FACULTY OF PHARMACY MAHIDOL UNIVERSITY

Economic Feasibility Study of Vaccine Production in Thailand

2012

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This report was commissioned by the World Health Organization (WHO), country office, Thailand

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Acknowledgments

I would like to express my gratitude to the following, for their useful suggestions and assistance:

- WHO Thailand office, for the research grant.
- Department of Disease Control: Dr. Suwanchai Wattanayingcharoen, Vice Director of the Department of Disease Control, for providing valuable comments.
- National Vaccine Institute: Dr. Charung Muangchana, director, and Dr. Unchalee Siripitayakunkit and staff of the National Vaccine Institute, for facilitating the project and providing comments.
- Government Pharmaceutical Organization:

  Mr. Somchai Srichainak, Deputy Director

  Mr. Sit Thirapakpoomanunt, Senior Expert

  Mr. Chakkrit Prapaipittayakun, Acting Director of Biological Product Department

  Mr. Ruengchai Kaweepornpoj, Head of Administration, Biological Product Department

  Mr. Pattharachai Lakornrach, Head of JE Production Section

  Mr. Chanasak Dechkum, Acting Head of Bacterial Vaccine Division

- Graduate students of the Mahidol University Pharmacy Administration Program: Ms. Siriporn Pooripussarakul, Ms. Tuangrat Phodha, Ms. Onwipa Rochchanathimoke and Ms. Chadarat Issararak, for data collection.

Executive Summary

The Thai cabinet approved the national agenda on vaccines in 2011. Vaccine production is a major part of the agenda. The goal is to strengthen the country's ability to produce vaccines for preventable diseases. To have evidence for planning and management, a feasibility study is required. This study aims to: develop an analysis model for an economic feasibility study of vaccine production; to develop an Excel-based template for an economic feasibility study of vaccine production; and to conduct preliminary analysis of the economic feasibility of vaccine production in Thailand. The study covers nine vaccines for diseases, i.e. diphtheria, tetanus, pertussis, acellular pertussis, hepatitis B, BCG (tuberculosis), dengue, Japanese encephalitis (JE) (cell-derived), and live attenuated JE. Descriptive feasibility analysis in terms of demand-supply mapping covers all nine vaccines. Cost-benefit analysis covers only three production programs, i.e. JE, DTP-HB (diphtheria/tetanus/pertussis–hepatitis B), and DTP-dT-TT (diphtheria/tetanus/pertussis–diphtheria/tetanus–tetanus toxoid).

Analysis of demand focused on countries in South and Southeast Asia. It was found that demand in terms of number of births was far beyond the production outputs of the various programs. In terms of supply, we found that the vaccine market is an oligopoly. There are producers both in Asian and Western countries. Cost-benefit analysis was employed as a method of economic feasibility analysis. Costs were composed of capital or investment costs (or fixed costs) and operating costs (variable costs). In addition to durable assets, cost of research and development or start-up cost, e.g. training, were categorized as capital costs. Benefits or revenue was determined by multiplying the unit price and the expected sold units of the vaccines. The

expected sold units were based on anticipated production units adjusted by production waste rate. All costs and benefits were discounted to present value. The program will be considered viable when net present value is more than zero. Analyses of each production program generated two extreme scenarios, scenario 1 and scenario 2. We found that scenario 1 of all programs resulted in loss benefit (costs higher than revenue). On the other hand, scenario 2 of all programs resulted in gain benefit (costs less than revenue).

Based on these findings, in addition to the local market, South and Southeast Asian countries can be potential markets as well, so the scale of production can expand in order to increase efficiency. For economic feasibility in terms of cost-benefit analysis of the programs, the findings were inconclusive. Scenario analysis found both positive and negative benefits. This was based on internal and external factors. Internal factors are related to resources used and efficiency of production (production waste). External factors are market prices and discount (interest) rate. Therefore, the programs have to be carefully implemented. This preliminary analysis and the analytical model can be a useful tool for program implementers and policy makers for decision making in adopting and monitoring the programs.

End-of-project status

This project was planned to be implemented from 4 March 2011 to 31 December 2011. However, this schedule was disrupted by major flooding in Thailand. Therefore, an extension was offered until 15 March 2012. The aim was to conduct an economic feasibility study of vaccine production in Thailand. Specific objectives were to develop an analytical model and an Excel-based template, and to conduct preliminary analysis of the economic feasibility of vaccine production in Thailand. All objectives mentioned were achieved by the end of the project. The research grant was used as planned. The final delivered project consists of a full report and a CD

containing cost-benefit analysis models. This material should be useful for stakeholders in the planning and management of vaccine production.

Data on use of resources

A summary of disbursement data was provided. The budget was expensed as planned without any problem.

Lessons learned

Economic feasibility analysis is related to business management. In business, a management plan is usually confidential. Although the study institute in this project is a state enterprise, the institute's staff was reluctant to provide information. To compromise, the analyses were conducted based on ranges of parameters. The findings are presented as a range of the final outcome. This could improve cooperation from the study institute.

Economic Feasibility Study of Vaccine Production in Thailand

Vaccination has been one of the most effective interventions for decreasing mortality and morbidity due to infectious diseases: for example, diphtheria, tetanus, polio and influenza. In Thailand, smallpox has been eradicated since 1962. Diphtheria and polio are expected to be eradicated in the near future. Mass immunization programs have been implemented for the control of tuberculosis, diphtheria, tetanus, pertussis, mumps, measles, rubella, hepatitis B, Japanese encephalitis, influenza and rabies.[1] Early vaccination programs have shown effectiveness and cost-savings in children.[2] This success of vaccination is threatened by several factors, such as research and development in vaccinology, investment, and potential markets for a vaccine. The common obstacles to new vaccine introduction include affordability, manufacturing capacity, accessibility, and quality assurance.

In the past, Thailand produced vaccines for smallpox, cholera, typhoid, diphtheria, tetanus, pertussis, BCG (tuberculosis) and JE (Japanese encephalitis). At present, due to good manufacturing practice (GMP) requirements and limitations of investment, only BCG and JE vaccines are produced, by Queen Saovabha Memorial Institute and the Government Pharmaceutical Organization (GPO), respectively. Thailand spends about 3 billion baht each year on vaccine procurement by government and private sectors; and 80% of vaccines are high-priced vaccines imported from other countries.[3] Due to the fluctuation of politics, limited budget, social concerns, and emerging and re-emerging diseases, importing vaccines may result in high costs, scarce supply, and risk in controlling epidemic diseases.[3] Also, neighboring countries, e.g. India, Vietnam and Indonesia, have invested in vaccine production for their own countries as well as for export. On 20 April 2011, the Thai cabinet approved the national agenda on vaccination. Vaccine production is a major part of the agenda. The goal is to strengthen the country's ability to produce vaccines for preventable diseases. The plan includes recommendations for human resources, research and

development, infrastructure development, and local production of vaccines. As part of the overall 10-year plan, nine vaccines for seven diseases are targeted as follows: four-year plans for diphtheria, tetanus, pertussis, and hepatitis B; five-year plans for BCG, acellular pertussis, and JE (cell-derived); and ten-year plans for dengue and live attenuated JE. Vaccines produced under this scheme will be sufficient for at least 800,000 newborn babies a year.

To obtain evidence for planning and management, a feasibility study is required. A feasibility study is an evaluation of a proposal, designed to determine if a business or project opportunity is possible, practical and viable.[4-6]

Objectives

This study aimed to conduct an economic feasibility study of vaccine production in Thailand. Specific objectives were to develop an analytical model and an Excel-based template, and to conduct preliminary analysis of the economic feasibility of vaccine production in Thailand.

Methodology

Study design: The project was designed as an economic feasibility study.

Study population: Institutes responsible for production of 9 vaccines under the national agenda.

Scope of the study: Nine vaccines for seven diseases, i.e. diphtheria, tetanus, pertussis, acellular pertussis, hepatitis B, BCG, dengue, JE (cell-derived), and live attenuated JE.

Process of the study: The project was composed of the following activities:

1. Systematic review of an economic feasibility study; the PubMed database was searched to retrieve articles relating to economic feasibility studies of vaccines.

