation and biological or chemical material obtained in the experiments and observations. Likewise, a record should be kept for the follow-up of the log books or laboratory notebooks, as well as the banks of chemical or biological material. Any record of primary data in electronic format requires a protocol that establishes the specific plan for storage and collection of backup copies to avoid accidents in the storage medium and computer equipment in the access to and safe-keeping of the data obtained.

Any documentary record of data or any sample that is part of a bank of biological or chemical material in the course of an investigation must be permanently accessible to all members of the research team. There is a mutual obligation between all of them with respect to the information, processing and interpretation of the data obtained.

All documentation (log books and laboratory notebooks, among others) and biological or chemical material obtained during research is the property of the Institute, since it is key

documented evidence that allows safeguarding the information obtained during research, not only for academic purposes but also to protect the possible knowledge generated, which may result in the generation of some intangible asset, hence the importance of always keeping it properly guarded in accordance with the criteria of the project's lead researcher. This material is an essential instrument for safeguarding the institution's innovation. If a collaborator of the research group changes institution and requires information obtained during his/her activity, the lead researcher may provide him/her with a photocopy of all or part of the record books; a copy of the existing electronic information; a photocopy of the data collection notebooks, or aliquots of the biological or chemical material available. When the change affects the lead researcher of the project, the provision of copies of documentation or biological or chemical material will be made under the supervision of the center's management.

All primary and original information (and biological or chemical material stored as a result of the research) must remain in storage for at least 10 years from the first publication of the results, except in those cases where longer periods are required by law. In the case of biological or chemical material, it may be stored for longer periods and its final destination will require the approval of the lead researcher.

Biological or chemical material and computerized data resulting from research must be publicly available and may be shared by third party researchers, with the exception of cases in which restrictions derived from their future commercialization have been established. The transfer will require: qualification for its proper use by the person making the request; due knowledge on the part of the researchers generating the material; a transfer protocol with the approval of the lead researcher responsible for the material, and the willingness of the applicant to cover possible production and shipping costs. The transfer may be limited for reasons of availability, competitiveness or confidentiality. The material or data must be anonymized, otherwise a new informed consent on the transfer will be required.

Quality and safety standards for the donation, procurement, testing, processing, preservation, storage and distribution of human cells and tissues.

Necessary measures shall be taken to ensure that the quality system includes at least the following documentation:

- Procedure manuals.
- Guidelines.
- Training and reference manuals.
- Information transmission forms.

- Data related to the donor.
- Information on the destination of cells or tissues.

In addition, care must be taken to ensure that this documentation is available for inspection by the competent authority or authorities.

In order to be appointed as a person in charge, he/she must possess at least the following qualifications and meet the following minimum requirements:

- Hold a degree, certificate or proof of formal qualification in the field of medicine or biology.
- Have at least two years of practical experience in relevant fields.

Any process that affects quality and safety should be included in the procedure manuals, and care should be taken to ensure that it is carried out under controlled conditions. In addition, special provisions should be included in the procedure manuals regarding the handling of cells and tissues to be discarded in order to avoid contamination of other cells and tissues in the processing environment and of the personnel.

Care shall be taken to ensure that all human tissues and cells are correctly identified at all times. An identification code must be assigned to each delivery or consignment of cells or tissues.

Acceptance or rejection of the cells and tissues received must be documented.

Cells and tissues must be kept in quarantine until donor testing and information requirements are met.

It must be ensured that all donations of human cells and tissues undergo laboratory testing in accordance with established requirements.

It shall be verified that storage conditions of the human tissues and cells received comply with the established requirements.

Development of research projects with stem cells obtained from supernumerary pre-embryonic stem cells.

Research projects that include in their development the use of frozen human pre-embryos left over from assisted human reproduction techniques must meet the following conditions:

- Identity and professional qualifications of the principal researcher and all project participants.
- In cases in which the projects involve or include the development of cell lines from embryonic stem cells, specification of the number, origin and center of origin of the pre-

embryos donated for these purposes to be used in the project, including the corresponding progenitors' informed consent form , both for the intended use and for other purposes.

- Material and human resources, as well as resources available for the development of the project.
- General information and current state of scientific knowledge in the field of research projects.
- Justification and objectives of the project, including, among others, the certification of its relevance and scientific excellence, as well as the impossibility of carrying out the planned research in the animal model.
- Description of the project and its phases and deadlines, including specification of its restriction to the basic scope or its extension to the clinical scope of application.
- Description of the financial conditions of the project and its budget, as well as a statement and commitment to its non-profit nature.
- Commitment to provide the corresponding public authority with the data that will allow identifying and knowing the conservation of the cell lines that may be obtained as a consequence of the development of the project, for the purpose of creating a registry of cell lines.
- Commitment to transfer cell lines that may be obtained during the development of the project free of charge for the development of other projects.

Research for genetic purposes

The collection, processing and/or storage of biological samples for genetic analysis shall comply with the provisions of the Biomedical Research Law and other applicable regulations. Without prejudice to the provisions of the legislation on protection of personal data, you must receive the following information in writing:

- Purpose of the genetic analysis to which he/she is consenting.
- Place of analysis and destination of the biological sample at the end of the analysis, whether it is the dissociation of the identification data of the sample, its destruction, or other destinations, for which the consent of the source subject will be requested under the terms provided for in this Law.
- Persons who will have access to the results of the analyses when they will not be subjected to dissociation or anonymization procedures.

- Warning about the possibility of unexpected discoveries and their possible significance for the subject, as well as the subject's ability to take a position in relation to receiving their communication.
- Warning of the implication that the information obtained may have for their relatives and the convenience that he himself, if necessary, transmit such information to them.
- Commitment to provide genetic counseling once the results of the analysis have been obtained and evaluated.

Good practices in research with humans

It is essential to obtain the approval of the Ethics Committee for Research with Medicines (CEIm) of the Hospital Universitario La Paz and to comply with the provisions regarding informed consent and information of the subjects participating in the research, as well as with the confidentiality of the data, samples and results obtained.

