

*Potential for
WHO-industry collaboration
on drug and vaccine
development for
HIV/AIDS*



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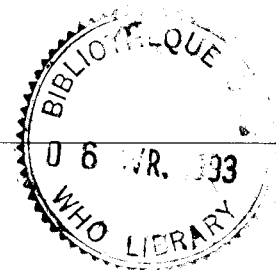
Introduction

The dimensions of the AIDS pandemic pose a unique challenge to health authorities worldwide. To date, an estimated 2.5 million adults and children have developed AIDS, with 12 million adults and one million children having been infected with the human immunodeficiency virus (HIV). The disease is spreading very rapidly in many regions of the world, particularly sub-Saharan Africa and South and South-East Asia. WHO estimates that an additional 20-30 million infections will occur during the 1990s, bringing the cumulative total by the year 2000 to 30-40 million men, women and children infected with HIV. In severely affected countries, the AIDS epidemic will have enormously disruptive demo-

graphic, social and economic consequences.

Drugs and vaccines are urgently needed to treat the increasing numbers of people with AIDS and to halt the expansion of the pandemic. In addition to the scientific challenge of developing these drugs and vaccines, there is the challenge of making them available and affordable to all people in need.

Close collaboration between countries, international organizations and the pharmaceutical industry will be essential in order to respond promptly and effectively to the global threat of the AIDS pandemic.



What the World Health Organization (WHO) can offer in collaborative activities with the pharmaceutical industry

The critical role played by WHO in collaborative activities with the pharmaceutical industry is to facilitate and support clinical trials of drugs and vaccines in developing countries. Research protocols are reviewed by international steering committees, and clinical trials are undertaken according to the highest ethical and scientific standards. WHO's substantial experience and reputation also facilitate the process of gaining regulatory approval from national and international authorities.

WHO can liaise rapidly with the public health sector of developing countries through member country governments in order to obtain permission for trials to be undertaken. It works closely with other United Nations agencies,

nongovernmental organizations and aid agencies in the coordination of a variety of activities related to the development, testing, utilization and supply of drugs and vaccines.

Through its network of contacts in the field in developing countries, WHO can provide "on-site" expertise and can facilitate the recruitment and training of local investigators. In addition, because of its local contacts and their knowledge of the socioeconomic and cultural context, WHO can ensure the smooth running of projects and the maintenance of good relations with local staff and government officials.

WHO experience in collaboration with the pharmaceutical industry in drug and vaccine development

WHO has collaborated closely with the pharmaceutical industry in drug and vaccine development activities. The Special Programme for Research and Training in Tropical Diseases (TDR), the Special Programme of Research, Development and Research Training in Human Reproduction (HRP) and, increasingly, the Programme on Vaccine Development (PVD) are major WHO programmes which have long and extensive experience of working in cooperation with the industry.

The following are examples of collaborative projects undertaken by WHO and the industry:

- research and development of drugs and vaccines
- identification and licensing of manufacturers, and design of manufacturing facilities
- identification and licensing of distributors to supply public and private sector markets
- development of quality assurance standards
- market assessments
- pursuance of regulatory approvals
- selection and registration of trademarks
- collection and distribution of royalties and fees
- technology transfer for local production.

Current WHO Global Programme on AIDS (GPA) activities of interest to the pharmaceutical industry

There are many ways in which the industry and WHO/GPA can usefully work together to advance the researching and development of HIV/AIDS drugs and vaccines. Three current GPA activities which are being carried out within the Office of Research and which are of immediate and particular interest are:

- the WHO Network for HIV Isolation and Characterization
- the preparation of vaccine evaluation sites in developing countries by the Vaccine Development unit (VAD)
- the preparation of field sites for drug efficacy studies by the Clinical Research and Drug Development unit (CRD).

All such activities are guided by international steering committees made up of experts in the field, who identify research priorities, review research proposals within their area of competence and make recommendations regarding the award of financial support.

WHO Network for HIV Isolation and Characterization

The HIV vaccines currently being developed in industrialized countries are based on well-characterized (prototype) HIV strains. But HIV has been shown to vary antigenically from region to region, and these vaccines may not be appropriate for use in developing countries where the antigenic structure of

variant HIV strains may be different. In addition to such geographic variation, temporal variation of strains within HIV-infected people and within regions also occurs. Systematic isolation and characterization of HIV from developed and developing countries, at regular intervals, would ensure that representative virus strains are available for vaccine development.

For this purpose, GPA has created the WHO Network for HIV Isolation and Characterization. Sample HIV strains from recent seroconverters at potential HIV vaccine field trial sites are systematically isolated and characterized at primary and secondary laboratories coordinated by GPA, and the data linked with data banks in developed countries. The information from the Network is monitored by the Steering Committee on Vaccine Development, and may be made available to interested parties with the objective of ensuring the development of suitable vaccines.

Preparation of vaccine evaluation sites in developing countries

There is broad international consensus that Phase I/II safety and immunogenicity trials of HIV vaccines should be conducted initially in the countries where the vaccines are developed and then be repeated in developing countries. One important reason for repeating these trials is that the side effects and the immune response observed in people living in developing countries may differ from those observed in developed countries owing to factors such as nutritional status or the presence of different endemic diseases. Larger-scale Phase III efficacy trials will need to be conducted in populations with a high incidence of HIV infection in both developed and developing countries. GPA will ensure that sites in developing countries are prepared for these vaccine evaluations so that such countries may fully participate in and benefit from the global effort of HIV vaccine development. Site

monitoring will be conducted by GPA staff, the Steering Committee on Vaccine Development and the GPA independent Data and Safety Monitoring Board.

