Research Benefits for Hypothetical HIV Vaccine Trials: The Views of Ugandans in the Rakai District

Author(s): Christine Grady, Jennifer Wagman, Robert Ssekubugu, Maria J. Wawer, David Serwadda, Mohammed Kiddugavu, Fred Nalugoda, Ronald H. Gray, David Wendler, Qian Dong, Dennis O. Dixon, Bryan Townsend, Elizabeth Wahl and Ezekiel J. Emanuel

Source: *IRB: Ethics & Human Research*, Mar. - Apr., 2008, Vol. 30, No. 2 (Mar. - Apr., 2008), pp. 1-7

Published by: The Hastings Center

Stable URL: https://www.jstor.org/stable/30033263

IRB

ETHICS
&
HUMAN RESEARCH

MARCH-APRIL 2008 • VOLUME 30, NUMBER 2

A PUBLICATION OF
THE HASTINGS
CENTER

Research Benefits for Hypothetical HIV Vaccine Trials:

The Views of Ugandans in the Rakai District

BY CHRISTINE GRADY, JENNIFER WAGMAN, ROBERT SSEKUBUGU, MARIA J. WAWER, DAVID SERWADDA, MOHAMMED KIDDUGAVU, FRED NALUGODA, RONALD H. GRAY, DAVID WENDLER, QIAN DONG, DENNIS O. DIXON, BRYAN TOWNSEND, ELIZABETH WAHL, EZEKIEL J. EMANUEL

Collaborative, multinational clinical research is complicated by thorny ethical issues, especially when sponsored by developed world entities and conducted in the developing world. An overarching ethical concern in all research is the possible exploitation of vulnerable individuals or populations. Exploitation, often understood as an unfair distribution of benefits,[1] may be more of a challenge in international research because of background disparities in health, health resources, and power between developed and developing countries.[2] Codes and guidelines have recommended provision of benefits to participants or the host community as one means of minimizing exploitation in international research.[3] Ensuing debates on the type and level of benefit that should be provided have focused on issues such as compensation to individual research participants and posttrial access to products proven effective.[4]

Although research participants are often reimbursed or compensated with money or other goods, researchers and members of research ethics boards sometimes disagree about what kind of reimbursement or compensation—and how much—is appropriate. International guidelines[5] note that participants may be reimbursed or compensated for time, travel, and inconvenience with money or free medical care in acceptable amounts approved by local research ethics boards, as long as amounts are "not so large or the medical services so extensive as to induce prospective subjects to consent to participate in the research against their better judgment."[6] Previous studies have shown that financial incentives may impact individuals' willingness to participate in HIV vaccine trials,[7] but few studies have directly assessed respondents' opinions about whether research participants should be financially compensated.[8]

International guidelines also address the provision of posttrial benefits, noting that "Medical research is only justified if there is

---

Christine Grady, Jennifer Wagman, Robert Ssekubugu, Maria J. Wawer, David Serwadda, Mohammed Kiddugavu, Fred Nalugoda, Ronald H. Gray, David Wendler, Qian Dong, Dennis O. Dixon, Bryan Townsend, Elizabeth Wahl, and Ezekiel J. Emanuel, "Research Benefits for Hypothetical HIV Vaccine Trials: The Views of Ugandans in the Rakai District," *IRB: Ethics & Human Research* 30, no. 2 (2008): 1-7.

a reasonable likelihood that the populations in which research is carried out stand to benefit from the results of the research,"[9] or directing research sponsors and investigators to "ensure that any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community."[10] Disagreement about posttrial benefits persists, and to date particular posttrial benefits have not been universally required by national regulations or research ethics committees. Some commentators insist that sponsors guarantee access to tested interventions after a trial, even if it requires enhancements to a community's health delivery infrastructures.[11] Yet doing so is "rarely a simple matter,"[12] and considerable uncertainty remains regarding what and how much should be guaranteed, and by whom.[13] One proposal—the fair benefits framework—suggests that host researchers and communities might negotiate for other benefits instead, such as public health measures or capacity building in health care or research, arguing that a *fair distribution* of benefits, rather than a particular *type* of benefit, is important for ethical international research.[14]

Little is known about the perspectives of research participants and other residents of developing country communities regarding these types of research benefits. This paper reports views related to two kinds of benefit in a hypothetical HIV vaccine study: 1) compensation to individual study participants, and 2) benefits to the community posttrial. This report is one part of a larger survey that aimed to describe perceptions of research benefits and harms[15] among residents in selected Ugandan communities that have participated in clinical research, including HIV vaccine preparedness studies, for almost two decades.

