Viet Nam

Ex-post Evaluation of Japanese Grant Aid Project

"The Project for Construction of the Facilities for Measles Vaccine Production in Viet Nam"

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0. Summary

This project has been highly relevant with the Viet Nam's development plan and Japan's ODA policy. Regarding development needs, there is a gap between the amount of measles vaccines which was regularly required at the time of planning and that of the time of ex-post evaluation. However, considering comprehensively that the number of cases of measles is still the highest among the six major infectious diseases of children at the time of ex-post evaluation, that outbreaks occur every few years, that the urgency of the project for providing stable supply of domestic measles vaccines is high and that the decrease in the required amount is due to the external factor which was not expected at the time of planning, it can be said that its relevance is high. Both project cost and project period were mostly as planned, therefore efficiency of the project is high.

This project established the physical and technical production capacity of 7.5 million doses per year of measles vaccines, which meet the World Health Organization (WHO) - Good Manufacturing Practice (GMP)[1], and achieved its objective to provide stable supply of the vaccines. Synergy effect with other projects has also been observed. On the other hand, the annual production quantity of measles vaccines at the time of ex-post evaluation is approximately 3.3 million doses, which is equivalent to 44% of its target at the time of planning or to 67% of its demand (required amount for regular vaccination) at the time of ex-post evaluation. The reason why the production amount remains 67% of its demand is that imported vaccines have been used for the second dose of regular vaccination, and this is an external factor for the executing agency. However, the government could have decreased imported vaccines for regular vaccination and could have increased the purchase amount of measles vaccines manufactured by POLYVAC as a counter-measure for 2010 and beyond. Although it was confirmed that it is possible that the annual production amount increases in the future, the effectiveness of the project at present is fair. Since it is only after 2011 when it is possible to measure the contribution of this Project to the achievement of the impact indicators, it is difficult to evaluate it at present. However, the indicators of the

1 GMP provides basic ideas about the good manufacturing practice and does not describe the detailed actions and methods. Each vaccine manufacturer needs to interpret the idea, to formulate its implementation plan and to carry it out. At the GMP assessment which is conducted every two years, there are Q&A sessions between the staff in a facility and inspectors regarding the interpretation of GMP, and the staff needs to explain logically and to provide evidence in order to persuade inspectors. Furthermore, because GMP assessment is conducted based on the latest knowledge in the world at that point, it is not easy to keep matching with the GMP.

expected positive indirect effects such as the ratio of two-dose vaccination of measles almost achieved those targets. No major problems have been observed in the operation and maintenance system, therefore sustainability of the project effect is high. In light of the above, this Project is evaluated to be highly satisfactory.

1. Project Description

Project Location

Measles Vaccines and Water for Injection produced by POLYVAC

1.1 Background

The Government of the Social Republic of Vietnam (hereinafter called "Vietnam") had been implementing the Expanded Program on Immunization (EPI) as one of the national programs since 1981 in order to provide an effective means of reducing the infant mortality rate and under five mortality rate and suppressing infectious diseases. At the time of planning, this Program was aimed at a higher EPI immunization rate and the efforts to establish the self-supply system of EPI vaccines (for polio, measles, diphtheria, whooping cough, tetanus and tuberculosis) had been made, enabling the domestic production of EPI vaccines except the measles vaccines. The vaccination rate in Vietnam was keeping 93% or more for the primary vaccination since 1993. However, the Primary Vaccine Failure (PVF)[2] and the Secondary Vaccine Failure (SVF)[3] had increased, resulting in the increase of patients after 1997. 19,000 cases of measles occurred in 2000, and the outbreak had occurred every 7 to 8 years. This fact showed the limit of the primary vaccination effect. Under this circumstance, the Government of Vietnam (GoVN) started to introduce the regular vaccination in two times gradually as recommended by WHO. Therefore, it was predicted that the domestic demand for measles vaccines would increase. On the contrary, it was also predicted that vaccines manufacturers in developed countries would shift from the production of measles vaccines at low costs to the high-profit vaccine production. Hence, it was concerned in Vietnam, which depended on importing measles vaccines, about

2 Primary Vaccine Failure: No immunization is obtained because the vaccine effect is reduced by the insufficiency of the low temperature storage system.

3 Secondary Vaccine Failure: If the measles infection is reduced, the immunization effect of measles vaccination cannot be sustained, causing the contraction of measles more than 10 years after vaccination.

whether measles vaccines could be imported in a stable quantity at a low price.

Under these circumstances, the GoVN requested the Government of Japan (GoJ) for this Project, the Measles Vaccine Production Facilities Construction Project. In 2003, the GoJ decided to implement the project of constructing the measles vaccine production facilities under the grant aid as a part of the former Poliomyelitis Vaccine Research and Production Center (current Center for Research and Production of Vaccines and Biologicals: POLYVAC)[4], which had produced vaccines under the direct control of the Ministry of Health in Viet Nam. Immediately after the completion of this Project, the Technical Cooperation Project for Strengthening Capacity for Measles Vaccine Production (2006-2010) was implemented.

1.2 Objective

The objective of this project is to provide stable supply of measles vaccines which matches the WHO - Good Manufacturing Practice (GMP) standard in Hanoi City by constructing the vaccines production facilities and the quality control facility, by providing the procurement of the equipment required for the vaccine production and by implementing technical guidance. The project summary is shown in Table 1.

Table 1 - Project Summary

Grant Limit/ Actual Grant Amount	2,277 million yen / 2,271 million yen
Date of Exchange of Notes	Detail Design: February 2003, Bidding and Civil Work: June 2003
Implementing Agency	Center for Research and Production of Vaccines and Biologicals (POLYVAC)
Project Completion Date	March, 2006
Main Contractors	Construction: Obayashi Corporation, Equipment: Mitsubishi Corporation and Ogawa Seiki Corporation
Main Consultant	Joint Venture: Nihon Sekkei, Inc. and JGC Corporation (Nikki)
Basic Design	"The Project for Construction of the Facilities for Measles Vaccine Production in Viet Nam", March 2002- September 2002
Detailed Design	May 2003-October 2003
Related Projects	"Technical Cooperation Project for Strengthening Capacity for Measles Vaccine Production in the Social Republic of Viet Nam", March 2006-March 2010[5]. Follow-up cooperation for technical transfer (April 2010- March 2011). Follow-up study (August 2010- November 2010). Follow-up cooperation for facility and equipment (January 2011-August 2011).

