



# The Ethics Charter of the Institut Pasteur

*October 2009*

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## *Preamble*

The Institut Pasteur wished to endow itself with an ethics charter that embodies the principles to which it adheres.

The Institut Pasteur seeks to affirm by the present charter its commitment to perform research according to the ethics rules recognised by the international community: good research cannot be conducted without ethics rules.

The Institut Pasteur is at the interface of research, public health, medicine, teaching and training, and sick patients. Research undertaken at the Institut Pasteur extends to many different fields, in both basic research and its applications. The Institut Pasteur and the institutes in the International Network are located in countries with varying ethics rules. Nevertheless, this diversity is countered by the unifying nature of the Pasteurian ideals that the Institut Pasteur would like to formalise in this charter. This charter aims to set forth the rules to which the Institut Pasteur adheres.

While maintaining the importance of intellectual freedom in scientific research and the numerous benefits bestowed upon society by scientific progress, the Institut Pasteur wishes to reaffirm the necessity of inscribing such research and the resulting progress in a rigorous ethical framework that contributes to the enforcement of ethics rules for research on living subjects and to the respect of human dignity and human rights.

The present charter was drawn up by the Ethical Vigilance Committee. It is published under the authority of the **President of the Institut Pasteur** and constitutes an ensemble of rules and reference texts for the Institut Pasteur and all persons working there, whatever the nature of their relationship to the organisation, and who are henceforth designated as "Personnel." The charter will be re-examined and updated every year to take into account the evolution of the national and international reference texts and the emergence of new ethical questions raised by research. All Personnel must respect the present charter.

## 1 Scope

While relying upon the major national and international texts in the field of ethics to which the Institut Pasteur is committed, this charter aims to set out rules to be applied to the activities of the Institut Pasteur. All research on human beings is inscribed in the framework of the ethics rules established by the international community, including most notably the Declaration of Helsinki in its current form,<sup>1</sup> the guidelines of the CIOMS,<sup>2</sup> UNESCO's Universal Declaration on Bioethics and Human Rights,<sup>3</sup> and the Oviedo Convention and its additional protocol regarding biomedical research.<sup>4</sup> Furthermore, all research must conform to the laws and regulations in effect in the country where it is conducted.\* This charter also aims to remind Personnel of the legal and regulatory documents that various internal services must maintain to ensure that Personnel remain well informed. These legal and regulatory texts are accessible on the Institut Pasteur internal website. This charter does not aim to establish administrative procedures. The Institut Pasteur has already established a number of relevant administrative bodies. Among these, three play a specific role regarding ethical matters and professional ethics:

First, the **Ethical Vigilance Committee** (CVE), directly attached to the President of the Institut Pasteur, may address or be asked to address any ethical questions that arise.

Furthermore, the Institut Pasteur has created a **Code of Professional Ethics** (CDS)<sup>5</sup> and a **Deontology Committee** (CVDC) devoted to professional ethics. The CDS aims to set clear rules of good conduct within teams and promotes the respect of persons and their scientific work. The CVDC can call upon the CVE to treat an ethical question, and the CVE can direct Personnel to the CVDC.

Lastly, the **Clinical Research Committee** (CoRC), operating under the authority of the Department of Medical Affairs, is responsible for all projects dealing with human subjects, including personal data, human biological samples and research on human subjects. The CoRC emits an opinion preceding the authorisation to begin research by the Department of Medical Affairs. This committee benefits from its **accreditation as an Institutional Review Board** (IRB) by the United States federal authorities. This accreditation qualifies it as an "ethics review committee" from the standpoint of international journals and American research institutes.

The Institut Pasteur in the present charter declares that the activities it supports or those undertaken by its Personnel are founded on the international reference texts, and is committed to respect the principles and obligations recommended therein.

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\* See chapter 2

## 2 Research on human subjects

The Personnel of the Institut Pasteur performs research on human subjects, including healthy volunteers and/or sick persons, as well as research using human biological samples and research using personal data. All research must avoid discrimination and/or stigmatisation of persons, families, and/or groups of persons.

The health of the patient must always be the primary concern of his or her doctor and of scientific researchers, whether or not they are medically qualified. This point is made explicit in article L.1121-2 of the French Code of Public Health, which states, **“The interests of persons participating in biomedical research must always take precedence over the interests of science and society.”** In this regard, the benefits obtained through research must be evaluated with respect to the risks assumed by all persons concerned, irrespective of whether they are research subjects in good or bad health or scientific, medical, or paramedical personnel.

The Institut Pasteur has several specialised laboratories in fields such as virology, bacteriology, parasitology, mycology, structural and cellular biology, neuroscience, development biology, genetics, cancerology, immunology, etc., and can contribute to the constant improvement of techniques for clinical diagnostics and epidemiology.

All members of Institut Pasteur Personnel wishing to undertake research on human subjects must contact the Clinical Research Department (PIRC), which will orient and advise researchers,<sup>6</sup> particularly with respect to applicable regulations, ethics rules and procedures to be followed according to the type of research. An authorisation from the Department of

Medical Affairs on behalf of the President, based on an opinion expressed by the CoRC, is indispensable before beginning any research using human subjects and/or human biological samples and/or personal data at the Institut Pasteur or involving its Personnel. These steps are summarised in an annexed schema.