The rights, safety, and welfare of research subjects are the most important considerations and should prevail over the interests of science and society. Before initiating a research study, foreseeable inconveniences and risks should be considered in relation to the anticipated benefit to the individual subject and to society. A research study should be initiated and continued only if the anticipated benefits justify the risks. It is important to emphasize that the medical care received by subjects and medical decisions affecting subjects should always be the responsibility of a qualified practitioner.

Within the section on Good Practices in Research involving humans, it is worth highlighting a section referring to clinical research with medical devices, which covers many types of devices, materials and products and machines of different varieties, including medical software, and which are classified according to the Spanish Agency of Medicines and Medical Devices (AEMPS).

The regulation of medical devices in Spain is essentially made up of three Royal Decrees (RD) which transpose the corresponding Community guidelines and which have been issued in development of the General Health Law and the Law on Medicines, currently replaced by the Law on Guarantees and Rational Use of Medicines and Medical Devices:

- RD 1616/2009, of October 26, 2009, which regulates active implantable medical devices, transposing Directive 90/385/EEC.
- RD1591/2009, of October 16, 2009, regulating medical devices, which transposes Directive 93/42/EEC.

- RD 1662/2000, of September 29, 2000, on medical devices for in vitro diagnostics, which transposes Directive 98/79/EC.

The legislation on medical devices, when defining the essential requirements that products must meet, refers to the need for this compliance to be demonstrated by means of a clinical evaluation. This means that the safety of the products and the benefits they offer must be supported by clinical data obtained with ethical and methodological criteria that are included in an annex to the legislation itself. The assessment of the benefit/risk ratio must also be supported, in order to determine whether the risks are acceptable in relation to the benefits provided.

Clinical trials

For the conduct of clinical trials with medicinal products managed by biomedical research foundations and carried out in the public healthcare centers of the Community of Madrid, a single contract model is required that incorporates, to the previously established one, the legislative modifications following the publication of Royal Decree 1090/2015, of December 4, which regulates clinical trials with medicinal products, the Ethics Committees for Research with medicinal products and the Spanish Registry of Clinical Studies, and, also, Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data and repealing Directive 95/46/EC (General Data Protection Regulation) and Organic Law 3/2018 of 5 December on the Protection of Personal Data and guarantee of digital rights, as well as the rest of the regulations in force on the protection of personal data that may be applicable.

The incorporation of these legislative modifications in a centralized manner facilitates the coordination and legal security of the research process in relation to clinical trials with drugs. In addition, the new legislation aims to give an important boost to clinical research with drugs, simplifying administrative processes and speeding up the conduct of simultaneous multicenter studies throughout Europe. It improves the delimitation of responsibilities of the participating agents, increases the safety of the trial subjects and, at the same time, increases the efficiency of the evaluation and communication processes involved.

For all these reasons, on April 19, 2019, the Directorate General for Planning, Research and Training ordered the adoption of a new single contract model for the conduct of clinical trials with drugs to be carried out in the healthcare centers of the Community of Madrid.

On our website, you can find the contract models with the applicable legislation and the necessary documentation:

http://www.idipaz.es/PaginaDinamica.aspx?IdPag=551&Lang=ES

http://www.idipaz.es/PaginaDinamica.aspx?IdPag=551&Lang=

Good practices in handling biological samples

The protection of personal privacy and the confidential treatment of personal data resulting from biomedical research activities will be guaranteed, in accordance with the provisions of current legislation and the **Data Protection Manual**. These guarantees will apply to biological samples that are a source of personal information.

Specifically, it will be taken into consideration that:

- The lead researcher must guarantee the correct safe-keeping and conservation of the data and biological material resulting from the research, during the period legally established for each type of project. In case personal data are collected, it is the lead researcher's responsibility to ensure compliance with current regulations, consulting with his/her institution about the necessary procedures.
- Every research protocol should establish standard procedures for data and biological material collection, recording, safe-keeping and preservation, in order to ensure consistent and accurate data. Any intermediate or final data must be matched with the original documents.
- Copies of the most relevant software used will be kept in order to be able to retrieve the original data in the future if necessary.
- It is advisable to assess the suitability of biological samples derived from research to be incorporated into the IdiPAZ Biobank, an aspect that should be considered at the time of obtaining the informed consent of the donor. For this provision, the approval of those responsible for the Biobank must be obtained prior to the collection of the samples.
- If the biological samples collected are intended to be kept for future research in the same line of research initially proposed, the lead researcher, in compliance with RD1716/2011, must constitute a collection of biological samples and register it in the National Registry enabled by the Carlos III Institute for these purposes or store them under the Biobank regime. The information and informed consent document must contain all the relevant aspects mentioned in RD 1716/2011 for these cases.

Assignment

For biological material under the Biobank regime, the institution in charge of safe-keeping all documentation and biological material resulting from research is IdiPAZ/FIBHULP.

Biological data and materials resulting from research may be transferred to third party researchers provided that they are covered by a protocol with a favorable assessment, both from a scientific and ethical point of view, and that any restriction derived from their future commercialization is respected. Such transfer will only be possible with the express consent of the source subject, under the terms and in accordance with the provisions of RD1716/2011.

The assignment may be limited for reasons of availability, competitiveness or confidentiality.

Nominal biological samples (coded samples and identified samples) are those that, from an ethical point of view, identify the person from whom they originate and should therefore be treated with the same ethical criteria and practices with which research on human subjects is treated.

Every researcher intending to transform identifiable samples into anonymous samples should obtain the consent of the sample holder and provide sufficient written assurances about the procedure to the Research Ethics Committee, including a description of the procedure to ensure protection of subjects from possible leakage of confidential information.

The subject is responsible for expressly authorizing and determining the destination and uses of his/her biological samples for research purposes (regardless of whether they were obtained for health care or research purposes).

- Any new use of identified biological samples requires the authorization of the person who provided it, of the person who obtained and conserves it, and, in any case, of the Research Ethics Committee.
- It is necessary that the subject authorizes the researchers to access clinical and analytical data relating to him/her.
- The subject must be correctly informed about the possible benefits and risks for him/her, and if applicable, for his/her family, the social or age group to which he/she belongs, or for third parties.
- In cases where it is foreseeable that a protocol will pose a risk to a particular group, this risk should be described in the informed consent process.

