# Support to Research and Development at the International AIDS Vaccine Initiative (P161232)

OTHER | World | Health, Nutrition & Population Global Practice |
Recipient Executed Activities | Investment Project Financing | FY 2017 | Seq No: 2 | ARCHIVED on 15-Nov-2017 | ISR30050 |

Implementing Agencies: International AIDS Vaccine Initiative, International AIDS Vaccine Initiative

## Key Dates

### Key Project Dates

Bank Approval Date:10-Feb-2017
Effectiveness Date:27-Feb-2017
Original Closing Date:30-Jun-2017
Revised Closing Date:30-Sep-2018

## Project Development Objectives

Project Development Objective (from Project Appraisal Document)
The Project Development Objective is to support the International AIDS Vaccine Initiative (IAVI) in the optimization and testing of one HIV vaccine candidate.

Has the Project Development Objective been changed since Board Approval of the Project Objective?
No

## Components

| Name |
|---|

## Overall Ratings

| Name | Previous Rating | Current Rating |
|---|---|---|
| Progress towards achievement of PDO | Moderately Satisfactory | Satisfactory |
| Overall Implementation Progress (IP) | Moderately Satisfactory | Satisfactory |

## Implementation Status and Key Decisions

The Project was restructured and the Amendment to the Grant Agreement with IAVI for additional financing was signed. This is an extension of the progress that was achieved during Year 1 of the project + the development of the new viral platform which will be helpful in research of other viruses. IAVI will develop an improved and optimized vaccine and several additional vectors with modifications to enhance the ability to induce immune response. A new cell line will be developed that can be used to produce vaccine material in a *standardized manufacturing process*, not "on demand" for phase 1 clinical trials. Finally, IAVI will organize a meeting with Coalition for Epidemic Preparedness Innovations and Global Health Innovative Technology Fund on the sidelines of UHC Forum in Tokyo in December 2017. The World Bank will participate at a senior level in that

meeting.

**Progress on Year 1 activities**

The year 1 work plan focused on advancing development of new modified VSVdG-Env.BG505 chimeras that have increased replicative capacity and/or ability to express increased quantities of Env. Investigating vaccines that can deliver increased antigenic stimulation is an important objective, because information gained from two prior experiments indicate that there is an antibody titer threshold that needs to be met to produce durable efficacy. IAVI's goal was to advance and test two vectors that would elicit a higher magnitude of immune response in rhesus macaques. Two approaches were used: 1) modified vector candidates were generated, 2) robust evolutionary potential of VSV was studied and used.

Progress has been made in developing 6 vectors. Virus was passaged to assess whether it may develop additional adaptive mutations that would enhance ability to replicate ("grow"). Mutant characteristics were successfully analyzed.

Vaccines were produced for a monkey study, and animals received their first immunization. The first glimpse of the immune response will be available the fall of 2017.

**Key Decisions**

To continue research and development activities at IAVI. The Bank team's assessment, including assessment by independent product development consultants, is that the Project is on track to achieve objectives by the end of September 2018.

## Risks

### Overall Risk Rating

| Risk Category | Rating at Approval | Previous Rating | Current Rating |
|---|---|---|---|
| Overall | -- | Low | Low |

Comments

The overall rating is based on the following sub-ratings used in the restructuring paper:

Research-related risks - High

Reputational risk - **Low** (downgraded from Moderate, due to research being limited to *in vitro* testing)

Financing arrangements - Moderate-Low

Donors - Negligible

Bank supervision and implementation capacity - Moderate-Low

## Results

### Project Development Objective Indicators

▸Vector has been optimized (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | -- | Y | Y |
| Date | 04-Jul-2016 | -- | 30-Jun-2017 | 30-Jun-2017 |

▸Vector testing has been initiated (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | Y | Y | Y |
| Date | 04-Jul-2016 | 30-Jun-2017 | 30-Jun-2017 | 30-Jun-2017 |

▸VSVdG-Env.BG505.1 vaccine vector has been evaluated (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | N | N | Y |
| Date | 06-Sep-2017 | -- | -- | 29-Jun-2018 |

▸Additional viral vectors have been developed (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | N | N | Y |
| Date | 06-Sep-2017 | -- | -- | 28-Sep-2018 |

Overall Comments

## Intermediate Results Indicators

▸Five genetically modified VSVdG-Env.BG505 vaccines have been isolated and characteristics have been analyzed (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | Y | Y | Y |
| Date | 10-Feb-2017 | 30-Jun-2017 | 30-Jun-2017 | 01-Mar-2017 |

