Principles and considerations for adding a vaccine to a national immunization programme

FROM DECISION TO IMPLEMENTATION AND MONITORING

World Health Organization

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Preface

This is a general guidance document that can be used as a reference for making decisions about and planning the introduction of a vaccine into a national immunization programme. It draws from the experiences of many countries that have introduced new vaccines.

This document is an update of the 2005 WHO Vaccine Introduction Guidelines and it brings together the recommendations and guidance from many recent guidelines, tools and other documents on specific aspects of immunization and on specific vaccines. It provides updated information relevant to many vaccines that are being introduced into national immunization programmes now and in the coming years, including pneumococcal conjugate, rotavirus, meningococcal A, rubella, human papillomavirus (HPV), Japanese encephalitis, and inactivated polio vaccines. For more detailed information about a specific vaccine or aspect of immunization, decision-makers and planners should consult vaccine-specific introduction guidelines and other tools developed by WHO, UNICEF and other partners. This document provides links to many of these guidelines and tools.

Drawing upon recent research findings,[1] this document also places new emphasis on the potential impact of vaccine introduction on the immunization programme and the overall health system. Suggestions are provided throughout the document on ways to minimize possible negative effects of introducing a vaccine on the immunization programme and health system, as well as ways to maximize the opportunities that a vaccine introduction can provide to strengthen these systems.

What is the purpose of this document?

- To assist countries in making informed decisions about adding a vaccine to a national immunization programme by considering its public health priority;

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01 See: Wang SA, Hyde TB, Mounier-Jack S, Brenzel L, Favin M, Gordon WS, Shearer JC, Mantel CF, Arora N, Durrheim D. New vaccine introductions: Assessing the impact and the opportunities for immunization and health systems strengthening. Vaccine 2013; 31 Supplement: B122-B128 (http://dx.doi.org/10.1016/j.vaccine.2012.10.116).

programmatic, economic and financial feasibility; and impact on the immunization programme and on the overall health system;

- To guide the planning of a smooth vaccine introduction;
- To suggest ways to use the opportunity provided by the introduction of the vaccine to strengthen immunization and health systems.

Who can use this document?

- Country-level decision-makers in the health sector and other government sectors;
- National immunization technical advisory groups;
- Immunization programme managers;
- Immunization advisors at the national, regional and global levels (e.g., from WHO, UNICEF, local and international NGOs);
- Partners and donors that support immunization activities in countries.

When do you need this document?

- When deciding if and when introducing a vaccine into an immunization programme is appropriate and feasible;
- After deciding to introduce a vaccine – to assist in planning the introduction in ways that strengthen the immunization programme and overall health system.

How can you use this document?

- As a technical tool to plan, implement and monitor the vaccine introduction;
- As a resource to readily access key guidelines and tools for specific vaccines and topics (through web links).

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Table of contents

Acronyms

AD	Auto-disable (syringes)
AEFI	Adverse event following immunization
AFRO	Africa Regional Office of WHO
AIDS	Acquired immunodeficiency syndrome
BCG	Bacille Calmette Guerin (TB vaccine)
CPAD	Compact pre-filled auto-disable device
cGMP	Current good manufacturing practice
cMYP	Comprehensive multi-year plan
CIOMS	Council for International Organizations of Medical Sciences
DALY	Disability-adjusted life-year
DQS	Data Quality Self-Assessment
dT	Diphtheria-tetanus vaccine
DTP	Diphtheria-tetanus-pertussis vaccine
DoV	Decade of Vaccines
EMA	European Medicines Agency
EMRO	Eastern Mediterranean Regional Office of WHO
EPI	Expanded Programme on Immunization
EURO	European Regional Office of WHO
EVM	Effective Vaccine Management
GAVI	GAVI Alliance (Global Alliance for Vaccines and Immunization)
GIVS	Global Immunization Vision and Strategies
GNI	Gross national income
GVAP	Global Vaccine Action Plan
HepB	Hepatitis B vaccine
Hib	*Haemophilus influenza type b*
HIV	Human immunodeficiency virus
HSCC	Health Sector Coordinating Committee
HPV	Human papillomavirus
IB-VPD	Invasive bacterial vaccine-preventable disease
ICC	Interagency Coordinating Committee
IEC	Information, education and communication

IHP	International Health Partnership
IPV	Inactivated polio vaccine
JE	Japanese encephalitis
KABP	Knowledge, attitudes, beliefs and practices
LMIS	Logistics management information system
MDG	Millennium Development Goal
Men A	Meningococcus A vaccine
MOF	Ministry of Finance
MOH	Ministry of Health
MMR	Measles-mumps-rubella vaccine
MR	Measles-rubella vaccine
NGO	Non-governmental organization
NHIS	National health information system
NITAG	National immunization technical advisory group
NRA	National regulatory authority
OPV	Oral polio vaccine
ORS	Oral rehydration salts solution
PAHO	Pan American Health Organization
PCV	Pneumococcal conjugate vaccine
PIE	Post introduction evaluation
PIRI	Periodic intensive routine immunization
QALY	Quality of life year
SEARO	South East Asian Regional Office of WHO
SIA	Supplemental immunization activity (campaign)
TB	Tuberculosis
TT	Tetanus toxoid vaccine
UN	United Nations
UNICEF	United Nations Children's Fund
VPD	Vaccine-preventable disease
VVM	Vaccine vial monitor
WHO	World Health Organization
WPRO	Western Pacific Regional Office of WHO


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1.

Introduction and background

1.1

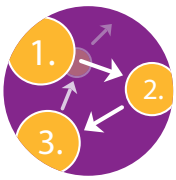
Introduction

The decision to introduce a vaccine into a national immunization programme presents many issues in prioritizing investments in the health sector. The challenge is to tackle key issues systematically, in order to provide the best available services in an appropriate, affordable, and cost-effective manner.

A "vaccine introduction" can mean the addition to an immunization programme of a vaccine against a disease not previously covered by an immunization programme (e.g., rotavirus or HPV vaccines). It can also describe the introduction of a new product formulation of a vaccine already in the programme (e.g., a liquid vaccine replacing a lyophilized vaccine), a new combination vaccine (e.g., DTP-HepB-Hib replacing previous individual vaccines for the various component antigens), or a vaccine that uses a new route of administration in place of a currently-used vaccine (e.g., an injectable vaccine replacing an oral vaccine). The extent to which new combinations, formulations or other changes constitute a "new vaccine introduction" will depend on the specific change in the vaccine and the potential issues that may arise and need to be addressed related to this change. Some changes in vaccines may require a full range of activities – from an evidence-based decision by policy-makers to additional training of health workers, a new communications and social mobilization campaign and so forth – while other vaccine changes may require only some of these activities. In this document, we use the term "new vaccine" to mean a new antigen, a new combination vaccine or other vaccine product that demands changes in the activities of an immunization programme for successful and widespread delivery to a population.

→ Chapter 2 of this document outlines the key factors to examine in making a decision about introducing a vaccine. These include the public health priority of the target disease, evidence of disease burden, and whether other prevention and control measures are a better option than vaccination. They also include the attributes of the vaccine and availability of its supply, whether the new vaccine

makes economic and financial sense, and the ability of the immunization programme and overall health system to handle the vaccine and adequately implement its introduction.



For countries that make the decision to introduce a vaccine, this document examines the many elements and steps needed to plan a smooth vaccine introduction and to allocate sufficient resources in order to do so (→ Chapter 3). These steps include deciding upon the service delivery strategy and schedule for the vaccine, selecting the exact product (including presentation and formulation), and procuring the vaccine. They also include steps to ensure the readiness of the immunization programme to introduce the vaccine by expanding the capacity of the cold chain and vaccine management systems to handle it, training health workers in managing and administering the new vaccine, creating awareness of and promoting its use amongst the public through social mobilization campaigns, and updating management information systems.

This document also outlines different aspects of monitoring and evaluating the vaccine introduction, including monitoring the coverage, safety and impact of the vaccination (→ Chapter 4).

Emphasis is placed throughout the document on the importance of considering the potential impact of introducing a particular vaccine on the financing, planning, implementation and other aspects of the immunization programme as a whole and on the overall health system. Suggestions on how to use the opportunity of a vaccine introduction to improve different aspects of the immunization programme and health system are presented in outlined boxes and in → Annex 1.

1.2

Background on global immunization efforts and the introduction of new and under-utilized vaccines

Immunization is one of the most successful global health interventions and one of the most cost-effective ways to save lives and prevent disease. Since the global Expanded Programme on Immunization (EPI) was launched in 1974, vaccination against six diseases (tuberculosis, diphtheria, tetanus, pertussis, poliomyelitis and measles) has prevented millions of deaths and disabilities. By 2012, an estimated 83% of the world's children under one year old received all three doses of DTP vaccine, an indicator of how well immunization programmes are functioning.[2]

Since the year 2000, most countries have added two other vaccines recommended by WHO for universal use – hepatitis B and *Haemophilus influenzae* type b (Hib) – to their routine immunization programmes, in many cases with support from the GAVI Alliance. The original six vaccines, along with hepatitis B and Hib vaccines, are estimated to save two to three million lives per year.[3] Other older, under-utilized vaccines that are increasingly being added to child immunization programmes include rubella vaccine, a 2nd dose of measles vaccine, inactivated polio vaccine (IPV), and for specific populations, yellow fever and Japanese encephalitis (JE) vaccines.

Several important life-saving vaccines have become available in recent years (→ Table 1). Pneumococcal conjugate and oral rotavirus vaccines – both recommended by WHO for universal use in child immunization programmes – are especially important in reducing child mortality. Pneumococcal disease and rotavirus diarrhoea together accounted for more than 900,000 deaths among children under five in 2008.[4] The availability of vaccines against human papillomavirus (HPV) provides an opportunity to reduce global cervical cancer morbidity and mortality by targeting a new group for routine immunization (9-13 year old girls). New or improved vaccines against diseases of regional importance, including a meningococcal conjugate vaccine against the Group A strain most prevalent in Africa and a single-dose live

02 Source: WHO/UNICEF coverage estimates 2012 revision. July 2013 available at http://www.who.int/immunization/monitoring_surveillance/data/gs_gloprofile.pdf
03 Ibid
04 WHO disease burden estimates from March 2012 are available at http://www.who.int/immunization/monitoring_surveillance/burden/estimates/en/index.html

attenuated JE vaccine (SA 14-14-2), are being introduced in endemic countries and have the potential to further reduce the infectious disease burden in some of the world's poorest countries.

A number of additional new or improved vaccines of public health importance are in advanced stages of clinical development and could be available on the market in the next several years (→ Table 1). These include malaria, dengue, new-generation tuberculosis and typhoid conjugate vaccines.

TABLE 1: New and upcoming vaccines of public health importance

Vaccine introduced in the global market since 2000	Vaccines in late stages of clinical development
• Rotavirus (oral) • Pneumococcal conjugate (10 and 13 valent) • Improved Japanese encephalitis vaccine (live, single-dose SA 14-14-2) • Human papillomavirus (HPV) • Meningococcal (A monovalent, tetra- and pentavalent conjugate vaccines) • Oral killed, whole-cell only cholera vaccine • Monovalent and bivalent oral polio vaccines	• Malaria (RTS,S) • Dengue • Typhoid Vi conjugate • Tuberculosis (new generation vaccines)

To meet the considerable challenges of getting these new vaccines into use in countries where they are needed the most and to increase the reach and performance of immunization programmes, the global health community in 2010 called for the "Decade of Vaccines" (DoV). The goal of the DoV is to extend by 2020 the full benefits of immunization "to all people, regardless of where they are born, who they are or where they live."[5] To realize this vision, a Global Vaccine Action Plan (GVAP) was developed and approved by the World Health Assembly in 2012, building upon the goals and progress of the WHO-UNICEF Global Immunization Vision and Strategy (GIVS).

05 Global Vaccine Action Plan, 2011-2020, p. 5 (see: http://www.dovcollaboration.org/action-plan/).

The goals of the GVAP by 2020 are to:

Achieve a world free of poliomyelitis;

Meet global and regional disease elimination targets (for measles, neonatal tetanus, rubella and congenital rubella syndrome);

Meet vaccination coverage targets in every region, country and community;

Develop and introduce new and improved vaccines and technologies;

Exceed the Millennium Development Goal (MDG) 4 target for reducing child mortality.

The GVAP has identified six strategic objectives to meet these goals (→ Box 1).

BOX 1. Strategic Objectives for the Decade of Vaccines

1. All countries commit to immunization as a priority.
2. Individuals and communities understand the value of vaccines and demand immunization as both their right and responsibility.
3. The benefits of immunization are equitably extended to all people.
4. Strong immunization systems are an integral part of a well-functioning health system.
5. Immunization programmes have sustainable access to predictable funding, quality supply and innovative technologies.
6. Country, regional, and global research and development innovations maximize the benefits of immunization.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1.3

Guiding principles for adding vaccines to national immunization programmes while strengthening immunization programmes and health systems

Experience has shown that the introduction of a new vaccine can have a significant impact – both positive and negative – on a country's health system. In recognition of this fact, the WHO Strategic Advisory Group of Experts (SAGE) on immunization has endorsed six guiding principles for countries to follow in planning and implementing a vaccine introduction while strengthening their overall immunization programme and health system (→ Box 2).

BOX 2. Principles for adding vaccines to national immunization programmes while strengthening immunization programmes and health systems

Optimal vaccine introduction into a national immunization programme that strengthens health systems benefits from:

1. A strong country-led, evidence-based decision-making, planning and prioritization process that is accountable and coordinated with other components of the health system.

2. A well-performing or improving and responsive immunization programme.

3. Seizing the opportunity to achieve:
   - A well-trained and motivated health workforce;
   - Quality education and communication about the new vaccine for the health workforce and community;
   - Functional cold storage, logistics and vaccine management systems;
   - Safe immunization practices and monitoring of adverse events;
   - High-quality monitoring and evaluation, including disease surveillance and immunization coverage monitoring;
   - Resource, performance and management accountability.

4. Maximizing opportunities to deliver vaccines as integral components of comprehensive health promotion and disease prevention and control efforts so that vaccines are delivered as part of a package of effective, feasible and affordable interventions based on national contexts.

5. Sufficient allocation of human and financial resources to introduce the new vaccine and sustain its use without adversely affecting other programmes and services.

6. A safe and efficacious vaccine that is appropriate for local use and is available with an uninterrupted, sufficient supply.

2.

Deciding on the introduction of a vaccine

2.1

Overview: issues to consider when deciding whether to introduce a vaccine into the national immunization programme

Different factors may prompt countries to consider adding a vaccine to their national immunization programme.[6] Systematic surveillance or laboratory-confirmed disease burden studies may reveal a high incidence or mortality from a vaccine-preventable disease (for example, pneumococcal disease or rotavirus diarrhoea). The disease may be spreading within a country, increasing in incidence or re-emerging (e.g., Japanese encephalitis, cholera). A new or improved vaccine coming onto the market or a new WHO recommendation may also spur countries to consider introducing a vaccine into their programme. Other "triggers" of vaccine introductions in recent years have included the availability of donor support (including funding through the GAVI Alliance), offers of vaccine donations from pharmaceutical companies[7] and political pressures. Regardless of the circumstances and sources of funding, it is important that countries undertake a systematic decision-making process based on a review of the evidence and consideration of the appropriateness and long-term financial and other consequences of introducing the vaccine.

The key issues to be considered before deciding to introduce a vaccine can be grouped into three areas (→ Fig. 1). The first area concerns the disease that the vaccine in question targets – whether it is a public health priority, the magnitude of the disease burden in the country and the existence and effectiveness of other strategies for preventing and controlling the disease. The second area relates to the vaccine – its safety, performance and other characteristics; its economic and financial attributes (cost, affordability, and cost-effectiveness); and whether the country can expect a reliable supply of the vaccine. The third area concerns the capacity of the immunization programme and underlying health system to successfully introduce the vaccine and to be able to continue to deliver it over the long term.

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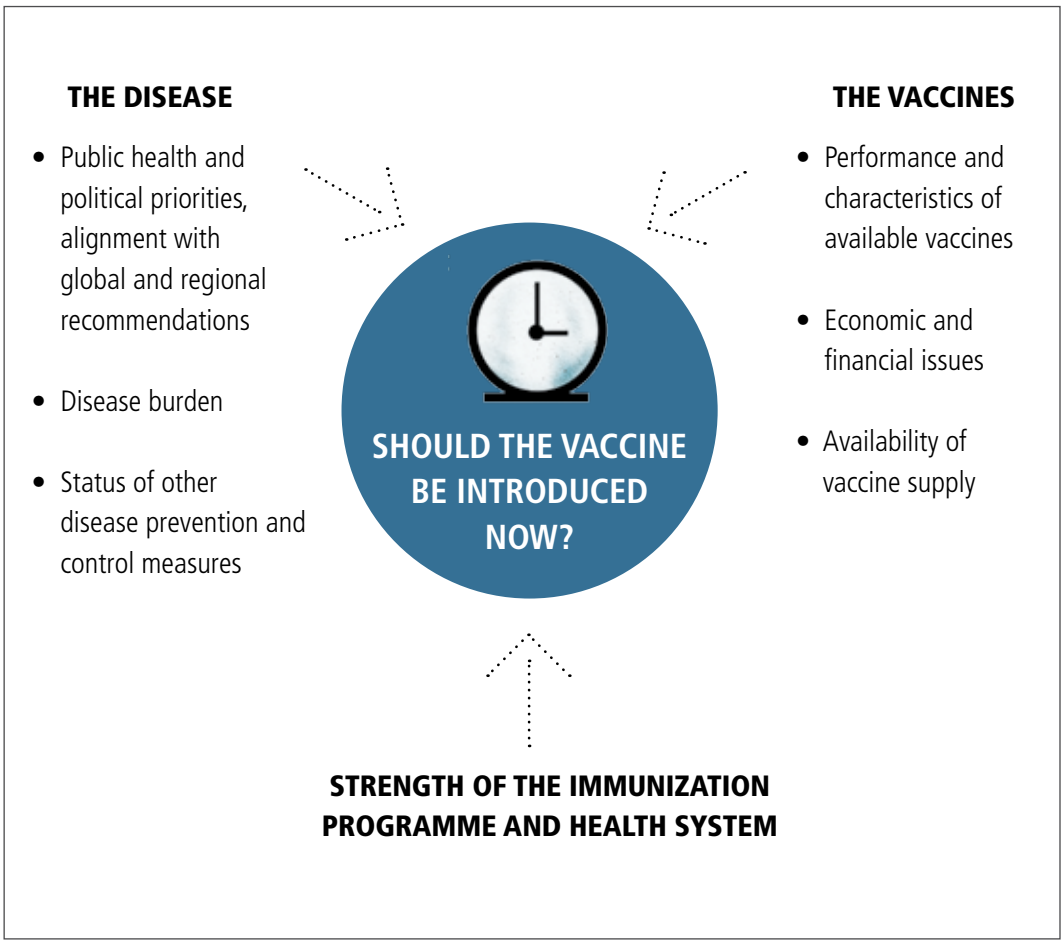
06 See: Mantel C, Wang SA. The privilege and responsibility of having choices: decision-making for new vaccines in developing countries. *Health Policy and Planning* 2012; 27:ii1-ii4.

07 See Box 13 in Section 3.4.2 for information on the WHO-UNICEF Joint Statement on Vaccine Donations.

Although it is recommended that each issue be addressed in a fully informed decision-making process, some factors may outweigh and override others, depending on the specific circumstances. In addition, each country must decide what locally-gathered evidence they require in order to make a decision, and for what types of evidence they can rely on country or regional estimates (e.g., disease burden, cost-effectiveness) prepared by other groups, instead of conducting their own studies.

As a result of this assessment of the issues, the decision might be to introduce the vaccine or not to introduce it at this time. Policy-makers may have to make further decisions about the scope of vaccination, target ages and schedule, and the specific vaccine product, since these have policy and financial implications. Countries that choose not to introduce a vaccine may decide to revisit the issue at a later date as more evidence of the disease burden or impact and cost-effectiveness of the vaccine becomes available, or as conditions change, such as the supply and price of the vaccine, financial resources, and the ability of the immunization programme and health system to handle the vaccine.

FIG. 1. Key issues to consider when deciding on the introduction of a vaccine



2.2

The disease

2.2.1

The public health and political priority of the disease

All countries need to set priorities to determine which health problems to address and what specific interventions to implement, given the many health issues and resource constraints that each country faces, especially developing countries. Health policy-makers may need to make a choice, for instance, between introducing a new vaccine and increasing access to anti-retroviral medicines for HIV/AIDS patients. The disease targeted by the vaccine should therefore be considered a public health priority by country policy-makers. Questions that can be asked in setting disease and vaccine priorities include the following:

Does the disease cause significant disease burden?

