

Evaluation Summary

1. Outline of the Project	
Country: the Lao People's Democratic Republic	Project Title: The Project for Development Innovative Research Technique in Genetic Epidemiology of Malaria and Other Parasitic Diseases in Lao PDR for Containment of Their Expanding Endemicity
Issue/Sector: Healthcare and medical treatment	Cooperation Scheme: Technical Cooperation Project (Science and Technology Research Partnership for Sustainable Development: SATREPS)
Division in charge: Health Team 4, Health Group 2, Human Development Department	Total Cost: 0.4 billion JPY
Period of Cooperation	(R/D): 1/May/2014 – 30/Apr/2019
	Partner Country's Implementing Organization: the Ministry of Health (MOH), the Center of Malariology, Parasitology and Entomology (CMPE), Institut Pasteur du Laos (IPL) (the leading organization of the <u>Laotian side</u>), the Lao Tropical and Public Health Institute (Lao TPHI) and the National Center for Laboratory and Epidemiology (NCLE)
	Supporting Organization in Japan: <u>the National Center for Global Health and Medicine (NCGM) (the leading organization of the Japanese side)</u> , the University of Tokyo (UT), University of the Ryukyus (UR), Juntendo University and Tokyo Medical and Dental University (TMDU).
	Other Related Projects: Japan Agency for Medical Research and Development (AMED)
1-1 Background of the Project	
<p>Parasitic diseases such as malaria and other trematode infections (Schistosomiasis mekongi, Opisthorchiasis viverrini, etc.) put a severe burden on the socioeconomics in the Lao People's Democratic Republic (hereinafter referred to as "<i>the Lao PDR</i>"). The Government of the Lao PDR has been putting efforts to improve the situation by taking various measures such as the distribution of the Long-Lasting Insecticide-Treated Nets as well as the provision of anthelmintic agents with the support of development partners. However, it is considered to be an urgent need to strengthen the countermeasures based on the scientific evidences to meet the international demands, not just for the Lao PDR, for effective infectious disease control measures as well as preventing the emergence of drug resistance, which are regarded as global issues.</p> <p>Accordingly, Japan International Cooperation Agency (JICA), based on the request of the Government of the Lao PDR, commenced a 5-year technical cooperation entitled "<i>the Project for Development Innovative Research Technique in Genetic Epidemiology of Malaria and Other Parasitic Diseases in Lao PDR for Containment of Their Expanding Endemicity</i>" (hereinafter referred to as "<i>the Project</i>") from May 2014 with the Lao counterpart organizations of the CMPE and IPL of the MOH, under the scheme of SATREPS.</p>	
1-2 Project Overview	
(1) Project Purpose	
Research results based on the methods for the genetic epidemiology diagnosis of malaria, Schistosomiasis mekongi and Opisthorchiasis viverrini are utilized in government services such as in diseases control.	
(2) Outputs	
1) More convenient and accurate methods (PCR method, LAMP method, etc.) for the diagnosis of malaria, Schistosomiasis mekongi and Opisthorchiasis viverrini are developed and utilized.	
2) Temporal and spatial epidemiological situations of pathogens and vectors of malaria, Schistosomiasis	

mekongi and *Opisthorchiasis viverrini* is monitored.

- 3) Mechanism of emergence and expansion of the drug resistant malaria is analyzed.
- 4) Based on the surveillance system using the developed diagnostic methods on malaria, *Schistosomiasis mekongi* and *Opisthorchiasis viverrini*, education for people is strengthened and endemicity is monitored together with the local government.
- 5) Capacity of researchers and administrative officers for the control of malaria and other parasitic diseases is strengthened.

(3) Inputs

The Japanese side:

- Dispatch of JICA experts: a total of 4 Experts (1 for parasitology research and a total of 3 Project Coordinators), a total of 101 M/M (Man/Month) / Short-term Experts: a total of 73 Experts, 15 M/M;
- Counterpart Researchers' visit to Japan: A total of 9 counterpart personnel for sharing the research progress and outcomes, discussion on the research plan of operation and so on. (a total of 61 days);
- Training in Japan: A total of 5 counterpart personnel for the training of malaria diagnosis, drug susceptibility test, genetic analysis, malaria epidemiological study, etc.;
- Provision of Equipment: DNA Sequencer, electrophoresis imaging system, multi-gas incubator, spectrophotometer, deep freezers, automatic electrophoresis apparatus, realtime-PCR system, etc.; and
- Overseas Activities Costs: procurement of reagents and consumables, travel costs, costs for training, etc.

The Lao PDR side:

- Allocation of Counterpart Personnel: A total of 20 counterparts such as Project Director, Project Manager, researchers;
- Facilities, Equipment and Materials: Laboratory and office spaces in IPL area, existing research instruments, equipment and/or devices in the IPL and provincial CMPEs and available data, information and/or specimens related to the Project.
- Local Costs: Utilities for the project office and costs other than that covered by JICA for equipment maintenance management etc.