2. Model development of an economic feasibility study; from the review, a model of economic feasibility was constructed for this study.
3. Supply-demand mapping. Global production of the target vaccines was reviewed. Target groups of customers both in Thailand and the potential international market were estimated. Based on these estimates, demand for the vaccines was forecasted.
4. Economic analysis of the vaccines; a systematic review of the efficacy of the vaccine, including cost-of-illness and cost-effectiveness analysis.
5. Estimation of costs of research and development (R&D); costs of R&D for all vaccines were reviewed. In addition, a field study was conducted by interview.
6. Cost-benefit analysis (CBA) of vaccine production was conducted.
7. An Excel-based template for the CBA was developed and transferred to stakeholders.

Cost-benefit analysis

Data were analyzed and presented in terms of total cost of each component, proposed price of the vaccine, and net present value. Sensitivity analysis was also conducted.

Expected benefits of the study

Thailand's National Vaccine Institute will use the results for management of the 10-year plan under the national agenda. Institutions responsible for vaccine production will have the knowledge and tools (Excel-based software) for economic feasibility analysis to monitor their action plans.

Results

Review of feasibility study

A product development plan involves many disciplines, including preclinical, clinical, post-marketing, and project management.[7] The key factors for successful vaccine production

are an understanding of the epidemiology and immunology of disease when proposing a vaccine design. Thus, it is necessary to determine whether a project opportunity is possible, practical and viable before starting the project.

A feasibility study can be categorized into economic or financial, technical or technological, and administration or management.[5, 6, 8-10]

Administration analysis

Common obstacles to new vaccine introduction in resource-limited countries are affordability, manufacturing capacity, accessibility, and quality assurance. Successful vaccine development requires both public and private financing, the latter making it possible to transform the science into a product that can be manufactured and sold on a large scale.[11] In poor countries, poverty leads to lack of demand for the creation of innovative health products.[12] Thus the prospective market for products needed in developing countries is commercially unattractive or offers an unfavorable return on investment (Figure 1).[13] Companies will naturally focus on areas that offer higher return on investment. Several factors make it difficult to attract the necessary investment in commercial research and development (R&D) for neglected diseases, including perceived and actual low market returns for these investments, distribution challenges in countries with poor health care infrastructure, and lack of awareness about these diseases in more developed countries.[14] Yet the health gap between industrialized and developing countries continues to widen. Although the private sector has exploited new technological capabilities for creating new drugs and vaccines directed primarily at chronic diseases common in industrialized countries, innovative pharmaceuticals have not been developed to treat neglected diseases in the developing countries.[14] For example, while malaria, tuberculosis (TB) and acquired immunodeficiency syndrome (AIDS) are killing millions and threatening the economic

stability of nations, there are a limited number of drugs and vaccines available to treat these diseases in developing countries.[14] Thus, a balance between R&D and commercialization is necessary in order to change health system, either by the reduction of commercial expenditures or increased prospects of revenue.

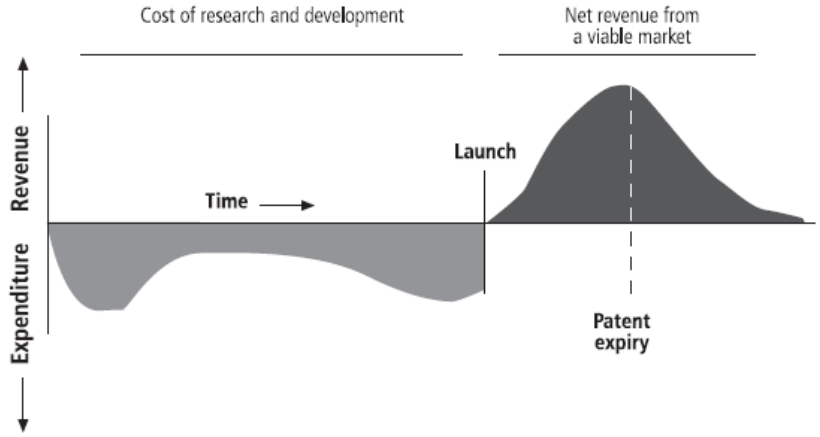

Figure 1 Industry costs and revenue associated with product development

The potential markets for vaccines are diverse, and predictive of the level of investment. Companies that usually devote the most resources to the development of a vaccine believe that there will be a substantial market in industrialized countries. They also consider the development path to be one of rapid uptake in industrialized countries but slow uptake in developing countries. However, if the potential market in industrialized countries was considered to be small, companies would be less likely to invest their resources in the development of a particular vaccine.

Views on the potential markets in developing countries are divided into two different outlooks. Smaller biotechnology companies with limited or no experience in supplying vaccines assume that there will be substantial markets in developing countries and that sales would be adequate if an effective vaccine were developed. In contrast, larger companies

already supplying vaccines for the global market attach little or no commercial value to markets in developing countries.

Technical and technological analysis

Improved knowledge of immune response mechanisms has brought about successes in vaccine development that offer protection against challenging pathogens. Systems biology is an interdisciplinary approach that systematically combines knowledge of a biological system to enable the prediction of the safety and effectiveness of vaccine.[15] Systems biology approaches applied to clinical trials can lead to the generation of new hypotheses that can be tested and ultimately lead to developing better vaccines (Figure 2).[16] Immune responses to vaccination in clinical trials can generate hypotheses about the biological mechanisms of a vaccine. Such hypotheses can then be tested in animal models or *in vitro* human systems. The results from such experiments can then guide the design and development of new vaccines. Such a framework seeks to bridge the gaps between clinical trials and discovery-based science, between human immunology and animal immunology, and between translational and basic science, and offers a continuous process of scientific discovery and vaccine invention.

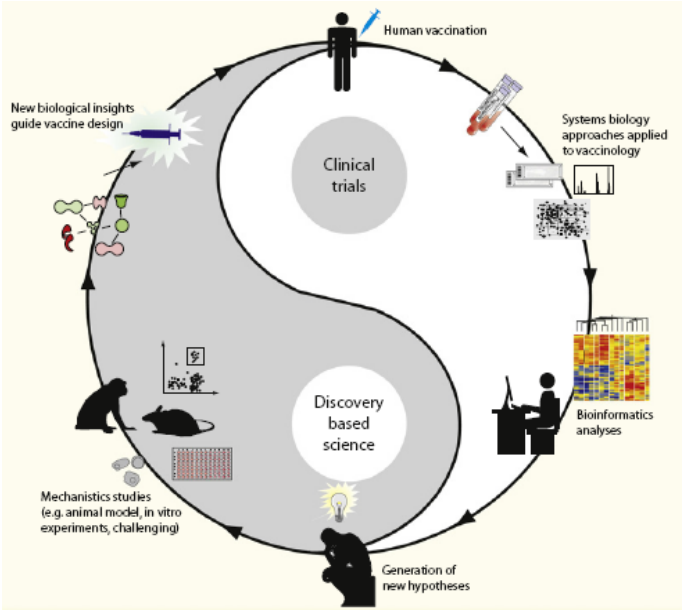

Figure 2 A framework for systems vaccinology

New vaccine technologies have resulted in protection against a wide range of communicable diseases, reducing the required number of injections, and improving safety and purity.[15] These technologies include cell culture, recombinant DNA technology, conjugation, combinations of vaccines, and new adjuvants (Table 1). After the introduction of new vaccines, the assessment of their real-world safety and effectiveness profile should be a matter of concern. The effectiveness of a vaccine dose does not vary geographically, but epidemiological characteristics of diseases may vary accordingly. For many pathogens, disease characteristics may also vary over time. Development of regulatory and manufacturing mechanisms to assess safety and effectiveness post-licensure are necessary to improve public confidence and increase vaccine acceptance and use.