The burden of disease that can be prevented by the vaccine is a key piece of evidence used to justify the need for a vaccine (see next section). The bulk of the infectious disease burden in many developing countries is due to respiratory and diarrhoeal infections, tuberculosis, malaria and AIDS. Existing and future vaccines that target these diseases will therefore be priorities in many countries, depending on the epidemiology of the specific diseases in each country. Vaccines against common causes of cancer, such as hepatitis B (preventing liver cancer) and HPV (preventing cervical cancer) vaccines, are also increasingly identified as priorities, given the new global focus on the prevention and control of non-communicable diseases.

Does preventing the disease contribute significantly to the goals and align with the priorities established in the national health and development plans?

The priorities of the immunization programme should be guided by the goals and priorities of the country's national health plan or strategy, national development plan

and other key policy documents. Many developing countries, for instance, have set goals to significantly reduce child mortality in order to contribute to the global Millennium Development Goal of reducing mortality in children less than five years old by two-thirds by 2015. Two major causes of child mortality worldwide are pneumonia and severe diarrhoeal disease. Vaccines that can substantially reduce the burden of these diseases, such as pneumococcal and rotavirus vaccines, will therefore align with national goals to reduce child deaths and should be considered priorities in many countries.

Is the disease perceived to be important to the public and the medical community?

The perceptions of the public and the medical community about the disease and the vaccine should be an important factor in determining its priority. The more visible and important the disease is to the community, the greater the acceptance of and demand for the vaccine will be. Some diseases, such as meningitis and dengue, may not cause high mortality, but because of the fear they engender amongst the public and clinicians (due to the difficulty in diagnosing and treating them) and the great disruptions in health services that outbreaks can cause, these diseases are often top priorities among political leaders, the medical community and the public in endemic countries. The vaccine may already be available in the private market and this can influence public awareness and raise equity issues. A qualitative study among key decision-makers, the medical community and the public will be useful to assess their perceptions about the vaccine and its likely impact. This assessment will also guide the development of a communications plan and appropriate messages for the public and health care providers to promote the vaccine.

Is the vaccine recommended by WHO and is control of this disease in line with global or regional priorities?

Country policymakers may also prioritize vaccines that have been recommended by WHO and/or that contribute to global and regional goals and strategies, such as the Decade of Vaccine's Global Vaccine Action Plan (GVAP). WHO issues recommendations for specific vaccines in Position Papers published in the *Weekly Epidemiological Review.*[8]

Does preventing the disease contribute to improving equity among socio-economic classes and population groups?

A number of vaccine-preventable diseases disproportionately affect certain segments

08 See: http://www.who.int/immunization/documents/positionpapers_intro/en/.

of the population, such as women in the case of HPV-related cancers, and poor and malnourished children in the case of pneumococcal disease. A strong argument can therefore be made that preventing these diseases through immunization will improve equity by reducing the disease burden among the highest risk groups. Inequities also arise from the fact that in many societies, health services are not accessible to the poorest or marginalized populations or to women and girls, due to their remoteness from health facilities, financial barriers or social taboos. Such barriers can prevent these groups from receiving other preventive services or effective and timely treatment. In contrast, immunization programmes in many countries have shown their ability to reach these marginalized populations more effectively than curative or other health services, and to achieve quite high coverage rates amongst these groups. Thus, equity is also improved by vaccinating populations for whom other preventive services, such as cervical cancer screening (in the case of HPV vaccine) or prompt treatment for acute pneumonia (in the case of measles, pertussis, Hib, and pneumococcal vaccines), are often out of reach.

2.2.2

Disease burden

An estimate of the magnitude of the disease and its impact on health in a country is critical information for policy-makers and national immunization advisory groups when making decisions about introducing a new vaccine. Disease burden data can include annual incidence, mortality, hospitalization and disability rates by age group and prevalence rates in the case of chronic diseases, such as cervical cancer and chronic hepatitis B virus infection.

Regular disease reports through the national health information system are one source of disease burden data. However, in many countries, reporting efficiency is poor and the degree of under-reporting is often unknown. And for syndromes that may be caused by different organisms, with more than one pathogen contributing to the pathology in some cases, laboratory diagnosis is required to estimate the pathogen-specific burden of disease. This is the case with pneumonia, diarrhoea and meningitis, which may be caused by different pathogens, including but not limited to those for which vaccines exist, such as rotavirus in the case of diarrhoea, Hib, meningococcus or pneumococcus in the case of bacterial meningitis, and Hib and pneumococcus in the case of pneumonia. However, many countries have limited capacity to conduct laboratory diagnosis, particularly microbiologic diagnosis.

Where facilities for laboratory diagnosis and/or rapid diagnostic tests are available, the proportion of diarrhoea and meningitis attributable to certain pathogens can be assessed. However, in the case of pneumonia, the specific bacterium causing the disease cannot be determined in many cases, even in sophisticated laboratories.

Furthermore, even if the diagnosis is accurate, it can be challenging to estimate the incidence rate of the pathogen-specific disease in the population, if the size of the catchment population to which these patients belong is not known, or if the site where laboratory testing is conducted does not capture all patients within the catchment population.

Given these difficulties, countries may decide to use country-specific estimates of disease burden derived from surveillance data, special studies and mathematical models when making policy decisions concerning the introduction of vaccines. WHO regularly publishes estimates of disease burden for each country for rotavirus, Hib, pneumococcal and meningococcal disease, which are derived using such methods.[9] Country-specific estimates are also available for cervical cancer and other HPV-related diseases.[10] Regional estimates or data from countries with similar social and demographic characteristics and environmental conditions in the region can also be used as a proxy for estimating a country's disease burden.

Despite its limitations in defining the burden of disease, countries may decide to conduct surveillance for the disease in question, since it provides empirical local data that may be used in mathematical models to estimate the local disease burden and because such surveillance may allow assessment of vaccine impact. For diseases such as rotavirus and invasive bacterial diseases (other than epidemic meningitis) that do not normally occur in localized outbreaks and are not targeted for eradication or elimination, country-wide surveillance is not required. Countries can instead conduct sentinel surveillance in one or more sites. These are typically hospitals capable of consistent case detection and investigation over time, that have laboratories capable of accurately diagnosing cases and that serve populations representative of the national or sub-national populations. For example, countries participating in the WHO Invasive Bacterial Vaccine-Preventable Disease (IB-VPD) surveillance network conduct meningitis surveillance in a minimum of 1-3 sentinel sites, depending on country size and population. This surveillance has allowed countries to estimate the proportion of bacterial meningitis caused by each of three vaccine-preventable organisms (*S. pneumonia*, Hib and *N. meningitides*). Data generated from this surveillance has been used to estimate the burden of Hib disease, thus informing decisions to introduce Hib vaccines. These surveillance data have also been used to document the impact of vaccination, thereby informing decisions to continue the use of these vaccines in the national programme.

For diseases, such as Japanese encephalitis and typhoid fever for which incidence and risk varies considerably within a country, the ability to detect and investigate suspected cases when and where they occur is required and thus establishing a

09 See: http://www.who.int/immunization/monitoring_surveillance/burden/estimates/Pneumo_hib/en/index.html and http://www.who.int/immunization/monitoring_surveillance/burden/estimates/rotavirus/en/index.html.
10 See http://www.hpvcentre.net/ or http://globocan.iarc.fr/.

small number of sentinel sites may be inadequate. Therefore, a system for collecting, transporting and testing samples from suspected cases in different parts of the country may be needed to identify high-risk areas and populations to target for vaccination.

Several tools and systems have been established in recent years to make surveillance of vaccine-preventable diseases more feasible in countries with limited resources and capacity. These include:

- International surveillance networks of sentinel sites and laboratories for rotavirus and IB-VPDs. These networks, coordinated by WHO, use standardized laboratory and data collection methods, have a system to monitor and implement quality assurance and quality control of participating laboratories, and provide technical assistance and training to countries;[11]
- A global network of measles and rubella laboratories, through which country-wide, case-based surveillance for rubella, linked to measles surveillance, provides data on rubella epidemiology and disease burden;[12]
- Surveillance protocols and guidelines for rotavirus, rubella, IB-VPD, and JE disease, as well as laboratory manuals for the diagnosis of bacterial meningitis and rotavirus and for HPV testing;[13]
- The WHO *Global Framework for Immunization Monitoring and Surveillance* (GFIMS).[14]

Once a vaccine is introduced, surveillance of the targeted disease is useful to monitor the impact on the disease and on the performance of the immunization programme. To monitor the impact on disease burden, surveillance would ideally begin prior to vaccine introduction (e.g., two or three years ahead of time) in order to obtain baseline data against which to compare once the programme is implemented. Surveillance practices should remain consistent over time so that changes in disease incidence and prevalence are not confounded by a change in surveillance methods. However, when multiple years of pre-introduction surveillance data are not available, strategies have been developed to estimate the impact of vaccination on the disease using data available in countries (see → Section 4.2 for more information about disease surveillance following vaccine introduction).

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11 See:http://www.who.int/immunization/monitoring_surveillance/burden/laboratory/IBVPD/en/index.html for the IB-VPD surveillance network and http://www.who.int/immunization/monitoring_surveillance/burden/laboratory/Rotavirus/en/index.html for the rotavirus surveillance network.

12 See: http://www.who.int/immunization/monitoring_surveillance/burden/laboratory/measles/en/index.html.

13 These tools can be found at the following websites: http://www.who.int/immunization/monitoring_surveillance/resources/en, http://www.who.int/immunization/monitoring_surveillance/burden/laboratory/Rotavirus/en/index.html (for rotavirus tools), http://www.who.int/immunization/monitoring_surveillance/burden/laboratory/IBVPD/en/index.html (for IB-VPDs), http://www.who.int/biologicals/vaccines/hpv/en/ (for HPV tools).

14 The WHO GFIMS may be found at: http://whqlibdoc.who.int/hq/2007/WHO_IVB_07.06_eng.pdf.

2.2.3

Other disease prevention and control measures

Decision makers need to consider other interventions and strategies to prevent and control the disease and compare these with the vaccine being considered. Comparisons should be based on the relative effectiveness and costs of the different interventions and should also consider the practicality and feasibility, the time required to have impact, the possibility of causing epidemiological changes over time and the adverse effects associated with each of the interventions.

Moreover, many of the newer vaccines, including Hib, pneumococcal and rotavirus vaccines, prevent only a portion of all cases of a syndrome, such as diarrhoea or pneumonia, and specific vaccines may not prevent all strains that cause disease. Significant reductions in the burden of these diseases require an integrated approach towards disease prevention and control that combines vaccination with other effective interventions. In the case of diarrhoea, such interventions include the promotion of early and exclusive breastfeeding and hand washing with soap, improvements in water and sanitation systems, access to treatment with oral rehydration therapy and zinc, and vitamin A supplementation, among others. Instead of weighing one intervention against another, an approach that combines various preventive and treatment interventions can have a much greater impact on reducing the disease than any single intervention alone, including vaccination. The introduction of new vaccines, such as pneumococcal, rotavirus and HPV vaccines, thus provide an excellent opportunity for countries to adopt integrated strategies towards disease control. See → Section 3.2.6 for more information on this topic.

2.3

The vaccines

2.3.1

Performance and characteristics of available vaccines

Vaccine safety, efficacy and effectiveness

Performance factors that decision-makers should consider include the vaccine's safety profile; efficacy, effectiveness and duration of protection; the age at which it can be administered or is most effective; and added benefits, such as indirect (herd) immunity and cross-protection against other diseases. The **safety** of a vaccine and the frequency and seriousness of any adverse reactions that it can induce is a critical factor for countries to consider. This is especially true for several newer and upcoming vaccines that are being introduced in developing countries without having first been used in industrialized countries and which thus do not have long safety records. The safety of a new vaccine is assessed in clinical trials before it can be licensed. However, these trials may not capture rare adverse events and thus post-marketing surveillance may be needed to further establish the vaccine's safety profile. Information on safety should be assessed carefully, weighing the risks against the benefit of the vaccine. To assist countries in assessing a vaccine's safety, WHO has prepared a series of fact sheets summarizing safety data for many vaccines, including observed rates of adverse events.[15]

For a vaccine to achieve licensure, there needs to be data on its **efficacy** in preventing disease in the target 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 have better immune responses. Efficacy may

15 These can be found at: http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/index.html.

also vary depending on age, nutritional status, co-infections and other factors. As a result, the efficacy of some vaccines, especially oral vaccines, may be lower in some populations than in others. Therefore, in estimating the likely efficacy of a vaccine in a specific country, careful consideration should be given to the range of data available and whether the studies were also performed in countries with similar disease patterns and health characteristics as in the country considering the vaccine.

It should be noted that vaccine **effectiveness** is a different concept which describes protection through programmatic implementation, and reflects the performance of the vaccine as actually delivered to the target population. Vaccine effectiveness is usually lower than vaccine efficacy as a result of programme-related factors such as errors in vaccine storage, preparation or administration of the vaccine, as well as incomplete coverage. On the other hand, the effectiveness of the vaccine can be greater than expected as a result of the vaccine's indirect (herd) effects, as has been demonstrated for several vaccines, including pneumococcal and Hib conjugate vaccines. Vaccines can also alter the epidemiology of a disease by changing the age pattern of people with disease or by changing the predominant strains causing the disease ("serotype replacement"). To monitor the overall impact of the vaccine, countries may consider appropriate disease surveillance activities following its introduction.

Other aspects of a vaccine's performance that have particular implications for an immunization programme are the age at which it becomes effective or has maximum effectiveness, and the duration of protection that it provides. Some new vaccines, notably HPV vaccine, are recommended for use later in childhood. Such vaccines cannot be incorporated into the infant immunization schedule and new delivery strategies, such as school-based vaccination, special campaigns, or new adolescent primary care health services, may need to be used. Vaccines with waning levels of protection may require repeat doses periodically or booster doses, which must be taken into account when assessing the costs and programmatic feasibility of the vaccination.

Characteristics of available vaccine products

Product selection, including the presentation and formulation of a vaccine, are more related to implementation and are addressed in → Section 3.3. However, characteristics of the vaccine product can have programmatic and financial implications. Thus, it is advisable for decision-makers to become familiar with the characteristics of all available products and to assess how they will impact programme costs and operations. Often when a new vaccine first becomes available, there are few product choices, but the selection may expand over time. Understanding and comparing the characteristics of the available vaccines can help a country assess their probable storage and transport requirements, wastage rates, auxiliary equipment

needed (e.g., syringes) and potential programmatic impact, such as an increased burden on health workers in preparing a vaccine for administration. Once a decision has been made to introduce a vaccine against a particular disease, decision-makers and technical advisory groups may decide to state a preference for a specific presentation or product, based on these considerations.

Vaccine product characteristics to consider include:

- **Number of doses required:** Immunization programmes typically prefer vaccines with as few doses as possible. The greater the number of doses, the more difficult it is to achieve high levels of coverage for the complete series and the higher the costs of storage, delivery and possibly the vaccine itself.

- **Formulation:**
  Combination versus monovalent products: Combination vaccines require fewer delivery devices (e.g., syringes) and less cold storage space, but they can be less flexible. For example, if purchasing DTP-HepB-Hib vaccine, there may be a need to also purchase monovalent hepatitis B vaccine separately for delivery of a birth dose.

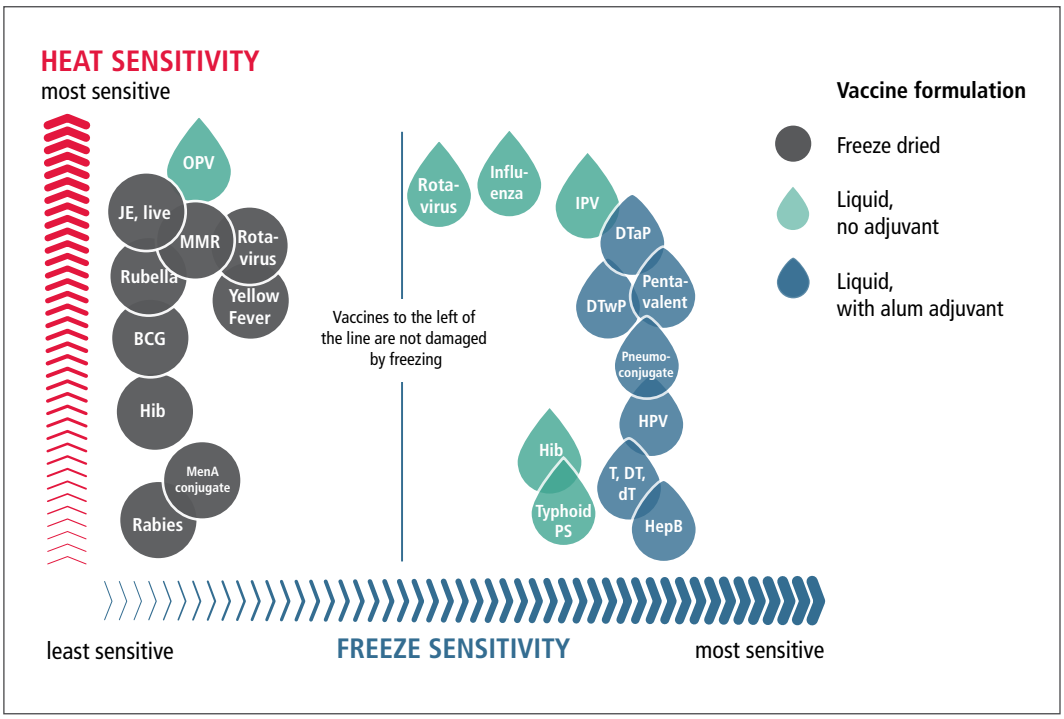
  Lyophilized vs. liquid products: Lyophilized products require diluents and reconstitution devices. They also require extra cold storage space at the peripheral level, since the diluents need refrigeration before reconstitution. Some lyophilized vaccines also result in higher wastage rates due to the need to discard the vaccine within six hours after being reconstituted. In addition, they create the risk that an incorrect diluent is used, possibly causing adverse events. On the other hand, lyophilized vaccines are often more heat stable than comparable liquid vaccines.

  Heat and freeze sensitivity: For a growing number of vaccines, guidance is provided on the label and in the licensing agreement for its use outside of the standard 2-8°C cold chain conditions (i.e., stating the number of days it can be stored at ambient temperatures). Decision-makers may therefore want to consider whether a more heat-stable product would facilitate the delivery of the vaccine, for instance for outreach or school-based delivery, which could significantly improve immunization coverage. Another important consideration is the sensitivity of the vaccine to freezing, which is relevant for several of the newer vaccines (→ Fig. 2 and → Box 14 in → Section 3.5.2).[16]

- **Presentation and packaging:**
  The number of doses per vial for the vaccine will affect wastage rates and cold chain capacity requirements at all levels of the system. The differences in storage

16 See also the WHO document, Temperature Sensitivity of Vaccines, which can be found at: http://whqlibdoc.who.int/hq/2006/WHO_IVB_06.10_eng.pdf.

FIG. 2. Temperature sensitivity of selected vaccines



Note: This graphic illustrates relative sensitivity across antigens, as the same type of vaccine from different manufacturers may have different vaccine vial monitors (VVMs). For more information, see → Section 3.3.4.

requirements for the same vaccine in single-dose vials and in 10-dose vials can be very substantial.

The volumes for the primary container and secondary container (cartons) will also affect cold chain storage, transport and waste disposal requirements. The WHO Vaccine Volume Calculator[17] is a useful tool that estimates the amount of storage space needed for various vaccine products and safe injection equipment or other delivery devices.

Novel presentations: Compact pre-filled auto-disable devices (CPADs), such as Uniject™, have been used for many years to deliver the birth dose of hepatitis B vaccine and are becoming available for other EPI vaccines, including DTP-HepB-Hib pentavalent vaccine. Some oral vaccines, including some rotavirus vaccines, are available in individual squeeze tubes placed into the mouth of the vaccine recipient. The sometimes higher cost per dose of novel presentations should be weighed against their advantages, such as reduced storage requirements or ease of use.

17 The vaccine volume calculator can be found at: http://www.who.int/immunization/programmes_systems/supply_chain/resources/tools/en/index5.html.

2.3.2

Availability of vaccine supply

It is critical for countries that are considering the introduction of a new vaccine to be aware of the current and future supply situation and likely future trends. There are many factors that affect the available supply and prices of vaccines. New vaccines are often produced by one or two manufacturers for the first several years after initial licensure. This can limit the global supply and keep prices high until more producers enter the market. Under-utilized vaccines may be in short supply because of a historical lack of demand. In addition, while the global supply of a vaccine may be adequate, countries may not be able to obtain the exact presentation and formulation that they prefer. This is especially true for new vaccines developed primarily for industrialized country markets, which may be lyophilized, be available only in pre-filled syringes that have large cold chain requirements or otherwise be more difficult for developing country immunization systems to handle.