2. Terminal Evaluation Team

Members	Dr. Kaname KANAI	Leader	Executive Technical Advisor to the Director General, Human Development Department, JICA
	Ms. Yukari MAEDA	Cooperation Planning	Staff, Health Team 4, Health Group 2, Human Development Department, JICA
	Dr. Yoichi INOUE	Evaluation Analysis	Senior Consultant, Consulting Division, Japan Development Service Co., Ltd.
	Mr. Katsumi ISHII	Planning and Evaluation	Deputy Manager, Division of International Collaboration, Department of International Affairs, AMED (Observing member)
Period of Evaluation	2/Oct/2018 – 20/Oct/2018		Study Type: Terminal Evaluation

3. Summary of Evaluation Results

3-1 Achievements

(1) Output 1

Concerning the LAMP-based DNA detection method for the diagnosis of malaria (*LoopampTM MALARIA*

Pan/Pf Detection Kit), the Project observed some problems in its operation in local clinical settings for proper laboratory diagnosis as well as the necessity of product improvement in all three (3) Station of Malariology, Parasitology and Entomology (SMPEs) under the Provincial Health Offices (PHOs), where kit was introduced by the Project. In addition, it is a common recognition among stakeholders that it is difficult to disseminate the Loopamp™ shown in the Outcome 1 within the framework of the Project, since the Project is required to obtain the prequalification of the Loopamp™ by WHO in advance of Lao MOH's authorization for the product as an official method. Given these circumstances, the Project is planning to introduce another five LAMP detectors to district health facilities in the areas of high malaria endemicity, and continue accumulating clinical cases as well as the efforts for improving the aforementioned challenges even following the completion of the Project.

Meanwhile, as was shown in the achievements of OVI's above, it seemed unnecessary to provide diagnostic services of both Schistosomiasis mekongi and Opisthorchiasis viverrini at local medical facilities in the endemic areas, in consideration of the characteristics of those diseases as well as the initiatives taken by the Lao government. Further, the Project, in accordance with the request from the MOH, has been providing testing services using PCR, LAMP and/or ELISA techniques for prevalence surveys performed in endemic areas. For these reasons, it is considered that there is little significance in aiming for "dissemination" (application in the Lao PDR as a laboratory testing service) as stipulated in the Output 1. Having said that, since the MOH expects the IPL to function as a reference laboratory for the diagnoses of Schistosomiasis mekongi and Opisthorchiasis viverrini, the IPL is necessitated to establish those DNA diagnostic techniques. Therefore, although it is different from the original assumptions, it can be understood that the Project has achieved the development and dissemination of diagnostic methods for both diseases in an alternative in accordance with the needs of the Lao PDR.

Summing up, it was confirmed that the Project established DNA detection methods for the three target diseases, and applied them to the project research subsequently. At the same time, the application of those methods to each disease control measure have practically contributed to the Lao PDR in the form suitable for the operation required for each of them. For these reasons, it is deemed that the Output 1 is generally achieved as of the time of the Terminal Evaluation in a manner different from the original plan.

(2) Output 2

The Project has clearly shown that the ratio of Falciparum malaria cases among reported cases of malaria in the Lao PDR is declining every year, while the ratio of Vivax malaria cases is increasing. Moreover, the active surveillance of community residents in endemic areas performed by the Project has shown that there are more asymptomatic carriers of Plasmodium vivax than expected. The Project also revealed that asymptomatic malaria infection without typical symptoms of malaria infection such as high fever existed to a certain extent. As the number of malaria patients continues to decline in recent years owing to the efforts of the Lao government and its partner organizations, the demonstration of the existence of asymptomatic carriers as reservoir by the time of the Terminal Evaluation has been an important achievement of the Project in consideration of future elimination of malaria. In relation to this, the Project has brought out the prevalence of G6PD deficiency through the genetic epidemiological analyses by testing its enzyme activity of community resident, since G6PD deficiency has the potential to trigger a severe adverse reaction (acute hemolytic anemia) when administering Primaquine in order to eradicate malaria from the hepatocytes. This is an important point in safely implementing radical eradication treatment for individuals with hypnozoites in hepatocytes; thus, it is deemed that the Project provided important evidences for considering mass drug administration of primaquine for extermination of Plasmodium vivax. As another achievement under the Output 2, the Project identified the first case of human infection with *P. knowlesi* in the Lao PDR. *P. knowlesi* is genetically similar to *P. vivax*, and it is known that not only the results of rapid diagnostic tests but also PCR may be mistakenly diagnosed as Vivax malaria. It is known that human infections with *P. knowlesi* can be severe in some cases, and many deaths have been reported

in Malaysia. Therefore, this research result of the Project warns that even if the diagnosis was Vivax malaria in a rapid diagnostic test, it is necessary to carry out the treatment with appropriate antimalarial drugs without fail.

In this way, concerning malaria, important epidemiological data has been gathered in the Project as of the Terminal Evaluation and those findings of advanced analyses using population-genetic techniques have also been published as scientific articles in international journals. Simultaneously, the Project has been providing the stakeholders of malaria control such as the MOH and WHO with those findings as convincing evidences for making policies, countermeasures and so on in the Lao PDR. Concerning Schistosomiasis mekongi and Opisthorchiasis viverrini, it became a common understanding that the said two diseases are not applicable to the analyses based on population genetics; therefore, it is deemed from general assessment that the degree of achievement of the Output 2 has largely been appropriate as of the time of the Terminal Evaluation.