For research on human subjects, legal and regulatory texts, as well as good practices, have the protection of persons as their primary goal. Thus, research including physical interventions on human beings may not commence without obtaining the free, informed, and express consent of the subject involved. In cases where the subject is unable to give consent due to his or her age or physical or mental state, more restrictive rules provide proper protection for the individual. However, the non-opposition of a duly informed person is often sufficient to permit secondary use of a biological sample for which consent was already given before sample was taken.

Under these conditions, the Institut Pasteur pledges that all research protocols involving human subjects that it promotes and/or finances, or that involve its Personnel, must be favourably vetted by an ethics review committee such as a committee for the protection of persons (CPP) and by the proper authorities as required by law before they are applied. When it assumes the role of sponsor of research involving human subjects and in submitting protocols to ethics committees, the Institut Pasteur will re-state its total commitment to the principles enounced in the present charter.

## *Research using human biological samples*

The Institut Pasteur has created a **Platform for Clinical Investigation and Access to Biological Resources** (ICAReB).<sup>7</sup> This structure provides Personnel with guidance on legislative and regulatory directives applicable to research using human biological samples. These texts protect the person from whom samples were taken, with respect to the inventory of samples maintained by health and research authorities, and including the protection of Personnel working on these samples. French law and regulatory statutes impose strict procedures for informing patients and obtaining their consent or non-opposition.<sup>8</sup> Thus, a sample may not be used for research purposes if the person from whom the sample was gathered is expressly opposed to its use for this purpose.

Research studies using **human stem cells** of embryonic or foetal origin must adhere strictly to legislation and regulatory statutes in the countries where they take place,<sup>9</sup> as well as those of the country of origin if different from the country where the research is undertaken.

Under no circumstances shall research promoted or supported by the Institut Pasteur or conducted by its Personnel or by the institutes of the Institut Pasteur International Network include the use of **embryos created solely for the purposes of research**.

Since **samples may be transferred** between French and non-French institutions, the Institut Pasteur would like to draw the attention of Personnel to the absolute necessity of contacting the ICAReB Platform when such transfers are envisaged. It is the duty of the Institut Pasteur to ensure proper respect of the intentions of the person from whom the sample was taken (notably by preserving anonymity), the interests of research teams, the various legislative and regulatory statutes, as well as to verify the intentions of the recipient(s). A contractual document between both parties to the transfer must be signed.

**The examination of the genetic characteristics of a person** must be preceded by the acquisition of his or her consent as strictly defined in French law, with which Personnel must duly comply. Moreover, the Institut Pasteur would like to draw the attention of the Personnel to the ethical questions that often arise in the course of research on genetic predispositions and vulnerabilities. The French National Ethics Advisory Committee for the Life Sciences and Health<sup>10</sup> (CCNE) has expressed several opinions on this subject to which the Institut Pasteur invites Personnel to refer.

## *Research using personal data*

Personal data are data for which a physical person can be identified, either directly or indirectly.

All personal data originate from a person. The collection, conservation and use of personal data for the purposes of research must respect this person and his or her dignity and integrity. Appropriate measures must be taken to protect him or her against discrimination or stigmatisation. As personal data may be the source of discrimination and/or stigmatisation, their collection, conservation and use must be regulated by specific protective measures.

The **possession of computer files containing personal data** (even if the files contain only the first and last initials or any other reversible code) must be declared and authorisation requested from the French data protection authority (CNIL). These files may not be exchanged with collaborators without prior anonymisation unless specific authorisation is obtained from the CNIL. Given the administrative delays, Personnel must begin the necessary steps at least six months prior to the creation of any such files, including soliciting the involvement of the PIRC when data pertain to its field of expertise, and in all cases soliciting the **Legal Department** and the **Department of Technical and Electronic Resources** regarding the appropriate information security measures.

## *Clinical trials*

The Institut Pasteur aims to fight disease and notably infectious, genetic, and immune diseases. The Institut Pasteur also conducts numerous research studies on cancer, neuroscience, and emerging diseases. The Institut Pasteur is committed to participating in the development of diagnostic tools, medicines, and other products that may be potentially useful in the field of health.

The Institut Pasteur participates in or sponsors certain clinical trials with the aim of providing an effective interface between basic and clinical research, notably in the areas of infectious and neurological diseases and cancerous pathologies.

Regarding **vaccine trials**, the Institut Pasteur is associated with the notion of preventive or therapeutic vaccines as an exemplar of the nexus between basic and clinical research. The Institut Pasteur is first and foremost involved in non-clinical vaccine research and in the early stages of preclinical and clinical research (Phase I and early Phase II). The Institut Pasteur also has a vaccine strategy working group that aims to define future orientations with regard to scientific and financial concerns, as well as intellectual property, promotion, and judicial responsibility for each candidate vaccine under development. The Institut Pasteur has also created a special partnership with the Pasteur/Cochin Clinical Investigation Centre (CIC), which allows it to hand off its involvement in the later phases of development, including the evaluation of vaccine efficacy and safety in patients.

The Department of Medical Affairs and the PIRC are responsible for clinical trials at the Institut Pasteur.

From a regulatory standpoint, the execution of all steps in a clinical trial must match a precise framework<sup>11</sup> at both the national<sup>12</sup> and international<sup>13</sup> levels.