In retrospective studies of nominal samples in which previously deposited samples are studied, the researcher is required to respect the will of the subjects who provided these materials, if they have expressed it. If they have not done so, it will be up to the Research Ethics Committee to assess whether it is possible to dispense with consent and approve the corresponding study. For this purpose, the Committee will take into account whether the exceptional situations contemplated in the applicable regulations are met.

In research projects, it is possible to use samples obtained in the context of care if the patients have given their consent, even if the objectives of these projects were not known at the time the samples were obtained. In this case, the Research Ethics Committee must determine whether such advance consent is valid for each specific project. In this case, consent should be obtained after informing the donor as explicitly as possible about the potential uses, including the most sensitive uses (genetic, reproductive biology, neuropsychiatric, etc.) for which they may be intended. The donor may determine whether the samples are to be anonymous or identifiable.

- When the samples were obtained initially for diagnostic or therapeutic purposes, their use for research may in no case compromise those purposes. The priority for the patient's interests after the biopsy is the anatomopathological study to establish the diagnosis and prognosis of the lesion. Therefore, histopathological examination has priority over any other possible use. The reasons for acting in this way are both ethical and in terms of quality of care.
- When, for health reasons, the source subject or his/her family needs it, they may use the samples, as long as they are available and not anonymized.
- Once consent to participate in a research protocol has been obtained, pathologists and researchers must agree to fulfill their respective specific purposes, while respecting the freely expressed will of the patient. The pathologist must protect the patient's medical healthcare interests; the researcher must ensure that the subject's willingness to participate in the research is fulfilled.
- Even when patients are invited to donate surplus samples obtained for their clinical care, which would normally be discarded, their freedom to give or withhold consent and to authorize the modalities of use of the samples must be sensitively respected. You will be informed that your refusal to consent to the alleged use of biological samples in research projects will in no way affect your clinical care. In this case, consent for research uses should be sought only after the samples necessary for clinical care have been obtained.

Since the conditions for obtaining research samples may vary from one protocol to another, specific rules are not established here and must be established by the interested parties for each specific situation.

The donor has the right to revoke consent, in whole or in part, at any time, and its effects, including the possibility of destruction or anonymization of the sample and that such effects will not extend to data resulting from research that has already been carried out.

Both the sponsor and the researcher must make a written commitment to the Research Ethics Committee to destroy the biological samples after completion of the studies unless the subject has given his/her authorization for their storage.

Good practices in animal research

IdiPAZ compliance with good practices and current national and European legislation follows the European Directive 2010/63/EU, which has been transposed into national legislation through the Royal Decree RD 53/2013, which establishes the basic rules applicable for the protection of animals used in experimentation and other scientific purposes. Following the current regulation under Order ECC/566/2015, personnel handling animals for scientific and research uses must have the knowledge, as well as the appropriate skills and attitudes for animal care, and that all necessary resources are available for the proper handling of animals with respect to facilities, husbandry, welfare and veterinary care.

IdiPAZ has adhered to the Agreement on Transparency in Animal Experimentation, promoted by the Confederation of Scientific Societies of Spain (COSCE), with the collaboration of the European Association for Animal Research (EARA) and launched on September 20, 2016.

Projects involving animal experimentation must comply with the provisions of current legal regulations and in particular with Law 6/2013, of June 11, amending Law 32/2007, of November 7, for the care of animals, in their exploitation, transport, experimentation and slaughter, as well as the aforementioned legislation.

Any research protocol involving animal experimentation shall never be implemented without the approval of the Animal Welfare Body (ABEW) and the Animal Experimentation Ethics Committee (CEEA).

The use of animals in experimentation may only take place when it pursues the following purposes:

- Fundamental research.
- Translational or applied research, and scientific methods for any of the following purposes:
  - The prevention, prophylaxis, diagnosis or treatment of disease, ill health or other abnormalities or their effects in humans, animals or plants.
  - The assessment, detection, regulation or modification of physiological conditions in humans, animals or plants.
  - Animal welfare, in particular the improvement of production conditions of animals raised for different purposes.

- The development and manufacture of pharmaceuticals, food, fodder and other substances or products, as well as the performance of tests to verify their quality, efficacy and safety, for any of the purposes indicated in the second paragraph.
- The protection of the natural environment in the interest of human or animal health or welfare.
- Research aimed at species conservation.
- Higher education or training for the acquisition or improvement of professional skills.
- Forensic and legal medicine.

The units destined for animal experimentation in the Institute are obliged to keep a registry book in which there is a record of all the animals used, as well as the number and species of animals acquired and the establishments of acquisition and their destination, once the experiment is finished. This register is kept for at least three years from the date of the last entry and is subject to periodic inspection by the competent authority.

Details concerning the identity and origin of any dog, cat or non-human primate are included in the corresponding record book of each unit used for animal experimentation.

Experiments may only be carried out by or under the responsibility of competent persons and care must be taken to ensure the protection of animals used for experimental and other scientific purposes, including teaching and, in particular, that the animals used are given adequate care; that they are not caused unnecessary prolonged pain, suffering, distress or injury; that any unnecessary duplication of procedures is avoided; and that the number of animals used in procedures is reduced to a minimum, applying alternative methods as far as possible.

Experiments should be performed under general or local anesthesia unless the latter is more traumatic to the animal than the experiment itself or is incompatible with the purpose of the experiment.

Good practices in research with biological agents

Projects involving the use of biological agents must comply with the provisions of Law 31/1995, of November 8, 1995, on the prevention of occupational hazards, and the Royal Decrees that develop it in terms of risks related to exposure to biological agents, such as Royal Decree 65/2006, of January 30, 2006, which establishes requirements for the import and export of biological samples.

Good practices in GMO research

Projects involving the use of genetically modified organisms must comply with the provisions of Law 9/2003, of April 25, 2003, on the Confined Use, Voluntary Release and Commercialization of Genetically Modified Organisms and Royal Decree 178/2004, of January 30, 2004, approving the general regulations for its development and implementing regulations.