(3) Output 3

Since chloroquine resistant Falciparum malaria was dominant in the Mekong region, the use of chloroquine is prohibited for its treatment in the Lao PDR. However, on conducting analysis of chloroquine resistant gene of *pfert* in the Project, it was confirmed that chloroquine-sensitive (wild type) Plasmodium falciparum is increasing. It is guessed that the decline in chloroquine selection pressure is one of the factors behind the increase in wild-type Plasmodium falciparum, however, there are still not enough samples to draw any definite conclusions. Meanwhile, the Project carried out massive survey for the analyses of the mutation on the *K13* gene that is considered to be related to the resistance against artemisinin. The analysis results revealed that artemisinin-resistant protozoa from Cambodia spread gradually from southern to northern parts of the Lao PDR as humans moved, reaching the northernmost Pongsavath Province by the end of 2017. These results suggest a risk that artemisinin-resistant malaria may spread from Pongsavath Province of the Lao PDR to Yunnan Province of China. From these research findings and outcomes, it is demonstrated that it is of greater importance to implement active surveillance on multidrug resistant genes in the Lao PDR. As aforementioned, the Project has gained important research findings and outcomes on the mechanisms of the emergence and dissemination of the drug resistance malaria as of the time of the Terminal Evaluation. Those findings and outcomes were published in international journals as academic articles, one of which was published in a world-class prestigious journal. Those have also been supplied to relevant organizations as important evidences for advancing countermeasures against malaria in the Lao PDR, in the region and even globally. For these reasons, the achievement level of the Output 3 is deemed to be significantly high at the time of the Terminal Evaluation.

(4) Output 4

Concerning malaria, the surveys and analyses on the endemicity, distribution and diffusion of the drug-resistant malaria have been carried out under the Output 1, 2 and 3. Regarding Schistosomiasis mekongi, the Project established the DNA detection method with high sensitivity and specificity in the IPL, and applied it to research on infection rates not only in humans but also vector snails and animals. The Project conducted a combined analysis of these infection rate results and geographic data from satellites provided through the Japan Aerospace Exploration Agency collaboration to create a risk map and to analyze risk factors for infection. Similarly, concerning Opisthorchiasis viverrini, and the Project developed the DNA detection method with high sensitivity and specificity, and used for the project research. It is worth noting that through the development of the DNA detection method for Opisthorchiasis viverrini, the Project revealed that the microscopic examination actually overestimated the prevalence of the disease by mis-distinguishing trematodes, which are morphologically similar to O. viverrini as O. viverrini to a certain extent. The research findings and outcomes obtained through these activities have been provided as convincing evidences not only to the MOH but also to the WHO and other organizations engaged in malaria

control in the Lao PDR and the region, and are used directly and indirectly for policymaking, surveillance and implementation of countermeasures.

It was not possible to construct a means for the prevention of infection of the inhabitants based on scientific evidence such as “*Position Deviance*” within the project period; nonetheless, the Project established DNA detection methods with high sensitivity and specificity in the IPL, which greatly contributed to functioning the Laos-Japan parasitology laboratory as a reference laboratory for those target diseases. Besides, the sharing of research findings and outcomes of the Project with stakeholders is deemed to directly contribute to the monitoring of the diseases in the Lao PDR. For these reasons, the Output 4 is considered to be largely achieved at the time of the Terminal Evaluation.

(5) Output 5

The Project has been advancing its activities with the emphasis on nurturing Laotian young researchers throughout the project period. As a result, the Laotian researchers became capable of planning field surveys, collecting samples and perform DNA analyses using advanced research instruments by themselves. Further, under the guidance of the JICA experts (researchers), they have been actively preparing abstracts and conference presentation slides in English and practicing presentations; as a result, some Laotian members made presentation of the project research orally in English at the National Health Research Forum. Meanwhile, the Project has offered basic and refresher training opportunities on malaria and parasitic disease control to a total of 156 health personnel engaged in parasitic disease control on the ground in districts and provinces. Not only has this made a contribution to measures for the prevention and control of target diseases, but it has also helped build a nationwide network, as a byproduct of training, for periodically collecting samples. In addition, the JICA expert (NCGM researchers) stationing in the IPL has been participating as an advisor in meetings on various infectious disease countermeasures held by the MOH, WHO and other partners, and continued to share technical advice and research findings and outcomes generously at meetings. In addition, the Project has provided direct support to the MOH by preparing implementation protocols for prevalence surveys and other activities, which may have contributed significantly to the capacity building of administrative officers and personnel in the national research institutes engaged in infection control in the Lao PDR.

As has been described, the Project has been offering various opportunities for capacity building for various human resources engaged in infectious disease countermeasure and research in the Lao PDR, and is expected to continue after the project period ends. Accordingly, the degree of achievement concerning the Output 5 is thought to generally be appropriate as of the time of the Terminal Evaluation.