From an ethical standpoint, clinical trials raise the same issues as those pertaining generally to research on human subjects. Two particular aspects can be mentioned:

- Because of the pathologies concerned, research necessarily involves populations possessing social and cultural specificities that must be taken into account in considering ethical issues.\*
- Partnerships and financing tools developed by the Institut Pasteur must facilitate access to treatment and tests approved for use in developing countries, notably via the involvement of the institutes in the Institut Pasteur International Network.\*

The Institut Pasteur is not accredited as a pharmaceutical establishment by the French Health Products Safety Agency (AFSSAPS) and is therefore not authorised to produce, receive or transport any medical product for use or testing in a clinical trial. In the context of partnerships that it may establish, the Institut Pasteur must therefore ensure compliance with legislative and regulatory statutes concerning the conditions for production, transport, and testing of these products.

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\* See the following sub-section

### *International research, notably in developing countries*

The **Institut Pasteur International Network** brings together more than thirty institutes and centres, united by the same missions, the same culture and the same values. The activities undertaken by the Institut Pasteur in developing countries may include research as well as service delivery, notably diagnostic services and vaccination, whether provided in a medical or research setting.

Research undertaken by the Institut Pasteur and/or its Personnel is essentially of two types: research on samples of human origin and clinical research. As was indicated in the preamble to the present chapter, all research protocols must be submitted to national health authorities and either a national ethics committee or, if such a committee does not exist in the country where the research is undertaken, an ad hoc committee. If the Institut Pasteur and/or its Personnel are participants in the project, the protocol must also be approved by a French ethics review committee such as the approved IRB within the CoRC at the Institut Pasteur.

National legislation of host countries for institutes in the International Network is not always in accordance with the major international reference texts cited in Chapter 1, nor with the present charter. In the case of a major contradiction, scientists may consult a ethics review committee. The Institut Pasteur Clinical Research Committee (CoRC) can help determine the procedure to be followed.

The line between research and other activities in the service of health, especially diagnostic services and vaccination, is tenuous and may fluctuate in countries where health systems are unable to provide care for all sick persons. The Institut Pasteur is a research institute that, as such, cannot substitute for national health systems in countries where it undertakes research projects. However, the Institut Pasteur remains committed to inscribing its action within the defined health needs of populations in collaboration with health authorities, particularly regarding access to treatments, skill transfers in the field of translational research, and the training of local personnel.

Research that is initiated in a developing country by one or more scientists from an industrialised country on behalf of the Institut Pasteur must be developed in partnership with scientists from the country where it will take place and must aim to fight disease and promote the health of populations.

The ethics procedures of the Institut Pasteur take into account the specificities of research in developing countries. These specificities call for special protections for persons living in cultural and political contexts with limited resources and heterogeneous systems for medical care. These procedures are essential where legislation does not provide sufficient personal protection.

The Institut Pasteur is committed to undertaking research only when it is in the interest of the population of the country where it takes place and to increasing its partners' awareness so that access to treatment is made possible. Links with various partners (notably NGOs, financing organisms, health networks, health authorities, and industrial laboratories) must be created ahead of time to guarantee access to the best possible care throughout the course of the study and when it terminates.

The Institut Pasteur reminds Personnel of their duty to return information and results to patients, partners, and authorities with whom research is undertaken in developing countries.

Research including diagnostic and prognostic activities without the provision of subsequent care for patients is ethically unacceptable. In these cases, patients must be oriented toward appropriate structures for medical care and researchers must ensure that such care can be provided, for example in the framework of partnerships.

Given these constraints, Personnel who are solicited to participate in a research project that they consider to be in contradiction with these ethics rules must inform the CVE.

### 3 Expertise activities

The expertise that the Institut Pasteur has historically provided in certain fields is now delegated to **National Reference Centres** (CNR) for diseases caused by bacteria, viruses, parasites, or fungi. The missions of the CNRs include providing expertise on microorganisms and the diseases they

cause, the development of new techniques, and microbiological and epidemiological surveillance. As such, the CNRs must store biological samples, make them available to the scientific community according to established criteria, and preserve the corresponding clinical and epidemiological data.

The creation of a database of clinical data necessitates the same precautions as those set forth in Chapter 2 of the present charter. While awaiting the validation of a consensual and official procedure with the French Public Health Institute (InVS), the heads of CNRs must be aware that the use of strains sent by their correspondents will be governed by an accord between the Institut Pasteur and the laboratory whence the sample originates, which stipulates the rules for publication and the transfer and use of strains, including patient's non-opposition. Transfer to any third party of biological

samples collected in the course of activities by the CNR must be the subject of an agreement explicitly precluding re-transfer and/or use for commercial purposes and that sets out the limits of the collaboration. Biological samples must always be transferred with a code preserving the anonymity of patients. Documents corresponding to this activity are currently under preparation. In case of doubt, the heads of CNRs are thus invited to contact the Legal Department of the Institut Pasteur.

## 4 Genetically modified organisms

A "genetically modified organism" (GMO) is defined as any organism (animal, vegetable, cellular, bacterial, viral, parasitic or fungal) whose genetic material has been modified other than by natural mutations.