Researcher responsibilities

Any research protocol that involves the use of the institution's own or other health care facilities or equipment, or of any research facility or equipment common to the institution, requires the approval of the person in charge of the institution, facility or equipment.

In any research grant application, the person responsible for the report is also responsible for the veracity of the resources committed.

When preparing a personal curriculum vitae, the researcher is responsible for the veracity of its contents. As proof of this, it is advisable to sign the curriculum vitae document. In the case of a collective curriculum vitae, the person responsible for the application must sign it.

It is advisable for the lead researcher, in collaboration with the rest of the researchers, to draw up a plan for communication and publication of the possible results of the research.

In addition, the application for grants for new research projects should be avoided as far as possible when this implies a delay in the publication of the results of projects that have already been completed.

Given that in clinical research the process of data collection is complex and not always repeatable, the lead researcher and staff collaborating in the research protocol must pay special attention to ensure that the protocol reflects the quality of data collection and data safekeeping.

6. PROTECTION OF PERSONAL DATA AND GUARANTEE OF CONFIDENTIALITY

Any research project involving the use of data that can be linked to individuals must ensure the protection of privacy and respect for the rights and freedoms of the participants and must observe compliance with current regulations, in particular Regulation 2016/679 on the Protection of Personal Data (RGPD) and Organic Law 3/2018 of December 5, 2018, on the Protection of Personal Data and guarantee of digital rights, as well as the provisions of Law 14/2007 on biomedical research.

In the processing of personal data, it is necessary to ensure security by controlling access to them, through any means that allows it. Hence IdiPAZ is obliged and is responsible for complying with current state and European legislation on data protection and has adopted a series of technical and organizational measures necessary to implement and demonstrate compliance with the provisions of that legislation.

In this regard, IdiPAZ has the figure of the *Data Protection Officer*, as required by art. 37 of the RGPD, as a key element in compliance and practice in data protection. For more information regarding the data protection policy of IdiPAZ, please consult the IdiPAZ website, and download the Data Protection Manual at the following link: **https://www.idipaz.es/ficheros/files/MPD%20FIBHULP.pdf**

As regards the right to confidentiality, the provisions of article 5 of Law 14/2007, of July 3, 2007, on Biomedical Research, and other applicable legal provisions will apply, by virtue of which, any person who accesses personal data in the exercise of his/her medical-healthcare functions and/or related to biomedical research will be subject to the duty of secrecy. This duty will persist even after the research or action within the project in question has ceased.

7. COLLABORATIVE PROJECTS

Whenever a collaborative research project is carried out, it is advisable to formalize a protocol that contemplates the terms under which the different groups from the same center or different centers agree on joint collaboration.

The lead researcher and collaborating personnel of research projects, not being responsible for the clinical treatment of the potential subjects, have the obligation not to interfere in any matter determined by the medical personnel responsible for those subjects.

The joint collaboration agreement, in addition to including the requirements of a research protocol, must also include:

- Unambiguous wording of all aspects of the research plan envisaged under the joint collaboration.
- Explicit distribution of the responsibilities, rights and duties of the participating groups or centers, both with respect to the tasks to be performed and the results to be obtained, including the determination of the custody and storage of the data or samples obtained.

- Criteria for updating the development of the studies among the different participating groups or centers.
- A preliminary draft of the plan for the presentation and dissemination of the results in any field.
- Procedures for storage and distribution of data and samples, as well as safeguarding confidentiality.
- All that is considered relevant, in addition to possible commercial implications, financing and resolution issues.

Research projects sponsored by the biomedical industry or other for-profit entities.

The following considerations should be considered with regard to the sponsorship of research by private entities in the public sector:

a) Industry has an urgent need to carry out certain types of research in public institutions, especially in terms of experimental and technological development.
b) Industry-sponsored research is desirable and necessary, as it promotes technology transfer and can provide important economic resources.
c) In scientific relations with industry, the necessary demarcations must be established to prevent the principles and purposes of intellectual freedom from being compromised.
d) Scientific personnel who benefit from public money and credibility have an obligation to always develop their findings in accordance with the public interest.

The totality of the data, the results of the trial, as well as all the works and industrial and/or intellectual property rights derived from the same, are the property of the promoter, and the parties are subject to the provisions of the applicable legislation. This circumstance will not prevent the lead researcher and FIBHULP from using the results in their professional activities. Safeguarding the industrial and/or intellectual property rights of the promoter and respecting what is established in the protocol.

Regarding the projects promoted by the industry, the totality of the data, the results of the trial, as well as all the works and industrial and/or intellectual property rights derived from the same, are property of the promoter, being the parties subject to what is established in the applicable

legislation. This circumstance will not prevent the lead researcher and FIBHULP from using the results in their professional activities. Safeguarding the industrial and/or intellectual property rights of the promoter and respecting what is established in the protocol.

> In accordance with the provisions of RD 1090/2015, the sponsor commits to publishing, once the trial is completed, the results obtained, whether positive or negative. This publication will take place in publicly accessible scientific media, preferably in scientific journals if the final results of the trial have not been submitted for publication by the sponsor, the lead researcher may disclose for professional purposes, and in scientific journals and publications, such data, discoveries or inventions, with mention, at least, of the sponsor according to the following criteria: trials with non-marketed products: within the first year after authorization and marketing in any country; trials conducted after marketing within one year after completion of the trial, unless publication in a peer-reviewed medical journal is ted or contravenes national legislation.

The sponsor must receive for review a copy of the text proposed for publication and/or dissemination, in accordance with the provisions of the protocol and, if nothing is indicated, at least forty-five (45) days before the date of submission to the scientific journal, and at least twenty (20) days before in the case of an abstract. In any case, the lead researcher may only use these data with the express written authorization of the sponsor.

All agreements of a financial nature between the sponsoring entity and the researcher or research group, as well as any other type of reward established in direct or indirect relation to the research, must be included in a single agreement between the sponsor and the institution on which the researchers depend. The financial agreements must be accessible to the bodies, committees and persons with responsibility for the matters agreed upon.

