

## Evaluation Summary

1. Outline of the Project	
Country: The Republic of the Philippines	Project Title: the Project for Prevention and Control of Leptospirosis in the Philippines
Issue/Sector: Healthcare and medical treatment	Cooperation Scheme: Technical Cooperation Project (under the scheme of “ <i>Science and Technology Research Partnership for Sustainable Development: SATREPS</i> ”)
Division in charge: Health Team 3, Health Group 2, Human Development Department	Total Cost: 350,000,000 JPY
Period of Cooperation (R/D): 1/Apr/2010-31/Mar/2015	Partner Country’s Implementing Organization: the College of Public Health, the University of the Philippines Manila
	Supporting Organization in Japan: the Kyusyu University, and the Chiba Institute of Science
	Other Related Projects: not applicable
<p>1-1 Background</p> <p>Leptospirosis is one of the bacterial (spirochetal) zoonoses widely distributed in tropical and sub-tropical regions, and develops hepatic damage (causing jaundice), renal failure, hemorrhagic diathesis, etc. in human cases. The severe type of leptospirosis is known as Weil's disease usually caused by <i>Leptospira interrogans</i>. Leptospire also infects animals such as rodents, canines, bovines and swine, and cause lethal disturbance as well as miscarriage and stillbirths. According to the WHO statistics in 1999, it is estimated that the number of newly infected cases and its case fatality rate were a half million and 23%, respectively. The pathogenic <i>Leptospira</i> has over 250 serovars and currently available vaccines are serovar-specific. Accordingly, it is necessary to identify endemic serovars in order to develop effective vaccines for prevention of the disease; nevertheless, respective panel antigens are needed for identification with highly advanced techniques. In addition, leptospirosis is sometimes misdiagnosed since clinical manifestation is similar to other infectious diseases such as malaria, hepatitis, dengue hemorrhagic fever and so on.</p> <p>Under these circumstances, the Government of the Philippines requested the Government of Japan to implement the technical cooperation aiming to enhance research and development capacity for prevention and control of leptospirosis. On the basis of the request from the Government of the Philippines, JICA, under the framework of “<i>Science and Technology Research Partnership for Sustainable Development</i>” (hereinafter referred to as “<i>SATREPS</i>”) launched the five-year technical cooperation project entitled “<i>the Project for Prevention and Control of Leptospirosis in the Philippines</i>” (hereinafter referred to as “<i>the Project</i>”) in April 2010 under the implementation structure consisting of the College of Public Health, the University of the Philippines Manila (hereinafter referred to as “<i>CPH-UPM</i>”) as a counterpart research institute from the Philippine side and the Kyusyu University (hereinafter referred to as “<i>KU</i>”) and the Chiba Institute of Science (hereinafter referred to as “<i>CIS</i>”) as research institutes from the Japanese side.</p> <p>1-2 Project Overview</p> <p>(1) Project Purpose</p> <p>Research and development (R&amp;D) capacity of CPH-UPM is enhanced for prevention and control of leptospirosis through the collaborative research.</p> <p>(2) Outputs</p> <ol style="list-style-type: none"> <li>0) The Leptospirosis Prevention and Control Center is established in CPH-UPM.</li> <li>1) The situation of leptospirosis in the Philippines is estimated through epidemiological studies.</li> <li>2) Rapid methods/tools are developed for the detection of anti-<i>Leptospira</i> antibodies and leptospiral antigens.</li> </ol>	

- 3) 抗レプト Vaccines are developed to prevent leptospirosis in animals.  
 4) Advocacy activities are enhanced regarding prevention and control of leptospirosis.

