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AIDS
Vaccine Initiative-
Conference
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# HIV VACCINES - ACCELERATING THE DEVELOPMENT OF PREVENTIVE HIV VACCINES FOR THE WORLD

## SUMMARY REPORT AND RECOMMENDATIONS OF AN INTERNATIONAL AD HOC SCIENTIFIC COMMITTEE

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## EXECUTIVE SUMMARY

The HIV epidemic continues to spread throughout the world despite current prevention efforts. The development and distribution of a safe, effective and inexpensive preventive HIV vaccine currently represents the best hope for controlling the global HIV/ AIDS pandemic.

In October 1994, 14 virologists, immunologists, and vaccinologists from 9 countries met in Paris to discuss the scientific barriers to the development of preventive HIV vaccines. The meeting was structured as a follow-up to a meeting held in Bellagio, Italy that identified a serious market failure in the development of HIV vaccines for the developing world and called for the establishment of a new global initiative. This report summarizes the discussions at the Paris meeting and proposes a preliminary scientific agenda for the initiative.

The proposed mission of the initiative is:

> **To ensure that safe and effective preventive HIV vaccines are developed appropriate for use throughout the world and, in particular, for use in those regions of the world most affected by HIV and AIDS.**

The initiative aims to accomplish this by complementing the on-going scientific activities with a new highly targeted applied vaccine development effort that is global in scope. It will be important that the initiative is flexible so that it can respond rapidly as new advances in knowledge are gained and that it has the freedom to undertake innovate development projects development projects entailing calculated scientific and financial risks. The initiative will not consider itself successful until a vaccine has been developed that is appropriate for widespread use in developing country settings (low cost, stable, easy to administer). The initiative will then work with other international and national agencies to assure global deployment.

The initiative's activities will be directed at vaccine product development and not at basic research, and will focus on the gaps in current efforts and on ensuring that the needs of developing countries are taken into account. This was viewed as best being accomplished by supporting the development of multiple empirical approaches in a parallel fashion. The initiative will not carry out any research and development activities directly, but rather award contracts to the companies, universities, and research institutions throughout the world where they can best be carried out. Critical to the success of the initiative will be the involvement of developed and developing country governments. The involvement of both the public and private sectors will also be vital especially as much of the expertise in vaccine research and development lies in the private sector.

To achieve its mission over the shortest time possible, an initial 7 year scientific research agenda has been proposed. The specific objectives of this scientific plan are:

> **To prove that a safe and effective HIV vaccine can be produced.**
>
> **To develop preventive HIV vaccines that are appropriate for use in developing countries.**

The strategies to do this include: **developing in parallel, approaches that have promise but are currently underexplored; developing candidate vaccines from subtypes found in those areas where the epidemic is spreading most rapidly; and ensuring that these products are safe and efficacious and move into clinical trials as quickly as possible.**

The consensus of the Paris meeting was that the initial efforts of the initiative should focus on multi-genic, multi-component vaccines and be directed at developing complex, replicating (e.g., live attenuated HIV and replicating virus vectors containing multiple antigens) and non-replicating vaccine approaches (e.g., whole killed HIV and pseudovirions), and also at encouraging the development and testing of vaccines corresponding to viral subtypes A, C, D and E. Valuable work is ongoing on various other approaches and this should continue at full speed; every effort will be made to ensure that the initiative is complementary to these efforts and does not interfere or compromise them.

The principal conclusions from the Paris meeting that influenced the direction of the scientific agenda were:

- Less risky peptide, subunit, and vectored vaccine strategies will be tried but may not work, and at best they may be only partially successful: therefore global efforts on other approaches should be intensified.

- A live attenuated approach has been successful in the SIV/monkey analog system, and theory and practice suggest that the more epitopes presented in a vaccine the lower the chances of immune escape: therefore there should be increased effort on developing approaches based on complex antigens and a focus on "build down" rather than "build up" strategies.

- No authentic animal model for AIDS caused by HIV-1 infection is currently available, and the *in vitro* correlates of protection in humans are still uncertain: therefore clinical trials in at-risk human populations will need to be done to obtain clear evidence of success or failure of any particular vaccine candidate or approach.

- The populations at greatest risk for infection, with the greatest need for an HIV vaccine, and where trials can most expeditiously be done, are in developing countries: therefore officials and scientists from developing countries should be full partners and included in the planning and execution of all stages of HIV vaccine research and development.

- Virus subtypes A, C, D, and E will probably continue to predominate in developing countries, while on a global scale subtype B will become relatively less important: therefore candidate vaccine products should be designed and tested against several subtypes, and should match the virus subtypes prevalent in countries where trials are to be performed.

- The development of preventive HIV vaccines will entail risks for all involved: therefore a strong emphasis on safety testing prior to and during human trials is essential.

- Incentives are lacking for industry to develop vaccines that are perceived as less safe or are directed at meeting the needs of developing countries and no governmental or international agencies have the mandate nor sufficient resources to actively champion these approaches: therefore a new initiative must take on this mission.

It is estimated that the proposed 7 year scientific research agenda, including associated administrative expenses, will cost approximately US$ 600 million.