Research Methods

■ ***Study Population.*** A cross-sectional ethics survey, "Perceptions of Benefits and Harms of Research" (BAHR), was conducted with participants drawn from the Rakai Health Science Program (RHSP, formerly the Rakai Project) in the rural Rakai District of southwest Uganda. The Rakai District was at the center of the HIV epidemic in Uganda; current HIV seroprevalence is estimated to be 15% and incidence 1.4/100 person-years.[16] RHSP is a population-based reproductive health research program that conducts extensive community HIV/STD epidemiological and behavioral studies, provides HIV/STD preventive services and HIV-related treatment, and undertakes large community randomized intervention trials. Trials have included STD control and male circumcision for the prevention of HIV/AIDS. In 1994, RHSP initiated a population-based prospective cohort study in 46 communities in the Rakai District. Annual interviews and biological samples, collected among consenting community members between 15 and 49 years of age and representing over 85% of age eligible residents, provide longitudinal data on HIV epidemiology, sociodemographic characteristics, behaviors, health status, and service utilization in these typical rural Ugandan communities.[17] All RHSP participants are provided with the benefits of health and HIV prevention education, access to free condoms, HIV testing, and counseling. All residents, whether participating in RHSP or not, have access to Rakai mobile and fixed clinics for STD treatment and general health care. At the time of the survey, antiretroviral therapy was not available through RHSP. The RHSP is a collaboration between the Uganda Ministry of Health (through the Uganda Virus Research Institute), and researchers from Makerere University (Kampala), Columbia University (New York), and Johns Hopkins University (Baltimore). Multiple U.S. organizations—including the National Institute of Allergy and Infectious Diseases, the Fogarty International Center, and the Bill and Melinda Gates Foundation—fund RHSP research.

BAHR participants included men and women randomly chosen from four groups: 1) individuals participating in three RHSP studies; 2) those who declined continued participation in the Rakai Cohort Surveillance Study; 3) community opinion leaders identified by a previous sociometric survey; and 4) unaffiliated residents of proximal communities not participating in RHSP studies. RHSP study participants were recruited from three specific studies: 1) the Rakai Cohort Surveillance Study (RCSS); 2) the Molecular Epidemiology Research (MER); and 3) the Bacterial Vaginosis Natural History Research (BV). A complex, stratified sampling mechanism was employed to ensure respondent representation from peri-urban, rural, and deep rural regions. A list of random names was generated by the Rakai study team for the BAHR study from the three research participant groups, the decliner group, and previously identified community opinion leaders. Community mobilizers who work as RHSP volunteers assisted in identifying potential respondents from the unaffiliated communities and other community leaders (Table 1, at http://www.thehastingscenter.org/pdf/irb_2008_mar_apr_Grady_tables.pdf).

■ ***Survey Design.*** Results reported here are respondents' views about individual compensation and posttrial community benefits in a hypothetical HIV/AIDS vaccine trial in Rakai District. These questions were part of a larger survey about perceptions of personal and community benefits and harms of research (BAHR). The survey was developed through: a comprehensive literature review; drafts of the survey by the U.S. and

Figure 1. Sample Questions on Posttrial Benefit

To answer the following questions, imagine that researchers are planning to test an HIV/AIDS vaccine in Rakai District.