(6) Project Purpose

As has been indicated so far, the Project has succeeded in acquiring important findings and research outcomes concerning endemicity of malaria (including asymptomatic carriers) and the mechanism that can contribute to drug resistance in the Lao PDR as of the time of the Terminal Evaluation, and these findings have even been published as scientific papers. Moreover, the simple and highly sensitive LAMP-based DNA detection methods were introduced to major research institutes in Vientiane (the CMPE and the IPL) as well as the SMPE of the PHOs covering the north, center and south of the country, and training of health personnel who are engaged in parasitic disease control at such facilities is being advanced. Moreover, as was indicated in the achievement of Outputs, the JICA long-term experts (NCGM researchers) stationed in the IPL have shared the research findings and outcomes and offered technical advice when participating in national conferences on malaria control.

Meanwhile, concerning *Schistosomiasis mekongi* and *Opisthorchiasis viverrini*, development work on the LAMP-based DNA detection method had been completed from the technical point of view. All WHO member countries are required to strengthen the “preparedness” against infectious diseases, in accordance with the International Health Regulations (IHR), by preparing options for testing and diagnostic methods.

Accordingly, the Project established DNA detection methods that have high sensitivity and specificity with respect to such parasitic diseases, and significantly contributed to the IPL to function as the reference laboratory for the said diseases in the Lao PDR. Furthermore, the research findings and outcomes gained using those detection methods have been used as the evidences for the betterment of the infection control in the Lao PDR.

As has been described above, the Project has created a variety of research findings and outcomes that will contribute to the countermeasure of parasitic diseases in the Lao PDR. The IPL Laos-Japan Parasitology Laboratory, which is the main body of the project implementation, has already been built into the system of infectious disease control in the Lao PDR as a supplying body of scientific evidences and as an implementation organization of direct countermeasures, making it an indispensable existence. In view of the above points, the achievement of the Project Purpose at the time of the Terminal Evaluation is highly satisfactory.

3-2 Summary of Evaluation Results

(1) Relevance

The relevance of the Project has been highly maintained hitherto.

The significance of taking measure for the control not only for malaria but also other parasitic diseases including Schistosomiasis mekongi and Opisthorchiasis viverrini, the target diseases of the Project, is clearly mentioned in the “*Eighth 5-year Health Sector Development Plan 2016-2020*”. The Plan stipulates the specific areas to be addressed as follows: capacity enhancement of both national and local laboratories (including human resource development and quality control) in accordance with the requirements of the IHR and other international standards; the reinforcement of infectious disease surveillance system; the control of drug resistance; and the strengthening of health education. Meanwhile, the Lao MOH, with the support of WHO, the Project (i.e., JICA experts and the IPL) and other stakeholders, issued the “*National Strategic Plan for Malaria Control and Elimination 2016-2020*” in January 2016. In the Strategic Plan, it is clearly mentioned that the CMPE of the MOH should introduce molecular diagnostic techniques to the provincial-level laboratories with the support of partner organizations as well as the IPL should take initiative to plan and implement the research on the drug-resistant malaria. These can be the results of the project’s efforts to demonstrate the necessity of addressing asymptomatic malaria cases and of researching the drug resistance; simultaneously, resulted in further enhancement of the relevance of the Project.

Meanwhile, the Government of Japan has been promoting aid activities for infectious disease control, and the “*Global Health Policy 2011-2015*” clearly come out with the promotion of the Neglected Tropical Diseases control, preparedness for emerging and reemerging infectious diseases and international collaboration for it. Furthermore, in its “*Basic Design for Peace and Health (Global Health Cooperation)*” and “*Basic Policy on Strengthening Countermeasures for Infectious Diseases that Pose a Threat to Global Society*”, both publicly announced in September 2015, the Government of Japan states to build a health security that is resilient to external factors such as public health emergencies and disasters and to strengthen Japan’s contribution and roles for the countries and regions facing the pandemic outbreaks of public health concerns. The Japan’s Aid Policy for the Lao PDR, issued in April 2012, stipulated the “*Improvement of health and Medical Services*” as one of four priority areas for assistances. Furthermore, following the adoption of “*Global Action Plan on Antimicrobial Resistance (AMR)*” at the WHO General Assembly held in May 2015, Japan has strengthened its effort to promote international cooperation for the control of AMR. For these reasons, the Project, aiming to contribute the improvement of health and medical services as well as the control of drug-resistant malaria in the Lao PDR through the collaborative research and technical cooperation, is deemed to be highly consistent with the Japan’s Aid Policies.

(2) Effectiveness

The effectiveness of the Project is high in general.

As was described in the Achievement of the Project Purpose, the Project obtained important research findings and outcomes of especially in malaria research with regard to the prevalence of the plasmodia (including asymptomatic carries) as well as the mechanism responsible for the emergence and expansion of drug resistance gene mutation. These research results have been published in a number of international journals as academic papers, and also, many presentations have been made by project members at domestic and international conferences (9 original articles published in international journals (Annex 7), 39 oral presentations at international conferences, 7 poster presentations and 18 oral presentations at conferences in Japan, as of October 2018). Besides, the JICA long-term expert (NCGM researcher) became a member of national level meetings and conferences for the control of infectious diseases in the Lao PDR and provided technical guidance on the basis of research findings and outcomes as well as his expertise and experiences as a scientist. As aforementioned, the Project has generated a number of research findings and outcomes that will contribute not only to the malaria control in the Lao PDR but also to the Greater Mekong Sub-region and even the global malaria countermeasures, and are practically used as evidences for the formulation of policies and action plans for malaria countermeasures. The IPL has also been contributing directly to the implementation of malaria countermeasures in the Lao PDR and the region. Therefore, the achievement level of the Project in malaria is very high in terms of both collaborative research and technical cooperation.

