

Evaluation Summary

1. Outline of the Project	
Country: The Socialist Republic of Viet Nam	Project Title : The Project for Strengthening Capacity For Measles Vaccine Production in Viet Nam
Issue/Sector: Healthcare and medical treatment	Cooperation Scheme : Technical Cooperation Project
Division in charge: Health Human Resources Division, Health Human Resources and Infectious Disease Control Group, Human Development Department, JICA	Total Cost : 430 JPY
Period of Cooperation	March 24, 2006 – March 23, 2010
	Partner Country's Implementing Organization: Center for Research and Production of Vaccines and Biologicals (POLYVAC)
	Supporting Organization in Japan: The Kitasato Institute, Research Center for Biologicals
	Other Related Projects: Japan's Grant Aid "The Project for the Construction of the Facilities for Measles Vaccine Production"
1-1 Background of the Project	
<p>The Vietnamese government has implemented the Expanded Program for Immunization since 1981 as effective measures to decrease infant mortality rate and to control infectious diseases. The government has promoted domestic production of EPI vaccines and resulted in producing domestically EPI vaccines other than measles vaccine(MV).</p> <p>Morbidity rate of measles is high especially for children and measles is one of the major causes of child death. Even though the measles vaccination cover rate has been kept as high as 90 %, the number of cases has shown an increasing trend since 1997 and reached 19,000 in 2000. The Vietnamese government has started provision of two doses of measles vaccine per child according to the WHO/WPRO's strategy. Therefore, it is estimated that the domestic demand for the vaccine will increase. On the other hand, international vaccine manufacturers have tended to shift from measles vaccine production to more profitable vaccines production, so there is a concern on stable supply of reasonable measles vaccine. Under these circumstances, domestic production of measles vaccine to secure stable supply is also an important issue for reducing prospective financial burden of the Ministry of Health.</p> <p>The Vietnamese government requested to the Japanese Government for grant assistance on measles vaccine production facility and technical cooperation to produce measles vaccine, which complies with WHO-GMP standard. In response to this, the Japanese Government made decision on construction of measles vaccine production facility as a part of POLIOVAC (currently POLYVAC) by grant aid and on technical cooperation project for strengthening capacity for measles vaccine production (hereinafter referred to as "the Project").</p> <p>The facility had been constructed since September 2004 and completed March 2006. In parallel with this, the Project has started for the purpose of making POLYVAC to be capable of producing measles vaccine complying with Vietnam-GMP, which has met WHO-GMP standard since 24 March 2006 for four years.</p>	

With the support by the Kitasato Institute technical transfer has been in place since July 2006.

This Terminal Evaluation aims to review the progress of the Project, identify its outstanding challenges and confirm the direction and plan of activities after the termination of the Project.

1-2 Project Overview

(1) Overall Goal

Measles Infection Rate in the Socialist Republic of Viet Nam will be decreased from the current level.

(2) Project Purpose

POLYVAC will be capable to produce necessary amount of measles vaccine for use of measles control activities in the Socialist Republic of Viet Nam complying with Viet Nam-GMP, which has met WHO-GMP standard.

(3) Outputs

- ① Staff of POLYVAC acquires appropriate technical skill to produce quality measles vaccine.
- ② Production and quality management meet Vietnam-GMP, which has met WHO-GMP standard.

(4) Input (as of the evaluation)

① Japanese Side

Dispatch of Experts	146 M/M(man/month), 204 times (Estimated numbers as of the end of the Project)
Provided Equipment	35,000 thousands JPY
Training in Japan	12 personnel (including 6 trainee dispatched by Vietnamese Budget)
Local Cost	27,557 thousands JPY (Estimated as of the end of the Project)

② Vietnamese Side

Counterparts	68 POLYVAC staff members
Equipment and Materials	Testing equipment, Equipment for MV manufacturing
Land and Facilities	Measles Vaccine Production Facility (MVPF), Project office in the administration building
Local Cost	Cost for low materials, Personnel cost, Energy bill, Facility maintenance cost, etc.

