Presidency of the Council of Ministers

OPINION OF THE NATIONAL BIOETHICS COMMITTEE ON THE EUROPEAN PROTOCOL ON BIOMEDICAL RESEARCH

19 November 1999

The NBC, as its meeting on 19 November 1999, examined the document prepared by the Steering Committee on Bioethics (the Council of Europe's CDBI) dated 29 July 1999 (Doc. CDBI-CO-GT2/99/10). This is the latest version of the work carried out on the drafting of a 'Protocol on biomedical research' in implementation of the 'European Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine' (the Oviedo Convention, 1997).

FOREWORD

While the NBC appreciates the results achieved by by the CDBI it notes that, in general terms, there has been a gradual distancing from the ethical positions elaborated to fully guarantee individuals undergoing trials, and from the overall philosophy which inspired the Helsinki Declaration on biomedical research involving human subjects. These diverging positions relate in particular to several very important issues that may be summarized as follows:

- the guarantees of good practice for trials and for the protection of the individuals taking part in them refer excessively to the laws of each individual state; this is a source of concern because most European countries have very little legislation dealing with this matter;
- unlike the position adopted in the Helsinki Declaration research may also be carried out on individuals who are unable to give their consent (albeit in compliance with specific indications to protect them).

Lastly, one particularly important feature of the draft Protocol is the lack of consistency between the positions taken up in the draft on biomedical research and the points previously established in the European Community framework by the 'guidelines for good clinical practice' adopted by the European Agency for the evaluation of drugs (CPMP/ICH/1995). This inconsistency betrays a lack of cooperation between the European agencies and an inadequate harmonization of the rules and regulations they produce.

RESERVATIONS

The NBC therefore considers it appropriate to make the following observations:

1) It is necessary to apply the safety guarantees established in the Protocol in their entirety (and not only the fundamental guarantees) to research carried out on human beings in countries which are not party to the Protocol (see art.10). A more effective form of legal protection should be provided for individuals from non-signatory states, particularly if they are less developed. For the purposes of applying the principle of individual self-determination, for example, it would appear appropriate to introduce a 'cultural mediator' from the local population, whenever required on account of the different cultural, economic and social environments in the country proposing the trial and the country in which the trials are to be performed. A 'cultural mediator' would guarantee that full information and a full understanding of the risks of the research, and in more general terms the risk/benefit ratio, is are made public. The results of the research should also be to the benefit of the population of the countries

in which it is carried out.

2) We are opposed to persist with placebo treatment when it is necessary to ascertain the greater effectiveness of new drugs on persons requiring treatment with traditional drugs (arts.12 and 19). The objection made to the previous draft of the document was that if a treatment is active, by definition the fact of not using it cannot be a matter of arbitrary choice. The following wording was therefore proposed 'placebo treatment may only be used in cases where there is no treatment of proven effectiveness'. The new version has accepted the emphasis made by the word 'only', but it still accepts the use of placebo treatment even when active treatment exists, even though it does specify that withdrawing or withholding active treatment must not present significant/considerable risks or burden. It should be quite clear that the use of placebo treatment when alternative treatment of proven effectiveness exists is a violation of the ethical code and is not in the interests of the patient. This cannot even be justified by reference to the interests of science and society. For whenever it is discovered that a particular treatment has a positive effect on changing the natural course of a particular condition or disease, the essential issue as far as science and society are concerned is to see whether the new treatments can produce a further improvement still. With regard to the treatment to be reserved to control groups, it would be preferable to speak of assuring them of the best treatment of proven effectiveness, using the wording of the Helsinki Declaration.

3) We would use the definition of 'minimal risk': this provides better guarantees for the patient than the other two wordings proposed, namely 'significant risk' or 'considerable risk'. The term 'integrity' should also be considered to comprise both mental and physical integrity. Consequently, consent must be requested both for physical and for psychological treatments.

4) No obligation is envisaged about giving clear information, when carrying out research projects, regarding the possible use of the findings and the documentation collected for industrial application and for patenting procedures and products.

5) Despite the improvements made to the text, some ambiguity still remains in the wording regarding experiments during pregnancy, whether this is designed to collect data regarding the mother's organism or data relating to the foetal organism, or whether they are trials being conducted for the health of the mother or of the foetus, which should guarantee mutual negative non-interference. It should also be clearly stated that non-therapeutic trials on pregnant and nursing women must exclude the maximum level of risk for the individuals involved.

6) The possibility of carrying out research on dependent persons (see art.24) or on persons deprived of liberty (art.25). In these cases, even though they are subject to different conditions, it may always be possible for unjustified influence to be brought to bear on them to secure their consent. As a secondary point, the Committee notes that research on dependent persons or persons deprived of liberty must be strictly limited to instances in which the individuals concerned can themselves benefit from the research.

ENDORSEMENT

As far as the amendments proposed by the Secretariat are concerned, the NBC

endorses the changes made, and particularly the introduction of the following points into the text:
1) further specification regarding the complex relations between researchers and the persons undergoing research with regard to the information required to be able to validly give consent (arts.11 and 12) and - in the case of persons unable to consent - further provisions taking account of any objections which that person may have expressed previously regarding participation in the research (art.20);
2) the clearer wording adopted regarding the restrictions on research on pregnant or nursing women (art.23) coupled with the remarks made above;
3) the clearer wording regarding the requirements for research on personal data (arts. 26 and 27);
4) the clearer wording regarding the protection of the confidentiality of personal data (art.29) and damages due in the case of breach of confidentiality (art.30);
5) the introduction in the new version of the requirements for research on biological materials which we have frequently advocated in the past (arts. 31, 32, 33, 34, 35);
6) the general statement that no research can be undertaken on human beings except when there is no alternative of comparable effectiveness (arts. 11 and 26).

CONCLUSIONS

In conclusion, the NBC notes the lack of any clear reference in the text to the need to spell out the purposes of the research, both from the point of view of the scientific analysis of the results and an ethical appraisal of the research, in the protocol submitted for approval to the authorizing authorities. We believe that it is a matter of absolute priority to indicate this, to establish the real relevance to human health and welfare of the objectives set for the research project, independently of the need to adopt sound procedures and guarantee the scientific validation of the research protocols.
The NBC has noted that the protocol does not cover experiments on embryos, and will return later to this subject with a reasoned opinion regarding the specific protocol currently being prepared for this purpose.
The NBC also notes that the draft protocol provides a much broader definition of research than previous versions, and also includes psychological, sociological research (relating to the Convention) and population studies. These are all issues that require further detailed discussion.

Lastly, the NBC believes that the role of Ethics Committee, which is given recognition in the protocol, must be more forcefully emphasized. The Ethics Committee must be entrusted with such fundamentally important tasks as examining and approving research projects, expressing a binding decision regarding their implementation. The Committee must also guarantee that no unjustified influence is brought to bear to obtain consent to experimentation and that patients are kept fully informed of all the possible unexpected adverse effects (which, if they materialize, are conditions for halting the research, and, if the trials are to be continued, the patient-s consent must once again be sought, and the Ethics Committee requested to issue an opinion on the amended protocols).
The NBC hopes that the final drafting of the 'Protocol' will take account of the

reservations expressed above regarding the present wording.