4 Former POLIOVAC: Poliomyelitis Vaccine Research and Production Center. POLIOVAC was renamed as the Center for Research and Production of Vaccines and Biologicals (POLYVAC).

5 The Project Purpose is "POLYVAC will be capable to produce necessary amount of measles vaccines for use of measles control activities in the Socialist Republic of Viet Nam complying with the Viet Nam GMP (VN-GMP) which has met WHO-GMP standard". The Overall Goal is "Measles Infection Rate in the Socialist Republic of Viet Nam will be decreased from the current level". Outputs are the followings: 1) Staff of POLYVAC acquires appropriate technical skill to produce quality measles vaccines, 2) Production and quality management meet Vietnam-GMP which has met WHO-GMP standard.

2. Outline of the Evaluation Study

2.1 External Evaluator

Junko Miura, Global Link Management Inc.

2.2 Duration of the Evaluation Study

Duration of the Study: From December, 2010 to November, 2011.

Duration of the Field Study: From April 3rd to 17th and From July 4th to 15th, 2011.

2.3 Constraints during the Evaluation Study

The use of the measles vaccines produced by POLYVAC started only after POLYVAC obtained sales license in November 2009. Thus, it is difficult to evaluate to what extent this Project has contributed to the indicators of the indirect effects such as the target population of the two-dose vaccination and the ratio of two-dose vaccination at present.

3. Results of the Evaluation (Overall Rating: A[6])

3.1 Relevance (Rating: ③[7])

3.1.1 Relevance with the Development Policy of Viet Nam

At the time of planning, the long-term policy for health and medicines for 2001-2010 highlighted the importance of public medical policy and preventive medicines and targeted the vaccination of measles vaccines for all the children concurrently and the introduction of two-dose regular vaccination by 2008 and the eradication of measles by 2010. The policy was also aiming for enhancing the procurement ratio of domestic measles vaccines to the extent possible.

At the time of ex-post evaluation, the guidance for the objectives and direction for the Expanded Program on Immunization (EPI) (2006-2010)[8] outlined the following targets regarding measles: 1) to reduce the measles prevalence rate to less than one per hundred thousand persons by 2010; and 2) to implement immunization campaigns in addition to regular vaccination in order to keep the two-dose vaccination rate for one-year-old and two-year-old children at 95% or more. Furthermore, the Five-Year Plan for the Health Sector for 2011-2015 is aiming to produce EPI vaccines including measles vaccines domestically and to meet the GMP standards. The objective of producing EPI vaccines domestically was also declared by the Vice Minister of the Government of Viet Nam at the conference "Investment in the

6 A: Highly satisfactory, B: Satisfactory, C: Partially satisfactory, and D: Unsatisfactory.

7 ③: High, ②: Fair, and ①:Low.

8 The guidance for the objectives and direction for the EPI (2011-2015) is currently under preparation. Hence, the guidance for 2006-2010 is the latest one.

pharmaceutical field towards 2020" in September 2010[9].

3.1.2 Relevance with Development Needs of Viet Nam

At the time of planning, in Viet Nam, among the six major infectious diseases of children (polio, measles, diphtheria, whooping cough, tetanus and tuberculosis)[10], both number of infected cases and the mortality in measles were the highest. In 2000, 19,000 cases of measles were reported annually, and this showed the limit of the primary vaccination effect. Under this circumstance, the GoVN started to introduce two-dose regular vaccination gradually since 2000. Whereas it was expected that the domestic demand for measles vaccines would increase in Viet Nam, vaccine manufacturers in developed countries started to shift from the production of measles vaccines at comparatively reasonable costs to the high-profit vaccine production. Therefore, there was an urgent need for stable supply of measles vaccines at a low price in Viet Nam, which depended on importing measles vaccines.

At the time of ex-post evaluation, among the six major infectious diseases of children, the number of cases of measles was the highest as follows: measles 5,358; tuberculosis 408[11]. The disease, of which the number of cases is the highest among the above six diseases between 2005 and 2009, was also measles. In addition, the number of suspected cases of measles in 2009 was approximately 23,056 cases[12], and outbreaks still occur. Considering the fact that the delay in the import process of measles vaccines affects the two-dose vaccination rate, the needs for stable supply of domestic measles vaccines still remain high.

In Viet Nam, the number of cases of rubella has been increasing. Therefore, pursuant to the recommendation by WHO, the Ministry of Health (MoH) is currently considering in introducing Measles Rubella (MR) vaccines for the second dose particularly for the fifteen to thirty five year-old women after 2013 and for the 18 month children after 2016. In order to respond to the shift in the development needs, POLYVAC is currently preparing the application for the JICA Technical Cooperation Phase II (tentative) in order to acquire the skills in MR vaccine production. As the government's policy is to replace one of two doses of measles vaccines with MR vaccines, the needs for measles vaccines still remain high.

Meanwhile, there is a gap between the amount of measles vaccines which was regularly

9 Source: Document of the government of Viet Nam (245/TT-VPCP).
10 Source: Health Statistical Yearbook, 2000.
11 Source: Health Statistical Yearbook, 2010. Data is that of 2009.
12 Source: Measles and Rubella cases confirmed by laboratory and others, Viet Nam, 2003-2011, WHO, 2011.

required at the time of planning and that of the time of ex-post evaluation. The following two can be raised as the reasons why the demand of measles vaccines at the time of ex-post evaluation was less than the estimated amount. First, as shown in the target group in Table 2, the target group at the time of planning included not only the under-one children and under-five children in the whole country including the mountainous high-risk area but also the total of 1.2 million children of 1-2 year old and 6-10 year old in the high-risk area. However, due to the synergy effect between the establishment of the cold-chain and measles eradication campaign after 2002, vaccination for the children of 1-2 year old and 6-10 year old in the high-risk area became unnecessary by the time of ex-post evaluation. Second, as shown in the number of target group in Table 2, the target population in the whole country at the time of ex-post evaluation is smaller than that of the planning by 0.6 million. Although the data on the number of births before 2002 could not be obtained, the average annual number of births from 2003 and 2008 was approximately 1,494,000[13], and this shows that the target population at present is smaller than its estimate of planning[14].