2. Terminal Evaluation Team

Team Leader:	Dr. Mitsuhiro USHIO	Executive Technical Advisor to the Director General, Human Development Department, JICA
GMP:	Dr. Hiroshi OHARA	Bureau of International Cooperation, International Medical Center of Japan
Cooperation Planning:	Mr. Shinji SATO	Infectious Diseases Control Division, Health Human Resources and Infectious Disease Control Group, Human Development Department, JICA

Evaluation and Analysis: Dr. Yoichi INOUE Consulting Division, Japan Development Service Co., Ltd.	
Period of Evaluation: November 1, 2009 – November 14, 2009	Study Type: Terminal Evaluation
3. Summary of Evaluation Results	
3-1 Achievements	
(1) Output 1	
<p>Activities under Output 1 were largely conducted without delay after the Mid-term Evaluation, and achievement of indicators was satisfactorily completed at the time of the Terminal Evaluation. Efficacy and safety of MV manufactured by POLVAC have been proven in clinical trials, therefore, which is implying technical transfer regarding MV production from seed virus has achieved. Moreover, POLYVAC staff members acquired technical skills of high quality.</p> <p>However, hands-on experiences as a manufacturer of MV is definitely insufficient. Strengthening of practical problem-solving capacity for inexperienced problems, such as abnormality and deviancy from tolerable limits, will be the future tasks. Strengthening of transferred techniques of MV production and data management/analysis will be required to acquire institutional self-sustainability.</p>	
(2) Output 2	
<p>Activities under Output 2 were largely conducted without delay after the Mid-term Evaluation, and achievement of indicators was satisfactorily completed at the time of the Terminal Evaluation, as well as activities under Output 1. Establishment of GMP system moved ahead steadily in POLYVAC as the MV manufacturer, resulting in the launching of MV to Vietnamese market through EPI.</p> <p>However, follow-up and additional guidance will be further required for the proper maintenance of GMP compliance at the commencement of routine manufacturing of MV in POLYVAC. Control of GMP-related documents should be further improved for the obtainment of prequalification from WHO.</p>	
(3) Project Purpose	
<p>The MV manufactured from imported bulk was shipped to the Vietnamese market in August 2009, followed by clinical trials for the verification of its efficacy and safety. The MV manufactured from seed virus is expected to be licensed for Vietnamese market in November 2009 by NRA as well. Moreover, POLYVAC acquired capacity to manufacture MV with sufficient doses for annual domestic demand of 7.5 million. It is suggested that POLYVAC has functioned as an MV manufacturer from these achievements.</p> <p>However, as aforementioned in “Achievements of Outputs”, strengthening of practical problem-solving capacity for inexperienced problems, such as abnormality and deviancy from tolerable limit, will be the future task.</p>	
3-2 Evaluation by Five Criteria	
(1) Relevance: The relevance of the Project is basically high at the time of the Terminal Evaluation.	
<p>In the Vietnamese long-term healthcare policy (2001-2010), the importance of public health and preventive medicine is emphasized. The Vietnamese Government has started provision of booster dose of MV in addition to first dose since 2006 according to the WHO/WPRO’s strategy. Although the MV coverage of two-dose MV immunization was kept as high as 97% in 2008, a significant measles outbreak was observed from the end of 2008. The number of suspected measles cases was more than 16,000 as of</p>	

September 2009, and this is the largest epidemic in the past decade. The Vietnamese Government has higher expectations of the achievements of the Project under the circumstance of the measles outbreak in terms of the increasing MV domestic demand, and the realization of self-supply of MV is currently recognized as a first priority in the Ministry of Health. Therefore, the Project Purpose is highly consistent with the Vietnamese health policy. On the other hand, WHO/WPRO also recommended to the Vietnamese government that providing measles-rubella vaccine instead of monovalent MV during supplementary immunization activities (SIAs) provides protection against rubella and prevention of congenital rubella syndrome. In case that the Vietnamese government adopted the MR vaccine for booster dose, the relevance of the Project might be reduced.

The healthcare cooperation area is regarded as the “improvement of basic social services” under “improvement of society and life, and disparity adjustment” in Japan’s country-by-country aid program for the Socialist Republic of Viet Nam issued in July 2009. Likewise, in the JICA’s country-by-country assistance implementation policy issued in April 2009, infectious disease control is described as follows; JICA emphasizes a long-term relationship with the National Institute of Hygiene and Epidemiology (NIHE), and provides assistances for the capacity enhancement and the acceleration of sustainability. JICA considers new assistances according to epidemic situation of the infectious diseases. Therefore, the Project meets the aid policies of Japan as well as JICA since the Project has been implemented with a good relationship with NIHE through regular information sharing and personnel exchange.

