Cooperation in the field of biomedical research between

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Contents

Opinion

Biomedical research projects involving French teams and teams from economically developing countries require special precautions, in order to guarantee the dignity and the safety of persons consenting to participate in research of general interest.

1. An agreement for cooperation between the governmental authorities of France, and of the countries or regions involved should specify the training and support conditions for the researchers and public health staff participating in the proposed study.

2. Prior studies, carried out by one or several teams, independent of those expected to implement the project, should make it possible to identify any social, political, religious or cultura1 specificities, likely to prevent project execution, or to make smooth progress more difficult.

3. All such projects should be submitted, before they are undertaken, to a specialised committee to be created (French consultative committee for the protection of persons consenting to biomedical research in developing countries, or CCPPVD).

This specialised committee should certainly include experts from the World Health Organization, with experience in the implementation or monitoring of such projects, and could be constituted under the aegis of ministerial departments responsible for Health, Research and Cooperation. This committee will be able to seek the advice of the National Consultative Ethics Committee.

4. The project will also be studied independently by an ethics committee of the country or region where the proposed study is to take place. A list of such local or regional ethics committees, as well as existing human rights defence committees, should be drawn up, published and brought up to date annually. In the absence of a local or national ethics or human rights committee, regional bodies operating under the aegis of the World Health Organization, of UNESCO or of the International Children's Centre could be called upon.

The analyses and opinions of the specialised committee (CCPPVD) and of the local, national or regional committees will be submitted to the authorities funding the project, and authorizing its implementation, before the project is launched.

In the present opinion, the National Consultative Ethics Committee recalls the intangible principles of no commercial use of the human body, and of consent.

5. Finally, the results of the study are the subject of a publication communicated to national

authorities, to the bodies having originated the project, and to the ethics committees involved in the process. These results must be accessible to the scientific community and to the public at large, through publication in a journal with peer review or in any other form.

Report

Prevailing international texts and recommendations

Since the publication of the Nuremberg Code (1947), several international bodies have proposed ethical rules with a general scope which are accepted by the majority of researchers involved in biomedical research. It is noted, however, that these recommendations are sometimes treated with disdain, especially for programmes concerning countries with different levels of economic development, and this occurs without any sanctions being applied.

Therefore, the rules of good conduct governing the design of biomedical research projects, sponsored from abroad and including vulnerable individuals or populations, must be clearly specified and re-affirmed yet again.

Already in 1964, the World Medical Association introduced into the Helsinki Declaration a statement of the basic principles of any biomedical research protocol involving human beings, and prescribed, even then, special precautions " when the subjects included in the protocol find themselves in a situation of dependence with respect to the promoter, or have to give their consent under pressure" (Article 10).

In 1981, the Manilla directives specified the modalities of application of previous principles " under the conditions prevailing in many countries, that are developing in technological terms" . They underscore. in particular, " the limitations of the informed consent procedure, and deal with the problems specific to research relating to communities, rather than to individuals" . In this case, it is noted that " consent constitutes an imperfect safeguard for the subject, and must always be supplemented by an independent examination of the ethics of the research proposal" .

In 1990, the Council of Europe, considering that " while medical research on human beings must take ethical principles into consideration, it must also be subject to legal rules" , declared that special protection must be extended to certain groups of people, and re-affirmed the principles that must govern medical research carried out in the twelve member states of the EEC.

The concept of vulnerable person or population

Following the path marked out by past international declarations, it now seems to us necessary to express what we mean by vulnerable person or population, for their fate is evoked in several of these texts, but the definition is not yet precise. For the ethical aspect of cooperation among countries with unequally developed economies, such a definition seems to us to be an indispensable pre-condition.

It must be considered that *a person or a population included in a biomedical research protocol is vulnerable, whenever the consent is absent or impeded, because the conditions required for free and informed acceptance cannot all be fulfilled.*

This impediment may be social, economic, political, legal or cultural in nature. Economic under-development constitutes, in and of itself, an obvious factor contributing to vulnerability of persons and populations.

