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# EMERGING BIOETHICAL ISSUES IN HEALTH RESEARCH: CONCERNS AND CHALLENGES IN THE AFRICAN REGION

## Report of the Regional Director

**EXECUTIVE SUMMARY**

1. The 20th session of the WHO African Advisory Committee for Health Research and Development (AACHRD), held in Dakar, Senegal, from 23 to 26 April 2001, noted with concern that, despite the significant increase in the amount of clinical research carried out in the Region in the past decade, especially in the field of HIV/AIDS, the bioethical aspects of these research endeavours have not received due attention by Member States. The Committee recommended that research bioethics be treated as an area for priority intervention in the Region. It is against this background that the Regional Director is bringing issues associated with research bioethics before the Regional Committee so that it can address the challenges faced by the Region.

2. This document presents key concerns and challenges about health research bioethics in the African Region and is meant to inform the Regional Committee of the gravity of the situation. It also makes suggestions for implementation by Member States and WHO. The Regional Committee is, therefore, requested to examine, improve and adopt the suggestions to address the challenges presented by bioethical issues involved in health research in the African Region.

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## INTRODUCTION

1. The progressive globalization of biomedical and behavioural research holds much promise for developing treatments that would prevent illness, cure disease and improve health. However, the globalization of research is raising concerns among African experts whether current regulations and guidelines can protect research subjects from ethical malpractices. While it is necessary to allow important international research to proceed in the African Region, the dilemma remains that the circumstances under which such research is being conducted markedly differs from that being carried out in developed countries.

2. The 20th session of the WHO African Advisory Committee for Health Research and Development (AACHRD), held in Dakar, Senegal, from 23 to 26 April 2001, noted with concern that, despite the significant increase in the volume of clinical research carried out in the past decade in the Region, especially in the field of HIV/AIDS, the bioethical aspects of this research have received little attention from Member States.

3. AACHRD was concerned that several factors have changed significantly with regard to the way clinical trials are being conducted in the African Region. The past decade, for example, has witnessed an increase in the commercialization of medical research. Clinical trials have become a big business globally and, as a result, there is an increasing tendency to conduct more research in developing countries and as cheaply and quickly as possible.

4. Furthermore, the AIDS epidemic in Africa and the resurgence of malaria and tuberculosis have brought to the fore unique and urgent ethical, legal and social issues with regard to clinical research in the African countries. And, more significantly, the progress achieved recently in human genomics research,[1] the creation of genetically-modified foods[2] and the gene therapy[3] have added to the major bioethical issues the Region is likely to face in the near future.

5. It is against this background that the Regional Director is bringing the issue of research bioethics before the Regional Committee. The Committee is requested to consider the challenges that the Region faces and provide suggestions and guidance on how to maximize and take advantage of new opportunities such as the recent advances in genomics research and how these can be used to fight disease. At the same time, the interest of African subjects as they increasingly participate in complex clinical trials needs to be safeguarded.

### Essential requirements for the ethical conduct of clinical trials

6. The essential ethical concerns in the treatment of human subjects in research include, among others, choosing the appropriate research question and design; ensuring prior scientific and ethical review of the proposed protocol; selecting participants equitably; obtaining voluntary informed consent; and providing appropriate treatment to participants during and after the trial. These concerns are consistent with the principles endorsed in international guidelines on research ethics.

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[1]Yamey G. Scientists unveil first draft of human genome. *BMJ* 2000; 321:7.
[2]Jones L. Science, medicine and the future-Genetically modified foods. *BMJ* 1999; 318:581-584.
[3]Russel S. Science, medicine and the future-Gene therapy. *BMJ* 1997; 315:1289-1292.

7. There are three basic ethical principles endorsed in international guidelines,[4] which provide an analytical framework for understanding many of the ethical issues arising from research involving human participants: *respect for persons*, *beneficence*, and *justice*. In order to be ethically sound, research conducted with human beings must, at a minimum, be consistent with these ethical principles. In addition, ethically-sound research must satisfy a number of important procedural requirements, including prior ethical review by a body that is competent to assess compliance with these substantive ethical principles.

