

Vaccine Introduction Guidelines

Adding a vaccine to a national immunization programme: decision and implementation

Immunization, Vaccines and Biologicals



World Health Organization

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Preface

What is the purpose of this guide?

- To assist an informed decision-making process to add a vaccine
- To ensure smooth introduction of the new vaccine
- To promote further strengthening of the immunization programme, taking the advantage of the newly added vaccine

When do you need this guide?

- Before introducing a vaccine in the immunization programme, to decide whether the introduction is feasible
- After deciding to introduce a vaccine, to conduct the operations
- After introducing a vaccine, to monitor the implementation and to evaluate the impact

How can you use this guide?

- As a technical tool to plan, implement and monitor the vaccine introduction
- As a supporting tool to advocate political decision-makers to introduce a vaccine

Who can use this guide?

- Country level decision-makers
- National immunization programme managers
- Consultants working on immunization

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Acronyms

The following acronyms are used in this document.

AD	auto-disable
AEFI	adverse event following immunization
AIDS	acquired immunodeficiency syndrome
CE	cost—effectiveness
CRS	congenital rubella syndrome
DALYs	disability adjusted life years
DTP	diphtheria–tetanus–pertussis (vaccine)
EPI	Expanded Programme on Immunization
FSP	financial sustainability plan
GAVI	Global Alliance for Vaccines and Immunization
GIVS	Global Immunization Vision and Strategies
GMP	good manufacturing practice
HBV	hepatitis B virus
HepB	hepatitis B vaccine
Hib	<i>Haemophilus influenzae</i> type b
ICC	interagency coordinating committee
IEC	information, education and communication
IPV	inactivated polio vaccine
JE	Japanese encephalitis
MDVP	multi-dose vial policy
Men A	meningococcus A (vaccine)
MNT	maternal and neonatal tetanus
MOH	ministry of health
MR/MMR	measles–rubella/measles–mumps–rubella (vaccine)
MYP	multi-year plan

NGO	nongovernmental organization
NID	national immunization day
NIP	national immunization programme
NRA	national regulatory authority
OPV	oral polio vaccine
RED	Reaching Every District strategy
TB	tuberculosis
VAPP	vaccine-associated paralytic polio
VVM	vaccine vial monitor
YF	yellow fever

1. Background

1.1 Purpose

This document aims to help:

- country decision-makers to decide whether to add a new vaccine to the national immunization programme (NIP);
- NIP managers to implement the operational steps to add the vaccine.

Covering policy and programmatic aspects together, the document is addressed towards both audiences, trying to provide guidance for a technically correct decision and implementation. It proposes a generic process to assess the available vaccines for introduction, followed by the common operational steps to introduce the vaccine(s). However, each vaccine presents its own specific issues, which are addressed in Annex 1.

1.2 Global Immunization Vision and Strategies: a renewed global commitment

Immunization is one of the most successful global public health interventions. Since the establishment of the Expanded Programme on Immunization (EPI) in 1974, millions of deaths and disabilities due to the six targeted diseases (diphtheria, measles, pertussis, poliomyelitis, tetanus and tuberculosis) have been prevented. Vaccines are now available against other diseases that are of public health importance globally or in some parts of the world. However, most developing countries did not have the means to access, evaluate and implement these newly developed vaccines. This situation led to a divergence in global vaccine utilization, and many children who were in most need were deprived of access to the new vaccine options.

In response to existing, new and anticipated challenges to immunization, WHO and UNICEF have jointly developed Global Immunization Vision and Strategies (GIVS) for 2006–2015 (1). In view of the marked differences between countries' capacities, priorities and resources, GIVS presents a range of immunization strategies from which countries will be able to select those most suited to their needs. It comprises goals and strategies under four main areas:

-
- 1) protecting more people in a changing world;
 - 2) introducing new vaccines and technologies;
 - 3) positioning immunization, other linked health interventions and surveillance in the health system context; and
 - 4) immunizing in a context of global interdependence.

GIVS aims to increase the use of traditional and new vaccines as well as contributing significantly to the achievement of Millennium Development Goals (2).

In conjunction with GIVS, countries are encouraged to develop or update comprehensive multi-year plans (MYPs) for immunization. MYPs provide national goals, objectives and strategies for up to five years based upon a situational analysis. The aim is to address all components of the immunization system, to make synergies between various initiatives (polio, measles, etc.) in a single plan and to integrate common activities to avoid duplication. GIVS may serve as a guide to ensure that the strategies in the plan are sufficiently comprehensive. MYPs also need to be linked to the national health and development plans, and include a budget consistent with the overall financial planning for health (3).

New vaccines present numerous issues in prioritizing investments of a national immunization programme. The challenge remains to tackle those issues systematically, providing the best available services in a cost-effective way. This guide provides national programme managers and decision-makers with a systematic approach to decision-making when facing the opportunities and challenges presented by adding a new vaccine product into national immunization programmes. For countries that make the decision to introduce a vaccine, the guide also examines the key elements for programmatic planning and for monitoring the impact of the additional vaccine.

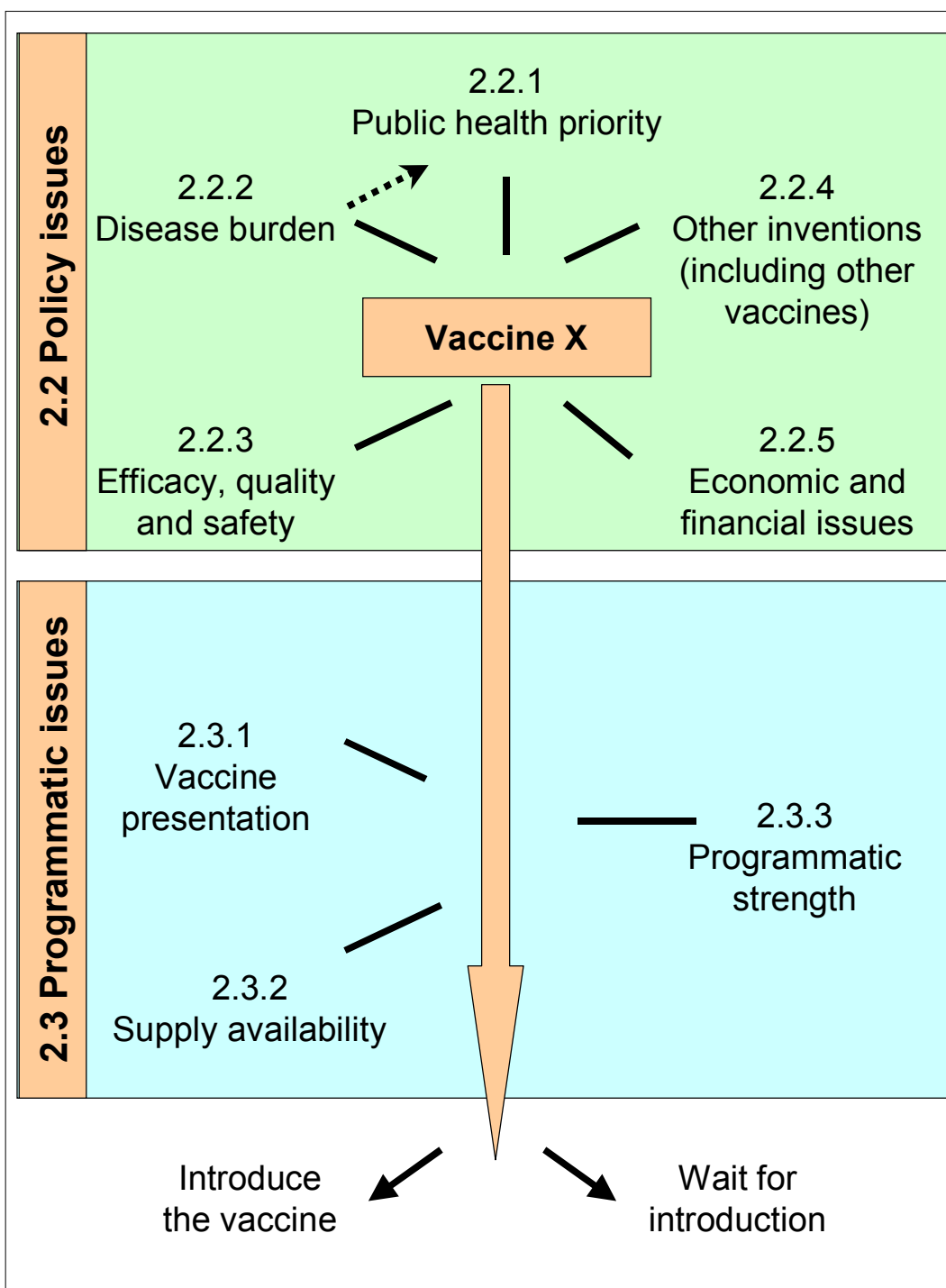
2. Deciding on the introduction of a vaccine

2.1 Overview

The flowchart (Figure 1) outlines the key issues to be considered before deciding to introduce a vaccine. A first group of issues, referred to as policy issues, leads high-level decision-makers to agree on whether the introduction of a particular vaccine is acceptable from an immunization policy perspective. The second group of issues, referred to as programmatic issues, addresses the feasibility of the vaccine introduction from a technical perspective. Although it is recommended that each issue is addressed in a fully informed decision-making process, some aspects of the flowchart may outweigh the other considerations, depending on the specific circumstances. As a result of this evaluation, the decision might be either:

- to introduce the vaccine;
- OR
- to wait until more evidence has been obtained (disease burden, cost-effectiveness, etc.), or until the conditions change (price, financial resources, supply, programme strength, etc.) before deciding on the introduction of the vaccine.

Figure 1: Key issues



2.2 Policy issues

2.2.1 *Public health priority*

Each country faces multiple health problems. Addressing those problems requires setting priorities to allocate the limited resources available to the health sector. The NIP may need to present rational arguments for introducing a particular vaccine, in order to convince the decision-makers. The burden of disease that can be prevented by the vaccine, as explained in the next section, provides one of the main pieces of evidence to set national health priorities.

Today HIV/AIDS, tuberculosis (TB), malaria, respiratory and gastrointestinal infections form the bulk of infectious disease burden in developing countries. Many of these infections are potentially vaccine-preventable and vaccine development studies are accelerating. For example, pneumococcus and rotavirus are responsible for an important proportion of respiratory and gastrointestinal diseases and vaccines are now becoming available against those infections. These diseases have their greatest impact in terms of mortality in the least-developed countries from sub-Saharan Africa and Asia among children under five.

The perception of the public and the medical community about the vaccine and the disease is a significant factor to identify its introduction as a priority. The more important and visible the disease is, and the safer and more effective the vaccine is perceived to be, the better the acceptance and uptake of the new vaccine will be. The vaccine may have already entered in the private market in that country, and this influences the public awareness as well as raising equity considerations. A qualitative investigation among key decision-makers, medical community, immunization partners and public will be useful to assess their perception about the vaccine and its likely impact. Moreover, this assessment will guide the design of appropriate messages for the public and health-care providers. News reports in print and electronic media may give valuable insight for this purpose. Any misperception or opposition to the vaccine should be investigated to determine the causes.

When deciding about the priority of a particular vaccine, it is also important to consider other vaccines that would become available in the near future. For example, introduction of a vaccine could be postponed if it was known that the same vaccine would be available shortly as a combination product that would facilitate introduction. Another issue in considering a particular vaccine would be to preserve limited financial resources, in situations where it is expected that another vaccine will become available in the near future against a disease that presents a greater burden.

