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Human Rights and Ethical Perspectives on HIV Vaccine Trials

Defining the Issue

Current and future clinical trials of preventive HIV vaccines embody several ethical concerns that may also have human rights implications. The ethical concerns fall into three categories: 1) questions relating to “standard of care” for trial participants; 2) questions relating to the design of future vaccine trials; and 3) concerns about access to successful products of vaccine research. The “standard of care” issue is the most pressing of the above three, given that there is, at the present time, no proven, efficacious, preventive vaccine.

Prominent international guidelinesⁱ and recommendationsⁱⁱ address these ethical concerns but arrive at rather different conclusions regarding what is owed to vaccine research subjects and to others, during clinical trials or after they are concluded. A number of human rights provisions may be considered relevant to these ethical concerns. As the issues at stake generally involve the conduct of researchers and the potential benefits to human subjects, rather than the conduct of governments per se, it remains unclear how and if attention to human rights norms and standards may be most useful to strengthening rights and responsibilities in HIV vaccine trials.

Ethical Principles and International Guidelines

Standard of care What level of care and treatment should be provided for trial participants who become infected with HIV during a trial? Three possible answers, along with relevant ethical principles and the position taken in leading guidelines, are provided below:

(i) *The best current treatment available anywhere in the world.* This (highest) level of treatment is supported by the *principle of beneficence* (maximize benefits and minimize harm to research subjects); the *principle of reciprocity* (people who make a significant contribution to an effort deserve something in return); and the *principle of justice as equality* (treat like cases alike). In this context, the “like cases” are vaccine trials conducted in different parts of the world. Since participants who become infected in vaccine trials in industrialized countries will have access to antiretroviral therapy (ART), this principle requires that participants in developing countries be provided with the same level of treatment.

None of the leading international guidelines mandates the highest standard of care for participants who become infected. The Declaration of Helsinki does not have a provision that is directly relevant. The CIOMS guidelines say, in a commentary, that there is no obligation, but it would be morally praiseworthy to provide treatment for a condition that an experimental vaccine is designed to prevent. The UNAIDS Guidance Document states that the *ideal* is to provide the best-proven therapy.

(ii) The highest attainable level of treatment available in the country where the trial is conducted. This level of treatment is supported by the principle of beneficence in a

somewhat weaker form than what exists for the best current treatment available. The UNAIDS Guidance Document (GP16) mandates this level of treatment as a minimum. The precise wording of this Guidance Point is derived from Article 12 of the ICESCR: “The right of everyone to the highest attainable standard of physical and mental health.”

(iii) The level of care provided in the public health system in the country where the trial is conducted. This (lowest) standard of care can be supported by the principle of justice as equity. The equity in this context refers to what HIV-infected individuals in the country who are not enrolled in a preventive vaccine trial normally receive. The international guideline that supports this standard of care is the Nuffield Council Report. Although Nuffield says it endorses UNAIDS GP 16, its recommendation states: “Where it is not appropriate to offer a universal standard of care, the minimum...that should be offered is the best available intervention as part of the national public health system for that disease.”ⁱⁱⁱ The “highest attainable” level of treatment may be higher than what the public health system provides in many developing countries. The National Bioethics Advisory Commission (NBAC) Report does not address this specific issue.

Choice of comparator in future randomized controlled vaccine trials. All of the international guidelines address this issue. Paragraph 29 of the Declaration of Helsinki, UNAIDS Guidance Point 11, and CIOMS Guideline 11 all agree that a placebo control is acceptable if there is no proven efficacious vaccine. If there exists a proven efficacious vaccine, paragraph 29 of Helsinki still applies (but see the caveat in the 2001 Clarification); CIOMS Guideline 11 still applies (but see the “exceptional” case in the commentary); UNAIDS Guidance Point 11 applies (but see the narrow exceptions). The requirement to provide a proven, efficacious vaccine to a control group is supported by the *principle of beneficence* (maximize benefits, minimize harms); and by the principle of *justice as equality* (applicable when the control group in a vaccine trial in an industrialized country would receive a proven, efficacious vaccine).

Both the NBAC Report and the Nuffield Council Report permit the use of placebo controls even if a proven efficacious vaccine exists. The recommendations in both reports allow the control group in developing countries to receive a “standard of care” lower than the best current method available elsewhere in the world. The only requirement is that the proposed comparator for the control group be justified to and accepted by the research ethics committee(s) reviewing the protocol.

Post-trial obligations to provide vaccine that proves efficacious. UNAIDS Guidance Point 2, and arguably, CIOMS Guideline 10 mandate provision of a proven efficacious vaccine to trial participants who received placebo. Paragraph 30 of the Declaration of Helsinki clearly mandates access to the “best current...method identified by the study.” However, the WMA has issued a potential “clarification” and a proposed replacement that would substantially weaken this paragraph.^{iv}

As for providing a successful product to the community or country where the trial was conducted, UNAIDS Guidance Point 2 mandates availability “as soon as possible”; CIOMS Guideline 10 requires that the product be made “reasonably available”. Helsinki does not mention wider access to successful products of research, and both NBAC and Nuffield deny that sponsors or researchers have any obligation to ensure access.

Significance of Human Rights

The significance of human rights norms and standards in relation to these ethical issues in HIV vaccine research may lie in identifying the accountability of the agents who have obligations related to the research and its aftermath. When governmental agencies sponsor, conduct, provide technical assistance, or collaborate in the design and conduct of HIV vaccine research, they have responsibility for any abuses of human rights that may occur in relation to the research. It may be that this then imposes a corresponding obligation on the part of government to comply with internationally recognized ethical principles for research. This holds for the government of the sponsoring country whose governmental research organization funds, designs, or conducts the research, and also the host country whose Ministry of Health must grant permission for the research to be conducted and in which local researchers collaborate with the sponsoring agency. Among governmental research agencies to which this would apply are the U.S. National Institutes of Health and Centers for Disease Control and Prevention, and the U.K. Medical Research Council. These organizations sponsor and conduct HIV research in their own countries as well as in many developing countries. Although the function of these agencies is limited to the sponsorship and conduct of research, the national governments of which they are a part have obligations under various international human rights documents.

The key human rights provisions relevant to the issues described above would seem to be Articles 12 and 15 of the ICESCR; General Comment on Article 12 (2000); and revised Guideline 6 (“Access to prevention, treatment, care and support”), Third International Consultation on HIV/AIDS and Human Rights, July 2002.

This Issue Paper was prepared by Ruth Macklin to facilitate discussion at the Reference Group’s August 2003 meeting.

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ⁱ World Medical Association, 1964, as amended by the WMA 52nd General Assembly, *Declaration of Helsinki* (Edinburgh, Scotland, 2000). Joint United Nations Programme on HIV/AIDS (UNAIDS), *Ethical Considerations in HIV Preventive Vaccine Research* (2000); CIOMS, *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (Geneva: CIOMS, 2002).

ⁱⁱ National Bioethics Advisory Commission, *Ethical and Policy Issues in International Research* (Bethesda, Maryland, 2000). Hereinafter, NBAC. Nuffield Council on Bioethics, *The Ethics of Research Related to Healthcare in Developing Countries* (London: Nuffield Council on Bioethics, 2002).

ⁱⁱⁱ Nuffield Council on Bioethics (2002), p. 96.

^{iv} The clarification and proposed replacement paragraph are scheduled for discussion at the WMA General Assembly, to take place in Helsinki, Finland, 10 – 14 September 2003..