

**PROJECT INFORMATION DOCUMENT (PID)
IDENTIFICATION/CONCEPT STAGE**

Report No.: PIDC85416

Project Name	Support to Research and Development at the International AIDS Vaccine Initiative
Region	OTHER
Country	World
Lending Instrument	IPF
Project ID	P161232
Borrower Name	International AIDS Vaccine Initiative
Implementing Agency	International AIDS Vaccine Initiative
Environment Category	B - Partial Assessment
Date PID Prepared	17-Aug-2016
Estimated Date of Approval	03-Oct-2016
Initiation Note Review Decision	The review did authorize the preparation to continue

I. Introduction and Context

Country Context

The project is not country-specific, hence not applicable.

Sectoral and Institutional Context

1. The need for a vaccine against Human Immunodeficiency Virus (HIV) remains urgent, with the epidemic contributing to reversals in health, food security, education and other measures of prosperity and stability. Approximately 5,753 people become newly infected with HIV each day. The pandemic is still outpacing current treatment and prevention efforts in many countries. There is no cure for HIV infection. However, effective antiretroviral medicines can control the virus and help prevent transmission so that people with HIV, and those at substantial risk, can enjoy healthy and productive lives. Another hope is that a vaccine can be developed against the virus. Its introduction will improve millions of lives around the world. Even though no vaccination is 100% effective, overall, immunization has proved to be one of the most cost-effective means to prevent vaccine-preventable diseases. It was estimated in 2012 that an HIV vaccine that is 50% effective and reaches 30% of the targeted population could avert more than 5 million new infections over a 10-year period, potentially saving millions of lives.

2. The International AIDS Vaccine Initiative (IAVI) was founded in 1996 with a global mandate to "ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world." Between 1996 and 2010, IAVI and its partners had achieved a series of "firsts" to reshape the landscape of AIDS vaccine R&D. These included: (1) Development and testing of the first vaccine candidates based on HIV subtypes circulating in Africa and India; (2) Conducting the first AIDS vaccine trials in Kenya, Rwanda, Zambia and India; (3) Establishing the first laboratory accredited for assessing immune responses against HIV from vaccine trials; (4) Identifying the first

potent and broadly neutralizing antibodies against HIV in more than a decade, which provided new targets on HIV for vaccine design; (5) Establishing the world's first Vaccine Design and Development Laboratory dedicated solely to the development of a safe and effective AIDS vaccine; and (6) Successfully advancing seven novel vaccine candidates from concept to clinical trials. IAVI was one of the first examples of Product Development Partnerships (PDP). The PDP's mission is to accelerate the translation of R&D from the bench to the bedside while supporting affordability and access to data.

3. Development of an HIV vaccine aligns with the development objectives of the Government of Japan and the World Bank. The previous project (P119051) built not only on the Bank's financial oversight capabilities but also used the Bank's convening power to bring different partners together and ensure technical oversight of this support. The Implementation Completion and Results Report (ICR3731) rated the project as Highly Satisfactory, based on high relevance of objectives design and implementation, high efficacy and substantial efficiency. IAVI-Sendai Vector project has been an innovative research and development initiative. As with all fundamental research, there are no guarantees that the eventual product will be an effective and efficient HIV vaccine. This risk was mitigated through managing external and internal expectations by clarifying that the World Bank was supporting a fundamental research that might or might not produce a viable vaccine, but would in any case contribute to the knowledge in the field. As modeling and economic analyses of a future HIV vaccine have demonstrated, even the most conservative scenarios (low efficacy and low coverage) of a preventive HIV vaccine appear to be cost-effective. The decision to participate in the current project was made in the environment of scarce information on possible outcomes of the HIV vaccine development. However, despite not being able to develop a viable vaccine, the project has yielded significant knowledge benefits that will be useful for further research. A high social value of a vaccine and projected savings of \$1.5 billion per year by 2070 justify current investments. However, new mechanisms of international cooperation and R&D incentive provisions will be needed to maximize the success of vaccine research and development.

4. Certain risks have been identified that impede the development of an HIV vaccine: the demand and return on investment are uncertain, high attrition rates and considerable amounts of time are required to design a viable candidate. Vaccines are global public goods with many positive externalities. The role of the governments and international organizations is undeniable in creating incentives to support vaccine R&D. At an early stage, push mechanisms might strategically lower cost of production as the costs will be subsidized. At a later stage, once a viable vaccine is on the market, pull mechanisms - creating demand through an advance market commitment - might help overcome market failures and increase the uptake of the vaccine.

5. Vaccine R&D is a potential area the World Bank could support, but there has been a reluctance to enter this area given the technical complexity and the perception that other players are better positioned to technically support R&D. As a result, the Bank has typically not engaged in this area except in a more indirect manner through its support of initiatives like IAVI through the Development Grant Facility (DGF). The partnership with the Ministry of Finance, Japan has provided continuity of financing to IAVI as it transitioned out of the catalytic support of the DGF.

6. The World Bank and others have recognized that international collective action is critical to ensure a supply of such GPGs. It is therefore an area the Bank could support but there has been a reluctance to enter this area given the technical complexity, inherent risks in financing research and the perception that other players are better positioned to technically support R&D.

