

## Evaluation Summary

1. Outline of the Project		
Country: the Socialist Republic of Viet Nam		Project Title: the Project for Determine the Outbreak Mechanisms and Development of a Surveillance Model for Multi-Drug Resistant Bacteria
Issue/Sector: Healthcare and medical treatment		Cooperation Scheme: Technical Cooperation Project (Science and Technology Research Partnership for Sustainable Development: SATREPS)
Division in charge: Health Division 2, Health Team 3, Human Development Department		Total Cost: 350 million JPY (as of the Evaluation)
Period of Cooperation	(R/D): 11/March/2012-10/March/2017	Partner Country's Implementing Organization: the National Institute of Nutrition (NIN); the Institute of Public Health (IPH); Thai Binh University of Medicine and Pharmacy (TBUMP); Can Tho University (CTU); Pasteur Institute Nha Trang (PINT); and Binh Dien Wholesale Market Company (BDWMC).
		Supporting Organization in Japan: the Global Collaboration Center, the Graduate School of Pharmaceutical Sciences of Osaka University; the Osaka Prefectural Institute of Public Health; Osaka Prefecture University; University of the Ryukyus
		Other Related Projects:
1-1 Background		
<p>In recent years, the emergence of multi-drug resistant bacteria, under the backdrop of antibiotic misuse in the fields of healthcare as well as livestock and fishery industries, is a global concern over the outbreak of refractory communicable diseases. Since the bacteria can be spread beyond national boundaries by globalized transfer of humans and products, global-scale countermeasures should be taken for preventing the emergence and spread of antimicrobial-resistant (AMR) bacteria. A previous study in the Socialist Republic of Vietnam (herein after referred to as ‘<i>Vietnam</i>’) showed that Expanded-Spectrum Beta-Lactamase (ESBL)-producing <i>Escherichia coli</i> (<i>E. coli</i>) was isolated from 33% of fecal samples in rural areas of the Red River Delta region. Another study also reported that 42% of healthy Vietnamese was estimated to be carriers of ESBL-producing bacteria. Thus, Vietnam has higher prevalence and spread of ESBL-producing bacteria than that in other countries, and it is concerned that the situation will further be serious. Though ESBL-producing <i>E. coli</i> is not pathogenic under normal conditions, the chemotherapy for infectious diseases will get severe damages given that genetic characteristics were transferred to pathogenic bacteria; thus, this can be regarded as an emerging global threat. For these reasons, it is an urgent need to grasp the actual situation of the spread of AMR bacteria in Vietnam and to conduct researches that contributes to the containment of it.</p> <p>On the basis of the request from the Government of Vietnam to the Government of Japan, JICA has implemented a technical cooperation entitled “<i>the Project for Determine the Outbreak Mechanisms and</i></p>		

*Development of a Surveillance Model for Multi-Drug Resistant Bacteria*” (hereinafter referred to as “*the Project*”) for five years from March 2011 under the scheme of the Science and Technology Research Partnership for Sustainable Development (SATREPS), under the implementing framework as aforementioned above.

With the project closure approaching in March 2017, JICA dispatched the Terminal Evaluation Mission to evaluate the Project by the “*Five Evaluation Criteria*” (*Relevance, Effectiveness, Efficiency, Impact and Sustainability*) based on their performances, progress of the project activities and implementation process of the Project as a joint evaluation with the Vietnamese side. On the basis of the evaluation results, a joint terminal evaluation team consisting of Vietnamese and Japanese members (hereinafter referred to as “*the Team*”) provided recommendations to relevant parties on the project activities to secure fulfillments of the Outputs and the Project Purpose as well as better sustainability of the benefits derived from the Project.

## 1-2 Project Overview

The Project aims to implement collaborative researches that contribute to the elucidation of outbreak mechanisms of multi-drug resistant bacteria and its surveillance and to enhance the research capacity of Vietnamese research institutes.

### (1) Project Purpose

Research capacity to continuously monitor the multi-drug resistant bacteria is strengthened.

