



## **Implementation of resolutions and decisions**

### **Ethical, scientific and social implications of cloning in human health**

Summary information is provided here on the outcome of the meetings held during the last three months of 1997, in which the ethical, scientific and social implications of cloning were discussed in relation to the potential biomedical applications of this technique in such areas of human health as reproductive health, xenotransplantation and medical genetics. This supplements section IX of document EB101/10.

#### **REPRODUCTIVE HEALTH**

1. The Special Programme of Research, Development and Research Training in Human Reproduction organized a second interregional and interdisciplinary meeting on cloning (Geneva, 24 October 1997), in conjunction with a regular session of its Scientific and Ethical Review Group.
2. The participants reviewed information from their organizations, countries and regions, which included statements made by governments and professional societies, general articles, and reports of official meetings and public debates, illustrating attitudes and responses to the potential uses of cloning in the area of human health. It appeared that the nature and extent of public information and debate on cloning and its potential advantages and disadvantages in the area of human health varied around the world. To facilitate discussion, it was agreed to distinguish between human cloning for reproductive purposes, that is to produce a human individual, and human cloning for nonreproductive purposes, that is to produce embryos for basic and applied research.

#### **Human cloning for reproductive purposes**

3. Current and proposed legal provisions in this area showed differences in attitudes and policies. Some countries have proposed a total ban on any research involving the cloning of human embryos. Others have proposed a ban on human cloning for reproductive purposes; yet others favour a moratorium. The rationale for the total and partial bans is usually based on concerns about the violation of human dignity. Those countries that have proposed a moratorium argue that further appropriate animal studies are needed to assess the safety of the procedure. These studies, which would have to be carried out at least in part on nonhuman primates and should

be multigenerational, would provide sufficient time and understanding of the procedure and its consequences to permit a fully informed public debate to take place.

4. The perception in some parts of the world, for example in sub-Saharan Africa, seemed to be that this is a high-technology intervention of little relevance to the health needs of the vast majority of the people. Other regions reported that some individuals and religious leaders might consider reproductive cloning acceptable in certain cases such as otherwise untreatable infertility, or to avoid inherited genetic diseases.

### **Human cloning for nonreproductive purposes**

5. Several participants reported interest among the scientific and medical communities of their countries and regions in the use of somatic cell nuclear transfer techniques to produce cloned human embryos for time-limited basic research on ageing and genetic diseases. Similarly, there was interest in using the procedure to produce cloned tissue and organs for possible future transplantation in the nuclear donor and perhaps other tissue-compatible recipients.

6. **Time-limited basic research involving cloned human embryos.** Some countries allow research, within prescribed time limits, on “spare embryos” obtained in assisted reproduction programmes and destined to be destroyed. However, many of these countries, and others, prohibit the production of human embryos specifically for research. In some countries this restriction only applies to research supported with public or federal funding and not to privately funded research; in others, legislation is being considered that would extend to both the public and private sectors. The participants felt that the value of such research needed to be discussed in view of its authorized time frame. Since it is likely to be very short, such research might not yield much useful information on, for example, inherited genetic disorders or genetic ageing.

7. **Production of cloned tissues and organs for transplantation.** This area was perceived as more complex. No ethical problems were envisaged with the use of somatic cell nuclear transfer techniques which would lead directly to cloned differentiated cells or tissues such as skin, for future use by the nuclear donor. However, ethical problems were foreseen with the production by cloning of fully formed and functioning organs, as participants could not envisage how such organs could be made without first producing a cloned embryo and allowing it to grow, at least partially, through the fetal stage of development.

### **International guidelines, regulation or legislation**

8. It was generally agreed that there was a need for international guidelines covering the technical and ethical issues of human cloning for both reproductive and nonreproductive purposes. WHO should play an active role in formulating such guidelines, and action was needed quickly. WHO should foster debate and provide countries with the necessary information and guidance to help them draft appropriate legislation and to avoid measures that might prohibit potentially beneficial research and lead to expatriate and/or clandestine activities.