Table 1 Vaccine technologies

Period	Cell culture	Recombinant DNA technology	Conjugation	Combinations	New adjuvants
1980s	Rabies	Hepatitis B	Hib	-	-
1990s	JE, varicella, hepatitis A, rotavirus	Acellular pertussis	Men C	DTP-Hib Hib-Hepatitis B DTaP-Hib	Influenza
2000s	Live influenza, rotavirus, herpes zoster, H1N1 influenza	HPV	PnC-7 PnC-10 PnC-13 Men ACWY	Hepatitis B and hepatitis A; DTaP-IPV and hepatitis B; Men ACWY; MMRV	HPV H1N1 influenza

JE = Japanese encephalitis; HPV = human papillomavirus; Hib = *Haemophilus influenzae* type b; Men C = meningococcal group C conjugate; PnC = pneumococcal conjugate; Men ACWY = meningococcal conjugate for groups A, C, W-135, and Y; DTP = diphtheria, tetanus and pertussis; aP = acellular pertussis; IPV = inactivated polio vaccine; MMRV = measles, mumps, rubella and varicella combination

Developing countries are now concentrating on the manufacture of the standard World Health Organization/Expanded Programme on Immunization (WHO/EPI) antigens (diphtheria, tetanus, pertussis, measles, BCG and oral polio vaccines) for local consumption. But over the last 15 years, several manufacturers in developing countries have worked with WHO and the United Nations Children's Fund (UNICEF) to officially "prequalify" their products for global distribution.[17] In the mid 2000s there was a global shortfall of influenza vaccine, and the production of influenza vaccine had to be expanded to developing countries. A major challenge was the need for rapid transfer of technology to ensure adequate production capacity. WHO has since facilitated technology transfer from established manufacturers or other technical sources for the rapid expansion of production of egg-based killed and live attenuated influenza vaccines.

Economic and financial analysis

In economic evaluation, the costs and consequences of a vaccination program are much broader than acquisition costs.[18] The comparisons between a new vaccine and the existing vaccine or no vaccine are conducted using clinical and economic data from clinical trials or modeling. There are three main forms of economic evaluation: cost-effectiveness analysis (CEA), cost-benefit analysis (CBA), and cost-utility analysis (CUA). CEA measures total net cost per unit of health outcome. CBA measures costs and consequences in monetary units. CUA measures total net costs per health outcome in terms of utility, such as quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs).[18, 19] There are many issues that may be problematic in economic evaluations, including indirect costs, herd immunity, utility, threshold, policies, perspectives, discount rate, and modeling.

Economic analysis is the most frequently used method for evaluating the efficiency of a new system. More commonly known as cost-benefit analysis (CBA), the procedure is to determine the benefits and savings that are expected from a candidate system and compare

them with costs. If benefits outweigh costs, then the decision is made to design and implement the system. An entrepreneur must accurately weigh the costs versus benefits before taking action.[13] CBA can be categorized into cost-based and time-based studies. Cost-based studies are important for identifying cost and benefit factors, which can be further categorized into development costs and operating costs. A cost-based study consists of an analysis of the costs to be incurred in the system and the benefits derivable out of the system. A time-based study is an analysis of the time required to achieve a return on investment. The future value of a project is also a factor.

Table 2 presents a summary of the criteria for a feasibility study of vaccines.[7, 12-14, 20]

Table 2 Criteria for feasibility study of vaccines

Administration criteria	Technical criteria	Economic criteria
Affordability 1. Price of medicines - Pricing policies and controls 2. Price of services - Price at point of use, including distributor mark-ups 3. User's income 4. Resources for financing	Product plan 1. Burden of disease 2. Product for prevention or treatment 3. Type-specificity of vaccine and formulation 4. Target population 5. Efficacy and safety profile 6. Age for immunization	Economic evaluation 1. Cost-benefit analysis 2. Cost-effectiveness analysis 3. Cost-utility analysis
Acceptability 1. Quality of products - Assurance of quality 2. Quality of services - Rational selection - Appropriate prescribing - Appropriate use, including patient compliance	Availability 1. Basic research 2. Discovery 3. Development 4. Marketing 5. Licensure	Market forecast Return on investment Regulatory issues Reimbursement Prices of competing products

Administration criteria	Technical criteria	Economic criteria
3. User's beliefs and attitudes - Social norms - Educational interventions - Variations with socioeconomic status of potential consumer acceptability		
Accessibility 1. User's location 2. Location of drug outlets 3. Infrastructural functionality, e.g. road networks 4. Distribution channels	Acceptability 1. Dosing schedule, volume, and number of doses 2. Concomitant use with other vaccines 3. Single or combination vaccine 4. Formulation-specific device	
Physical availability 1. Medicine supply 2. Medicine demand 3. Supply-chain efficiency 4. Reliable sources of supply 5. Availability where needed		

Model development for an economic feasibility study

CBA is composed of the costs and benefits of the program. Costs are composed of cost of research and development, cost of production, and cost of management and marketing activities. Benefits are from revenue of products sold. To calculate revenue, unit price is estimated from the market price, or from the break-even price based on cost-effectiveness analysis (CEA) in case there is no market price. In this situation, cost-of-illness analysis is needed for CEA and for policy makers to estimate disease burden (Figure 3).

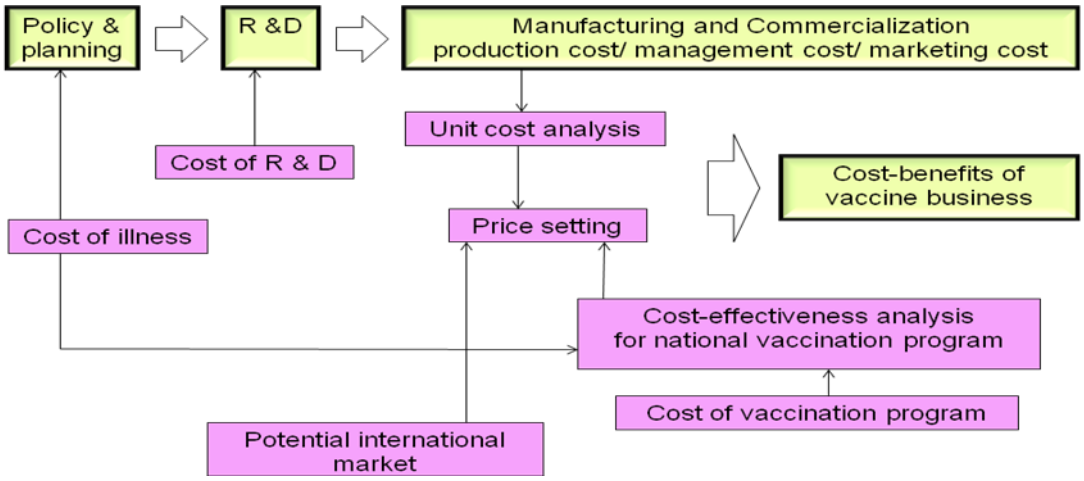

Figure 3 Conceptual framework of economic feasibility study of vaccine production

Demand-supply mapping

To explore feasibility, a descriptive analysis of demand and supply is also useful. For a national immunization program (NIP), the number of annual births in target countries could reflect the size of the potential market. This study focused on countries in South and Southeast Asia. In Table 3, demand is presented in terms of population, number of annual births, and Global Alliance for Vaccines and Immunization (GAVI) eligibility by country.[21] In addition to the number of births, information on vaccines under the NIP reflects real potential customers (Table 4).

In terms of supply, current producers of target vaccines and market prices are presented in Tables 5 and 6. The prices presented were from the following sources:

- purchasing prices of the National Health Security Office (Thailand)[22]
- UNICEF purchasing prices[23]
- CDC vaccine prices[24]

Most of the producers are based in developed countries. There are some producers in Asia, i.e. India, Indonesia, Japan and Korea.

Table 3 Details of potential markets

Country	Population	Annual Births	GAVI-eligible
Southeast Asia			
Brunei	400,000	8,000	no
Cambodia	14,805,000	367,000	yes
Indonesia	229,965,000	4,174,000	no
Laos	6,320,000	172,000	yes
Malaysia	27,468,000	550,000	no
Myanmar	50,020,000	1,016,000	yes
Philippines	91,983,000	2,245,000	no
Singapore	4,737,000	37,000	no
Thailand	67,764,000	977,000	no
Timor-Leste	1,134,000	46,000	no
Vietnam	88,069,000	1,485,000	yes
South Asia			
Bangladesh	162,221,000	3,401,000	yes
Bhutan	697,000	15,000	no
India	1,198,003,000	26,787,000	yes
Maldives	309,000	6,000	no
Nepal	29,331,000	730,000	yes
Pakistan	180,808,000	5,403,000	yes
Sri Lanka	20,238,000	364,000	no

***** Eligibility for Global Alliance for Vaccines and Immunization (GAVI) support in 2011 is determined by a gross national income (GNI) per capita below or equal to US$1,520 (according to World Bank data for the latest available year).