2.2.2 Disease burden

The burden of disease is usually expressed in the terms below.

- *Incidence rate*—how many new cases occur per year per standard unit of population, affecting which age groups?
- *Prevalence rate*—how many cases exist at a given time, per standard unit of population? This indicator is essentially relevant for chronic conditions, such as disease sequelae or chronic hepatitis B virus (HBV) infection.
- *Hospitalizations*—how many cases are hospitalized per year?
- *Disability*—how many cases suffer a long-term disability?
- *Mortality*—how many cases die per year?

National burden of disease studies, if conducted, may provide valuable information on the particular disease and its importance compared to the other health conditions. In the absence of such studies or country-specific epidemiological data, data from countries of similar social and demographic characteristics in the region or regional estimates can be used. When incomplete data are available (e.g. because the condition is difficult to measure), mathematical models can also help make inferences on the total disease burden. Data from models should, however, be used cautiously with a clear understanding of the range of uncertainty that rests on the underlying assumptions used to build those models.

Public health surveillance

Surveillance systems aim to collect data from public and private health facilities, hospitals and laboratories: on incidence, hospitalizations, disability and mortality from diseases. In practice, surveillance data are rarely complete in many countries, due to numerous weaknesses in the surveillance system. As many more diseases will become vaccine-preventable in the future, strengthening surveillance systems to integrate the largest number of relevant vaccine-preventable diseases is a worthy investment. Surveillance not only provides disease burden data for deciding on vaccine introduction, but enables national managers to assess the impact of a specific vaccine after the introduction.

Special studies

When the surveillance data are not conclusive, special studies may be needed to assess the burden of a particular disease. Even a good surveillance system may not provide the necessary evidence, if the data is on the clinical syndrome rather than the causative organism. Because those studies can be costly, the added value of getting local disease burden data as opposed to extrapolating existing data from neighbouring countries must be carefully considered.

WHO has prepared rapid assessment tools, reference surveillance protocols and guidelines to assess the burden of *Haemophilus influenzae* type b (Hib) (4, 5), rotavirus (6), shigella (7), respiratory syncytial virus (8), rubella (9) and yellow fever (YF) (10).

Example: Estimating the burden of Hib

Haemophilus influenzae type b causes a range of clinical conditions, the most important ones being meningitis and pneumonia. However, not all meningitis and pneumonia cases are caused by Hib. Estimating Hib meningitis incidence requires ensuring the completeness of Hib isolation from sentinel sites for bacterial meningitis surveillance with high quality laboratory testing. Estimating the full burden of Hib disease also requires factoring in the incidence of severe pneumonia. WHO Hib Rapid Assessment Tool provides a methodology to generate these estimates.

2.2.3 Vaccine efficacy, quality and safety

In order for a vaccine to be licensed, it needs to have data on its **efficacy** in preventing disease in the immunized populations. These data are obtained from controlled studies, where considerable efforts are made to ensure that every aspect of the immunization is delivered under ideal conditions. In those trials, vaccines tend to be given to healthier people who may present a better immune response. Efficacy may also vary depending on age, nutritional status, co-infections, and other factors. As a result, the efficacy of some vaccines is lower in developing countries than in industrialized countries. Therefore, in estimating the likely efficacy of the vaccine in the country, careful consideration needs to be given to the range of data available, and whether the studies were also performed in countries with similar disease epidemiology to the one considering the vaccine.

It should be noted that vaccine **effectiveness** is a different concept which describes protection under programmatic implementation and reflects the performance of the vaccine in the actual target population. Programmatic factors like errors in vaccine storage, preparation or administration, which can impair the vaccine, are more likely to occur in the field. Therefore vaccine effectiveness is usually lower than vaccine efficacy. It should be monitored as part of the post-marketing surveillance activities that also include surveillance for adverse events following immunization (AEFIs).

Vaccines being considered for introduction should meet international standards of quality and safety. A vaccine may induce adverse reactions that need to be included in assessing its overall impact. The **safety** of a new vaccine is assessed by clinical trials before it is considered for use. However, these trials may not capture rare adverse events, thus post-marketing surveillance is still needed to further establish the safety profile. There should also be data about the impact on safety and efficacy on other routine vaccines that are given at the same time. Information on safety needs to be assessed carefully, weighing the risks against the benefit of the vaccine. The risk:benefit ratio may vary between countries. In developing countries where disease morbidity and mortality is high, the expected benefits may far outweigh the risk of adverse events.

2.2.4 *Other interventions (including other vaccines)*

The new vaccine needs to be compared with other existing vaccines against the same disease as well as with other control strategies. Comparisons will be based on relative effectiveness and costs of the different interventions, and need to also consider practicality/feasibility, timeliness of effect, possibility of causing microbiological and epidemiological changes over time, and any adverse effects of each of the options. If an alternative control strategy or an existing vaccine is more advantageous, then the new vaccine does not need further consideration.

Acellular pertussis vaccine has been compared with whole-cell pertussis vaccine in randomized trials. The acellular vaccine caused fewer reactions, but none of these caused long-term effects. On the other hand, the whole-cell vaccines tend to offer better immunity (11). Currently, wealthier countries, where the burden of pertussis is lower, have adopted acellular vaccines. For developing countries, the traditional whole-cell vaccine remains the best control strategy for pertussis (12).

2.2.5 *Economic and financial issues*

Traditional immunization programmes represent one of the best buys in the health sector—significant health impacts can be achieved for cents per dose. However, new vaccines are much more expensive than the traditional vaccines. For example at 2005 UNICEF prices, the vaccine costs for fully vaccinating an infant with the traditional Expanded Programme on Immunization (EPI) vaccines is about US\$ 0.80 (excluding shipping, insurance and wastage). Adding HepB to the schedule doubles the vaccine cost per infant to US\$ 1.60, and adding Hib vaccine increases the cost to approximately US\$ 10 per infant. Even when the vaccine and non-vaccine costs are considered together, introduction of vaccines may lead to a considerable increase in the costs of the immunization programme. Therefore, it is important to carefully evaluate the costs and benefits of adding new vaccines as well as to measure their potential impact on limited national health budgets.

Assessing the economic and financial implications of new vaccines can provide valuable information for decision-making for both governments and their development partners as to: (i) whether a particular vaccine is cost effective relative to other uses of scarce resources; (ii) what the long-term resource requirements of the new vaccine will be and how this compares with government budgets in order to assure its sustainability; (iii) the magnitude of the potential funding gap for a new vaccine and whether additional domestic or external funding could be mobilized to fill this gap; and (iv) the potential prospects for financial sustainability of the new vaccine, once introduced.

Cost-effectiveness

Cost-effectiveness (CE) analysis is a tool that is used to evaluate and compare among alternative uses of scarce resources. This approach can help determine whether investment in a new vaccine achieves greater or lesser health outcomes relative to investment in another type of vaccine presentation or public health programme.

In cost-effectiveness analysis, the cost of an intervention (US\$) is divided by the intervention's effectiveness, resulting in a cost-effectiveness ratio, such as the cost per fully immunized child, cost per death averted, or cost per disability adjusted life years (DALYs). Interpretation of these ratios needs to be done on a relative basis in comparison with other estimates. A general rule of thumb is that a CE ratio which is less than three times the gross national income (GNI) per capita of a country would be a worthwhile investment overall. Interventions with lower CE ratios are better investments than those with higher ones, from an economic perspective.

When comparing introduction of a range of new vaccines, it is appropriate to evaluate the **additional costs** above the costs of the immunization programme associated with each alternative. However, when comparing introduction of a new vaccine relative to using the same level of resources for another health programme, it is important to evaluate the **total costs** with the new vaccine.

Total costs for new vaccines are compared to the potential cost savings as a result of reduced treatment for disease. There are several published methods and approaches to cost-effectiveness analysis, which can be found at http://www.who.int/immunization_financing/tools/en/. An annotated bibliography and additional information on economics of immunization is available from WHO (13).

Fiscal impact

A decision to introduce a new vaccine should include the affordability of the vaccine to the country, and the magnitude and timing of future funding gaps. Affordability is a subjective concept and relates to whether a new vaccine can be introduced and absorbed into an immunization budget over the medium to long term without significantly affecting available resources for other public health priorities.

Analysis of fiscal impact evaluates expected programme costs with the new vaccine, and estimates of future programme resource requirements. Immunization programme costs are often divided into programme-specific costs and shared costs.

Programme-specific costs reflect the value of resources used 100% for the immunization programme:

- time of health personnel who spend 100% of their time on immunization
- vaccines
- injection supplies
- cold-chain equipment
- vehicles which are used 100% of the time for immunization, etc.

Shared costs reflect the value of resources used by the immunization programme, but which are also shared with other health services and interventions:

- time of health personnel who do other work in addition to immunization
- buildings
- equipment
- vehicles, etc.

The WHO *Guidelines for immunization multi-year planning and costing* (3) includes a standard method for estimating programme costs as part of the MYP.

Once programme or strategy costs including the new vaccines are estimated, they can be compared with a range of indicators like:

- programme costs with and without the new vaccine as a proportion of total government health budget or government health expenditures for a particular year;
- programme costs with and without the new vaccine as a proportion of total health expenditures (which includes private expenditures);
- programme costs with and without the new vaccine as a proportion of gross domestic product (GDP);
- per capita estimates of programme costs with and without the new vaccine; and
- programme costs with and without the new vaccine per child that has received the third dose of diphtheria–tetanus–pertussis vaccine (DTP3).

Interpretation of these indicators is subjective, and ideally these indicators should be compared with those for other public health interventions and programmes to have a better sense of relative impacts. However, if the programme-specific costs with a new vaccine represent a substantial share (more than 5%) of total government health budget or expenditures in a particular year, the programme may be pushing the limits of affordability, and will require significant efforts to mobilize resources and sustain the new vaccine in coming years.

Financial sustainability

Financial sustainability refers to the timely mobilization of needed resources to cover the costs of an intervention into the future. It is only one aspect of sustaining an immunization programme, which also requires sufficient human resources and government commitment, among other factors. It is related to sustaining the financing of the entire immunization programme after introduction, not just the financing of new vaccines.

The analysis of financial sustainability first begins with an evaluation of current and future resource requirements. These can then be compared with current and future financing of different programme line items by source of funding per year. Funding sources include the central ministry of health (MOH) budget and donor funds where necessary. Donors tend to finance cold chain equipment, vaccines, vehicles and supplies, while the government funds are used to support labour and operational costs.

The financial gap (total resource requirements minus expected available funding) can be estimated per year. The composition of funding gaps varies greatly from country to country, with some countries having significant underfunding of capital expenditures, and others with recurrent expenditure under funding, excluding new vaccines. Evidence on the expected financing gap can be useful in government budget negotiations and in discussions with donor organizations about the need for more resource mobilization. Other potential sources of funding which remain to be explored

include funding from local governments, resources from debt relief, development loans, the private sector (foundations and nongovernmental organizations/[NGOs]) and social insurance.