Recourse to the techniques of genetic engineering has been accompanied by the creation of a prescriptive regulatory framework on the security of GMOs, including procedures for the evaluation of biological risks, confinement measures, and operating procedures designed to protect humans and their environment. **Official approval is required**. The High Council on Biotechnologies, which incorporates the Commission on Genetic Engineering (CGG), evaluates the risks incurred by GMOs (including in kits for medical analysis that use GMO components) and the procedures used to obtain and work with them. Basing itself on European regulations and French law, this Council proposes a classification of GMOs by group according

the degree of pathogenicity, as well as laying out the confinement measures necessary to minimise the risks presented by GMOs in general and during their construction.<sup>14</sup> At the Institut Pasteur, the **Department of Hygiene, Security, Quality Control, the Environment and Sustainable Development** coordinates the use of GMOs.

At the Institut Pasteur, the manipulation of GMOs conforms to rules on confinement. This includes all operations during the course of which organisms are genetically modified or in which GMMs (genetically modified microorganisms) are cultivated, stored, destroyed, eliminated, or used in any other manner. Specific confinement measures must be taken to limit the contact of these microorganisms with all other organisms and with the environment so as to ensure the safety of the latter. According to the law, the notion of confinement extends to the use of genetically modified animals and plants in specialised facilities or green houses.

Manipulations of GMOs must adhere to the appropriate conditions of confinement. Only a thorough and complete application of all security norms can provide real protection of experimenters, the environment, and the experimental biological material.

For all questions regarding GMOs, members of Personnel should refer to the Department of Hygiene, Security, Quality Control, the Environment and Sustainable Development. All Personnel involved must inform themselves of the regulations in effect and strictly adhere to them; they must also declare all cases of use, import or export of GMOs.<sup>15</sup>

## 5 Fundraising

The Institut Pasteur is a private state-approved non-profit foundation that, for its operating costs, depends in part on public generosity. Thus, the Institut Pasteur employs fundraising to support its activities.

Furthermore and above all, the Institut Pasteur is an institution dedicated to research, public health, and the prevention of diseases. Thus, the Institut

## 6 Intellectual property and its promotion

The question of the **promotion and exploitation of inventions** is particularly important. Thus, a co-ordinator of these matters is present in each scientific department in order to facilitate steps taken by Personnel. As the Institut Pasteur also encourages members of Personnel to publish their results, it does not wish to delay the publication of articles but simply to draw attention to the possibility and potential benefits of exploiting results.

Third parties to whom GMOs are transferred must comply with rules in effect at the Institut Pasteur and do so in a contractual transfer agreement called a "**Material Transfer Agreement**" (MTA) corresponding to the material to be transferred, for which the **Department for Research Applications and Industrial Relations** is responsible. Instructions are available on the website of the Department of Hygiene, Security, Quality Control, the Environment and Sustainable Development.

Pasteur refuses to associate these activities and its sources of funding with structures whose products are medically recognised as being harmful to health.

The President of the Institut Pasteur may solicit an opinion from the CVE on the appropriateness of accepting funds from certain persons or parties.

Regarding the development of health-related products such as diagnostic tests or any other inventions that could be produced or fabricated for generalised use, the absence of a patent may preclude an indispensable partnership with an industrial partner, preventing the invention from being produced and, therefore, from being used in the field of health and/or healthcare.

In the case of existing agreements with industrial partners for the development of Pasteurian inventions, the Institut Pasteur attaches particular importance to clauses relative to access to these inventions in developing countries.

Research activities and the expertise of Personnel can have financial implications that raise ethical questions. In particular, operations including the physical or legal transfer or purchase of biological samples, as well as the exploitation of knowledge and discoveries that may follow, must be subject to heightened vigilance with respect to the principle of the non-commercialisation of the human body.<sup>16</sup> The promotion and exploitation of knowledge and discoveries must take into account the work of all research teams and platforms involved.

## 7 Communication

It is the duty of scientists to communicate the results of their research in a format that is intelligible by the greatest possible number of people. As a foundation recognised for its contributions to the public good, the Institut Pasteur has a **duty to inform** its partners (medical and scientific bodies, universities, teaching bodies, businesses), as well as public authorities, donors, and the general public. An internal text sets out rules for communicating with the media.<sup>17</sup>

As noted by the CCNE, the transmission of scientific information via the media always entails a risk of deforming its meaning.<sup>18</sup> Moreover, vulgarisation – that is, translation into comprehensible terms for non-specialists – poses problems regarding presentation and commentary.

Furthermore, Personnel who possess specific competences are frequently solicited by industrial firms to provide purely intellectual services in the context of a **consulting contract**. To participate in such activities, Personnel must request permission from the President. Because of the potential for conflicts of interest, particular attention will be paid in situations where Personnel are solicited by the same partner both for a personal contract and an expertise activity involving a laboratory at the Institut Pasteur.

As such, Personnel are reminded of the following recommendations: authorship of papers must be apportioned with respect to the equitable contribution of each author and the accepted rules of professional ethics within the international community; results must first be accepted for publication in a peer-reviewed journal before being diffused to the greater public; the incentive to publish must not incite teams to neglect their obligations with respect to ethics rules and professional ethics; neither must institutional policies regarding communication engender neglect of this type. Personnel must not take advantage of the lack of scientific understanding in the media to publish results without an in-depth examination by knowledgeable persons, nor must they create false hope or unnecessarily discourage sick people.