### **Conclusions**

9. Participants agreed that it was too soon to come to conclusions about global opinions on the use of human somatic cell nuclear transfer procedures for reproductive or nonreproductive purposes. They felt that a comprehensive and international debate was first needed on this subject, as well as within each region and society concerned. At this stage, it would be appropriate to continue with a moratorium on the use of cloning for reproductive purposes, but WHO could take action to clarify the technical procedures and ethical requirements of nonreproductive cloning with a view to producing international guidelines in this area.

## XENOTRANSPLANTATION

10. Transplantation is a life-saving intervention which has gained general acceptance, but the donation of human organs and tissues has not kept pace with demand. In many parts of the world, the shortage is exacerbated by insufficient national capacity to provide chronic and expensive treatments such as dialysis.

11. Xenotransplantation - the transplantation in humans of animal cells, tissues or organs - is at present an area of clinical research which may become part of medical practice. There is preliminary evidence that porcine cellular grafts can endure in human recipients. A subsequent stage would involve using animal cells, tissues and organs as temporary transplants. If reasonable standards of safety and efficacy can be ensured, xenotransplantation could become an economical option and help improve equitable access to transplantation. It could also offer the prospect of treatment for diseases with no other effective therapeutic intervention, such as refractory Parkinson's disease or Huntington's disease.

12. Development of this biomedical technology, however, requires careful consideration and monitoring. Current research is exploring ways of overcoming the immunological problems associated with xenotransplant rejection. Strategies are being elaborated and refined to modify the recipients' immune systems, and genetically to engineer animals to serve as a source of cells, tissues and organs. This includes the use of cloning technology as a means of producing suitable animals for xenotransplantation.

13. A WHO consultation on xenotransplantation (Geneva, 28 to 30 October 1997) stressed that due attention should be paid to ethical, social and religious values and perceptions, which will have a major influence on the ultimate acceptance or refusal of xenotransplantation. It expressed the view that use of cloned, transgenic, or otherwise genetically engineered animals as sources of cells, tissues or organs might be considered acceptable as long as the dignity and identity of humans were respected, human health was protected, and animal welfare was adequately taken into account. If a country authorized the practice of xenotransplantation, it should also determine the species of animals to be used for that purpose, whether the genetic engineering of animals was acceptable, and how principles of animal welfare could be integrated into such use.

14. Xenotransplantation raises important issues regarding informed consent, human rights and community interests. Basic principles of biomedical ethics such as beneficence, nonmaleficence, autonomy and justice should be applied, in a balanced manner, to both the recipient and the community. They both have a right to expect that the principle of precaution will be exercised. It should be made clear that a balance of risks, not a total absence of risk, is expected. The potential psychological impact of xenotransplants should be carefully monitored and counselling provided to the recipients and their immediate contacts, including health care providers.

15. Cultural and societal responses to xenotransplantation are difficult to predict. They will differ from place to place and may change over time. Scientists, health professionals, and other partners involved, such as religious leaders and the media, can play an important role in providing public information and fostering debate on this technology's potential safety, efficacy and desirability. A major influence on people's attitude towards xenotransplantation will be their perception of the scientific validity and medical justification of the procedure. It is imperative to ensure accountability, protection of public interests and minimization of risk.

16. An important concern of researchers and public health authorities is the prevention and management of zoonoses - the transmission of potentially infectious agents from animals to xenotransplant recipients and, through secondary transmission, to their contacts and the wider human population. WHO has produced detailed guidance on this subject. The consultation carefully considered the various issues related to zoonotic risk and the measures necessary to deal with them.

17. Since the potential advantages and risks of xenotransplantation cross national boundaries, development of this technology is a public health issue which must be dealt with at both national and international levels. National policies should be framed and international collaboration built up in order to promote safety, efficacy,

equity and ethical practice. Compatibility and cooperation between national programmes and registry systems will facilitate the international exchange of information and the notification and investigation of zoonotic infection and disease. WHO has a major role to play by enhancing awareness of xenotransplantation developments among all Member States and providing them with the necessary guidance on the issues raised by the potential use of this technology. WHO can foster debate in different cultural, religious and social environments on the ethical issues raised by organ transplantation in general, and xenotransplantation in particular.