Long-term sustainability of vaccine procurement should be a central consideration for any government. Interrupting the use of a vaccine in the infant immunization schedule can have several serious implications for equitable health outcomes. For instance, in countries where universal rubella vaccination of infants has been adopted, an interruption to the continuous supply and procurement of rubella-containing vaccines could result in a risk of greater burden of congenital rubella syndrome than would have resulted without temporary use of the vaccine. In most cases, there will be negative consequences on the perception of the NIP from the public and health-care workers as well as the costs associated with switching products. There may also be the loss of funding for traditional vaccines (e.g. DTP component of a combination vaccine with HepB and/or Hib). Therefore, if there are doubts about the sustainability of introducing a new vaccine, this should not proceed unless it is clear that short-term use of the new vaccine will not have negative consequences.

2.3 Programmatic issues

2.3.1 Vaccine presentation

The presentation of a vaccine includes options like monovalent/combination, single dose/multi dose, liquid/lyophilized (requires reconstitution). Product selection and its implications are more related to implementation and are explained in more detail in Section 3.2. However, it is useful to consider the available presentations of the vaccine in the market at this stage, as it may have direct implications on the decision-making. WHO has developed a tool to assist national managers in selecting vaccine product formulations that are supplied through UNICEF (14).

The country may not have a chance to introduce the most preferred option because of high cost or lack of availability. In some cases, the country may be faced with a choice of delaying the introduction until the preferred formulation/presentation is available, or starting with another option and then moving to the preferred option at a later stage.

2.3.2 Supply availability

In considering the available options, it is important to be aware of the current and future supply situation in consultation with UNICEF and WHO. Initially, the new vaccines might be produced by a limited number of manufacturers and it might take time for the vaccine market to reach a level of maturity in terms of both supply and price. Procurement of the vaccines that have a limited global supply can present challenges. Particularly countries with a large population might need to postpone the introduction, or adopt a phased introduction strategy until the supply reaches a level that meets the demand. In addition to the current supply situation, the future trends should also be consulted before moving into introduction. For example, in case a country utilizes a greater quantity of the new vaccine than had first been anticipated (due to high wastage, increased demand, etc.) it might be difficult to obtain additional vaccine in time and there might be a risk of temporary stock-out.

2.3.3 Programmatic strength

The overall NIP performance should be assessed ahead of any new vaccine introduction to identify any areas that need strengthening. Even for countries that are not currently considering adding a vaccine, the indicators below can be useful to prepare for the future, when countries are going to have an increasing number of new vaccines. Adding a vaccine will provide greater benefits through well functioning delivery systems. New vaccine introduction can affect the NIP in two ways. It may help to strengthen the programme through raising demand by adding new resources and increasing public interest, or it may cause additional burdens and worsen performance in a poorly performing system. If the current programme is failing to reach a large proportion of children, then the new vaccine will be able to offer only limited benefits to those who most need it.

If the vaccine is already being used in the private sector, this may have implications for vaccine impact, advocacy and communication; and it may even affect disease burden, depending on the share of the private sector in overall immunizations.

The following checklist outlines possible criteria that could be used in assessing the strength of the NIP to accommodate a new vaccine, alongside with the findings from the other immunization programme reviews. It is obvious that there would not be many developing countries which could fulfil all the criteria listed here before introduction. However, the aim of this list is to assist with identifying weak areas that could be improved.

Criteria for assessing the national immunization programme readiness for new vaccine introduction

1) Obtaining full benefit from existing vaccines

- An immunization multi-year plan and annual work plans are in place, with regular updating of policies.
- Immunization coverage reflects satisfactory access and limited drop out. Each NIP should set its own coverage targets in the MYP considering the regional targets and global targets in GIVS.
- Specific objectives are met or well under way for already existing vaccines. For example timely (i.e. within 24 hours) coverage with HepB birth dose is achieved where relevant, catch-up measles vaccination has been conducted, or two-dose measles strategy has been established.

2) Financially sustainable programme

- The NIP is able to mobilize and use resources for existing programme strategies with secure current and future financing.
- MYPs include a budget linked with the national health budget to secure vaccine supply and other costs.
- There is a capacity to expand the programme without threatening financial sustainability.

3) Functional cold chain

- National cold-chain policy and vaccine management systems include an updated cold-chain inventory as well as plans for the maintenance and replacement of equipment.
- The cold chain has adequate volume capacity and performance for existing vaccines at all levels.
- Cold space is able to meet any additional demands of the new vaccine, with an adequate spare capacity to meet campaign or unforeseen needs.

4) Well managed vaccine stock

- There are two-year to five-year forecasts for all existing vaccines (including planned/likely campaigns) and the new vaccines, including the transition period when existing vaccines are being replaced.
- There is effective monitoring of wastage for all vaccines, with acceptable levels of wastage compared to coverage.
- Vaccine stock-outs at national or subnational levels are infrequent.

5) Safe immunizations and monitoring of adverse events

- All vaccines are given with auto-disable (AD) syringes.
- Proper diluents and reconstitution methods are used for lyophilized vaccines.
- There is capacity to procure, distribute and dispose of additional injection materials for new vaccine.
- There is capacity to investigate and respond to adverse events following immunization.

6) High quality disease surveillance

- There is timely, reliable and comprehensive surveillance for major vaccine-preventable diseases.
- There is surveillance with pre-introduction baseline data to monitor impact of new vaccine.

2.4. Decision-making process

The driving force to consider the introduction of a vaccine might come from different sources: such as the NIP itself, country decision-makers, international organizations, the academic community or private sector. Although each country has its own mechanisms for an informed decision-making process, it is important to ensure that all interested parties are consulted and the implications of all possible options are discussed.

The key steps in this process can be suggested as outlined below.

- Identify stakeholders of the immunization programme.
- Identify funding sources (government agencies or donors).
- Establish a task force to bring together all parties. One of the existing committees could be used as a forum for this purpose, if available:
 - inter-agency coordinating committee (ICC); or
 - advisory committee on immunization.
- Elaborate policy and programmatic issues by reviewing existing evidence, identifying the need for additional information and assessing the possible options.

Many countries already have one or more advisory committees that provide technical and programmatic advice to the NIP. For countries that do not already have such a committee, establishing one should be considered to aid with the assessment process for adding a vaccine. The committee members are usually selected from the scientific community, immunization partners and programme implementers. They may also have knowledge of future developments, and thus help with the current decision-making.

Country example 1: South Africa

South Africa introduced Hib vaccine in 1999 with its own resources. Several local studies had documented the importance of Hib disease burden, including non-meningitis Hib. In addition, data were available from the Gambia, Finland and the United States of America showing impact of Hib vaccination. There was a strong lobby of paediatricians supporting Hib vaccine introduction. South Africa therefore developed an extensive process outlining financial implications and long-term prospects for Hib vaccine introduction. This was accompanied by political lobbying and the case was presented to national and provincial decision-makers. Hib vaccine was introduced in June 1999 as a combination with DTP, following an open tender system and supported by domestic funding.

The successful introduction process in South Africa resulted from a comprehensive approach and the unquestioned availability of the vaccine of choice. The availability of clear disease burden data was critical to convince decision-makers. The data from other countries on the effectiveness and impact of the vaccine was helpful because they demonstrated the potential disease control that could be achieved by the programme. The availability of internal financing resources ensured the long-term viability of the approach.

Country example 2: Finland

Finland has been administering the Hib vaccine to infants in monovalent form since 1987. The country decided to switch to a combination product in 2005, while assessing the possibility of introducing pneumococcal conjugate vaccine. Finland has taken a four-step approach in the process of decision-making for all new vaccines:

- 1) expected public health benefit
- 2) safety of vaccine individually
- 3) safety effects on population level
- 4) cost-effectiveness.

Using the well established technical working groups and advisory committees within the government structure, the two vaccines were evaluated according to those factors.

The impact of Hib immunization on the disease was dramatic. The high incidence which was documented by studies in the pre-vaccination era showed a sharp decrease in a few years and stayed very low, enforced by consistently high (96%) immunization coverage. Moreover, the vaccine impact was greater than estimated due to the herd effect. According to the National Registry, adverse events associated with Hib vaccine were minimal. Although the decision to introduce Hib vaccine had been made without an economic evaluation, a later study showed that the vaccination cost per child was low enough compared with the associated treatment costs.

The evaluation for pneumococcal conjugate vaccine exposed a different picture. The estimated impact of the vaccine in the country could be documented based on the existing evidence on disease burden and vaccine efficacy. Pneumococcal vaccine was feasible in terms of public benefits, safety and effects on the population. However, introduction of the vaccine in routine immunization was not found cost effective in the economic analysis. Therefore the country decided not to introduce pneumococcal conjugate under these circumstances.

Country example 3: United Republic of Tanzania

The United Republic of Tanzania indicated its intention to WHO to introduce hepatitis B (HepB) vaccine in the mid-1990s already, because serological data suggested that the prevalence of the carriage of hepatitis B surface antigen (a marker for the high risk of liver cancer) was high. However, the country could not introduce the vaccine due to lack of financial resources. In 1999, the United Republic of Tanzania and Zanzibar signed a memorandum of understanding with a WHO Collaborative Centre in Italy (Naples) to introduce hepatitis B vaccine. By the time GAVI became available as a resource for hepatitis B vaccination there was already strong conviction that this vaccine was needed. In the case of Hib, a rapid assessment was conducted in 2001 to establish the disease burden. No Hib cases were identified in laboratory records, indicating how invisible the disease was in the country. Based on hospital data of pneumonia and meningitis and on data from a reproductive and child health survey, the rapid assessment indicated that between 3300 and 3450 deaths caused by Hib meningitis could occur every year among children less than 5 years of age. The consensus meeting held in December 2001 led to the decision not to apply for Hib vaccine introduction because the burden of Hib disease compared to the cost of vaccination was not convincing. As a result, DTP–HepB combination vaccine was introduced in January 2002. Although the United Republic of Tanzania has not introduced Hib vaccine, the EPI programme remains interested in introducing it. To do so, its main challenge will be to convince senior Ministry of Health officials about the long-term prospects for financial sustainability.

3. Implementing the decision

3.1 Updating the immunization multi-year plan

Once a decision has been taken, the rationale, strategies and activities needed for the vaccine introduction have to be identified and integrated into the national comprehensive immunization multi-year plan (MYP). This can either be done by updating an existing MYP, or developing a new one if the time span of the existing MYP is close to the end.

It will be useful to consider the points below when updating an MYP to include new vaccine introduction.

1. Experience from previous vaccine introductions (if applicable).
2. Information on the specific disease to be prevented with the new vaccine:
 - surveillance data and trends
 - disease burden and cost-effectiveness of vaccination
 - public health importance and public demand.
3. Programmatic objectives:
 - expected immunization coverage
 - disease-reduction goals.
4. Implementation aspects:
 - product selection
 - vaccination schedule
 - introduction strategy
 - supply needs
 - cold-chain readiness
 - vaccine wastage
 - injection safety
 - AEFI monitoring
 - revision of records and reporting tools
 - staff training and supervision
 - information, education and communication
 - financial sustainability
 - vaccine impact evaluation.

As in the case of all activities in the MYP, those activities for the new vaccine introduction should identify the responsible institution, the budget and a timetable. Introduction of a new vaccine represents a major addition to the MYP, affecting, in particular, the costing of the whole programme. Work backwards from the planned date of introduction, and identify all the critical activities that need to happen before the start of the introduction. For example, if the updated MYP includes staff training on the new vaccine that will happen over three months, and a further three months is needed to develop the training materials and process, the process must start at least six months ahead of the planned start date.