Table 4 List of production-target vaccines in the national immunization program

Country	BCG	DT	DTwP	DtwPHep	DTwPHep	DTwPHibHepB	HepB	TT	Td	Tdap	JE	Dengue
Southeast Asia												
Brunei	/	/					/					
Cambodia	/				/		/	/			/	
Indonesia	/	/			/		/	/				
Laos	/					/	/	/				
Malaysia	/	/	/			/	/	/			/	
Myanmar	/		/				/	/				
Philippines	/		/			/	/	/				
Singapore	/						/		/	/		
Thailand	/		/	/			/		/		/	
Timor-Leste	/		/					/				
Vietnam	/		/				/	/			/	
South Asia												
Bangladesh	/		/					/				
Bhutan	/			/		/		/				
India	/	/	/				/	/			/	
Maldives	/	/	/				/	/				
Nepal	/				/			/			/	
Pakistan	/					/		/				
Sri Lanka	/	/	/			/	/	/	/		/	

Table 5 Price of vaccine/dose in 2010 (US$)

Manufacturer	Producing country	BCG-20	DT-10	DTP-10	DTP-20	DTPHepB-10	DTwPHib-10	DTwPHibHepB-1	DTwPHibHepB-2	DTaP-10	DtaPIPV-10	DTaPHepIPV-10	DTaPHibIPV
InterVax	Canada	0.0685	0.0995										
Japan BCG Laboratory	Japan	n/a											
Sanofi Pasteur	France		20.39	0.4			3.2			23.76			75.33
Serum Institute of India	India	0.057	0.105	0.178	0.141	0.69			2.25				
Statens Serum Institut	Denmark	0.138											
PT Bio Farma (Persero)	Indonesia			0.16									
Aventis Pasteur Canada	n/a[1]			n/a[2]	n/a[2]								
CSL	n/a[1]				n/a[2]								
GlaxoSmithKline Biologicals	n/a[1]								2.95	21.44	48		
Shantha Biotechnics	n/a[1]					0.72		2.7					
Crucell	n/a[1]							3.2					
Panacea Biotec	n/a[1]							2.965					
Novartis Vaccines and Diagnostics	German						n/a						
Biological E.	India												
LG Life Sciences	Korea												
Merck	USA												
Heber Biotec	Cuba												
GlaxoSmithKline	Germany, Belgium									20.96	48	70.72	
MassBiologics	USA												

n/a[1] = not available (There are production plants in many countries. There is no information on country of production.) n/a[2] = prices are not available in 2010.

n/a = not available (There are production plants in many countries. There is no information on country of production.)

Table 6 Price of vaccine/dose in 2010 (US$) (continued)

Manufacturer	Producing country	HepB-1	Hep-2	Hep-6	Hep-10	TT-10	TT-20	Td-10
InterVax	Canada					0.08	0.05	0.093
Japan BCG Laboratory	Japan							
Sanofi Pasteur	France							
Serum Institute of India	India				0.21	0.07	0.05	0.094
Statens Serum Institut	Denmark							
PT Bio Farma (Persero)	Indonesia					0.09		
Aventis Pasteur Canada	n/a							
CSL Limited	n/a							
GlaxoSmithKline Biologicals	n/a							
Shantha Biotechnics	n/a		0.29	0.34	0.23	0.08		
Crucell	n/a							
Panacea Biotec	n/a							
Novartis Vaccines and Diagnostics	German						n/a	
Biological E. Limited	India						0.03	
LG Life Sciences	Korea	0.4			0.175			
Merck	USA				23.2			
Heber Biotec	Cuba				n/a[2]			
GlaxoSmithKline	Germany, Belgium				21.37			
MassBiologics	USA							15

n/a[1] = not available (There are production plants in many countries. There is no information on country of production.) n/a[2] = prices are not available in 2010.

n/a = not available (There are production plants in many countries. There is no information on country of production.)

Economic analysis of the target vaccines

The review focuses on those vaccines which as of yet have not been included in the NIP. Economic information is useful to forecast the potential of their being included in the NIP, resulting in the possibility of becoming a potential market.

Economic analysis of acellular pertussis vaccine

Pertussis, or whooping cough, is a highly communicable respiratory disease caused by *Bordetella pertussis*. Pertussis occurs mainly in infants and young children. Adolescents and

adults are significant sources of transmission of *B. pertussis* to unvaccinated young infants. Pneumonia is a common complication, while seizures and encephalopathy occur more rarely. Estimates from WHO suggest that in 2008 about 16 million cases of pertussis occurred worldwide, 95% of which were in developing countries, and that about 195,000 children died from the disease [25].

Whole-cell pertussis (wP) vaccines were originally developed from killed bacteria in the 1940s, but they caused serious and permanent nervous system disorders such as convulsions, encephalopathy and hypotonic-hyporesponsive episodes, as well as minor adverse effects such as anorexia, drowsiness, fever, irritability and fretfulness, prolonged crying, vomiting, and local adverse events (e.g. erythema, swelling and injection site pain).[26, 27] This led to a fall in immunization rates, which resulted in an increase in the incidence of whooping cough. Concerns about the safety of wP vaccines prompted the development of acellular pertussis (aP) vaccines in the 1970s. These aP vaccines are less likely to provoke adverse events because they contain purified antigenic components of *Bordetella pertussis*.[27] They have fewer adverse effects (less fever, irritability, and injection site pain) than wP vaccines. The immune response induced by wP and aP vaccines is also different: wP vaccines selectively induce Th1 cells, while aP vaccines induce Th2 cells.[28] For long-term immune responses, these different effects may be masked by subclinical pertussis infection.

In Thailand, a study comparing the immunogenic and economic evaluation of a combined DTP-HB (diphtheria, tetanus, pertussis–hepatitis B) regimen with separate DTP and HB regimens was conducted in Chiang Rai province.[29] To shift from the separate regimen to the combined regimen would cost 1,641 baht for each additional seroconversion. This study was not able to demonstrate that DTP-HB vaccine had more cost savings than the vaccines given separately, as baseline vaccine coverage was already high and cold storage capacity was entirely adequate.

Caro et al. (2005)[30] reviewed the economic burden of pertussis, including direct and indirect costs. Direct medical costs for pertussis would include hospitalizations, emergency room/physician visits, laboratory tests and medications. Direct nonmedical costs would include additional child care provision or travel expenses incurred for medical consultations. Typically the direct costs of pertussis are higher in infants, for whom the disease burden is considerably greater and hospitalization is more common. The direct medical costs of pertussis depend on the rate of hospitalization and the severity of complications, such as pneumonia and encephalopathy, which are highest in infants. The indirect costs of pertussis are a consequence of the illness, even though no direct expenditure has occurred. These include costs associated with time diverted from normal activities (e.g. as a consequence of visits to the physician) and reduced work productivity, both of which may be caused by either individual illness or illness in a family member. Indirect costs can be expected to be relatively higher in adult cases, in whom illness is most directly linked to time lost from paid work activities, but can also be high for cases in infants and young children, where working parents are required to stay at home to care for their children.

Westra et al. (2010) conducted a literature search to estimate the cost-effectiveness of three new immunization strategies: immunization of the infant at birth, immunization of the parents immediately after birth of the child (cocooning), and maternal immunization during the third trimester of pregnancy.[31] Each strategy was compared with the current Dutch pertussis vaccination schedule (5 doses) using an acellular pertussis vaccine. The total pertussis-related costs were estimated at €971,000 (US$1,359,000) and €14,781,900 (US$20,694,700) annually from the payer and societal perspectives, respectively. Pertussis costs per case for infants ranged from €660 (US$900) for infants 11 months of age to €7,060 ($9,900) for newborn infants. From the payer's perspective, the cost-effectiveness of cocooning and maternal immunization were estimated to be similar, with incremental cost-

effectiveness ratios (ICERs) of €4,600 (US$6,400)/QALY (95% CI, €2,200–€17,800 [US$3,100–$24,900]) and €3,500 (US$4,900)/QALY (95% CI, €1,700–€15,000 [US$2,400–$21,000]), respectively. From the societal perspective, cocooning and maternal immunization were estimated to be cost-saving, with savings of up to €7,200 ($10,100) and €5,000 ($7,000) per QALY gained, respectively. This study estimated that both cocooning and maternal immunization were cost-effective (and even cost-saving) interventions that might be added to the current Dutch national immunization program. These estimates were mainly due to reductions in cases among the parents, which likely would not be severe and therefore would remain unreported. Immunization at birth was not cost-effective. Cocooning was the most expensive intervention to implement; however, it resulted in the highest number of QALYs gained (mainly in adults). Maternal immunization would offer better protection of infants, due to maternally acquired antibodies.