(3) Input (as of the Review)

the Japanese side

Dispatch of JICA Experts: Long-term Experts: A total of 2 persons (Project Coordinator), and Short-term Experts: 56.7 Man Months (a total of 80 Experts, 1,702 Days)

Provided Equipment: Research instruments such as real-time PCR system, microscopies (dark field, inverted), micro-plate reader, etc. (Total Cost: PHP 40,143,468 (≒ JPY 82,399,035))

Training in Japan: 12 researchers (A total of 395 days/person)

Overseas Activities Costs: approx. JPY 17,300,000 (Approx. PHP 6,600,000 / USD 147,000)

Others: Costs for renovation of existing laboratories for the establishment of the LepCon Center: A total of PHP 16,522,596.26 (≒ USD 369,000)

The Philippine side

Counterparts: 26 personnel

Land and Facilities: Provision of office space and furniture

Local Cost: PHP 21,138,628 (approx. USD 471,056 / JPY 45,950,000)

2. Terminal Evaluation Team

Members	Dr. Kaname KANAI	Leader	Executive Technical Advisor to the Director General, Human Development Department, JICA
	Ms. Ayako OI	Cooperation Planning	Deputy Director, Health Team 3, Health Group 2, Human Development Department, JICA
	Dr. Yoichi INOUE	Evaluation and Analysis	Senior Consultant, Consulting Division, Japan Development Service Co., Ltd.
	Dr. Hiroshi KIDA	Infectious Disease Control	Evaluation Committee Member of JST – SATREPS / Specially Appointed Professor, Head, Hokkaido University Research Center for Zoonosis Control
	Ms. Yuko SATO	Planning and Evaluation	Assistant Program Officer, Department of International Affairs (Research Partnership for Sustainable Development Group), JST
Period of Evaluation	23 November to 10 December 2014		Study Type: Terminal Evaluation

3. Summary of Evaluation Results

3-1 Achievements

(1) Output 0

Although there was delay in the renovation work and the procurement of research equipment, the Leptospirosis Prevention and Control Center (LepCon Center) was established in January 2012. In addition to the research activities, the Center provides diagnostic services to suspected cases from hospitals of Metro Manila, and the services are expanded outside of Manila in cooperation with health facilities in provinces in nine regions. Moreover, the LepCon Center is utilized for research activities of under-graduate, graduate and post-graduate students as well as for the training of laboratory technicians from the neighboring countries.

The LepCon Center is recognized as the most significant institution for research, clinical diagnostic services and education for Leptospirosis, and is highly appreciated by the DOH and the DOST. Therefore, Output 0 has been fully achieved.

(2) Output 1

With supporting data from the past, epidemiological information on *Leptospira* in human, domestic

animals, livestock and environment was obtained and analyzed. The data is utilized not only for the analysis on burden of disease, but also for the development of diagnostic methods and vaccines and advocacy activities. The epidemiological data is contributing to patient treatment from the continuation of diagnostic services as well as surveillance of outbreak and monitoring of prevalent serovars.

According to the disease burden study, disability-adjusted life year (DALY) per 100,000 inhabitants was estimated as high as 25.76, and indicated that leptospirosis had the high burden of disease. Economic burden and factors which have correlation with antibody prevalence rate had also been identified. Moreover, the hotspots of leptospirosis were identified using an analysis of environmental factors. Based on the epidemiological research, a statistical estimation model (predictive equation) was developed for predicting the number of leptospirosis cases using the data of precipitation, relative humidity, temperature, sea level altitude and population size of selected Barangays.

These research results can be used to craft the related health policies and guide program planning for the prevention and control of leptospirosis in the Philippine. Further, the research outcomes were summarized in scientific articles and published in peer-reviewed international journals. Therefore, it can be concluded that the Output 1 have been achieved in general within the project framework.

### (3) Output 2

As of the time of the Terminal Evaluation, the Project has developed MCAT and ELISA-based method that detects leptospiral antibody in serum as well as the immunochromatography-based method that detect leptospiral antigen in urine. An ELISA-based method that detects urinary antigen demonstrated insufficient sensitivity to detect antigen that are excreted in urine infinitesimally; however, other methods are deemed to be utilized for practical use at laboratories with sufficient sensitivity and specificity. The Project has developed a testing method to detect urinary leptospiral cells quantitatively using the real-time PCR. On the other hand, through the research and experimental activities, testing skill of the existing antibody detection method of MAT has significantly improved at the LepCon Center.

As has been described, the Project has developed many detection/diagnostic methods that meet various needs in the Philippines such as clinical testing services at local laboratories with insufficient equipment, mass screening and so on. For these reasons, it is considered that the Output 2 is achieved in general at the time of the Terminal Evaluation.