3.2 Vaccine formulation and presentation

The NIP manager should assess the available options for formulation (combination/monovalent, lyophilized/liquid) and presentation (vial/ampoule/prefilled injection device, vial size) with respect to programme requirements. These factors might affect various aspects of the NIP such as:

- immunization schedule
- number of injections per visit
- cold storage space
- vaccine wastage
- injection safety equipment
- staff training and supervision
- recording and reporting mechanisms
- programme costs.

The assessment should lead to a decision on one or more preferred options, or a ranking of options, as well as planning the steps to tackle the issues. Cost considerations need to be included, not just for the price of the vaccine but for the programmatic costs of the different options. For example, a lyophilized formulation brings the additional costs for reconstitution syringes, their disposal, additional storage space and transport. Multi-dose vials tend to have lower costs per dose and will place fewer burdens on the cold chain, but will have higher wastage rates. Annex 2 describes a comprehensive example of how different product options could be evaluated according to their programmatic impact.

It is possible to use several vial sizes or vaccine presentations in a country programme. For example, many countries administering monovalent HepB with a birth dose prefer to use one-dose or two-dose/vial presentations for the birth dose and the larger vial size presentation for the subsequent two doses. As another example, if the country would like to introduce DTP–HepB or DTP–Hib+HepB combination vaccines but also has to administer a HepB birth dose due to the high prevalence of hepatitis e antigen in pregnant women, and the consequent high rate of perinatal transmission of virus from mother to baby; plans should be made to introduce both monovalent HepB and one of the combination vaccines.

In some instances the country may choose to start with one vaccine presentation, and then move to the preferred presentation at a later stage when it becomes available.

Managing a switch from one vaccine formulation/presentation to another can be as demanding as introducing a new vaccine. Any change needs to be preceded by adequate planning and training.

Example: Country X has been using the 10-dose DTP–HepB but is not happy with the high wastage rate due to the dispersed population and a system extensively relying on outreach activities. Multi-dose vial policy (MDVP) is difficult to apply because of the long period between the outreach sessions. When a new manufacturer starts to produce 2-dose DTP–HepB, the NIP immediately decides to switch to that presentation. However, districts encounter a lot of confusion and stock-outs in the first months as, according to their current system, they would order vaccine by the number of **vials**. The situation resolves when the system is revised to order the vaccine need in **doses**.

3.3 Phased or countrywide introduction

Phased introduction of a new vaccine may be considered in the following circumstances outlined below.

- A pilot implementation is needed to identify and address programmatic challenges, especially if it is the first experience with vaccine introduction. In that case, an evaluation needs to be made at the end of the pilot project to document lessons learnt.
- The capacity to train and supervise staff, update forms etc. is limited, thus the national staff could support provinces/districts in turn.
- The new vaccine is going to replace an existing one, and the country wants to use up the old vaccine before transitioning.
- Introduction in some parts of the country presents programmatic challenges that need to be addressed, such as limited cold-chain capacity.

On the other hand, a national roll-out will lead to a faster impact, as well as allowing national promotion of the event. It may also have the advantage of easier acceptance by the community.

3.4 Procuring the vaccine and safe injection supplies

The updated MYP should specify the activities to calculate the requirements for new vaccine and supplies, and to place an order with sufficient lead time to ensure continued supply. Procurement of the new vaccine will need to be integrated with the mechanisms used for the other vaccines. For all vaccines, a vaccine stock-management system needs to be established to ensure the right quantities of vaccines with “bundled” safe injection supplies to arrive at the right place at the right time, while tracking wastage.

The new vaccine introduction offers an opportunity to strengthen vaccine stock management because of the increased focus on vaccine procurement and supply system. For all vaccines there is a need at national and subnational levels to:

- count stock before placing an order, to adjust the order;
- compare vaccine use with immunization coverage to calculate wastage; and
- forecast future needs.

3.4.1 Forecasting supply needs

Forecasting vaccine supply needs for the first time is based on **target population, coverage, and wastage factor** (15). Often, there is considerable uncertainty about these parameters leading to compounded uncertainty about estimated vaccine requirements. It is better to overestimate rather than to underestimate the initial supply needs, provided that the procured vaccine has a long enough shelf life to avoid the risk of vaccine expiry. The subsequent orders must be adjusted based on actual usage and current stock levels, so that any initial surplus due to over-ordering is used up. The forecast also needs to be adjusted with any new data on population, coverage, wastage or usage.

The example below shows how to do a five-year vaccine forecast (Table 1).

Table 1: How to do a five-year vaccine forecast

	Definitions and formulas	Year 1	Year 2	Year 3	Year 4	Year 5
Population to be immunized	a	20 000	100 000	102 000	104 040	106 121
Total number of doses in immunization schedule	b	3	3	3	3	3
Estimated coverage with first dose	c	75%	80%	85%	90%	90%
Wastage factor	d	1.18	1.18	1.18	1.18	1.18
Annual need	$e=(a*b*c*d)$	53 100	283 200	306 918	331 471	338 102
Buffer stock	$f=(e - e')/4$	13 275	57 525	5 930	6 138	1 658
End-of-year balance	g	20 500				
Total	$e+f-g$	45 875	340 725	312 848	337 609	339 760

Partial introduction in year 1

End-of-year balance will be entered each year

Key to table 1:

- a: Population to be immunized** can be based on the most reliable source – like the census data with growth projections – or the number of children vaccinated in polio national immunization days (NIDs). For vaccines given in early infancy (DTP, HepB, Hib), estimated births should be used as the target population. For the vaccines given in late infancy (measles, yellow fever) the number of surviving infants is a better choice.

$$\text{Surviving infants} = \text{births} - (\text{births} \times \text{infant mortality rate})$$

When a new vaccine is progressively phased in, the target population is accordingly adjusted for the areas to be covered in that year.

- b:** Total number of doses of the concerned vaccine in the immunization schedule.
- c: Coverage** will need to be initially estimated based on the coverage of an existing vaccine given at the same time. For example, DTP coverage can be used as a proxy to estimate HepB coverage. If the vaccine is given as a series, it is preferable to use the coverage of the first dose in order to factor in drop-out and to avoid any potential stock-outs. Although this method leads to some overestimation in the first year, the quantities are balanced in the subsequent years when the end-of-year balance (g) is deducted from the total need. At the same time, efforts need to be made to reduce drop-out rate.
- d: Wastage** will depend on the type and presentation of the vaccine, the vaccination strategy (fixed site/outreach), population density, number of doses per vial, the number of children at each session, and whether the multi-dose vial policy (16) is used. For a new vaccine where there is no data, the likely wastage should be based on wastage for an existing vaccine with the greatest similarity of presentation and formulation.

Wastage factor	1.05	1.11	1.18	1.25	1.33	1.43	1.54	1.67	1.82	2.00	2.22	2.50
Corresponding wastage rate	5%	10%	15%	20%	25%	30%	35%	40%	45%	50%	55%	60%

$$\text{Wastage factor} = 1 / (1 - \text{wastage rate})$$

- f: Buffer stock** is usually accepted as 25% of the annual need, and aims to cover any delay in the next shipment or overuse of vaccine. It is a rolling stock to be maintained over the years. In order to make adjustments according to the changing vaccine requirement (especially in cases of phased introduction as shown in this example), the total requirement of the previous year (e') is subtracted from the total requirement of the current year (e), which is then divided by 4.
- g: End-of-year balance** is calculated at the end of each year, and deducted from the total need of the following year. Thus the forecast is not static and should be revised annually.

3.4.2 *Assuring vaccine quality*

Many developing countries prefer to use vaccines procured through UNICEF. In this case, vaccines have already been prequalified by WHO through a standardized process (17) and packaging and shipping conditions are identified to ensure that cold chain is maintained between the point of manufacture and point of delivery. The person who receives the vaccines needs to make sure that they have been transported according to international packing guidelines, and that the individual batches have received the batch release certificates from the national regulatory authority (NRA) in the country of manufacture. Batch release certificates issued by the country NRA should not be confused with the internal release documents of the manufacturing company. Checking for the various quality aspects of vaccine requires completing the vaccine arrival report (18).

For countries purchasing their own vaccines, the documents and conditions to ensure the quality of vaccine and shipping conditions should be included in the tender specifications. These include: the batch release certificates issued by the NRA in the country of manufacture; the list of countries where the vaccine is licensed; the product file including safety and efficacy data and clinical studies. Vaccine vial monitors (VVMs), cold chain monitor card, packaging and shipping conditions may be considered in this regard by the countries. Technical documents should be reviewed by an expert committee to ensure the quality of the vaccine.

National regulatory agencies are responsible for ensuring that products released for public distribution (pharmaceuticals and biological products, including vaccines) are evaluated properly and meet WHO standards of quality and safety.

All countries should have an NRA capable of performing at least two functions: licensing and postmarketing surveillance. Ideally the NRAs need to fulfil six critical control functions, particularly in vaccine-producing countries, and they need to exercise them in a competent and independent manner, backed up with enforcement power. These six functions are:

- 1) a published set of requirements for licensing,
- 2) surveillance of vaccine field performance,
- 3) system of lot release,
- 4) use of laboratory when needed,
- 5) regular inspections for GMP, and
- 6) evaluation of clinical performance.

The documented performance of these functions according to established indicators will be essential to guarantee vaccine quality. These critical control functions depend on vaccine source, as shown in Table 2.

Table 2: Relation of critical functions to vaccine source

Vaccine source	Licensing	Surveillance	Lot release	Laboratory access	GMP inspections	Clinical evaluation
UN agency	x	x				
Procured	x	x	x	x		
Produced	x	x	x	x	x	x

The new vaccine introduction provides an opportunity to improve vaccine quality, check on arrival for all vaccines, and strengthen the licensing framework. WHO gives ongoing support to countries to assess their NRAs as well as maintaining the Global Training Network (<http://www.who.int/vaccines-access/quality/gtn/>) as a means of providing educational resources to vaccine regulatory and production staff in countries.

3.5 Immunization strategy

3.5.1 Routine immunization schedule

Selecting the optimal schedule for immunization requires balancing the need for:

- early protection;
- matching with the existing schedule to the extent possible;
- minimizing the number of visits; and
- implementing the most effective schedule to reduce disease burden.

The vaccine introduction may also offer an opportunity to streamline the schedule by reducing the number of visits required. WHO recommends the following schedule for infants (Table 3).

Table 3: Recommended immunization schedule for infants

Age	BCG	OPV	DTP	HepB(1)	HepB(2) ^a	Hib	YF ^b	Measles
Birth	X	X ^c			X			
6 weeks		X	X	X	X	X		
10 weeks		X	X	X	X ^d	X		
14 weeks		X	X	X	X	X		
9 months							X	X ^e

^a HepB option (2) with birth dose is recommended where perinatal transmission is frequent, as in Eastern Asia. If HepB is given as a combination, the birth dose must be given as monovalent making a total of four doses of HepB.

^b Only in countries at risk for yellow fever.

^c Only in countries that are still polio endemic.

^d In countries using HepB vaccine as a combination.

^e A second opportunity for measles should be provided for all children either as part of the routine schedule or through regular mass immunizations targeting the susceptible age group. Once measles control improves, the first dose should be given at age 12 months.

In case the new vaccine replaces an existing one in the schedule, transitional arrangements will be needed for the children who had already started their immunization schedule with the old vaccine.