The Steering Committee on Vaccine Development has initially recommended four countries — Brazil, Rwanda, Thailand and Uganda — as sites for HIV vaccine trials. National authorities and scientists in each of these countries have developed plans for strengthening field sites and undertaking vaccine trials.

These four countries receive funding directly from GPA and other international AIDS research programmes for site development in order to:

- provide an environment in which national and international investigators, approved by all parties, may work towards the common goal of HIV vaccine development

- ensure that appropriate research procedures are followed and that the quality of the data is acceptable to the regulatory agency in the country of origin of the vaccine.

The development of the vaccine evaluation sites involves:

- basic on-site infrastructure strengthening and training, including the training of investigators in good clinical and laboratory practices (GCP and GLP)
- obtaining advice and endorsement from the Steering Committee on Vaccine Development regarding the technical and ethical integrity of study protocols
- the dissemination of information from the sites, in accordance with the established practices of the international scientific community

- having access to biological samples, when necessary, for testing in highly specialized laboratories outside the country
- the importation of supplies and vaccines for research, without import taxes or other trade barriers
- the attendance of investigators and technical staff from the site at scientific meetings, conferences and courses within and outside the country
- coordinating the activities necessary for data management and safety monitoring.

The Steering Committee on Vaccine Development makes recommendations about the selection of appropriate candidate vaccines to be tested at the GPA-supported sites once such products have met its criteria for study. Countries are encouraged

by GPA to select vaccines for study based on these recommendations.

GPA works closely with manufacturers to ensure that they have the necessary access to the Steering Committee on Vaccine Development and to the developing country sites and input into protocol development in order to ensure that regulatory needs are met.

GPA also maintains close collaboration with the major regulatory authorities for biologicals in order to ensure that the results of vaccine trials carried out at GPA-supported sites can be used by the pharmaceutical industry for the licensing of products.

Preparation of field sites for drug efficacy studies

Three priority issues for GPA in HIV/AIDS drug development are:

- prophylaxis and treatment of common and important secondary HIV-related symptoms and diseases such as pruritus, diarrhoea, tuberculosis, and candidiasis in both children and adults
- prevention of sexual transmission of HIV
- prevention of perinatal transmission of HIV.

The Steering Committee on Clinical Research and Drug Development of GPA's Clinical Research and Drug Development Unit (CRD) defines the technical approaches and ethical standards for studies in these priority areas and identifies candidate drugs based on their merits for safe and effective use in developing countries. Prophylaxis and treatment trials include drugs for

treating the major HIV-related diseases, such as tuberculosis and candidiasis, and drugs which have the potential to decrease the sexual transmission of HIV (e.g., vaginal virucide preparations) and perinatal HIV transmission (e.g., antiretrovirals and/or passive antibody preparations).

CRD ensures the development of technically and ethically sound protocols to address these three priority research issues, and provides guidance to developing countries wishing to conduct these studies. Clinical trial sites, occasionally in conjunction with vaccine trial sites, are being strengthened in developing countries and this activity will include infrastructure strengthening to equip the sites for the conduct of clinical trials, development of standard operation procedures and training of developing country scientists in clinical trials methodology and good clinical and laboratory practices. As for vaccine trial sites, these sites will:

- provide an environment in which national and international investigators, approved by all parties, can work towards the common goal of HIV/AIDS drug development
- ensure that appropriate research procedures are followed and that the quality of the data is acceptable to the regulatory agency in the country of origin of the drug.

GPA ensures the dissemination of information from these sites, the importation of drugs and supplies for research without import taxes

or other trade barriers, attendance of investigators at international scientific meetings and conferences, and coordination of the activities necessary for data management and safety monitoring through the GPA independent Data and Safety Monitoring Board.

GPA maintains at all times close collaboration with the major drug regulatory authorities in order to ensure that the results of drug trials carried out at GPA-supported sites can be used by the pharmaceutical industry for the licensing of products.

Ongoing collaborative activities between WHO/GPA and the pharmaceutical industry

Collaboration between WHO/GPA and the pharmaceutical industry was accelerated in May 1991 at a meeting on AIDS drug and vaccine supply, co-sponsored by WHO and the United Nations Development Programme (UNDP). Two working groups were established, with members from WHO and the International Federation of Pharmaceutical Manufacturers Associations (IFPMA), to address issues relating to the development, testing, utilization and supply of drugs and vaccines for HIV/AIDS.

A second meeting on AIDS drug and vaccine supply was held in Geneva on 30 July 1992. Participants encouraged the

ongoing dialogue with WHO in areas of mutual interest such as information exchange, research, and the development and worldwide availability of drugs and vaccines. Several major international drug regulatory authorities including the US Food and Drug Administration (FDA) and the Medicines Evaluation Board, the Netherlands, also attended the meeting and offered to provide continued guidance to ensure the acceptability of clinical trial data generated in other countries, including developing countries.

This collaboration has provided a mechanism for information exchange regarding such topics as the current and projected need for drugs for HIV infection and HIV-

related diseases in developing countries, potential HIV immunization strategies and vaccine needs, potential mechanisms to ensure developing country access to safe and effective drugs for HIV/AIDS, international harmonization of drug regulatory criteria, and patent and liability issues arising from the collaborative development of drugs and vaccines.

By the year 2000, developed countries will have invested billions of dollars of public and private funds in the search for

AIDS drugs and vaccines. If WHO and the pharmaceutical industry can successfully collaborate now, then future observers may well report that the recognition of AIDS as a global threat prompted a public sector-pharmaceutical industry response to the needs of developing countries that went beyond “business as usual” to result in the accelerated development and widespread availability of safe and effective drugs and vaccines for HIV/AIDS.