Rules of good conduct for the design of biomedical cooperation projects with developing countries

Partnership

The design of a protocol for research sponsored " from outside" must always be approached from a partnership point of view, and cannot be viewed as an assistance programme. This means that it must have been seen as desirable by local or regional personalities, with a view to improving the health of the population, and that it must not flow from a public health policy grounded solely in the market and offered from the outside, even if the agreement of certain political authorities is forthcoming.

The achievement of this partnership requires that there be, during and certainly not after the scientific design phase, a study of the project's acceptability and of its implementation conditions in the country where it is to occur. Close cooperation with a local or regional scientific and ethics committee must therefore be established. This committee must be independent of the governments and researchers promoting the project. In the absence of local scientific or ethics representatives, the regional committees of the WHO for research on medication, or representatives of the International Children's Centre, especially for studies of vaccines, could be either the partner as such, or the consultant of the mandatory local partner. In any event, the teams conducting these preliminary studies, of the project's acceptability for the populations concerned, must include expert sociologists and anthropologists, who are neutral and independent of the project's promoters. These teams must also inform the researchers of the public health needs of the countries where the project is to be implemented, of the population's nutritional status, of the local climate's influence on public health, etc. The independent experts, who know the host region well, must be able to identify any risk of deviation from the research protocol because of local political or cultural influences, for this may be decisive for the project's completion and for analysis of its results.

The protection of persons

The probable benefit of the proposed research for the populations concerned must be clearly set out. The safety of persons who consent to research with a therapeutic goal requires that the attendant risk be carefully calculated, and evaluated in the light of the expected benefit. in any event, prior animal experimentation is absolutely necessary.

Any research involving children must be subject to full respect for the rules defined by the International Children's Centre and the Convention on the Rights of the Child: consent must be given by the parents, or by the one parent who exercises parental authority. The concept of consent by the child itself is now recognized, and the child's opinion will have to be sought, as a function of level of maturity.

The report of the National Consultative Ethics Committee on "Ethics and Pediatrics", published in 1992, emphasizes that " giving due consideration to the cultural level, the linguistic abilities, the beliefs and the traditions of the child, the parents and the community is obligatory. Any study, research work or trial carried out primarily on children from disadvantaged communities, and not in a position to decide freely, must be rejected vigourously, except, of course, when the disorder or illness to be combated manifests itself only in such communities" .

These concepts, as defined for the child, who is simply a specific vulnerable person, must be extended to vulnerable persons in general.

Moreover, an insurance policy must be foreseen and included in the protocol, in order to indemnify victims of therapeutic hazard attributable to the research project.

Preliminary evaluation of the project

The scientific and ethical quality of projects authorized, funded or executed in whole or in part by public or private organizations or promoters from countries with a high level of development, in particular from France in so far as the National Consultative Ethics Committee is concerned, and the competence of teams entrusted with implementing these projects, must be systematically evaluated by a specialised body.

A Consultative Committee for the Protection of Persons Consenting to Biomedical Research in Developing Countries could well be constituted under the aegis of interested ministerial departments, responsible for Health, for Research and for Cooperation. This committee would especially include specialists in this type of research, coming from different scientific and medical disciplines, with sufficient representation of the human sciences. It should also include members of international institutions, such as the WHO or the International Children's Centre. This specialised Committee could submit projects to the National Consultative Ethics Committee, as required and when they involve issues within the latter's domain of competence.

In short, any project for cooperation between France and a country with a level of economic and technological development far below its own should be subject, before its authorisation and funding, to two evaluation exercises: by the French consultative committee for the protection of persons consenting to biomedical research in developing countries, and by a local, national or regional scientific and ethics body from the location where the project is to take place.

The final decisions of the supervisory authorities and funding bodies must be taken with due consideration for the opinions of these committees.

Finally, the research results must, of course, be the subject of a final report addressed to the governmental and supervisory authorities concerned, to organisations having provided funding, and to protection of persons and ethics committees having examined the project. These reports have to be available for communication to anyone expressing an interest, or even better, be published in a scientific journal with a peer review system.

The principles enumerated above will be submitted by the National Consultative Ethics Committee to other ethics committees or equivalent bodies around the world, as well as to international organisations concerned about the issues of biomedical cooperation among countries with very different levels of economic development.

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