Example: Country X decides to launch the DTP–HepB+Hib combination vaccine from January next year, to replace the DTP and monovalent HepB which were administered previously. They have reviewed the options for transitioning:

- **Option 1:** All children who come to the health centres from January will be given the relevant dose of the new vaccine. No catch-up activity will be conducted for children who start the schedule with the old vaccine, thus they will complete the schedule with the new one.

Pros: Simpler implementation for the staff.

Cons: Stocks of old vaccines will not be used; some children will not receive three doses of Hib.

- **Option 2:** Children who have already started will complete the schedule with the old vaccine. Only the newcomers will be given the new vaccine starting from January.

Pros: Opportunity to use up the old vaccines.

Cons: Complicated implementation; unequal treatment of children in the same visit may lead to parental objection.

In cases where each vaccine is administered separately, creating an extra visit for the new vaccine should be avoided if possible. Limiting the number of visits will increase the chances of the children becoming fully immunized. On the other hand, this may cause multiple injections to be given in the same visit. It has been observed that multiple injections are quite acceptable among health staff and the community, with some additional staff training and appropriate communication with the parents.

3.5.2 Catch-up immunization

A “catch-up” programme when introducing the vaccine for the first time in infants may be considered for two reasons:

- to increase immunization coverage rapidly among infants; and
- to reduce the susceptible population in age/population groups which are at high risk but would have been missed out as they would not benefit from routine immunization.

The initial catch-up campaign may be planned if the disease has a low transmission rate, and not many people in the population acquired natural infection and immunity in the pre-vaccination era. One example could be rubella immunization, as its primary aim is to prevent infection in pregnancy that can lead to the congenital rubella syndrome (CRS). Vaccination of infants only would take very many years before impact on CRS is seen, thus vaccination of adult women is also recommended to provide direct protection to those at risk. Another example could be vaccinating those health staff against hepatitis B that is at increased risk for bloodborne infections.

Another issue that can be considered in this regard is to decide which age group to include when the implementation of the new vaccine is launched. There will always be children who have received one or two doses of the existing vaccine, and it is a question whether to provide them with the full series of the new vaccine, which may require additional visits. Similarly, mothers may demand that older children who are fully vaccinated with the existing vaccines should also benefit from the new antigen. The decision for this arrangement needs to be taken at country level. In general, it is recommended that infants coming after the new vaccine introduction date should have priority in receiving the new vaccine but, if it is feasible, older children can be included to complete their vaccine series.

Catch-up campaigns implemented years after the vaccine is introduced should be considered separately from the initial catch-up campaigns. These are conducted against the build-up of susceptible cohorts due to low coverage of immunization. An example of this is measles catch-up campaigns, done many years after introduction of measles vaccine in infancy to protect the children who did not receive vaccine in infancy due to low coverage or failed to respond to the first dose.

3.6 Cold-chain readiness and vaccine management

3.6.1 *Estimating additional cold chain requirements*

The updated MYP should include calculations of the impact of the new vaccine on cold chain requirements at national and subnational levels. A tool to calculate vaccine volumes has been developed and is being updated by WHO (19). This tool only calculates the cold chain volume need of infant vaccines and does not include buffer stock and supply intervals.

Alternatively, WHO guidelines for establishing or improving primary and intermediate vaccine stores (20) include two worksheets that can be used for this purpose. Worksheet 1 calculates the net storage volume required for each antigen based on programme needs; Worksheet 2 further calculates refrigeration capacity to store what is calculated in Worksheet 1. As for Worksheet 1, “packed volume per dose” should be taken from *Guidelines on the international packaging and shipment of vaccines* (18).

3.6.2 *Ensuring adequate functional cold chain capacity*

Using the data on the additional storage requirements for the new vaccine, including the buffer stock, cold-chain storage and transport capacity at each level need to be assessed to see if additional equipment will be needed to cater for the new vaccine. Also it should be considered whether there may be seasons of the year when more vaccines have to be stored because of anticipated breaks in the supply chain. Conversely, less vaccine may be used at some times of the year due to the difficulty in accessing communities (e.g. seasonal flooding or extreme winter conditions).

This assessment provides an ideal opportunity to establish a national cold-chain inventory, which describes the type of equipment and its status in every part of the country. Included in that inventory should be the expected life of the item so that a planned replacement programme can be instituted. This inventory should be updated every two to three years. The vaccine introduction can be used as an opportunity to raise support from the government or immunization partners for replacing the non-functional equipment and procuring additional, if necessary.

3.6.3 *Wastage optimization*

It is important to minimize wastage. In addition to saving funds, monitoring and preventing wastage can be an indicator of good programme management. However, reducing wastage can be at the expense of coverage when health workers become reluctant to open a multi-dose vial for only one child, or insufficient vials are taken on outreach. In countries with a dispersed population and extensive outreach, a higher wastage rate may be acceptable not to lose programme efficiency. Therefore, the appropriate goal is wastage optimization, which means to minimize preventable wastage without compromising coverage or safety.

Because of the higher cost of new vaccines, increased attention is likely to be given to wastage, and this should be used to improve monitoring of wastage (21). The vaccine introduction can provide the impetus for establishing a wastage monitoring system. Wastage monitoring needs to be integrated with coverage monitoring, and information on both should be fed back to subnational levels. Where possible, wastage should be categorized into opened and unopened vial wastage, analysed by each administrative level, and compared with coverage data. Adding the vaccine usage data to the monitoring system is also important to obtain data on actual use to adjust the estimated vaccine needs in the forecast.

3.7 Immunization safety

3.7.1 Safe injection supplies and waste disposal

The new vaccine may require additional injections and/or additional reconstitution syringes leading to a need for more safe injection supplies. If not already in place, the updated MYP can work on the practical distribution of the vaccine and its diluents; “bundled” with matching amounts of safe injection supplies—safety boxes, auto-disable syringes and reconstitution syringes. This can start with the new vaccine, and eventually be expanded for all vaccines.

Similarly, the new vaccine may increase the volume of used injection material that requires disposal and the introduction may be an opportunity to address waste-disposal issues.

3.7.2 Adverse events following immunization

All NIPs should have a working surveillance system for AEFIs to track any expected and unexpected adverse events and to interrupt the use of the vaccine if necessary. As there may be special concerns around any new intervention, it will be important to have the capacity to investigate and communicate results related to any community concerns around AEFI. If there is no AEFI surveillance system in the country, adding a new vaccine would be an appropriate time to start establishing one. Moreover, if there are any new procedures for preparing or administering the vaccine there may need to be special surveillance to ensure that there are no programme errors leading to AEFI.

It is worth keeping in mind that some of the adverse events are actually coincidental events mistakenly related to the vaccination. Adequate investigation of a cause and effect relationship, with the involvement of scientific experts, will be crucial to avoid rumours that may hamper the programme.

3.8 Staff training and supervision

Vaccine introduction is usually an opportunity to provide refresher training to staff and supervisors on all aspects of NIP, including specific aspects related to the new vaccine.

Training for vaccine introduction will include aspects related to:

- details regarding the disease and the new vaccine (schedule, safety, efficacy, AEFI);
- storage, preparation and administration of the vaccine, including avoidance of freezing;
- record keeping and reporting of doses administered; and
- monitoring and reporting the vaccine wastage, and using approaches like the multi-dose vial policy (MDVP) to reduce it.

Adults may learn better and convert their knowledge into behaviour through the act of doing rather than by passive listening. Hence, the traditional form of classroom-based training is relatively ineffective. If any classroom-based training is considered, it should involve role plays and stimulate small-group discussions by the trainees, rather than just be organized as a sequence of presentations and lectures.

3.9 Advocacy, social mobilization and communication

Advocacy efforts usually start in the decision-making process to ensure that funds can be made available and political commitment can be provided for new vaccines that are cost effective and have an important public health impact. But, advocacy for immunization needs to go beyond the initial decision, by communicating the benefits expected from the addition of the new vaccine, building trust and awareness for the new vaccine and immunization programme in general, creating demand in the community, and showing the impact of immunization in preventing disease burden. The impact of some vaccines can be visible in a couple of years, especially if the strategy includes an initial catch-up campaign. In others like HepB, prevention (i.e. liver cancer) will occur several decades after delivery of immunization in that cohort; this means special advocacy efforts are needed.

Advocacy might be best characterized as any effort to influence policy and decision-makers, to fight for social change, to transform public perceptions and attitudes, to modify behaviour, or to mobilize human and financial resources. There are several steps to take in order to conduct an effective advocacy and communication effort (22):

- 1) gathering information
- 2) building a plan
- 3) creating messages and materials
- 4) building a strong coalition
- 5) engaging policy and decision-makers
- 6) informing and involving the public
- 7) working with mass media
- 8) monitoring and evaluation.

For all of these strategies, the foundation is good science and finding the effective and appropriate media to communicate the messages. A range of channels should be used to deliver the messages, including community volunteers and health workers, as well as the mass media. At the national level, the ICC is the primary body to be involved in and plan for the advocacy activities. However, there are other immunization partners like NGOs, ministries of finance and education, other donor agencies, the private sector, universities and community and religious leaders. Obtaining the support of these partners will be extremely useful in communicating the information regarding the new vaccine to the community and in refreshing awareness of immunization. Since immunization is primarily a medical intervention, most of the key opinion leaders are in the medical community. Involving prominent academicians in scientific advisory committees or clinical evaluations of the vaccines might be very effective for advocacy purposes.

Advocacy and communication plans also need to be prepared to address possible AEFI due to the new vaccine, to deal with community concerns, to respond to rumours and other negative publicity about the new vaccine.

The development of information, education, and communication (IEC) resources can be useful both for advocacy and for health worker training. Before preparing any material, there should be a needs assessment to make sure that the appropriate material is developed. As well as developing new material, existing IEC material that is used in the programme may need to be adapted to reflect the addition of the vaccine.

In addition, IEC materials can be used:

- to encourage disease reporting to improve surveillance;
- to give advice on care after immunization for dealing with the common minor vaccine reactions;
- to improve the reporting of more severe AEFI; and
- to encourage return for the next visit.

3.10 Supportive supervision

After vaccine introduction, the implementation should be periodically reviewed through supportive supervision, which also includes “on-the-job training” (23). This involves assessing the health worker’s delivery of the service, praising the worker for achievements and correct practices, and providing advice on how to improve on deficient areas. To be effective, there needs to be ongoing follow-up to ensure that the suggested practices are being used and, if not, to address the obstacles to doing so. Therefore, supportive supervision requires considerable inputs from skilled supervisors. It is an ongoing process needed for the NIP that can be started with the vaccine introduction, if not implemented earlier.

Supportive supervision is one of the elements of the Reaching Every District (RED) strategy for improving overall coverage, and any work on RED should be integrated with that of vaccine introduction. The new vaccine may be used as an aid to coverage improvement, by providing additional incentives for immunization.

3.11 Information systems

Adding a vaccine will generally require updating the forms and vaccination cards used for recording and reporting vaccine administration, forms for ordering vaccines and vaccine stock ledgers, and any other forms that list the NIP vaccines. When the change involves substituting one vaccine for another, it is possible to use the same forms, knowing that any record written after the start date relates to the new vaccine. Although it is preferable to adapt the forms to reflect the vaccine that is actually used, this can also be accomplished when they need reprinting.

In addition to the forms, the various systems that use the information will also need to be updated to reflect the addition of the new vaccine. This includes the systems that aggregate immunization coverage data from subnational levels upwards, including reporting at national level to UNICEF/WHO. In many countries these data are not managed by the immunization programme, but by a national health information system or similar. Early communication with the national health information system is needed to make sure of adequate lead time to change the system.