Countries can consult the list of vaccine products that have been WHO pre-qualified.[18] In addition, UNICEF's product menu for GAVI-supplied vaccines provides an indication of the general availability of each product (good, limited, very limited), as well as recent weighted average prices paid by UNICEF.[19]

Introducing a vaccine with a limited global supply can present serious challenges for immunization programmes. Global shortages and stock-outs in countries can occur if one of the few producers (or the sole producer) experiences production problems, if supply cannot keep pace with a sudden increase in global demand – for instance, as a result of massive donor support – or if there is greater than expected demand from more profitable markets, such as high-income countries. Also, once the vaccine has been introduced, countries may have less flexibility to procure additional quantities if they have underestimated their needs due to higher than expected wastage rates or increased demand. This was the situation for several years with the DTP-HepB-Hib pentavalent vaccine in the early to mid-2000s, when there was a sole producer and demand exceeded supply, requiring some countries to postpone introduction or use alternative products.

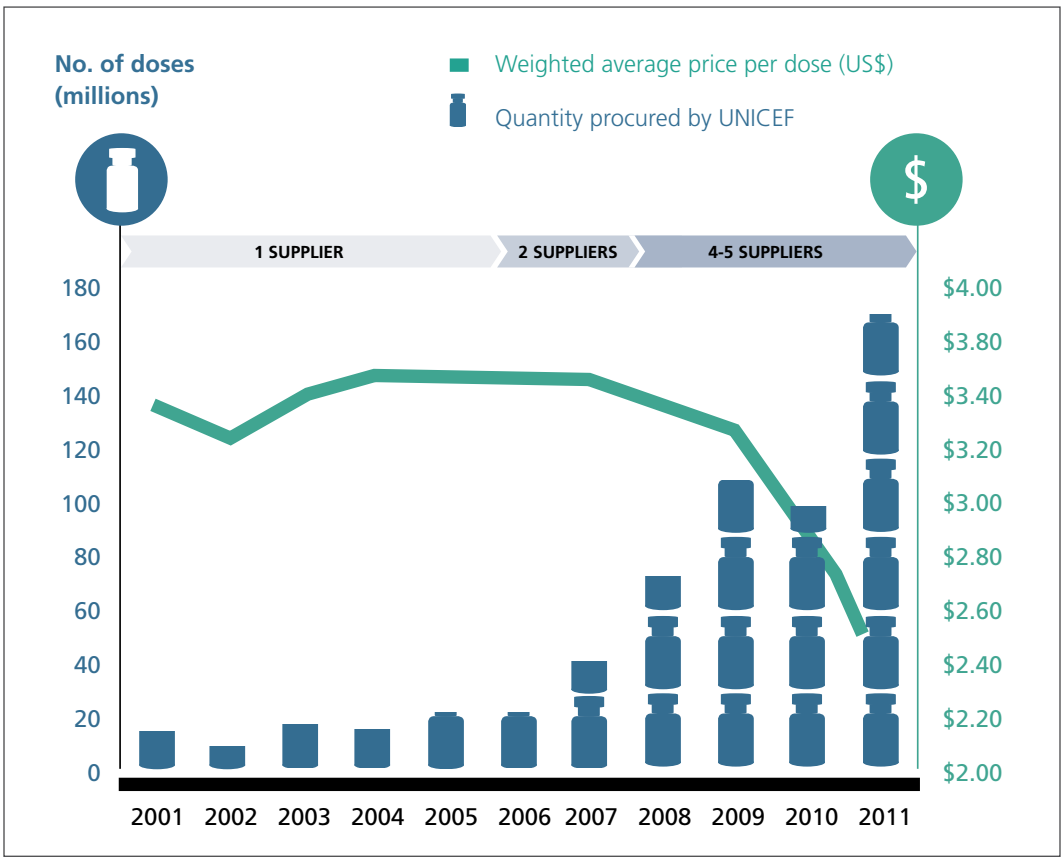
To avoid these problems, countries, especially those with large populations, may need to delay introducing the vaccine or adopt a phased introduction strategy until a more healthy market develops. A healthy market is defined as one in which there are several producers, a global supply that meets the current and projected demand, and competitive and falling prices. Increasingly, healthy markets develop once

18 The list of pre-qualified vaccines can be found at: http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/index.html.
19 The product menu can be found at: http://www.unicef.org/supply/index_gavi.html.

high-quality producers from low and middle-income countries acquire the technology to produce the vaccine, as these producers often have large production capacities and relatively low production costs, resulting in price declines. It took a number of years for such a market to develop for pentavalent vaccine, once several new producers began to manufacture the vaccine (→ Fig.3). A lesson learned from the pentavalent vaccine experience is that the more technologically complex a vaccine product is to develop and produce, the longer it takes for a healthy market to develop.

If a country wants to target a specific disease in spite of a limited global supply of the exact vaccine product (e.g., presentation or formulation) that it prefers, one option is to use a different product until the preferred one becomes available in sufficient quantities. However, this approach will result in additional product introductions into the immunization programme. Depending on the differences between the products or presentations, this may have either a negligible impact or be almost equivalent to a full new introduction. It may also have implications for stock management and may create a need for retraining of immunization personnel.

FIG.3. Change in the UNICEF DTP-HepB-Hib pentavalent vaccine market over time: Volume of sales, number of suppliers and average price per dose, 2001 – 2011



Source: UNICEF Supply Division. Note: Data based on year purchase order was placed

In recent years, global immunization partners, including WHO, the GAVI Alliance, the Bill & Melinda Gates Foundation and large procurers of vaccine, such as UNICEF and the Pan American Health Organization (PAHO) Revolving Fund, have been able to influence vaccine supplies and to accelerate the development of healthy markets. They have done this by creating demand for new vaccines in many countries, thereby spurring production among existing or new producers. Other ways they have influenced the markets include purchasing large quantities and developing long-term contracts with producers, both of which help to reduce prices.

There are a number of ways in which individual countries can improve the security of their supply and minimize the likelihood of stock-outs. These include preparing accurate forecasts of vaccine needs, monitoring vaccine uptake, improving stock management, monitoring and reducing vaccine wastage, ensuring timely payments to producers and entering into multi-year contracts with suppliers.

2.3.3

Economic and financial issues

Because of the much higher costs of many of the new vaccines as compared to the traditional EPI vaccines (BCG, OPV, DTP and measles), the cost of adding a new vaccine to the national programme and how it will be financed are important considerations when making a decision about new vaccine introductions. The cost of the traditional EPI vaccines in the infant schedule in low-income countries totals around $1.35 (for the vaccines only), based on 2011 UNICEF average prices and excluding shipping, insurance and wastage. Adding all the vaccines now recommended by WHO for universal use, that is hepatitis B, Hib, rotavirus and pneumococcal conjugate vaccines, would increase the vaccine costs alone to more than $30 per child.[20] The operational costs – both the short-term costs of preparing the introduction and longer-term costs – must also be considered (see below). Therefore, decision-makers – even in countries eligible for GAVI support – must carefully evaluate the costs and benefits of adding the new vaccine, as well as its potential short- and long-term impact on national health budgets.

An assessment of the economic and financial implications of adding a vaccine to the immunization programme can answer the following critical questions for governments and their development partners:

20 This cost assumes average UNICEF prices for 2012 and the use of the combination DTP-hep B-Hib vaccine.

- Is the new vaccine and associated operational costs affordable? That is, what are the long-term resource requirements as compared to the available budget?
- What are the main cost drivers for countrywide introduction of a new vaccine?
- What will be the potential funding gap for the new vaccine?
- Can additional domestic or external funding be found to fill this gap and what are the prospects for financial sustainability of the new vaccine?
- Are the available vaccines cost-effective against established cost-effectiveness thresholds and compared to other vaccines or health interventions?
- Using a cost-effectiveness analysis, is it possible to assist decision-makers with determining the vaccine price that would provide value for money or what would be affordable for the country?

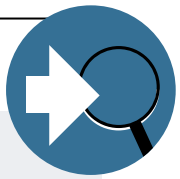
While a number of different economic analyses can be conducted, the three most common and practical ones used in making decisions about new vaccines are:

1) Cost-effectiveness analysis to determine the relative worth or value of the new vaccine;
2) Analysis of its fiscal or budgetary impact and affordability; and
3) Estimation of the funding gap and financial sustainability.[21]

In conducting economic analyses, it is important to distinguish between programme-specific versus shared costs, between full costs of the programme with the new vaccine versus incremental costs of adding the new vaccine, and between financial (budgetary) versus economic costs. Different types of analyses require using different types of costs which depend on the policy question to be answered and who is asking the question (i.e., the perspective of the analysis). See → Annex 2 for more information. There are now a series of tools and guidelines to assist countries in conducting these analyses (→ Box 3).

21 There are also analyses of the broader economic impact and value of vaccines and immunization programmes that may be useful for decision-makers to be aware of, such as the macro-economic impact of certain vaccines and the impact of childhood vaccination on cognitive development and hence on society's future work force. For more information, see: Deogaonkar R, Hutubessy R, van der Putten I, Evers S, Jit M. Systematic review of studies evaluating the broader economic impact of vaccination in low and middle income countries. BMC *Public Health*. 2012 Oct 16;12:878.

BOX 3. Tools to help conduct economic analyses for new vaccines*



- ***WHO Guidelines for estimating costs of introducing new vaccines into the national immunization system*** provide a standard method for estimating incremental costs for a new vaccine. The guide can be found at: http://whqlibdoc.who.int/hq/2002/WHO_V&B_02.11.pdf.

- ***Immunization costing and financing: A tool and user guide for comprehensive Multi-Year Planning (cMYP)*** enables countries to estimate the costs, the financing needs of their immunization programmes to meet their goals for the next several years, including the addition of new vaccines and other activities, as well as the funding gaps. The tool and user guide can be found at: http://www.who.int/immunization/programmes_systems/financing/tools/cmyp/en/.

- ***The WHO Guide for standardisation of economic evaluations of immunization programmes*** is a practical guide on conducting, interpreting and presenting cost-effectiveness analyses for immunization programmes, including the addition of new vaccines. The guide can be found at: http://whqlibdoc.who.int/hq/2008/WHO_IVB_08.14_eng.pdf.

- ***The WHO Cervical Cancer Prevention and Control Costing (C4P) Tool*** is a user-friendly computerized tool that estimates the incremental resources required, including operational costs, to add HPV vaccine to an existing immunization programme. The tool estimates the cost per dose, the cost per fully-immunized girl, the total costs of adding the vaccine to the programme, as well as the expenditures required for the initial investment for HPV vaccine introduction. It also allows the user to estimate the cost of various vaccine delivery strategies. There is also a module to estimate the cost of implementing cervical cancer screening and treatment. The tool can be found at: http://www.who.int/immunization/diseases/hpv/cervical_cancer_costing_tool/en/.

- **ProVac/TriVac models for calculating cost-effectiveness of new vaccines:** PAHO has created user-friendly computerized tools for specific vaccines (including rotavirus, pneumococcal conjugate and HPV vaccines) to estimate the costs and cost-effectiveness of vaccination. The tools produce charts showing disease incidence and deaths with and without vaccination, and calculates treatment cost savings, cost per DALY averted and other cost-effectiveness ratios. E-learning courses for specific vaccines, including rotavirus and pneumococcal conjugate vaccines, provide guidance in estimating the impact of vaccination. These tools can be found at: http://new.paho.org/provac.

* Many of these and other tools are available at http://www.who.int/immunization/programmes_systems/financing/en

Economic analyses to support decisions about HPV vaccination in low- and middle-income countries: a consensus report and guide for analysts. Jit M, Levin C, Brison M, Levin A, Resch S, Berkhof J, Kim J, Hutubessy R.BMC Med 2013 Jan 30;11(1):23. This is a consensus report of a WHO expert group that prioritized key questions to be addressed when considering economic analysis to support HPV vaccine introduction in low and middle income countries.

Results from evaluations of models and cost-effectiveness tools to support introduction decisions for new vaccines need critical appraisal. Hutubessy R, Henao AM, Namgyal P, Moorthy V, Hombach J. BMC Med 2011 May 12;9:55. doi: 10.1186/1741-7015-9-55. This article describes WHO assessments of economic analytical tools to support vaccine introduction decisions for pneumococcal, rotavirus and human papillomavirus vaccines. The objectives of these assessments were to provide decision-makers with a menu and appraisal of existing cost-effectiveness tools for new vaccines rather than to endorse the use of a single tool.

OneHealth Tool is a software tool developed through the International Health Partnership (IHP+) that provides a single framework for planning, costing, impact analysis, budgeting and financing of health strategies at the country level, with a focus on integrated planning and health systems strengthening. The primary purpose of this tool is to assess health investment needs in low- and middle-income countries. It is designed in a modular format that allows for costing of specific interventions as well as of health system components. Currently infant and HPV vaccines are included. It can be found at: http://www.internationalhealthpartnership.net/en/tools/one-health-tool/.

Making choices in health: WHO guide to cost-effectiveness analysis presents the WHO-CHOICE methodology for "generalized cost-effectiveness analysis." This allows for broad-based decision-making and priority setting at the national level by comparing the cost-effectiveness of new vaccines to that of other public health interventions. The guide also provides country and regional estimates of health care costs used for cost-of-illness analyses. It can be found at: http://www.who.int/choice/cost-effectiveness/generalized/en/.

The WHO Guide to identifying the economic consequences of disease and injury provides a framework for "cost-of-illness" studies that can address a number of microeconomic (e.g., level of households, firms or governments) or macroeconomic policy questions concerning the economic consequences of disease or injury. Resulting estimates can inform decision-makers about the overall magnitude of economic losses and their distribution across a number of key drivers or categories of cost. The guide can be found at: http://www.who.int/choice/economicburden/en/.

Costs to consider when introducing a vaccine to the national immunization programme

When estimating the cost of adding a new vaccine to the national immunization programme, it is important to consider all of the activities and changes that the vaccine introduction will require. These include activities to prepare for the introduction, such as expansion of the cold chain system, social mobilization activities to promote the new vaccine and training of health workers. They also include costs that are sometimes forgotten, such as the cost of surveillance of the disease targeted by the new vaccine; the cost of repairing, expanding or constructing incinerators to handle the waste disposal needs of the new vaccine; and other "hidden costs" (discussed further in → Section 3.1). Often these activities are not planned in detail or budgeted until after the decision to introduce the vaccine is made. However, policy-makers need to be aware of these costs to avoid any surprises and to ensure that sufficient funds are available for a successful introduction.

As discussed throughout this document, a country may use the opportunity of a new vaccine introduction to strengthen different aspects of the immunization programme or health system, such as AEFI surveillance and reporting, and supportive supervision. These improvements may result in additional costs that, together with their benefits, also need to be taken into account.

Cost-effectiveness analysis

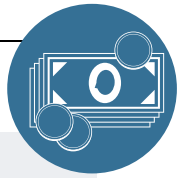
A cost-effectiveness analysis for a new vaccine is used to answer the question: Is adding the vaccine to the national immunization programme a good value for money to achieve a certain result, such as preventing deaths and hospitalizations? The analysis estimates the economic cost of incorporating the new vaccine into the immunization programme, after subtracting the estimated cost savings resulting from the vaccination, such as savings in treatment costs and/or the reduction of productivity losses of parents or caregivers. It also estimates the impact of the new vaccine to derive the estimated cost per death or illness prevented, or the combined impact on morbidity and mortality expressed as the cost per disability-adjusted life year (DALY) averted or quality of life year (QALY) gained. These cost-effectiveness ratios are then compared to those of other interventions or against established cost-effectiveness thresholds which can help clarify how much country decision-makers are willing to pay for additional health gains (see → Box 4).

Cost-effectiveness analyses are useful to answer such questions as:

- Should a new vaccine or technology be introduced into the national immunization programme?
- Which vaccine against a particular disease should be chosen?

- Is geographically targeted or universal vaccination more cost-effective for this disease?
- Would it be more cost-effective to introduce a vaccine alone or in combination with other interventions against the targeted disease?

BOX 4. Cost-effectiveness analyses



In **cost-effectiveness analyses**, the value of a vaccine is expressed in ratios, such as the cost per death averted, cost per illness prevented, or cost per disability-adjusted life year (DALY) averted. The decision-makers' valuation of a unit of health gain (or ceiling ratio) is important in cost-effectiveness analyses as the relative value against which acceptability is defined, although in practice, values are usually chosen arbitrarily. WHO's Commission on Macroeconomics and Health considers that a cost/DALY averted of less than the gross national income (GNI) per capita of the country or region is "very cost-effective", while a cost/DALY averted of less than three times the GNI is "cost-effective" – that is, a worthwhile investment. Interventions with lower cost-effectiveness ratios are better investments than those with higher ones from an economic perspective.

The cost-effectiveness of a vaccine must be weighed against other considerations discussed in this chapter, such as the public health priority of the disease, its impact on improving equity, and the effectiveness of other prevention and control measures. Cost-effectiveness analyses can also be challenging and time-consuming, especially to obtain accurate estimates of cost-of-illness and vaccine delivery costs per child, and to model the impact of the vaccine on disease transmission. Furthermore, technical capacity to use cost-effectiveness models or tools and to interpret the results may be lacking. As a result, evidence about the cost-effectiveness of vaccines in low-income and middle-income countries is often scarce. In addition, policy-makers in these countries often do not have the benefit of using results from an array of cost-effectiveness studies conducted in their country, unlike their counterparts in countries such as the USA, the UK and The Netherlands. There are a number of models for conducting cost-effectiveness analyses for vaccines, including the ProVac and WHO-CHOICE methodologies (see → Box 3 above). Responses to the tool comparison exercises for HPV, rotavirus and pneumococcal vaccines (see 7th bullet in → Box 3) demonstrate that modelling groups are prepared to share their models and expertise to work with stakeholders in low-income and middle-income countries.

Analysis of impact of the vaccine introduction on the national budget and affordability

All decisions about whether to introduce a new vaccine should include an analysis of whether the country can afford the vaccine and associated operational costs both in the short- and long-term. An analysis of the budgetary or fiscal impact estimates the **financial costs** – that is the actual expenditures – of adding the new vaccine and its effect on the budget over time. The electronic costing tool for a comprehensive multi-year plan (cMYP) (described in → Box 3) can be useful in estimating these costs. A new vaccine may be considered affordable if it can be introduced and absorbed into the immunization budget over the medium to long term without significantly affecting available resources for other vaccines or other public health priorities. The analysis should include the cost of co-financing the portion of vaccine doses that GAVI-supported countries must procure and pay for themselves. It should also include all of the inputs needed to successfully deliver the vaccine and make necessary programme changes, as described above and in → Section 3.1.

To decide whether adding the new vaccine to the immunization programme is affordable, the financial cost is often compared to the overall government health budget, the overall economy or in terms of the cost per population or per person vaccinated. Common indicators used include:

- Share of the new vaccine cost as a percentage of the total immunization programme costs or total vaccine costs;
- Programme costs with and without the new vaccine as a proportion of the total government health budget or government health expenditures for a particular year;
- Per capita estimates of programme costs with and without the new vaccine;
- Programme costs with and without the new vaccine as a proportion of gross domestic product (GDP).

These indicators should ideally be compared to those of other public health interventions or programmes to have a better sense of their relative impact on the budget. However, if the programme-specific costs with a new vaccine represent a substantial share of the 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 the coming years.

Estimation of the funding gap and financial sustainability

Once the costs of the programme with the new vaccine are estimated, they can be compared with current and future financing by funding source per year to estimate the annual funding gap for the next several years. The cMYP tool provides automatically-generated graphs and tables showing the funding gap, based on current and projected financing, including the breakdown of the gap by different programme components (e.g., vaccines, personnel, transport).

Long-term financial sustainability of the immunization programme with the addition of the new vaccine should be a major consideration for any government. Suspending the use of a vaccine due to a lack of funding can have serious implications for disease control and for equitable health outcomes. If funds are diverted from other health programmes to pay for the new vaccine, careful planning is needed to ensure that other priority health programmes and services are not adversely affected.

As the costs of many of the new and upcoming vaccines increase, and with competition to fund other important health interventions, such as AIDS treatment with anti-retroviral drugs, it is increasingly important for countries to develop a variety of effective strategies to achieve financial sustainability for new vaccines and for the immunization programme as a whole. These strategies can be grouped into three categories: 1) mobilizing additional resources, 2) increasing the reliability of funding and 3) improving programme efficiency to minimize the additional resources needed.[22] These strategies are discussed further in → Annex 2.