Considering that outbreaks occurred in 2005 and 2009, the government changed its policy to provide eighteen-month-old children with the second dose of the vaccines after 2011 in order to raise the vaccination rate of children between one and five year old particularly. If there is no major change with the future population, it is expected that there is no major change with the target population for vaccination in the coming years.

13 Data Source: WHO Bulletin 2011, Original data: UNICEF.

14 Birth rate is also declining between the planning and the ex-post evaluation. Birth rate was 18.62 in 1999, 17.91 between 1999 and 2004, 17.75 between 2004 and 2009, 16.59 between 2009 and 2014 (projection). “Health in Asia and the Pacific”, WHO.

Table 2 - Target population for regular vaccination and the amount of measles vaccines required for regular vaccination

	Plan (2002)	Mid-term evaluation of the Technical Cooperation (2007)	Ex-post evaluation (2011)
Target age	Under one year old infant:1.8 million persons, Under five year old children: 1.8 million persons, Children in high risk zones in mountainous areas (1-2 year old: 0.6 million persons, 6-10 year old: 0.6 million persons)	First dose: 9 month old infants x 1.6 million Second dose: under six year old children[15] x 2.5 million	First dose: 9 month old infants x 1.5 million Second dose: 18 month old children x 1.5 million
Target population	Total: 4.8 million persons/year	Total: 4.1 million persons/year	Total: 3 million persons/year
Required amount of vaccines (Note 1)	4.8 million/year x wastage factor figure 1.5 (Note) =7.2 million/year + contingency 0.3 million/year = 7.5 million/year	4.1 million/year x wastage factor figure 1.5 = 6.15 million/year	3 million/year x wastage factor figure 1.5 =4.5 million/year + contingency 0.4 million/year = 4.9 million/year

Source: Ex-ante evaluation summary sheet (2002), Mid-term Evaluation of the "Technical Cooperation Project for Strengthening Capacity for Measles Vaccine Production in the Social Republic of Viet Nam"(2007) and data from the National Institute of Hygiene and Epidemiology (NIHE), 2011.

Note : Wastage Factor Figure= 100/(100-Wastage Rate). Wastage rate is about 33%, the yield rate is 67%. The above wastage factor rate was calculated based on the condition that ten doses are contained in one vial and that vaccines are formulated in freeze-dry. For example, if only one person is vaccinated in six hours after a vial is opened, the rest of nine doses in the vial are disposed.

3.1.3 Relevance with Japan's ODA policy

At the time of planning, priority areas of the Japan's ODA policy towards Viet Nam (ODA Country-wise Databook, 2002) were human resource & institutional development, upgrade of economic infrastructure such as electricity and transportation, development of agriculture and rural areas, education, health and medical system, and environment. As this Project was included in the health and medical system, the project was consistent with the Japan's ODA policy.

In light of the above, This project has been highly relevant with the Viet Nam's development plan and Japan's ODA policy. Regarding development needs, there is a gap between the amount of measles vaccines which was regularly required at the time of planning and that of the time of ex-post evaluation. However, considering comprehensively that the number of cases of measles is still the highest among the six major infectious diseases of children at the time of ex-post

15 At the time of planning, the target group for the 2nd dose was five year old children. In the guidance for the objectives and direction for the EPI (2011-2015), it was under-six children (before entering school). These are considered the same meaning substantially.

evaluation, that outbreaks occur every few years, that the urgency of the project for providing stable supply of domestic measles vaccines is high and that the decrease in the required amount is due to the external factor which was not expected at the time of planning, it can be said that its relevance is high.

3.2 Efficiency (Rating: ③)

3.2.1 Project Outputs

The outputs were completed almost as planned. The output of the project is shown in Table 3.

Table 3 - Output (planned and actual)

Items	Planned	Actual
Japanese Side	<Facility> - Construction of Vaccine Production Building and Animal Test Building - Electrical works of Mechanical Building <Equipment> Water supply unit, vial washing machine, filling machine, autoclave, laminar flow unit, incubator, dry oven, freezer, etc. <Soft component> Technical guidance regarding the three steps out of six steps of validation (Design Qualification: DQ, Installation Qualification: IQ and Operation Qualification: OQ) [16], preparation of GMP related documents, and the technical guidance for operation and maintenance.	As planned.
Vietnamese Side	<Facility> - Administration Building, Parking Garage, Canteen, Security Guard House - Architectural and structural works of Mechanical Building - Wells, incinerator, site works, etc. <Equipment> Furniture, lockers, shelves, etc.	As planned. except incinerator. Incinerator was removed from the list because it was not approved due to the regulation of Hanoi City.

Source: Basic Design Report (2002) and Questionnaire Answer.

Front of the MVPF Building

Signboard of the building installed in 2006

Filling and labeling room

16 Regarding Performance Qualification (PQ), Media Fill Test (MFT) and Process Validation (PV), technical guidance was provided by the Technical Cooperation Project.

3.2.2 Input

3.2.2.1 Project cost

The Exchange of Note (E/N) ceiling amount of this project was 2,277 million yen, and the estimated cost by the GoVN was 230 million yen. However, the actual cost for the Japanese side was 2,271 million yen (99.7% of the plan), and the actual local cost was equivalent to 547 million yen[17]. Therefore, the Japanese Grant component was within the plan whereas the GoVN component was increased compared to its planned cost. It was because the estimate did not include the cost for seeds, expense for test production, operation and maintenance cost and because the market price was escalated. Thus, the increase of the cost can be justified.

3.2.2.2 Project period

The planned project period was 35 months from May 2003 to March 2006[18]. The project period was as planned.

Both project cost and project period were mostly as planned, therefore efficiency of the project is high.

3.3 Effectiveness (Rating: ②)

3.3.1 Quantitative effects

(1) Annual Production Quantity of Measles Vaccines

Table 4 shows the annual production quantity of measles vaccines at the facility constructed by this Project.