### (4) Output 3

As of the time of the Terminal Evaluation, the inactivated vaccines and OE vaccines were prepared and demonstrated the increase of corresponding antibody titer after inoculating it upon experimental animal and protective capacity by challenging *leptospire*. The Project currently use low protein medium to culture *leptospire* for the development vaccines. Though this vaccine can be applicable to clinical use, however, there is a concern that it might cause allergic reaction after inoculation due to protein used in the process of *leptospire* culture. Currently, the Project is putting more efforts to improve the safety of vaccines by trying to culture *leptospire* with protein-free medium.

Under the Output 3, vaccines for animals are supposed to be developed under the framework of the project; nonetheless, the Project is aiming to develop vaccines for human in future. With an eye on the development of vaccines for human, the Project used leptospiral strains endemic in human. The Project has succeeded in preparing effective inactivated vaccines and OE vaccines in animal testing. For these reasons, the achievement level of the Output 3 is deemed to be appropriate within the framework of the Project.

### (5) Output 4

The knowledge and skills survey for health workers and distribution of posters and fans developed for the public based on the KAP survey were implemented with the research grants obtained by the Philippine side with the support of the JICA experts. The seminar for nurses to be implemented in February 2015 will likewise be supported by JICA.

The trainings for health workers and advocacy work using posters and fans are on-going, and, these activities are likely to continue beyond the project period with support from the Philippine Government. However, although improvement of knowledge of the health workers and people could be expected to a certain extent, it was not possible to evaluate the achievement level of Output 4 because implementation of aforementioned activities were limited due to external factors and the assessment of the effectiveness

of the activities had not been confirmed.

#### (6) Project Purpose

A significant volume of research outcomes were obtained through the joint research, and capacity building of researchers was achieved through the Project. The LepCon Center, a research facility set up by the Project, is fully functional and being utilized not only for the Project research, but also for diagnostic services and educational and training purposes.

Based on the achievements of the Outputs explained above and the Project Purpose below and considering the other supporting factors, it can be concluded that the Project Purpose has been achieved in general.

### 3-2 Summary of Evaluation Results

#### (1) Relevance

The relevance of the Project is highly maintained as of the time of the Terminal Evaluation

With regard to the consistency of the Project Purpose with the Philippine Health Policies as well as the needs of the target groups that were confirmed at the Ex-ante Evaluation of the Project in August 2009, there wasn't any alteration of the Philippine health policies, the needs from the target group and the Japan's Aid Policies so as to undermine the relevance of the Project, that is to say, the consistencies are being maintained at the time of the Terminal Evaluation.

In particular, the majority of patients with leptospirosis are male labor population; therefore, the disease causes substantial social and economic burden in the Philippines. The Project revealed that delay in leptospirosis diagnosis, attributed to limited medical facilities that can provide laboratory diagnosis in the Philippines, is one of the major reasons for the delayed diagnosis. Moreover, since weak water drainage system vulnerable to high precipitation frequently causes submergence and/or flood in some areas, the residents in those areas are laid open for the risk of leptospiral infection. For these reasons, the rationale of assistant approaches of the Project to conduct researches regarding advocacy activities, vaccine development and diagnostics development for its prevention, protection and early initiation of treatment is gained in order to realize effective and comprehensive measures for prevention and control of leptospirosis. Besides, it is necessary to grasp epidemiological information of leptospiral serovars in endemic areas to develop novel vaccines and diagnostics because more than 250 serovars of pathogenic *leptospire*s are recognized and endemic strains vary according to areas.

#### (2) Effectiveness

The effectiveness of the Project is considered to be high in general at the time of the Terminal Evaluation.