Meanwhile, concerning Schistosomiasis mekongi and Opisthorchiasis viverrini, the Project has almost completed development work on the LAMP-based DNA detection methods for each parasitic disease, and they are used as sensitive, specific and reliable DNA diagnostics in the prevalence surveys conducted by the MOH and WHO. The MOH also calls for the IPL to function as a reference laboratory in these diseases from the perspective of IHR compliance. In addition, as with the malaria control countermeasures mentioned above, the JICA long-term expert (NCGM researcher) is assigned as a temporary member of the Advisory Committee on Parasitosis hosted by the MOH and WHO, and the Project has been continuing to share research findings and outcomes and providing technical advice throughout the project period. Thus, concerning Schistosomiasis mekongi and Opisthorchiasis viverrini, the Project has also contributed to the infectious disease countermeasures the Lao PDR in a different way than originally assumed. Thus, concerning Schistosomiasis mekongi and Opisthorchiasis viverrini, the Project has also contributed to the infectious disease countermeasures the Lao PDR in a different way than originally assumed.

As aforementioned, on top of the research findings and outcomes gained from the project collaborative research, the Project has been putting efforts to capacity development not only of Lao young researchers but also health administrative officers and medical professionals on the ground through joint research work and trainings provided by the Project. For these reasons, it is deemed that the Project Purpose has generally been accomplished at the time of the Terminal Evaluation.

(3) Efficiency

The efficiency of the Project is high in general.

Meanwhile, as was described in the “*Verification of Implementation Process*” section, the IPL Parasitology Laboratory is operated as the Lao-Japan Joint Laboratory, headed by the Chief Advisor of the Project (NCGM department director) and the JICA long-term expert is assigned as the Laboratory Manager to organize research activities as well as other managerial work in the Lao PDR. The IPL hold a weekly meeting with the participation of all laboratory heads chaired by the Director of the IPL to share the progress and achievements as well as to discuss managerial issues. At the initiative of the JICA long-term expert (NCGM researcher) stationed in the IPL, the liaison and coordination of the research collaboration amongst the Japanese research institutes such as the UT, the UR, the TMDU and the Juntendo University. Meanwhile, the project coordinator has changed approximately one year before the end of the project period; nonetheless, the coordination work was properly taken over to the successor. Thus, the liaison and coordination amongst the whole players have adequately been continued throughout the project t period.

Meanwhile, it usually took longer-than-expected time (approx. 2 to 4 months) to go through procedures for acquisition of tax exemption certificates for research instruments, reagents, etc. from the Lao authority concerned in accordance with the R/D. The Mid-term Review mission had observed that similar problems had happened in other IPL laboratories. In particular, the reagents with short expiration dates can be used in the experiment for a shorter period of time. Following the time of the Mid-term Review, the IPL has appealed to the relevant ministries and agencies for problem solving, but it has not been resolved even at the time of the Terminal Evaluation. In addition, the Project implemented researches following the acquisition of ethical clearance by the relevant authorities concerned both in Japan and the Lao PDR. Accordingly, the Project submitted research proposals to the National Ethics Committee for Health Research properly; however, it took, in many time, more-than-expected time for the Project to receive the results of the review by the Committee. Although these issues did not have a significant negative impact on achieving the Outputs and the Project Purpose, it negatively affected the smooth progress of the Project.

(4) Impact

The following positive impacts are confirmed and/or expected by the implementation of the Project.

The IPL Parasitology Laboratory has been operated as the Lao-Japan Joint Laboratory, and the researchers of the NCGM is proactive in doing operational management of the Laboratory. The JICA experts have been working on the project research activities in consideration of nurturing Lao researchers, and it is deemed that the capacity of those researchers has significantly been enhanced in comparison with that in the beginning of the Project. Moreover, the Laotian young researchers in the IPL sometimes accompanied the JICA long-term expert (NCGM researcher) to attend the various meeting opportunities at the national level, and experienced and learned the theory and practice of the infectious disease control as well as the practical application of research outcomes to the society. Having said that, it is recognized that they are still young researcher and less experienced to run and to maintain or even enhance the research capacity of the IPL Parasitology Laboratory by themselves; from the project-designing stage, it had not been anticipated to hand over the project research to the Laotian staff in the IPL Lao-Japan Parasitology Laboratory. Further, as has been mentioned, the IPL Lao-Japan laboratory is already regarded as a part of the implementation system of the infectious control in the Lao PDR, and the NCGM is decided to sustain the collaborative research in the IPL even following the termination of the Project; therefore, it is highly expected that the research activities will further be enhanced and expanded hereafter on the project's research outcomes and human resource development as a strong steppingstone.