- After the trial, do you think researchers should provide some benefit to everyone in the community, whether or not they participated in the trial? YES NO
- What type of benefit should researchers offer communities? (open-ended)
- Which ONE of the following benefits do you think researchers should provide for the community where the trial takes place?
  - Free provision of the HIV/AIDS vaccine, if it is found to work for people who do not have HIV/AIDS
  - Free treatment of opportunistic infections for people who have HIV/AIDS
  - Free provision of drugs which treat HIV/AIDS for people who have HIV/AIDS
  - Free general medical care for everyone in the community
  - Other
- As well as providing [insert response from above], if the HIV/AIDS vaccine works, do you think researchers are also required to provide the vaccine to the community for free? YES NO

Ugandan authors; revisions by survey professionals; translation into the local language (Luganda) and back-translation into English by Rakai Program staff; pilot testing; and final revisions. Pilot testing was conducted in December 2002 with 54 individuals in three different communities that were not subsequently involved in the BAHR survey. Pilot testing evaluated the interview strategy, the process of informed consent, the questionnaires and survey procedure, and quality control procedures. The overall BAHR survey also assessed perceived personal and community benefits and harms from research, including psychological, scientific, local medical, and economic benefits or harms. Both structured and open-ended responses were elicited. Questions about compensation and posttrial benefit included dichotomous yes/no choices, open-ended questions, and multiple choice questions. For sample questions, see Figure 1. The instrument is available from the authors upon request.

■ ***Survey Administration.*** Interviews were conducted between January and August 2003 by specially trained Ugandan personnel independent of other RHSP activities. Research assistants explained the purpose and nature of the study and invited interested individuals to a prearranged interview in a central place in each community cluster. For individuals who did not keep their appointments, research assistants conducted home visits to reschedule the interview. Respondents gave written informed consent and were reimbursed for their travel (2,500 Uganda shillings, approximately US$1.50)

■ ***Human Subjects Approval.*** This study was reviewed and approved by the Institutional Review Board of the U.S. National Institute of Allergy and Infectious Diseases and the Science and Ethics Committee of the Uganda Virus Research Institute. Identifiers were not included on the questionnaires, and RHSP staff had no access to the completed surveys.

■ ***Statistical Methods.*** Data were double-entered into a FoxPro database with built-in range, cross checks, and edits. Data were analyzed using SAS Version 9.1 for Windows. The analysis was descriptive and examined responses of the entire study population, as well as those within respondent groups. Univariate and multivariate analysis examined associations between age, gender, school status, marital status, religion, and participation status and the outcome variables of interest. Univariate analysis was done by χ^2 tests. Logistic regression models estimated the adjusted odds ratios and 95% confidence intervals of factors associated with answers to questionnaires. Models were adjusted for age, gender, and statistically significant covariates identified in the univariate analysis. For questions with multiple answers, a nominal logistic regression model was used.

Results

A total of 915 adults were interviewed—517 research participants, 100 decliners, 103 unaffiliated persons, and 195 opinion leaders. Overall, 60% of respondents were male, mean age was 31.3 years (range 18–49), and 72% were married. Sixty-five percent of respondents were Catholic, 17% Protestant, and 14% Muslim. More than half (58%) reported some primary education, 23% had some secondary education, and 16% had some postsecondary education; 93% were identified as literate. Most participants (92%) lacked electricity, and the majority owned bicycles (65%) but not cars. Overall, opinion leaders were older, better educated, and more likely to own a bicycle than the other groups (Table 2, at http://www.thehastingscenter.org/pdf/irb_2008_mar_apr_Grady_tables.pdf).

■ ***Individual Participation and Compensation.*** Most respondents (77%) said previous participants in Rakai Program studies should receive highest priority for enrollment in a hypothetical HIV vaccine study, while 14% said anyone in the Rakai District should get priority, and 7% thought priority should be given to Rakai residents who had not previously participated in research. Respondents recruited from the three active RHSP studies (RCSS, MER, and BV) were more likely than the other groups to say previous participants should have priority.

Overall, 73% (668) said researchers should compensate individual participants in research (Table 3, at http://www.thehastingscenter.org/pdf/irb_2008_mar_apr_Grady_tables.pdf). No significant differences were noted by age, gender, school status, or religion between those who did and those who did not think researchers should compensate participants. Participants in the three active Rakai studies were less likely to favor compensation than other groups (adjusted OR 0.68 [95% CI 0.50, 0.93] p = 0.016), although no difference was seen between active research participants who were receiving payment and those who were not. Of 668 respondents who favored compensation, 53% said it was warranted due to possible negative effects of participation, and 30% as a sign of appreciation for their participation.