22 See: Kamara L, Milstein JB, Patyna M, Lydon P, Levin A, Brenzel L. Strategies for financial sustainability of immunization programs: a review of the strategies from 50 immunization program financial sustainability plans. *Vaccine* 2008; 26(51):6717-26.

2.4

Strength of the immunization programme and health system

When deciding whether to introduce a vaccine into the national immunization programme, decision-makers must consider the potential impact of the introduction on both the programme and on the overall health system, including its ability to provide other critical health services. If there are already serious weaknesses in the immunization programme, adding the new vaccine may cause additional burdens and thus worsen the programme's performance. For example, if the current programme is failing to reach a large proportion of the target population, the new vaccine may be able to offer only limited benefits to those who need it most.

Decision-makers must also decide whether the immunization programme and health systems are capable of handling, storing and administering the additional vaccine adequately, considering its number of doses and schedule, storage space requirements, heat stability and freeze tolerance and other specific characteristics. Looking beyond the immunization programme, if the current workforce is insufficient, inadequately trained or poorly motivated to handle the current package of health services, adding a new vaccine to the programme may result in more stress on these workers, poor coverage of the new vaccine and perhaps other vaccines, and less time and attention paid to other critical health services.

Another issue that policymakers should consider is whether the prevailing attitudes amongst the public towards vaccines or the immunization programme are conducive to adding the vaccine in question at this particular time, and if not, whether the communication campaign for the new vaccine introduction will sufficiently address public concerns to prevent them from having a negative impact on public acceptance and uptake of the new vaccine or vaccines in general. Safety concerns about several new vaccines, as well as the rise of anti-vaccine movements and misinformation from the media, have resulted in low initial acceptance of some new vaccines in a number of countries. Thus, to ensure a successful introduction, it can be critical to conduct an assessment of the current climate towards vaccines in the country, of the potential impact of the vaccine introduction on the uptake of other vaccines in the programme, and of the health sector's ability to develop strategies or interventions to prevent negative perceptions from derailing the new vaccine introduction.

The introduction of a vaccine into the national immunization programme may also present opportunities to improve the programme and the overall health system. For example, the training of health workers for the new vaccine presents opportunities to refresh their skills and knowledge in key aspects of immunization. The vaccine introduction can also provide an impetus for the country to establish a National Immunization Technical Advisory Group (NITAG), or if one already exists, can lead to strengthening its ability to make evidence-based decisions. In addition, the addition of a new vaccine can result in improved planning, upgrading of the cold chain and logistics system, and improved monitoring and evaluation of programme performance.

Therefore, it is important to conduct a situation analysis (or "pre-introduction assessment") of the immunization programme in order to identify weak areas that need to be strengthened before a vaccine is introduced or areas that can be explicitly strengthened in the process of introducing the vaccine. This review should allow sufficient time to address identified weaknesses (see → Section 3.1 for further discussion of pre-introduction assessments). Data from a recently-conducted EPI review, coverage survey, Effective Vaccine Management (EVM) assessment, or a post-introduction evaluation (PIE) for a previously-introduced vaccine (see → Section 4.4. on PIEs) could be used to assess the current strength of the programme. At the same time, it is also critical to identify major health system-related issues that can affect the performance of the immunization programme and to develop strategies to address them.

→ Box 5 lists possible elements or benchmarks that can be used to assess the strength of the national immunization programme to accommodate a new vaccine. While, ideally, a country should meet all of these conditions before introducing a vaccine, it is obvious that many countries may not be able to do so. Therefore, the items in this list should not be viewed as prerequisites that must all be met before a country can add a new vaccine to its programme. Rather, the list can assist in identifying weak areas that could be improved prior to or in parallel with the vaccine introduction. In the case of multiple, serious deficiencies, the list can help provide evidence of the need to delay introduction of the vaccine until major areas are strengthened.

Once a decision to introduce a vaccine has been made, an immunization programme manager should develop a New Vaccine Introduction Plan as well as detailed implementation plans with timelines. WHO has prepared templates for a New Vaccine Introduction Plan (see → Annex 3) as well as Excel templates for a New Vaccine Introduction Checklist, Activity List & Timeline (see → Annex 4 and Excel worksheets at: http://www.who.int/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines/).

BOX 5. Elements to assess when deciding upon the readiness of the immunization programme to add a vaccine

1 A strong decision-making and accountability process that is transparent, coordinated and integrated with the overall health sector:

- The vaccine introduction fits in with the priorities and plans outlined in the national health sector plan, national development plan, or other key government policy documents.
- There is a functioning National Immunization Technical Advisory Group (NITAG) or equivalent technical committee to make recommendations to the government about the vaccine introduction, based on a rigorous and transparent review and analysis of epidemiological, economic and other relevant evidence.
- The plan or proposal for the new vaccine has been reviewed by a Health Sector Coordinating Committee (HSCC) or similar mechanism to ensure coordination of health programmes and funding requests.
- All key decision-makers in relevant agencies (e.g., Ministry of Health, Ministry of Finance and, for vaccines delivered through schools, the Ministry of Education) are involved in making the final decision about introducing the vaccine.

2 A well-performing or improving immunization programme to obtain the full benefit from existing vaccines:

- An immunization multi-year plan and annual work plans are in place, with regular updating of policies.
- Overall coverage rates of existing vaccines meet national targets or reflect satisfactory improvement and have not fallen in the last five years.
- Drop-out rates between vaccine doses have decreased in the past five years or are at acceptable levels.
- Differences in coverage rates between high- and low-performing districts and between the lowest and highest income groups (e.g., quintiles) are decreasing or are at acceptable levels.
- Specific objectives are met or well underway for vaccines already in the programme. For example, high coverage with DTP-HepB-Hib is achieved, catch-up measles vaccination has been conducted, as needed, or a two-dose measles strategy has been established.

③ **A sufficient or expanding, well-trained and motivated health workforce:**

- A situation analysis has been conducted of the size and distribution of the health workforce in terms of its ability to provide the current package of health services and to add the new vaccine to the national immunization programme.
- If additional personnel are deemed necessary to handle the extra workload created by the addition of the vaccine, they are included in the immunization multi-year plan and budget, and in the national health sector plan and budget.
- Appropriate pre-service and in-service training and on-site supportive supervision of health staff is provided.
- If staff turnover is a critical problem, there is a realistic plan and budget in place (as part of the national health plan) to replace staff and reduce the turnover rate.

④ **Functional vaccine management, cold chain and logistics systems:**

- National cold-chain policy and vaccine management systems include an updated cold chain equipment inventory as well as plans for the maintenance and replacement of equipment.
- The cold chain system has adequate volume capacity and performance for vaccines already in the programme at all levels (central, provincial/regional, district, and facility). This includes adequate temperature monitoring and ability to pinpoint and correct problems with freezing of vaccines.
- Cold storage space is sufficient or is being expanded to meet any additional demands of the new vaccine at all levels of the health system, with adequate spare capacity to meet campaign or unforeseen needs.
- There is sufficient dry storage space at all levels to accommodate injection materials for the current vaccines and the new vaccine, as well as for medicines and other health commodities.
- Vaccine stock-outs at national or sub-national levels have been infrequent in the last five years.
- There are two-year to five-year forecasts for all vaccines already in the programme (including for planned or likely campaigns) and for the new vaccine, including the transition period when current vaccines are being replaced.
- There is effective vaccine wastage monitoring and acceptable levels of wastage that do not compromise the coverage targets.

5 Safe immunization practices and monitoring and management of adverse events

- All injectable 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 properly dispose of additional injection materials for the new vaccine.
- There is in place a surveillance and reporting system for adverse events following immunization (AEFI) that is capable of investigating and responding to possible adverse events, or there are plans to improve this capacity with training.

6 High-quality disease surveillance and immunization coverage monitoring

- There is appropriate surveillance to meet the country's disease control objectives and according to the country's capacity. It is essential that, whatever surveillance strategy is used, the epidemiological and laboratory methods comply with surveillance quality standards, as failure to do so will entail the risk of misleading results.
- Credible data exist on coverage of all vaccines provided through the national immunization programme, including a breakdown by sub-national levels.
- Vaccination coverage evaluation surveys are conducted periodically to validate routinely-collected data and ideally include coverage data by socio-economic group and gender.

7 A financially sustainable programme

- The decision to introduce the vaccine has been based on a careful consideration of the short-term additional costs associated with new vaccine introduction, as well as the longer-term financial implications for sustaining the programme (e.g., after donor support ends).
- The government has committed to financing the national immunization programme, and budget allocations and disbursements have increased over time.
- The vaccine introduction, including co-financing for donor-supported vaccines, will be funded with additional resources and should not adversely affect the supply of other vaccines, other immunization programme components, or other critical health services and programmes.
- Multi-year plans include a budget that is linked to the national health budget to secure current and future funding for vaccines and other costs.

BOX 6. Maximizing the opportunity of a new vaccine introduction to strengthen the immunization programme and overall health system

The introduction of a vaccine provides many opportunities to improve a country's overall immunization programme as well as its health system. Many of the activities carried out to prepare, implement and monitor the vaccine introduction provide opportunities to improve the immunization programme as a whole and to identify best practices that could be applied to other health programmes and services. These activities include using an evidence-based decision-making process; preparing multi-year plans and budgets based on a programme assessment; training health workers on the new vaccine; improving and expanding the cold chain; strengthening disease surveillance and AEFI monitoring and reporting systems; and conducting advocacy and communications activities to promote the new vaccine.

Conversely, the immunization programme can learn from the best practices of other health programmes. These synergies become more possible as countries integrate the introduction of vaccines and other health activities into a national health strategy or plan, such as by adopting the International Health Partnership Plus (IHP+) process aimed at incorporating all donor-funded health projects into "one plan, one budget and one report" (see: http://www.internationalhealthpartnership.net/en/key-issues/national-health-planning-jans/).

Low-income countries often receive financial and technical support from partners for the introduction of a vaccine, which expands the possibilities for creating long-term benefits to immunization and other health programmes. These possibilities remain unfulfilled, however, unless the immunization programme, health ministry and partners have the interest and time to plan and execute initiatives that take advantage of the opportunities provided by this support. Some vaccine introductions in recent years may have been rushed, with insufficient time for planning and preparation. Advocating for sufficient lead time may be key to translating the ideas in this box into reality.

Health ministries should therefore examine weaknesses in the immunization programme and in different components of the broader health system and use the opportunity of the new vaccine introduction and accompanying funding to strengthen these areas. Below are examples of how countries have used the introduction of a new vaccine to improve immunization programmes and health systems:

- In a **South American** country, the introduction of DTP-HepB-Hib (pentavalent) vaccine provided the impetus to strengthen many components of the immunization programme as well as the health system, with technical and financial support from external donors. Improvements were made to the training of health workers on new norms and procedures, injection safety and waste management practices; the immunization information system at all levels;

and monitoring, supervision and evaluation. Improvements were also made to the vaccine management and logistics system – practically eliminating once frequent vaccine stock-outs. The government also used this opportunity to establish a system of accreditation of public and private health facilities to ensure standards of quality, equity, efficiency and effectiveness.

In a **West African** country, the introduction of the meningococcal A vaccine in 2010 led to the re-activation of the country's National Committee on Post-Marketing Surveillance to review and respond to reports of adverse events following immunization (AEFI). The committee included representatives from the National Medicines Agency, National Technical Centre for Disease Control, WHO, Ministry of Defence, National Health Inspectorate and key hospitals. Regional AEFI committees were also established. The national committee developed improved guidelines and training modules on AEFI surveillance for health workers. The importance of the committee was recognized by the Government. This led to expansion of the committee's mandate to include post-marketing surveillance of other medical products.

In preparation for its simultaneous introduction of pneumococcal and rotavirus vaccines in 2008,* **Peru** conducted a systematic assessment of its primary health care workforce, including a review of its size and distribution and an evaluation of the average available time spent on medical consultations. The review identified a human resource gap for immunization of 40%. The country's plan included a substantial increase in the proportion of operational budgets allocated to human resources. These changes facilitated the reallocation and increase in the number of public health nurses in proportion to the increase in the number of vaccines provided by the immunization programme, and ensured that each health post had at least one nurse. The increase in the health workforce, together with management improvements, was seen as playing a significant role in Peru's successful introduction of the two vaccines.

More ideas on health system strengthening as part of a vaccine introduction can be found in → Annex 1.

* Gordon WS, Jones A, Wecker J. Introducing multiple vaccines in low- and lower-middle-income countries: issues, opportunities and challenges. *Health Policy and Planning* 2012; 27; ii7-ii26.

2.5

The decision-making process

There is increasing recognition among governments, donors and international agencies of the importance of having a systematic and transparent process for making a decision about introducing a vaccine into the national immunization programme. Also critical is that key stakeholders both in and outside of the health sector are consulted to obtain their input and buy-in and to ensure ownership of the vaccine introduction and its alignment with the national health plan or strategy and budget. If the process is perceived as secretive, rushed or not thorough, it can lead to opposition among powerful leaders or groups, negative reports in the media and a lack of community acceptance of the new vaccine. On the other hand, a decision made in a systematic way with the input of all key stakeholders and that addresses their concerns is more likely to result in a successful introduction of the vaccine.

More and more countries are recognizing the need to establish a National Immunization Technical Advisory Group (NITAG) to make recommendations to the government about the national immunization programme, based on a rigorous review of the evidence. NITAGs should consist of national experts in a broad range of disciplines – such as senior paediatricians, immunization and vaccine experts, epidemiologists, public health experts, health economists, health system experts and social scientists – who are capable of analyzing the different types of evidence and issues that should be considered in making an informed decision. NITAG members should have a broad health perspective to ensure that the impact of the vaccine on the immunization programme and overall health system is considered. The committee and its members must be perceived as objective, independent and not representing a particular interest group. The independence of the NITAG and its reliance on evidence-based decision-making reinforces the credibility of the decision, helps resist pressure from interest groups and enhances the ability to secure government and/or donor funding for the vaccine. NITAGs function best when they are supported by a secretariat or technical sub-committee to collect and synthesize the evidence.[23]

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23 More information and references on NITAGs can be found at: http://www.who.int/immunization/sage/national_advisory_committees/en/index.html at the Supporting Independent Immunization and Vaccine Advisory Committees (SIVAC) Initiative website: http://www.sivacinitiative.org/, and at the NITAG resource centre of the SIVAC Initiative: http://www.nitag-resource.org.

Decisions about introducing a vaccine should be approved not only by top decision-makers within the health and finance ministries, but also by other relevant agencies and ministries, as necessary, including the Ministry of Education, in the case of vaccines that may be delivered through schools. In addition, the country's Health Sector Coordinating Committee (HSCC) or similar group should be involved in reviewing any plans for the new vaccine introduction to ensure that they are consistent with the national health plan and priorities and that they are not contradictory or duplicative with other plans. HSCCs can also help ensure that plans for the vaccine introduction are coordinated with other sectors of society, such as civil society and NGOs, in order to secure their buy-in and assistance in planning and implementing the new vaccine introduction. In addition, Inter-agency Coordinating Committees (ICCs) play an important role in many countries by coordinating partner financing and activities, including the preparation of proposals for support for new vaccines and the subsequent roll-out and evaluation of the vaccine introduction.

TABLE 2. Groups involved in making decisions and in coordinating plans for introducing a vaccine into national immunization programmes

Group or agency	Description/role
National Regulatory Authority (NRA)	An agency responsible for assuring the quality of the medical products, including vaccines, used in the country and in issuing licenses for new products
National Immunization Technical Advisory Group (NITAG)	A group of experts responsible for advising the government on technical issues related to the national immunization programme, including vaccine introductions, based on scientific evidence
Inter-agency Coordinating Committee (ICC)	A committee made up of representatives of the MOH, WHO, UNICEF and other national and external partners to improve coordination among partners for the support of immunization programmes
Health Sector Coordinating Committee (HSCC)	The highest level group in a country responsible for coordinating and monitoring of the national health sector plan and for ensuring that all new activities, including a vaccine introduction, are consistent with the national health strategy, national health plan and budget

The NITAG and government policy-makers may have to make decisions beyond just whether or not to introduce the vaccine, especially if there are policy and financial implications. These decisions can include:

- Whether to implement nationwide or geographically-targeted vaccination. Certain diseases, such as Japanese encephalitis, meningococcal disease, yellow fever and cholera, may pose a threat primarily in certain high-risk areas or for specific populations in the country and thus nationwide immunization may not be necessary or cost-effective. Evidence such as the disease burden by geographic area and the cost-effectiveness of nationwide vs. targeted vaccination can assist in making this decision;

- The age group and schedule. Some newer vaccines, including HPV vaccine, are given to populations other than infants. Thus, the feasibility of reaching older age groups and the need for alternative delivery strategies, such as school-based immunization, may have to be considered;
- Whether or not to conduct catch-up immunization and for which age groups. Catch-up immunization for older age groups, when coupled with routine immunization for infants or young children, can rapidly reduce transmission of a disease. However, the larger the age group to be immunized, the higher the costs and logistical challenges.
- The choice or preference of vaccine, formulation and presentation, in consideration of the costs, storage requirements, and training needs for each product.

These issues are discussed further in → Chapter 3.

BOX 7. Country example: Sudan[24]

The Federal Ministry of Health in **Sudan** established a national immunization technical advisory group (NITAG) in April 2009 through a ministerial decree in response to the availability of several new vaccines supported by the GAVI Alliance, and with encouragement from the WHO Eastern Mediterranean regional office. The Government recognized the need to have a stronger

24 This country example is about Sudan in 2009 before the new country of South Sudan was created.

scientific rationale for decisions to introduce new vaccines into the national immunization programme. The NITAG consisted of 11 core (voting) members – mainly from academia and all independent from the Ministry of Health – and included experts in paediatrics (including the Chair), epidemiology, immunology, public health, pharmacology, community medicine, and health economics. Non-core members who did not vote included representatives from different MOH departments (e.g., surveillance, public health), WHO and UNICEF. The EPI manager and staff served as the committee's secretariat.

Once the NITAG was formed, it decided to first consider the introduction of rotavirus vaccine, in part because epidemiological data were already available from sentinel site surveillance that had been set up as part of a global rotavirus surveillance network supported by WHO, U.S. CDC and other partners. Surveillance data from 2007 – 2010 showed a high burden of the disease – with 36% of stools tested from children hospitalized with acute gastroenteritis or diarrhoea testing positive for rotavirus infection. The NITAG also examined additional data from local hospitals and reviewed data on the safety of rotavirus vaccines. In addition, the committee conducted an assessment of the readiness of the immunization programme to handle the rotavirus vaccine by examining the logistics and cold chain system, the training needs for health workers and other key programmatic issues, and determined that the programme was indeed ready. Based on this body of evidence and on WHO recommendations regarding rotavirus vaccines, the NITAG made a recommendation to add the vaccine to the national immunization programme.

To build support for the new vaccine within the medical community, the EPI organized a forum for paediatricians soon after the recommendation was made. In response to their concerns about the safety of rotavirus vaccines, the MOH decided to conduct post-marketing surveillance of intussusception (obstructed bowel syndrome) and of the vaccine's impact on disease following the vaccine introduction. A retrospective study of intussusception in major hospitals going back three years was conducted to obtain baseline data on the incidence of this condition.

The introduction of Rotarix® vaccine was launched nationwide in July 2011 in a well-publicized ceremony officiated by the President's health advisor. By December 2011, coverage for the second dose reached 74%. Prospective intussusception surveillance using a standard protocol was also instituted.

BOX 8. Country example: Portugal

In 2008, the government of **Portugal** introduced HPV vaccine for 13 year old girls by adding the vaccine to its existing school-based immunization programme. Coverage for all three vaccine doses reached 84% for the first birth cohort vaccinated. The success of this programme has been attributed to the building of a strong and comprehensive evidence base – consisting of epidemiological, socio-behavioral and economic data – and the communication of this evidence to the medical establishment, the public and the media in order to build trust and create demand for the vaccine.

National estimates of cervical cancer incidence and mortality from the Globocan database maintained by the International Agency for Research on Cancer (IARC) and other sources revealed quite high rates, indicating that coverage of cervical cancer screening was insufficient. The National Vaccine Committee also examined the results of a survey on sexual behavior among girls and women, which found a high rate of sexual activity among teenagers. In addition, an economic analysis found that HPV vaccination would be cost-effective.

To build support from the medical community, this multi-faceted evidence was included in letters from the Ministry of Health to health professionals and in training materials for health workers in preparation for the vaccine introduction.