Scuffham and McIntyre (2004) compared the potential costs and health consequences of three strategies – a parental vaccination strategy, a birth vaccination strategy and a 1 month vaccination strategy – with the current practice in Australia of commencing vaccination at 2 months.[32] Vaccination at birth was estimated to cost (SD) an additional A$33.21 (SD = A$1.60) per infant and to reduce cases, deaths and DALYs by 45%. Vaccination at 1 month was estimated to cost an additional A$43.24 (A$8.98) per infant and to reduce morbidity by approximately 25%. Parental vaccination at birth was the most expensive alternative, costing an additional A$73.38 (A$4.98) per infant and reducing pertussis morbidity by 38%. The costs per DALY averted were A$330,175 (A$15,461), A$735,994 (A$147,679), and A$787,504 (A$48,075) for the birth, 1-month, and parental vaccination strategies, respectively.

Economic analysis of Japanese encephalitis (JE) vaccine

Japanese encephalitis is a disease that is transmitted from animals to humans by a mosquito vector, *Culex tritaeniorhynchus*. Japanese encephalitis virus (JEV), a mosquito-borne flavivirus, is the most common cause of encephalitis, especially in East Asia, South Asia and Southeast Asia.[33, 34] The virus is transmitted between mosquitoes and vertebrate hosts (e.g. pigs and birds) to humans as dead-end hosts. JEV transmission is seasonal; the disease usually peaks during the rainy season in subtropical and tropical areas.[35, 36] The World Health Organization estimates that there are 30,000–50,000 clinical cases reported annually in Asia. Approximately 10,000 of those die, mostly children under the age of 15 years.[34]

Japanese encephalitis is an important public health problem in Asia, and there is no specific antiviral treatment. Several organizations (e.g. WHO, UNICEF, and the Bill and Melinda Gates Children's Vaccine Program) promote and support introduction of JE vaccine for routine immunization in affected countries.[37] There are three JE vaccines that are used on a large scale: inactivated mouse brain-derived vaccine, inactivated primary hamster kidney cell-derived vaccine, and live attenuated primary hamster kidney cell-derived vaccine (SA 14-14-2 strain). Serious adverse events have not been documented; however there have been reports of mild effects (arm soreness, injection site redness, and swelling) and moderate effects (fever, headache, and myalgia).[35]

The introduction of JE vaccines for routine use in several countries depends on several factors: the disease burden; the availability of resources for vaccine purchase; the acceptability of JE vaccines; vaccine-associated adverse events; the perceptions of policy makers concerning the need for and cost-effectiveness of JE vaccines; and competing public health priorities.[38]

In Thailand, an economic analysis was conducted of a Japanese encephalitis vaccination program in children aged 18 months and 6 years from a public health system perspective.[39] Cost analysis covered the costs of JE vaccination (including wastage and supplies) and savings associated with the long-term effects of cases of JE prevented: treatment of acute JE illness, deaths and mental retardation. The number of JE cases prevented per 100,000 population due to vaccination was 123.7 for the 18-month-old child program compared to 152.9 for the 6-year-old child program. The overall cost of the 18-month-old child program was US$1,944,000, with cost savings of US$9,020,451. The net cost savings and cost-savings-to-cost ratio were US$7,076,451 and 4.6, respectively. The 6-year-old child program cost US$3,528,000, saved US$10,121,521, and gave a net savings of US$6,593,521 and a cost-savings-to-cost ratio of 2.87. The cost-effectiveness ratio was valued at US$15,715 for the 18-month-old child program and US$21,661 for the 6-year-old child program. The 18-month-old child program would save US$72,922 for each case of JE prevented, compared with US$66,197 for the 6-year-old child program. The JE vaccine is a cost beneficial vaccination. Children under 3 years of age should be the first priority because of the greater cost-effectiveness. A JE vaccination program is worth implementing unless the incidence of JE is less than 3 per 100,000 population; otherwise, the cost of the vaccine has to be reduced.

Another study was conducted in China.[40] This study assessed the cost-effectiveness of inactivated and live attenuated Japanese encephalitis (JE) vaccines given to infants and children in Shanghai followed up to the age of 30 years. In comparison with no JE immunization, a program using the P3 vaccine would prevent 420 JE cases and 105 JE deaths and would save 6,456 DALYs per 100,000 persons; the use of the SA 14-14-2 vaccine would prevent 427 cases and 107 deaths and would save 6,556 DALYs per 100,000 persons. The total direct costs associated with the treatment of JE and sequelae during the 30-year follow-

up of 100,000 neonates who were not vaccinated would be US$738,315, and the corresponding costs of using the P3 and SA 14-14-2 vaccines would be US$390,069 and US$225,859, respectively. The savings per 100,000 neonates would thus be US$348,246 and US$512,456, respectively. Consequently, the use of the SA 14-14-2 vaccine would be expected to result in a 47% greater financial savings than that associated with the use of the P3 vaccine. For each JE case prevented, the use of the P3 and SA 14-14-2 vaccines would additionally save US$829 and US$1,200, respectively. The use of the P3 vaccine in Shanghai was cost-saving to the health care system; and similarly high levels of JE control might be achieved using the SA 14-14-2 vaccine, with even greater cost savings.

In Indonesia, a study assessed the cost-effectiveness of a primary hamster kidney cell-derived, live attenuated JE vaccine (SA 14-14-2 strain) from a health care system perspective.[41] In China, two hypothetical birth cohorts – one immunized with SA 14-14-2 and the other unimmunized – were modeled for JE risk over 11 years after JE immunization.[40] The two-dose JE immunization program was found to avert 54 JE cases, 5 deaths and 1,224 lost DALYs among these children. Treatment of JE cases without the immunization program would cost the health care system US$71,144. A JE immunization program that costs US$99,464 would reduce the costs of treating acute JE illness from US$29,200 to US$3,926, and the costs of treating long-term disability from US$41,944 to US$5,639 because of the decreased number of JE cases following the immunization program. Therefore, the net cost of the vaccination program would be US$37,886, and the net cost of each JE case, each death averted and each DALY saved would be US$700, US$6,998 and US$31, respectively. This program was thus highly cost-effective.

In the case of Cambodia, a study aimed to evaluate the costs and effectiveness of introducing a live attenuated vaccine (SA 14-14-2) into the immunization program, both from a provider and societal perspective.[41] The incidence was highest (15.24 per 100,000) in

children from 5 to 10 years of age, followed by children up to 5 years of age (11.28 per 100,000) and children from 10 to 15 years of age (7.66 per 100,000). Vaccination could potentially avert up to 2,888 JE cases, 376 deaths and 2,354 disabilities due to JE, and reduce the disease burden by 52,392 DALYs over the 15-year analytical period. From a societal perspective, up to US$1.46 million of economic burden due to JE could be saved. The combination of a campaign among children 1–10 years of age in the first year, together with routine vaccination in 9-month-old children in the second year, was most costly and most effective; whereas routine vaccination in 9-month-old children was least costly and least effective.

Economic analysis of dengue vaccine

Dengue fever and dengue hemorrhagic fever are major causes of morbidity and mortality in tropical and subtropical regions of the world, including Thailand. We reviewed two studies of the burden of dengue illness and ne study on the cost-effectiveness of dengue vaccine in Thailand.

A study on the burden of symptomatic dengue infection in children at a primary school was conducted in Thailand in 1998.[42] The study prospectively collected data to assess the burden of dengue illness in children at a primary school in Kamphaeng Phet province in northern Thailand. A total of 2,214 children were recruited from grades 1 to 5 (children aged 5 years to 15 years) at 12 local primary schools. Volunteers were assessed three times during the dengue season, from June to November every year. Samples were collected for dengue serology. Cases were identified on the basis of absences from school, visits to a school nurse, visits to a public-health clinic, or admission to a hospital. DALYs lost due to dengue were estimated. It was found that dengue accounted for 328 (11%) of the 3,056 febrile cases identified in 2,114 children during the study period. The mean burden of dengue was 465.3 (SD = 358.0; range = 76.5–954.0) DALYs per million population per year, accounting for

about 15% of DALYs lost to all febrile illnesses (3,213.1 [SD = 2,624.2] DALYs per million per year). Non-hospitalized patients with dengue illnesses represented a substantial proportion of the overall burden of disease, with 44–73% of the total DALYs lost to dengue each year. The infecting dengue serotype was an important determinant of DALYs lost: DEN4 was responsible for 1% of total DALYs lost, DEN1 for 9%, DEN2 for 30%, and DEN3 for 29%.