On top of that, several positive impacts of the Project have been observed or expected as follows: 1) Efforts for the acquisition of the prequalification for the LAMP-based DNA detection method for the diagnosis of malaria through the collaboration between the NCGM and the *Eiken Chemical Co., Ltd.*; 2) Cooperative research with the *neopharma Japan Co., Ltd.* for research on antimalarial Activity of a substance; 3) Collaboration with the MOH and the Ministry of Agriculture and Forestry through the prevalence surveys on Schistosomiasis mekongi and the development to the "One-Health" approach; 4) Collaboration with the MOH and the Ministry of Agriculture and Forestry through the prevalence surveys on Schistosomiasis mekongi and the development to the "One-Health" approach; 5) Promotion of Inter-laboratory collaboration for cross-cutting research in the IPL; and 6) Nurturing Japanese young researchers (Postgraduate students).

(5) Sustainability

A self-sustainability as well as a self-deployment of the benefits provided by the Project can be expected to some extent.

From the political and institutional aspects, the significance of the control of malaria and other parasitic diseases will be maintained even after the termination of the project period since the significance is clearly stated in the "*Eighth 5-Year Health Sector Development Plan 2016-2020*". Especially for malaria, the

MOH, jointly with the Development partner organizations, has strengthened efforts to achieve the elimination of Falciparum malaria by 2015 followed by the elimination of all types of malaria by 2030. Therefore, it is anticipated that the importance of research outcomes, which will be presented to the MOH and other stakeholders, will be maintained even after the end of the project period since the outcomes are expected to be used as solid basis for making decisions, policies and countermeasures by the said agencies. The Japanese research organizations are anticipated to continue the joint research at the IPL even following May 2019 when the cooperation period is over. Effective infectious disease countermeasures have been implemented through various collaborations between research institutes and the governmental organizations. However, it is desirable that the MOH and other related organizations will provide more support to the implementation of joint research and the utilization of research findings and outcomes for policymaking, implementing countermeasures, etc. in the Lao PDR, even after the completion of the project period.

Concerning the financial sustainability, the NCGM has decided to continue the joint research at the IPL even after the end of the project period, by utilizing financial support from Japanese private companies as well as by acquiring the competitive research funds in Japan. The IPL also has commenced two projects financially-supported by the US Foundation, and some of these budgets have become available in all IPL laboratories since July 2018. Specifically, \$1,000 per month are provided for each IPL laboratory for the purchase of experimental consumables and is expected to continue for two years. Accordingly, the budget for maintaining collaborative research at the IPL is considered to be secured for the time being after the project period ended.

As for the technical aspect, the NCGM has decided to continue collaborative research at IPL after the completion of the Project. The research and testing technologies provided through the Project will continue to remain in the IPL, and research results and technical advice will also be shared with relevant organizations engaged in infectious diseases control in the Lao PDR in a sustainable manner. On the other hand, the Laotian researchers have enhanced their capacity in comparison with that at the beginning of the Project, however, the efforts for capacity development should be continued with a long-term point of view.

3-3 Factors that promoted the attainment of the Project

(1) Concerning the project design

None in particular.

(2) Concerning the implementation process of the Project

At the time of the interviewing opportunities, the CMPE of the MOH as well as WHO showed their recognition that the Project (i.e., JICA experts and the IPL researchers) is an important partner who can provide scientific evidences such as research findings and outcomes for helping them to develop policies and/or countermeasures. Based on such recognition, the JICA long-term expert, as a representative of the IPL Parasitology Laboratory has been assigned as a member of the said meetings and provided technical guidance based on the project research findings and his expertise and experiences.

On the basis of the establishment of such relationship of mutual trust and collaboration amongst the stakeholders through the implementation of the Project, the Project has been providing the scientific evidences for policymaking, cooperating by providing testing services, receiving the funding support from partner organizations, implying the ideal collaboration has been continued from the technical and financial standpoint. Simultaneously with the implementation of project research activities, the Project has been putting efforts to apply the research findings and outcomes to the policy making, countermeasure, etc. as well as to establish the relationship of mutual trust and cooperation with relevant organizations. As a consequence, the Project has made a great contribution to the infectious disease control in the Lao PDR; at the same time, the effectiveness of the Project was enhanced significantly.

3-4 Factors that impeded the attainment of the Project

(1) Concerning the project design

None in particular.

(2) Concerning the implementation process of the Project

There were several cases that it took a couple of months to obtain certifications of tax exemption on the basis of the R/D for the research instruments as well as reagents, which were brought from Japan. Some reagents with relatively short valid period had been shortened the days for expiration date since it had been kept in the customs for a certain period of time. The IPL has been calling for the improvement of this issue to the relevant governmental agencies such as the Ministry of Health and the Ministry of Finance throughout the project period; nevertheless, nothing has resolved as of the time of the Terminal Evaluation. Though it had not caused critical influence on the project activities, it is deemed to hinder the smooth implementation of project activities to some extent. Thus, this is regarded as a hindering factor against the efficiency of the Project.