In response to an open-ended question about the type of compensation they thought desirable, 55% (40% of the total sample) said money, 23% suggested health care, and 15% suggested food. Older respondents were significantly more likely to choose money than younger respondents (OR 4.60 [1.76, 12.3], p = 0.033). Respondents suggested a wide range of amounts from as low as 1,000 USh (about US$0.60) to as high as 5,000,000 USh (approximately US$3,000).

From a list of types of compensation, 44% chose the combination of travel reimbursement plus a health/hygiene-related item as the *one* type of compensation they would prefer in an HIV vaccine trial over other options listed, including money alone. This choice (travel plus a health item) was chosen most frequently by each of the respondent groups, and significantly more frequently by older respondents than younger (OR 0.28 [0.11, 0.73], p = 0.0009). Differences between participants and nonparticipants, or participants and decliners, were not significant. When asked why they would prefer this type of compensation, the most common reason (47%) was to protect against other diseases, followed by the high cost of travel associated with study participation (18% overall).

■ ***Posttrial Community Benefits.*** Most respondents (80%) said researchers should provide posttrial benefits to everyone in the local community regardless of their participation in the research (Table 4, at http://www.thehastingscenter.org/pdf/irb_2008_mar_apr_Grady_tables.pdf). When unprompted, 59% of those who said researchers should provide posttrial benefits to communities (47% of the total) suggested health care services as the posttrial benefit they thought researchers should provide; another 25% said clinics, dispensaries, and clean water; 28% said money; and 16% said the vaccine.[18] Females selected money more frequently than males (OR = 1.70 [1.22, 2.38], p = 0.0019), and active research participants more than nonparticipants (OR = 1.58 [1.11, 2.23], p = 0.01). Just 16% (12.8% of the total) offered that researchers should provide the vaccine if proven effective.

From a list of types of benefit, 44% chose free provision of the HIV/AIDS vaccine for uninfected people if found effective as the *one* benefit researchers should provide for the community, 29% chose free general medical care, and 21% free provision of HIV drugs (Table 4, at http://www.thehastingscenter.org/pdf/irb_2008_mar_apr_Grady_tables.pdf). Opinion leaders were more likely than the other groups to choose the benefit of free HIV vaccine. No other differences between respondent groups were found.

Of the 56% who chose a community benefit *other* than the HIV/AIDS vaccine from the list, just over half (55% [31% of the total]) gave as their reason the level of poverty in the community. Twenty-four percent said they wanted to help HIV-positive individuals. Three quarters (74% [41% of the total sample]) of these respondents, and females less often than males (OR 0.52 [0.35, 0.78], p = 0.0017), said the HIV vaccine should be provided *in addition to* the other benefit they chose. The most common reason given for this answer was poverty.

■ ***Providing Posttrial Vaccine: To Whom and How?*** Most respondents (86%) chose making the HIV vaccine available to more people at some cost rather than to fewer people for free (12%) as fairest in the event the HIV/AIDS vaccine was found to be effective, but resources prevented RHSP from giving it to everyone free (Table 5, at http://www.thehastingscenter.org/pdf/irb_2008_mar_apr_Grady_tables.pdf). Very few respondents (2% overall) said that RHSP had a responsibility to provide free vaccine to everyone regardless of the circumstances. No differences were found between respondent groups.

When asked which entity they believed should provide funds to enable Ugandans to access a vaccine, 50% chose the Ugandan government, 10% chose the vaccine manufacturer, and 40% a local or international aid organization. Females were less likely than males to choose the Ugandan government over other possibilities to subsidize the cost of the vaccine (OR 0.61 [0.47, 0.79], $p = 0.0011$).

When asked who should decide about community benefits in the HIV/AIDS vaccine trial (results not shown), 31% said the Local Council 1 chairman (LC1s represent the most grassroots level of elected government in Uganda), 22% said research participants, 22% said Ugandan researchers, and 11% said community members. Support for research participants as decision-makers did not vary by respondent group.

Discussion

This is the first published study to describe the views of individuals in a developing community about two controversial types of benefits associated with research: compensation to individuals for research participation and posttrial benefits to the community.

