One might answer that the requisite standard should be that in a developed country or, alternatively, one might answer that it ought to be that in a developing country. Each possibility has its proponents; each can point to an international ethics document to support its case. While the text of the *Declaration of Helsinki* is ambiguous on this issue, the intention of its authors is not. In a press release, the WMA states: ''The WMA opposes the notion that the nonavailability of drugs should be used as a justification to conduct placebo-controlled trials. Dr Human [former WMA Secretary General] said that 'this would lead to poor countries of the world being used as the laboratory of research institutions of the developed world' '' (18). Adopting a local standard of care in isolation surely would present just such a risk to developing countries. No one to our knowledge is, however, suggesting such a move.

Proponents of a local standard of care point out that other protections will prevent exploitation. Central to these protections is the requirement that research be ''responsive to the health needs and the priorities of the population or community in which it is to be carried out'' (CIOMS 10). It is difficult to imagine an exploitive study that would both pass a local standard of care threshold and meet the health needs and priorities of the community in the developing country. Furthermore, the adoption of a local standard of care threshold also must not be allowed to take advantage of inefficiencies in a developing country's health care system. One may morally distinguish between the stated policies and objectives of a health care system (de jure local standard of care) and its implementation in the field (de facto local standard of care). The former, and not the latter, should guide the choice of a control treatment for a clinical trial (19). Thus, in a country that has an imperfectly implemented policy of universal provision of a vaccine, that vaccine should not be withheld from the control group in a trial of a new vaccine for that same indication.

5. What other medical care must be provided to research subjects?

The controversy surrounding the tenofovir HIV prevention trials precipitated an international debate as to ethical obligations to research subjects infected with HIV during the course of a prevention trial. The ethical principle of justice grounds the obligation to compensate subjects for research-related injury. This obligation is reflected in the CIOMS document, ''Investigators should ensure that research subjects who suffer injury as a result of their participation are entitled to free medical treatment for such injury and to such financial or other assistance as would compensate them equitably for any resultant impairment, disability or handicap'' (CIOMS 19).

Just what constitutes a research-related injury in the context of a prevention trial requires careful consideration. Childress, in his seminal paper on the topic, uses a positional-risk test: ''It asks whether the injury would have been avoided if the injured party had not been in that position (i.e., a research participant)'' (20). The UNAIDS document correctly traces out the implications of this standard for HIV vaccine studies: ''HIV infection acquired during participation in a biomedical HIV prevention trial should not be considered a compensable injury unless directly attributable to the prevention product being tested itself, or to direct contamination through a research-related activity'' (UNAIDS 9). Thus, the development of infection because of risk behaviors of the research subject is not a research-related injury for which treatment must be provided.

The UNAIDS document goes on to identify an unprecedented obligation to treat all infection in prevention trials, even infection that is not a research-related injury. It states: ''Participants who acquire HIV infection during the conduct of a biomedical HIV prevention trial should be provided access to treatment regimens from among those internationally recognized as optimal'' (UNAIDS 14). The document cites ethical principles of beneficence and justice as the foundation of this obligation, despite the existence of an unanswered refutation of the claim (21). We are concerned that the widespread adoption of this purported obligation would have a chilling effect on international vaccine research.

6. What is owed to research participants at the conclusion of the study?

A further protection for research subjects and the communities in which they live is afforded by the obligation to share research benefits with study participants. The precise scope of this obligation is, however, a matter of controversy. In the very least, researchers have an obligation to persons who actually participated in the trial. Thus, the *Declaration of Helsinki* requires that, ''At the conclusion of the study, patients entered into the study are entitled . . . to share any benefits that result from it, for example, access to interventions identified as beneficial in the study. . .'' (WMA 33). But might obligation be reasonably construed as broader than this? Some have argued that it may be.

The CIOMS document broadens the scope of this requirement considerably in its position that the researcher and sponsor have an obligation to ensure that ''any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community'' (CIOMS 10). The CIOMS document takes the further step in suggesting that researchers and sponsors have an obligation to ''see that biomedical research projects for which they are responsible in such countries contribute effectively to national or local capacity to design and conduct biomedical research, and to provide scientific and ethical review and monitoring of such research'' (CIOMS 20).

The UNAIDS document requires that trial sponsors and developing countries come to an agreement on post-trial access to treatment. It states, ''[T]rial sponsors and countries should agree on responsibilities and plans to make available as soon as possible any biomedical HIV preventive intervention demonstrated to be safe and effective . . . to all participants in the trials in which it was tested, as well as to other populations at higher risk of HIV exposure in the country'' (UNAIDS 19). The document goes on to claim that ''making a successful HIV biomedical HIV prevention product or intervention reasonably available to the population where it was tested can be sustained as a basic ethical requirement'' (UNAIDS 19).

The feasibility of these recommendations for the provision of treatment to entire community, population, or country may be questioned. For instance, it would have been very difficult, or even economically impossible, after completing the rotavirus vaccine trials in periurban Lima, where 800 infants participated, to provide the vaccine broadly (22). The cost of the vaccine when introduced in the U.S. market was US$27 per dose (23). If the scope of the