Instituto de Investigación Sanitaria La Fe

CODE OF ETHICS AND DEONTOLOGY IN CLINICAL AND BIOMEDICAL RESEARCH

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This document has been reviewed and approved by the Research Committee, the different Research Ethics Committees of the Hospital Universitari i Politècnic La Fe (hereinafter acronym), the Integrity Committee of the Instituto de Investigación Sanitaria del Hospital La Fe (hereinafter IIS La Fe).

This code of ethics is also approved by the Management of IIS La Fe, by the Governing Board of IIS La Fe and by the Board of Trustees of IIS La Fe.

It will be distributed to all personnel linked to IIS La Fe (research, teaching and/or support) of the Institution through the IIS La Fe intranet.

This *Code of Ethics and Deontology in Clinical and Biomedical Research replaces the previous Code of Ethical Recommendations in Biomedical Research (CREIB).*

Contents

1. Presentation:

Could we speak of a bioethical code?

The code of ethics and deontology in clinical and biomedical research is a set of recommendations and commitments on the practice of scientific activity, designed to promote the quality of research and innovation carried out in the Institution and to prevent problems of integrity and transparency in the behaviour of workers in this type of context. Their content is complementary to what is already provided for in existing ethical and legal norms.

Research and innovation in health sciences is the driving force that promotes the responsiveness of the healthcare system to the growing needs of society as a whole.

The continuous progress of scientific and technological knowledge in the bio-health field makes it necessary to define and establish a bioethical framework that encompasses the different elements involved: the participation of human beings in such research, the appropriate use of animals in experimentation, the responsible use of biological samples, the appropriate use of personal data and data derived from research, and the responsibility of the work teams.

The interrelation between clinical practice and research gives rise to translational research.

However, an understandable desire for the advancement of knowledge cannot justify any means employed for this purpose. All biomedical research and innovation must take into account the rights of the individual, the rights of other current and future patients, the objectives to be achieved and their future application for the benefit of patients and society, which must be supported at all times by truthful information.

For this reason, and in order to guarantee acceptable ethical behaviour guidelines, compatible with the development and promotion of biomedical research and innovation, the IIS La Fe has elaborated the present bioethical and deontological code in clinical and biomedical research, on the basis of which the activity and research carried out by the Institution's employees must be governed.

2. Basic bioethical principles in clinical and research practice.

- Principles of non-maleficence. "Primum non nocere" ("first do no harm").
- Principles of beneficence. "I will carry out that regimen, which according to my power and discernment will be for the benefit of the sick."
- Principle of autonomy. The right of every competent and informed person to participate actively in making decisions that affect them in any way.
- Principle of fairness. The researher is responsible for allocating available health resources, not only to the individual but also to the population at large or to a group of patients.

Translated to the operation and organisation of IIS-La Fe, IIS-La Fe has an obligation to promulgate the values defined in this code to guide decision-making. IIS-La Fe employees have the responsibility to reflect on these values, articulate them correctly and accept them as normative within the organisation's culture.

3. Research Ethics Officers: Duties and Obligations

All researchers are ethically responsible for their work and must guarantee the quality and integrity of the work they perform.

The ethical obligations of the researcher and support personnel are regulated by the normative principles of scientific practice in human beings, experimental animals, good laboratory practices, and protection of the personal and family privacy of the persons involved in the research. In addition, the Director, Group Leader or Coordinator who holds the position, will have the obligation and responsibility to ensure that the work derived from his/her activity complies with the established ethical criteria. To this end, they must, if necessary:

- Create an open, respectful and equitable work environment for all collaborators, especially protecting the interests of personnel in training.
- Tutor and encourage the intellectual development of young researchers and trainees, facilitating their participation in training courses and scientific meetings related to the subject of their research and other cross-cutting topics of interest and direct relation to their work.
- Meet regularly with their team members to review, evaluate the activity and establish relevant action plans.
- Share with the work team all information related to the activity (projects, Platform functions,...), establishing competencies, responsibilities, duties and obligations among team members.
- Check and supervise the adequacy of resources, control the expenses derived from the activity and authorise the relevant payments.
- In case of joint collaboration, formalise in writing the scope and terms of such joint collaboration between groups from the same centre or from different centres.
- Supervise the publication of the research results, ensuring that the order of the signatories is in accordance with the relevance of their contribution to the project.

- Formalise in writing the distribution of the intellectual and industrial property derived from the joint collaboration when a project foresees the participation of different centres.

In the case of jointly developed projects, and more or less independently, by more than one Group or Center, there will be in each of them a person responsible for overseeing compliance with ethical standards in the development of their respective sub-projects. However, the final responsibility will be of each of the principal investigators, Directors or Group Heads of each line of research of each Group or Center.