### (2) Outputs

- 1) The wide spread mechanisms of multi-drug resistant bacteria in Vietnam are clarified microbiologically, pharmacologically and anthropologically.
- 2) A comprehensive monitoring system for antibiotics residue and antibiotic-resistant bacteria over the process from food production to intake is developed.
- 3) Researchers and technical staff related to food safety monitoring at the targeted research institutes are trained.

### (3) Input (as of the Evaluation)

#### The Japanese Side

Dispatch of JICA Experts: Long-term Experts: 1 person (Project Coordinator), Short-term Experts: a total of 288 persons)

Provided Equipment: Ion Personal Genome Machine (PGM™) Sequencer, Real-time PCR System, High Speed Refrigerated Micro Centrifuge, High-speed Micro Centrifuge, Bioanalyzer, Automated Microbial Identification System, Clean Bench, etc.

Local Cost: approx. JPY72,854,000 (≒ USD 660,310)

Training in Japan: a total of 35 persons (149.4 M/M)

#### The Vietnamese Side

Counterparts: 27 persons (NIN: 6 persons, TBUMP: 5 persons, PINT: 5 persons, IPH: 4 persons, CTU: 3 persons, BDWMC: 4 persons)

Land and Facilities: Office space in NIN, IPH, TBUMP, CTU, PINT

Local Cost: approx. JPY 13,778,000 (≒ USD 113,109)

2. Terminal Evaluation Team			
Members	Dr. Kaname KANAI	Leader	Executive Technical Advisor to the Director General, Human Development Department, JICA
	Ms. Sangnim LEE	Cooperation Planning	Health Advisor, Health Team 3 & 4, Health Group 2, Human Development Department, JICA
	Dr. Yoichi INOUE	Evaluation and Analysis	Senior Consultant, Consulting Division, Japan Development Service Co., Ltd.
	Prof. Dr. Haruo WATANABE	Infectious Diseases Control Research	Program Officer, International Collaborative Research Program, Department of International Affairs, the Japan Agency for Medical Research and Development (AMED) Professor, the Graduate School of the International University of Health and Welfare
	Ms. Keiko SAITO	Planning and Evaluation	Deputy Manager, Division of International Collaboration, Department of International Affairs, AMED
Vietnamese members	Dr. Tran Viet Nga	Deputy Director, the Vietnam Food Administration, MOH	
	Dr. Le Danh Tuyen	Director, NIN, Ministry of Health	
Period of Evaluation	14/Aug/2016 - 27/Aug/2016		Study Type: Terminal Evaluation
3. Summary of Evaluation Results			
3-1 Achievements			
(1) Output 1			
<p>The Project demonstrated the actual situation of the spread of AMR bacteria especially for ESBL-producing bacteria in Vietnam through the collaborative research. It is notable that the Project firstly revealed the prevalence of ESBL-producing <i>E. coli</i> in general inhabitants, the actual status of antibiotics usage for human and animals as well as the contamination of antibiotics residues in food products.</p> <p>The Project also gained the findings, which can explain the possible mechanisms of the spread of antibiotics resistance characteristics such as plasmid-mediated horizontal transmission of the drug resistance gene, recombination of particular drug-resistance gene to resident microbiota and/or its chromosome. Further, the Project obtained findings with regard to the mechanisms of the induction of multi-drug resistance as well as dose-dependent prolongation of colonization period of ESBL-producing <i>E. coli</i> using project-developed carrier model mice.</p> <p>Meanwhile, the Project observed the possibility that the public health interventions might contribute to the reduction of the prevalence of ESBL-producing <i>E. coli</i> in community inhabitants; nevertheless, it seemed that continuous and detailed research will be required to determine the causal relationship between the intervention and the reduction.</p>			
(2) Output 2			
The Project has developed an inspection manual for isolating and subsequent characteristic analysis in			

conformity with the International Organization for Standardization (ISO) standards jointly with the Vietnamese and Japanese research institutes in 2013. The Project also developed an operational method with reporting forms, information items for database and so on. The Project commenced monitoring operation for ESBL-producing bacteria and residual antimicrobials in accordance with the manual in June 2014, and updated the manual in 2015. The monitoring activities have been continued on the basis of the unified manual at the initiative of the three national institutes (i.e. NIN, PINT and IPH) as of the time of the Terminal Evaluation.

