Internal Ex-Post Evaluation for Technical Cooperation Project (Science and Technology Research Partnership for Sustainable Development: SATREPS)

conducted by Indonesia Office: January 2019

Country Name	Identification of Anti-Hepatitis C Virus (HCV) Substances and Development of HCV and Dengue Vaccines
Republic of Indonesia	

I. Project Outline

Background	In Indonesia, the number of individuals with chronic hepatitis C was estimated at approximately 7 million (2008). Some of persistent infection of Hepatitis C Virus (HCV) principally is predicted to develop liver cirrhosis and hepatic cancer subsequently, resulting to death. The number of death cases caused by HCV was estimated at over 200,000. Although the Interferon (IFN) + Ribavirin (RBV) combination therapy significantly improved the rate of viral clearance in comparison to the conventional IFN monotherapy, it was limitedly effective for around the half of the infected persons and it was very costly. As for the situation of Dengue viral infection, the numbers of diagnosed and fatal cases of Dengue Fever/Dengue Hemorrhagic Fever were estimated at over 100,000 and over 1,000, respectively. Treatment of dengue viral infection is primarily symptomatic treatment, and preventive vaccines and/or antivirals effective for dengue viral infection remain to be developed. Also, from the aspect of afferent infectious disease, it was regarded as an urgent issue not only in Indonesia but also worldwide. Under those situations, the project was approved as a SATREPS[1] project. As a project of SATREPS for development of antiviral drugs against HCV and vaccines for HCV and dengue, the project aimed at boosting self-reliant research and development capacity of the University of Indonesia and Airlangga University. The research theme for development of novel antivirals as well as therapeutic and/or preventive vaccines with low cost and high efficacy and safety (tolerability) and development of dengue preventive vaccine was highly valuable for not only Indonesia but also other developing countries.		
Objectives of the Project	Through collaborative research activities with Japanese research institutes, the project aimed at enhancing research capacity of University of Indonesia and Airlangga University for development of anti-HCV agents and vaccines against HCV and Dengue virus, thereby contributing to implementation of pre-clinical trial of these agent and vaccines and application of the developed research techniques and equipment for other medicine development.		
	Project Purpose: Research capacity of Indonesian research institutes, for the development of anti-HCV agents and vaccines against HCV and Dengue virus, are enhanced through collaborative research activities with Japanese research institutes.		
Activities of the project	Project site: Jakarta and Surabaya. 1. Main activities: 1) Collaborative research activities for identification of novel compounds with anti-HCV activity from medical plants and natural products, 2) Generation of candidates of HCV therapeutic/preventive vaccines, 3) Generation of candidates of dengue virus preventive DNA vaccine, etc. 2. Inputs (to carry out above activities) Japanese Side 1) Experts from Japan: 62 persons 2) Training in Japan: 18 persons 3) Equipment: Nuclear magnetic resonance system, DNA microarray, liquid chromatography mass spectrometer (LC/MS), etc. 4) Local cost: cost for research equipment, etc. Indonesian Side 1) Staff allocated: 41 persons 2) Land and facilities: office and research space at space at UI and AU, etc. 3) Local cost.		
Project Period	February 2010 to February 2014	Project Cost	(ex-ante) 350 million yen, (actual) 501 million yen
Implementing Agency	University of Indonesia (UI) and Airlangga University (AU)		
Cooperation Agency in Japan	Kobe University, Research Center for Medicinal Plant Resources, National Institute of Biomedical Innovation.		

II. Result of the Evaluation

[Special Perspectives Considered in the Ex-post evaluation]

- Though Overall Goals were not set at the ex-ante evaluation, the following two were considered as envisaged Overall Goals at the Terminal Evaluation which can be considered as "actions/efforts for utilization of the research outcomes by the project": 1) The pre-clinical trial is conducted on: i) Anti HCV agent candidates, ii) Candidate vaccines against HCV, and iii) Candidate vaccines against Dengue virus, and 2) Research techniques and equipment introduced by the project are applied for other medicine development. Therefore, the achievement level of the envisaged Overall Goals were verified at the ex-post evaluation as a part of positive impacts of the SATREPS project.