## **RESEARCH AND REGIONAL PARTICIPATION IN THE ETHICAL DEBATE**

18. The meeting of the global ACHR (Geneva, 21 to 24 October 1997) endorsed the report of its Task Force on Organ Transplantation, including the recommendation for improving equitable access to organ transplantation. It also endorsed recommendations to ensure adherence to the best technical and ethical practices for transplantation from either cadaveric or live donations and for the potential development of xenotransplantation. It was agreed that the regional bodies of ACHR should be asked to help collect information on, and foster awareness and understanding of, organ transplantation in their regions, and that the network of WHO collaborating centres in this area of activities would be strengthened.

19. In response to resolution WHA50.37, ACHR decided to include consideration of the ethical and social questions raised by cloning in its future activities. It expressed the view that the issues of responsible parenthood and of the social and ethical regulation of research should not be limited to cloning only but seen in a broader perspective. Such issues should be analysed within the broader context of the relations between biomedical technology, social perceptions and parental expectations regarding, for example, disability and possible genetic defects.

## **GENETIC AND HEREDITARY DISORDERS**

20. WHO convened a panel of experts (Geneva, 15 to 16 December 1997) to review proposed guidelines on genetic counselling. The meeting also considered some major ethical issues which arise from current research and advances in medical genetics, particularly from the human genome project.

21. The medical application of genetic knowledge must be carried out with due regard to the general principles of medical ethics, which include: doing good, not doing harm, offering autonomy of choice after information is given, and facilitating personal and social justice. Genetics itself teaches us that there is no such thing as a “superior” or “inferior” genome, and that humankind depends for its richness and survival on its complex genetic diversity.

22. The group discussed the issue of reproductive cloning, defined as use of a genome from an existing individual to create a new, but near genetically identical, individual via nuclear or cell transfer. Members expressed the view that human cloning for reproductive purposes was not ethical and should not be permitted. The statements and decisions made by various international bodies in this regard were noted. Cell cloning in cell cultures for medical purposes was a different matter and might be of great clinical value in the treatment of some diseases such as cancer.

23. Regarding gene testing during pregnancy, the group considered that it should be offered to those who wished it, but that there should be no pressure on couples to have such testing. The results of the test should not be used to compel a couple either to continue or to end an affected pregnancy. The group acknowledged that the ethical beliefs of individuals and the histories and legal positions of countries differed but stressed that, to the

extent possible, the ultimate decision on issues of genetics in the context of reproduction should rest with the woman or the couple.

24. The advances in human genetics which have occurred during the past 20 years have revolutionized our knowledge of the role of inheritance in health and disease, not only for single gene disorders but also for predisposition to cancer, heart disease, mental disorders and even susceptibility to infectious diseases. WHO should take the initiative to promote the public health applications of medical genetics, especially in developing countries, and their integration into national health policies and services. This could be done through pilot programmes and medium-term strategies, which include testing for genetic factors of common diseases, counselling services, access to care, and social support services.

25. When used properly, genetic knowledge can play a very important part in helping to achieve better health for all worldwide. Gene screening and testing can make a cost-effective contribution to public health planning in any country, but should not be compulsory. Genetic data should be used to the advantage of members of a family or ethnic group, not to stigmatize or discriminate against them. Confidentiality and nondiscriminatory use of data should be protected, if necessary by legal means. To maximize the benefits and minimize the risks, education in genetics should be developed not only for health professionals but also for the general public in all cultures.

26. On the issue of justice and equitable access for all to the benefits of genetic knowledge, the group recognized that patenting was part of the normal process of product development, in genetics as in other medical fields. Deep concern was expressed, however, that patenting had the potential to impede international collaboration, especially between developed and developing countries, to the ultimate detriment of health care for those who needed it most. The group expressed the view that patents on gene sequences should only be granted in the context of inventions of methods or procedures of proven utility.

27. With these important points in mind, the Member States of WHO should give urgent consideration to ethical development of the public health applications of genetic knowledge, and foster dialogue and cooperation in this field.

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