Table 4 - Annual Production Quantity of Measles Vaccines

(unit: million doses per year)

Indicators	Target for the 1st year and 2nd year	Target for the 3rd year and beyond	Actual for the 1st year (2009)	Actual for the 2nd Year (2010)	Actual for the 3rd Year (2011)
Vaccines manufactured from imported bulk	0.5	0	Approximately 0.3	0	0
Vaccines manufactured from seed virus	0	7.5	Approximately 2.37	Approximately 2.39	Approximately 3.3
Annual Production Amount of Measles Vaccines (Note 1)	0.5	7.5	Approximately 2.67	2.39 Note 2	3.3

Source: Targets are from the Ex-ante Evaluation Summary. The actual figures and prospect for 2011 are from POLYVAC production management record.

Note 1: Because it is necessary for POLYVAC to produce more than ordered, the annual production amount of the measles vaccines is more than the amount purchased by MoH.

Note 2: This figure does not include 0.3 million, which was abandoned because its quality was not guaranteed due to the frequent black-out in the production process.

17 78,196,648,000VND. Calculated based on the average exchange rate between May 2003 and March 2006: 1VND=0.0070.

18 The installation of the small items such as lockers was completed in June 2006.

By the year of 2009, the first year after the commencement, the production capacity of 7.5 million doses per year was obtained. Meanwhile, as shown Table 4, the actual annual production quantity in 2011 remains as low as 3.3 million doses per year against the target for the third year of 7.5 million doses per year (approximately 44% of its target). 3.3 million doses per year is equivalent to 67% of the required amount for regular vaccination (4.9 million doses per year). The reason why the production amount remains 67% of its demand is that the Global Alliance for Vaccination and Immunization (GAVI) started in 2007 providing the MoH with the budget for purchasing measles vaccines for the second dose of regular vaccination and for campaigns and as a result that imported vaccines has been used for them. Because GAVI's supply of imported vaccines is a tentative action until the year of 2012, it is highly possible that the amount of the order from the MoH to POLYVAC will increase after 2013 and that the annual production quantity will increase up to 4.9 million doses per year accordingly.

Other possibilities which affect the annual production amount are as follows.

1) As noted in the section of relevance, after 2013, if the government of Viet Nam adopts a policy of replacing the second dose of measles vaccines with MR vaccines, there is a possibility that the annual production amount will decrease by half. On the other hand, if an environment enables POLYVAC to produce MR vaccines, the total production amount of measles vaccines and MR vaccines will be maintained at the same level of the current status.
2) As described below, if the National Regulatory Authority (NRA) acquires accreditation and POLYVAC obtains prequalification from WHO, it becomes possible to use the vaccines of POLYVAC for campaign[19] and to export, which makes it possible to utilize the production capacity more than now.

Because only the vaccines which obtained prequalification from WHO is allowed for vaccination with the assistance by international organizations, the government of Viet Nam cannot purchase the vaccines manufactured by POLYVAC, which has not obtained prequalification from WHO yet. In addition, it is an essential requirement that the NRA obtains accreditation from WHO before POLYVAC applies to WHO for prequalification. The approval and authorization services related to the measles vaccines produced in this Project were undertaken by the NRA. In Vietnam, NRA consisting of four agencies[20] are

19 So far, the required vaccine for large scale campaigns has been imported with the funds from GAVI, UNICEF and WHO.

20 Four agencies include Drug Administration of Vietnam (DAV), Department of Science and Training (DST), Vietnamese Administration of Preventive Medicine (VAPM) of the Ministry of Health, and National Institute for Control of Vaccine and Biologicals (NICVB). At the time of planning, CENCOBI (current NICVB) were responsible for all the six functions as NRA, and

responsible for six approval and authorizations functions[21]. However, NRA has not acquired accreditation from WHO so far[22]. Following the unofficial assessment by WHO in December 2008, another unofficial assessment was conducted in May 2011. The relevant agencies are to undertake necessary steps towards official assessment based on the roadmap for strengthening the NRA, which was formulated in May 2011. At the same time, POLYVAC is planning to confirm the quality of measles vaccines by the GMP assessment, which is conducted every two years (the next one will be conducted in 2012), and to prepare for applying the pre-qualification from WHO. In order to achieve it, it is desirable for the government to acquire the accredititation of the NRA from WHO as early as possible.

(2) Proportion of Annual Supply Amount of Measles Vaccines by POLYVAC to the Total Supply Amount of Measles Vaccines in Viet Nam

Table 5 - Annual Supply Amount of Measles Vaccines produced by POLYVAC against the Total Supply Amount of Measles Vaccines in Viet Nam

Indicators (unit)	2009 Actual	2010 Actual	2011Actual
Purchased Amount of POLYVAC Measles Vaccines by MoH (million doses)	1.3	2	3.2 (Note 2)
Imported vaccines supplied by GAVI (million doses)	1.74	1.58	1.7
Imported vaccines supplied by UNICEF/WHO (million doses)	0	8.1 (Note 1)	0
Total (million doses)	3.04	11.68	4.9 (Note 3)
Ratio of POLYVAC vaccines against the total supply in Viet Nam (%)	43	Regular vaccination only: 56 Including campaign: 17	65

Source: Questionnaire Answer from NIHE and EPI Plan for 2011, NIHE.

Note1: Campaigns were implemented for 7.3 million of 1-5 year old children.

Note 2: While the annual production amount is 3.3 million doses per year, the purchased amount of POLYVAC vaccines by the Ministry of Health is 3.2 million doses per year.

Note 3: 4.9 million doses per year is the total amount calculated based on the target population of 3 million persons, which the Ministry of Health planned.

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those functions had been strengthened by the assistance by WHO. However, due to the change of the policy of the government of Viet Nam, the above departments of the Ministry of Health and NICVB became responsible for the functions, thus the process for strengthening NRA is behind the original schedule. Authorization by two committees, the Ethics Committee and the Licensing Committee, is also the requirement for NRA, but the problem of conflict of interests between the members of the two committees has been pointed out by WHO, and they have been receiving guidance from WHO.

21 Six functions include the followings: authorization/approval of clinical trials, marketing authorization and licensing activities, GMP regulatory inspection, laboratory access, NRA lot release, and post-marketing activities including surveillance of adverse events following immunization.

22 It was also agreed in the Minutes of Discussion at the time of planning that the government of Viet Nam would obtain accreditation for NRA.