1 Relevance

<Consistency with the Development Policy of Indonesia at the time of ex-ante evaluation and project completion>

One of the priorities in the "Indonesia Sehat (Healthy Indonesia) 2010" issued by the Ministry of Health in 1999 was control of infectious diseases, which was still effective at the time of the project completion. Also, development of anti-HCV agents and vaccines against HCV and Dengue virus is prioritized in the "Science and Technology Policies (Research on MADAT[2])" (2010-2014).

<Consistency with the Development Needs of Indonesia at the time of ex-ante evaluation and project completion >

In order to decrease patients with chronic hepatitis C and HCV victims, development of novel antivirals as well as therapeutic and

[1] Science and Technology Research Partnership for Sustainable Development.

[2] MADAT stands for malaria, avian influenza, dengue fever/dengue hemorrhagic fever, HIV/AIDS and tuberculosis.

preventive vaccines with low cost and high efficacy and safety (tolerability) was needed. Also, development of dengue preventive vaccine was regarded as an urgent issue not only in Indonesia but also worldwide. The project was consistent with these needs at the time of both the ex-ante evaluation and project completion.

<Consistency with Japan's ODA Policy at the time of ex-ante evaluation>

In the Country Assistance Program for Indonesia (2004), one of the priority areas for assistance was creation of a democratic and fair society. Assistance for combatting infectious diseases was included in this area.

<Evaluation Result>

In light of the above, the relevance of the project is high.

2 Effectiveness/Impact

<Status of Achievement for the Project Purpose at the time of Project Completion>

The Project Purpose was achieved. It is judged that, through collaborative research activities with Kobe University and National Institute of Biomedical Innovation of Japan, UI and AU enhanced their research capacity for development of anti-HCV agents and vaccines against HCV and Dengue virus. They succeeded in determination of candidates of anti-HCV substance and HCV and Dengue vaccines for pre-clinical trial (Indicator 1). Part of their research outcomes were summarized in academic journals (Indicator 2).

<Continuation Status of Project Effects at the time of Ex-post Evaluation>

The project effects have continued. Since the project completion, UI has continued research activities for anti-Dengue drug development with competitive grants, based on the research output produced by the project. Also, UI started discussion with Kobe University for collaboration for new anti-bacterial substances. As well, AU has continued researches related to anti-HCV for identifying bioactive compounds derived from plants, involving undergraduate and graduate students. Also, the Institute of Tropical Diseases (ITD) of AU has conducted a collaborative research with Kobe University for identifying bioactive compounds of anti-Dengue derived from plants[3]. A PhD graduate has continued a research on anti-HCV from bio marine resources, with research equipment and techniques developed by the project. On the other hand, AU's research focus has been shifted from anti-HCV to anti-amoeba and anti-malaria. One reason is that researches related to HCV are difficult due to its characteristics of mutation, and another reason is it requires long time from in-vivo analysis to approval and release as drugs, according to a professor of AU. Because of AU's new SATREPS project[4] which deals with development of lead compounds of anti-malaria and anti-amebic agents in addition to the project, they have been able to expand their research area.

The implementation system for development research introduced by the project has sustained at both UI and AU, such as preparation of the Standard Operating Procedures (SOP) and progress review. All of the major provided research equipment have been utilized, except LC/MS due to troubles of the uninterruptible power supply (UPS) and compressors at AU, however, of which some parts were already replaced and prepared for use.

<Status of Achievement for Envisaged Overall Goal at the time of Ex-post Evaluation>

Although no Overall Goal was set forth at the time of ex-ante evaluation, this ex-post evaluation attempted to verify achievement level of the envisaged Overall Goals mentioned above. As of the ex-post evaluation, for pre-clinical trial on anti HCV agent candidates and candidate vaccines against HCV and Dengue virus, (envisaged Overall Goal 1), only the in-vivo analysis (mice) has been conducted on anti-Dengue virus vaccines. It should be noted that this had been expected by the Terminal Evaluation Team, and no responsibility of UI and AU sides had been officially mentioned for realizing the pre-clinical trial. Another expected impact is application of the research techniques and equipment introduced by the project for other drug development. Techniques such as cytotoxicity evaluation and MTT assay[5] and equipment have been utilized for researches on anti-obesity, anti-bacteria, anti-cancer, anti-amoeba, and so on (envisaged Overall Goal 2).