BOX 9. Country example: Paraguay

The introduction of pneumococcal conjugate vaccine (PCV) into the national immunization programme in **Paraguay** was a priority among top health officials. However, the Ministry of Health recognized the need to develop a strong evidence base to make an informed decision about which, if either, of the two available PCVs to introduce, given the relatively high costs of these vaccines compared to traditional childhood vaccines and other competing health priorities. To do this, the MOH took the unusual step of issuing a ministerial decree to establish a national team to collect and analyze evidence on the need for and potential impact of the vaccine. The team consisted of the EPI manager, the PAHO immunization focal point, a health economist and a paediatrician.

A recommendation from the country's National Immunization Technical Advisory Committee came within a year of the ministerial decree and the introduction of PCV-10 was launched one year later (January 2012).

There were several factors contributing to the relatively rapid approval of the new vaccine introduction, despite the fact that a financial analysis showed that it would double the entire national immunization programme budget. First, the ministerial decree served as a high-level mandate that enabled the data collection team to collect needed information from relevant agencies in a short period of time. Second, the TriVac cost-effectiveness tool developed by the ProVac Initiative assisted the team in determining the data needs to make a transparent and compelling case, in analyzing the cost-effectiveness and financial feasibility of the different pneumococcal vaccines and schedules, and in presenting the results in user-friendly charts. The fact that most of the evidence was gathered locally by a national team with no conflicts of interest also strengthened the case for the vaccine. These data included disease burden estimates (from extrapolated sentinel site surveillance and from regional sources), data on utilization and costs of health services to treat pneumococcal disease in children and incremental vaccination programme costs. The disease burden data showed a high incidence of clinical pneumonia and related mortality in children under five (≈22,000/100,000) as compared to neighboring countries. The analyses showed that PCV-10 would prevent more illness due to acute otitis media than PCV-13 and thus would be slightly more cost-effective due to savings in the cost of treating this illness. The team's report also identified data gaps, including poor and erratic local disease burden data.

The team's report formed the basis for the Committee's recommendation to introduce PCV-10 and to improve disease surveillance systems to inform future decisions. The report was also used by the EPI manager and Minister of Health to successfully lobby members of Parliament and the Ministry of Finance to finance the vaccine and enhance disease surveillance, logistics and communications around the vaccine introduction. The process of a comprehensive analysis using primarily local data to justify new vaccine introductions has become institutionalized in the country and was undertaken to inform a decision about HPV vaccine introduction.

3.

Planning and managing the vaccine introduction

3.1

Planning for a successful vaccine introduction

3.1.1

Updating immunization plans and policies and integrating them with the national health plan

Once the decision to introduce the vaccine has been made, the comprehensive multi-year plan (cMYP) and budget need to be updated to include all of the activities to prepare for, implement, monitor and evaluate the introduction. The cMYP is normally a three to five year plan that sets out the goals, objectives, strategies, indicators, and activities to achieve these milestones for the entire national immunization programme. It integrates into one plan all routine immunization activities, supplemental immunization activities (SIAs) and other related initiatives. The immunization programme budget and financing plan also needs to be updated to incorporate the vaccine introduction (as discussed in → Section 2.3.3).[25]

As discussed in → Chapter 2, developing or updating the multi-year plan should begin with a situation analysis of the current performance of the immunization programme. Updating the plan to include the new vaccine thus presents an opportunity to identify weak areas of the immunization programme and health system that may impede the successful introduction of the vaccine or progress of the overall immunization programme, and to make plans to strengthen these areas. To assist in the detailed planning for the new vaccine introduction, WHO has developed a template New Vaccine Introduction Checklist as a useful tool to determine what changes and activities are needed and the time required to ensure a successful vaccine introduction (see → Annex 4).[26]

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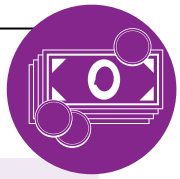
25 Guidelines for developing a cMYP and the cMYP costing and financing tool can be found at http://www.who.int/immunization/programmes_systems/financing/tools/cmyp/en/

26 The electronic version of the WHO New Vaccine Introduction Checklist, Activity List, and Timeline can be found at: www.who.int/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines/

In planning for a vaccine introduction, it is also critical to consider all possible effects of this addition on the national immunization programme and on the health system, including possible new burdens and stresses. For instance, some newer vaccines, such as rotavirus vaccine, require more time to administer to infants than other routine EPI vaccines. Based on a situation analysis of current services, programme planners may need to consider if additional health workers or an increase in the number of EPI sessions will be required to ensure both high coverage of the new vaccine and that other immunization and health services do not suffer. Vaccine introductions can also require new delivery strategies, expansion of cold chain and dry storage systems, additional waste management facilities and expansion of disease surveillance and programme monitoring to include the newly-targeted disease. Many of these changes may incur additional costs that must be added to the budget (see → Box 10).

BOX 10. Possible costs to include when estimating funding needs for a vaccine introduction



- Training of all relevant health workers at all levels, including refresher training;
- An increase in personnel, such as EPI staff or health workers, to handle the additional work load with the new vaccine, an increase in salaries or other personnel costs;
- An increase in the number of EPI sessions due to the extra time needed to administer the new vaccine and/or due to an increase in demand for immunization services that the new vaccine may generate;
- Expansion of the cold chain, dry storage and vaccine transport systems and associated inputs, including:
  - Extra fuel to operate additional cold chain equipment and vehicles required to accommodate the new vaccine (especially for vaccines with large storage requirements);
  - Possible additional personnel costs for more frequent vaccine deliveries (if storage capacity is insufficient to handle the added requirements of the new vaccine initially);
  - Maintenance and repair of additional equipment and vehicles needed to accommodate the new vaccine;
- Repairs, expansion or addition of waste management facilities to handle the additional waste (e.g., vials, AD syringes) generated by the new vaccine;
- Development and implementation of an effective social mobilization plan;
- Costs of new delivery strategies, such as school-based vaccination, that may result in new costs such as teacher training, additional transport or per diems;
- Revision and printing of child health cards, immunization forms, vaccine stock forms, guidelines and procedures;
- Pre-introduction visits to districts to monitor readiness for the introduction and immediate post-introduction supervisory/monitoring visits to identify and resolve major bottlenecks or issues affecting the introduction;
- Establishment or strengthening of disease surveillance for the new vaccine, including expansion of laboratory capacity, as needed;
- Support for overall programme monitoring and evaluation, such as a vaccine coverage survey and a post-introduction evaluation;
- Strengthening AEFI surveillance, reporting and management for the new vaccine and all EPI vaccines.

3.1.2

Developing a vaccine introduction plan

In addition to updating the multi-year plan to include the new vaccine, an immunization programme should develop a detailed introduction plan. → Annex 3 presents a template for a vaccine introduction plan that countries can use and adapt. An immunization programme will then need to outline all activities and steps required for a successful vaccine introduction by programme component, stipulate what institutions and government departments are responsible for each activity and include a timeline and detailed budget, with an indication of availability of funds. → Annex 4 presents a template New Vaccine Introduction Checklist, Activity List & Timeline which may be used to develop a country's detailed activity list and timeline that list all activities required for the introduction, estimates the time required for each one, sets deadlines, and identifies a timeline.[27]

In developing the introduction plan, programme planners should identify short-, intermediate-, and long-term objectives and targets for the introduction in order to track progress with the various components and phases of the introduction. Short-term objectives may be immediate activities to be completed before the new vaccine introduction, for example, all relevant health management information system (HMIS) forms have been updated to include the new vaccine and have been distributed to all health facilities at least two weeks before the introduction. Some examples of intermediate-term objectives might be improved AEFI monitoring as a result of improved health worker knowledge of AEFI monitoring from recent new vaccine introduction training, improved distribution of AEFI protocols and forms, and improved supportive supervision. Long-term objectives may be a reduction in morbidity and mortality of the poorest children (as a result of successful social mobilization and delivery of the new vaccine) or successful delivery of integrated disease prevention and control services to populations that have traditionally been hard to reach.

Monitoring of progress or barriers to reaching the objectives, targets, and milestones should be conducted regularly by the EPI team and technical sub-committees and the results reported to the ICC or other national coordinating body overseeing the introduction. As activities get underway, the programme may have to make adjustments to the list of activities and the timeline to address unforeseen problems or delays. The New Vaccine Introduction Activity List maybe used as a dynamic management tool to check whether targets and milestones will be met on time and if not, what adjustments must be made to ensure a smooth introduction.

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27 Templates for a New Vaccine Introduction Plan, a New Vaccine Introduction Checklist, Activity List & Timeline are available at: http://www.who.int/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines/

Based on country experiences with recent vaccine introductions, it is critical that enough time is allowed to plan and implement all of the many activities involved in introducing a vaccine and that the introduction not be rushed. For instance, if staff training is estimated to take four months to complete throughout the country and it will take three more months to plan the training and develop the training materials, the process needs to begin at least seven months before the planned launch of the new vaccine. Similarly, if the cold chain system needs to be expanded before a vaccine is introduced, the time to procure and install new equipment and, if necessary, expand or construct new space, needs to be planned – recognizing that these multiple steps may take up to a year or more.

To ensure that a country and all its regions and districts are ready to introduce a new vaccine, some national immunization programmes have conducted visits to selected districts several weeks before the planned introduction date to assess readiness – for example, to check if all relevant health workers have been trained, the new cold chain equipment for individual health facilities is in place, the IEC materials and updated HMIS forms have arrived, social mobilization activities are well underway, and so forth. Such pre-introduction monitoring visits can identify key potential bottlenecks and problems that need to be resolved before the vaccine is introduced, and in some instances, can lead countries to decide to either phase in the introduction – starting with the best-prepared districts – or even move back the introduction date to allow more time for the country to be ready. If countries plan on conducting such visits, they should be included in the budget for the vaccine introduction.

Given the many diverse programme components and technical areas of an immunization programme, when preparing a vaccine introduction, many countries have established technical sub-committees for such areas as advocacy and communications; cold chain, logistics and vaccine management; training and supervision; AEFI surveillance, etc. These sub-committees can play a critical role in assessing, preparing for and implementing the various aspects of a vaccine introduction. Thus, if countries do not have active sub-committees for particular technical areas, the introduction of a vaccine into the national immunization programme can provide the stimulus for establishing or re-activating such committees. The technical sub-committees and other groups involved in planning and implementing the vaccine introduction should include a broad range of stakeholders and community, political and religious leaders (as appropriate) to ensure their buy-in, minimize potential negative impacts, and improve the likelihood of a successful introduction. Involving health workers in the planning also helps to ensure their cooperation and input in developing practical strategies, as well as in identifying and addressing potential problems in implementing the vaccine introduction.

BOX 11. Questions to ask when planning for a vaccine introduction to ensure broad cooperation with key stakeholders and coordination with other health programmes

- Have the national immunization policy and national health sector plan been revised to include the introduction of the vaccine?
- Do time periods for the revised cMYP align with those of the national health plan or strategy? If not, is it possible to modify the time periods so that they coincide?
- Are key officials involved in the planning for the vaccine introduction, including preparation of the revised cMYP, such as representatives from:
  - MOH Planning Department, Planning Commission or equivalent;
  - Primary health care or health services divisions of the MOH;
  - Immunization programme, including the EPI manager;
  - Ministry of Finance;
  - Other relevant ministries or government agencies, such as the Ministry of Education for school-based vaccination programmes?
- Do active technical sub-committees exist for all critical programme components (e.g., advocacy and communications, cold chain and vaccine management, training) and are they actively involved in the planning and implementation of the vaccine introduction?
- Are representatives of different stakeholders (e.g., professional associations, civil society organizations, NGO health care providers, women's groups) involved in planning and implementing the vaccine introduction?
- Are health workers at all levels of the health system involved in the planning of the vaccine introduction?

3.2

Choosing the immunization strategy

Below are general guidance and points to consider when choosing the immunization strategy for a new vaccine. Several introduction guidelines for specific vaccines, including Hib, rotavirus, pneumococcal conjugate, HPV, and 2nd dose of measles vaccines have been developed that provide more detailed guidance for these vaccines.[28]

3.2.1

Phased or simultaneous introduction

Countries will need to decide whether to introduce a vaccine in a phased manner or all at once throughout the nation or, in the case of a geographically-targeted vaccine, in all targeted areas at the same time. A national roll-out will lead to a faster impact, as well as allow for nationwide promotion of the vaccine introduction. However, it may make more sense for some countries to take a phased approach to introduction. A phased-in introduction of a vaccine may be considered in the following circumstances:

- A pilot implementation is needed to identify and address programmatic and logistical challenges, such as the ability of health care workers to understand and adjust to a new, more complicated vaccine schedule, a new vaccine delivery device or vaccine delivery strategy;
- The capacity to train and supervise staff is limited and thus national staff can only support a certain number of provinces or districts at a time;
- 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 will present programmatic and logistical challenges that need to be addressed (e.g., limited cold chain capacity); and

28 These guidelines can be found at: www.who.int/immunization/programmes_systems/policies_strategies/Vaccine_intro_resources/en/.

- Countries with large birth cohorts may want to rationalize the use of limited resources or limited vaccine availability by introducing the vaccine in a phased manner over time.

3.2.2

Deciding whether to introduce more than one vaccine at a time

In recent years, a number of countries have introduced more than one vaccine at the same time, mainly pneumococcal conjugate and rotavirus vaccines. These experiences show that there are both gains – in efficiencies and cost savings – and challenges in simultaneously introducing more than one vaccine into the national immunization programme. Efficiencies can be gained by expanding the cold chain and logistics system all at once to accommodate both vaccines (versus expanding it incrementally for each one), by training health workers on both diseases and vaccines during one training activity, and by updating reporting forms and management information systems to reflect the addition of both vaccines. In addition, introducing pneumococcal and rotavirus vaccines simultaneously, as part of a coordinated strategy to reduce childhood pneumonia and diarrhoea, can generate significant public attention, stimulate more integrated interventions against both diseases, and lead to a more rapid decline in childhood morbidity and mortality than if each vaccine were introduced separately.

However, the simultaneous introduction of vaccines may require a sharp increase in the national immunization programme budget to cover the costs of the new vaccines, a significant expansion of the cold chain system, and an increase in the health workforce. Financial constraints in many countries may not allow for such a sudden expansion of the immunization programme budget. Simultaneous vaccine introductions also have the potential of further stressing weaknesses in routine immunization programmes and add complexity to the planning and implementation of a vaccine introduction. The greater the differences between the vaccines being introduced, the greater the challenge in training health workers in their use, in developing clear and effective communication messages and strategies, and in planning and implementing other aspects of the introduction. These may include differences in the immunization schedule and age limits, or in packaging and temperature requirements for each vaccine, or the way the vaccines are administered. Before deciding whether to introduce more than one vaccine at the same time, countries should consider all of these factors and the immunization programme's ability to handle the added complexity and budgetary requirements of a multiple vaccine introduction.

3.2.3

Optimal schedule for routine immunization and eligibility

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

- early protection;
- minimizing the number of visits and simplifying the schedule; and
- implementing the most effective schedule to reduce disease burden.

The addition of a new vaccine may also offer an opportunity to review and revise the entire national immunization schedule. For example, the introduction of a vaccine for older children, such as HPV vaccine, may prompt countries to add booster doses of other EPI vaccines, such as measles and dT, to the immunization schedule for these children at the same time. In such cases where a revision to the schedule results in one or more new immunization contacts, it can provide opportunities to revitalize and boost immunization services and to offer catch-up vaccination to children who have missed vaccine doses. However, in countries where immunization programmes are weak, adding one or more new contacts is unlikely to be successful if not accompanied by efforts to improve access and coverage and to secure sufficient human and financial resources to do so. Thus, before a new contact is added to the schedule, policy-makers should analyze both the costs and benefits of this change.

Adding a new vaccine can also provide the opportunity to streamline the schedule by reducing the number of visits required. However, parents and health workers may object to multiple injections being given during the same visit. The immunization programme should therefore consider the acceptability of the new schedule among both health workers and parents, and address these concerns in the training of health workers and in communications with the public. To determine the level of acceptability and how to address these concerns, programmes can consider conducting qualitative research, such as focus group discussions, with parents and frontline health workers (discussed further in → Section 3.8).

Recommended vaccine schedules for routine immunization, based on WHO Position Papers, are published in Summary Tables, along with a User's Guide.[29] These tables provide information on the optimal age for the first dose, minimum and maximum intervals between doses, and the timing and number of booster doses, if required. In addition, children often come late for their vaccinations or their schedule has been interrupted. This can pose a challenge to health workers, who may not know how many doses to give to a child who starts a vaccination series late, or whether or not to repeat doses if the series was interrupted. To guide national programmes, one of these published summary tables also summarizes WHO recommendations for interrupted or delayed routine immunizations.

When a new vaccine is introduced or is replacing an old vaccine (e.g., pentavalent replacing DTP or IPV replacing OPV), health workers also need clear instructions on which children are eligible to receive the new vaccine. This can be especially confusing in cases where children have already started their vaccinations before the new vaccine is introduced. For example, if a country introduces pneumococcal conjugate vaccine, the programme needs to decide whether to restrict eligibility to children born after a certain date, or to provide the vaccine for all children who are under a certain age (e.g., 12 months) at the time of introduction. It also needs to decide what the upper age limit is. If the immunization program decides to vaccinate all children under 11 or 12 months during the first year of introduction – essentially conducting "catch-up" vaccinations – it should take into account the fact that such a target population is equivalent to nearly two birth cohorts when calculating its vaccine and other supply needs for the year of introduction. This is because, in this scenario, eligible children will include many of the children born during the previous year plus all children born in the current year. If the new vaccine is co-administered with other vaccines and a child has completed the series for these vaccines but is within the age of eligibility for the new vaccine at the time of introduction, the programme must decide whether or not this child should receive the new vaccine.

The immunization programme should think through different possible scenarios and provide clear guidance to health workers during their training and in job aids, field manuals and other guidance documents. Having defined criteria and communicating them clearly will also enable more accurate forecasting of vaccine needs (see → Section 3.4.3) and prevent stock-outs. In addition, it will help reduce confusion among parents who may not understand why their child cannot receive the new vaccine. Therefore, particular attention needs to be paid to this issue when designing communication messages for the public.

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29 The Summary Tables on WHO recommended vaccine schedules for routine immunization and User's Guide may be found at: http://www.who.int/immunization/policy/immunization_tables/en/.

3.2.4

Catch-up and supplemental immunization campaigns

Countries may also decide to conduct supplementary immunization activities (SIAs) or "catch-up" or "speed-up" campaigns for the new vaccine to rapidly increase immunity in older age groups that are outside of the immunization schedule. Typically, catch-up campaigns are intended to reduce or interrupt transmission of the targeted disease, often with the goal of elimination or eradication. One example is the mass rubella vaccination campaigns that have taken place in Latin America for older children and adults up to 39 years of age. Vaccinating only infants with measles-rubella (MR) or measles-mumps-rubella (MMR) would take many years before its impact on congenital rubella syndrome is seen. On the other hand, vaccinating a large age group that includes adults can provide direct protection to women at risk and rapidly reduce or interrupt the transmission of endemic disease. Another example is the mass vaccination campaigns for meningococcal A conjugate vaccine that have been taking place in African countries in the Meningitis Belt. These campaigns target all 1-29 year olds before routine infant immunization is introduced in order to rapidly reduce transmission of the disease.

Other diseases that are amenable to catch-up immunization with new or under-utilized vaccines are JE, HPV and typhoid vaccines. In considering such campaigns and the high costs that they can incur, careful attention needs to be paid to the age group to be targeted, in order to maximize the gains, while limiting the costs. In addition, as described in → Section 3.2.3 above, identification of the targeted age group is needed to enable clear communication to health workers and the public in order to reduce confusion about eligibility for the vaccine.

Unlike with routine immunizations given either during regular immunization sessions or in periodic intensive routine immunization (PIRI) activities, all age-eligible persons are vaccinated in supplemental campaigns, regardless of their vaccination history (i.e., prior doses of the vaccine). In addition, the supplemental doses are not generally recorded on individual immunization records, such as vaccination cards and immunization registries.

3.2.5

New delivery strategies

Vaccines that are targeted for ages beyond infancy may require countries to establish new delivery strategies and venues. Vaccine delivery in schools may be a practical means of reaching school-aged children with primary vaccination (e.g., possibly for HPV or typhoid vaccines) or for booster doses (e.g., dT vaccine). This is especially

true if school enrolment rates are sufficiently high for the groups targeted for the vaccine. Nationwide measles campaigns that used schools as a key delivery platform have been successful in achieving high vaccination coverage in many low- and middle-income countries. Countries can build upon this experience and the links established with the education sector to deliver vaccines that may be appropriate for a school-age group.