8. LABORATORY NOTEBOOKS

What is the laboratory notebook?

The Laboratory Notebook is a support, like a diary, in which all the data of the investigation are recorded, with the objective of documenting the hypotheses, experiments, results obtained and their analysis or interpretation. This Notebook also collects the incidents or problems of any kind that have occurred during research and must show precisely what was done over the course of it, who did it and when, so that it is possible to reproduce the same process following the annotations.

The Laboratory Notebook is a fundamental source of information to know the development of research and it is a key element to determine the authorship and ownership of an invention.

The Laboratory Notebook will provide a complete record of the activity of the research personnel, and it is key documented evidence of their role in the work they are performing and their ownership of it.

The Laboratory Notebook and the information contained therein is the property of IdiPAZ.

Format

The Laboratory Notebook must have the pages numbered and in chronological order with the date of the annotation and the signature on each of its pages. It must be complete and it is not possible to delete pages. If there are pages that are not used or that want to be crossed out, the appropriate thing to do is to draw a diagonal line over them indicating that they are incorrect.

What information is recorded

- The materials used, the quantity and their origin, whether commercial, internal or from third parties.
- All observed results or data, including negative ones.
- All variables such as time, temperature, quantities needed, etc. that will allow another person with similar training and experience to duplicate the experiment using that notebook.
- The lab notebooks should be arranged in chronological order, so that when one experiment ends, the next one begins.
- If an experiment is to be started before the previous one ends, the page where the experiment continues should be noted on the last page of the unfinished experiment.
- If there is a prolonged period of inactivity, it is necessary to include an explanation, which may range from technical or scientific reasons, or even vacation periods.
- The Notebook must include the name and surname of each researcher involved in the registered research.

Additional material

Any other supporting material required to be used in the course of research should be recorded, referenced and considered part of the permanent record.

In these cases, it is important to consider the following aspects:

- All data that have not been stored in the official notebook must be recorded in an annotation explicitly referenced in the notebook.
- When original printed material such as photographs, tables, graphs, etc. have been generated, they should be added to the notebook in a reliable format, not susceptible to being misplaced.
- Materials that have been glued to notebook pages should be signed so that part of the rubric is on the paper and part on the additional material.

Notebook signatures

On a preferably weekly basis, the pages added to the Notebook during that period must be countersigned by the Co-signer. This Co-signer must be able to understand the work being done but cannot be listed as a co-inventor on any patent application based on the data recorded therein.

The function of this "co-signature" is to attest that the page has been written and signed by the researcher under these exact conditions.

Storage and custody of the Notebooks

- The Notebook must be kept in a protected place and its custody will be the responsibility of the person in charge for the group or PI or person delegated by him/her.
- The notebook can be stored for an unlimited period of time so that it can be used at any time.
- The information generated by a computer can be stored on a dated, write-protected medium. The media should be kept in a safe place and referenced in the Laboratory Notebook. If possible, the media should be kept sealed, dated and write-protected.

Interruption/termination of contract

In the event that the researcher in charge of the Notebook interrupts or terminates his or her employment relationship, the person in charge of the group or LR must ensure that the transition is carried out in compliance with the rules established for the conservation and protection of the research.

To this end, the research personnel who discontinue this relationship must commit to making an orderly transition of the record of research activities in the Laboratory Notebook to whoever is designated so that the application standards are not affected.

Duties of the group leader

The research personnel in charge of the research must comply with the following obligations:

- Provide as many notebooks as necessary.
- Make sure that the Notebook is used correctly.
- To be responsible for the safe-keeping of all the research group's notebooks.
- Ensure that the notebook is received should its user leave the research group, as well as ensure that the notebook is correctly passed on to future employees.
- If the LR is the one who will terminate his/her employment relationship, he/she should deliver the Notebooks to the Scientific Director of IdiPAZ.

Obligations for the user of the Notebook

Similarly, the Lab Notebook user must:

- Notify his/her manager in good time of the need to order new Notebooks.
- Fill out and sign the Notebook correctly.
- Give the Notebook to the LR should he/she leave his/her job.

Good practices in Laboratory Notebooks

- It is signed using the researcher's full name.
- The start date of the experiment and the dates on which each of the actions leading to its conclusion were carried out must be recorded.
- All annotations must be legible, and it must be possible to photocopy them.
- Corrections are made by marking the incorrect entry and marking and dating the corrections.

9. COMMUNICATION OF RESULTS

Research results should be made public as a legal requirement, whereas non-publication, delay in publication or exaggeration of the importance of the results for clinical practice or health policies is considered unacceptable practice. The results obtained should be fully disseminated, regardless of whether they are considered positive or negative.

Plagiarism and falsification of results is unacceptable and may be grounds for sanction.

In the event of an error in a study that underestimates or overestimates its conclusions, a correction note should be published as soon as possible.

In those projects with funding, the regulations established by the funding agencies on the dissemination and communication of results must be respected.

Authorship of scientific papers

The authorship of a research paper implies:

- Having contributed substantially to the conception and design of the work or analysis and interpretation of the data.
- Having participated in the drafting of the article or the analysis and critical revision of its important intellectual content.
- Accepting in writing the final version of the original paper submitted for publication.

In review articles it is essential that the authors have participated in the critical analysis of all the works cited.

It is the indivisible responsibility of all co-authors to ensure that the ethical requirements on authorship are met and to prevent anyone from appropriating the status of author without deserving it, or from being excluded from it when he or she has justly earned it. The rigorous demand of the aforementioned requirements is not incompatible with a generous attitude on the part of the research works, which judiciously shows the noble desire for promotion of the younger researchers.

The eagerness to highlight the valuable contributions of these collaborators must always be present in the Institute.

It is unacceptable to accept the status of author based solely on the employment relationship or hierarchical position.

It is not considered good practice for the director of a department to routinely appear as co-author on all papers published by members of his or her department. They should only do so when they have fulfilled, with respect to each specific paper, the requirements indicated.