Another study was on the economic impact of dengue fever/dengue hemorrhagic fever in Thailand at the family and population levels.[43] This study was conducted in the city of Kamphaeng Phet, located in Kamphaeng Phet province in Thailand. The study population consisted of persons hospitalized with laboratory-confirmed dengue virus infection in 2001. A cluster sampling design was used to select participants from the study population. Surveys were administered primarily via home visits, but the telephone was used when available. Information was collected on the self-reported direct economic costs of hospitalization, including transportation costs, costs associated with staying at the hospital for extended periods (any food and lodging expenses), and hospitalization costs incurred by the family. Respondents were also asked to recall the number of workdays missed while taking care of the child, and the number of days of school that the child missed. The duration of illness was assessed in terms of the number of days the child was ill pre-hospitalization, the number of days the child was ill in the hospital, and the days post-hospitalization. Calculations were based on five-year age groups (0–4, 5–9, 10–14, 15–20 and >20 years old) and a standard life expectancy of 82.5 years for females and 80.0 years for males. The study found that financial loss in terms of direct costs of hospitalization, indirect costs due to loss of productivity, and the average number of persons infected per family was approximately US$61 per family. This amount was more than the average monthly income in Thailand. DALYs were

calculated using selected results from a family-level survey, and resulted in an estimated 427 DALYs per million population in 2001.

A third study was an economic evaluation of dengue vaccine in Thailand.[44] A Markov simulation model was applied to evaluate the potential health and economic value of administering a dengue vaccine to a dengue-naive individual (≤ 1 year of age) from a societal perspective. It was found that a ≥ 50% efficacious vaccine was highly cost-effective (<1 × per capita gross domestic product [GDP], US$4,289) up to a total vaccination cost of US$60; and cost-effective (<3 × per capita GDP, US$12,868) up to a total vaccination cost of US$200. When the total vaccine series was US$1.50, many scenarios were cost-saving.

Cost-benefit analysis of the study vaccines

Cost-benefit analysis is an economic evaluation method to compare the value of all resources consumed or costs in program implementation against the value of the outcome or benefits from the program.[45]

Costs are composed of capital or investment cost (or fixed costs) and operating cost (variable costs). In addition to durable assets, costs of research and development or start-up costs (e.g. training) are categorized as capital costs.[46, 47] Capital costs are calculated as equivalent annual economic cost by the following formula[48]:

Capital cost = Current price / annuity factor

Annuity factor = $[1-(1 + r)^{-n}] / r$

where n = useful years

r = discount rate

Useful life used in this study is based on information from the Thailand Ministry of Finance,[49] and in the case of useful years of technology from research and development, from the GPO project's administrators. Benefits consist of revenue from products sold. Analyses are usually presented in three forms, i.e. net present value (NPV), internal rate of return (IRR), and benefit-to-cost ratio (BCR):

Net present value = benefits - costs
Internal rate of return = (benefits - costs) / costs
Benefit-to-cost ratio = benefits / costs

For a multi-year program, costs and benefits must be discounted as in the following formula:

$$NPV = \sum_{t=0}^{n} \frac{Bt - Ct}{(1+r)^t}$$

where *NPV* = net present value of the program
Bt = benefits or revenue from selling in year *t*
Ct = total costs of production and business management in year *t*
r = discount rate

The commonly used discount rate is the current yield on long-term government bonds.[45] Alternatively, WHO and Thai National Guidelines on Health Technology assessment recommend 3%.[46, 50] Recently, the average interest rate of 15-year Thai government bonds was 8.19%.[51]

The program will be accepted when NPV >0 or BCR >1 or IRR >minimum acceptable rate of return (i.e. interest rate of government bonds).[45] Feasibility analysis is based on projected data and assumptions; there is necessarily some uncertainty. In terms of economic analysis, sensitivity analysis must be conducted to answer "what if" scenarios.

Some studies have employed one-way sensitivity analysis.[52] Reference parameters are assumed to be the following:

Useful years of building	15 years
Useful years of equipment	10 years
Useful years of vehicles	5 years
Useful years of training	15–20 years
Useful years of R&D	15–20 years
Discount rate (%)	3.0–8.19%
Forecasted inflation rate	4.53%
Administration/marketing cost (% of price)	5.0–30%
Annual price increase (%)	0–4.53%
Production waste (% product)	25–30%
Forecasted birth rate increase (%)	0

Prices of the vaccines were from the reviewed market prices. Administration/marketing cost was added to production cost. This was assumed to account for 5%–30% of the price. Price increases were assumed to be 0%–4.53%. Revenue was from multiplication of unit price times expected sold units of the vaccines. The expected sold units were derived from expected production units adjusted by production waste rate. In this study the production waste rate was assumed to be 25%–30%, in accordance with calculations by the Government Pharmaceutical Organization (GPO) staff. The forecasted inflation rate of 4.53% was based on the average of 1979–2011.[53] Due to family planning campaigns, birth rate was assumed to be constant.

Due to a limitation of data availability, three production programs were evaluated: JE, DTP-HB and DTP-dT-TT. Data on production plans and resources used were collected from the GPO as program operator. The analytical models were modified based on comments by the National Vaccine Institute (NVI) and GPO staff. Analysis of each production program generated two extreme scenarios: scenario 1 and scenario 2. For scenario 1, the analysis used

the lowest vaccine price (based on market prices), a discount rate of 8.19%, production waste of 30%, and administration/marketing costs of 30% of the price. Scenario 2 used the highest vaccine price (based on market prices), a discount rate of 3%, production waste of 25%, and administration/marketing costs of 10% of the price. Scenario 1 of all programs resulted in a loss benefit (costs higher than revenue). On the other hand, scenario 2 of all programs resulted in a gain benefit (costs less than revenue). For the JE vaccine, the net benefit (profit) would be 5.498 billion baht for a 28-year program, or approximately 196 million baht per year. In the case of DTP-HB, the net benefit gain would be 1.021 billion baht for a 17-year program, or approximately 60 million baht per year. And for the DTP-dT-TT vaccine, the net profit would be 410 million baht over the course of a 17-year program, or approximately 24 million baht per year. Details are presented in Tables 7–18.

Table 7 Parameters of JE; scenario 1

Parameter	Value
Useful years of building	15
Useful years of equipment	10
Useful years of vehicles	5
Useful years of training	15
Useful years of R&D	15
Discount rate (%)	8.19
Forecasted inflation (%)	4.53
Administration/marketing cost (% of price)	30
Annual price increase (%)	0
Production waste (% product)	30
Forecasted birth rate increase (%)	0
Price per dose (baht)	120