These criteria are applicable to the Platforms and to the administrative staff, taking into account their administrative organisation.

The IIS La Fe, through its Ethics and Scientific Committees, will ensure that all the activity (research, technological development, innovation, support, management...) is in accordance with the agreed ethical standards, as an institution, the subsidiary responsible for the derived actions.

In the case of research projects developed at IIS La Fe, the Research Committee will act as guarantor of the veracity and technical quality and may propose the actions it deems appropriate for this purpose; likewise, the Research Ethics Committee will be the regulatory body when deciding on issues affecting the dignity and privacy of individuals.

4. Conducting clinical and biomedical research projects: design and development

Any clinical, biomedical, technological or innovation research must be formulated in writing through a research project.

The project must have an adequate experimental design, including the background, general and specific objectives, methodology, work plan and schedule, available and necessary resources, and the participating team.

All projects must be approved by the corresponding Institutional Committees (Drug Research Ethics Committee, Animal Experimentation Ethics Committee, External Biobanks and Research Collections Ethics Committee and Research Commission); no study can be initiated without express written approval for the project. In some cases, authorisation or classification by the appropriate Regulatory Bodies will also be required. However, there may be projects that, due to their nature, do not require these opinions.

All research projects will require an opinion from the Research Commission.

Likewise, all projects developed within the scope of the IIS La Fe must be formally notified through the channels established by the Institution and must have the following notifications and authorisations:

a) Notification to the person in charge of the research group, platform or clinical-care service

The principal investigator must notify the head of the clinical-care service (Head of Service/Head of Unit) or Platform to which they are assigned of their intention to carry out the project, and obtain their agreement in writing. This agreement shall be presented together with the rest of the documentation for its evaluation. In case of conflict between the researcher/s and their hierarchical superior, the Research Commission will mediate for its solution, recording it in writing through its resolution.

b) Authorisation of the center

Any research or action project that involves the use of proprietary or external health care facilities or equipment, or of any research facility or equipment that is not exclusively for proprietary use, will require the prior approval of the person in charge of the Institution, centre, facility, Platform or equipment to be used.

Regarding Clinical Trials or Post-Authorization Studies, the Authorisation of the Center will be given by the signature of the corresponding Contract. The aforementioned trial or study will have been evaluated by the Ethics Committee for Research with Drugs or the corresponding Research Ethics Committee according to the guidelines set forth in the legislation in force.

In research projects, the IIS La Fe will authorise the start of the study, notifying the Principal Investigator, once it has been approved by the corresponding committees.

Other necessary considerations for the realisation of any research in the Institution are:

Liability Insurance

If necessary, according to current legislation, the studies should be carried out under the cover of a civil liability insurance policy, and the corresponding committees will verify the possible civil liability that the investigators or the Institution may incur during their performance, determining whether such activity would be covered by the Institution's liability insurance, or if so, whether a special and/or additional policy should be taken out, in accordance with current regulations.

Damages to the trial or study subject as a consequence of a low-intervention clinical trial and or observational study are included in the Civil Liability Policy underwritten by the Conselleria de Sanidad Universal, since August 1, 2016.

Statement of sources of financing

The sources of financing for given research must be explicitly declared to the corresponding Committees and the Research Commission at the time of requesting approval, when this is not an explicit provision of services to third parties covered by a contract that regulates it.

All the agreements adopted between a private sponsoring entity and the center on which the person in charge of the research depends, will be included in the corresponding agreement (or agreements). The agreement will necessarily include everything related to the economic considerations directly or indirectly related to the research. These agreements will be accessible to the bodies, committees and persons with responsibilities on the agreed matter.

In the case of Clinical Studies, whether they are clinical trials or observational studies,

the signing of an economic research contract between the IIS La Fe, the Management of the centre, the Promoter and the Investigator will be mandatory, where the amounts that the latter will receive as a consequence of their participation in the trial or study will be reflected.

Rejection of the secret investigation

Under no circumstances should the secrecy of a protocol or part thereof be accepted. This is different from the fact that, for reasons of competitiveness and confidentiality, the temporarily restricted distribution of certain protocols or parts thereof may be agreed upon.

Exceptionally urgent investigations

When safety or public health circumstances require an investigation to begin immediately, especially if it involves humans or experimental animals, the initiation of activities should also be explained in an action protocol, even if it is simplified. Simplified or urgent protocols, as soon as possible, should be reviewed and processed according to the procedures required in the regular protocols.

Protocol and its modifications

The sponsor of a clinical trial or observational study, the principal investigator, or the person delegated by them will be responsible for submitting all the necessary documentation to the corresponding committees and will be obliged to inform of any subsequent modification that essentially affects the nature of the research or action that they intend to develop. This is indispensable when the research or action directly involves people, experimental animals or material of human embryonic origin or if the primary objectives of the research are modified.