To avoid this risk of fictitious or usurped authorship, it is recommended that the contribution and order of signature of each of the presumed authors be detailed at the time the study protocol is submitted.

All contributions from formal collaborations or others that directly or indirectly support the research work that do not involve scientific authorship should be properly acknowledged. Their omission would be considered misappropriation of intellectual authorship.

The acknowledgements section should include those contributions that are limited to functions such as obtaining resources or collecting data and do not justify their authorship (e.g., facilitating patient recruitment or providing materials or analytical data). All contributions should be accompanied by an explicit mention of the assistance provided.

Authors are responsible for obtaining the written consent of the persons who are acknowledged by name.

The Institute has an affiliation policy that is mandatory for the members of the Institute, which includes the correct identification of the scientific production of the researchers of the Instituto de Investigación Sanitaria del Hospital Universitario La Paz. It also includes the correct way to mention funding entities in acknowledgements of publications, as well as the use of support platforms.

Recommendations for the signature

The following rules are recommended for establishing the order of authors:

- The first author is the person recognized by the rest of the group as the most important for the conception and development of the research and is the one who has written the first draft of the article prior to its publication.
- The last author should be the one who is ultimately responsible for the research protocol.
- The rest of the authors can be ordered according to the importance of their contribution or simply in alphabetical order.
- The right is reserved to justify the order of signatures in a footnote.
- It may be the case that two authors have shared the same effort in the development of the research and preparation of the manuscript. In these cases, and under the recognition of the rest of the group, both authors can be considered as first authors, and this should be explicitly reflected in the publication of the original.

The edition of internal drafts, memories, work or technical reports and any other writing addressed to third parties must include the authors of the research or inquiry, in the same terms in which they would be included if it were a scientific publication.

In the case of publications of multicenter studies with the participation of a large number of people, collective authorship and the designation of an editorial committee should be accepted. In the case of establishing a nominal list of authors, the order should be established according to objective criteria.

Individual centers may negotiate independently with the Editorial Committee for separate publication of their contribution.

In all cases, the head of the department may review the manuscript before it is submitted for publication and may offer advice and recommendations. He/she will always retain the right to make the authors include a statement of exclusion of responsibility that will save his/her personal responsibility or that of the department.

Publishing practices

The Publication of results is essential if scientific knowledge is to be used effectively and in the public interest. Publication makes results available to the scientific community for verification, contrast and replication and initiates a process of development of new results based on the first ones.

The communication and dissemination of research results to the media should be subsequent to their scientific publication. This would only be justified for public health reasons.

In these cases, the authors will consider the possibility of having the results reviewed in parallel, as a matter of urgency, in a scientific publication, or they will agree on the scope of this exceptional communication with the editors of the publications in which they have planned their definitive publication.

The researcher with overall responsibility for the research program will be the one who must authorize the publication of the content (integrity of the results, adequate peer review, adequate protection of intellectual property rights) and its place of publication.

The publication of the results of research involving individuals is an ethical imperative.

Any contribution from formal collaborators or others who assist the research in a manner directly related to it should be properly acknowledged, avoiding unjustified references.

Acknowledged persons have the right to decline to be mentioned, so the authors will try to obtain their written permission.

In the publication of the results, the following must be explicitly stated:

- The centers to which the authors belong.

- The centers where the research was conducted.
- The independent ethical committees that have supervised the research protocol.
- Basic information on the ethical/legal acceptance of the study protocol, as well as a description of the scientific method used.
- Any financial aid or other type of sponsorship received, with its identification.
- It is also advisable to report all these details in communications in congresses or other types of presentations prior to publication.
- Quality should take precedence over quantity. It is not considered good scientific practice to proliferate publications with multiple authors in order to increase quantity.
- Redundant or duplicate publication is considered an unacceptable practice. Authors should not publish the same data in different journals.
- Fragmented publication in small blocks would only be justified by a legitimate need to advance findings by publishing preliminary data. An IdiPAZ affiliation policy is available at the following link: https://www.idipaz.es/ficheros/files/Normativa%20de%20filiaci%C3%B3n%20IdiPAZ-V5.pdf.

10.PEER REVIEW

Generally, researchers should seek to have their scientific output evaluated in terms of content and not only in quantitative terms, following the current trend set out in the framework of the San Francisco Declaration on Research Assessment (DORA).

On the other hand, the evaluations carried out by the Institute are mainly based on peer review, who may examine and criticize a manuscript submitted for publication, a report for which an individual or collective grant is requested, a clinical or experimental protocol submitted for review by an ethics committee, or a report to be made during an on-site visit.

Persons agreeing to contribute to the peer review process must observe the following rules:

- All information provided must be treated with the utmost confidentiality and may not be shared with any other colleague or copied or retained without explicit permission.
- Under no circumstances may experts use this confidential information for their own benefit until the information has been previously published.
- Reviews should be objective, based on scientific criteria and not on personal opinions.

- Any invitation to participate in a peer review should be declined in the event of any actual or potential conflict of interest (personal relationship, commercial interest, professional colleagues from the same center/university).
- When the advisors convened as experts do not feel that they are sufficiently expert in the subject matter to be critiqued, they should clearly communicate this.

11.GOOD DISSEMINATION PRACTICES

The dissemination of research results to the general public must be done in an honest and understandable manner, avoiding alterations or exaggerations in the impact or importance of the results. The information should be contrasted, truthful and adequately treated for the target audience, using accessible and understandable language that avoids misinterpretations of the results.

It must be possible to clearly identify membership in the organization and, under no circumstances is it possible to adopt positions that could compromise the image of the organization. In the case of public actions in which personal opinions are given, it shall be made clear that they are personal and do not represent the organization.

IdiPAZ staff should rely on the organization and its communication and outreach experts to make interventions on behalf of the institution.

Likewise, all IdiPAZ personnel commit to complying with the dissemination criteria proposed in funded projects, taking charge of ensuring that the organizations involved are correctly mentioned and that the requirements for advertising logos and corporate identity are met.