## KEY CONCERNS IN THE AFRICAN REGION

### Ethical review

8. Although several countries in the Region have instituted national guidelines on research ethics, and although in some countries, ethics review is becoming more established, many difficulties and challenges to local review still remain. These include: lack of experience with and expertise in ethics review principles and processes; conflict of interest among ethics review committee members; lack of resources for maintaining and sustaining the review committees; the length of time it can take to obtain approvals; and problems involved in interpreting and complying with international regulations. In some cases, there is political interference - or at least heightened political pressure - to obtain approvals whereby it would mean that valuable research funds would flow to a particular institution.

### Voluntary informed consent

9. The requirement to obtain voluntary informed consent from individuals before they are enrolled in a research trial is a fundamental principle of research ethics. However, despite the centrality of voluntary informed consent and its underlying principles, problems of interpretation and application remain for researchers and ethics review committees. Part of the problem relates to the nature of research participants in the African context. Most of them are poor, illiterate and are, therefore, extremely vulnerable. There may also be constraints in obtaining voluntary consent in settings in which the belief system of potential research participants does not explain present-day health and disease concepts and terms of modern medical science and technology. A related concern is how voluntary participation can be ensured in settings in which community leaders may exert pressure on an entire community to enroll in a proposed clinical trial.

### HIV/AIDS epidemic

10. Sub-Saharan Africa accounts for more than 70% of the world's HIV/AIDS cases. There are controversies surrounding the research being conducted on AIDS in Africa. The ethics of the placebo-controlled trials in the prevention of mother-to-child transmission of HIV have been debated extensively,[5, 6, 7] which is illustrative of the complexity of conducting research in Africa. To date, the issue of placebo-controlled trials has still not been resolved, and it would not be surprising to find that these trials are still

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[4]Council for International Organisation of Medical Sciences (CIOMS) in collaboration with the World Health Organisation (WHO). *International guidelines for biomedical research involving human subjects. Geneva: CIOMS, 1993.*

[5]Lure P, Wolf SM. Unethical trials of interventions to reduce perinatal transmission of human immunodeficiency virus in developing countries. *N Engl J Med* 1997; 337:883-85.

[6]Editorial. The ethics industry. *Lancet* 1997; 350:897.

[7]Clarke M, Collinson A, Faal H, Gaye A, Jallouu M, Joof-Cole A, *et al*. Ethical issues facing medical research in developing countries. *Lancet* 1998; 351:286-287.

going on in the Region. An editorial in the *New England Journal of Medicine* by Marcia Angell[8] highlights several pertinent issues, namely, that:

(a) the goals of research must always be secondary to the well-being of the participants;

(b) only when there is no effective new treatment is it ethical to compare a potential new treatment with placebo; and

(c) even informed consent in the African context is not protection enough, because of the asymmetry in knowledge and authority between researchers and their subjects.

11. There seems to be a general retreat from the clear principles enunciated in the Nuremberg Code and the Declaration of Helsinki as applied to research in the Third World. The Declaration of Helsinki requires that control groups in a clinical trial should receive the *best currently available treatment* and not *locally available treatment*, as often spelt out in research protocols in the Region. The problem is that the so-called *locally available* treatment works out in many cases to no treatment at all. This problem is compounded by the fact that, for some diseases facing African populations, there may be no effective treatment, and, therefore, a placebo control may be justified.

12. Another concern in HIV/AIDS research relates to the recent developments in vaccine trials. These trials have posed very complex ethical issues, namely:

(a) whether it is ethical to perform trials in Africa which are aimed at researching HIV subtypes that are more predominant in developed nations and not on the continent or in the particular African country where the research is being conducted;
(b) the difference between 'community consent' as opposed to 'individual consent' that standard drug trials insist on; and
(c) as in the case of other HIV/AIDS trials, what happens to the research participants after the trial is over, especially with regard to providing access to the 'best available treatment'.

**Concerns related to new and major advances in genomics**

13. The recent advances in genetics have revolutionized the knowledge about the role of inheritance in health and disease. Their application in medicine will offer exciting possibilities to better health. However, there are global concerns about the use and exploitation of genetic data and genome technology, and some nations are concerned that benefits of new advances coming to developing countries may be limited.

14. WHO is uniquely equipped to consider new ethical issues that arise from developments in human genetics by virtue of its mandate to assist Member States in their efforts to promote the health of their people and to provide leadership in health-related ethical issues.