## 8 Confidentiality and protection of sensitive information

The Institut Pasteur considers it important that users of computers and other electronic devices understand both the value of electronically stored data and the risks that are potentially incurred with respect to the storage and diffusion of such data, such as the pirating of files, the introduction of viruses, or other negligent or harmful activities.

In order to protect the integrity of its computer systems and more particularly the data stored therein, the Institut Pasteur has created an Information Security Charter as well as procedures on information security accessible by all Personnel on the internal website.<sup>19</sup> The Institut Pasteur would like to draw the attention of Personnel to the risks engendered by the transport of data, whether on a laptop computer, a USB key, via messaging systems or by any other means.

Regarding specific kinds of data such as personal biomedical data and data stored by the National Reference Centres associated with the Institut Pasteur, the Department of Technical and Electronic Resources has put in place specific computer

programs. All Personnel are asked to recall that only data that are strictly necessary to the task at hand, whether regarding patients or healthy volunteers, must be stored electronically and anonymity must be strictly maintained. Electronic measures must be taken to achieve these goals within the framework of the law on information security and liberties.<sup>20</sup> In particular, the storage of such files, their use and above all their distribution must be declared to the CNIL.\*

The diffusion of sensitive information to third parties may constitute a violation of confidentiality agreements to which the Institut Pasteur adheres with respect to third parties. It is therefore essential to ensure the protection of sensitive information and to examine scrupulously situations where the diffusion of such information might be envisaged. Before communicating sensitive information to a third party, the Legal Department must be consulted in order to determine whether a confidentiality agreement or any other specific protective measure is necessary.

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\* See chapter 2

## 9 Hygiene and security

Respect of the rules on hygiene and security is obligatory for all Personnel, whether they work on the Paris campus or in one of the institutes of the Institut Pasteur International Network. These rules are presented to all new employees regardless of

their status during an obligatory two-day training session (one-half day for employees staying less than 3 months) organised by the **Department of Hygiene, Security, Quality Control, the Environment and Sustainable Development**.

**Bio-safety and bio-security rules** on the manipulation of pathogenic microorganisms, GMOs, and human biological samples must be imperatively and rigorously respected, not only to protect the experimenter and his or her colleagues but also to prevent the dissemination of pathogenic microorganisms into the environment. Thus, isolation categories (1, 2, and 3) in accordance with European legislation shall govern the manipulation of such specimens (BSL-2 or BSL-3), as well as animal experimentation (A-2 or A-3) and transfers to a third party (class A or B) of such microorganisms, be they bacterial, viral, parasitic or fungal. The transfer of microorganisms between research teams on the Paris campus is subject to the same rules and authorisations. The physical transfer of microorganisms, even those that have not been genetically modified, must be accompanied by an MTA when the exchange takes place between an on-campus entity and an exterior entity.

Personnel are reminded that the use, import, export, detention, and transfer, as well as the acquisition and transport of certain infectious agents and toxins, is governed by law<sup>21</sup> and must receive prior authorisation from the AFSSAPS.

The manipulation and transfer of human biological samples must be carried out according to rules set out in Chapter 2.

Personnel are reminded that reagents and techniques used during diagnostic or therapeutic procedures on humans must have been developed according to international norms and standards.\*

Thus:

- all commercially available reagents must be used according to the manufacturers' instructions, including expiration dates, so as not to modify the expected performance in terms of sensitivity and specificity
- techniques and reagents that are not officially approved may not be used in diagnosis if quality assurance has not been performed according to the established rules throughout production, and if the procedures leading to approval (comparison to standard reagents, quality control, validation of the samples used to develop the method, publication of results in an international peer-reviewed journal, etc.) have not been followed
- reagents that have not received official approval may not be used in treatment (vaccines, serums, antibodies, etc.) if their development involved human or animal tissue or liquids or if their production or the procedures leading to approval were not performed according to the international rules (WHO) and good clinical and laboratory practices, including all phases of pharmacokinetic and safety testing in animals and in humans.

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\* See chapter 2

## 10 Use of research for offensive military purposes or bioterrorism

A significant portion of Pasteurian research involves the detection of infectious agents or the toxins they produce, the control of such agents using vaccines and treatments, and fundamental aspects of their biology.

It is indispensable to store and manipulate these biological or toxic agents strictly for the benefit of public health, knowledge acquisition, the treatment and prevention of emerging risks of intentional or accidental origin, as well as the development of possible countermeasures. However, such research still runs the risk of being used for offensive military objectives or for criminal purposes by terrorist groups. This risk is increased both by recent progress in biotechnology and by the code of secrecy generally imposed by military authorities for research projects to which they contribute, a policy that conflicts with the ideal of transparency and the free exchange of experimental data that usually characterises scientific research.

## 11 Research using animal models

The use of animal models for biomedical research is an essential step in the scientific activities preceding research on human beings that, understandably, raises questions from the general public. Indeed, the public justifiably requests information on the utility of such experiments, the possibility of obtaining comparable results without using living animals, and the conditions in which animals are kept.