POLYVAC is a sole manufacturer for measles vaccines in Viet Nam[23]. As shown in Table 5, the proportion of supply of POLYVAC vaccines to the total supply in Viet Nam is increasing from 2009 to 2011 year by year as long as the regular vaccination is concerned. Although the second dose of vaccines will be provided by GAVI up to the year of 2011, all the vaccines for regular vaccination except the second dose has been procured by POLYVAC.

3.3.2 Qualitative Effects: Technical Production Capacity

As mentioned in the section of efficiency, technical guidance was provided in this Project regarding the three steps of validation (Design Qualification, Installation Qualification and Operation Qualification), and the POLYVAC staff acquired the related skills by the project completion. In addition, GMP related documents required for obtaining a facility license were prepared, and POLYVAC obtained the facility license from the NRA one month after the project completion in April 2006. Furthermore, POLYVAC passed a GMP assessment for the first time in 2008 during the Technical Cooperation Project, and as a result, POLYVAC came to be able to sell measles vaccines on the domestic market in 2009.

3.3.3 Synergetic effect with Technical Cooperation Project and other contributing factors

This Project and the Technical Cooperation Project for Strengthening Capacity for Measles Vaccine Production (hereinafter refers as “TC Project”) share the same objective of producing and of supplying the measles vaccines which match with the GMP in stable manner. This objective was achieved only three years after the project completion by providing the facility and the equipment with this Project and by establishing the production and quality control technology skills with the TC Project. For the successful achievement of the above objective, there were various partnerships with other organizations and linkage with other cooperation forms including the TC Project even before the planning of this Project and until the implementation of the TC Project.

1) In 1990’s, the government of Japan provided POLYVAC with equipment for establishing the production technology of polio vaccines. POLYVAC had established a production technology of polio vaccines before the commencement of this Project, which contributed to the smooth establishment of production technology of measles vaccines which is similar to that of polio vaccines.
2) Since 1997, the essential staff required for the measles vaccine production including the Director and the managers of each department had received training regarding the

23 In Viet Nam, four national vaccine manufacturers such as POLYVAC, IVAC, VABIOTEC and Darat Vaccine Center produce nine kinds of vaccines, and they produce different kinds of vaccines exclusively.

measles vaccine production and quality control in the Kitasato Institute, from the experts, who were involved in the soft component of this Project and the TC Project, thereby having built a mutual trust essential for smooth technical transfer prior to this Project and the TC Project;

3) In 2002, POLYVAC and the Kitasato Institute signed the technical transfer agreement on the measles vaccines production and the seed virus (AIK-C Strain);
4) The MoH, POLYVAC, WHO and the Kitasato Institute exchanged opinions closely and formulated the plan of this Project;
5) The expert in the Kitasato Institute, who had been a member in the mission of the Basic Study of this Project, was involved in the soft component of this Project as a process licenser. The ten experts in the soft component were involved in the TC Project. Through their commitment in the whole process, the blue print of this Project from the beginning to the success in GMP assessment was shared with the implementing agency and implemented steadily; and
6) The preparation of the plan for the TC Project had already started before the completion of this Project, and the technical transfer required for GMP assessment went smoothly because the TC Project started just after this Project completion.

In light of the above, this project established the physical and technical production capacity of 7.5 million doses per year of measles vaccines and achieved its objective to provide stable supply of the vaccines. Synergy effect with other projects has also been observed, and the indirect effect indicators almost achieved those targets as described later. On the other hand, the annual production quantity of measles vaccines is equivalent to 44% of its target at the time of planning or to 67% of its demand at the time of ex-post evaluation. The reason why the production amount remains 67% of its demand is that imported vaccines have been used for the second dose of regular vaccination, and this is an external factor for the executing agency. However, considering the facts that POLYVAC had acquired production capacity of 7.5 million doses per year of measles vaccines and that it obtained sales license by November 2009, the government could have decreased imported vaccines for regular vaccination in consultation with GAVI and increased the purchase amount of measles vaccines manufactured by POLYVAC as a counter-measure for 2010 and beyond. In light of the above, the effectiveness of the project is fair.

3.4 Impact

3.4.1 Intended Impacts

At the time of planning, it was expected that the project would contribute to the improvement in the followings: 1) target population of the two-dose vaccination, actual vaccinated population

and vaccination rate; and 2) infant vaccination rate, cases of measles including adults, prevalence rate and mortality rate caused by measles.

Although it is difficult to evaluate to what extent this Project has contributed to the indicators of the indirect effects at present, the indicators of the indirect effects almost achieved those targets as described below. The reason why it is difficult to evaluate the contribution is that the immunization by using the vaccines produced by POLYVAC started after POLYVAC obtained its sales license in November 2009 and that it is possible to measure the contribution after 2010 at the earliest. However, as described in page 11, there is a possibility that this Project will contribute more in the future because the proportion of supply of POLYVAC vaccines to the total supply in Viet Nam is increasing year by year, and it is also expected to increase in 2011.

3.4.1.1 Two-dose vaccination target population, actual vaccinated population and vaccination ratio

Table 6 shows the target population for two-dose vaccination, actual vaccinated population and vaccination ratio.

Table 6 - Target population for two-dose vaccination, vaccinated population and vaccination ratio

Indicators (unit)	2001 Actual	2002 Actual	2003 Actual	2004 Actual	Target for 2005 -2010	2005 Actual	2006 Actual	2007 Actual	2008 Actual	2009 Actual	2010 Actual
Target population (persons)	2,200,000	9,000,000	11,000,000	1,000,000	2,400,000	NA	1,471,146	1,351,164	1,228,861	1,526,671	1,536,461
Vaccinated population (persons)	288,902	6,640,859	NA	NA	>2,280,000	NA	1,466,129	1,244,860	1,175,120	1,471,627	1,500,635
Vaccination Rate (%)	13.1	73.8	NA	NA	>95%	NA	97.9	92.1	95.6	96.4	97.7

Source: The target for 2005-2010 is from the Ex-ante Evaluation Summary. Actual figures are from the questionnaire answer from NIHE.

Note 1: The actual target population for two-dose vaccination between 2001 and 2004 was the children between nine-month old and ten year old. The target for target population for two-dose vaccination for 2005 and 2010 at the time of planning was the total of 1.8 million five-year-old children in the whole country and the total of 0.6 million six to ten year-old children in the high-risk area; 2.4 million children in total.