4. Regulatory requirements in scientific practice

a) Regulations in biomedical research

- **Human research**

The subject who participates in any research, either actively or with the transfer of biological material, must have clear and precise knowledge about the purpose, possible inconveniences and risks that may arise, the benefits of carrying out such research and, of course, the voluntary nature of the research in which the individual is going to participate. Obtaining the express, specific and written consent of the participants, as well as maintaining the confidentiality of the data, samples and results, is the responsibility of the principal investigator of the project or of their collaborators, who may also foresee the use of the sample for other research projects related to the one initially proposed. It must guarantee the protection of the rights, safety and welfare of the subjects in accordance with the principles of the Declaration of Helsinki, and the credibility of the research results.

Informed Consent signed by the subject/patient or their representative, as the case may be, is an essential requirement for participation in any research project, whether or not the usual healthcare practice provided to the patient is modified, as well as in the case that biological samples of the patient are to be used in research or for the use of their clinical data for research purposes. Consent is formalised through the signature of the patient or his/her legal representative.

In relation to retrospective studies, the Ethics Committees allow the collection of data from the patient's clinical history without the need for consent. It is a requirement that the data identifying the patient must have been dissociated in the study (the patient's personal identification data is preserved and separated from those of a clinical-healthcare nature).

It will be the responsibility of the Principal Investigator (or someone from the group with sufficient competence) to explain, in an adequate manner and in accordance with the age and cultural capacity of the patients likely to be included in the study, all the relevant aspects that they need to know in order to give informed consent, by means of the **Patient Information Sheet**. Likewise, the guarantees for maintaining data confidentiality should be adequately explained, allowing them to make a voluntary and reasoned decision regarding their participation in the study.

In accordance with current legislation, in the case of children[1] or incapacitated persons, the parents or legal guardians will be responsible for giving their consent and signing the Informed Consent.

All protocols involving the participation of both healthy volunteers and patients or based on obtaining clinical information from biological samples from human beings must be written, reviewed and approved by the Drug Research Ethics Committee (**CEIm**), where aspects related to the relevance, methodology and ethics of each particular project are assessed. According to the legal regulations, the corresponding Committee will be the body in charge of ensuring compliance with the legal regulations on drugs or medical devices used in a non-habitual or randomised manner, and will have to approve the conduct of the study. This committee will evaluate, among other things, the validity of the Informed Consent and the Patient Information Sheet.

In case the research involves the study of genome data or requires the use of human embryos, even indirectly, a specific, informed consent that complies with Spanish regulations must be elaborated and presented. Any research protocol that involves the collection, treatment and/or conservation of biological samples for genetic analysis will comply with the specific provisions of the legislation in force. In the case that samples stored in the Biobank of Hospital La Fe are used at any time during the study, they must also be approved by the **External Ethics Committee of Biobanks and Research Collections (CEBCI)**.

All research protocols involving the collection, treatment and/or conservation of biological material of human embryonic origin must have the corresponding permission from the Ministry of Health (Commission of Guarantees for the Donation and Use of Human Cells and Tissues, attached to the Carlos Institute of Health), with the prior approval of the specific reference CEI.

[1] If the child is older than 11, they will be provided with information adapted to their age. In this case, they will also sign the Informed Consent form.

In the case of obtaining inducible stem cell lines (IPs), they must be sent to the Official Cell Line Bank in order to comply with current legislation.

Finally, the research studies in advanced therapy (whether gene therapy, cell therapy or tissue engineering) must comply with the specific legislation. In addition, as they are considered drugs, they must comply with the legislation in force regarding studies with drugs or clinical trials.

When the clinical study foresees the collection of biological samples, the potential participant must be informed of what is foreseen in relation to the future use of the samples. In accordance with Royal Decree 1716/2011, of November 18, 2011, the samples may be destroyed after the end of the study, or incorporated into a collection or an authorised biobank. In the last two cases, the biobank or the person responsible for the collection should be informed, as well as the location where the samples will be kept. This information should also be clearly specified in the project. When the final destination of the samples once the project or clinical trial is finished is a private collection, they should be registered in the ISCIII. There should be a registry of the private collections in the centre and their respective registration communications in the ISCIII. Regardless of the regime in which it is found, RD 1716/2011 applies, so the quality requirements of the aforementioned legislation should be met.

Financial compensation

If there is any possible financial compensation for participation in the study, as well as that received by healthy volunteers, it will be stated. Provided that such compensation does not influence the subject's decision to participate in the study.