The Project identified the major antibiotic residues in each food item as follows: Sulfamethazine for pork; Quinolones for shrimp and fish; and Tilmicosin, Sulfaclozine and Enrofloxacin for poultry. Therefore, the Project started internal discussions regarding the possibility of expansion of target antibiotics on the basis of the said findings in the Joint Coordinating Committee (JCC) meeting held in May 2016.

### (3) Output 3

For the purpose of capacity building about Vietnamese researchers and technicians with an eye on the achievement of the Super Goal, the Project organized a long-term training (5 persons in Ph.D. courses in Japanese universities) and short-term training courses (a total of 32 participants in 13 courses. Trainees were also provided training opportunities such as participating lecture seminars and workshops in Japan. In Vietnam, the Project has continued technical training and workshops (a total of 159 participants in 8 courses), Scientific Meetings geared to Vietnamese researchers and technicians. Notably, the training courses held in Vietnam were budgeted by the Vietnamese side with the financial support of the Ministry of Health (MOH).

In particular, the research in the field of AMR basics as well as the establishment of monitoring system was rather new in the Vietnamese research institutes; therefore, it is considered that the establishment of research base for AMR and/or food safety is significant achievements under the Output 3 through the collaborative research as well as the above-mentioned training courses and workshops. Those who participated in the Project are supposed to lead the research in the field of AMR and/or food safety in Vietnam in future.

### (4) Project Purpose

As described in “the Achievement of Outputs”, the Project gained many research findings and published a total of 18 research articles in international journals as of the time of the Terminal Evaluation. Eight (8) out of 18 articles were authored by Vietnamese researchers, implying that the capacity enhancement of Vietnamese researchers and functional improvement of Vietnamese research institutes.

Meanwhile, the Project is supposed to propose policy recommendations for better AMR control in Vietnam, in particular, evidences and practical measures for the practical implementation of “*the National Action Plan to Combat with AMR 2013-2020*” (NAP-AMR) through the Comprehensive Report. As of the time of the Terminal Evaluation, the Project works on the finalization of the Report with the guidance of stakeholders such as the VFA of the MOH.

For these reasons, it is deemed that the Project Purpose is generally achieved as of the time of the Terminal Evaluation as the Vietnamese project members had enhanced their research capability as expected to continue the monitoring of AMR in Vietnam through the Project.

### 3-2 Summary of Evaluation Results

#### (1) Relevance

The relevance of the Project is further enhanced at the time of the Terminal Evaluation in comparison with that at the time of the commencement of the Project.

The government of Vietnam has long been putting the emphasis on infectious disease control as well as food hygiene. The MOH, in advance of the publication of “*Antimicrobial Resistance Global Report on Surveillance*”, prescribing a policy package to combat AMR, by the World Health Organization (WHO) in February 2014 has officially announced a “*Decision to approve the National Action Plan on Antimicrobial Resistance in the Period from 2013 to 2020*” (No. 2174/QD-BYT) in June 2013 right after the commencement of the Project. This national plan describes the actions and roadmap for strengthening and improving national surveillance system on drugs and AMR bacteria, such as the development of testing protocol with forms and norms, the determination of operational method, the enhancement of function/capacity of research institute and human resource and so on. Further, since the AMR is obviously regarded as a multi-sectoral issue, all the stakeholders engaged in the combat of AMR in Vietnam are supposed to take “*One Health*” approach. In June 2015, multi-stakeholders of AMR such as the MOH, the MARD, the Ministry of Industry and Trade, the Ministry of Natural Resources and Environment and development partners in Vietnam signed on the Aide Memoire of “*Multi-Stakeholder Engagement to Combat Antimicrobial Resistance in Vietnam*”. This document prescribes the roles and activities, which are supposed to be borne by each stakeholder.