Note 2: The target population in 2002 and 2003 are more than that in other years because campaigns were carried out in the country.

As shown in Table 6, against the plan of target population of the two-dose vaccination for 2005-2010 (2.4 million persons per year), the actual target population between 2006 and 2010 was approximately 1.5 million persons per year, which is smaller than that of planning. The reasons are the followings. The target population for two-dose vaccination for 2005-2010 included the total of 1.8 million five-year-old children in the whole country and the total of 0.6 million six to ten year-old children in the high-risk area; 2.4 million children in total. However, as mentioned in the section of relevance, because the total of 1.2 million children of one to two year-old and six to ten year old in the high-risk area were no longer included in the target population of regular vaccination, the target population for two-dose vaccination became only

five-year-old children in the whole country. In addition, regarding the target population for two-dose vaccination, the total of 1.8 million five-year-old children was estimated at the time of planning. However, according to the data after 2006, the actual target population varies between 1.2 and 1.5 million children under six.

Meanwhile, the target of 95% for the vaccination rate was achieved between 2006 and 2010 except in 2007. The reason why the vaccination rate in 2007 was 92.1%, which went below its target, was the delay in the import process of the vaccines[24]. This shows the necessity of producing measles vaccines domestically.

3.4.1.2 Infant vaccination rate, cases of measles, prevalence rate and mortality rate caused by measles

Infant vaccination rate, cases of measles, prevalence rate and mortality rate caused by measles are shown in Table 7. Infant vaccination rate achieved its target for 2010. In addition, the mortality rate was zero between 2005 and 2010, and achieved its target for 2010. On the other hand, the number of measles cases cannot be compared with a target because a target was not established. Since outbreaks occur every five years after 2000, there are still urgent needs for vaccination of measles. The reason why the prevalence rate could not achieve its target was because an outbreak occurred between 2009 and 2010.

Table 7 - Infant vaccination rate, cases of measles including adults, prevalence rate, and mortality rate caused by measles

Indicators (unit)	1996 Actual	1997 Actual	1998 Actual	1999 Actual	2000 Actual	2005 Actual	2006 Actual	2007 Actual	2008 Actual	2009 Actual	2010 Target	2010 Actual
Infant vaccination rate (%)	96.0	96.0	95.8	93.8	96.6	98.6	96.4	87.9	95.6	96.4	>95%	97.7
Suspected cases of measles (persons)	5,156	6,507	6,507	13,511	17,436	11,604	6,461	5,286	3,425	23,056	NA	15,196
Confirmed cases of measles (persons)	NA	NA	NA	NA	NA	410	1,978	17	352	7,818	NA	3,404
Prevalence rate (per 100 thousand persons)	6.8	8.6	13.2	17.7	21.2	0.5	2.4	0.02	0.41	6.22	<1.0	3
Mortality rate (per 100 thousand persons)	9	0	8	18	10	0	0	0	0	0	<1.0	0

Source: Actual figures between 1996 and 2000 as well as the target for 2010 are from Ex-ante Evaluation Summary. The figures for the suspected cases between 2008 and 2010 are from "Measles and Rubella cases confirmed by laboratory and others, Viet Nam, 2003-2011", WHO, 2011. The figures for the confirmed cases between 2005 and 2008 are from the above WHO document and the questionnaire answer from NIHE. The figures for the confirmed cases for 2009 and 2010 are from the above document from WHO.

Note: The prevalence rate is the figure calculated by NIHE based on the number of confirmed cases.

3.4.2 Other Impacts

3.4.2.1 Impacts on the Natural Environment

No major problem has been observed regarding the impacts on the environment. Every year, POLYVAC has passed the environmental inspection by the Hanoi People's Committee. Among

24 Source: Interview with NIHE.

the Working Groups which will be explained in the section of sustainability later, Environment Pollution Management Working Group and Environment Monitoring Working Group are responsible for environment issues.

3.4.2.2 Land Acquisition and Resettlement

There was no resettlement of residents. No problem has been observed with the land acquisition process.

3.4.2.3 Impacts on the Research and Development of Rota Virus Vaccines

Since 2000, POLYVAC has promoted research and development of vaccines against Rota Virus, which induces diarrhea. It was confirmed that the knowledge and experiences in GMP management, which was acquired through this Project and the TC Project, is useful in the research and development of Rota Virus vaccines. In Viet Nam, about half cases of diarrhea of under-five children have been caused by Rota Virus. The vaccines against the Rota Virus has not been produced domestically, thus vaccines of seven dollar per dose has been imported[25]. POLYVAC is currently applying to the MoH for the manufacturing and sales license of the Rota Virus vaccines. If POLYVAC obtains the license, then it is possible to supply the vaccines at the reasonable price in stable manner as a single manufacturer for the vaccines in Viet Nam.

In light of the above, the indicators of the indirect effects almost achieved those targets.

Since it is possible to measure the contribution of this Project to the achievement of the impact indicators only after 2010, it is difficult to evaluate it at present. However, there is a possibility that this Project will contribute more to the impact indicators in the future because the proportion of supply of POLYVAC vaccines to the total supply in Viet Nam has been increasing year by year. As other impact, the knowledge and experiences in GMP management, which has been obtained by this Project, have been applied in the production and management of other types of vaccines. No particular negative effects were observed.

3.5 Sustainability (Rating:③)

3.5.1 Structual Aspects of Operation and Maintenance

Whereas the number of staff working for measles vaccine production was sixty three at the time of planning, that of the time of ex-post evaluation is sixty four. The number of staff meets the requirement in carrying out operations in accordance with the GMP. The GMP management consists of the three departments: Project Management (PM), Quality Control (QC) and Quality Assurance (QA), and the responsibility of each department is clear. Seven working groups[26] are

25 Source: Interview with WHO.

26 Established working groups so far include the followings: 1) Calibration/validation, 2) Formalin

responsible for each specialized mandate in cooperation with the above departments. For example, Risk Management Working Group, in collaboration with QC and other related departments, identifies the causes of anomalies and deviations, discusses and decides the counter-measures and preventive measures, and shares the decisions and the information in the organization.