Notification and action in case of possible adverse events

The investigator is responsible for collecting and, if appropriate, notifying the sponsor of all adverse events that occur during the clinical trial. This requires that, prior to the start of the trial, the investigator understands what an adverse event is, when it is classified as serious and/or unexpected, how it should be recorded, and when and to whom it should be reported. It should be taken into account that all related serious and unexpected adverse events should be reported immediately to the study sponsor in accordance with current legislation. This information should be clearly reflected in the study protocol.

The reporting period begins once the subject signs the informed consent until, if the protocol does not specify otherwise, 28 days after receiving the last dose of the study medication. Likewise, after this time, the investigator should notify the sponsor of any serious adverse event the subject presents if they consider it related to the study medication. The investigator should follow up on the adverse event until it resolves or stabilises.

When the investigator or the IIS La Fe acts as the study's sponsor, they are also obliged to notify the health authorities, when appropriate, about the adverse events according to the current legislation.

Interferences between the care process and research activity

When the biomedical research or clinical study to be carried out involves patients (inpatients or outpatients) in any of the healthcare institutions dependent on the Health Department to which the Hospital Universitario y Politécnico La Fe is subscribed, the researchers must inform in writing all those responsible for the healthcare process of the nature and type of the project or clinical study in which the patient is included, leaving a record of the same in the patient's clinical record.

In the event of a conflict that may distort the proper development of the care process, the Research Commission or the corresponding Committees, as the case may be, will be in charge of determining the final solution in each case, after evaluating all the reasonable elements of judgment available.

It is also possible that any person involved in research tasks, whether staff of IIS La Fe or an employee of the Valencia "La Fe" Department, may request the Director of IIS La Fe the resolution of a conflict by the Commission for the Resolution of Interpersonal Conflicts of IIS La Fe.

- **Research with experimental animals**

Any research procedure involving animal experimentation must always have the approval of the **Ethical Committee on Animal Experimentation** (CEEA). The purpose of the CEEA is to protect the animals used for experimentation and, in particular, to ensure 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 the procedures is reduced to a minimum, applying, as far as possible, alternative methods. In this way, and in compliance with current legislation, it will be the body responsible for following the Reduction, Refinement and Replacement standard in all experimental procedures carried out with animals.

b) Regulations in scientific practice

- **Good clinical and laboratory practices**

It is necessary for researchers to be trained in Good Clinical Practice (GCP)[2] standards that address international ethical and scientific quality requirements for the design, conduct and reporting of clinical studies involving human subjects.

Non-clinical studies intended for health safety or environmental testing, the results of which are intended for submission to the competent regulatory authorities, should be conducted according to the principles of Good Laboratory Practice.

A Biosafety manual and a Quality Policy must be available in each group and platform.

- **Personnel protection**

To work in the laboratory, it is necessary to follow a series of regulations and recommendations regarding personal habits (prohibition of eating and smoking, keeping the workplace clean and tidy, use of personal protective equipment, etc...) as well as for the handling of products.

Basic research uses a large number of techniques with different physical, chemical and biological means (radioactivity, chemical agents, etc.). In this regard, it is worth mentioning the existence of several technical guides published by the Ministry of Labor based on Royal Decrees for working with biological or chemical agents.

All research personnel must attend the informative/training sessions held by the Prevention Service of Hospital La Fe.

Anyone who needs to handle radioisotopes for research must have the necessary training and the corresponding permit to enter the radioactive facility.

Likewise, any person who performs animal experimentation must have the necessary training and accreditation.

Depending on the type of service/platform, there will be common safety requirements and other specific ones.

- **Waste management and disposal**

The standards established by the Environmental Management System of Hospital La Fe must be complied with regarding the storage, treatment, collection and disposal of waste generated as a result of the research carried out, with the aim of guaranteeing the conservation of the environment and the protection of people.

[2] (In the web page of the Spanish Agency of Medicines you can find the Guide of GOOD CLINICAL PRACTICE STANDARDS, this document is the annotated translation made by AGEMED of the Good Clinical Practice Guide published in the European Commission's web page).

5. Recording, documentation, storage, custody and total or partial transfer of data and samples of biological material.

Protection of personal data. Any research protocol that involves the use of institutional computer files or the creation of databases with information on human beings must guarantee the anonymity of the participants and must be subject to current legislation on data protection (Organic Law 15/1999 of December 13, 1999, on the Protection of Personal Data and Royal Decree 1720/2007, of December 21, 2007, approving the Regulations for the development of Organic Law 15/99).

In order for researchers or collaborators who are not Hospital personnel to have access to the Center's clinical records, they must request access to the "Information Systems of the Valencia La Fe Department" from the Hospital's IT Service in order to carry out the appropriate research protocol. This request must be processed by the Head of the Service that oversees the research.