First, the majority of individuals believe that participation in clinical research merits some compensation for individual participants. This, however, did not necessarily mean monetary compensation. While most (73%) respondents thought participants in clinical trials should be compensated, just over half said that such compensation should come in the form of money, while many indicated that food or healthcare would be an appropriate or even a preferred form of compensation. These choices may reflect the socioeconomic status and basic needs of this cohort. Further, the most common choice from a list of possible forms of compensation was travel reimbursement plus a health/hygiene related item, a choice that may have been influenced by knowledge of the usual form of compensation in the RHSP or that could perhaps reflect an interest in health as a major motivation for research participation. That almost 30% of respondents indicated no compensation was necessary is intriguing and merits further exploration, especially given how easy it is to say yes to a question like this. Although we did not explore whether respondents were concerned about inducement or other possible negative effects of compensation, given the potential importance for future studies, further research to clarify reasons respondents said no to compensation would be helpful.

Second, the majority of respondents thought that researchers should provide some benefit to the community after a trial, yet only 16% suggested providing the vaccine tested in the study. When asked to choose from a list of possible posttrial benefits, many more—yet still less than half of respondents (44%)—chose offering free HIV vaccine to the community. The others chose general medical care or care specific to HIV-infected individuals. Although we do not know all of the reasons that only some respondents selected the benefit of the tested vaccine, their choices suggest that community members chose tangible, pressing needs in their community that they see as a higher or more immediate priority or as affecting a greater number of people than making the tested product "reasonably available."[19] Many respondents explained their choices based on poverty in their community. Even if an HIV vaccine was recognized as a possible future benefit for the community, respondents were aware of more current needs for food and health care. A quarter of respondents did not opt for vaccine provision even when given the option of *adding* the HIV vaccine to the other chosen benefits, however, and this finding warrants further study.

Third—and surprisingly—active research participants were less likely than others to say that researchers should compensate participants, but more likely to say that money should be provided to the community as a posttrial benefit. The reasoning behind these choices was not explored. It is possible that the active research participants wanted to give responses that reflect what they had been told by researchers regarding compensation. In RHSP, even when compensation is offered, it is not emphasized, and participants are frequently reminded that research participation is voluntary.

Fourth, respondents overwhelmingly preferred that in the event the RHSP could not afford to offer a proven effective vaccine for free, it be offered at some cost to a larger number of people, rather than free to a smaller number. Respondents most often placed responsibility for subsidizing a vaccine on their own government or local and international aid organizations. Only 10% chose the pharmaceutical company sponsor as responsible for paying for the vaccine. This choice could reflect lack of knowledge about the sponsors of research, distrust in pharmaceutical companies, awareness of the need for a sustainable approach to providing HIV vaccine to Ugandans, and/or other factors.

There is growing recognition in the literature that public-private partnerships—with governments, international organizations, pharmaceutical companies, and others—may be the most economically and politically sustainable way to make effective research products available to developing country communities.[20] Host country governments, researchers, and research sponsors should work collaboratively to make the results of research—as well as the tested product when appropriate and possible—available to individuals and communities. UNAIDS recommends that all stakeholders, including members of the involved communities, take part in those negotiations.[21] Respondents in this survey demonstrated their readiness to be engaged in this type of process. Of importance, community concerns are already given voice through community representation on local ethics committees and local community advisory boards in many vaccine and community preparedness studies. Town-hall-type meetings and other mechanisms for including more community members in the discussion may also be valuable.

Importantly, these data suggest that the voices, concerns, and preferences of those most affected by international research should be included when decisions are made about research benefits and when formulating and implementing ethical guidelines. This is not to suggest that such benefits should be limited to what communities ask for, as their expectations could be small and relatively uninformed. However, it does suggest that when decisions are made about the type and level of benefit that is "best" for minimizing the exploitation of communities, the views of such communities should be considered and used to expand the foundation laid by sound ethical guidance.

These survey findings are limited in that they reflect the views of people in one region of one country to one kind of hypothetical trial (HIV vaccine), and as such may not be generalizable to other groups. Individual perceptions about these issues can be influenced by education and knowledge about specific issues, local infrastructure, authoritative structures, and needs. In addition, this is a highly studied population because of the longstanding presence of the RHSP in Rakai,[22] and thus, respondents may be more familiar with and supportive of research than other communities with less exposure or familiarity. Nonetheless, their views on participant compensation and posttrial benefits associated with research make a valuable contribution to continued dialogue about these issues. Although alone maybe not determinative, the needs and preferences of research participants themselves and others in involved communities should be carefully considered when debating appropriate and fair benefits associated with research.