3.5.2 Technical Aspects of Operation and Maintenance

All the required documents for GMP such as the Standard Operating Procedures (SOP) and validation have been prepared, and the operations have been almost carried out in accordance with the GMP. GMP assessment is conducted every two years, and POLYVAC passed twice in 2008 and 2010. The next GMP assessment will be the first one after the TC Project and the follow-up cooperation, thus it will become a touchstone for the future of POLYVAC.

As contributing factors for POLYVAC to maintain such high skills, the following three points were identified:

1) two-thirds of the staff working in the measles vaccine production is the staff who has experiences in the production of polio vaccines;
2) the staff has strong commitment and motivation for learning as know from the fact that the staff turn-over rate is low[27] and that they learn Japanese from their own motivation; and
3) the staff has been keen to observe the GMP strictly under the supervision of the Kitasato Institute during the TC Project and the follow-up cooperation.

On the other hand, at the time of Terminal Evaluation of the TC Project, following challenges remained for POLYVAC: the response to anomalies and deviations, reasonable materials and test kits for the reduction of production costs, and change validation in the production process. For this objective, the follow-up cooperation for technical transfer was implemented between April 2010 and March 2011. The situation in the last half year is described as below.

1) Production record and sanitation record in the final production process have been continuously kept in daily operation;
2) In the late 2010, anomalies and deviations occurred due to the biological contamination during the bulk production process. Because the response was not satisfactory, guidance was provided for investigating causes and for taking steps to

Fumigation, 3) Environmental Pollution Control, 4) Environment Monitoring, 5) Procurement Control, 6) Risk Management, 7) Document Control, 8) Clinical Trial, and 9) Pre-qualification. WG-2 and WG-8 finished their tasks, and WG-9 was established in 2010.

27 0.017% excluding the retired.

prevent similar incidents in future by the Japanese experts during the follow-up cooperation. The direct cause was that the top of the culture bottle was loose, and the indirect cause was that the young staff was in charge of the process after the retirement of the skilled staff;

3) Change validation has been almost properly conducted in accordance with the change control procedure. However, for example, a trouble occurred because the procedure was not followed before changing the manufacturer of test materials for the bulk production. During the follow-up cooperation, it was instructed to obtain test lot in advance and to follow change control procedure;

4) Training has been conducted in accordance with the annual training plan. Because the individual training records had not been fully filled, it was recommended in the follow-up cooperation report that format of the individual training records be improved in order to understand better the skill level of each person.

3.5.3 Financial Aspects of Operation and Maintenance

(1) Cash Flow Status of POLYVAC

The production and procurement plan for EPI vaccines are managed by NIHE under the supervision of the MoH, thus POLYVAC receives orders from NIHE and supplies NIHE with the products. POLYVAC is supposed to cover the O&M costs by the revenue. There is no plan for privatization for the time being. In case that the financial situation becomes worse, it is expected that the government provides support. Cash flow statement of POLYVAC is shown in Table 8.

Table 8 - Cash Flow of POLYVAC

(Unit: million VND)

	Items	2008	2009	2010	Prospect for 2011
Income	Subsidy from MOH	16,000	12,273	0	0
	Total Sales Income	9,284	16,351	23,802	34,864
	Measles vaccines	NA	7,109	10,983	16,667
	Polio vaccines	NA	6,585	11,235	16,397
	Other income	NA	2,657	1,800	1,800
	Total Income	25,284	28,624	23,802	34,864
Expenditure	Operation cost	24,684	27,637	25,070	28,646
	Maintenance cost	582	727	619	954
	Total Expenditure	25,266	28,364	25,689	29,600
Surplus/Deficit		18	260	-1,887	5,264

Source: POLYVAC Questionnaire Answer

As shown above, although there have been surpluses from operating activities in 2008 and 2009, POLYVAC experienced deficit in 2010. The reasons for deficit include the

followings: sales of measles vaccines remained as little as 200 million doses, and the counterpart funds from the MoH were terminated along with the completion of this Project and the TC Project. However, it is expected that surpluses equivalent to twenty million JPY is created along with the increase in sales to 3.2 million doses in 2011. Furthermore, as GAVI will terminate its assistance in providing imported vaccines in 2012, there is a prospect that sales income will increase along with the increase in sales after 2013. After 2013, if MR vaccines are introduced and if POLYVAC cannot produce MR vaccines, then its income may decrease. On the contrary, if environment enables POLYVAC to produce MR vaccines, its income may increase because the unit price of MR vaccines is higher than that of measles vaccines.

Looking at POLYVAC as a whole, the income from polio vaccine department is stable. It can be judged that management base of POLYVAC may not be at risk even if measles vaccine department experiences slight deficit.

The production costs and purchase price are shown in Table 9. The estimated production cost at the time of planning (twenty four JPY), is almost the same as the estimated production cost (twenty two JPY) as of now based on the case of producing the full capacity of 7.5 million doses per year. However, because the annual production quantity remains as little as two to three million doses per year, the actual production cost is estimated twice or more than the planned costs. The reason why the production costs are expensive is that the many kinds of test reagents were imported from Japan.

During and after the follow-up cooperation, POLYVAC has been trying to reduce the production costs through the change validation of test reagents and kits. Nevertheless, there is a limitation due to the following reasons: 1) the order remains as little as two to three million doses; and 2) it is necessary to take required steps to replace test reagents and to change production process in order not to cause anomalies and deviations from the GMP.

Table 9 – Unit price of production costs and purchase price

	Unit price of production cost			Sales price approved by the Ministry of Finance	Purchase price by MoH in 2010
	Estimate at the time of planning	In the case 5 million doses are produced	In the case 7 million doses are produced		
VND	NA	9,474	5,674	7,420	5,491
JPY	24	37	22	29	21

Source: The estimate is from the Basic Design Report, and others are from documents by POLYVAC.
Note: The estimate at the time of planning is that estimated based for the second year and beyond after the integrated production from seed virus started. The actual JPY was calculated based on the following exchange rate: 1 VND = 0.003890 JPY as of April 2011.

Although POLYVAC needs to make continuous efforts in reducing production cost, it can be

said that there is no problem in financial aspect for the following reasons: 1) there have been surpluses from operating activities in the past four years except 2010; 2) it can be judged that surpluses are secured if the current level of production amount (3.2 million doses/year) is maintained; 3) the management base of POLYVAC is stable as a whole; and 4) in case that the financial situation becomes worse, it is expected that the government provides support.