▸VSVdG-Env.BG505 mutants have been isolated after serial passage under conditions that select for viruses with increased replicative fitness. Mutant virus characteristics have been analyzed. (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | Y | Y | Y |
| Date | 10-Feb-2017 | 30-Jun-2017 | 30-Jun-2017 | 01-Mar-2017 |

▸A decision to test new VSVdG-Env.BG505 vaccines or revise a macaque study to evaluate the requirement for three doses have been made. (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | Y | Y | Y |
| Date | 10-Feb-2017 | 30-Jun-2017 | 30-Jun-2017 | 31-Mar-2017 |

▸Candidate vaccines have been produced for a preclinical study. (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | Y | Y | Y |
| Date | 10-Feb-2017 | 30-Jun-2017 | 30-Jun-2017 | 01-Jun-2017 |

▸Preclinical study in non-human primates has been commenced. (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | Y | Y | Y |
| Date | 10-Feb-2017 | 30-Jun-2017 | 30-Jun-2017 | 30-Jun-2017 |

▸Determination of construction feasibility and replicative capacity of VSVdG-Env.BG505 with Env in position 2, 3 or 5 (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | N | N | Y |
| Date | 20-Jun-2017 | -- | -- | 02-Apr-2018 |

▸VSVdG-Env.BG505 position 1 vector with Matrix protein (M) modifications that will dampen the innate immune response rescued (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | N | N | Y |
| Date | 20-Jun-2017 | -- | -- | 01-Jan-2018 |

▸VSVdG-Env.BG505.1 vector with M modifications evaluated for genetic stability and replicative capacity (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | N | N | Y |
| Date | 20-Jun-2017 | -- | -- | 28-Sep-2018 |

▸Initiate VSVdG-Env.BG505 position 1 vector vaccine rescue in Early Development Laboratory (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | N | N | Y |
| Date | 20-Jun-2017 | -- | -- | 28-Sep-2018 |

▸Feasibility of VERO-CD4/CCR5 cell line also expressing VSV glycoprotein G is demonstrated (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | N | N | Y |
| Date | 20-Jun-2017 | -- | -- | 29-Dec-2017 |

▸Conduct serial passage of VSV New Jersey vector to improve replicative capacity and fitness of the virus (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | N | N | Y |
| Date | 20-Jun-2017 | -- | -- | 29-Dec-2017 |

▸Evaluate VSV New Jersey vector for improved fitness and utility as a vaccine platform (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | N | N | Y |
| Date | 20-Jun-2017 | -- | -- | 28-Sep-2018 |

▸Initiate VERO CD4/CCR5 VSV G expressing cell line in Early Development Laboratory (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | N | N | Y |
| Date | 06-Sep-2017 | -- | -- | 28-Sep-2018 |

▸Organize and facilitate meeting in conjunction with UHC Forum in December in Tokyo on Japanese investments in global health R&D (Yes/No, Custom)

| | Baseline | Actual (Previous) | Actual (Current) | End Target |
|---|---|---|---|---|
| Value | N | N | N | Y |
| Date | 06-Sep-2017 | -- | -- | 01-Jan-2018 |

Overall Comments

The Year 2 work plan includes *four* Specific Aims and is scheduled to conclude in September 2018:

**Specific Aim 1** includes a range of activities needed to characterize a new redesigned vaccine, which was modified to express increased quantities of Env. A hypothesis is that the increased Env expression will improve immunogenicity and efficacy.

In **Specific Aim 2**, IAVI will develop several additional vectors with different strategic modifications designed to enhance immunogenicity. New vectors will be developed and characterized in year 2, and will be available for preclinical evaluation in an animal model in the following year.

**Specific Aim 3** switches emphasis to essential work on vaccine production process. The current laboratory method used to produce vaccine virus will support a phase 1 clinical trial, but not development of a standardized manufacturing process. To solve this problem, IAVI will investigate whether it is possible to modify IAVI's current Vero cell line to generate a new cell that can be used to produce vaccine material. By the end of the current grant, IAVI expect that feasibility of making the cell line will be determined.

**Specific Aim 4** is designed to advance the VSVdG chimeric virus vector platform by developing one to two new vectors based on viruses that are related to a current vector VSV. This will broaden the number of vaccines that can be prepared using this technology, which might be immediately important, as both our VSVdG-Env.BG505 vaccine and the Merck VSVdG-ZEBOV/GP vaccine are based on the same VSV vector.