As with other aspects of the immunization programme, the additional needs from vaccine introduction lead to an opportunity to review how information is gathered and used for the NIP. It is important for the NIP to improve the quality of routinely reported data and to use that data to improve programme performance at all levels.

4. Monitoring impact

Immunization, unlike some health interventions, has a service delivery indicator (immunization coverage) that is closely linked to an impact indicator (morbidity/mortality). In general, they both should be monitored at national and subnational levels to target areas or population groups in greatest need, identify best and worst practices, and address problems with vaccine effectiveness.

Monitoring the impact is also important for advocacy and long-term sustainability of the programme. The best argument for additional resources is to show that the resources given to the programme have been effectively used, both in terms of reaching the target population and by reducing the disease burden. WHO is in the process of developing impact assessment protocols for HepB, Hib and meningococcal vaccine immunization programmes.

4.1 Coverage monitoring

The primary method for countries to evaluate the new vaccine introduction is through monitoring immunization coverage at district level, which should cause a reduction in disease over time. If the new vaccine is administered separately, comparison of its coverage and drop-out rate with that of other vaccines provides valuable insight in programme performance. Each level of the NIP should regularly analyse the data from the sub-levels and provide feedback. Obviously, this relies on the quality of the data produced by the programme, and the new vaccine introduction may be a useful prompt to assess and improve data quality for routine coverage reporting. The timeliness of coverage may be particularly important for the new vaccine, for example, delivery of the birth dose of hepatitis B vaccine within 24 hours. However, a more important aspect is the use of data at the level it is collected. This can be a powerful intervention to improve performance, staff morale and engagement and data quality.

Coverage surveys may be done periodically to validate routinely reported data as well as to find out reasons for failure to immunize. However, coverage surveys have their own biases, and the primary effort should be to improve the quality of routinely reported data.

4.2 Disease and AEFI surveillance

The ability to monitor the impact on disease will depend on the nature of the disease being prevented and the existing surveillance system. Mostly, the disease related to the new vaccine would not already be a part of the existing disease surveillance system and it will need to be integrated in the system. This may be a national comprehensive surveillance from both community and hospital sources, or a sentinel surveillance operating in selected sites. In addition, there is a need to establish laboratory capacity to confirm the diagnosis. The costs of supporting the surveillance system and laboratory should be included in the overall programme costs.

A key aspect of getting disease data is to compare it with coverage data to ensure that the impact on disease is in line with what is expected for the level of coverage in that area. Obtaining the immunization status of all disease cases, and comparing immunization coverage of cases with immunization coverage in the overall population provides a method of estimating vaccine effectiveness that is also useful for programme monitoring. However, there are important biases in the method, so the estimates need to be carefully interpreted (24).

Another aspect of impact that could be included is AEFI surveillance. In addition to providing another dimension of information on the impact of the vaccine, AEFI surveillance is important in maintaining confidence in the programme and to identify safety issues including those due to programmatic mistakes.

4.3 Special studies

Because surveillance may not provide timely and direct evidence of the impact of vaccination on disease, special studies might be considered. The assessment of HepB programmes is one example where the impact on chronic disease may not be evident for decades after vaccination. In this case, the impact of HepB vaccination can be assessed with a serosurvey of chronic infection.

4.4 Assessing overall implementation

WHO has developed a post-introduction evaluation checklist, to assess the implementation of the new vaccine 6 to 24 months following introduction (Annex 3). Because this assessment addresses several components of immunization programmes, it is recommended that it is combined with other ongoing evaluations such as EPI reviews, surveillance evaluations or other similar system evaluations.

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Annex 1:

Specific issues for selected vaccines

WHO has provided detailed technical information for the implementation of each available vaccine in the *Core Information for the Development of the Immunization Policy*¹. Here, specific issues related to the vaccine introduction are described for new and underused vaccines.

¹ World Health Organization. *Core information for the development of immunization policy, 2002 update*. Geneva, WHO, 2002 (WHO/V&B/02.28). Available at <http://www.who.int/vaccines-documents/DocsPDF02/ww57.pdf> accessed on 16 September 2005.

Issues related to introduction of new and underused vaccines

Vaccine	Issues for introduction	Impact assessment	References
Hepatitis (B) (HepB)	<ul style="list-style-type: none"> • The vaccine is very safe and highly effective (85–98% with three doses). WHO recommends introduction in all countries. • A determination of the role of perinatal transmission (useful for birth dose considerations) can be made based on the overall seroprevalence of HBsAg, age-specific prevalence of HBsAg, and the prevalence of the HBeAg in pregnant women. • Combination products may not be used at birth; therefore, programmes including the birth dose will need to include monovalent HepB vaccine in the supply. • HepB vaccine is sensitive to low temperatures and can be damaged by freezing. On the other hand, it is quite heat stable and use with a vaccine vial monitor (VVM) allows greater flexibility in transportation and storage. 	<p>WHO provides comprehensive guidance on impact assessment for hepatitis B immunization as well as on conducting simple serosurveys that may be useful in certain circumstances to guide prevention and assist in advocacy efforts. Guidelines on assessing the impact of HepB immunization programmes, and on the HepB vaccine coverage and HBV infection marker survey, are in preparation in WHO.</p>	<ul style="list-style-type: none"> • <i>Hepatitis B immunization. Introducing hepatitis B into national immunization services</i> (fact sheet). Geneva, WHO. Available on the Internet at http://www.who.int/vaccines-documents/DocsPDF01/www598.pdf accessed on 16 September 2005. • Hepatitis B vaccines—WHO Position Paper. <i>Weekly Epidemiological Record (WER)</i>, 2004, 28:255–263. Available on the Internet at http://www.who.int/vaccines-documents/PP-WER/wer7928.pdf accessed on 16 September 2005. • <i>Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents</i>. Geneva, WHO, 2001 (WHO/V&B/01.31). Available on the Internet at http://www.who.int/vaccines-documents/DocsPDF01/www613.pdf accessed on 16 September 2005.
Haemophilus influenzae type b (Hib)	<ul style="list-style-type: none"> • Challenges to the introduction of Hib vaccine include demonstration of disease burden in most Asian countries, as well as in Central and Eastern Europe. • Another main challenge to date has been long-term financing as one dose of Hib vaccine costs at least US\$ 2.50 in 2004. 	<p>Hib vaccine introduction can be assessed for its impact on the programme performance (DTP3 coverage prior to and after Hib vaccine introduction) and on the occurrence of disease. The most specific indicator is laboratory-confirmed meningitis. However, in most developing countries this is usually only available through sentinel sites. Other end-points include vaccine effectiveness against clinical meningitis or radiological pneumonia. These can be assessed by carefully designed case-control studies. Guidelines on assessing the impact of Hib immunization programmes on childhood meningitis are under development at WHO.</p>	<ul style="list-style-type: none"> • <i>Haemophilus influenzae type b immunization. Introducing Haemophilus influenzae type b conjugate vaccine into national immunization services</i> (Fact sheet). Geneva, WHO, 2001 (WHO/V&B/01.29). Available at http://www.who.int/vaccines-documents/DocsPDF01/www599.pdf accessed on 16 September 2005. • <i>Introduction of Haemophilus influenzae type b vaccine into immunization programmes. Management guidelines, including information for health workers and parents</i>. Geneva, WHO, 2000 (WHO/V&B/00.05). Available at http://www.who.int/vaccines-documents/DocsPDF99/www9940.pdf accessed on 16 September 2005. • The WHO Position Paper on <i>Haemophilus influenzae type b conjugate vaccines</i>. <i>Weekly Epidemiological Record</i>, 1998, 73: 64–68. Available on the Internet at http://www.who.int/vaccines-documents/PP-WER/wer7310.pdf accessed on 16 September 2005.

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Issues related to introduction of new and underused vaccines (continued)

Vaccine	Issues for introduction	Impact assessment	References
Yellow fever (YF)	<ul style="list-style-type: none"> Yellow fever vaccine is contraindicated for infants less than 6 months of age, immune-deficient persons and persons with egg allergy. The risk of disease should be weighed against the risk of vaccination in pregnant women and in persons with symptomatic HIV infection. These are important factors to consider before planning a mass preventive vaccination campaign. Severe adverse reactions are extremely rare but, when they occur, infants and elderly seem more susceptible. Another challenge for introduction is maintaining high vaccination coverage, as at least 80% of the infants need to be vaccinated for effective disease control. 	<p>There are plans to assess YF vaccine introduction impact by the outcome indicators of immunization programme like vaccination coverage, as well as disease incidence and frequency of outbreaks.</p>	<ul style="list-style-type: none"> Adverse events following yellow fever vaccination. <i>Weekly Epidemiological Record</i>, 2001, 76(29):217–218. Available at http://www.who.int/wer/pdf/2001/wer7629.pdf accessed on 16 September 2005. Monath TP. Yellow fever: an update. <i>Lancet, Infectious Diseases</i>, 2001, 1:11–20. Available in pdf format on the report CD. <i>District guidelines for yellow fever surveillance</i>. Geneva, WHO, 1998 (WHO/EPI/GEN/98.09). Available at http://www.who.int/vaccines-documents/DocsPDF/ww9834.pdf accessed on 16 September 2005. <i>International travel and health</i>. Geneva, WHO, 2002. Available at http://www.who.int/ith accessed on 16 September 2005. Silva J et al. <i>Vaccine safety: yellow fever vaccine. Report of the Technical Advisory Group on Vaccine Preventable Disease</i>. Washington DC, Pan American Health Organization, 2000. <i>The immunological basis for immunization. Module 8: Yellow fever</i>. Geneva, WHO, 1993 (WHO/EPI/GEN/93.18). Available at http://www.who.int/vaccinesdocuments/DocsPDF-ibi-e/mod8_e.pdf accessed on 16 September 2005. WHO position paper on yellow fever vaccine. <i>Weekly Epidemiological Record</i>, 2003, 78:349–360. Available at http://www.who.int/vaccines-documents/PP-WER/wer7840.pdf accessed on 16 September 2005. Yellow fever. Geneva, WHO, 1998 (WHO/EPI/GEN/98.11). Available at http://www.who.int/vaccines-documents/DocsPDF/www9842.pdf accessed on 16 September 2005.