3.5.4 Current Status of Operation and Maintenance

Cleanliness of the facility, control of areas in accordance with the bio-safety, and wearing protective suits are strictly maintained. The equipment, spare-parts, raw materials and consumables are properly managed by the control system. The procurement of the materials and spare-parts are controlled by the Procurement Management Working Group appropriately. In general, operation and maintenance status of the facility and equipment is satisfactory. Although there are following problems, actions have been undertaken by either POLYVAC itself or under the follow-up cooperation, thus those problems are expected to be solved.

1) Some problems such as the distortion of connection pipes due to the subsidence of the buildings without bearing piles along with the land subsidence in Hanoi City, the distortion of drainage pipes along with the land subsidence in the compound, cracks in the buildings, etc. In order to respond to these issues, the follow-up cooperation for facility and equipment was implemented from January 2011 to August 2011;
2) one of the CO_2 incubators has not been used because the grass door is broken, but it can be used after the grass door is provided by the follow-up cooperation;
3) Because Incubator D could not perform the expected functions at the Performance Qualification (PQ) test, it has not been used. POLYVAC purchased the same type of incubator, and has been using. Incubator D has been used for drying grass equipment in the cleansing room in the QC Department.; and
4) There was no job register of the calibration equipment, thus the Japanese consultant instructed the staff to prepare a job register during the follow-up cooperation.

Freeze Dryer

Indicators of temperature of each facility

Shelf of spare-parts with spare-parts list

In light of the above, sustainability of the project is fair considering the following three aspects: 1) in the past six months, the response to anomalies and deviations was not satisfactory, and validation for reducing production cost was not properly carried out in accordance with the change control procedure, but no major technical problems are currently observed; 2) although POLYVAC needs to make continuous efforts in reducing production cost, there is no major problem with the financial aspect; and 3) although there are some problems with the status of the O&M, those are expected to be solved by the follow-up cooperation and so on.

4. Conclusion, Recommendations and Lessons Learned

4.1 Conclusion

This project has been highly relevant with the Viet Nam's development plan and Japan's ODA policy. Regarding development needs, there is a gap between the amount of measles vaccines which was regularly required at the time of planning and that of the time of ex-post evaluation. However, considering comprehensively that the number of cases of measles is still the highest among the six major infectious diseases of children at the time of ex-post evaluation, that outbreaks occur every few years, that the urgency of the project for providing stable supply of domestic measles vaccines is high and that the decrease in the required amount is due to the external factor which was not expected at the time of planning, it can be said that its relevance is high. Both project cost and project period were mostly as planned, therefore efficiency of the project is high.

This project established the physical and technical production capacity of 7.5 million doses per year of measles vaccines, which meet the World Health Organization (WHO) - Good Manufacturing Practice (GMP), and achieved its objective to provide stable supply of the vaccines. Synergy effect with other projects has also been observed. On the other hand, the annual production quantity of measles vaccines at the time of ex-post evaluation is approximately 3.3 million doses, which is equivalent to 44% of its target at the time of planning or to 67% of its demand (required amount for regular vaccination) at the time of ex-post evaluation. The reason why the production amount remains 67% of its demand is that imported vaccines have been used for the second dose of regular vaccination, and this is an external factor for the executing agency. However, the government could have decreased imported vaccines for regular vaccination and could have increased the purchase amount of measles vaccines manufactured by POLYVAC as a counter-measure for 2010 and beyond. Although it was confirmed that it is possible that the annual production amount increases in the future, the effectiveness of the project at present is fair. Since it is only after 2011 when it is possible to measure the contribution of this Project to the achievement of the impact indicators, it is difficult to evaluate it at present. However, the indicators of the expected positive indirect effects such as the ratio of two-dose vaccination of measles almost achieved those targets. No

major problems have been observed in the operation and maintenance system, therefore sustainability of the project effect is high. In light of the above, this Project is evaluated to be highly satisfactory.

4.2 Recommendations

4.2.1 Recommendation to POLYVAC

Continuous efforts in enhancing the response to anomalies and deviations, reducing the production cost and human resource development (Effectiveness and sustainability)

It is recommended for POLYVAC to make continuous efforts towards the GMP inspection in 2012, paying attention to the learning from the follow-up cooperation including the following three points:

1) to strictly follow the change control procedure without fail before replacing materials with more reasonable ones in order to prevent anomalies and deviations;
2) to repeat in-house training in accordance with the annual training plan as well as to develop the staff who are expected to teach subordinates in future; and
3) to improve the formats of the training records in order to understand the individual technical level properly.

4.2.2 Recommendations to the Ministry of Health (MoH)

(1) Review of purchase price of measles vaccines

If the purchase amount of measles vaccines from POLYVAC by MOH continues to be limited and if POLYVAC continuously experiences deficit, it is recommend for MOH to consider increasing the purchase price.

(2) Efforts for Strengthening National Regulatory Authority (NRA)

It is recommended for the MoH to make further efforts in obtaining the accreditation of the NRA in accordance with the roadmap for strengthening NRA, which was agreed in May 2011.

(3) Build a framework for introducing MR vaccines

As mentioned in the section of relevance, there is an urgent need for preventing not only measles but also rubella. If the government of Viet Nam officially adopts a policy to replace the second dose of measles vaccines with MR vaccines after 2013, it is required to build a framework to implement the policy. For example, it is required to precisely estimate the MR vaccines amount based on the target population, to review how to obtain the vaccines, to estimate the cost and to secure the budget, to provide a domestic vaccine manufacturer with technical and financial support required for establishing technology in

producing MR vaccines, and to secure required budget for purchasing domestically produced vaccines.

4.2.3 Recommendations to JICA

(1) Assistance in building a framework for introducing MR vaccines (Effectiveness and sustainability)

If there is a request from the government of Viet Nam for establishing a production technology of MR vaccines in a domestic vaccine manufacturer, it is one of ideas for JICA to consider transferring the production technology of MR vaccines from the perspectives of effectiveness and sustainability.

(2) Strengthening National Regulatory Authority (NRA)

In cooperation with the government of Viet Nam, WHO and UNICEF, it is recommended for JICA to support four relevant agencies of NRA in taking necessary steps in stable manner towards the NRA official assessment along with the roadmap for strengthening NRA.