Disclaimer

The authors of this article are responsible for its contents. No statement in this article should be construed as an official position of the National Institutes of Health, Public Health Service, or Department of Health and Human Services.

Acknowledgments

The authors gratefully acknowledge the contributions of the 915 respondents, the Ugandan interviewers and research assistants, the RHSP study team, Lone Simonsen and Erica Heiman for help with initial statistics, and all those who provided critical feedback on the manuscript. This study was funded by the Department of Bioethics, Clinical Center, National Institutes of Health.

■ **Christine Grady, RN, PhD,** is Head, Section on Human Subjects, Department of Bioethics, Clinical Center, National Institutes of Health, Bethesda, MD; **Jennifer Wagman, MHS,** is Senior Research Program Coordinator, Department of Population, Family, and Reproductive Health, Bloomberg School of Public Health, Johns Hopkins University, Bethesda, MD; **Robert Ssekubugu** is Research Assistant, Rakai Health Sciences Program, Uganda Virus Research Institute, Entebbe, Uganda; **Maria J. Wawer, MD, MSc,** is Professor, Department of Population and Family Health Sciences, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; **David Serwadda, MB, ChB, MMed, MPH,** is Associate Professor, Institute of Public Health, Makerere University, Kampala, Uganda; **Mohammed Kiddugavu, MB, ChB, MPH,** is Investigator, Rakai Health Science Program, Uganda Virus Research Institute, Entebbe, Uganda; **Fred Nalugoda, BSc, MHS,** is Director of Field Activities, Rakai Health Sciences Program, Kalisizo, Uganda; **Ronald H. Gray, MD,** is Professor, Department of Population and Family Health Sciences, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; **David Wendler, PhD,** is Head, Unit on Vulnerable Populations, Department of Bioethics, Clinical Center, National Institutes of Health, Bethesda, MD; **Qian Dong, MS,** was a statistics fellow at National Institute of Allergy and Infectious Diseases, National Institutes of Health, while writing this paper and is currently Senior Statistician, Merck & Co., Inc., Rahway, NJ; **Dennis O. Dixon, PhD,** is Mathematical Statistician, Biostatistics Research Branch, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD; **Bryan Townsend, MA,** was a student at the NIH Department of Bioethics while writing this paper and is currently a student at Yale Law School, New Haven, CT; **Elizabeth Wahl** was a Fellow, NIH Department of Bioethics, while writing this paper and is currently a student at Yale University Medical School, New Haven, CT; and **Ezekiel J. Emanuel, MD, PhD,** is Chief, Department of Bioethics, Clinical Center, National Institutes of Health, Bethesda, MD.

References

1. Wertheimer A. *Exploitation.* Princeton, NJ: Princeton University Press, 1996.

2. Macklin R. *Double Standards in Medical Research in Developing Countries.* Cambridge, UK: Cambridge University Press, 2004; National Bioethics Advisory Commission. *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries.* Vol. 1. Bethesda, MD, 2001; Emanuel E, Wendler D, Killen J, Grady C. What makes clinical research in developing countries ethical? Benchmarks of ethical research. *Journal of Infectious Diseases* 2004;189:930-937.

3. Nuffield Council on Bioethics. *The Ethics of Research Related to Healthcare in Developing Countries.* 2002. http://www.nuffieldbioethics.org/go/print/ourwork/developingcountries/introduction>; Council for International Organizations of Medical Sciences (CIOMS). *International Ethical Guidelines for Biomedical Research Involving Human Subjects.* Geneva: CIOMS, 2002. http://www.cioms.ch/frame_guidelines_nov_2002.htm; see ref. 2, National Bioethics Advisory Commission 2001, recommendation 1.3; World Medical Association. *Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects.* October 2000. Principle 19. http://www.wma.net/e/policy/b3.htm.