(2) Effectiveness: The effectiveness of the Project is generally high at the time of the Terminal Evaluation for the following reasons, while the achievement of technical skills of the staff members in POLYVAC should be further improved.

Achievement of the Project Purpose of “MV manufacturing complying VN-GMP” can be attributed to the achievement of the Outputs of “Improvement of technical skills for MV manufacturing” and “Compliance of VN-GMP standard”. Since the relationship between the Project Purpose and Outputs is logically correct, it is considered that the Project took the most effective approach to achieve the Project Purpose. Furthermore, it is considered that the effectiveness of the Project is high since indicators for the Project Purpose and Outputs are sufficiently fulfilled. Obtainment of capacity to manufacture sufficient amount of MV for domestic demand in Viet Nam would be very challenging as an attainment target in the setting of four-year project period. These results are attributed to the unified cooperation and persistent efforts of all concerned, especially the staff members in POLYVAC and Japanese experts. The number of level-4 staff members has steadily increased as the result of continuous activity of technology transfer.

However, POLYVAC is just standing at the start line as an MV manufacturer, so the hands-on experiences as a manufacturer of MV is insufficient. Practical problem-solving capacity for inexperienced problems, such as abnormality and deviancy from tolerable limit, will only be acquired by practical experiences through the routine business. Though the operational skills for MV manufacturing are achieved to sufficient level, strengthening of transferred techniques of MV production and data management/analysis of various kinds of validation remain as future tasks.

Working groups consisting of representatives from each division, were phased in according to the progress of the Project, as recommended by Japanese experts from the beginning of the Project period. As of the time of the Terminal Evaluation, eight self-organized working groups of Calibration/Validation, Formalin Fumigation, Environmental Pollution Control, Environmental Monitoring, Procurement Control, Risk Management, Document Control and Clinical Trial are functioning for solving various

kinds of problems arising from arising in and out of the Project. The working groups were organized by POLYVAC voluntarily under the indirect support from Japanese experts, and contributed to the achievement of Outputs. Additionally, issuance of certificates of ability to POLYVAC staff members contributed to the clarification of official responsibilities and job description, and boosted motivation.

- (3) Efficiency: The efficiency of the Project was generally high at the time of the Terminal Evaluation for the following reasons, even though several unexpected external factors vitiated the efficiency of the Project.

Due to the effective input and the effort by the concerned people, the 2 outputs of the Project were achieved with in a time frame of 4 years.

Dispatch of Japanese experts has been conducted on schedule mostly, and efficiently modified in accordance with progress of the Project activities and the local situation. As for the general outline of experts' activities for technical transfer, necessary MV production-related and GMP-related documents and teaching materials were drafted by experts in Japanese during domestic service in Japan, and translated from Japanese to Vietnamese by national staff members of the Project in Viet Nam. During the period of field activities in Viet Nam, the experts conducted the training and guidance to POLYVAC staff members intensively by using the translated documents and the materials. During the unattended period of Japanese experts in Viet Nam, technical advice and guidance were efficiently continued via communication tools such as international call and e-mail.

On the other hand, The relative electrical shortage is a growing problem amidst the recent significant economical development and industrialization in Viet Nam, especially in Ha Noi. In POLYVAC, power outages have caused frequent stoppages of the production line. Though POLYVAC is capable of producing 7.5 million doses of MV per year at its production rate, it cannot be denied that the frequent power shortages affect the practical production of 7.5 million doses.

- (4) Impact: To achieve the overall goal, POLYVAC requires some continuous support. The following positive or negative impacts are confirmed or expected in line with the implementation of the Project.

① Probability of MV production covering domestic demand

Currently, the annual consumption of MV for routine EPI is estimated at 5 million doses. POLYVAC acquired the capacity to manufacture 7.5 million doses of MV per year, which fulfills the domestic demand. According to the significant outbreak of measles in Viet Nam, an ad-hoc and massive EPI campaign is expected to be launched by the Vietnamese government in the near future. Taking the additional consumption necessary for the campaign into account, the current capacity of MV manufacturing of 7.5 million doses per year is not enough.