It is the obligation of the Principal Investigator or the Promoter of the Clinical Trial (as applicable):

- To provide the system for collecting data, records and biological or chemical material resulting from the execution of the research, as well as the plan for their custody and conservation. All data resulting from the experiments or observations of the research should be collected without exception. This information should be permanently recorded in databases, log books or any other relevant format, and in a condition to be reviewed by third parties. The records shall also include changes, errors, negative, unexpected or discordant results, as well as the person performing or observing them.

- Adequate conservation of the records and/or research data collection notebooks for the period of time established by the legislation in force[3]. The necessary means and infrastructure must be provided for the proper custody and conservation of the different documentation and the resulting biological or chemical material. In the case of data recorded on electronic media, a specific plan for backup copies and their physical location must be included.

- All persons who are part of the research team will have access to the information and interpretation of the data obtained. The person responsible for the research will have a single record of the various data collection instruments (notebooks, databases, etc.) and of the custody of samples, access to which must be made available to third parties.

- All primary documentation (data collection notebooks, databases, etc.) and biological or chemical material obtained in the course of research is the property of the center to which the person responsible for the project is attached.

- All primary and original information, as well as biological or chemical material stored as a result of any research project must be kept for at least 10 years from the first publication of the results, except in those cases in which the law allows shorter periods or requires longer periods.

[3] Ranges from 5 years to 15 years for the identification codes of subjects undergoing Clinical Trials.

- The data and materials resulting from research must have public status and be able to be shared by third parties, except for cases in which restrictions derived from their possible future commercialisation have been established. The transfer will require prior knowledge of the applicant's intended use, knowledge of the request by the research team, a transfer protocol with the approval of the person responsible for the research, and the willingness of the applicant to bear any production and shipping costs. The transfer may be limited for reasons of availability, competitiveness or confidentiality. Material or data from individuals should be shared without the possibility of identifying the source subjects; otherwise, specific consent for disclosure by the donors is required. Appropriately codify patient data and/or corresponding biological samples, when required, in order to maintain confidentiality and security to protect the identity of the patients.

- To ensure that clinical samples are not, under any circumstances, the direct or indirect subject of commercial transactions for profit, not being understood as the repercussion of the costs of handling, management and transfer of such samples in accordance with current legislation (Law 14/2007 on Biomedical Research (chapter three) and Royal Decree 1716/2011, of November 18, which establishes the basic requirements for authorisation and operation of biobanks for biomedical research purposes).

6. Declaration of conflict of interest

All researchers (Principal Investigator or Collaborator) must communicate in writing to the Research Committee through the IIS La Fe, all aspects that involve or may involve conflicts of interest in relation to a particular study.

In exchanging or transferring knowledge and technology with private entities, the public interest must always prevail, so agreements must be made with total transparency. In addition, the management of the centers will establish the necessary boundaries to protect the intellectual freedom of their researchers, and avoid disproportionate confidentiality commitments or unjustified restrictions on the publication of the results obtained.

The existence of conflicts of interest affecting the Principal Investigator and/or collaborating researchers, or their relatives, in relation to the research for which they are responsible, must be clearly stated and made public.

The existence of interests or links of any kind with the entities or companies financing a specific research project must be reported to IIS La Fe in order not to compromise the ethical integrity of the research project in question. This communication must be made prior to the start of the research project or clinical trial and must be accompanied by the documentation of the same.

The Research Commission, as well as the corresponding Ethics Committees, will be in charge of settling these conflicts of interest and advising, where appropriate, the non-participation of a given investigator in a research project if, in the opinion of these bodies, their impartiality could be compromised.

In this matter, both researchers and members of the various Ethics Committees must comply with instruction no. 1/2017 of the Conselleria de Sanitat Universal i Salut Publica on "Declaration of interests in relation to health organisations, societies and companies".

According to the aforementioned instruction, in case any person who participates in committees/commissions or groups of experts who exercise actions may influence the decision-making of the Conselleria de Sanitat Universal i Salut Publica, the corresponding institutions or the IIS La Fe must make a written declaration of interests before the start of their actions.

7. Mentoring of research personnel in training

Any person who joins a research group of the entity, through a contract or grant, in order to acquire some training, will be assigned at least one tutor or responsible researcher, who will be responsible for the educational process of the trainee.

The **tutor** will inform IIS La Fe about the research personnel in training under their charge, as well as about their progress, and will set the objectives, advise and guide this personnel so that the formative and chronological expectations are fulfilled according to the initial purposes. To this end, the tutor commits to:

a. Interacting personally and on a regular basis with the trainees under their charge to supervise the tasks entrusted to them and to ensure their fulfilment.
b. Promoting the holding of regular meetings to discuss the progress of assigned tasks and contribute to the scientific and methodological updating of trainees
c. Ensuring the working conditions of personnel undergoing training, as well as their adequate preparation in occupational risk prevention matters
d. Updating the trainees in relation to the existing legal norms affecting scientific practice.