However, the use of schools for campaign delivery of a one-time dose of vaccine requires a different level of resources and planning than the use of schools for the routine delivery of multiple doses of vaccine. The WHO School Vaccination Readiness Assessment Tool may be used by countries to help determine if using schools as routine vaccination sites would be an effective and practical means of vaccinating school-age children.[30] In countries without existing infrastructure for vaccine delivery through schools, the delivery costs of routine school-based vaccination can be quite high. The affordability of school-based vs. other delivery strategies should therefore be examined before such a strategy is routinely implemented. Analysis of a country's cost of delivering HPV vaccine through various strategies, including through school, can be done by making use of the HPV vaccine module of the *WHO Cervical Cancer Prevention and Control Costing (C4P) Tool* (see → Box 3 in Chapter 2).

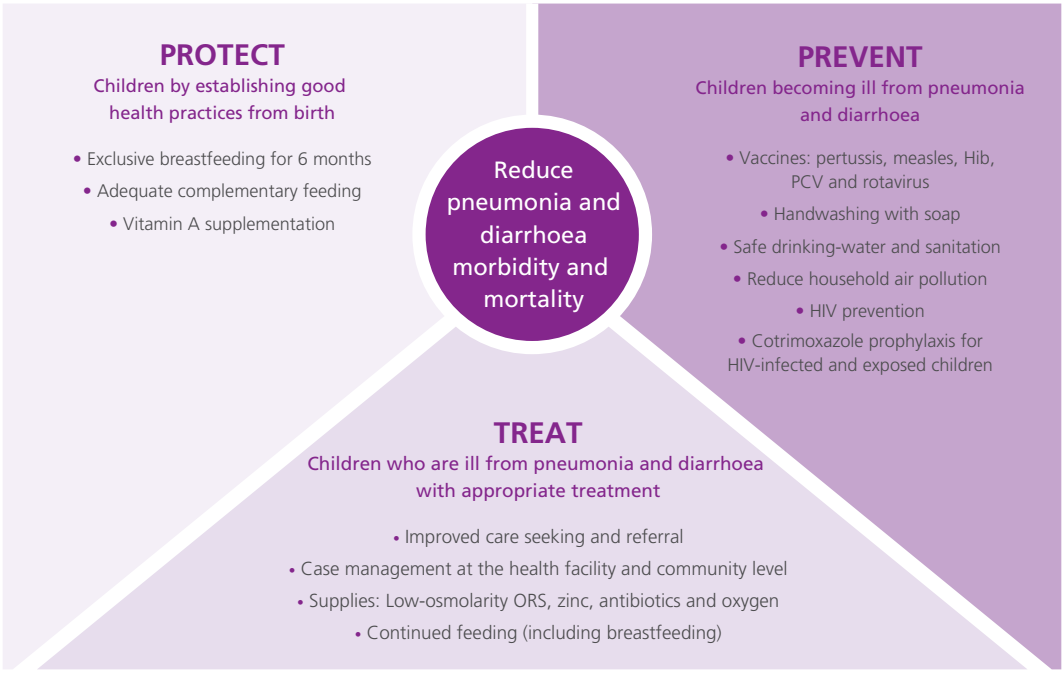
3.2.6

Using the opportunity of a new vaccine introduction to implement integrated approaches towards disease control and health promotion

Many of the new vaccines target diseases or syndromes that cannot be completely prevented or controlled by the vaccine alone. While pneumococcal and Hib vaccines can significantly reduce the burden of pneumonia, other interventions are also critical to its prevention and control. These include the promotion of exclusive breastfeeding for the first six months of life, adequate nutrition, and case management with antibiotics. Similarly, the prevention and control of childhood diarrhoeal illnesses requires a package of interventions, including the promotion and use of oral rehydration salts (ORS) solution and zinc to treat the disease, along with preventive measures such as rotavirus vaccination, the promotion of exclusive breastfeeding and hand washing with soap, vitamin A supplementation, and efforts to improve drinking water and sanitation. The introductions of Hib, pneumococcal and rotavirus vaccines in developing countries thus provide an excellent opportunity to

30 The WHO School Vaccination Readiness Assessment Tool may be found at: http://www.who.int/iris/bitstream/10665/90566/1/WHO_IVB_13.02_eng.pdf.

FIG. 4. Framework for coordinated approaches to pneumonia and diarrhoea control



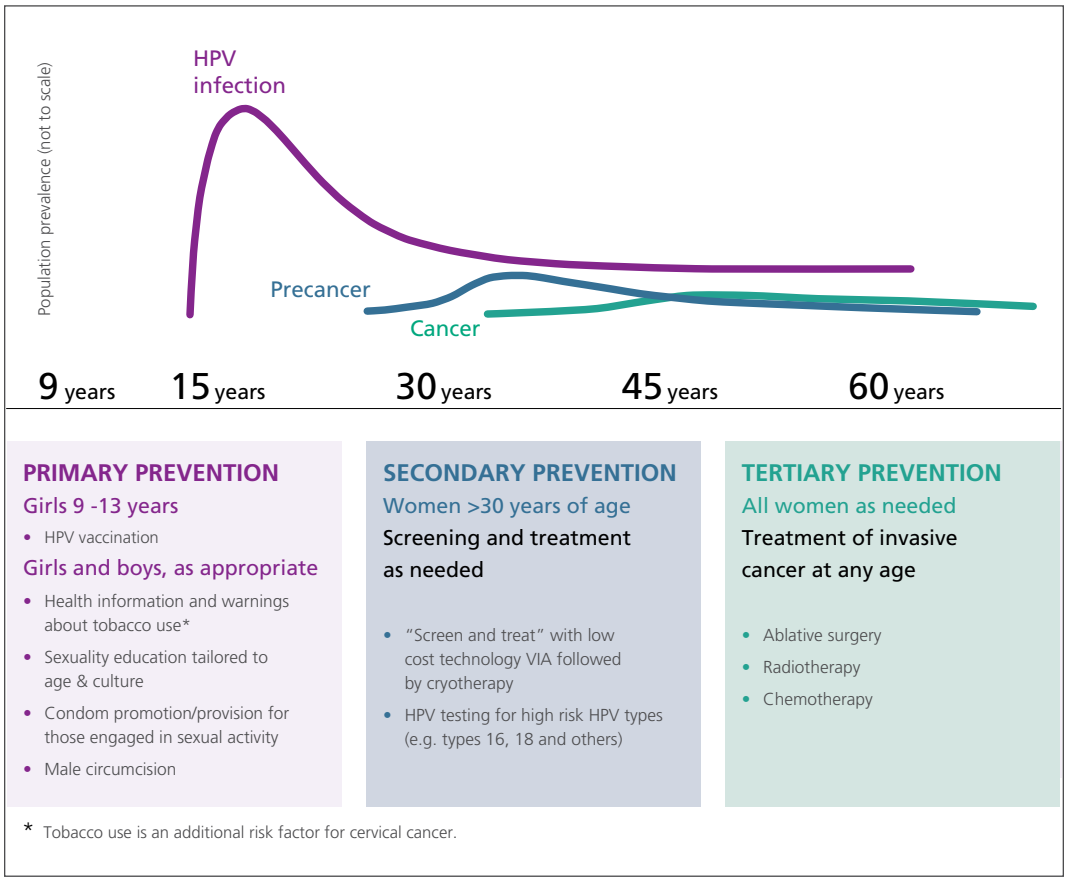
simultaneously scale up the use of other complementary interventions and to create synergies between them in order to maximize benefits. To guide countries in developing integrated approaches to controlling the two greatest causes of child mortality and morbidity, WHO and UNICEF developed the integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD) (see framework in → Fig. 4).[31]

31 World Health Organization, United Nations Children's Fund. Ending preventable child deaths from pneumonia and diarrhoea by 2025: the integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD). Geneva, Switzerland: World Health Organization; 2013. Available at http://www.who.int/maternal_child_adolescent/news_events/news/2013/gappd_launch/en/index.html

Similarly, the introduction of HPV vaccine provides two important opportunities to implement integrated approaches towards disease control and health promotion: 1) the opportunity for countries to develop comprehensive national strategies for the prevention and control of cervical cancer, including cervical cancer screening, treatment and palliative care; and 2) the opportunity to provide other health services or health education messages to 9-13 year old children. A comprehensive approach to cervical cancer prevention and control through delivery of effective interventions across the life course of girls and women is shown in → Fig. 5 and described in the WHO Guidance Note "*Comprehensive cervical cancer prevention and control - a healthier future for girls and women*."[32]

Immunization programmes should therefore consult with colleagues from other departments and health or education programmes to identify opportunities to provide age-appropriate packages of services whenever a new vaccine is introduced.

FIG. 5. Overview of possible programmatic interventions over the life course to prevent HPV infection and cervical cancer



32 World Health Organization. WHO Guidance Note Comprehensive cervical cancer prevention and control - a healthier future for girls and women. Geneva, Switzerland: World Health Organization; 2013. Available at: http://www.who.int/immunization/documents/diseases/ISBN_978_92_4_150514_7/en/index.html.

BOX 12. How a vaccine introduction can provide the opportunity to improve coverage and timeliness of other vaccinations and maternal and child health services

There are a number of ways in which a vaccine introduction provides the opportunity to reach underserved populations or age groups with other immunizations and health services that they would not otherwise receive.

For example, the **high demand for the new vaccine** – spurred by effective communications and social mobilization activities – can bring in children or adolescents who have not previously been immunized or are behind in their immunization schedules. This has been shown to be especially true for vaccines, such as pneumococcal and meningococcal vaccines, that target highly visible and frightening diseases well known to the community. Countries may want to assess the potential for this increased demand through formative research (e.g., KABP surveys discussed in → Section 3.8), and take the opportunity of this potential demand to get children up-to-date on all their vaccinations and to provide them with other preventive and curative health services both during routine visits and special campaigns. For instance, the new vaccine can be added to the package of services provided during Child Health Weeks (or Days) or during periodic intensive routine immunization (PIRI) activities. The popularity of and awareness about the new vaccine could increase attendance of these integrated health campaigns, thus increasing access to other critical health services.

A number of countries have also combined efforts to provide immunization and malaria control interventions. These include distributing long-lasting insecticide-treated bednets (LLINs) at PIRI events and at routine immunization sessions, as well as using immunization activities to provide anti-malarial treatment for home use.

Some new vaccines target **new age groups**, such as school-age children, adolescents and adults. The introduction of vaccines targeting children beyond infancy – such as HPV, meningococcal conjugate and rubella vaccines– provides opportunities to reach these older children, often through school-based programmes, with other age-appropriate vaccines (e.g., TT and dT boosters) and other health interventions. These can include the distribution of de-worming medicines and iron tablets, and treatment of trachoma and schistosomiasis.

To avoid missing opportunities to increase coverage of other vaccines and critical health services when introducing a new vaccine, immunization programme managers should ask themselves the following questions:

- Will there be a particularly high demand for the vaccine amongst the public?
- Will delivery of the vaccine involve new delivery strategies that can provide new opportunities to deliver other critical, age-appropriate vaccinations and health services? Which ones?
- Will the vaccine target new age groups that can be reached with other health services?
- Can the new vaccine be provided at PIRIs, Child Health Weeks or other periodic campaigns?
- What other opportunities are there to combine the introduction of the new vaccine with other health services (e.g., zinc distribution, de-worming medication, pneumonia and diarrhoea prevention and control interventions)?
- What is the experience with integrating delivery of these other interventions with vaccination?
- What are the drawbacks or benefits of integrating service delivery?

3.3

Selecting the vaccine, presentation and formulation

As described in → Section 2.3.1, the characteristics of vaccine products can have a profound impact on the immunization programme and costs. The immunization programme should assess the available options for formulation (e.g., combination vs. monovalent, lyophilized vs. liquid) and presentation (e.g., vial vs. pre-filled syringe for injectable vaccines, squeeze tube vs. vial for oral vaccines) with respect to programme requirements and costs. The price per dose of a vaccine should not be the sole driver for solid decision-making. Rather, an analysis of all of the costs, advantages and disadvantages of introducing a specific product into the immunization programme should be conducted. Some general issues and guidance when considering product characteristics are as follows:

3.3.1

Safety

Product formulations and presentations should be selected that are least likely to result in programmatic errors and that correspond with the training levels and capacities of the health workers providing immunizations. This is especially important in areas where refresher training and supportive supervision are difficult to provide and health care worker turnover is high. For example, single component vaccines will require less training and are therefore less likely to result in programmatic errors than vaccines that require combining the contents of two or more containers, such as lyophilized vaccines or those that require the co-administration of two separate components (e.g., vaccine and a separate antacid).

3.3.2

Ease of use

In some situations, the time required to prepare a vaccine is critical, such as during campaigns with long lines of waiting clients or during outreach activities. For these situations, a vaccine product that is easier to use and takes less time to prepare can be extremely valuable and can help to increase coverage. Such easy-to-use products might include oral vaccines in squeeze tubes or injectable vaccines in compact pre-filled auto-disable devices (CPADs). These presentations can also facilitate the ability of community-based health care providers to deliver immunizations, such as the birth dose of HepB delivered in homes using CPADs. Immunization programmes may also decide to select products that are similar to those already in use to minimize the burden on health care workers. Programmes should therefore evaluate the trade-offs between cost on the one hand and ease-of-use and time savings on the other.

3.3.3

Vaccine wastage rates and missed opportunities

Vaccines with a higher number of doses per vial can result in higher wastage and thus increased costs, especially if the vaccine must be discarded within hours after the vial is opened. This can also result in a failure to immunize if health workers are reluctant to open a vial for a few clients or if they limit the number of days per week that a vaccine is offered in order to reduce wastage. Selection of the number of doses per primary container (e.g., vial) must therefore take into consideration the costs of wastage versus missed opportunities. In general, it is preferable to have fewer doses per vial for expensive vaccines; for vaccines that must be discarded within short time periods, such as lyophilized vaccines that have been reconstituted or unpreserved vaccines in multi-dose vials; or when session sizes are small.

3.3.4

Cold chain, transport and storage requirements

Vaccine products vary greatly in terms of their storage requirements. Vaccines in single or two-dose vials take more space, but overall fewer doses are needed since wastage rates are minimal for these products. As discussed in → Section 3.5, the programme should evaluate the cold chain, storage and transport requirements for each of the available products for the vaccine under consideration. The assessment should also look at the auxiliary equipment needed (e.g., injection materials), and the quantity of vaccine that must be purchased to off-set vaccine wastage.

In addition, vaccine products can have vastly different sensitivities to heat and freeze damage. One way to assess heat stability is to review the type of vaccine vial monitor (VVM) assigned to the product, as it indicates the number of days of stability of the vaccine at 37°C. A product with a VVM2 is stable for two days at 37°C, while a product with a VVM30 is stable for 30 days at this temperature. This information can be found on the product insert or, for all WHO pre-qualified vaccines, on the WHO website for pre-qualified vaccines.[33] If power outages are frequent or if the vaccine will be used for outreach activities, a more heat-stable vaccine will be preferable.

Similarly, some vaccines are more sensitive to freezing than others. If freeze exposure is a concern due to the use of ice packs, reliance on non-WHO pre-qualified refrigerators or cold ambient temperatures, a vaccine product that is less freeze-sensitive should be selected, if available (for more information, see also → Box 14).

33 The WHO website that lists the WHO pre-qualified vaccines may be found at: http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/index.html.

3.4

Assuring quality and procuring the vaccine and injection supplies

3.4.1

Assuring vaccine quality

The establishment of international norms and standards for vaccines

WHO's Expert Committee on Biological Standardization (ECBS) develops standard specifications for the production and quality control of vaccines, and establishes standard vaccine preparations. These standards – published in a series of guidelines and technical reports for specific vaccines – provide guidance to producers to ensure the safety and quality of vaccines. They also serve as the standard of acceptability against which vaccines are assessed by national regulatory authorities during the licensure process and by WHO for pre-qualification.[34]

WHO pre-qualification of vaccines

All vaccines procured through UNICEF (which can include GAVI-supported vaccines), the PAHO Revolving Fund, and other United Nations agencies must be pre-qualified by WHO. Pre-qualification ensures that the vaccines meet WHO-recommended standards of quality, safety and immunogenicity and has become a globally recognized "seal of approval". The pre-qualification process relies on the continual oversight by the national regulatory authority (NRA) responsible for monitoring the product (normally the NRA in the country of manufacture). Thus, a vaccine can be pre-qualified only if the NRA of record is fully-functional. The pre-qualification process also requires that the vaccine meet WHO recommendations for safety and efficacy, that lot consistency is demonstrated through testing at WHO contracted laboratories, and that the production process complies with current Good Manufacturing Practice (cGMP).

34 These standards can be found at: http://www.who.int/biologicals/vaccines/en/.

An important added value of pre-qualification is that it ensures that clinical data are relevant for the target population – such as children in developing countries – at the recommended schedules, and that the vaccine is suitable for use under programmatic conditions found in developing countries.

Many countries that procure vaccines through an international bidding process use the list of pre-qualified vaccines as a reference. Some countries require that all vaccines purchased by the national immunization programme be WHO pre-qualified.

National Regulatory Authorities (NRAs)

A national regulatory authority (NRA) plays a key role in assuring the safety, efficacy and quality of vaccines used in a country. WHO has developed an assessment tool with standard criteria and benchmarks for evaluating NRAs, and has identified six key functions that NRAs need to perform, depending on the source of the vaccines (→Table 3).

TABLE 3. Required functions of a country's national regulatory authority according to where the country obtains vaccine

	VACCINE SOURCE		
	UN agencies	**Procured directly from producers**	**Produced in country**
Marketing authorization and licensing	X	X	X
Post-marketing surveillance	X	X	X
NRA lot release		X	X
Laboratory access		X	X
Regulatory inspections			X
Regulatory oversight of clinical trials*			X

* This function is also required in any country where a vaccine clinical trial is undertaken, regardless of where the vaccine is produced.

NRAs in countries that procure all of their vaccines through UN agencies must perform at least two functions: 1) issue marketing authorizations and licenses for the vaccines, manufacturers and distributors, based on a published set of licensure requirements; and 2) conduct post-marketing surveillance, including monitoring of adverse events following immunization (AEFI). NRAs in countries that purchase vaccines directly from producers must perform two additional functions: lot releasing to verify the consistency of quality and safety of different batches, and providing access to a laboratory to test vaccine samples.

NRAs in countries producing vaccines have two further requirements: regulatory inspections of manufacturing facilities and distributors to ensure compliance with current Good Manufacturing Practice and Good Distribution Practice, and regulatory oversight of clinical trials held in the country. All countries where trials are conducted, in fact, should have an NRA capable of authorizing and monitoring these studies, regardless of the source of the vaccine. WHO is assisting countries in strengthening their review and oversight of vaccine clinical trials through the establishment of the Developing Country Vaccine Regulators Network (DCVRN)[35] and regional networks (e.g., the African Vaccine Regulatory Forum), as well as through training, guidelines development and technical assistance.

To adequately perform these functions, NRAs must be competent, independent from public and private producers and have clear enforcement power. The documented performance of these functions is critical to guarantee vaccine quality in a country.[36]

Some countries without NRAs capable of evaluating vaccines choose to buy only vaccines licensed by highly-regarded NRAs, such as the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and NRAs in other high-income countries. This strategy ensures the selection of high-quality vaccines. However, since few vaccines produced by emerging producers have been licensed in high-income countries, this approach can restrict the choice to vaccines manufactured in these countries, which are more expensive and may not be available in presentations suitable to local conditions in developing countries.

The vaccine introduction provides an opportunity to strengthen a country's NRA, by, for instance, improving the inspection of shipments to ensure that all documents and materials specified in the tender are present (e.g., vaccine vial monitors, batch release certificates, cold chain monitoring cards); strengthening the framework or procedures for licensing vaccines; and improving vaccine quality control. To strengthen NRAs in low- and middle-income countries, WHO provides training to NRAs and

35 See: http://www.who.int/immunization_standards/vaccine_regulation/dcvrn/en/.
36 More information about NRAs can be found at:
http://www.who.int/immunization_standards/national_regulatory_authorities/role/en/index.html

vaccine producers through the Global Learning Opportunities for Vaccine Quality (GLO/VQ).[37] WHO also provides technical assistance to countries in assessing and formulating institutional development plans to improve their NRAs.

3.4.2

Procurement options

Countries have a number of options for procuring a new vaccine. These include national (self) procurement, such as through an international tender and bidding process; purchasing through a pooled procurement mechanism, such as UNICEF or the PAHO Revolving Fund; or accepting a vaccine donation.

If the country is already procuring vaccines on its own, adding the new vaccine to the national procurement process may not be too complicated. If more than one manufacturer produces the preferred product, competitive bidding, such as a Limited International Bidding process in which only selected qualified suppliers are invited to bid, is encouraged to ensure the lowest possible price. However, if a country is not currently self-procuring vaccines, starting such a process with a new vaccine may be difficult.