12.MANAGEMENT OF INDUSTRIAL AND/OR INTELLECTUAL PROPERTY AND EXPLOITATION OF RESULTS

Research staff must respect the intellectual and industrial property policies of IdiPAZ. If the results obtained in research may lead to inventions or applications potentially susceptible to be protected for their commercial interest, they should go as soon as possible to the Innovation Support Unit of IdiPAZ, in order to receive the advice and support necessary for their potential protection and exploitation.

For more information on the management of these rights, as well as their exploitation, please refer to the Regulations on the Protection and Exploitation of Research Results, published on the IdiPAZ website.

13.CONFLICT OF INTEREST

Conflict of interest is understood as all those situations in which the judgment of a person, with respect to the main interest of scientific knowledge, is influenced by a secondary interest, such as economic, academic, political or personal gain.

Being in a conflict-of-interest situation does not inherently present any ethically unacceptable behavior, as long as the objectivity and integrity of the design, development, interpretation and publication of the research has not been compromised.

Attention should be paid to actual, perceived and potential conflicts of interest. How one is perceived to act can influence the attitude of others and discredit the Institute as a whole.

All members of the Institute are expected to recognize when they find themselves in a conflict-of-interest situation, declare it to their superiors and handle it in an ethically correct manner.

When faced with a conflict of interest, researchers should ask themselves, "*Will I feel comfortable when others know or perceive a secondary interest in this matter?*" If the answer is no, they should act responsibly to maintain the highest degree of objectivity by resolving the conflict of interest or by alienating themselves from the affair.

In the case of research financed by for-profit entities, all agreements reached with the sponsor must be included in a contract or agreement expressly stating the financial, intellectual property and industrial agreements. These agreements must be accessible to the institutions and persons with oversight on the matter.

14.IT SECURITY

At IdiPAZ, we abide by Order 1943/2005, of the Regional Minister of Health and Consumer Affairs, which approves the code of good practice for users of computer systems of the Regional Ministry of Health and Consumer Affairs, given the need to ensure the proper use of Information Technology and Communications that the Regional Ministry of Health and Consumer Affairs makes available to those responsible for files and treatments.

This makes it necessary to establish security measures and guidelines of conduct with the objective of facilitating the knowledge of the application of these measures and guidelines to persons with access to personal data in the development of their functions.

15.ETHICAL PRINCIPLES AGAINST FRAUD

Ending corruption and fraud in all its forms is the basis for building just and inclusive institutions and societies.

Our SDG 16 aims to ensure equal access to justice for all, reducing corruption and bribery and creating accountable and transparent institutions.

FIBHULP's anti-corruption policy establishes that all employees of FIBHULP and any third party acting for or on its behalf do not have any interest or commitment that conflicts with or prevents them from performing their work duties in an ethical and proper manner, and that all activities are carried out in strict compliance with such ethical standards and applicable legislation. FIBHULP considers integrity and transparency to be essential and applies a zero-tolerance policy for any corrupt practices.

Furthermore, employees of FIBHULP and of any third party acting on behalf of FIBHULP shall not, under any circumstances, directly or indirectly, contact with or authorize payments of any kind to any of FIBHULP's suppliers for the purpose of obtaining an improper advantage or unduly influencing the making of any decision. The concept of "payments" includes payments or promises of payment, in kind and/or in cash, as well as any other offer of goods or services.

In this way, FIBHULP/IdiPAZ establishes its commitment in the fight against fraud and corruption, reflecting compliance with the code of conduct for action against fraud, corruption and conflicts of interest, which can be found at the following link on the IdiPAZ website: https://www.idipaz.es/ficheros/files/C%C3%B3digo%20de%20conducta%20fraude.pdf

16.FUNCTIONS AND COMPOSITION OF ETHICS COMMITTEES

Research Ethics Committee-CEIm:

The objective of carrying out the purpose of the CEIm is to ensure the protection of the rights, safety and welfare of subjects participating in a clinical study and to provide public assurance in this regard, through an opinion on the study protocol. The composition of this Committee has

been established according to current regulations and can be consulted on the IdiPAZ website: https://www.idipaz.es/PaginaDinamica.aspx?IdPag=38&Lang=ES

Animal Welfare Body

Body authorized by the Directorate General of Environment, Ministry of Environment and Land Management for the evaluation of projects in which experimental animals are used according to RD 53/2013 of February 1. The composition of this body can be consulted on the IdiPAZ website: https://www.idipaz.es/PaginaDinamica.aspx?IdPag=45&Lang=ES

17. REPORTING CHANNEL

Research misconduct, according to the Office of Research Integrity (ORI), is the invention, falsification, plagiarism or other practices that deviate in a significant way from those commonly accepted by the scientific community for the proposal, conduct or presentation of research results.

Some research deviations are as follows:

- Manipulating authorship or denigrating the role of other researchers in publications.
- Republishing substantial portions of one's own previous publications, including translations, without acknowledging or properly citing the original ("self-plagiarism").
- Cite selectively to improve one's own results or to please editors, reviewers, or peers.
- Retain research results.
- Allowing sponsors to compromise independence in the research process or in the presentation of results that introduce bias.
- Unnecessarily expanding the bibliography of a study.
- Maliciously accusing a researcher of misconduct or other wrongdoing.
- Misrepresenting the achievements of the research.
- Exaggerate the importance and practical relevance of the results.
- Inappropriately delaying or hindering the work of other researchers.
- Employing one's own professional experience to encourage breaches of research integrity.
- Ignoring alleged breaches of research integrity by third parties or covering up inappropriate reactions to misconduct or other breaches by institutions.

- Establish publications or provide support for publications that do not comply with the research quality control process ("abusive publications").

As part of IdiPAZ's social responsibility management system and the attention to our stakeholders, we have enabled the following complaint channels:

CODE OF CONDUCT	You can report a breach of the Code of Conduct using the following **form**
CODE OF ETHICS AND GOOD SCIENTIFIC PRACTICES	Anyone having knowledge or well-founded suspicion of a breach of the Code of Ethics and Good Scientific Practice may report it through the e-mail address codigoetico@idipaz.es.
HARASSMENT PROTOCOL	Any aggression or behavior involving discrimination based on sex, sexual orientation or sexual harassment shall be reported to the following e-mail address igualdadydiversidad@idipaz.es.