The tutor must be especially diligent with the scientific personnel in training, avoiding their involvement in tasks outside of their training.

8. Publication, protection and dissemination of results

Dissemination and publication of results

Consistent with the principles of academic freedom and intellectual integrity, the Principal Investigator in research projects (including when acting as a Promoter in a clinical study), has the primary authority to make judgments regarding the use and communication of the data and/or any other material generated by his/her original research.

In the preparation of scientific papers to be published, the following rules should be followed:

a) Authorship

- Authorship must be based on a substantial contribution[4] to the conception, design, execution, analysis or interpretation of the results.
- Mere participation in data collection does not justify authorship, although it should be acknowledged in the acknowledgements section. In research in which samples or reports made by third parties are to be used, it is advisable to establish a prior collaboration agreement specifying the aspects of their intellectual contribution to the project.

[4] Each author must have participated sufficiently in the work to be able to accept public responsibility for its content, or have contributed to the preparation of the resulting communications, reports or publications

- The order of appearance of the authors in any publication derived from the research project should be a joint decision of the Principal Investigator and all collaborators. As a general rule, the order of signature will be as follows: a) the first author is the one who has contributed the most to the work, both in the design and in the collection and analysis of the data and has prepared the first draft of the article, b) the last author is the senior person who directs and/or has the maximum responsibility in the project, and c) the other authors may appear in order of importance.
- The principal investigator should openly discuss the possible problems derived from multiple authorship, such as the inclusion of several authors in the same paper or the sequence of their appearance, with their collaborators before starting any research project.
- When no single author can assume responsibility for the entire content of a paper, their specific contribution should be identified separately, except in cases where the editorial rules already regulate this issue.
- Any person linked to the research group who, because of their hierarchical position or employment relationship, requests to be listed as an ex officio author violates academic freedom and commits an act of injustice, if not an abuse of authority. Conversely, the omission of the name of any person who has made proven contributions according to the criteria expressed in the previous section is an act of misappropriation of intellectual property by the rest of the authors.
- All authors must be involved in the development of the drafts of the article by reviewing the content and must read and approve in writing of the final version of the manuscript.
- The edition of memoirs, work or technical reports or any other writing addressed to third parties must always include the list of the authors of the research or investigation, the centre or centres on which they depend, and the grants received in the same terms as if it were a scientific publication or a patent.
- In the preparation of the personnel's Curriculum Vitae, the author is responsible for the veracity of its content. In this sense, they must always sign the curriculum vitae document provided. In the case of a collective Curriculum Vitae, it is sufficient for it to be signed by the person responsible for the application.

b) Content

- It is unethical to submit for publication as one's own, the work done in whole or in part by another person/s (plagiarism or misappropriation), to falsify data or results of the research process and to suppress or alter information relevant to the understanding of the project or its results (scientific fraud).
- The content, place and time of disclosure should be mutually agreed upon by the different groups and centres participating in the project.
- It is ethically unacceptable to publish the same work (redundant or repeated publication) or part of the same work (partial publication) in more than one biomedical journal, except when the nature of the work justifies it (compilation review).
- It can only be declared that the work has the approval of the Research Ethics Committee, when the research object of publication has been carried out under the premises determined by the original approved protocol.
- All publications must state the name of the institution(s) where the research work was carried out.
- The results of the research project should preferably be published in Accredited Scientific Journals, and the scientific results should not be published in a premature or sensationalist manner.
- It is necessary to publish negative results or results different from the expectations foreseen in the research project.

- Failure to publish the results of a research study or excessive delay may constitute serious misconduct for misuse of resources. Publication of the results of clinical studies in which one participates is an ethical and legal imperative.
- Both in publications and patent or utility model files, it is necessary to include the reference of all work directly related to the research and, at the same time, avoid unjustified or honorific references. The reference to third-party works must sufficiently acknowledge their merit.

c) Deadlines

Communication and dissemination of research results to the media prior to their acceptance for publication in Scientific Journals or Conferences is not considered acceptable.

Prior or premature dissemination or publication of results can only be justified exceptionally for public health reasons. In these cases, the authors must ensure that the results will be reviewed in parallel, as a matter of urgency, by a scientific publisher. Likewise, the editors of the journals in which the results are to be definitively published should be informed of the scope of the previous communication.