JE = Japanese encephalitis

Table 8 Cost-benefit analysis of JE; scenario 1

Year	Number produced (vials)	R&D and production cost	Admin/market cost	Total cost	Benefit (revenue)	Net benefit
1	-	4,127,392	-	4,127,392	-	(4,127,392)
2	-	8,600,863	-	8,600,863	-	(8,600,863)
3	-	11,742,512	-	11,742,512	-	(11,742,512)
4	-	23,873,322	-	23,873,322	-	(23,873,322)
5	-	40,488,701	-	40,488,701	-	(40,488,701
6	-	52,138,621	-	52,138,621	-	(52,138,621)
7	-	52,937,666	-	52,937,666	-	(52,937,666)
8	-	52,654,445	-	52,654,445	-	(52,654,445)
9	1,800,000	77,963,461	34,520,576	112,484,038	80,548,012	(31,936,026)
10	1,800,000	75,785,784	31,907,363	107,693,147	74,450,515	(33,242,633)
11	1,800,000	75,785,784	29,491,971	105,277,755	68,814,599	(36,463,156)
12	1,800,000	75,785,784	27,259,424	103,045,208	63,605,323	(39,439,885)
13	1,800,000	75,785,784	25,195,881	100,981,665	58,790,390	(42,191,275)
14	3,600,000	75,785,784	46,577,099	122,362,882	108,679,897	(13,682,986)
15	3,600,000	75,785,784	43,051,205	118,836,989	100,452,811	(18,384,177)
16	3,600,000	75,785,784	39,792,222	115,578,006	92,848,518	(22,729,488)
17	3,600,000	75,785,784	36,779,944	112,565,728	85,819,870	(26,745,858)
18	3,600,000	75,785,784	33,995,697	109,781,481	79,323,293	(30,458,188)
19	5,400,000	75,785,784	47,133,326	122,919,110	109,977,760	(12,941,349)
20	5,400,000	75,785,784	43,565,326	119,351,109	101,652,427	(17,698,683)
21	5,400,000	75,785,784	40,267,424	116,053,207	93,957,322	(22,095,885)
22	5,400,000	75,785,784	37,219,173	113,004,957	86,844,738	(26,160,219)
23	5,400,000	75,785,784	34,401,676	110,187,460	80,270,578	(29,916,882)
24	5,400,000	75,785,784	31,797,464	107,583,248	74,194,082	(33,389,165)
25	5,400,000	75,785,784	29,390,391	105,176,175	68,577,579	(36,598,596)
26	5,400,000	75,785,784	27,165,534	102,951,317	63,386,245	(39,565,072)
27	5,400,000	75,785,784	25,109,098	100,894,882	58,587,896	(42,306,986)
28	5,400,000	75,785,784	23,208,336	98,994,120	54,152,783	(44,841,336)
Total present value	81,000,000	1,764,456,876	687,829,131	2,452,286,006	1,604,934,638	(847,351,368)

Table 9 Parameters of JE; scenario 2

Parameter	Value
Useful years of building	15
Useful years of equipment	10
Useful years of vehicles	5
Useful years of training	15
Useful years of R&D	15
Discount rate (%)	3
Forecasted inflation (%)	4.53
Administration/marketing cost (% of price)	10
Annual price increase (%)	4.53
Production waste (% product)	25
Forecasted birth rate increase (%)	0
Price per dose (baht)	150

Table 10 Cost-benefit analysis of JE; scenario 2

Year	Number produced (vials)	R&D and production cost	Admin/market cost	Total cost	Benefit (revenue)	Net benefit
1	-	3,507,798	-	3,507,798	-	(3,507,798)
2	-	6,901,054	-	6,901,054	-	(6,901,054)
3	-	9,410,635	-	9,410,635	-	(9,410,635)
4	-	19,590,484	-	19,590,484	-	(19,590,484)
5	-	34,902,346	-	34,902,346	-	(34,902,346)
6	-	46,970,136	-	46,970,136	-	(46,970,136)
7	-	47,871,686	-	47,871,686	-	(47,871,686)
8	-	47,725,330	-	47,725,330	-	(47,725,330)
9	1,800,000	85,474,879	21,314,049	106,788,929	159,855,370	53,066,441
10	1,800,000	84,233,284	21,630,656	105,863,940	162,229,921	56,365,980
11	1,800,000	84,233,284	21,951,966	106,185,250	164,639,744	58,454,494
12	1,800,000	84,233,284	22,278,048	106,511,333	167,085,363	60,574,031
13	1,800,000	84,233,284	22,608,975	106,842,259	169,567,311	62,725,052
14	3,600,000	84,233,284	45,889,634	130,122,918	344,172,252	214,049,335
15	3,600,000	84,233,284	46,571,295	130,804,579	349,284,714	218,480,135
16	3,600,000	84,233,284	47,263,082	131,496,367	354,473,118	222,976,751

Year	Number produced (vials)	R&D and production cost	Admin/market cost	Total cost	Benefit (revenue)	Net benefit
17	3,600,000	84,233,284	47,965,146	132,198,430	359,738,592	227,540,163
18	3,600,000	84,233,284	48,677,638	132,910,922	365,082,282	232,171,360
19	5,400,000	84,233,284	74,101,070	158,334,354	555,758,024	397,423,670
20	5,400,000	84,233,284	75,201,794	159,435,079	564,013,458	404,578,380
21	5,400,000	84,233,284	76,318,870	160,552,154	572,391,522	411,839,369
22	5,400,000	84,233,284	77,452,538	161,685,823	580,894,037	419,208,215
23	5,400,000	84,233,284	78,603,047	162,836,331	589,522,852	426,686,521
24	5,400,000	84,233,284	79,770,646	164,003,930	598,279,842	434,275,912
25	5,400,000	84,233,284	80,955,588	165,188,872	607,166,911	441,978,039
26	5,400,000	84,233,284	82,158,132	166,391,417	616,185,992	449,794,576
27	5,400,000	84,233,284	83,378,540	167,611,824	625,339,046	457,727,223
28	5,400,000	84,233,284	84,617,075	168,850,359	634,628,063	465,777,704
Total present value	81,000,000	1,902,786,749	1,138,707,789	3,041,494,538	8,540,308,416	5,498,813,878

Table 11 Parameters of DTP-HB; scenario 1

Parameter	Value
Useful years of building	15.00
Useful years of equipment	10.00
Useful years of vehicles	5.00
Useful years of training	15.00
Useful years of R&D	15.00
Discount rate (%)	8.19
Forecasted inflation (%)	4.53
Administration/marketing cost (% of price)	30.00
Annual price increase (%)	-
Production waste (% product)	30.00
Forecasted birth rate increase (%)	-
Price per dose (baht)	21.04

DTP-HB = diphtheria/tetanus/pertussis–hepatitis B

Table 12 Cost-benefit analysis of DTP-HB; scenario 1

Year	Number produced (vials)	R&D and production cost	Admin/market cost	Total cost	Benefit (revenue)	Net benefit
1	-	3,980,344	-	3,980,344	-	(3,980,344)
2	-	9,073,664	-	9,073,664	-	(9,073,664)
3	3,000,000	43,400,962	16,176,332	59,577,294	37,744,774	(21,832,519)
4	3,000,000	42,213,516	14,951,872	57,165,387	34,887,700	(22,277,687)
5	3,000,000	41,066,233	13,820,096	54,886,329	32,246,891	(22,639,438)
6	3,000,000	39,957,755	12,773,990	52,731,746	29,805,977	(22,925,768
7	3,000,000	38,886,771	11,807,069	50,693,839	27,549,827	(23,144,012)
8	4,000,000	37,852,010	14,551,117	52,403,127	33,952,607	(18,450,520)
9	4,000,000	36,852,249	13,449,677	50,301,926	31,382,580	(18,919,346)
10	4,000,000	35,886,303	12,431,610	48,317,913	29,007,089	(19,310,824)
11	4,000,000	35,886,303	11,490,604	47,376,908	26,811,410	(20,565,497)
12	4,000,000	35,886,303	10,620,828	46,507,131	24,781,933	(21,725,199)
13	6,000,000	35,886,303	14,725,334	50,611,637	34,359,113	(16,252,524)
14	6,000,000	35,886,303	13,610,707	49,497,010	31,758,315	(17,738,694)
15	6,000,000	35,886,303	12,580,450	48,466,753	29,354,384	(19,112,370)
16	6,000,000	35,886,303	11,628,179	47,514,482	27,132,417	(20,382,065)
17	6,000,000	35,886,303	10,747,989	46,634,292	25,078,640	(21,555,651)
Total present value	65,000,000	580,373,928	195,365,854	775,739,781	455,853,658	(319,886,123)

Table 13 Parameters of DTP-HB; scenario 2

Parameter	Value
Useful years of building	15.00
Useful years of equipment	10.00
Useful years of vehicles	5.00
Useful years of training	15.00
Useful years of R&D	15.00
Discount rate (%)	3.00
Forecasted inflation (%)	4.53
Administration/marketing cost (% of price)	10.00
Annual price increase (%)	4.53
Production waste (% product)	25.00
Forecasted birth rate increase (%)	-
Price per dose (baht)	39.03