18. MONITORING OF THE CODE OF ETHICS AND GOOD SCIENTIFIC PRACTICES

In order to monitor compliance with the Code of Ethics and Good Scientific Practice, a subcommittee of the IdiPAZ Internal Scientific Committee will be set up to carry out an annual audit of a project managed by the Institute's Research Foundation.

19. NORMATIVE AND LEGAL FRAME OF REFERENCE

- Law 10/2013 of July 24, 2013, which transposes into Spanish law Directives 2010/84/EU of the European Parliament and of the Council of 15/12/2010 on Pharmacovigilance and 2011/62/EU of the European Parliament and of the Council of 8/06/2011 on the prevention of the entry of counterfeit medicines into the legal supply entry and amends Law 29/2006 of July 26 on guarantees and rational use of medicines and health products, and Law 28/2009 of December 30 which amends the previous one.
- Order SCO 256/2007, of February 5, 2007, which establishes the principles and detailed guidelines for good clinical practice and the requirements for authorizing the manufacture or importation of research medicinal products for human use, as well as Order SCO/362/2008, of February 4, 2008, which amends the previous Order.

- Law 1/1998, of March 2, 1998, on Foundations of the Community of Madrid. In accordance with Article 23, the trustees may contract with the foundation, either on their own behalf or on behalf of a third party, with the prior authorization of the Protectorate of Foundations.
- It is agreed to be performed in accordance with the Principles contained in the Declaration of Helsinki (2013), and in accordance with the ICH (International Conference of Harmonization Guideline) standards for Good Clinical Practice (GCP), as well as with deontological standards and national and international anti-corruption legislation, contained in the OECD Convention adopted on November 21, 1997, also contained in the Foreign Corrupt Practices Act (FCPA) that may be applicable to any or all of the parties to this contract.
- Oviedo Convention on Human Rights and Biomedicine. Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine. Oviedo, April 4, 1997.
- Council of Europe Convention on Human Rights and Biomedicine, ratified by Spain on July 23, 1999.
- UNESCO Universal Declaration on the Human Genome and Human Rights.
- Royal Decree 577/2013 regulating pharmacovigilance of medicinal products for human use.
- Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.
- SAS Order 3470/2009, which publishes the guidelines on observational post-authorization studies for medicinal products for human use and the regulations of the Autonomous Community of Madrid.
- Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data.
- Law 14/2007, of July 3, 2007, on Biomedical Research. Organic Law 3/2018, of December 5, 2018, on Personal Data Protection and guarantee of digital rights.
- REGULATION (EU) 2016/679 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 27 April 2016 on the protection of individuals with regard to the processing of personal data and on the free movement of such data and repealing Directive 95/46/EC (General Data Protection Regulation).

- Charter of Fundamental Rights of the European Union (2000/C364/01).
- Spanish Constitution (art.18.4), relating to the fundamental rights of citizens.
- Royal Decree 1090/2015 of December 4, 2015, which regulates clinical trials with medicinal products, the Ethics Committees for Research with medicinal products and the Spanish Registry of Clinical Studies.
- Amendment of Royal Decree 223/2004, on clinical trials with medicines, for its adaptation to the International Convention on the Rights of Persons with Disabilities, in application of Royal Decree 1276/2011, of September 16, on regulatory adaptation to the International Convention on the Rights of Persons with Disabilities.
- Decree 39/1994, of April 28, 1994, which regulates the competences regarding clinical trials with medicinal products of the Community of Madrid.
- Law 14/2006, of May 26, 2006, on assisted human reproduction techniques.
- Royal Decree 1825/2009, of November 27, 2009, approving the Statute of the National Transplant Organization.
- Royal Decree 2132/2004 of October 29, 2004, which establishes the requirements and procedures to request the development of research projects with stem cells obtained from surplus pre-embryonic stem cells.
- Royal Decree-Law 9/2014, of July 4, establishing the quality and safety standards for the donation, procurement, evaluation, processing, preservation, storage and distribution of human cells and tissues and approving the coordination and operating rules for their use in humans.
- Royal Decree 120/2003, of January 31, 2003, which regulates the requirements for the performance of controlled experiments, for reproductive purposes, of fertilization of previously frozen oocytes or ovarian tissue, related to assisted human reproduction techniques.
- Law 14/2006, of May 26, 2006, on assisted human reproduction techniques.
- Law 30/1979, of October 27, 1979, on organ extraction and transplantation.
- Royal Decree 1716/2011, of November 18, establishing the basic requirements for the authorization and operation of biobanks for biomedical research purposes and the treatment of biological samples of human origin, and regulating the operation and organization of the National Register of Biobanks for biomedical research and Order ECC/1404/2013, of June 28, amending its annex.

- Royal Decree 65/2006, of January 30, 2006, establishing requirements for the import and export of biological samples and Order SAS/3166/2009, of November 16, 2009, amending its annexes.
- Law 32/2007, of November 7, for the care of animals, in their exploitation, transport, experimentation and slaughter and Law 6/2013, of June 11, which amends it.
- Royal Decree 53/2013, of February 1, establishing the basic rules applicable to the protection of animals used in experimentation and other scientific purposes, including teaching.
- Order ECC/566/2015, of March 20, establishing the training requirements to be met by personnel handling animals used, bred or supplied for experimental and other scientific purposes, including teaching.
- Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes.
- Law 9/2003, of April 25, 2003, which establishes the legal regime for the confined use, voluntary release and commercialization of genetically modified organisms, and by Royal Decree 178/2004, of January 30, 2004, which approves the General Regulations for the Development and Implementation of said Law (amended by Chapter V of Royal Decree 367/2010, of March 26, 2010 and by Royal Decree 191/2013, of March 15, 2013).
- Law 41/2002, of November 14, 2002, basic law regulating patient autonomy.
- Law 31/1995, of November 8, 1995, on Occupational Risk Prevention.


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