Both in communications to congresses or other types of previous presentations and in the definitive publication of results, the following must be explicitly stated: a) the institutions or centres to which the authors belong or belonged and the place where the research was carried out, b) the independent ethics committees that supervised the research protocol, as well as the specific permissions obtained, and c) the grants, financial aid or sponsorship received.

The IIS La Fe, after the accredited publication of these results, through its Communication Area, will collaborate in the dissemination of the relevant scientific findings to society. Such dissemination will be carried out through all available social media (written and on-line press, radio, television and others), in an objective manner and free of unjustified sensationalism.

The results of a clinical trial can be made public in the Program of Clinical Studies of Medicines and Medical Devices in the Valencian Community (PECME) website of the Regional Ministry of Health (Conselleria de Sanitat).

Protection of results (Intellectual property)

If the results obtained in a research project may lead to inventions or applications potentially susceptible to be protected due to their commercial interest, the person responsible for the project has the obligation to communicate this to the IIS La Fe Management through the Innovation Area, and prudently manage the publication of the results in scientific journals taking into account this possibility.

- Researchers who have participated in a project, and collaborated in a real way in it, have the right to the recognition of the intellectual property (inventorship) of their findings in a shared manner with all those who contributed to it.
- The research protocols, records and original data collection notebooks are the property of the institutions where the research has been developed, being the researchers, and in a subsidiary way, the Principal Investigator, responsible for their custody for the times and periods established by the legislation in force.
- The new materials generated in the course of a research project (new cell lines, transgenic animals, antibodies, etc.), are the intellectual property of the researchers (authorship) and industrial property of the Institution. They may be transferred or licensed to third parties with the explicit agreement of the parties. The researcher must inform IIS La Fe of their intention to cede these materials to third parties, and the latter must ensure that a cession agreement is formalised that safeguards the interests of the researcher and the Institution.
- The human material obtained (sera, biopsies, tissues, etc.) are the property of the institution and the IIS La Fe, which, by virtue of its Framework Agreement, will be responsible for establishing the rules that make possible its access to third parties, with the knowledge of the Responsible Investigator, following the recommendations of the relevant Ethics Committee.

- When the research personnel participating in a project promoted by the industry contributes essentially to its design and execution, the necessary agreements will be established with the promoting entity to share the corresponding industrial and intellectual property. In these cases, if the sponsor so requests, in order to properly ensure the protection of inventions or developments derived from the trial or study, the Principal Investigator agrees to delay the submission of any proposed publication for a period not exceeding 6 months.

- When the research group offers a technical service, or the research personnel participates exclusively in the collection of data of a protocol developed by third parties, the conditions of communication and publication of the results obtained will be established by mutual agreement with the sponsoring entity, always taking into account the precepts foreseen in the previous section.

9. Values of the Institution

The IIS La Fe manages the scientific policy and research linked to the Hospital La Fe de Valencia.

We are a multidisciplinary team with a service calling whose **mission** is to generate biomedical, clinical and health knowledge, promoting its effective translation to improve the quality of life of patients and society, leading cutting-edge biomedical research, and committed to cooperation, talent and innovation.

The **values** that we want to promote from IIS La Fe are:

- Integrity
- Calling for Service
- Excellence
- Transparency
- Innovation
- Sustainability

In order to promote the Institute's values, there are specific committees for each of the values.

10. Dispute resolution procedure

- All IIS La Fe staff and the Valencia La Fe Health Department staff, attached to the Research Area, are entitled to adequate protection in terms of safety and health at work and under the consideration that all forms of harassment at work constitute a psychosocial risk. As part of their preventive obligations, both IIS La Fe and the Valencia La Fe Health Department must contribute to identifying and eliminating such matters.

- Considering violence at work as an emerging risk in the workplace, the IIS La Fe and the Valencia La Fe Health Department are committed to allocating human and material resources, as well as organisational measures necessary to prevent and address, where appropriate, the consequences of this type of behavior.

- In order to make it possible to act against any type of conduct that could be classified as harassment, the Management of IIS La Fe and the Management of the Research Area of the Valencia La Fe Health Department have developed a procedure for the prevention and resolution of conflicts regarding violence in the workplace, in which the rights of those affected parties will be safeguarded in the necessary context of prudence and confidentiality.

- The "Commission for the Resolution of Interpersonal Conflicts in the Research Area", hereinafter "Commission", will have the mission of analysing and investigating the situations that arise in accordance with the provisions of this procedure.

11. Responsible use of resources and facilities

- All IIS La Fe staff and the Valencia La Fe Health Department staff, attached to the Research Area must protect the assets of IIS La Fe and the hospital or third parties, such as users and suppliers, which are in the centre's facilities. This includes not only misuse but also theft and uses outside the professional field.