4. See ref. 2, National Bioethics Advisory Commission 2001; Participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries. Moral standards for research in developing countries: From "reasonable availability" to "fair benefits." *Hastings Center Report* 2004;34(3):17-27.

5. See ref. 3, CIOMS 2002; see ref. 2, Declaration of Helsinki 2000; UNAIDS. *Ethical Considerations in HIV Preventive Vaccine Research.* 2000. Guidance Point 10. http://www.who.int/vaccine_research/diseases/hiv/en/JC072-EthicalCons-E.pdf.

6. See ref. 3, CIOMS 2002, Guideline 7.

7. Celentano DD, Beyrer C, Natpratan C,

et al. Willingness to participate in AIDS vaccine trials among high risk populations in northern Thailand. *AIDS* 1995; 9(9):1079-1083; Jenkins RA, Tougsa K, Markowitz LE, et al. Willingness to participate in HIV-1 vaccine trials among young Thai men. *Sexually Transmitted Infections* 2000;76(5):386-392.

8. Russell M, Moralejo D, Burgess E. Paying research subjects: Participants' perspectives. *Journal of Medical Ethics* 2000;26:126-130.

9. See ref. 2, Declaration of Helsinki 2000, Principle 19.

10. See ref. 3, CIOMS 2002, Guideline 10.

11. Glantz LH, Annas GJ, Grodin MA, Mariner WK. Research in developing countries: Taking "benefit" seriously. *Hastings Center Report* 1998;28(6):38-42; Shapiro H, Meslin E. Ethical issues in the design and conduct of clinical trials in developing countries. *NEJM* 2001;345:139-142.

12. Nuffield Council on Bioethics. *The Ethics of Research Related to Healthcare in Developing Countries: A Follow Up Discussion Paper*. 2005. http://www.nuffieldbioethics.org/.

13. See ref. 2, National Bioethics Advisory Commission 2001; See ref. 11, Glantz et al. 1998; Cooley DR. Distributive justice and clinical trials in the third world. *Theoretical Medicine* 2001;22:151-167; Benatar SR. Review: Distributive justice and clinical trials in the third world. *Theoretical Medicine* 2001;22:169-176; Lie RK. Justice and international research. In: Levine RJ, Gorowitz S, Gallagher J, eds. *Biomedical Research Ethics: Updating International Guidelines*. Geneva, Switzerland: CIOMS, 2000, p. 27-40; Benatar SR. Justice and international research: A response to Reidar K. Lie. In: Levine RJ, Gorowitz S, Gallagher J, eds. *Biomedical Research Ethics: Updating International Guidelines*. Geneva, Switzerland: CIOMS, 2000, p. 41-50.

14. Participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries. Fair benefits for research in developing countries. *Science* 2002;298:2133-2134; see ref. 4, Participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries 2004.

15. Thiessen C, Ssekubugu R, Wagman J, et al. Personal and community benefits and harms of research: Views from Rakai, Uganda. *AIDS* 2007;21(18):1493-2501.

16. Kiwanuka N, Robb M, Kigozi G, et al. Knowledge about vaccines and willingness to participate in HIV vaccine trials. *Journal of the Acquired Immune Deficiency Syndromes*. 2004;36(2):721-725.

17. Wawer MJ, Gray RH, Sewankambo NK, et al. A randomized, community trial of intensive sexually transmitted disease control for AIDS prevention, Rakai, Uganda. *AIDS* 1998;12(10):1211-1125; Wawer MJ, Serwadda D, Gray RH, et al. Trends in HIV-1 prevalence may not reflect trends in incidence in mature epidemics: Data from the Rakai population-based cohort, Uganda. *AIDS* 1997;11(8):1023-1030; Wawer MJ, Sewankambo NK, Serwadda D, et al. Control of sexually transmitted diseases for AIDS prevention in Uganda: A randomised community trial. Rakai Project Study Group. *Lancet* 13;353(9152):525-535.

18. Numbers add up to more than 100% because some respondents suggested more than one thing.

19. See ref. 3, CIOMS 2002.

20. Widdus R. Public-private partnerships: An overview. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2005, 99(supp 1):1-8

21. See ref. 5, UNAIDS 2000.

22. See ref. 15, Kiwanuka et al. 2004.