France has signed and ratified the Biological and Toxin Weapons Convention (BTWC).<sup>22</sup>

Members of Personnel must not agree to participate in work that could intentionally lead to the aggressive use of chemical, biological, or toxic agents against human beings, animals or plants, or that otherwise represent a threat to biodiversity. As it is often difficult to evaluate the risk of this occurring, members of Personnel confronting this situation are encouraged to notify the CVE and the office of the President of the Institut Pasteur. This procedure is obligatory when research involving pathogenic biological agents and/or their toxins is financed by the General Delegation for Ordnance (DGA), an office within the French Ministry of Defence, or with laboratories operating under its umbrella.

The use of animals in research projects at the Institut Pasteur is carefully overseen and the teams in charge of such projects are conscious of the ethical concerns at stake.

The scope of the present charter extends only to living vertebrate animals, in coherence with the regulatory texts currently in force.

The experimental use of living vertebrates is governed by European<sup>23</sup> and French<sup>24</sup> regulatory arrangements that all research institutions are required to respect. The French texts require that all establishments performing animal experimentation be approved, that lead investigators in charge of protocols be authorised to perform such experiments, and that all persons involved in animal experiments receive appropriate training. Certain protocols must be declared and justified at the Prefecture before any research can begin.<sup>25</sup> Finally, any person possessing non-domestic species must have a certificate of capacity.<sup>26</sup> Moreover, the Institut Pasteur expects Personnel working with animals to be aware of good practices in the development of research protocols for use on vertebrates.

These procedures are currently being harmonised with those of public and private research institutions that, over the past 15 years, have progressively created specialised committees to evaluate experimental protocols and formulate recommendations to maximise animal welfare, above and beyond regulatory obligations.<sup>27</sup>

Conscious of its responsibilities, the Institut Pasteur is committed to promoting the development of experimental methods that avoid the use of animals whenever and wherever possible, and to overseeing the proper treatment of animals by Personnel and in particular the strict adherence to regulations. It also actively encourages project leaders to submit systematically their protocols for examination by the Regional Committee on Ethics and Animal Experimentation (CREEA), according to the procedures laid out in the guidelines created by the Inter-professional Working Group on Ethics Committees (GRICE), which can be found on the Institut Pasteur internal website.<sup>28</sup> Ethics examination is a means to improve the quality of research, including animal experimentation.

The Institut Pasteur requires a favourable opinion from the CREEA for protocols including level 2 or higher pain levels (procedures practised on living vertebrates, causing stress or minor pain of short duration).<sup>29</sup> Prior authorisation from the Institut Pasteur President is also required for protocols reaching pain levels 3 or higher<sup>30</sup> and for all protocols making use of non-human primates.

The same procedures are to be applied when research is conducted at the initiative of the Institut Pasteur, including in internal and external collaborations and service agreements.

Personnel involved in the conception of protocols and their implementation must keep in mind the “3 R’s” rule – replace, reduce, refine.<sup>31</sup> Protocols must indicate how this rule and good practices have been respected.

The Institut Pasteur is especially attentive to the pain of animals.

The Institut Pasteur is dedicated to the respect of ethics rules recognised by the international community and is committed to ensuring that the research it undertakes is in accordance with these rules.



Alice Dautry

President

Annex

**Procedure for submitting a research project to the Clinical Research Committee (CoRC)**

Who submits?	What type of research?	Where to send the request?	How?	When?
A researcher, an investigator, or a group of researchers or investigators from the Paris campus or one of the institutes of the International Network	<ul style="list-style-type: none"> <li>▪ on human subjects (epidemiology, physiopathology, treatment or vaccine trials, etc.)</li> <li>▪ using components or products originating in the human body (laboratory or surgical waste, etc.)</li> <li>▪ research using personal health data</li> </ul>	To the <b>Clinical Research Department (PIRC)</b> , which coordinates the CoRC	By post or by email ( <a href="mailto:pirc@pasteur.fr">pirc@pasteur.fr</a> )	<ul style="list-style-type: none"> <li>▪ When all necessary documents are ready</li> <li>▪ Before beginning any or all regulatory procedures (notably for the CPP)</li> </ul>

**Logging of the project in the clinical research database at the Institut Pasteur  
Designation of a project representative**

**Evaluation by the Clinical Research Committee - CoRC (monthly meetings)**

1. Presentation by the project's designated representative (a member of the Clinical Research Committee)
2. Examination of the study's compliance with regulatory, legal, ethical and organisational standards
3. Drafting of a recommendation

**Department of Medical Affairs**

**Request for additional information, possibly requiring re-examination by the CoRC**

**Authorisation to begin the study**

**Refusal to begin the study**

**If necessary, revision of the project**

**Notification of project leaders regarding the decision of the Department of Medical Affairs based on the recommendation of the CoRC**



## Acronyms

AFSSAPS	French Health Products Safety Agency
BTWC	Biological and Toxin Weapons Convention
CDS	Code of Professional Ethics
CCNE	French National Ethics Advisory Committee for the Life Sciences and Health
CGG	Commission on Genetic Engineering
CIC	Clinical Investigation Centres
CIOMS	Council for International Organisations of Medical Sciences
CNIL	French data protection authority
CNREEA	French national working group on the ethics of animal experimentation
CoRC	Clinical Research Committee
CPP	Committee for the Protection of Persons
CREEA	Regional Committee on Ethics and Animal Experimentation
CVDC	Deontology Committee
CVE	Ethical Vigilance Committee
DGA	General Delegation for Ordnance
GMO	Genetically Modified Organism
GRICE	Inter-professional Working Group on Ethics Committees
MGM	Genetically Modified Microorganism
ICAReB	Platform for Clinical Investigation and Access to Biological Resources
NGO	Non Governmental Organisation
PIRC	Clinical Research Department
WHO	World Health Organisation
WHOCC	Collaborating Centre of the World Health Organisation