- The aforementioned personnel must take care of the facilities, equipment and spaces, making rational use of the available resources such as materials, water, light, etc. It is not allowed to remove, eliminate or destroy assets of the IIS La Fe or the hospital except those authorised by donation, transfer or expiration.

- All personnel of the IIS La Fe and the Valencia La Fe Health Department personnel assigned to the Research Area, must inform their superiors of situations of deterioration of the facilities, equipment and spaces.

- The aforementioned personnel must comply with all applicable environmental regulations and other requirements that the organisation subscribes to in relation to the use of the facilities.

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12. Monitoring and compliance with the code of ethics

- It is the obligation of all IIS La Fe employees and the Valencia La Fe Health Department staff, attached to the Research Area, to know and respect the code of ethics.
- If, in the performance of work any employee has doubts about the conduct to be adopted in a situation, they must consult their manager or corresponding tutor before taking any action.
- Any employee or collaborator may propose any change to the content of the code of ethics by communicating it through their manager or corresponding tutor, which will be subsequently reviewed by the Integrity Committee of the Hospital La Fe Health Research Institute before proceeding with its processing.
- To ensure compliance with the code of ethics, internal and external audits may be carried out on Corporate Social Responsibility issues.

13. Applicable legal and ethical regulations

- UNESCO Universal Declaration on the Genome and Human Rights of November 11, 1997.
- Council of Europe Convention of April 4, 1997, on Human Rights and Biomedicine and its Additional Protocol of January 12, 1998, prohibiting the cloning of human beings.
- Nuremberg Code. Nuremberg International Tribunal 1946
- Universal Convention on Human Rights and Biomedicine. Council of Europe 1996.
- Declaration of Helsinki. World Medical Association, 1964-2013
- Asturias Convention. Council of Europe, 1997.
- The Spanish Constitution of 1978 (especially its articles relating to the value of freedom, real and effective freedom and equality, the dignity of the person, inviolable rights and interpretation of rights and freedoms, the right to life, physical and moral integrity, personal freedom, the right to health protection, and the defense of consumers and users).
- Law 14/2007 of July 4, 2007, on Biomedical Research.
- Royal Decree 1716/2011 Biobanks.
- Royal Legislative Decree 1/2015 of July 24, 2015, approving the revised text of the Law on Guarantees and Rational Use of Medicines and Medical Devices.
- Law 41/2002, of November 14, 2002, basic law regulating patient autonomy and rights and obligations regarding clinical information and documentation.

- Organic Law 15/1999 of December 13, 1999, on the Protection of Personal Data (BOE December 14; 298: 43088-43099).
- Royal Decree 1720/2007, of December 21, 2007, approving the Regulations for the development of Organic Law 15/99.
- Law 31/1995 of November 8, 1995, on the Prevention of Occupational Risks (BOE no 269 of November 10).
- Royal Decree 1090/2015, of December 4, regulating clinical trials with drugs, the Ethics Committees for Research with drugs and the Spanish Registry of Clinical Studies (BOE no. 307, of December 24).
- COUNCIL DIRECTIVE 93/42/EEC of June 14, 1993 on medical devices.
- Royal Decree 1591/2009, of October 16, 2009, which regulates medical devices (BOE no.268, of November 6).
- Royal Decree 1616/2009, of October 26, 2009, which regulates active implantable medical devices (BOE No. 268, of November 6).
- Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.
- Instruction document of the Spanish Agency for Medicines and Health Products for the conduct of clinical trials in Spain (Version dated May 9, 2016).
- Regulation (EC) 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products.
- Royal Decree 477/2014, of June 13, regulating the authorisation of non-industrially manufactured advanced therapy medicinal products.
- Royal Decree 1527/2010, of November 15, 2010, regulating the Commission of Guarantees for the Donation and Use of Human Cells and Tissues and the Registry of Research Projects.
- 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 rules of coordination and operation for their use in humans.
- 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.
- 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.
- Royal Decree 665/1997, of May 12, 1997, on the protection of workers against risks related to exposure to carcinogenic agents during work.
- Royal Decree 951/1997, of June 20, 1997, approving the General Regulations for the Development and Execution of Law 15/1994, of June 3, 1994, which establishes the legal regime for the confined use, voluntary release and commercialisation of genetically modified organisms, in order to prevent risks to human health and the environment.
- Royal Decree 178/2004, of January 30, 2004, approving the General Regulations for the development and execution of Law 9/2003, of April 25, 2003, which establishes the legal regime for the confined use, voluntary release and commercialisation of genetically modified organisms.
- Royal Decree 1369/2000, of July 19, 2000, amending Royal Decree 822/1993, of May 28, 1993, which establishes the principles of good laboratory practices and their application in the performance of non-clinical studies on chemical substances and products.