Important assumption for the achievement of MV self-sufficiency covering domestic demand is a certain magnitude of financial assistance from the Ministry of Health to POLYVAC until it achieves financial independence followed by MV manufacturing revenue stabilization. The Ministry of Health is recognize the needs of support strongly until POLYVAC acquires the prequalification from WHO. Vice-Minister of the Ministry of Health also has great interest in the achievement of the Project from the perspective of infectious disease control in Viet Nam. Therefore, it is expected that the Ministry of Health will provide continuous financial support to POLYVAC.

② Probability of MV export for neighboring countries via UN Agencies

In the usual inspection manner for prequalification, the inspection team from WHO will devote a

substantial amount of time working on the inspections in line with the current WHO-GMP (WHO-cGMP), and will order a certain amount of improvement to the inspected party. In the case of POLYVAC, basic techniques and procedures in regard to validation complying with the GMP standard have just been transferred from the aspect of quality assurance. Several issues also remain such as strengthening of practical problem-solving capacity for inexperienced problems of abnormality and deviancy from tolerable limit, as well as maintenance of transferred technical skills. Therefore, it is suggested that technical assistances, by any means, will be essential for POLYVAC to acquire the prequalification from WHO to export MV products.

An important assumption for the achievement of exporting POLYVAC-made MV products is the accreditation of the six necessary functions of NRA (supervision of clinical trials, GMP inspection, lot release, licensing, laboratory access and post-marketing surveillance). As of the time of Terminal Evaluation, only three out of six functions are at an acceptable level. And, the serious conflict of interest for members of the ethical committee and the licensing committee is a remaining issue of major concern to date. A positive impact is observed for the functional enhancement of NRA functions through the indirect assistance of the Project (described under “Impact” in detail). However, in case of taking into consideration some assistance for activities aimed at the acquisition of the prequalification from WHO, the acquisition of accreditation of NRA functions is one of the important assumptions. JICA should assess the following issue; the aforementioned “conflict of interest” can be a “killer assumption” for the assistance.

Additionally, to export the POLYVAC-made MV product, it is a pre-condition that POLYVAC is a capable of manufacturing a sufficient amount of MV product for export above the fulfillment of the domestic demand. It is expected that POLYVAC is theoretically capable of manufacturing MV products up to 15 million to 20 million doses per year (i.e. around 2.5 times the current production capacity) under the right circumstances. In that case, there are several critical problems such as securing qualified human resources, training and guidance for new personnel, procurement of sufficient materials for MV production, and addition of the freeze dryer that determines the production rate. The electrical power shortage is suspected to be worse than ever before in case of the production increase. In that case, therefore, additional power generator will be required.

- (5) Sustainability: Under the current circumstances, it is difficult for POLYVAC to assure a self-sustainability without continuous assistances by any means.

① Political and Institutional Aspects

The Ministry of Health has particularly large expectations for the impact of the Project outputs on the EPI in Viet Nam, and the Project is afforded top priority on the health agenda in Viet Nam. The Project Purpose is highly consistent with the health policy and principles, especially for the national EPI. Therefore, it is believed that the policies regarding national EPI will be sustained and enhanced. Though POLYVAC has the capacity to manufacture up to 7.5 million doses per year, the more POLYVAC manufacture MV products, the more the size of the overall deficit expand in POLYVAC or the Vietnamese government inversely. Meanwhile, the domestic demand of MV product will increase according to the implementation of nationwide countermeasures such as massive campaign for MV immunization against the measles outbreak taken place currently in Vietnam. Therefore, the Vietnamese government should utilize the MV manufacturing capacity of POLYVAC, acquired though the implementation of the Project, by the allocation of the expenses for purchasing

POLYVAC-made MV products as well as the equipment investment for MV production increase.

To export the POLYVAC-made MV products to the international market through United Nations agencies, it is required for NRA to acquire the accreditation from WHO prior to the application for prequalification of POLYVAC to WHO. In other words, the acquisition of NRA accreditation from WHO is an important pre-condition. Under the circumstances, the Ministry of Health is addressing the functional enhancement of NRA under the leadership of the vice-minister.