15. In July 2000, an inter-cluster initiative was launched at WHO headquarters to develop an agenda and a work plan on ethical, legal and social issues (ELSI) related to genomics, with emphasis on developing countries.

16. Within this context, the WHO Director-General has requested the Global Advisory Committee on Health Research (ACHR) to prepare a special report on 'genomics and health'. The report will focus primarily on scientific issues and the potential of genomics in improving health in developing countries.

[8]Editorial. The ethics of clinical research in the Third World. *N Engl J Med* 1997; 337:847-849.

The fifty-first session of the Regional Committee provides a timely opportunity to express the views of the Region and to emphasize that these should be reflected in the Global ACHR's special report as well as in the future WHO agenda and related work plan.

17. Some of the concerns for the African Region in the new genomics research include the following:

***(a) Coping with the genomics revolution***

18. The extent to which the African Region will be affected by the progress made in the gene therapy, cloning of DNA, xenotransplantation (the transplantation in humans of animal cells, tissues or organs) and other genomic research advances are not yet quantified. But the challenges already faced in the United States of America regarding gene therapy[9] are educative. The death of a patient in one trial and, more importantly, the fact that the United States Food and Drug Administration (FDA) found '18 specific violations of government protocols' at the research institute in question brings into question whether Africa would have the capacity to monitor as well such trials in the near future. Based on the FDA report, it would seem wise to ensure that regulatory bodies do not provide ethical approval for gene therapy trials in Africa, and if there is a specific need to perform one, it must be on the implicit condition that the trial would require clearance from the national regularly authority or a similar body with the capacity to do so.

19. Regulations with regard to the conduct of human cloning trials in the developed world have become more prohibitive. There is a concern that these trials may be conducted in countries which have not yet legislated against them or which do not have the capacity to monitor them. Thus, although genetic interventions hold great promise for the betterment of human health, vigilance should be exercised lest they contribute to racism, stigmatization, discrimination or development of a ruthless social policy.

***(b) Genetically-modified foods***

20. Hunger and poverty are major impediments to good health in the Region. The promise of genetically-modified foods that are resistant to pests, can survive droughts and do not require current storage methods, are possible solutions to the problems. But there are also complex ethical, social and legal issues involved in genetically-modified foods. In an increasingly globalized world, the introduction of these foods into African markets without the knowledge or consent of consumers may occur. Concerns about their safety and the fact that regulatory bodies in the Region may not be capable of judging the safety of these products are real and justified. Several instances where maize and other crops have been genetically modified with genes that confer antibiotic resistance may pose a serious public health problem in African countries.

21. The issue of genetically-modified 'golden' rice, with high amounts of vitamin A, could have major and serious consequences on the people. As an example, it is known that vitamin A is teratogenic if taken in excessive amounts by women in the first trimester of pregnancy.[10] This is important because a majority of pregnant women in the African setting present themselves for antenatal care for the first time only during the second trimester.

22. So, although genetically-modified foods provide an opportunity for the Region, it does mean that the Region would have to develop the complex regulatory bodies needed to examine and approve the use of these products and monitor the effects they possibly could have on public health.

[9] Ciment J. Gene therapy experiments put on clinical hold. *BMJ* 2000; 320:336.
[10] Jick SS, Terris B, Jick H. First trimester topical tretinion and congentital disorders. *Lancet* 1993; 341:1181-2.

### *(c) Development of new drugs and vaccines*

23. Over the past decade many African countries have witnessed a decline in life expectancy to almost below 40 years. Some countries lose one child in five to infectious diseases, while in some countries, like Botswana, two of their young people in five fall prey to AIDS.[11] The human genome undoubtedly offers unprecedented opportunities to all countries to understand the mechanisms of disease and to develop new drugs and vaccines. Some countries such as Brazil, India, Indonesia and Korea have biotechnology industries capable of producing new, high-quality and low-cost generic drugs.[12] Brazil, China, South Africa and Viet Nam, are endeavouring to develop their own essential vaccines, although they are doing so in the face of competition from multinationals. Of concern is the fact that new drugs and vaccines are being developed for export for profit rather than selling them cheaply to local populations.