## Notes

1. Declaration of Helsinki of the World Medical Association. Ethics principles applicable to medical research involving human beings, last revised in October 2008 in Seoul: <http://www.wma.net>
2. International Ethical Guidelines for Biomedical Research Involving Human Subjects. Council for International Organisations of Medical Sciences (CIOMS). Adopted in 1993, revised in 2002: [http://www.cioms.ch/frame\\_guidelines\\_nov\\_2002.htm](http://www.cioms.ch/frame_guidelines_nov_2002.htm)
3. The Universal Declaration on Bioethics and Human Rights, adopted 19 October 2005. [http://portal.unesco.org/shs/en/ev.php-URL\\_ID=1372&URL\\_DO=DO\\_TOPIC&URL\\_SECTION=201.html](http://portal.unesco.org/shs/en/ev.php-URL_ID=1372&URL_DO=DO_TOPIC&URL_SECTION=201.html)
4. Convention for the protection of human rights and the dignity of the human being with regard to the application of biology and medicine: Convention on Human Rights and Biomedicine: <http://conventions.coe.int/Treaty/Commun/QueVoulezVous.asp?NT=164&CM=8&DF=01/09/2009&CL=ENG>
5. Code of Scientific Ethics [in French]. [http://webcampus.pasteur.fr/jcms/c\\_51222/code-dedeontologie](http://webcampus.pasteur.fr/jcms/c_51222/code-dedeontologie)
6. Clinical Research Department [in French]. [http://webcampus.pasteur.fr/jcms/c\\_82379/pirc](http://webcampus.pasteur.fr/jcms/c_82379/pirc)
7. ICAREB [in French]. [http://webcampus.pasteur.fr/jcms/c\\_80673/investigation-clinique-et-access-auxressources-biologiques-icareb](http://webcampus.pasteur.fr/jcms/c_80673/investigation-clinique-et-access-auxressources-biologiques-icareb)
8. Research on human biological samples [in French]. [www.legifrance.gouv.fr](http://www.legifrance.gouv.fr). See "Code de la santé publique" [Public Health Code], especially articles L. 1243-3, L. 1243-4, L. 1211-2, L. 1221-8-1.
9. Research on human embryonic stem cells. In France, an authorisation from the Agency on Biomedicine is necessary. See article L. 2151-5 of the Public Health Code.
10. Genetic characteristics. <http://www.ccne-ethique.fr/opinions.php>. N°097 - Ethical issues arising out of the delivery of neonatal genetic information after screening for genetic disorders (the examples of cystic fibrosis and sickle-cell disease) (2007-05-10); N°086 Problems connected to marketing self-test kits for HIV screening and diagnosis of genetic disease.(2004-11-04); N°083 Generalised prenatal screening for cystic fibrosis (2003-03-25); N°076 Regarding the obligation to disclose genetic information of concern to the family in the event of medical necessity (2003-04-24); N°046 Opinion and recommendations on "Genetics and medicine: from prediction to prevention." Reports. (1995-10-30); N°036 Opinion on the use of somatic gene therapy procedures. Report (1993-06-22); N°030 Ethical issues raised by mandatory genetic testing for female participants in the Albertville games (1992-01-27); N°027 Opinion that the human genome should not be used for commercial purposes. Report. Thoughts relating to ethical problems of human genome research (1991-12-02); N°025 Opinion regarding the application of genetic testing to individual studies, family studies and population studies (Problems related to DNA "banks," cell "banks" and computerisation) (1991-06-24); N°019 Opinion on embryo research aiming to achieve pre-transfer genetic diagnosis for which a moratorium was declared in 1986 (1990-06-18); N°017 Opinion concerning the dissemination of DNA analysis identification techniques (genetic fingerprinting) (1989-12-15)
11. Clinical trials [in French]. <http://afssaps.sante.fr/htm/5/essclin/indesscl.htm>
12. National framework: Law on the public health policy n° 2004-806 of 9 August 2004 and the Decree on its application n°2006-477 of 26 April 2006, Law on Research n°2006-450 of 18 April 2006, Laws 2004-800 and 2004-801 of 6 August 2004 regarding bioethics and the protection of persons with respect to personal health data.
13. International framework: ICH norms, topic E6, CPMP/ICH/135/95; European directives 2001/20/CE and 2005/28/CE on good clinical practices, authorisations for the production or importation of pharmaceutical products; guidelines of the European Medicines Agency (EMA): "The rules governing medicinal products in the European Union"
14. GMO. Principles for Classification and Official Guides of the Commission on Genetic Engineering. Ministry of Research and Higher Education, Commission on Genetic Engineering. <http://www.enseignementsup-recherche.gouv.fr/commiss/genetique/index.htm>
15. GMO. Directive 90/219/CE of 23 April 1990 modified by directive 98/81/CE of 26 October 1998. Also see the European Community Regulations n°1946-2003 of 15 July 2003 on cross-border movements of GMOs. Their transposition essentially concerns the environmental, rural, public consumption and public health codes.
16. Non commercialisation of the human body. Also see the opinion of the CCNE: N°077 Ethical issues raised by collections of biological material and associated information data: "biobanks," "biolibraries": <http://www.ccne-ethique.fr/opinions.php>
17. Rules for communicating with the media [in French]. [http://webcampus.pasteur.fr/jcms/c\\_100834/no-054-relations-avec-les-medias](http://webcampus.pasteur.fr/jcms/c_100834/no-054-relations-avec-les-medias)