<Other Impacts at the time of Ex-post Evaluation>

Based on the project experience, a patent on Hepatitis strain research model was applied in Japan. No negative impacts such as bio hazards from researches on HCV and dengue vaccines have not occurred at UI or AU.

<Evaluation Result>

Therefore, the effectiveness/impact of the project is high.

Achievement of the Project Purpose and Overall Goal

Aim	Indicators	Results
(Project Purpose) Research capacity of Indonesian research institutes, for the development of anti-HCV agents and vaccines against HCV and Dengue virus, are enhanced through collaborative research activities with Japanese research institutes.	1 At least one candidate of anti-HCV substance and one each candidate for HCV and Dengue vaccines are determined for pre-clinical trial.	Status of achievement: Achieved (Continued). (Project Completion) - Eighteen (18) anti-HCV compounds have been identified, two (2) of which with strong activity are regarded as final candidates for future pre-clinical trials in the Project. - HCV genomic region to be integrated into anti-HCV recombinant varicella vaccine candidate was identified. - Dengue virus genomic region to be integrated into dengue DNA vaccine (serotypes 1 to 4) was determined, and the dengue DNA vaccine candidates were generated. (Ex-post Evaluation) - The Faculty of Medicine of UI won a competition-based research fund for anti-Dengue drug development in 2017/18 (2 billion Indonesian Rupiahs (IDR). - At AU, ITD has continued collaborative researches with the Faculty of Pharmacy and Faculty of Science and Technology related to anti-HCV.

[3] AU was supposed to conduct researches for development of drugs against HCV, and the bioactive compound of anti-Dengue was unintentionally found during other research activities.

[4] "Project for Searching Lead Compounds of Anti-malarial and Anti-amebic Agents by Utilizing Diversity of Indonesian Bio-resources" (2015-2020). Indonesian research institutes including AU has implemented the project in collaboration with Japanese universities and other organizations.

[5] It is a method which is widely used to investigate cell proliferation, activity and toxicity.

	2. More than 2 research papers, in which first author is an Indonesian researcher, are published for each research subject in peer-reviewed journals with its impact factor more than 1.0.	Status of achievement: Achieved (Continued). (Project Completion) - Two or more research papers in each research group were either published or in the process of reviewing in peer-reviewed journals with the impact factors of 1.0 or higher. (Ex-post Evaluation) - Since March 2014, four and five research papers in which the first author is an Indonesian researcher of UI and AU, respectively, have been published in the journals with the impact factors of 1.0 or higher.

Source: Terminal Evaluation Report and data/information provided by UI and AU.

3 Efficiency

Although the project period was as planned, the project cost exceeded the plan (ratios against the plan: 100% and 143%, respectively). Outputs were produced as planned. Therefore, the project efficiency is fair.

4 Sustainability

<Policy Aspect>

Development of anti-HCV agents and vaccines against HCV and Dengue virus is prioritized in the "National Dengue Vaccine Consortium on Development of Dengue Vaccine" (2015-2020) of the Ministry of Research, Technology and Higher Education (RISTEKDIKTI). Thus, it is backed up at least until 2020.

<Institutional Aspect>

UI has sustained an appropriate organizational structure for utilizing research outputs produced by the project. The Indonesia Medical Education and Research Institute (IMERI) was established under the Faculty of Medicine of UI in 2017. IMERI has 12 research clusters including ones for drug development and infectious diseases, and the number of the assigned staff including research assistants has been sufficient, according to the Faculty of Medicine. AU's organizational structure has been sufficient, with assigned 18 staffs at the Center for Natural Product Medicine Research and Development (NPMRD). UI and AU has conducted bimonthly meetings for sharing research progresses and next work plan, but no other arrangement for collaboration, since research themes have been demarcated among them.