Countries that are self-procuring vaccines are in a better position to obtain competitive prices and favourable terms when they have substantial knowledge about the market for the new vaccine. This means being aware of all qualified suppliers, new and future suppliers and products coming onto the market, as well as the range of prices that countries and other buyers are paying for the vaccine. To increase the transparency of price information, UNICEF now publishes data on current and past contracted vaccine prices that it has obtained from specific suppliers.[38] Assistance that WHO offers to countries considering or currently conducting self-procurement of vaccines includes independent assessments of current procurement procedures or of a country's preparedness to conduct self-procurement; assistance to achieve identified improvements following an assessment; and occasional regional training sessions and workshops to assist in developing vaccine procurement action plans specific to each country's needs.

Countries can also procure vaccines and safe injection supplies through UNICEF, the PAHO Revolving Fund (for countries in the Americas), or other sub-regional pooled procurement mechanisms, such as the Gulf Cooperation Council (GCC) group purchasing programme. Pooled procurement can range from simply sharing supplier

37 See http://www.who.int/immunization_standards/vaccine_quality/gtn_index/en/.
38 See http://www.unicef.org/supply/index_57476.html.

and pricing information amongst countries in the group to having joint tenders and contracts with producers. This concept is becoming more attractive to countries as they add more, increasingly expensive vaccines to their immunization programmes. Groups of countries are exploring such mechanisms, including middle-income countries in the WHO Eastern Mediterranean region.

Donations from vaccine producers can be another means of initially obtaining a new vaccine. Donations should be an exception and may be most appropriate for research projects, for vaccine demonstration projects, and for emergency situations, such as epidemics. While properly managed vaccine donations can be useful to immunization programmes, they can actually have a negative impact if the donated vaccine does not align with the priorities and needs of the national immunization programme, or if the government has no control over the specifications of the vaccine. Furthermore, if the vaccine is to be part of the routine immunization schedule, there needs to be a plan in place before accepting the donation for sustaining the vaccine supply after the donation ends, such as having already negotiated a vaccine price with the supplier. To provide guidance to countries, WHO and UNICEF have issued a Joint Statement on Vaccine Donations, which stipulates minimum requirements that should be met before countries accept vaccine donations (→ Box 13). It is also important to note that the country has the responsibility for the licensure, management, deployment and monitoring of the vaccine, including AEFI monitoring.

Additional information and resources on vaccine procurement can be found at http://www.who.int//immunization/programmes_systems/procurement/en.

BOX 13. Five minimum requirements for "Good Donation Practice" from WHO-UNICEF Joint Statement on Vaccine Donations

1. **Suitable vaccine:** The vaccine is epidemiologically and programmatically appropriate for the immunization programme: that is, the donated vaccines are consistent with the goals, priorities and practices of the immunization programme of the country for which it is being donated.

2. **Sustainable use:** Prior to the donation of a vaccine that is new to the recipient country, efforts should be undertaken to assure sustainable use of the vaccine (including negotiation of price) after the period of donation, if the vaccine is meant to be included in the routine immunization programme of the country.

3. **National officials informed:** Responsible officials of the national immunization programme in the recipient country should be informed of all donations that are being considered, prepared, or actually under way, and the donation should only be accepted and the vaccine shipped upon their confirmation.

4. **Supply requirements:** All donated vaccine should have at least 12 months shelf life remaining or a shelf life sufficient to fulfill the intended purpose of the donation (e.g., to mount a response to an epidemic or emergency or for use in a preventive campaign). Donations of vaccine for use in routine immunization programmes should provide for a minimum of 12 months' supply. Injectable vaccines should be provided with auto-disable syringes and safety boxes for safe disposal. All donations must be delivered to the designated site(s) with all costs of transport and insurance paid for by the donor and other costs (e.g., customs clearance, in-country distribution) should be precisely assessed and funding secured before acceptance of the donation.

5. **Licensed vaccine:** The vaccine is subject to prescribed licensing and/or other control procedures set up by the recipient government. It should also be licensed for the intended use by the National Regulatory Authority of the producing country.

Source: WHO-UNICEF Joint Statement on Vaccine Donations, August 7, 2010, WHO/IVB document number 10.09; available at: http://whqlibdoc.who.int/hq/2010/WHO_IVB_10.09_eng.pdf

3.4.3

Forecasting supply needs

Accurate forecasting of vaccine and injection supply needs is critical to prevent stock-outs as well as overstocks that can result in wastage due to expiry

of vaccines. Forecasting the needed quantity for a new vaccine is based on considering the size of the target population, the estimated vaccination coverage rate and the wastage factor. When a new vaccine is introduced, making clear decisions about who is eligible to be vaccinated and effectively communicating that information to health workers and the community is important. As described in → Section 3.2.3, some decisions on eligibility may inadvertently result in mini-catch-up campaigns during the first year of introduction. Decisions on eligibility for vaccination need to be incorporated into the planning and forecasting of supply needs.

The estimated size of the target population can be based on census data with growth projections. For vaccines given in early infancy, the estimated number of births should be used as the target population, while vaccines given to older infants and children (e.g., MMR, yellow fever, DTP boosters) should be based on the number of surviving infants or children, taking infant and child mortality rates into account. For HPV vaccine which is targeted for 9-13 year old girls, country-specific estimates of the population of girls by year of age from national census data, from WHO estimates, or from the UN Population Division should be used.[39] In settings where eligibility is not defined by a single year of age and instead broader target populations are described (e.g., all infants under 12 months or all girls in a school grade), special attention is needed to understand and gather data on the actual size of the target population in order to avoid significant miscalculations in forecasting.

Estimated wastage should be based on actual wastage of an existing vaccine with the greatest similarity in presentation and formulation.

Often, there is considerable ambiguity about these parameters, leading to uncertainty about the estimated vaccine requirements. It is better to overestimate rather than underestimate the initial supply needs, provided that the procured vaccine has a long shelf life and provided there is a sufficient global supply and financial resources. Subsequent orders should be adjusted based on actual usage and current stock levels, so that any initial overstock is used up. The forecast also needs to be adjusted with any new data on population, coverage, wastage or usage.

WHO has developed a Vaccine Forecasting Tool to assist national immunization programmes in conducting multi-year forecasts of vaccine and injection supply needs for both routine immunizations and special campaigns.[40] This Excel tool also helps calculate vaccine and supply costs, as well as storage capacity needs and costs.

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39 Population estimates of the 9-13 year old age cohort by country and by year of age are available at http://www.who.int/immunization/diseases/hpv/WHO_population_estimates_9-13_year-old_cohort/en/index.html.
40 The Vaccine Forecasting Tool, along with additional information on vaccine forecasting, can be found at: http://www.who.int/immunization/programmes_systems/supply_chain/resources/tools/en/index2.html.

3.5

Determining vaccine management, cold chain and logistics needs for the new vaccine

Some of the new vaccines have large storage requirements that can place a significant strain on a country's vaccine storage and transportation system at all levels of the health system. These requirements need to be considered when determining whether the national immunization programme is ready to introduce the new vaccine, and in selecting the specific product and presentation (discussed in → Section 3.3). Several factors affect the volume required for a vaccine, including the number of doses per vial, whether the product is a single-antigen vaccine or a combination, its packaging, the interval between vaccine deliveries to each level of the distribution system and whether it is being used in routine immunization sessions or in campaigns.

3.5.1

Estimating additional storage requirements for the new vaccine

The cold chain and vaccine transport system should have the additional capacity to store the new vaccine at the maximum stock level, including a buffer or safety stock, at **all levels** of the distribution system. The maximum stock level for national or primary stores should be a six-month supply. Countries need to estimate the added requirements of the new vaccine not only in terms of cold storage, but also the space required for transporting the vaccine, as well as the dry storage needs for auto-disable syringes and safety boxes.

The WHO Logistics Forecasting Tool is an Excel tool designed to help national immunization programmes determine the net storage volume and transport requirements of vaccines, diluents and injection supplies per child, and the added requirements for a new vaccine, new formulation or presentation.[41] The tool is populated with automatically-updated information on volume, transport requirements, amount of waste generated and storage costs for all WHO pre-qualified

41 The WHO Logistics Forecasting Tool and the Vaccine Volume Calculator can be found at: http://www.who.int/immunization/programmes_systems/supply_chain/resources/tools/en/index5.html.

products, and is linked to the cMYP costing tool. For quick assessments of impact on the cold chain of different vaccine products and presentations, the Vaccine Volume Calculator can be used.

To determine if additional capacity is required to accommodate the new vaccine, the national immunization programme should conduct an up-to-date inventory of all equipment involved in the storage and transport of vaccines and related supplies at all levels of the system. This includes an inventory of all cold chain equipment, including their storage capacity, age, working status and the expected life of the equipment so that a planned replacement programme can be instituted, if not already in place. The inventory should also include all vehicles used in delivering vaccines, as well as dry storage space capacity. Various tools are available to assist in performing a cold chain equipment inventory, including the Cold Chain Equipment Manager.[42]

From the updated inventory and estimate of additional needs for the vaccine, the gap in storage and transport capacity can be determined. Countries can consider several options for filling this gap. The most common option is to expand capacity by buying additional equipment and expanding or building additional cold rooms. The introduction of a new vaccine thus provides an opportunity to raise support from the government and immunization partners for replacing non-functional equipment and for procuring additional equipment, if necessary. Since countries may be introducing several additional vaccines in the foreseeable future, it is advisable to take a longer-term perspective instead of incrementally expanding the system each time a new vaccine is introduced. This is the time to critically re-think the existing immunization supply chain and determine whether its design is optimal (e.g., number of levels and supply points, frequency of shipments) to plan the capacity needed to accommodate other vaccines being considered for future introductions.

Countries have adopted shorter-term solutions to address the gap in vaccine storage and transport capacity until it can be expanded. These strategies have included:

- Shortening the interval between vaccine deliveries from the supplier. For example, if vaccines are received every six months, decreasing the supply interval to three or four months (but not further) will reduce the volume of vaccine required per shipment.
- Increasing the frequency of vaccine deliveries to provinces and districts. If, for example, vaccine deliveries are increased from once per quarter to once a month, the required storage capacity at the national and provincial levels is lower. However, this will incur additional transportation costs (for drivers' salaries and per diem, fuel, vehicle maintenance) that must be taken into account.

42 The Cold Chain Equipment Manager may be found at http://www.path.org/publications/detail.php?i=1569.

3.5.2

Updating the logistics management information system (LMIS)

The logistics management information system (or stock management system) must be updated to include the new vaccine. This computerized system, if properly maintained, is critical to ensure an adequate supply of vaccine and injection supplies – that is, the avoidance of both overstocks and stock-outs – at all levels of the system by providing real-time information.

The LMIS also helps maintain proper handling and storage conditions, including temperature tracking. Proper temperature tracking requires upgrading from temperature monitoring devices that simply display current temperatures to those that provide a historic record of temperatures over time. In addition, by recording the movement of vaccines from their arrival in country to central storage and distribution down the chain, a well-maintained LMIS enables the national immunization programme to trace individual vaccines or batches, in case there are suspected adverse events after immunization (AEFI) or other safety issues.

Forms and components of the LMIS that need to be updated when a new vaccine is added include:

- Order forms for vaccines and injection equipment
- Manual or computerized stock records for vaccines and injection equipment
- Vaccine wastage reports
- Temperature monitoring and alarm systems (upgrading from instant readers to temperature recorders).

BOX 14. Freeze-sensitive vaccines and the need to prevent accidental freezing

Many of the vaccines that countries are introducing are sensitive to freezing temperatures, including hepatitis B, liquid Hib, inactivated polio, pneumococcal conjugate and HPV vaccines (see → Fig. 2 in section 2.3.1). Studies have shown that accidental freezing of vaccines along different parts of the cold chain is pervasive in both developed and developing countries and that protecting vaccines from freeze damage remains one of the most poorly addressed problems in vaccine management.*

The most common causes of exposure to freezing temperatures are transporting them in cold boxes at the local level with deep-frozen ice packs, incorrectly positioning vaccines in cold rooms and refrigerators, and inadequate temperature monitoring.

Before introducing a freeze-sensitive vaccine, countries may want to consider conducting a temperature monitoring study of the vaccine cold chain system, from central stores to points of delivery, using electronic data loggers. This will enable the immunization programmes to pinpoint where problems with freezing are occurring and to take correction action before the new vaccine is introduced. A study protocol for temperature monitoring in the vaccine cold chain can be found at: http://whqlibdoc.who.int/hq/2011/WHO_IVB_05.01_Rev.1_eng.pdf.
More information may be found in the *WHO Aide-mémoire for preventing freeze damage to vaccines* at http://www.who.int/immunization/documents/WHO_IVB_07.09/en/index.html and the WHO document, *Temperature Sensitivity of Vaccines* found at: http://whqlibdoc.who.int/hq/2006/WHO_IVB_06.10_eng.pdf.

* Matthias DM, Robertson J, Garrison MM et al. Freezing temperatures in the vaccine cold chain: a systematic literature review. Vaccine 2007; 25: 3980-3986.

3.6

Ensuring injection safety and safe waste disposal for the new vaccine

Most of the new vaccines recommended by WHO for inclusion in the immunization schedule are injectable. As health workers provide more and more injections during busy immunization sessions, this increases the risk of human errors, such as not handling the injection materials properly or administering the vaccine through the wrong route. Additional injections per child also increases the safe injection supplies needed, such as auto-disable (AD) syringes, safety boxes and, in the case of lyophilized vaccines, reconstitution syringes. WHO recommends that in the budgetary, procurement and delivery process, vaccines be "bundled" with matching quantities of injection supplies to ensure appropriate quantities of these supplies at the point of use. The bundling should take into account different wastage rates for vaccines and supplies. If a bundling strategy is not already in place, it can start with the new vaccine and eventually be expanded to all vaccines in the immunization programme.

The new vaccine may also significantly increase the volume of used injection material that requires safe disposal. For instance, in many countries, adding the three-dose pneumococcal conjugate vaccine to the infant immunization schedule will increase the number of syringes to be disposed of from seven per child to ten – a 43% increase.[43] As part of the pre-introduction assessment, countries should assess the additional waste management needs with the new vaccine and determine whether incinerators need to be repaired or expanded or additional ones built to handle the increased needs. WHO has published a handbook on safe management of health-care waste.[44]

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43 This is in the case of a country that provides BCG, a birth dose of hepatitis B, three doses of DPT-HepB-Hib, and two doses of measles-containing vaccine.

44 The WHO handbook on safe management of health-care waste can be found at: http://apps.who.int/iris/bitstream/10665/85349/1/9789241548564_eng.pdf.
For more information on safe injection practices, see: http://www.who.int/injection_safety/en/.

3.7

Training and supervision of health personnel

3.7.1

Staff training

One of the key elements in the successful introduction of a vaccine is sufficient, high-quality training of all health workers involved in immunization, as well as supervisors and immunization programme staff, about the new vaccine and the disease(s) it prevents. Several of the newer vaccines present new challenges to health workers. These challenges include more complex handling and storage requirements due to increased temperature sensitivity, more complicated immunization schedules and the targeting of ages beyond infancy and early childhood.These challenges make adequate training for the new vaccine all the more critical.

Training in preparation for the new vaccine introduction should cover the following topics:

- The disease and the new vaccine (composition, safety, efficacy, side effects);
- The immunization schedule incorporating the new vaccine, and determining which vaccines and doses to provide to children who are "off-schedule" or who are already partially immunized with other vaccines before the launch of the new vaccine;
- Storage, preparation and administration of the vaccine, including avoidance of freezing the vaccine and techniques for optimal administration;
- Recordkeeping and reporting of doses administered using new forms;
- Educating parents about the new vaccine, the disease(s) it targets, the schedule, possible side effects, and what to do in the case of serious adverse events;
- The delivery of other interventions that prevent or control the disease(s) targeted by the new vaccine, such as vitamin A and zinc supplementation, and the promotion of exclusive breastfeeding and hand washing to prevent pneumonia and diarrhoea (e.g., for Hib, pneumococcal and rotavirus vaccines);

- Monitoring of coverage, drop-out and vaccine wastage rates.

The training should also include refresher training to health workers and supervisors on other major aspects of the immunization programme, especially areas where previous programme assessments have identified weaknesses. The training for the new vaccine provides an opportunity to refresh immunization and health workers' skills and knowledge in such critical areas as:

- Vaccine forecasting and ordering;
- Cold chain management, including understanding the multi-dose vial policy and interpreting vaccine vial monitors (VVMs);
- Safe injection and waste disposal practices;
- AEFI surveillance and reporting;
- Effective strategies for communicating about vaccines and immunization with parents and the community;
- Data collection and analysis, including estimating denominators (the target population) to calculate coverage rates and estimating drop-out rates.

An initial step in planning and designing the training programme is to conduct an assessment of the knowledge, skills and practices of health workers involved in immunization. This information may already be available from a recent programme evaluation. The assessment should highlight the areas where refresher training is especially needed and also inform the development of training materials that are written at the appropriate level for different levels of health workers. A detailed

training plan and budget should then be prepared and incorporated into the cMYP and annual EPI plan. The plan should include the numbers of levels of training, the length of each level of training, materials to be used and identification of trainers.

As much as possible, the number of levels through which the training is rolled out (e.g., cascade training) should be minimized to maintain high quality of the training. The training for a new vaccine should be conducted not too far in advance of the vaccine introduction; ideally training for frontline health workers should take place two or three weeks prior to the new vaccine launch. It is also important that the training be followed by supportive supervision to ensure that health workers actually use the skills learned and apply them correctly (see → Section 3.7.2).

The training methods used are also critical to ensure effective learning. People have different learning styles, and studies have shown that adults learn more effectively by doing rather than by passively listening to a lecture. Instead of consisting simply of a series of lectures and presentations, the training should involve a mix of activities, such as small group discussions, question-and-answer sessions, skills practice, role-playing (e.g., to practice communicating with parents), and field visits – all of which can reinforce key messages. Immunization programmes may want to involve experts from training institutes, universities, training units of the Ministry of Health and others to assist in designing and conducting training that uses effective teaching methods based on adult learning principles.

Countries should also establish procedures and mechanisms to monitor the quality of the training, especially at lower levels of the health system (e.g., if a cascade training approach is used). Administering pre- and post-tests at all trainings is one commonly-used method to evaluate the effectiveness of the training. Another method that countries have been using is to have national-level trainers attend local-level training sessions to monitor their quality, supervise the local trainers and serve as resource persons.

WHO has developed training packages for several new vaccines, including pneumococcal conjugate, rotavirus and HPV vaccines. These packages include handbooks for health workers, modules on different topics in Powerpoint slide format, and review exercises.[45] Other WHO immunization training resources include the Immunization in Practice modules, a series of modules on immunization training for Mid-Level Managers (MLM),[46] numerous job aids, and a WHO e-learning course on Vaccine Safety Basics.[47]

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45 Training manuals for various new vaccines maybe found at: http://www.who.int/immunization/documents/training/en/index1.html.
46 These can be found at http://www.who.int/immunization/documents/training/en/.
47 The WHO Vaccine Safety Basics course can be found at: http://www.vaccine-safety-training.org/.

BOX 15. Questions to ask when planning training for the introduction of a new vaccine

- Does the training fit in with the training plans and policies outlined in the national health plan?
- Has an assessment of the capabilities, skills and knowledge of health workers in the area of immunization taken place or is such an assessment planned to inform the training for the new vaccine, including refresher training?
- Is the training schedule and timing planned to minimize disruptions in health services and the "training load" of workers?
- Does training for the new vaccine include sufficient refresher training on immunization practices (e.g., injection safety, communications, cold chain maintenance, data collection and analysis)?
- Does the training include information on other interventions for health workers to promote or provide for a coordinated approach to disease control?
- Is information on the new vaccine being added to the curricula for medical and nursing students (pre-service training)?
- Will the training provide health workers with new skills that can be applied more broadly to other health services (e.g., in disease surveillance, safe injections, adverse events monitoring, data analysis and reporting)?
- Are there procedures in place to monitor the quality of the training, including training of health workers at the local (e.g., sub-district) level?

3.7.2

Supportive supervision

Once the vaccine is introduced, implementation should be reviewed through supportive supervision, which also includes on-the-job training. To ensure a smooth introduction, some immunization programmes have intensified supportive supervisory visits for the first month or so following the vaccine introduction. Supportive supervision has been shown in several countries to significantly improve health worker performance. Unlike traditional hierarchical supervision that

focuses on inspection and finding fault, supportive supervision emphasizes improving a clinic's or health worker's performance through two-way communications, coaching, mentoring and joint problem solving. Together, the supervisor and health workers identify and address weaknesses on the spot, thus preventing poor practices from becoming routine, and also point out good practices. This process involves establishing health facility-specific goals, indicators and milestones, against which progress is measured during supervisory visits. To be effective, there needs to be regular follow-up visits to ensure that suggested improvements are being carried out and if not, to address obstacles to doing so.