18. Scientific communication. Also see the opinion of the CCNE, N°045, "Ethical questions arising from the transmission of scientific information concerning research in biology and medicine. Report (1995-05-31)": <http://www.ccne-ethique.fr/opinions.php>
19. Information security procedures [in French]. <http://www.pasteur.fr/infosci/utlinfo/SSI/>
20. Electronic information. Law 78-17 of 6 January 1978 on computers, electronic files, and personal liberties. <http://94.247.233.54/en-savoir-plus/textes-fondateurs/>
21. Decree of 30 July 2004 regarding the use, importation, exportation, detention, and transfer, whether or not for consideration, as well as the acquisition and transport of certain agents responsible for infectious diseases, pathogenic microorganisms, and toxins. Authorisation is delivered for each operation by the Executive Director of the French Health Products Safety Agency (AFSSAPS). It must be conserved by the bearer to be presented at the request of relevant authorities.
22. Despite its insufficiencies (the states who have signed the convention are not required to declare these arms, nor show proof of their elimination, and, above all, the convention does not include any methods for verification), this convention incites the commitment of the scientific community as well as national civil and military authorities. Resolution 1540 of the United Nations Security Council (2004), which aims to limit the proliferation and dissemination of biological weapons, reinforces this obligation. It is necessary to establish criteria for risk-benefit analyses of projects or sensitive publications, that is, the critical point beyond which their real or perceived dangers prevail upon the advantages relative to the public good. The French Academy of Sciences, on the model of the National Academy of Sciences (United States) and the Royal Society (United Kingdom), proposes founding such an evaluation on questions including the following: Can results be used for offensive military purposes or for terrorist acts? What would be the technical prerequisites for offensive purposes of this type, including by a non-state organisation? Would the expected results allow for the optimisation of known types of weapons?
23. Research using animal models. Directive 86/609/CEE
24. Research using animal models. Decree 87-848 of 19 October 1987
25. Research using animal models. Protocols including procedures that risk exposing animals to intense pain without use of anaesthesia or an analgesic. Decree 2001-464 of 29 May 2001
26. Research using animal models. Article R.213-4 of the Rural Code
27. Public research institutes are thus required to have a Regional Committee on Ethics and Animal Experimentation (CREEA), all of which are founded on a common charter. The jurisdiction of these committees is currently up to the determination of researchers. The Inter-professional Working Group on Ethics Committees (GRICE), which brings together ethics committees from public and private research institutions, published a "Guide for ethics evaluations of studies using animals" in 2008, with the objective of harmonising practices to create homogeneity at the national level. Finally, the primary mission of the French National Committee on Ethics and Animal Experimentation (CNREEA) is to draw up and publish a national charter on the ethics of animal experimentation. [www.enseignementsup-recherche.gouv.fr](http://www.enseignementsup-recherche.gouv.fr) [in French]
28. Research using animal models [in French]. [http://webcampus.pasteur.fr/jcms/c\\_91648/accueil](http://webcampus.pasteur.fr/jcms/c_91648/accueil) and [http://webcampus.pasteur.fr/jcms/c\\_96931/evaluation-ethique-des-protocoles](http://webcampus.pasteur.fr/jcms/c_96931/evaluation-ethique-des-protocoles)
29. Research using animal models [in French]. [http://www.bvet.admin.ch/themen/tierschutz/00781/00795/index.html?lang=fr&download=NHZLpZeg7t,lnp6l0N TU042l2Z6ln1ae2lZn4Z2qZpn02Yuq2Z6gpJCDdH12e2ym162epYbg2c\\_JjKbNoKSn6A--](http://www.bvet.admin.ch/themen/tierschutz/00781/00795/index.html?lang=fr&download=NHZLpZeg7t,lnp6l0N TU042l2Z6ln1ae2lZn4Z2qZpn02Yuq2Z6gpJCDdH12e2ym162epYbg2c_JjKbNoKSn6A--)
30. Research using animal models [in French]. [http://www.bvet.admin.ch/themen/tierschutz/00781/00795/index.html?lang=fr&download=NHZLpZeg7t,lnp6l0N TU042l2Z6ln1ae2lZn4Z2qZpn02Yuq2Z6gpJCDdH12e2ym162epYbg2c\\_JjKbNoKSn6A--](http://www.bvet.admin.ch/themen/tierschutz/00781/00795/index.html?lang=fr&download=NHZLpZeg7t,lnp6l0N TU042l2Z6ln1ae2lZn4Z2qZpn02Yuq2Z6gpJCDdH12e2ym162epYbg2c_JjKbNoKSn6A--)
31. Research using animal models [in French]. <http://extranet.inserm.fr/recherche-pre-clinique/l-experimentation-animale>



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