As of the time of the Terminal Evaluation, the Project has revealed the epidemiological picture of leptospirosis in Metro Manila, and demonstrated the protective capacity and safety of inactivated vaccines and OE vaccines in animal testing. Moreover, the Project is at a final stage of validation of testing methods as follows: an antibody detection method using endemic serovars in the Philippines (MCAT); an antibody detection method (ELISA method); as well as a urinary antigen detection method (immunochromatography method) that can detect wide range of serovars endemic in the Philippines. Detection capability of existing methods such as MAT has also significantly improved through the project research activities. For these reasons, it can be said the Project provides options of diagnostics with high sensitivity and specificity that meet the various needs and situations in the Philippines. Though the achievement level of Output 4 could not be evaluated since several activities are still on-going, the Project publishes many research articles in international journals with regard not only to project-related research outcomes but also to other scientifically-important findings and evidences as of the time of the Terminal Evaluation. Therefore, it is considered that the Project has generally attained its objectives in terms of research outcomes within a framework of the Project.

Meanwhile, the LepCon center was established in the CPH-UPM with support of the Project, and a lot of novel research technologies have been transferred to CPH-UPM through collaborative research activities, and necessary research instrument have been installed and utilized. For these reasons, certain improvements not only in research outcomes but also human resource/organizational development have

been manifested through the implementation of the Project.

### (3) Efficiency

The Project has progressed efficiently to a maximum extent throughout the project period.

Monitoring activities for the whole project matters have been conducted at the JCC. Science-oriented matters such as progress of research activities and generation of research outcomes have been monitored regularly and through the Scientific Symposia. Moreover, the Japanese Chief Advisor visited research institutes in the Philippines at approx. three months interval and had discussions and consultations closely with the Philippine Project Manager, leaders of research groups, JICA experts in the Philippines. In addition to that, direction and monitoring of the Project have been continued on a regular basis via e-mail and so on.

All the instruments and equipment introduced under the support of the Project have been used effectively for the implementation of the research activities. On top of this, other research groups are also allowed to use research instruments, equipment and facilities under the strict supervision by the Philippine researchers. The LepCon Center has been used for researches and/or special studies of graduate and under-graduate students as well. For these reasons, facilities, research instrument, equipment and other materials provided under the support of the Project have contributed not only to project research activities but also to capacity development of young researchers and students. In addition, novel technologies and knowledge obtained at the Training in Japan were effectively utilized for the research activities of the Project, and even shared to other researchers and scientists proactively.

### (4) Impact

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

Several basic technologies for the novel diagnostics are likely to be developed during the project period. The novel diagnostics each have unique characteristics, which determines the applicable situation. However, in order for those novel diagnostics to be applied for clinical practices, it requires registration and/or commercialization as diagnostic test kits. On the other hand, the Project has attempted to develop inactivated vaccines, OE vaccines and DNA vaccines. At the time of the Terminal Evaluation, protection capacity against homologous leptospire challenge was confirmed with inactivated vaccines and OE vaccines by animal experiment. With this, it can be evaluated that the Project had achieved the intended research outcomes for the development of vaccines within the project framework, however, requires further enhancement of the research for the practical application for clinical use in the future. In the Philippines, novel diagnostics are recognized by the DOH and pharmaceutical products including vaccines is registered with Food and Drugs Administration. It is desirable that by the end of the project period, the requirement for the registration process such as clinical performance test shall be confirmed and relevant government institutes are consulted on it.

In addition to the above, the Project has studied the disease burden of leptospirosis in Metro Manila taking into account the epidemiology data. The results of the knowledge survey of the health workers, subsequent trainings and the advocacy work using the IEC materials will be confirmed after the time of the Terminal Evaluation. The Project expects that these results be reflected in the policy and program of leptospirosis control by the DOH in future. It is desirable that the consultation with DOH on this matter is considered by the end of the project period and even after.

### (5) Sustainability

Self-sustainability as well as self-deployment of the benefits provided by the Project can be fairly expected as of the time of the Terminal Evaluation.

As was described at “*Relevance*” section, prevention and control of leptospirosis is regarded as one of the important program for infectious diseases from the perspectives of health as well as science and technology policies. Moreover, severe typhoon damage since 2009 had triggered outbreaks of leptospirosis. These incidences, unfortunately, promoted the importance of prevention and control of leptospirosis further. For this reason, political sustainability is anticipated after the end of the project period. Having said that, the DOH will be the responsible entity for the implementation of disease control using the research outcomes. Therefore, it is desirable for the Project to consult with the DOST

and the DOH on the future direction of the researches before the end of the project period.