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Issues related to introduction of new and underused vaccines (continued)

Vaccine	Issues for introduction	Impact assessment	References
Japanese encephalitis	<ul style="list-style-type: none"> Further studies are needed to document the safety of administering Japanese encephalitis (JE) vaccine concomitantly with the measles vaccine. If the first dose of JE vaccine could be given at the same visit with the first dose of measles, this will fit better into the schedule of the national immunization programme (NIP) and may help to increase coverage. In countries having a good surveillance and laboratory framework, impact of JE vaccination on other flavivirus infections should be monitored. Studies from China and Thailand and experience gained in Sri Lanka since 1988 indicate that routine immunization to control JE vaccine is cost effective; moreover, new vaccines could possibly be cost-saving in comparison to current vaccines. It is believed that, when the live attenuated and vero cell JE vaccines become available in the global market and have been prequalified by WHO, the vaccine cost will be markedly reduced. 	<p>Introduction of immunization has led to a marked reduction of disease in several countries. In combination with vector control measures and environmental management, near elimination has been achieved in countries with widespread immunization programmes such as China (Province of Taiwan), Japan and the Republic of Korea. Elimination has been achieved mainly by immunization in Sri Lanka. Impact can be measured in terms of a reduction in rates of encephalitis or in rates of JE if specific diagnostic tools are available. WHO is currently developing standards for surveillance of JE in endemic countries, and there are also improved diagnostic tools under development.</p>	<ul style="list-style-type: none"> WHO Position Paper on Japanese encephalitis vaccines. <i>Weekly Epidemiological Record</i>, 1998, 73(44):337–344. Available at http://www.who.int/vaccines-documents/PP-WER/wer7344.pdf accessed on 16 September 2005. Halstead SB, Tsai TF. Japanese encephalitis vaccines. In: Plotkin SA, Orenstein WA (eds), <i>Vaccines</i>. Philadelphia, W.B. Saunders Co., 2004. <p>Note: CVP/PATH conducts a Japanese encephalitis project in collaboration with WHO. More information can be found at http://www.childrensvaccines.org/html/jep.htm accessed on 16 September 2005.</p>
MMR/MR	<ul style="list-style-type: none"> While many countries have readily replaced single-antigen measles vaccine with measles–mumps–rubella (MMR) or measles–rubella (MR) vaccines, to prevent a potential gradual increase in rubella susceptibility among women of childbearing age and a paradoxical increase in congenital rubella syndrome (CRS) incidence, efforts are needed to assure that women of childbearing age are also protected against rubella. A strong laboratory-based surveillance mechanism is a must for identification of rubella outbreaks following the introduction of MMR or MR into the NIP. A screening programme should be available for females entering childbearing age because, once the vaccine is introduced into the NIP, the susceptibility of adults getting rubella will be increased. 	<p>When high coverage is achieved and sustained with MMR vaccine over time, major decreases in measles, mumps and rubella incidences have been documented. Moreover, countries that have implemented comprehensive strategies for rubella control have demonstrated the elimination or near elimination of CRS.</p>	<ul style="list-style-type: none"> The WHO position paper on rubella virus vaccines. <i>Weekly Epidemiological Record</i>, 2000, 75:161–169. Available at http://www.who.int/vaccines-documents/PP-WER/wer7520.pdf accessed on 16 September 2005. The WHO position paper on mumps virus vaccines. <i>Weekly Epidemiological Record</i>, 2001, 76:346–355. Available at http://www.who.int/vaccines-documents/PP-WER/wer7645.pdf accessed on 16 September 2005. The WHO Position Paper on Measles virus vaccines. <i>Weekly Epidemiological Record</i>, 2004, 79:130–142. Available at http://www.who.int/vaccines-documents/PP-WER/wer7914.pdf accessed on 16 September 2005.

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Issues related to introduction of new and underused vaccines (continued)

Vaccine	Issues for introduction	Impact assessment	References
<p>Inactivated polio vaccine (IPV)</p>	<p>Oral poliovirus vaccine (OPV) remains the vaccine of choice for the polio eradication initiative. In 1988, only five countries used inactivated poliovirus vaccine (IPV) exclusively (Finland, France, Iceland, the Netherlands, and Sweden) and Denmark used a sequential schedule. With the progress towards polio eradication, many industrialized countries have revised their recommendations for routine immunization, and replaced OPV with IPV to ensure continued high population immunity and prevent vaccine-associated paralytic poliomyelitis (VAPP). Currently, more than 30 countries use IPV exclusively or in a sequential schedule.</p>	<p>Since poliovirus transmission has been eliminated in most countries, assessment of vaccination coverage with IPV provides a proxy of "population immunity" expected to prevent any imported poliovirus from spreading and establishing endemic or epidemic transmission.</p>	<ul style="list-style-type: none"> Introduction of inactivated poliovirus vaccine into oral poliovirus vaccine-using countries. WHO position paper: <i>Weekly Epidemiological Record</i>, 2003, 78:241–252. Available at http://www.who.int/vaccines-documents/PP-WER/wer7828.pdf accessed on 16 September 2005.
<p>Rotavirus</p>	<ul style="list-style-type: none"> The efficacy of this vaccine in developing countries in Africa and Asia is yet to be determined. Further trials are proposed by WHO and the Rotavirus Vaccine Programme for this purpose. The safety, immunogenicity and efficacy of rotavirus vaccines in HIV-infected children are currently being investigated. Potential interference with other routine EPI vaccines, including live OPV, are currently being investigated. One of the vaccines has already been shown to have no interference with OPV. Due to the large volume of the vaccine, the impact on cold chain space should be considered before introduction. 	<p>WHO will work on the development of a tool to assess the impact of vaccination in countries.</p>	<ul style="list-style-type: none"> <i>Report of the meeting on future directions for rotavirus vaccine research in developing countries</i>. Geneva, 9-11 February 2000. Geneva, WHO, 2000 (WHO/V&B/00.23). Available at: http://www.who.int/vaccines-documents/DocsPDF00/www531.pdf accessed on 16 September 2005. <i>Generic protocol for (i) hospital-based surveillance to estimate the burden of rotavirus gastroenteritis in children and (ii) a community-based survey on utilization of health care services for gastroenteritis in children. Field test version</i>. Geneva, WHO, 2002 (WHO/V&B/02.15). Available at: http://www.who.int/vaccines-documents/DocsPDF02/www698.pdf accessed on 16 September 2005. Rotavirus vaccines, an update. <i>Weekly Epidemiological Record</i>, 2003, 78:2–3. Available at: http://www.who.int/vaccines-documents/PP-WER/wer7801.pdf accessed on 16 September 2005. <p>Note: GAVI supports the development of new rotavirus vaccines through a special project. More information can be found at http://www.rotavirusvaccine.org/ accessed on 16 September 2005.</p>

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Issues related to introduction of new and underused vaccines (continued)

Vaccine	Issues for introduction	Impact assessment	References
Pneumococcus conjugate	<ul style="list-style-type: none"> • While 9-valent and 11-valent formulations are expected to cover >75% of the serotypes causing severe disease in all regions of the world, actual data confirming this is limited from some regions. Therefore obtaining local and/or regional data on serotype distribution may be required. • Pneumococcal vaccines are likely to be substantially more expensive than the current NIP vaccines. Therefore, a strong economic case will be required to convince governments and donors about vaccine introduction, which involves estimating local disease burden and vaccine cost-effectiveness. • Once the vaccine has been introduced, continued surveillance documenting the impact of the vaccine on disease will be required to sustain the vaccine programme. This will be especially important for countries who are first to introduce the vaccine. Surveillance should be conducted in vaccinated and unvaccinated persons in order to assess the beneficial effects of herd immunity and the risks of serotype replacement. 	<p>Vaccine impact assessment would be similar to that used for Hib vaccine.</p> <p>In addition, surveillance would be required to monitor for replacement disease with non-vaccine serotypes of pneumococcus.</p>	<ul style="list-style-type: none"> • WHO Position Paper on pneumococcal vaccines. <i>Weekly Epidemiological Record</i>, 2003, 78 (14):110–119. Available at: http://www.who.int/vaccines-documents/PP-WER/wer7814.pdf accessed on 16 September 2005. <p>Note: GAVI supports the development of 9-valent and 11-valent pneumococcal vaccines through a special project. More information can be found at http://www.preventpneumo.org/ accessed on 16 September 2005.</p>

Issues related to introduction of new and underused vaccines (continued)

Vaccine	Issues for introduction	Impact assessment	References
Meningococcal vaccines	<p>Meningococcus A conjugate:</p> <ul style="list-style-type: none"> • It is anticipated that the low price of the vaccine negotiated by the Meningitis Vaccine Project will be affordable for the African countries. • A well planned and coordinated strategy for introduction will guarantee widespread use of this needed vaccine. This requires not only a sound plan, but the buying in of the user countries. • Estimating local disease burden and vaccine cost–effectiveness should be integral components. 	<p>Vaccine impact assessment will be based on the results of surveillance activities, which are already well established in the African meningitis belt countries. These activities take advantage of processes put into place for other diseases and pathogens.</p>	<ul style="list-style-type: none"> • <i>Control of epidemic meningococcal disease. WHO practical guidelines.</i> Geneva, World Health Organization, 1998 (WHO/EMC/BAC/98.3). Available at: http://www.who.int/entity/csr/resources/publications/meningitis/whomc98bac983.pdf accessed on 16 September 2005. • Jodar L et al. Meningococcal conjugate vaccine for Africa: a model for development of new vaccines for the poorest countries. <i>Lancet</i>, 2003, 361 :1902–1904. Available in pdf format on the report CD. • Lapeyssonie L. La méningite cérébrospinale en Afrique. <i>Bulletin of the World Health Organization</i>, 1963, 28 (Suppl.): 1–114. Available in pdf format on the report CD. • Guibourdenche M et al. Epidemics of serogroup A <i>Neisseria meningitidis</i> of subgroup III in Africa, 1989–94. <i>Epidemiology and Infection</i>, 1996, 116:115–120. • Greenwood B, Manson Lecture. Meningococcal meningitis in Africa. <i>Transactions of the Royal Society of Tropical Medicine and Hygiene</i>, 1999, 93:341–53. • Ramsay ME et al. Efficacy of meningococcal serogroup C conjugate vaccine in teenagers and toddlers in England. <i>Lancet</i>, 2001, 357:195–196. Available in pdf format on the report CD. • Trotter CL et al. Effectiveness of meningococcal serogroup C conjugate vaccine 4 years after introduction. <i>Statistics, Economics, and Modelling Department, Health Protection Agency Communicable Disease Surveillance Centre, United Kingdom. Lancet</i>, 24 July 2004, 364(9431):365–367. <p>Note: CVP/PATH supports the development of meningococcal conjugate vaccine through a special project. More information can be found at http://www.meningvax.org accessed on 16 September 2005.</p>

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Issues related to introduction of new and underused vaccines (*continued*)

Vaccine	Issues for introduction	Impact assessment	References
Other meningococcal vaccines	<ul style="list-style-type: none"> • A combination Men A/C vaccine with DTP, HepB and Hib is expected to be licensed in 2007. • The price might be beyond the reach of the least developed countries. However, it might be a programmatically feasible option for countries already considering/using pentavalent and planning to add the meningococcal vaccine. 		

Annex 2:

Case study: Assessment of vaccine presentation options

In 2004, country X planned to integrate both HepB and Hib antigens into the national immunization programme, with a preference for combination vaccines. On enquiring the supply situation, it has occurred that both DTP–HepB and DTP–HepB+Hib vaccines will be unavailable for introduction in 2004 and will only become available at the end of 2006.

The manager of the national immunization programme has consulted the partner institutions and worked on a number of options for introduction of HepB and Hib vaccines including programmatic impact, to be discussed by the interagency coordinating committee.

Option 1: Delay introduction until preferred combination vaccine available

Advantages	Disadvantages
<ul style="list-style-type: none"> • It allows minimal programmatic changes and training costs. 	<ul style="list-style-type: none"> • A large number of cases of preventable disease and deaths continue to occur.
<ul style="list-style-type: none"> • It has low impact on the cold chain. 	<ul style="list-style-type: none"> • An expensive combination results in increased costs and difficulty with financial sustainability.
<ul style="list-style-type: none"> • There is no impact of extra injection on caregiver acceptance. 	<ul style="list-style-type: none"> • There may be further delays in the availability of the vaccine.
<ul style="list-style-type: none"> • There is low injury potential from multiple injections. 	