The Project aims to generate research outcomes (evidences), which contribute to the AMR control in Vietnam through the joint effort of Vietnamese and Japanese research institutes, at the same time, to enhance the capacity of researchers and research function of Vietnamese counterpart organizations from the viewpoint of technical cooperation under the framework of SATREPS. Therefore, it is considered that the Project Purpose and/or the Outputs stipulated in the PDM meet the needs of Vietnam as well as international demands (incl. Japan) directly or indirectly.

#### (2) Effectiveness

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

The project research, especially after the mid-term of the project period, the project research activities were accelerated, and a lot of findings and/or research outcomes were obtained in the fields of microbiology, pharmaceutical sciences, anthropology, or its combination. These achievements include publications in international journals and presentations at international and domestic conferences. Specifically, a total of 18 research articles have been published in peer-reviewed international journals, 8 out of which were authored by Vietnamese researchers, implying that Vietnamese researchers or Vietnamese counterpart organizations have enhanced their capability of AMR research.

Besides, it is notable that one of the strong points of the Project can be a cross-cutting approach for AMR research, covering from the basic and epidemiological research in microbiology and pharmaceutical sciences, the pragmatic research in pharmaceutical sciences and anthropology for food safety and community awareness raising, respectively. Furthermore, it can be of great importance that the Project

firstly revealed that the actual status of AMR such as the prevalence of ESBL-producing *E. coli* in healthy residents, the actual status of antibiotics usage for both human and animals (i.e. livestock, fishery products, etc.) the actual situation of antibiotics residues in foods, etc. in Vietnam. On top of these achievements, through the implementation of the Project, research environment, implementation system of collaborative research and basic technologies for the implementation of AMR research in the Vietnamese counterpart organizations; in parallel, Vietnamese young researchers raise their research capability through domestic and international training opportunities. For these reasons, it is deemed that the Project Purpose was achieved in general both from the viewpoint of sciences and technical cooperation.

### (3) Efficiency

The Project has been operated efficiently to a maximum extent though some internal issues had affected the smooth operational management in the first half of the project period.

As has been described, the Project had spent certain amount of time and efforts to liaison and coordination as well as common understanding of the Project at the beginning of the project period. From the viewpoint of the effective utilization of time resources, these incidents hindered the efficiency of the Project to an extent. However, the project activities were accelerated owing to the efforts of the JICA and JST/AMED as JCC member organizations for intercession and coordination, and consequent unification of understanding regarding challenges and measures for better collaborative research amongst all the stakeholders of the project at the time of the Mid-term Review. Particularly, under the careful and detailed liaison and coordination organized by Project Management Unit such as detailed planning of Japanese researchers' visits to Vietnamese institute as well as the implementation of meetings and research activities, the progress management of the Project was improved and successfully continued with the same view of the goal to compile the research findings and outcomes into the Comprehensive Report.

Concerning the collaboration with external resources, from the perspectives of confidentiality of research information as well as intellectual properties under the research project, active collaboration with external resources has been discouraged contrary to usual technical cooperation projects. For this reason, the Project has no record to work with external resources as a collaborative research. However, in the process of finalization of the Comprehensive Report, the Project has started preliminary discussions with major envisaged users of the report of the MOH and the MARD. It is anticipated that more detailed and pragmatic discussions will be proceeded for the evidence (research outcomes)-based policy planning in a multi-sector manner through the 9 working groups responsible for the implementation of the NAP-AMR at the initiative of the Medical Service Administration (MSA) of the MOH.