7. The technical basis for further investments in HIV vaccine research is strong. While immune correlates for protection against HIV infection are currently unknown, it is generally hypothesized that antibodies, cell-mediated immune responses and mucosal immunity may all be needed in an effective preventive HIV vaccine. Among the goals for an efficacious vaccine is eliciting protective mechanisms at the primary interface for HIV infection, the mucosa. Although there is demonstration that parenterally administered vaccines could provide such protection, it will may require mucosal administration of vaccines to achieve optimal protection at those surfaces. Further, there is great interest in the potential for replicating vectors to elicit optimal responses, in terms of profile and magnitude.

8. Global investment in the R&D of a preventive vaccine for HIV has been significant in the past decade. More than 30 candidate vaccines have been developed and only a few have been tested for efficacy in people. None of them have proven efficacious enough in long-term protection to be introduced into clinical practice. In the previous project with IAVI, and other projects of other organizations, the end product has not been yet attained, but incremental progress and knowledge has been successfully gained. This uncertain and prolonged product development pathway has discouraged the pharmaceutical industry to further invest into vaccine R&D against HIV and other pathogens of poverty.

9. Although it is assumed that an HIV vaccine would be made available at a low price, its cost is uncertain. This prevents us from making estimates around cost-effectiveness. Several studies have modeled the introduction of the vaccine in low- and middle-income settings. Despite heterogeneity in methodology, modeling studies yielded similar results. Even the vaccine with limited efficacy will provide cost savings to society. At a price of \$20 per vaccine dose, vaccination will be cost-effective even with limited efficacy (30%). A higher price (\$65 per dose) will reduce the cost-effectiveness of the intervention, but vaccination will continue to be cost-effective if efficacy is at least 70%.

10. In a previous project, IAVI successfully constructed vaccine candidates using Sendai Vector (SeV) as vector encoding HIV immunogens; conducted virulence and pre-clinical safety studies in animals with the SeV-Gag vaccine candidate; obtained approval to conduct a phase 1 trial for the SeV-Gag vaccine candidate from medicines regulatory authorities in UK, Rwanda and Kenya; developed a scalable Vero-cell expression and purification process for production of clinical trial material of SeV-Gag; conducted the Phase I clinical trial of SeV-Gag in humans to assess its safety and immunogenicity.

11. As evident from the previous 5-year project, collaboration between the WBG and IAVI significantly contributed to the progress on the quest for an HIV vaccine. IAVI's work contributed to building research and broader Health System infrastructure in African countries where clinical trials took place. Knowledge has been generated about the replication-competent vectors which can be translated to other promising vaccine candidates that will be studied in the current project.

12. In 2016, Japan is the presiding country for the G7 Ise-Shima Summit, and a continued commitment to IAVI and the global effort to find a HIV vaccine remains a priority of Japan in its work on Global Health. WBG and the Government of Japan view the current project as a vehicle to improvement of R&D environment in order to prepare for emerging epidemics and strengthen health systems - including regulatory, clinical, and research components.

13. This project meets the WBG's role as a financier of global public goods in addressing diseases of poverty and aligns with WBG's efforts in strengthening research and delivery systems for immunization. Investments in immunization are a critical component of Universal Health Coverage and a strong force for poverty reduction.

Relationship to CAS/CPS/CPF

Not applicable

II. Project Development Objective(s)

Proposed Development Objective(s)

To support the International AIDS Vaccine Initiative (IAVI) in the development of a novel HIV vaccine candidate through a program of fundamental translational research and product development.

Key Results

Research has been conducted to optimize the replicating vector platform for a candidate HIV vaccine.

III. Preliminary Description

Concept Description

The project will entail further research to optimize the replicating vector platform. The applied research required to optimize vaccine vector design to ensure efficacy and safety of a vaccine for wide-scale usage is considerable. Informed by the studies conducted as part of the project P119051 using Sendai virus vector candidate, the research in the current project will include iterative design and the systematic investigation of modified vectors and vaccination regimens in order to identify the most practical effective route and dose, mainly in a series of monkey studies. The research will help identify and characterize the immunologic mechanisms that provide protection, which will inform improvements in the HIV vaccine candidates as well as direct how the vector can be used to develop vaccine candidates against pathogens of poverty. The project might consider clinical trials in humans at a later stage.

IV. Safeguard Policies that Might Apply

Safeguard Policies Triggered by the Project	Yes	No	TBD
Environmental Assessment OP/BP 4.01	x		
Natural Habitats OP/BP 4.04		x	
Forests OP/BP 4.36		x	
Pest Management OP 4.09		x	
Physical Cultural Resources OP/BP 4.11		x	
Indigenous Peoples OP/BP 4.10		x	
Involuntary Resettlement OP/BP 4.12		x	
Safety of Dams OP/BP 4.37		x	
Projects on International Waterways OP/BP 7.50		x	
Projects in Disputed Areas OP/BP 7.60		x	

V. Financing (in USD Million)

Total Project Cost:	2	Total Bank Financing:	0
Financing Gap:	0		
Financing Source			Amount
Free-standing TFs for HDNVP			2

VI. Contact point**World Bank**

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