In addition, as a non-research activity, IAVI will organize a technical meeting with other global public-private partnerships (PPPs) in product development in global health, namely Coalition for Epidemic Preparedness Innovations (CEPI) and Global Health Innovative Technology Fund (GHIT), on the sidelines of the UHC Forum 2017, to be held in Tokyo in early December. The aim of this activity is to coordinate and align to the extent possible the strategies of the PPPs to maximize the investments by the Japanese government, and to further engage corporate and research partners in Japan in the activities of the global PPPs.

## Data on Financial Performance

### Disbursements (by loan)

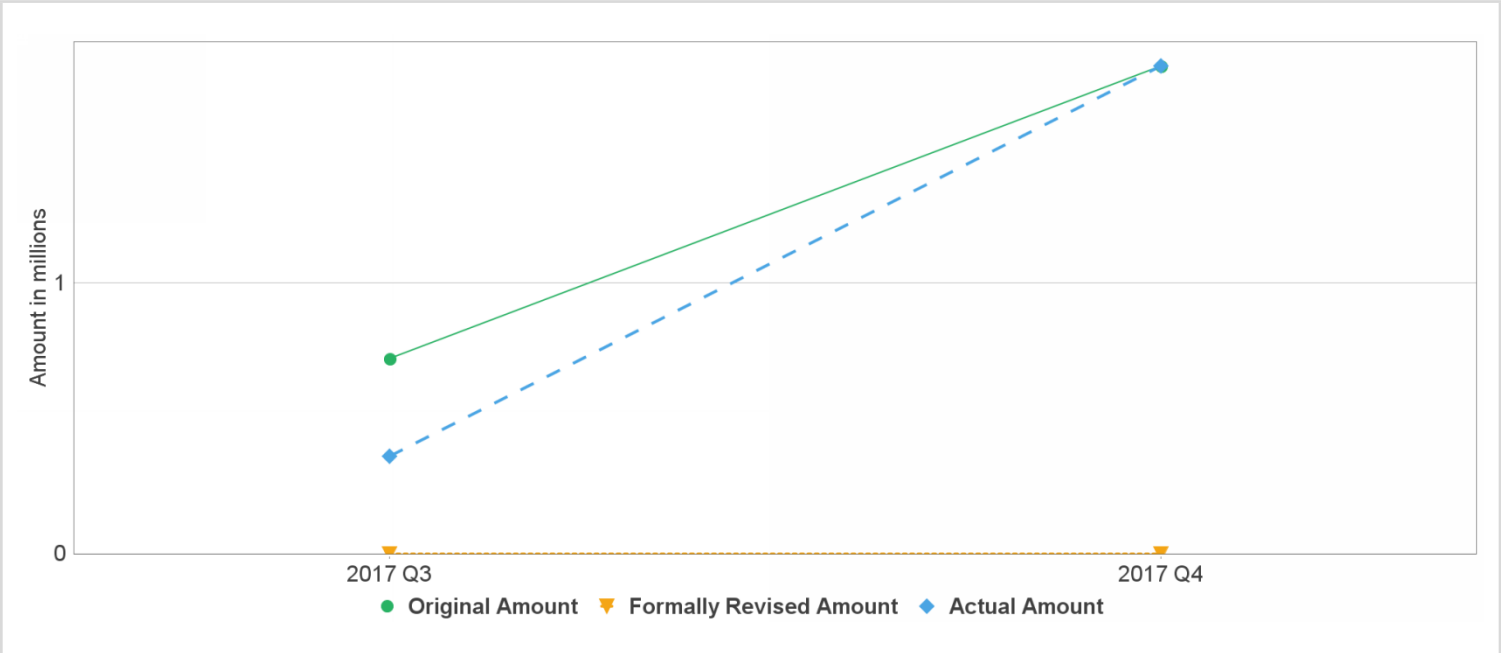
| Project | Loan/Credit/TF | Status | Currency | Original | Revised | Cancelled | Disbursed | Undisbursed | Disbursed |
|---|---|---|---|---|---|---|---|---|---|

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| P161232 | TF-A4434 | Effective | USD | 3.59 | 3.59 | 0.00 | 1.80 | 1.79 | | 50% |

### Key Dates (by loan)

| Project | Loan/Credit/TF | Status | Approval Date | Signing Date | Effectiveness Date | Orig. Closing Date | Rev. Closing Date |
|---|---|---|---|---|---|---|---|
| P161232 | TF-A4434 | Effective | 08-Feb-2017 | 27-Feb-2017 | 27-Feb-2017 | 30-Jun-2017 | 30-Sep-2018 |

### Cumulative Disbursements




## Restructuring History

Level 2 Approved on 28-Sep-2017

## Related Project(s)

There are no related projects.