Option 2: Administer DTP vaccine plus monovalent HepB vaccine; delay Hib vaccine introduction until preferred combination is available

Advantages	Disadvantages
<ul style="list-style-type: none"> • It is easy to handle (no reconstitution). 	<ul style="list-style-type: none"> • Two injections are given per child per session.
<ul style="list-style-type: none"> • There is much less wastage: all liquid products can be kept for subsequent sessions. 	<ul style="list-style-type: none"> • More needles / syringes are required.
<ul style="list-style-type: none"> • It is less expensive. 	<ul style="list-style-type: none"> • More injection waste is produced, which needs to be disposed of safely.
<ul style="list-style-type: none"> • It has good long-term financial sustainability 	<ul style="list-style-type: none"> • It does not address Hib disease burden early.

Option 3: Administer DTP vaccine plus monovalent HepB vaccine plus monovalent Hib vaccine

Advantages	Disadvantages
<ul style="list-style-type: none"> • These are easy to handle (no reconstitution) unless Hib vaccine is lyophilized. 	<ul style="list-style-type: none"> • Three injections would be given per child per session.
<ul style="list-style-type: none"> • There would be much less wastage: all liquid products can be kept for subsequent sessions. 	<ul style="list-style-type: none"> • Many more needles / syringes would be required.
<ul style="list-style-type: none"> • This would allow for transition to DTP–HepB + Hib monovalent with minimal change to the programme. 	<ul style="list-style-type: none"> • Much more injection waste would be produced, which needs to be disposed of safely.
<ul style="list-style-type: none"> • This would address preventable disease and death burden immediately. 	<ul style="list-style-type: none"> • There would be increased social mobilization costs associated with product switching.
<ul style="list-style-type: none"> • There would be a long-term reduction in programmatic complexity. 	<ul style="list-style-type: none"> • There would be a large impact on the cold chain.

Option 4: DTP–Hib vaccine plus monovalent HepB vaccine

Advantages	Disadvantages
<ul style="list-style-type: none"> • This is a similar product to pentavalent vaccine—will be easier to shift from lyophilized DTP–Hib to lyophilized pentavalent. 	<ul style="list-style-type: none"> • This option is more expensive than option 3.
<ul style="list-style-type: none"> • Two injections would be required per child per session (instead of three with the monovalents). 	<ul style="list-style-type: none"> • There would be more wastage, as reconstituted lyophilized products have to be discarded by the end of the session. (Of note the pentavalent vaccine comes in 2-dose vials, while the DTP–Hib comes in 10-dose vials. There would be a possibility to get some of the DTP–Hib in 1-dose vials for a similar price but in limited quantity.)
<ul style="list-style-type: none"> • Both vaccines seem amply available. 	<ul style="list-style-type: none"> • Due to high wastage, the forecasted vaccine amounts may be insufficient, resulting in stock-outs.

Summary of information relating to new vaccine options

Vaccine	HepB monovalent	Hib monovalent	DTP-Hib	DTP-HepB	DTP-HepB+Hib (penta)
Presentations	<ul style="list-style-type: none"> 1, 2, 6 and 10 dose vial. The discussion below refers to the 10-dose vial. 	<ul style="list-style-type: none"> 1- and 10-dose vial. Liquid (only 1-dose vial) or lyophilized. The discussion below refers to the lyophilized 10-dose vial. 	<ul style="list-style-type: none"> 1- to 10-dose vial. Lyophilized only. The discussion below refers to the liquid + lyophilized 10-dose vial. 	<ul style="list-style-type: none"> 10-dose vial. 	<ul style="list-style-type: none"> 2-dose vial.
Supply situation	Supply of this vaccine is plentiful.	Supply of this vaccine is plentiful.	Available.	Limited supply of this vaccine in 2004 and 2005. Additional quantity is expected to be available in mid/late 2006.	Limited supply of this vaccine in 2004 and 2005. Additional quantity will be available in mid/late 2006. However, the waiting list of countries will also be a factor in identifying those that could receive it next.
Current cost ^a	Cost per dose: US\$0.23-0.48 (depends on manufacturer)	Cost per dose: US\$2.25	Cost per dose: US\$2.58	Cost per dose: US\$1.21	Cost per dose: US\$3.65
Volume per dose	3.1 – 5.9 cm ³ per dose	4.8 cm ³ per dose (including both vaccine and diluents)	11.8 cm ³ per dose (including both vaccine and diluents)	3.0 cm ³ per dose	11.3 cm ³ per dose
Programmatic issues	<ul style="list-style-type: none"> Requires an extra injection. Could be used for a separate birth dose if required. May be used for health worker immunization. 	<ul style="list-style-type: none"> Requires an extra injection. 	<ul style="list-style-type: none"> Substitution for DTP injection – easier to implement. Combination vaccine. Single manufacturer as of 2004. 	<ul style="list-style-type: none"> Substitution for DTP injection – easier to implement. Single manufacturer until 2005 or 2006 at least. If birth dose is warranted, additional monovalent HepB would be required. 	<ul style="list-style-type: none"> Substitution for DTP injection – easier to implement. Single manufacturer until 2006 at least. If birth dose is warranted, additional monovalent HepB would be required.
Logistics issues	<ul style="list-style-type: none"> Multi-dose vial policy applies, therefore wastage should be low. Requires increased cold storage space. 	<ul style="list-style-type: none"> Requires increased cold storage space. 	<ul style="list-style-type: none"> Multi-dose vial policy does not apply to lyophilized vaccines, high wastage (50%) expected. Requires increased cold storage space. 	<ul style="list-style-type: none"> Multi-dose vial policy applies, therefore wastage should be low. Requires increased cold storage space. 	<ul style="list-style-type: none"> Multi-dose vial policy does not apply to lyophilized vaccines; only 2-dose vials will keep wastage low (10%). Requires increased cold storage space.

^a UNICEF prices as of 2004.

Annex 3:

Checklist for post-introduction evaluation

Following the introduction of a new vaccine into a national immunization programme, the process and outcomes should be evaluated to identify and correct problems. These evaluations should be conducted within the first 6–12 months of introduction for maximum benefit to the programme. Because they cover several components of the immunization programme, they should be integrated into routine supervision and monitoring activities, or into other immunization-related field assessments— e.g. EPI reviews, acute flaccid paralysis (AFP) surveillance reviews, injection safety assessments, maternal and neonatal tetanus (MNT) and measles assessments.

Findings and recommendations from monitoring and supervision should be addressed directly with the staff to improve the quality of the national immunization programme. In addition, recommendations from more formal evaluations should be discussed by the interagency coordinating committee. These recommendations should be followed up and regularly reviewed for progress.

The following set of indicators may be used as a basic checklist for new vaccine evaluation, and be adjusted according to country conditions.

Option A: Review data through routine reporting system and available studies

Records and forms	Are there updated records and reporting forms that include the new vaccine in use, and is the new vaccine coverage reportedly as timely and as complete as in the case of other vaccines?
Vaccine coverage	Are coverage rates of new vaccine similar to that of simultaneously administered traditional ones? (Comparing HepB1 and Hib1 to DTP1, HepB3 and Hib3 to DTP3, yellow fever to measles.)
	Are drop-out rates of new vaccine similar to those of simultaneously administered traditional ones? (Comparing HepB1–HepB3 and/or Hib1–Hib3 drop-outs to DTP1–DTP3 drop-outs.)
	Is there a difference between coverage rates of traditional vaccines for the periods prior to and after new vaccine introduction? Any difference may suggest the effect of new vaccine introduction on the immunization programme, provided that other possible causes are ruled out.
	Is the coverage rate of HepB birth dose (where applicable) similar to the expected percentage of births taking place in health institutions/with the assistance of health workers?
Vaccine wastage	Is the wastage rate of new vaccine similar to that of traditional vaccines with the same type (liquid/lyophilized) and vial size?

Option B: Discuss at the national level

Pre-implementation phase	Were the following conducted prior to introduction? <ul style="list-style-type: none"> • Disease burden and cost-effectiveness estimations • Financial sustainability planning for future years • Advocacy and social mobilization • Training and material development • Cold-chain capacity assessment
Planning and operations	Is the implementation in progress according to the initial plan (countrywide/phased introduction, key dates)?
	Is there a transition plan, if the country has or is planning to switch from one vaccine presentation to another?
	Is the new vaccine need adequately forecasted, procured and distributed?
	Are specific adverse events following immunization (AEFIs) for new vaccine recognized and reported in timely fashion?
	Is surveillance for the new vaccine-related disease or condition in place?
Vaccine management	Have vaccine stock-outs been experienced since introduction?
	Is a vaccine freezing assessment ¹ planned or conducted (for freeze-sensitive vaccines)?
Impact assessment	Is there a plan to assess the impact of new vaccine implementation? Which methods are considered (programme outcome indicators, routine surveillance, serological surveys)?
	What is the overall perception of introduction as judged by decision-makers and NIP team?

Option C: Observe during field visits

Health worker practice	Are correct practices observed during handling, reconstitution and administering of vaccines?
Immunization safety	Are auto-disable syringes and safety boxes used, and appropriately disposed of?
Vaccine management	Do health facilities experience vaccine freezing for freeze-sensitive new vaccines?
	Do health facilities experience stock-outs for the new vaccine?
Vaccine wastage	Is vaccine wastage recorded and monitored at the health facility level?
	Is it consistent with the assumptions at national level?
Health worker knowledge	Do the health workers need additional training and supportive supervision on new vaccine?
Community acceptance	Is the new vaccine well received by the community and the health workers?
	Can families name the new vaccine and the disease it prevents?

¹ Children's Vaccine Program. *Preventing Vaccine Freezing in the Cold Chain*. Seattle, PATH, 2003. Available at http://www.childredivaccine.org/files/Freeze_Prevention_Materials.zip accessed on 25 September 2005.



The World Health Organization has managed cooperation with its Member States and provided technical support in the field of vaccine-preventable diseases since 1975. In 2003, the office carrying out this function was renamed the WHO Department of Immunization, Vaccines and Biologicals.

The Department's goal is the achievement of a world in which all people at risk are protected against vaccine-preventable diseases. Work towards this goal can be visualized as occurring along a continuum. The range of activities spans from research, development and evaluation of vaccines to implementation and evaluation of immunization programmes in countries.

WHO facilitates and coordinates research and development on new vaccines and immunization-related technologies for viral, bacterial and parasitic diseases. Existing life-saving vaccines are further improved and new vaccines targeted at public health crises, such as HIV/AIDS and SARS, are discovered and tested (*Initiative for Vaccine Research*).

The quality and safety of vaccines and other biological medicines is ensured through the development and establishment of global norms and standards (*Quality Assurance and Safety of Biologicals*).

The evaluation of the impact of vaccine-preventable diseases informs decisions to introduce new vaccines. Optimal strategies and activities for reducing morbidity and mortality through the use of vaccines are implemented (*Vaccine Assessment and Monitoring*).

Efforts are directed towards reducing financial and technical barriers to the introduction of new and established vaccines and immunization-related technologies (*Access to Technologies*).

Under the guidance of its Member States, WHO, in conjunction with outside world experts, develops and promotes policies and strategies to maximize the use and delivery of vaccines of public health importance. Countries are supported so that they acquire the technical and managerial skills, competence and infrastructure needed to achieve disease control and/or elimination and eradication objectives (*Expanded Programme on Immunization*).

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