The CPH-UPM had secured funds provided from the PCHRD-DOST for the research activities, which had greatly contributed to the financial sustainability of the Project. Given that there are research grants already secured for new research topics beyond the project framework, financial sustainability can be expected at great extent. Meanwhile, it should be noted that the operation and maintenance costs of the LepCon Center is covered by the Project and the overhead cost of the research grants. Thus, it is desirable for the CPH-UPM to secure fixed budget for its operation and maintenance costs, given that the LepCon Center is an important asset of the CPH-UPM.

The enhancement of research competency of Philippine counterparts, the Project Purpose, has been consistently and consciously implemented in the Project. Through on-site training in the Philippines by JICA experts and also the Training in Japan, acquisition of the technical skills for epidemiological researches and the development of inactivated vaccines have satisfactorily advanced enough to organize the research activities by themselves. However, transfer of the core technology for the development of novel diagnostic method is on-going, and it is likely that it would take some time for the Philippine researchers to be able to develop the methods independently. Therefore, the Project is expected to have an internal discussion on the concrete ways and timeframe to complete such technical transfer within the project period to the extent possible.

### 3-3 Factors that promoted the attainment of the Project

#### (1) Concerning the project design

No specific factor that promoted the attainment of the Project was observed from the aspect of project designing.

#### (2) Concerning the implementation process of the Project

Both Philippine and Japanese research institutes have been working together with mutual respect and prestige under the equal partnership. This has enabled the Project to progress their research works smoothly, resulting in the good achievement of the Project Purpose.

### 3-4 Factors that impeded the attainment of the Project

#### (1) Concerning the project design

Full operation of research activities was delayed for several months at the initial phase of the Project since it took longer-than-expected time to procure and install research instruments and related equipment. Further, renovation of laboratory facility was delayed for approx. six months.

#### (2) Concerning the implementation process of the Project

Research subjects or a part of them, led by the CPH-UPM, are conducted using research grants obtained by their self-reliant efforts. However, some research activities could not be commenced as scheduled because it took longer-than-expected time for some research proposals to be approved.

### 3-5 Conclusions

Based on the strong ownership of the Philippines side and the excellent cooperation between CPH-UPM and the Japanese researchers, the intended Outputs were mostly achieved and the Project Purpose is likely to be achieved by the end of the project period. Based on the five evaluation criteria, Relevance, Effectiveness, Efficiency and Sustainability of the Project were all assessed high in general and the positive Impact is highly expected for the prevention and control of leptospirosis in future.

In addition to the research outcomes originally planned, the Project was able to obtain multiple research findings of scientific value, and they have been published in peer-reviewed international journals. As for the utilization of research outcomes, discussion has been initiated between the Project and a private company for the development of diagnostic “kit”. Moreover, it is assessed that the capacity of Philippine researchers had been enhanced owing to the assistance of Japanese researchers with passion and commitment. The LepCon Center, a research facility set up under the support of the Project, is fully functional, and is serving researchers of other research groups and post-graduates for their research and capacity building.

Another significant aspect of this project is that from the beginning of the project period, CPH-UPM had secured research grants from external institutions for their part of research activities. There were

sometimes delays due to the approval process; however, it had developed a foundation for the LepCon Center to be self-reliant and sustainable beyond the SATREPS project period. The cooperation established between the CPH-UPM and other institutions such as the DOH, the DOST, health facilities and the LGUs is also a positive indication that the research can be sustained and expanded.

### 3-6 Recommendations

#### 1. Maintaining the functions of the LepCon Center

- 1) For the long-term and sound management of the LepCon Center, the Team recommends the CPH-UPM to continue internal and external discussion with relevant institutions such as the DOH for securing the operation and maintenance costs. For example, support of leptospirosis surveillance by the DOH, the utilization of tuition fees with the UPM, conducting training courses for health human resources, and charging for the diagnostic services, which is currently done for free. It should be noted that due attention should be paid for any actions taken not to hinder the health seeking behavior of the patients.
- 2) Currently, research assistants employed using the research grants play a significant role in the actual operations of the LepCon Center in terms of research operation and laboratory management. In order to sustain the technical level and function of the Center, it is desirable for the CPH-UPM to start discussions amongst stakeholders of the Center about practical measures for it, such as considering the continued employment of research assistants, technical transfer to permanent staff and so on.