### (4) Impact

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

The Project revealed that the prevalence of the community residents with ESBL-producing *E. coli*, the actual situation of antibiotics usage for human and animals (livestock and fisheries), and consequent contamination of ESBL-producing *E. coli* and antibiotics residues in foods through the collaborative research; indeed, these findings are very useful for AMR control in Vietnam in future. In addition, the Project developed the monitoring procedures for ESBL-producing *E. coli* and Ampicillin (an antibiotic

residue) as well as gained several findings regarding the effects of public health interventions on the reduction of the prevalence of community healthy residents with ESBL-producing *E. coli*. The Project is supposed to have pragmatic discussions with ministries engaged in AMR control in Vietnam regarding the development of policies and countermeasures on the basis of the Comprehensive Report, compiled from the research findings and outcomes of the Project; therefore, it is deemed that the Project will contribute to the achievement of the Super Goal of the prevention of the spread of multi-drug resistant bacteria in Vietnam in future.

Meanwhile, the positive impacts derived from the Project are as follows: 1) Effect of public health intervention with population approach on the prevalence of healthy residents carrying ESBL-producing *E. coli*; 2) Development of the mouse model as experimental carrier; 3) Construction of a research network amongst Vietnamese research institutes; 4) Discovery of novel vancomycin-resistant enterococcus (*Enterococcus saigonensis*); 5) Actual situation of Colistin abuse for livestock; and 6) Improvement of food quality control at BDWMC.

#### (5) Sustainability

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

Political and Institutional Aspect: Political importance of food safety management in the framework of infectious disease control in Vietnam are maintained or even strengthened, and it is assumed to be continued even after the end of the Project. Practical application of the research results is highly expected in SATREPS. This project has produced the considerable number of research outcomes that could contribute to the national response to AMR. The Project is also expected to have proactive discussion with these related ministries on the feasible application of recommendations in the comprehensive report into the AMR response in Vietnam.

Financial Aspect: Financial sustainability would be ensured if the monitoring systems developed by the project are integrated into the existing monitoring system or applied as a part of public system in Vietnam. The project is required to have consultation with related ministries and propose specific budget information of operating the developed monitoring models so that related ministries consider future budget allocation. On the other hand, it would be efficient investment to Vietnam ministries if they provide financial support for further researches as much as possible to the research institutes that have already built capacities throughout this Project.

Technical Aspect: The project implementing institutions of the Vietnamese side have acquired the skills of AMR research and the research environment including laboratories was well equipped through this project. In addition to the area of AMR research, they gained a range of knowledge and skills of other research such as public health, epidemiology and biosafety, that are helpful to strength general research capacity, through both training in Vietnam and training (short term, long-term) in Japan. SOP of the established protocols in each institute was developed. Therefore, sustainability from technical aspect can be expected to some extent.

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

#### (1) Concerning the project design

No major promoting factor has been observed as far as the project plan is concerned.

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

The Project encountered a difficult situation regarding project management, to be more precise, coordination and unified understanding amongst players of the Project, at the initial phase of the project period. On the basis of the request from the Vietnamese side, JICA and JST, as JCC member organizations, jointly ventured to resolve the situation, and as a result, the project management has improved significantly at the initiative of newly-established Project Management Unit. This countermeasure, taken by the JCC members in right time and right way, contributed to the improvement of project management.

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

#### (1) Concerning the project design

No major obstacles have been observed as far as the project plan is concerned.

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

Since the delays of the project approval and some other operational and managerial issues negatively affected smooth implementation of the project research activities, it is recognized as hindering factors against efficiency and the effectiveness of the Project.

### 3-5 Conclusions

Research capacity on AMR in Vietnam was considerably strengthened through the Project. This Vietnam and Japan collaboration research project produced numbers of evidences and findings that contribute to the further development of evidence-based policies in Vietnam. Therefore, this project reaches almost success.

The delay in partial research activities at the early stage of the project period affected efficiency of the project implementation as hindering factors. However, the relevance of the Project is further enhanced due to the increased importance of AMR response in the global level. The effectiveness of the Project is considered to be high in general, and sustainability can be expected because of confirmed research outcomes so far. Positive impact on the prevention of AMR spread can be expected through this project. As one of impact found, the Project discovered a novel strain of *Enterococcus* with vancomycin-resistance characteristics from the food samples, and named *Enterococcus saigonensis*.

