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Hard-won consensus on AIDS vaccine trial guidelines

Following an intense two-day session at the World Health Organization's Geneva headquarters on June 25–26th, an *ad hoc* group convened by the Joint United Nations Programme on HIV/AIDS (UNAIDS) reached an eleventh hour consensus on guidelines covering ethical considerations in anti-HIV vaccine trials. The guidelines—to be published later this year—are not legally binding, but UNAIDS hopes that they will be voluntarily adopted by all groups conducting HIV vaccine trials.

Although agreement was reached readily on many questions, one difficult issue came to the fore and dominated most of the meeting: what level of long-term health care should be guaranteed to all participants that become infected in the course of a trial?

The answer may have far reaching implications. And given the mixed backgrounds and agendas of the meeting's 84 participants—people living with HIV/AIDS, vaccine researchers, legal and medical ethicists and representatives from the pharmaceutical industry—it was little wonder that very different views were expressed during the lively and oftentimes emotionally charged debate.

Established ethical guidelines for clinical trials, such as those adopted by the World Medical Association Declaration of Helsinki, are quite clear on the issue. They demand that all subjects receive the very best care available. But to hold HIV vaccine trials to this standard could make it almost impossible for developing countries to attract trials from overseas groups, as the sponsor would be committed to the logistical nightmare of providing a life-long regimen of advanced antiviral drugs to a community ill-equipped to administer them. The cost of antiviral therapy—US$10,000–20,000 annually—is also likely to put some sponsors off.

Major Rubaramira Ruranga, an HIV positive man from Uganda, pointed out that such a commitment would not only be totally impractical in Uganda but also may act as an unethical inducement to join the trial for those who see themselves as at very high risk in a country where no treatment for HIV infection or AIDS is otherwise available.

In support of this view, Courtney Bartholomew, Director of the Medical Research Foundation of Trinidad and Tobago, stated that in his capacity of government advisor on HIV and AIDS, he would not countenance guidelines calling for guaranteed triple therapy for trial subjects who became infected. When challenged as to whether this was the view of others in his country, he replied that it did not matter since he was "the government" and would "not allow it."

Bartholomew, Ruranga and others proposed that the guidelines establish a more pragmatic level of health care. At a minimum, those becoming infected should receive a level of care better than the minimum offered to the country's HIV positive population, but not necessarily the world's best-known treatment.

Some attendees, in particular representatives from Brazil and other South American countries, feared that such a relaxation of the Helsinki guidelines would place HIV vaccine trials at the top of a slippery slope. It would allow governments to drop their overall standard of HIV treatment to attract outside trial support. It might even, they argued, give rise to a competitive system in which trial sponsors would 'shop around' for those countries offering the lowest baseline therapy and willing to accept the least commitment from the sponsor.

The group came close to acknowledging that they were unlikely to reach consensus on this issue. However, Thai representatives Natth Bhamarapravati and Vichai Chokevivat urged a further effort. They sought concrete guidance to take back to the Thai government in light of the imminent Aidsvax Phase III trial to be hosted in Thailand later this year (*Nature Med.*, **4**; 753, 1998). Neither the Thai government nor the industrial sponsor, VaxGen, have plans to provide triple therapy for those who become infected in the course of the trial.

In response to this plea, Barry Bloom, head of UNAIDS Vaccine Advisory Committee and other UNAIDS representatives made a final attempt to establish some common ground. Although the group could not claim unanimous approval, Ruth Macklin, a member of the UNAIDS Ethical Review Committee, recorded in the minutes the consensus opinion that the guidelines should call for the "highest practically attainable standard of care" for those infected in the course of the trial, but would stop short of demanding "the best proven treatment." That an agreement was ultimately minuted may have been missed by some attendees (*Science*, **281**; 22, 1998).

After the meeting Bloom told *Nature Medicine* that the desire to see ethical guidelines that would "allow trials to reach developing countries" had won the day.

Adrian J. Ivinson, New York

Budget cut indicates policy changes at the WHO

A budget cut proposed by the World Health Organization (WHO) for healthcare training, equipment and inter-country programs on diseases such as malaria and polio in South East Asia, is fuelling speculation that the WHO is short of money. It may also be a sign that the new director general, Gro Harlem Brundtland, means to take firm action in shaking up the organization and re-directing funds. The South East Asia Regional Office (SEARO) budget, which currently stands at US$100 million, will be reduced by 12 percent over six years beginning in 2000.

The WHO stresses that budget allocations for all of its regions (Africa, the Americas, the Eastern Mediterranean, Europe, the Western Pacific and South East Asia) have remained unchanged since the inception of WHO 50 years ago, and are no longer based on relevant and objective criteria. But there is evidence that the Organization may be short of money. Of the $418,751,000 pledged by member nations for 1998, only 32 percent had been collected as of July 1st—a rate of collection significantly lower than that in 1997.

SEARO director Uton Muchtar Rafei says that the formula for distributing the loss across the member countries will be determined at the regional committee meeting next month in New Delhi, which will be attended by Brundtland.

Under the new policy, budgets will be fixed according to a "development index" formula. The index has been immediately attacked as flawed by SEARO member countries. Africa will become the primary beneficiary region because of the deterioration in socioeconomic conditions there, and