<Technical Aspect>

Researchers of both IMERI and NPMRD have sustained a sufficient capacity to implement research activities using the research outputs by the project, as they have yearly won research funds from RISTEKDIKTI, university and other agencies. Besides, AU has made efforts for technical capacity development by conducting joint researches with private companies and other research institutes and by involving young researchers in the SATREPS project. Both universities have sustained skills and knowledge for operation and maintenance of the facility and equipment installed by the project based on SOP or by asking technicians and service agents for repair when necessary.

<Financial Aspect>

IMERI has received competitive funds from FMUI, RISTEKDIKTI and a private fund. Among from these fund sources, FMUI's fund has reached 20,700 US dollars (USD) for dengue vaccine researches for 2020. One of the researches who worked for the project has got 86,900 USD in 2018 and 89,700 USD for 2019 for the biomarker research on dengue infection. According to the Research Coordinator of the FMUI, these funds have been sufficient. As well, NPMRD has obtained funding from the university (250 million IDR in 2016 and expenses from the SATREPS project in 2017 and 2018), which has been sufficient, according to the Research Coordinator of AU. Both of IMERI and NPMRD have continuously secured budgets for operation and maintenance of the research facility and equipment installed by the project, by collecting service charges from clients.

<Evaluation Result>

Therefore, the sustainability of the effects is high.

5 Summary of the Evaluation

The Project Purpose was achieved, and the project effects have continued. Through collaborative research activities with a Japanese university and research institute, both UI and AU enhanced their research capacity for development of anti-HCV agents and vaccines against HCV and Dengue virus. Since the project completion, the two universities have continued research activities on drug development against Dengue virus and HCV, respectively, while AU's research focus has been shifted from anti-HCV to anti-amoeba and anti-malaria. Regarding sustainability of the research outputs, both UI and AU have sustained an appropriate organizational structure and staffing. Financially, both have gained competitive research funds from the university and external institutions. As for the project efficiency, the cost exceeded the plan.

Considering all of the above points, this project is evaluated to be very satisfactory.

III. Recommendations & Lessons Learned

Recommendations for Implementing agency:

- According to UI, it requires much preparation to win competitive funds, in terms of human resources, facility and equipment. Besides these funds, for further promotion of research activities, it is recommended to RISTEKDIKTI to establish a scheme of block grant (subsidy assigned for each university) for conducting research activities. It should be considered to involve the industry sector (private companies related to drag development) as fund providers.

Lessons learned for JICA:

- Overall Goal had not been set forth at the time ex-ante evaluation, as it would take more than several years to implement the pre-clinical and clinical trial of anti-HCV agent candidates and candidate vaccines against HCV and Dengue virus after they are determined by the project. And, no responsibility of UI and AU sides had been officially mentioned for realizing these trials as of the project completion. If the project expects implementing agencies (research institutions) to sustain activities to achieve specific goals after the project completion, it should be written and officially agreed before the project completion. And, capacity building should be done for responsible stakeholders to conduct necessary activities, depending on set goals, during the project period. For example, in projects for drug development, if goals are set as determination of active compound (in-vitro), pre-clinical trial (in-vivo), or clinical trial, responsibilities should be clarified and necessary training should be given for stakeholders such as university researchers, research coordinators, pharmaceutical companies, the Ministry of Health, an ethical committee, and medical institutions, before the project completion.

- In the project, special equipment including the nuclear magnetic resonance system and LC/MS were provided as necessary for medicine department. IMERI and NPMRD could not only implement research activities as planned, but also have provided rental services for researchers within and outside the universities. These equipment have been utilized by many users, and furthermore rental fees have been collected. Thus, when providing equipment which can be utilized beyond the project activities, it is effective to provide paid rental services unless it affects the project activities from the project period or after the project completion. By spending the collected fees for payment of operation and maintenance of the equipment, financial sustainability will be enhanced.

A researcher explain the Nuclear Magnetic Resonance (NMR) equipment for Structure elucidation of chemical compound (Airlangga University)

Elisa reader equipment for reading the antigen – antibody bond (University of Indonesia)