### 3-6 Recommendations

#### (1) The Comprehensive Report of the Project

##### For the project team

To continue making efforts in developing and completing the comprehensive report so that this report contributes to the implementation and further improvement of the existing NAP-AMR of Vietnam.

##### 1) For final edition

- To accelerate the discussion about the comprehensive report with related ministries (1. MOH



departments including VFA and MSA, 2. MARD departments including the NAFIQAD, the Department of Animal Health and the Department of Cooperatives and Rural Development, and so on).

- To reflect synthesized findings gained from microbiological, pharmacological and anthropological researches in the comprehensive report.
- To describe the information of resources (personnel, material, costs and so on) which is necessary to implement the developed models such as food monitoring and community intervention.

2) For utilization

- To have timely and intensive discussion with the related ministries in order to incorporate the scientific evidences achieved by the project team into the policy making for the AMR control. Considering that national response to AMR requires multi-sectoral collaboration in any country, strength of collaboration between the related ministries is important from perspectives of food safety in Vietnam.
- To accelerate the provision of information on the scientific evidences of AMR prevalence and the developed monitoring system of AMR bacteria and antibiotics residues in foods, and to exchange opinions for the use of the information with related working groups of NAP-AMR.

(2) The monitoring system of AMR bacteria and antibiotics residues in foods developed by the Project  
For the project team

- From the perspective of risk management to the AMR-bacterial spread, continuous monitoring of antibiotics residues and AMR bacteria including ESBL-producing *E. coli* in food products is crucial, in addition to the monitoring on AMR of human and livestock. The mission recommends the Project team to have consultation with the related ministries about necessary resources (e.g. budgets) to sustain and improve the monitoring model.

(3) Community intervention

For the project team

- To complete community intervention through population approach that is feasible, appropriate and sustainable in the context of Vietnam by utilizing the project results.

For related ministries (e.g. MOH, MARD, MST, MOIT, MONRE)

- To support the further study of community intervention through population approach in order to obtain the solid and confirmative evidences, because the community intervention is probably effective for the reduction of the prevalence of ESBL-producing *E. coli* in the community.

(4) Control of antibiotics use

For the related ministries

- The project research revealed that at least one antibiotic residue was detected in approx. 12% of foods (meats and fisheries products) investigated and approx. 4% (ranging from 1.6% to 9.1%) of which exceeded the maximum residues level stipulated in the Vietnamese standards. Simultaneously, approximately 60 % of Vietnamese healthy residents carried ESBL-producing *E. coli*. These results imply inappropriate use of antibiotics to human, animals and fishes.

Therefore, in order to reduce the selective pressure of antibiotics residues on AMR, continuing national level-dialogue among related ministries is expected for further development of multi-sectoral collaboration on antibiotics control and the monitoring system.

- The investigation of the Project revealed that the use of Colistin is used very frequently for livestock. It is known that the abuse of Colistin is of great risk for the emergence of superbugs. The Project has just identified Colistin resistance gene-carrying *E. coli* from both human and food samples collected in Vietnam; thus, prompt actions should be taken by the ministries engaged in AMR control to prevent the emergence and spread of Colistin resistance gene.

#### (5) Human resource development

##### For the related ministries

- To further support the capacity development for human resources and research activities in institutes of Vietnam in order to keep the developed research network on AMR, as the project created a unique research network among Vietnamese national institutes, universities and private sector, and produced good results useful for the development of the NAP-AMR in Vietnam.

#### 3-7 Lessons Learnt

A liaison and coordination system should be strictly established at the time of project designing or very early stage of the project in case that many stakeholders such as research institutes, universities and ministries/authorities are involved in a project.

#### 3-8 Follow-up

AMED's plan from the perspective of research needs to follow-up.