Table 14 Cost-benefit analysis of DTP-HB; scenario 2

Year	Number produced (vials)	R&D and production cost	Admin/market cost	Total cost	Benefit (revenue)	Net benefit
1	-	3,219,387	-	3,219,387	-	(3,219,387)
2	-	7,619,700	-	7,619,700	-	(7,619,700)
3	3,000,000	45,236,276	11,036,064	56,272,340	82,770,478	26,498,138
4	3,000,000	45,811,642	11,199,997	57,011,639	83,999,981	26,988,342
5	3,000,000	46,395,554	11,366,366	57,761,920	85,247,748	27,485,828
6	3,000,000	46,988,140	11,535,207	58,523,346	86,514,049	27,990,703
7	3,000,000	47,589,528	11,706,555	59,296,083	87,799,161	28,503,078
8	4,000,000	48,199,850	15,840,598	64,040,448	118,804,483	54,764,035
9	4,000,000	48,819,238	16,075,900	64,895,138	120,569,248	55,674,111
10	4,000,000	49,447,826	16,314,697	65,762,523	122,360,228	56,597,705
11	4,000,000	49,447,826	16,557,042	66,004,868	124,177,812	58,172,945
12	4,000,000	49,447,826	16,802,986	66,250,812	126,022,395	59,771,583
13	6,000,000	49,447,826	25,578,876	75,026,702	191,841,568	116,814,866
14	6,000,000	49,447,826	25,958,834	75,406,660	194,691,253	119,284,594
15	6,000,000	49,447,826	26,344,436	75,792,262	197,583,269	121,791,007
16	6,000,000	49,447,826	26,735,766	76,183,592	200,518,244	124,334,652
17		49,447,826				126,916,081

Year	Number produced (vials)	R&D and production cost	Admin/market cost	Total cost	Benefit (revenue)	Net benefit
	6,000,000		27,132,909	76,580,735	203,496,816	
Total present value	65,000,000	735,461,923	270,186,231	1,005,648,154	2,026,396,735	1,020,748,580

Table 15 Parameters of DTP-dT-TT; scenario 1

Parameter	Value
Useful years of building	15
Useful years of equipment	10
Useful years of vehicles	5
Useful years of training	15
Useful years of R&D	15
Discount rate (%)	3
Forecasted inflation (%)	4.53
Administration/marketing cost (% of price)	30
Annual price increase (%)	0
Production waste (% product)	30
Forecasted birth rate increase (%)	0
Price per dose (baht); DTP	4.88
Price per dose (baht); dT	2.84
Price per dose (baht); TT	0.88

DTP-dT-TT = diphtheria/tetanus/pertussis–diphtheria/tetanus–tetanus toxoid

Table 16 Cost-benefit analysis of DTP-dT-TT; scenario 1

Year	Number produced (vials)	R&D and production cost	Admin/market cost	Total cost	Benefit (revenue)	Net benefit
1	-	4,470,687	-	4,470,687	-	- 4,470,687
2	-	5,794,990	-	5,794,990	-	- 5,794,990
3	4,000,000	11,001,670	1,820,446	12,822,116	14,504,951	1,682,836
4	4,000,000	10,978,791	1,715,945	12,694,736	14,082,477	1,387,741
5	4,000,000	11,217,794	1,617,443	12,835,237	13,672,308	837,071
6	4,000,000	11,264,375	1,524,595	12,788,970	13,807,994	1,019,025
7	4,000,000	11,469,559	1,437,077	12,906,635	13,405,820	499,184
8	4,000,000	11,575,261	1,354,583	12,929,843	13,015,359	85,516
9	4,000,000	11,668,411	1,276,824	12,945,235	13,613,476	668,241
10	4,000,000	11,826,293	1,203,529	13,029,822	13,216,967	187,145
11	4,000,000	11,826,293	1,134,442	12,960,734	12,832,007	- 128,728
12	4,000,000	11,826,293	1,069,320	12,895,613	13,352,540	456,927
13	4,000,000	11,826,293	1,007,937	12,834,229	12,963,631	129,402
14	4,000,000	11,826,293	950,077	12,776,370	12,586,049	- 190,320
15	4,000,000	11,826,293	895,539	12,721,831	12,219,466	- 502,366
16	4,000,000	11,826,293	844,131	12,670,424	11,863,559	- 806,865
17	4,000,000	11,826,293	795,675	12,621,967	11,518,018	- 1,103,949
Total present value	60,000,000	184,051,878	18,647,562	202,699,440	196,654,622	- 6,044,818

Table 17 Parameters of DTP-dT-TT; scenario 2

Parameter	Value
Useful years of building	15
Useful years of equipment	10
Useful years of vehicles	5
Useful years of training	15
Useful years of R&D	15
Discount rate (%)	3
Forecasted inflation (%)	4.53
Administration/marketing cost (% of price)	10
Annual price increase (%)	4.53
Production waste (% product)	25
Forecasted birth rate increase (%)	0
Price per dose (baht); DTP	12.20
Price per dose (baht); dT	5.49
Price per dose (baht); TT	1.51

Table 18 Cost-benefit analysis of DTP-dT-TT; scenario 2

Year	Number produced (vials)	R&D and production cost	Admin/market cost	Total cost	Benefit (revenue)	Net benefit
1	-	4,470,687	-	4,470,687	-	- 4,470,687
2	-	5,794,990	-	5,794,990	-	- 5,794,990
3	4,000,000	11,001,670	1,625,398	12,627,068	33,830,277	21,203,210
4	4,000,000	10,978,791	1,601,498	12,580,289	34,332,805	21,752,516
5	4,000,000	11,217,794	1,577,948	12,795,742	34,842,797	22,047,054
6	4,000,000	11,264,375	1,554,745	12,819,120	36,475,585	23,656,464
7	4,000,000	11,469,559	1,531,884	13,001,442	37,017,407	24,015,964
8	4,000,000	11,575,261	1,509,358	13,084,619	37,567,277	24,482,658
9	4,000,000	11,668,411	1,487,164	13,155,575	40,456,635	27,301,060
10	4,000,000	11,826,293	1,465,296	13,291,588	41,057,592	27,766,004
11	4,000,000	11,826,293	1,443,749	13,270,042	41,667,477	28,397,435
12	4,000,000	11,826,293	1,422,520	13,248,812	44,723,182	31,474,370
13	4,000,000	11,826,293	1,401,602	13,227,895	45,387,517	32,159,622
14	4,000,000	11,826,293	1,380,992	13,207,285	46,061,720	32,854,435
15		11,826,293				33,558,959

Year	Number produced (vials)	R&D and production cost	Admin/market cost	Total cost	Benefit (revenue)	Net benefit
	4,000,000		1,360,686	13,186,978	46,745,937	
16	4,000,000	11,826,293	1,340,677	13,166,970	47,440,319	34,273,349
17	4,000,000	11,826,293	1,320,963	13,147,256	48,145,015	34,997,759
Total present value	60,000,000	184,051,878	22,024,481	206,076,359	615,751,541	409,675,182

Excel-based templates for CBA

The templates were developed as Excel-based software. The models are specific for each program, and are composed of input, calculation and output sheets. The models were handed in to the GPO and NVI for further simulation analyses, and were submitted in a CD together with this report.

Discussion and conclusion

In terms of potential market focus on South and Southeast Asia, most of the countries include the target vaccines in their NIPs. Therefore, all birth cohorts were converted to doses of vaccines needed. When comparing production plans, the number of vaccines produced was comparable to the amount of vaccines produced to meet the demand in Thailand. Therefore, the production scale can be expanded to other countries to reduce the fixed cost per unit; then unit cost can be reduced. However, there are other existing competing producers, both in Asia and developed countries. Those producers may have a large market share, and with production at more efficient levels than those in Thailand. Therefore, they can reduce prices when faced by competition.

Regarding cost-benefit analysis of the programs, there is a range of losses and gains (profit) for all three programs. The findings are based on internal and external factors. Internal factors are related to resources used and efficiency of production (production waste).

External factors are market prices and discount (interest) rate. Therefore, the programs have to be carefully implemented.

There were some limitations of this study. In essence, estimates of costs of R&D, production, and administration/marketing costs were roughly forecasted as marginal costs to existing GPO facilities. Therefore, the program costs tend to be underestimated in terms of economic cost concepts. However, the study has produced Excel-based models for all programs. These can be continually revised based on the availability of more accurate data. The findings of this study could be useful as a tool for program implementers and policy makers in decision making and for adopting and monitoring these programs.

In conclusion, there is enough demand for designed production levels of all programs. However, the vaccine market is an oligopoly. Business success is thus not only based on production feasibility but also on marketing or business strategies which are beyond the scope of this study. In addition, these analyses should be revised as more accurate data become available.

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