② Financial Aspects

The MV from imported bulk has already been launched on the Vietnamese market. The MV from seed virus is expected to be licensed in December 2009 as well. Moreover, POLYVAC has acquired the capacity for a sufficient amount of MV manufacturing, which meets the domestic demand. From the aforementioned achievements of the Project, it is expected that POLYVAC will obtain a certain level of financial independence. However, current manufacturing cost for MV is rather expensive since the prices of raw materials are rising globally, and most of the reagents are still procured from Japan. Therefore, it is required that the Ministry of Health continue financial support to POLYVAC until it becomes capable of operation and maintenance of the facilities and equipment as well as procurement of consumables. As for POLYVAC, it is required to conduct validation to switch over the reagents from Japanese-made to inexpensive products. However, it would be technically difficult for POLYVAC to conduct the validations autonomously due to its lack of experience.

A certain amount of budget should be allocated for additional freeze dryer, private power generator, and hiring of new staff members.

③ Technical Aspects

In the usual inspection manner for prequalification, the inspection team from WHO will devote a substantial amount of time working on the inspections in line with the current WHO-GMP (WHO-cGMP), and will order a certain amount of improvement to the inspected party. In case of POLYVAC, basic techniques and procedures in regard to validation complying with the GMP standard were just transferred from the aspect of quality assurance. Several issues also remain such as strengthening of practical problem-solving capacity for inexperienced problems of abnormality and deviancy from tolerable limit, as well as maintenance of transferred technical skills. Therefore, technical assistances, by any means, will be essential for POLYVAC to acquire the prequalification from WHO to export MV products.

3-3 Conclusions

POLYVAC acquired the capacity for VN-GMP-compliant MV manufacturing of sufficient amounts for domestic demand by the time of the Terminal Evaluation. Setting of a four-year project period was rather challenging to achieve the Project Purpose of practical MV manufacture and launch into the Vietnamese market. Therefore, these achievements showed that a technology transfer with high relevance, effectiveness and efficiency was executed by the Project.

However, the impact of the Project from the aspect of achieving Overall Goal as well as sustainability of the Project cannot be evaluated, since POLYVAC has just started as an MV manufacturer, and also several issues remain to be conquered such as the compliance of GMP standard and practical problem-solving capacity for problems arising from inexperience such as abnormality and deviancy from tolerable limit and so on. According to the aforementioned reasons, the Team concludes that POLYVAC requires assistances to complement its lack of experience as an MV manufacturer aspiring to become an MV exporter as well as

stable self-supply of MV for the domestic demand including the campaigns.

3-4 Recommendations

Based on the review on the achievement of the activities and the outputs of the Project, both sides confirmed the recommendations as follows:

- (1) It is required for the Ministry of Health to continue the procurement of the MV manufactured by POLYVAC in order that they can use the full capacity for Vietnam-GMP-compliant MV manufacturing through the Project and to raise domestic supply for MV rapidly.
- (2) It is needed that the Ministry of Health continue financial support to POLYVAC until it becomes capable of operation and maintenance of the facilities and equipment as well as procurement of consumables independently with the income from MV products.
- (3) POLYVAC is required to conduct validation to switch over the reagents from Japanese-made to inexpensive products one by one for reducing high manufacturing cost.
- (4) NRA is required to enhance its six functions regarding WHO accreditation as soon as possible so that POLYVAC could become an exporter of MV in the near future.
- (5) POLYVAC staffs need to strengthen practical problem-solving capacity for inexperienced problems of abnormality and deviancy from tolerable limit with Japanese experts' support by the end of the Project.
- (6) Since there being no alternative sources of import for Specific Pathogen Free (SPF) eggs causes high manufacturing cost, it is recommended for POLYVAC to keep persistent discussion with concerned Ministries to convince them to approve importing the SPF eggs even when the exporting countries report Highly Pathogen Avian Influenza (HPAI) infection among poultries.
- (7) It is suggested that POLYVAC continues staff training in order to strengthen and maintain the knowledge and skill regarding GMP standard.
- (8) The first version of Vietnam-GMP was released in 2002 and the revised version released in 2004 is currently valid. It will be necessary for the MOH to consider the revision in case of the new recommendation coming from WHO as the compliance with Vietnam-GMP, which has met WHO-GMP standard, is the essential component of the Project.