3-5 Conclusions

The Terminal Evaluation Mission confirmed that "*Relevance*" of the Project has highly been maintained, and that "*Effectiveness*", "*Efficiency*", and "*Sustainability*" were also generally high. The Project has also created a number of positive "*Impact*" as of the time of the Terminal Evaluation; thus, it is expected to contribute significantly to the countermeasure of malaria and parasitic diseases in Lao PDR in future.

In particular, the Project has established the cooperative relationships with relevant ministries, national agencies and other partner organizations by providing scientific evidences and technical advices as well as by assisting the national surveys, which are beneficially utilized for the infectious disease countermeasures in the Lao PDR. Under such liaison and cooperation, the Project also proceeded various project activities to date. As the result, various scientific research results have been created, and it has directly contributed to the infectious disease countermeasure in the Lao PDR.

With regard to malaria, as a result of the establishment of cooperative relationship with local health professionals through the provision of technical training to them, the Project obtained sufficient number of clinical samples from malaria suspected patients and analyzed them proactively; consequently, the Project revealed that the present state of asymptomatic malaria carriers, which is recently regarded to be important for strengthening the initiatives for malaria elimination. In addition, the important research findings and outcomes on the emergence and diffusion of the drug-resistant malaria are gained, which had impacted to the commencement of novel international research collaboration (supervision) for preventing from crossing border.

On the other hand, concerning Schistosomiasis mekongi and Opisthorchiasis viverrini research, the Project had developed DNA detection methods based on the novel gene amplification technology, and the developing work for the methods has largely been completed from a technical standpoint within the cooperative period. These DNA detection methods are established as diagnostic methods in the IPL, enabling the IPL to function as a reference laboratory for these diseases, and are also used for the national prevalence surveys conducted by the MOH.

These research findings and outcomes are disseminated to the world through the publications of research articles in international journals, and many presentations has also been made at academic conferences. Thus, the achievement of the Project from an academic standpoint is very large. Besides, by taking the opportunities of field sampling activities, the Project has been providing health education regarding the prevention of infectious diseases geared to community residents jointly with the health professionals, resulted in the steady contribution to the community health. The Project has also consistently addressed the fostering of Laotian young researchers through its research activities, and the staff of the IPL Lao-Japan Parasitology Laboratory has reached the level where they can make oral presentations in English at domestic and international

conferences at the time of the Terminal Evaluation. Though further self-study and continuation of guidance from Japanese researchers are also required to stand alone as researchers, it is deemed that the Project has made a significant achievement from the viewpoint of JICA's technical cooperation.

Even after the completion of the Project, Japanese research institutes are supposed to continue international joint research at the IPL by utilizing research funding from companies and scientific research grants in Japan. The Japanese research institutes will move on to the preparations for the acquisition of WHO pre-certification for the LAMP-based malaria DNA diagnostic kit, detailed research on asymptomatic malaria carriers, and further, novel research on the substance with antimalarial activity. Those international collaborative researches are also anticipated to continuously contribute not only to scientific research outcomes but also to the countermeasure of infectious diseases in the Lao PDR hereafter.

3-6 Recommendations

(1) To the Project

1) Promotion of the "One-Health" approach

The Project had gained an experience of inter-sector collaboration with the Ministry of Agriculture and Forestry, such as the implementation of the joint survey. From the aspect of the significance of the collaboration with other organizations, it is anticipated that this kind of cross-sectoral activities such as the regular cross-sectoral meeting become widely be done, in order to promote the "One-Health" approach.

2) The effort to explanation of the practical operational procedures at the time of introduction of LAMP detectors

The Project is planning to introduce another five LAMP detectors to district health facilities in the areas of high malaria endemicity, and continue accumulating clinical cases even following the completion of the Project. At the time of introduction, it is necessary that the Project should put efforts to publicize the performance and utilization of the kit to the local stakeholders; at the same time, to introduce the practical operational procedures of the testing services, such as algorithms for selecting eligible patients for genetic diagnosis by LAMP method and specimen transfer method, etc.

Meanwhile, the Project experienced that LAMP reagents under storage could easily deteriorate with moisture, enough to affect the measurement results as false positive, in usual environment of laboratories in the Lao PDR, and the problem can happen in hot and humid malaria-endemic areas such as Southeast Asia and Africa where the LAMP-based malaria DNA detection methods were expected to be used. Though the current reagent packaging would not cause any problem of the testing results in the usage of mass survey of asymptomatic malaria carriers, it is recommended for the Project, jointly with the *Eiken Chemical Co., Ltd.*, to resolve the problem by improving the "Product", such as individual packaging of reagents, in consideration the usage in practical clinical settings.

(2) To the MOH

1) Improvement of internal quality control system in local clinical laboratories

Capacity of local laboratory staff has significantly been enhanced through the implementation of the Project, it is confirmed that a problem concerning the quality control toward laboratory testing results from the LAMP-based DNA detection method for diagnosing malaria, introduced by the support of the Project. In particular, the Project, with the support of the *Eiken Chemical Co., Ltd.*, developed and introduced the Standard Operating Procedure (SOP) for the said testing by providing the staff with its training; nevertheless, it is found that there is no monitoring mechanism for the compliance of the SOP. This is regarded not only the issue of the Project but also a challenge of the clinical laboratories in whole country; therefore, it is recommended that the NCLE, in charge of laboratory quality control and assurance, will take action for the construction and even improvement of the Internal Quality Control (IQC) mechanism immediately.