#### 2. Consolidation of technical transfer

The techniques acquired through leptospirosis researches and the research instruments and equipment provided have versatility and are applicable to other researches and education of microbiology. With the aim to further enhance the research capacity of the CPH-UPM, the Project is expected to make an effort to the extent possible for the consolidation of research techniques until the end of the project period.

#### 3. Practical application of research outcomes and achievements

- 1) In order for the diagnostic methods developed by the Project such as MCAT, ELISA and immunochromatography method to be recognized and/or registered and commercialized product(s), the CPH-UPM is requested to start discussing the necessary procedures with the relevant department of the DOH.
- 2) Given the urgent need for the rapid diagnostic kit, the Project is expected to promote discussions with pharmaceutical and/or medical device enterprise(s) interested in developing a diagnostic kit using the immunochromatography-based urinary antigen detection method.
- 3) For the development of vaccines for livestock, and for humans as the ultimate goal of the research, it is desirable for the Project to develop a mid/long-term strategic plan aiming for the practical application of vaccines for clinical use.

#### 4. Expansion of target areas for the epidemiology study

The target areas for the research on burden of disease and advocacy conducted under the Project is the Metro Manila. However, given the different situations of urban and rural settings, it is expected for the CPH-UPM to expand the target area and to conduct the research in rural areas.

#### 5. Consultation with relevant government institutes

By the end of the project period and even after, the Project is advised to continue consultation with the DOST and the DOH on the direction of future research in order to secure technical and financial assistance and the utilization of research outputs for the disease control measures.

#### 6. Publicity of research outputs

Those involved in the Project are expected to publicize the research outcomes and achievements acquired through media, seminars, etc. during the remaining project period and beyond.

### 3-7 Lessons Learnt

1. From the beginning of the Project, there was a positive relationship between the Philippines and the Japanese researchers to conduct a joint research. This was because one of the Japanese researchers had been involved in research on Leptospirosis with the CPH-UPM from the 1980s and KU and CIS had been conducting joint research with CPH-UPM since 2006. It was observed that smooth implementation of research activities was due to the mutual understanding among researchers which was generated over the years. Moreover, one of the Philippine researchers who joined the research lab of the Japanese Chief Adviser supported efficient communication between the Philippines and Japanese researchers. When implementing a research project, it is crucial to have or to establish a certain level of mutual understanding and relationship between the Japanese and counterpart researchers.
2. Lepcon Center, including necessary equipment, was established at the outset of the Project as a research lab for epidemiology study and development of diagnostic methods and vaccines. When the Lepcon Center was established, a regular meeting to discuss operation and maintenance issues was organized with the initiative of the Philippines researchers. In these regular meetings, any issues on the facility or the equipment were raised and immediately dealt with using budget of CPH-UPM. As a result, the Lepcon Center has been maintained well, and is continuously utilized by the researchers, students and for training programs. The Lepcon Center is highly likely to be maintained by the Philippines researchers after the Project. When establishing research facilities and procuring equipment under the Project, setting the rules and routines for operation and maintenance by the counterpart at the beginning, and not at the end of the Project, is the key to sustainable management.
3. In addition to the SATREPS budget, CPH-UPM has obtained research grants from PCHRD-DOST, and allocated the funds for research activities and operation and maintenance of Lepcon Center. CPH-UPM also received research grants for research projects outside of SATREPS Project. Such effort by CPH-UPM not only secured enough budget for the Project activities, but it also enhanced the autonomy and sustainability of CPH-UPM. In order to increase capacity and sustainability of the counterpart, it is suggested to promote the counterpart to apply and obtain research grants outside of SATREPS.
4. The Project was able to obtain intended research outcomes for the development of rapid diagnostic methods and vaccines for animals. However, SATREPS is a scheme which requires practical application of research outcomes. In order to fulfill this, it was desirable that the Project had activities on promoting practical application of research outcomes such as developing plans, starting approval processes and consultation with private entities. If such activities were included in the Project framework, it will push forward the practical application of research outcomes beyond the Project period.