### *(d) Privatization of genomics research*

24. The privatization of genomics research techniques has led to several patents being registered. A case in point is the AIDS vaccine research in Kenya where Kenyan researchers discovered that their intellectual and legal claim to the vaccine produced in collaboration with their colleagues from the United Kingdom was not registered. It was asserted by the latter that patent registration required more than just participation in a trial. Therefore, good understanding of the intellectual property regulations is essential if the rights of African researchers are to be protected.

### *(e) General issues*

25. Genetic research and development must be accompanied by public education and debate involving all relevant sectors of society. Ethical concerns in this area should be given serious consideration and dealt with carefully at both national and international levels. Individuals have the right to retain control over their genetic material and the information derived from it. Access to and use of this material must be defined through consent, contract or law. Furthermore, genetic information should not be used as the basis for refusing employment or insurance.

## DEALING WITH THE PROBLEM

26. Noting that research bioethics has not received due attention in the African Region, and coupled with the challenges posed by recent advances in genomics, the Regional Director has decided that the subject be treated as a priority area for intervention in the Region. There are clearly issues that could be addressed at the levels of the Member States and the Regional Office.

### The role of Member States

27. Member States should ensure that health research conducted in their territories is limited to those studies that are responsive to the health needs of the country. They should not allow studies which are sponsored by external agencies unless such studies have received the prior approval of an ethical review committee of the host country.

28. Whenever possible, all collaborative research should develop and implement strategies that assist in the building of local research capacity. All collaborative projects should specify plans for including or identifying funds or other sources necessary to build such capacity. Capacity-building may include, but should not be limited to, the following activities:

(a) establishing and strengthening independent and competent ethical review mechanisms;

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[11] Editorial. Genetics and developing countries. *BMJ* 322: 1006-1007

[12] Sidely P. Drug companies sue South African government over generics. *BMJ* 2001; 322-447.

(b) strengthening the research capacity of national institutions;

(c) developing technologies for health care and biomedical research appropriate to the African situation;

(d) training of research and health care staff; and

(e) educating the community from which research participants will be drawn.

29. Health authorities should be encouraged to form an independent, legally-recognized national ethics committee. This committee should be different in composition and function from a scientific review committee. Wherever possible, ethics review committees should be decentralized to local institutional levels and should include members who come from other walks of life besides health. They should receive orientation on the ethics of research.

30. Externally-sponsored research entails two ethical obligations:

(a) The external sponsoring agency should submit the research protocols for ethical and scientific review to its country's research regulatory authority. These protocols should be established in accordance with the standards applicable in the country of the sponsoring agency, and the ethical standards applied should in no way be less exacting than they would be in case the research was carried out in that country.

(b) After scientific and ethical approval in the country of the sponsoring agency, the appropriate authorities of the host country, including a national or local ethical review committee or its equivalent, should satisfy themselves that the proposed research protocols and standards meet their own ethical requirements.

**The role of WHO**

31. WHO should assemble and circulate existing international guidelines and relevant training materials on research bioethics to all Member States and major research and training institutions in the Region.

32. WHO should encourage Member States to include bioethics in the curricula of all training institutions and make it a part of continuing health education. In addition, it should support regional forums and other similar efforts to promote research bioethics in the Region.

33. For WHO to play the leadership role in matters of bioethics, it would be advisable for the Organization to consider appropriate mechanisms to this effect. Furthermore, WHO could help facilitate the establishment of a regional mechanism to ensure the coordination of matters related to bioethics.

34. WHO should advocate for the protection of intellectual property with appropriate international and regional bodies, including the World Intellectual Property Organization (WIPO).

**CONCLUSIONS**

35. Ethical behaviour is not only an essential ingredient in sustaining public support for research, it is also an integral part of the process of planning, designing, implementing and monitoring research involving human subjects. Just as good science requires an appropriate research design, consideration of statistical factors and a plan for data analysis, it must also be based on sound ethical principles. Only then can research succeed in being efficient and cost-effective, while at the same time embodying appropriate protection for the rights and welfare of human participants.

36. The relationships and ultimately the level of trust established among individuals, institutions, communities and countries are determined by complex and often contradictory social, cultural, political, economic and historical factors. It is essential, therefore, that research sponsors, the countries from which they come, the host countries and researchers themselves must work together to enhance collaboration by creating an atmosphere that is based on trust and respect.