2) Coordination with related development partners for effective trainings

Regarding the training on communicable diseases for the lab staffs and officers in rural area which was provided by the Project, the Department of Communicable Disease Control and other relevant departments within MOH should continue to work closely and coordinate with WHO and other partners which are conducting various trainings, in order to make them more effective without duplication.

3) Improvement of the situation regarding the certification of tax exemption for reagents, research instruments and equipment.

When reagents, research instruments and equipment were brought from Japan to the Lao PDR, it took longer time than expected to go through procedures for acquisition of tax exemption certificates for them from the Lao authority concerned in accordance with the R/D. Especially, some reagents with relatively short valid period had been shortened the days for expiration date since it had been kept in the customs for a certain period of time.

Having said that, it is acknowledged that this issue cannot be solved by the MOH alone but is regarded as a complex issue involving the Ministry of Finance, the Ministry of Planning and Investment, and other relevant agencies. Not only all laboratories in the IPL but also any research institutes engaged in the infectious disease control in the Lao PDR are being affected by the issue. In other words, the relevant ministries and agencies should acknowledge the negative impact of the issue on infectious disease countermeasures in the Lao PDR, and are expected to make further efforts to resolve the issue, at the initiative of the MOH, by convening inter-ministerial consultations and so on.

4) Smooth implementation of ethical review for the research proposal

The Project implemented researches following the acquisition of ethical clearance by the relevant authorities concerned both in Japan and the Lao PDR. Accordingly, the Project submitted research proposals to the National Ethics Committee for Health Research properly; however, it took, in many time, more-than-expected time for the Project to receive the results of the review by the Committee. The Project sometimes have to put a special consideration for the timing of survey especially for malaria and Schistosomiasis mekongi, thus, the Committee is recommended to improve this situation for smooth implementation of ethical reviewing.

5) Further cooperation to promote international joint research work in IPL with Japanese research institutes

The Japanese research organizations such as NCGM are anticipated to continue the joint research at the IPL even following May 2019 when the cooperation period is over. MOH should provide more support to the implementation of joint research and the utilization of research findings and outcomes for policymaking, implementing countermeasures, etc. in the Lao PDR, because of the importance of IPL as the national referral laboratory for the investigation of parasitic diseases and for provision of evidences for policy making and as a cooperation agency for national surveys. It is expected that the MOH will involve Lao and Japanese researchers to participate in conferences on countermeasures for infectious diseases and promote the utilization of research findings more actively.

(3) To the Lao young researchers

1) Further Self-Help Endeavor to enhance International Competitiveness

It is important for the Lao young researchers to come in touch with the advanced scientific research by themselves, in order to acquire international competitiveness. To achieve it, the Lao young researchers are advised to continue self-help efforts even following the termination of the Project further, such as reading more English papers, holding journal club, capturing novel scientific information, obtaining Ph.D. degree in the future, and increasing other options for capacity enhancement.

3-7 Lessons Learnt

(1) Significance of proactive information sharing with stakeholders in light of the practical application of the research findings and outcomes to society

This project, with the full-understanding of the scheme objectives of the SATREPS, has been providing scientific evidences on malaria, Schistosomiasis mekongi and Opisthorchiasis viverrini to relevant organizations such as the MOH and WHO in a timely and effective fashion. The JICA long-term expert (NCGM researcher), stationed in the Lao PDR, has been participating countermeasure meetings at various levels in Lao PDR, and not only sharing information but also providing advices from a professional perspective and coordinating collaborative countermeasure activities, contributing greatly to the control of infectious diseases in Lao PDR and even the Greater Mekong Sub-region, thereby maximizing the relevance, effectiveness and impact of the Project.

Many research institutions such as universities do not disclose research findings and outcomes until it is published in academic journals or other publications in order to maintain the confidentiality of their research results. Having said that, the principle of SATREPS is the practical application of research outcomes to society; therefore, projects are required to promote the information sharing and collaboration with future users (e.g. governmental authorities) of the research outcomes even within the project period as well as to provide necessary assistances in a timely manner, in order to fulfill the said principle.

(2) Allocation of resident researcher(s)

In the Project, one researcher from a Japanese implementing organization was stationed in the Lao PDR, and not only the implementation of international joint research but also managerial affairs with related organizations were conducted exclusively. The establishment of such an implementation system enabled the smooth construction of a research system and the development of human resources as a technology cooperation project, and also led to technical assistance to the Lao government and international organizations in a timely manner. Since the social application of research findings and outcomes has strongly been taken into account in SATREPS, it is recommended for SATREPS projects to allocate researcher(s) stationed in the host country as much as possible to enhance the effectiveness of international joint research, and to promote information sharing and collaboration with not only the host country but also international organizations in the region, while giving due consideration to the confidentiality of research results.

3-8 State of the follow-up