When introducing a new vaccine, supervisors can play an important role in the training process, including conducting training needs assessments, developing training curricula and job aids, and conducting training sessions for health workers.

Supervisory visits following a new vaccine introduction should not focus solely on the new vaccine, but should also look at overall performance of the immunization programme and practices related to all immunizations (such as injection safety practices and cold chain maintenance). Supervisors together with the health workers should examine what impact, if any, the new vaccine introduction has had on the provision of other immunizations and other health services or programmes. For instance, has coverage of other EPI vaccines increased or decreased since the new vaccine was introduced, and if so, why? If the vaccine has brought in new, previously-unimmunized children, what other interventions and services can the clinic provide to take advantage of their visit? The supervisor together with the health staff can find ways to resolve negative effects of the new vaccine introduction and capitalize on any positive effects.

If supportive supervision is not currently being practiced in the delivery of essential health services, including immunization, the introduction of a new vaccine can provide an opportunity to institute such a system. This may require the purchase of additional vehicles, training of supervisors, per diems for visits, and transportation expenses – all of which should be included in the updated cMYP and budget.

Resources on supportive supervision include the *Guidelines for Implementing Supportive Supervision* developed by PATH[48] and a module in the Mid-Level Managers (MLM) training series.[49]

48 These can be found at: http://www.path.org/vaccineresources/files/Guidelines_for_Supportive_Supervision.pdf.
49 These can be found at: http://www.who.int/immunization/documents/training/en/.

3.8

Advocacy, communications and social mobilization

A comprehensive and coordinated set of advocacy, communications and social mobilization activities for the vaccine introduction is critical to create and sustain the support of policy-makers and opinion leaders, as well as community acceptance of and demand for the new vaccine. These activities help build demand by communicating the benefits expected from adding the vaccine to the immunization programme and build trust and awareness for the vaccine and the programme in general.

One best practice is to develop an advocacy and communications plan for the new vaccine. The plan should draw from the existing communications plan or strategy for the national immunization programme, if one exists, and be aligned with the Ministry of Health's overall health promotion and communication strategy. A technical sub-committee on advocacy and communications can be helpful in developing and implementing the plan. To ensure that the communications activities are effective in reaching all key target audiences and that messages about the new vaccine are appropriate for each audience, the sub-committee should include representatives from different sectors of society, such as parents, community leaders, women or children's associations, religious or ethnic groups and health workers. The sub-committee should also include experts in health promotion and social mobilization from the Ministry of Health.

The communications plan and subsequent activities, materials, and messages will be most effective if they are informed by a study of the public's knowledge, attitudes, beliefs and practices (KABP) about the targeted disease, the vaccine, and immunization in general. KABP studies can range from a series of focus group discussions to more detailed community and household surveys. They should target a range of different groups, including community and opinion leaders, health workers, and parents. The study can identify gaps in the public's knowledge and attitudes about the disease, misperceptions and concerns about the vaccine, inaccurate perceptions among health workers concerning parents' attitudes and acceptability, and other factors that may affect the public's acceptance and thus uptake of the vaccine, such as the influence of anti-vaccination groups.

To improve acceptance among health workers, parents and others in the community, information, education and communications (IEC) messages and activities should also address issues and concerns identified in the KABP study or others that may arise due to the nature of the vaccine. Such issues can include:

- The fact that the vaccine will not protect against all causes of the syndrome (e.g., diarrhoeal disease in the case of rotavirus vaccine, and meningitis and pneumonia in the case of Hib and pneumococcal vaccines);
- Limits on what age groups can receive the vaccine (e.g., to answer or pre-empt questions from parents about why their older children are not getting the vaccine);
- An additional injection per visit resulting from the new vaccine.

IEC activities and materials should also go beyond promoting just the new vaccine itself. They should include messages about the importance of children being up-to-date on all of their immunizations. The materials should also include information on other interventions to prevent or control the disease or syndrome targeted by the vaccine. Messages for Hib and pneumococcal vaccines, for instance, can include information to parents about how to recognize the signs of pneumonia in infants, as well as the importance of exclusive breastfeeding, hand washing and seeking prompt treatment.

It is also important to develop materials tailored for different target audiences, such as physicians, health workers, journalists, as well as the general public. A range of different channels and media to deliver the messages should be used, including health workers, community volunteers and mass media (e.g., radio and television spots). Obtaining the support from and participation of respected political leaders and a broad range of influential groups and members of society in promoting the new vaccine can be critical to communicate information about the vaccine to the community, to renew awareness of immunization, and to allay possible safety concerns about the vaccine and correct misinformation. These partners can include opinion leaders (such as leading physicians), civil society, academics, community and religious leaders, and the private sector. It is also important to inform and educate the media about the new vaccine in advance of the introduction and to obtain their support in getting messages out, since they can have a major influence on public perceptions about vaccines. One effective way to do this is to hold one or more media workshops or seminars before the vaccine introduction, which can lead to a substantial amount of free publicity, such as newspaper articles, radio and television interviews and programmes concerning the new vaccine. Some countries have also found that starting the vaccine introduction on a well-publicized launch date can be a successful strategy to promote the new vaccine and create public awareness and demand.

Risk communications for the new vaccine is important to build trust with the public. This involves including information on possible side effects in the IEC materials and when communicating with parents and the community. Awareness among health workers and the public of possible adverse events will also facilitate early recognition and treatment of side effects, which may reduce their consequences.

Another component of risk communications is the preparation of a crisis communications plan for the new vaccine. This allows for a rapid and effective response to adverse events following immunization (AEFI), to anti-vaccine movements, and to any allegation that can have a negative effect on public acceptance of the new vaccine and trust in the immunization programme. A poor response to a real or imagined adverse event can rapidly lead to a loss of trust in the immunization programme that can take years to rebuild. Since the exact nature of the crisis will not be known until it arises, it is not possible to plan for a detailed response ahead of time. However, countries can have in place the basic elements of a crisis plan. These elements include:

- AEFI committees at different levels (e.g., national, provincial) that can meet immediately to discuss an action plan;
- Identified, well-respected spokespersons at all levels;
- Clear channels of communication with various media;
- Engagement with credible opinion leaders to address misconceptions and rumours;
- Training of health workers in how to communicate with the public about AEFIs and safety concerns; and
- An AEFI action plan with specific roles for immunization programme partners.

More information about communications strategies for new vaccines may be found in the document, "*Communications Framework for New Vaccines and Child Survival*", developed by UNICEF, WHO, U.S. CDC and other partners, as well as in other documents.[50]

Finally, to maintain political and public support for the new vaccine, it is important to periodically disseminate information to policymakers and the media on the impact of the new vaccine in reducing the disease burden, as well as achievements of the overall immunization programme.

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50 *Communications Framework for New Vaccines and Child Survival* may be found at: http://www.mchip.net/node/508. *HPV Vaccine Communication: Special considerations for a unique vaccine* may be found at http://www.who.int/iris/bitstream/10665/94549/1/WHO_IVB_13.12_eng.pdf

BOX 16. Useful tips for advocacy, communications and social mobilization activities

- Establish a sub-committee to help plan and implement advocacy, communications and social mobilization activities and sensitize its members about the new vaccine and targeted disease;
- Conduct formative research on knowledge, attitudes, beliefs and practices (KABP) about the new vaccine, the disease it targets, other vaccines, and immunization in general to inform communications activities and messages for the new vaccine and to pre-empt potential negative public reactions to the vaccine;
- Educate and inform the media about the disease, the vaccine and the vaccine introduction well in advance (e.g., through a media workshop);
- Educate and mobilize a broad range of stakeholders (e.g., community and religious leaders, the private sector, NGOs, universities) to promote the new vaccine and the immunization programme;
- Train health workers in how to communicate with parents and the community about the disease, ways to prevent it and the new vaccine, as well as in effective communication methods. Develop job aids to assist them in conveying these messages;
- Include messages about other prevention and control measures for the target disease or syndrome in communications about the new vaccine;
- Include the promotion of all childhood vaccines in IEC activities, messages and materials;
- In communications to parents and the community and in the training of health workers, include information about possible side effects and what to do if a child has an adverse reaction;
- Before the vaccine introduction, establish a crisis communication plan to be able to rapidly respond to reports of severe adverse events or other potential crises;
- Assess the need for and added value of starting the vaccine introduction with a well-publicized launch;
- Disseminate information on the progress of the new vaccine introduction, its impact on disease burden (as possible) and performance of the overall immunization programme on a regular basis to policymakers and the media.

3.9

Updating information systems

Adding a vaccine to the national immunization programme requires updating child immunization or health cards, immunization registries, tally sheets and other forms used to record and report vaccinations. Various components of the Logistics Management Information System, such as vaccine order forms and stock records, and any other forms that list the vaccines provided by the national immunization programme, also need to be revised.

All other components of the National Health Information System (NHIS) that include vaccines and vaccine-preventable diseases must also be updated to reflect the addition of the new vaccine. These include forms and databases related to disease surveillance, AEFI monitoring, and immunization coverage from the sub-national levels upwards. Updating electronic health information systems requires sufficient leadtime to change the system, and thus the NHIS should be informed about the new vaccine well ahead of the vaccine introduction. In addition, measures should be put in place to recall out-dated data collection forms to avoid confusion created by having different versions of the same forms in circulation.

As with other aspects of the immunization programme, the changes required by the addition of the new vaccine provide an opportunity to review and improve how information is gathered and used for the national immunization programme.

4.

Monitoring and evaluation

4.1

Coverage monitoring

A primary method for countries to evaluate a vaccine introduction is by monitoring immunization coverage at all levels. This is routinely done using administrative data from immunization registries, vaccination cards and tally sheets. If the new vaccine is administered separately (i.e., not in combination with other vaccines in the same injection), comparison of its coverage and dropout rates with that of other vaccines can identify problems with the vaccine introduction, such as low community acceptance, vaccine stock-outs at the local level and other areas of programme performance that require corrective action. Each level of the national immunization programme should regularly monitor coverage from the sub-levels and provide feedback. The *Global Framework for Immunization Monitoring and Surveillance* (GFIMS) recommends that this occur at least once a month.[51] Analysis of coverage and dropout data allows the programme to develop plans to improve coverage and to reach people who have been missed or who have not completed the vaccination series. Coverage data at the health facility level can also be a powerful motivator to health workers to improve performance.

In addition, it is important to record the timeliness of vaccination to monitor whether children are being vaccinated within the recommended schedule to maximize the benefits of the vaccines. Forms and charts used to monitor coverage should therefore record both vaccinations administered on time and those given beyond the recommended schedule.

The introduction of a vaccine can affect the coverage of other EPI vaccines. For instance, a new vaccine in high demand may bring previously unimmunized children into the clinic. They can then be caught up with other vaccines, resulting in increases in coverage of all routine vaccines. On the other hand, rumours about the safety of a new vaccine may dissuade parents from bringing their children to immunization sessions, reducing overall immunization coverage. Immunization programmes should therefore examine coverage rates of all EPI vaccines before and after the new

51 GFIMS may be found at http://whqlibdoc.who.int/hq/2007/WHO_IVB_07.06_eng.pdf.

vaccine is introduced to identify trends and pinpoint problems, as well as to identify opportunities to further enhance coverage.

Obtaining high quality data on immunization coverage can be challenging in many countries. Obtaining accurate denominators – that is, the total number of people in the target population – can be especially difficult due to population movement, inaccurate census estimates or projections, or multiple sources of population data, all with different estimates. This is particularly true for age groups beyond infancy, such as the target population for HPV vaccine (9-13 year old girls)[52] and for meningitis A campaigns (1-29 year olds). The new vaccine introduction can be a useful prompt to assess and improve data quality for routine immunization coverage reporting. Countries can use the WHO Data Quality Self-Assessment (DQS) tool to assist in diagnosing problems with their immunization monitoring systems and in identifying appropriate remedial steps.[53]

Coverage of the new vaccine should also be assessed through population-based immunization coverage surveys, which WHO recommends be conducted every three to five years to validate routinely reported data for all vaccines included in the national programme. Coverage surveys often collect additional information to inform programme improvements, such as coverage disaggregated by specific groups (e.g., income groups and gender) and reasons for non-immunization. The surveys should use methods recommended by WHO, such as the immunization coverage cluster survey methodology, or be incorporated into broader surveys, such as the UNICEF Multiple Indicator Cluster Surveys (MICS) or the USAID-funded Demographic and Health Surveys (DHS).[54]

52 For guidance on this topic, please see the WHO report of the Meeting on HPV vaccine coverage and impact monitoring, 16-17 November 2009 which may be found at: http://whqlibdoc.who.int/hq/2010/WHO_IVB_10.05_eng.pdf.
53 The WHO Data Quality Self-Assessment (DQS) Tool may be found at: http://www.who.int/immunization/monitoring_surveillance/routine/coverage/DQS_tool.pdf.
54 More information and resources, including a reference manual for conducting immunization coverage cluster surveys, can be found at: http://www.who.int/immunization/monitoring_surveillance/routine/coverage/en/index.html.

4.2

Disease surveillance

The ability to monitor the impact of a vaccine on disease will depend on the nature of the disease being prevented and the existing surveillance system. While disease surveillance is ideally an important and integral component of an immunization programme, in countries with limited resources, but with convincing indirect evidence of the disease burden, the absence of a robust surveillance system should not be an impediment to the use of a vaccine with obvious benefits.

Countries may choose to establish national surveillance using hospitals and community sources, such as public health clinics, building upon existing disease surveillance systems as much as possible. For example, JE surveillance could be added to existing surveillance systems for polio, measles and rubella, supported by virology laboratories. However, for many of the diseases targeted by new vaccines – including rotavirus, Hib, pneumococcal and meningococcal disease – sentinel site surveillance in one or more sites, with laboratory capacity to confirm the diagnosis, will be sufficient. Adding surveillance of the disease to sentinel sites already conducting high-quality, laboratory-confirmed surveillance of other vaccine-preventable diseases or other infectious diseases can save costs, increase efficiencies and ensure quality and timeliness of the surveillance. For vaccines that prevent cancer, such as HPV and hepatitis B vaccines, an important surveillance strategy is to have a well-functioning cancer registry. The costs of supporting the surveillance system should be included in the overall costs of the immunization programme or other appropriate budget.

Surveillance of the disease targeted by the new vaccine would ideally begin two or three years before the vaccine is introduced to obtain consistent baseline data on disease incidence, mortality and epidemiological patterns (e.g., prevailing serotypes, age distribution). Such a time period will allow for seasonal and yearly fluctuations, if that is relevant to the disease being studied. However, in the absence of multi-year surveillance data, approaches have been developed to assess the impact of vaccination using data available in countries. These approaches are detailed in manuals developed by WHO on assessing impact of Hib and pneumococcal conjugate vaccines[55] and on assessing the impact of rotavirus vaccines.[56]

The main reasons for conducting surveillance of the disease targeted by the new vaccine are:

- To measure the impact of the vaccine on disease incidence, morbidity and mortality. This impact can be assessed, for example, through sentinel site surveillance by documenting a decrease in disease occurrence in the years following introduction of the new vaccine. Vaccine impact can include indirect (herd) protective effects in non-vaccinated populations and age groups. This has been seen, for instance, with pneumococcal vaccination in many countries, which has reduced the incidence of invasive pneumococcal disease in non-vaccinated groups such as the elderly. Evidence of the overall impact and effectiveness of the vaccination can be critical to maintaining political and

55 This manual may be found at: http://www.who.int/iris/bitstream/10665/75835/1/WHO_IVB_12.08_eng.pdf.
56 This manual may be found at: http://whqlibdoc.who.int/hq/2008/WHO_IVB_08.16_eng.pdf.

financial support for the programme, especially in low-income countries, once donor support ends and governments must cover the costs themselves;

- To monitor other epidemiological changes in the disease, such as shifts in age patterns or in the types or sub-types of the organism (e.g., in the case of Hib and pneumococcal disease), as well as to detect outbreaks;
- To monitor performance of the immunization programme and identify programme weaknesses. A higher than expected incidence of the disease could be due to low or spotty vaccination coverage or to weaknesses in the cold chain that could result in a reduction in the vaccine's potency, such as by inadvertent freezing of the vaccine. For instance, comparing the distribution of cases of the targeted disease to vaccine coverage data and obtaining the immunization status of cases can help to pinpoint the problem (i.e., cases among those vaccinated may indicate a problem with the vaccine). Using surveillance data to identify and address these problems is a practical means of improving immunization programme performance.

Once surveillance begins, the system and methods for identifying suspected cases, laboratory diagnosis and analysis should remain consistent. Otherwise, changes in surveillance methods could confound the analysis of the impact of the vaccination programme on the disease.

Disease surveillance may also be linked with AEFI surveillance. For example, surveillance of intussusception can take place at the same sentinel site hospital(s) where rotavirus surveillance is being conducted.

WHO has numerous resources to provide guidance on surveillance of vaccine-preventable diseases, including WHO Standards for Surveillance of VPDs, the *Global Framework for Immunization Monitoring and Surveillance*, and protocols and guidelines for conducting surveillance and laboratory diagnosis of specific vaccine-preventable diseases. As mentioned in → Section 2.2.2, WHO has also established international surveillance networks for several vaccine-preventable diseases that provide technical support and training.[57]

57 These and further resources and information may be found at: http://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/en/index.html and at http://www.who.int/immunization/monitoring_surveillance/resources/en/index.html.

4.3

Vaccine safety monitoring (vaccine pharmacovigilance)

It is increasingly important that any country introducing a new vaccine be able to adequately monitor its safety, including detecting and investigating possible reactions or adverse events following immunization (AEFI). This is especially true as a growing number of new vaccines such as meningococcal conjugate A vaccine, rotavirus vaccine and in the future, malaria and dengue vaccines, are introduced primarily in low-and middle-income countries or are introduced in these countries around the same time as they are introduced in high-income countries. For these vaccines, there will not be the years of experience and large body of safety data from countries with well-developed safety monitoring systems as there were for older vaccines such as rubella, IPV, hepatitis B and Hib vaccines. While safety is assessed during clinical trials, these studies may not capture rare adverse events that become apparent only once the vaccines are used on a large scale. Not being able to promptly deal with suspected severe vaccine-related adverse events can cause concern amongst the public, especially in countries with active anti-vaccine groups. This can lead to low utilization of the vaccine and potentially of other vaccines as well, and may reduce public confidence in the immunization programme as a whole.

An AEFI has been defined by the Council for International Organizations of Medical Sciences (CIOMS) and WHO as an "untoward medical occurrence [unfavourable or unintended sign, abnormal laboratory finding, symptom or disease] which follows immunization and which does not necessarily have a causal relationship with usage of the vaccine."[58] CIOMS/WHO have classified vaccine-associated AEFIs into five categories (→ Box 17). They can be due to a reaction to the vaccine itself ("vaccine product-related reaction") – with most reactions being mild and short-term – or to a defect in the vaccine or administrative device ("vaccine quality-related reaction). They can also be coincidental and not related to the vaccine or how it is administered ("coincidental event") or a result of the vaccine recipient's anxiety about the vaccination ("immunization anxiety-related reaction"). Alternatively, AEFIs can result from programme errors "(immunization error-related reactions"). Such errors include contamination of the vaccine or diluents during handling or by using reconstituted vaccine beyond the recommended timeframe of six hours, improper sterilization of injection equipment, and administering the vaccine at the wrong site or through the wrong route. AEFI surveillance can therefore be an effective way to detect problems with the handling and administration of vaccines and to correct these mistakes through training and supervision of health workers.

BOX 17. Cause-specific definitions of vaccine-associated adverse events following immunization (AEFI) from CIOMS/WHO

- **Vaccine product-related reaction:** Caused or precipitated by a vaccine due to one or more of the inherent properties of the vaccine product.
- **Vaccine quality defect-related reaction:** Caused or precipitated by a vaccine that is due to one or more quality defects of the vaccine product, including its administration device as provided by the manufacturer.
- **Immunization error-related reaction:** Caused by inappropriate vaccine handling, prescribing or administration and thus by its nature is preventable.
- **Immunization anxiety-related reaction:** Arising from anxiety about the immunization
- **Coincidental event:** Caused by something other than the vaccine product, immunization error or immunization anxiety.

58 See the CIOMS/WHO document, "*Definition and application of terms for vaccine pharmacovigilance*" at: http://www.vaccine-safety-training.org/tl_files/vs/pdf/report-of-cioms-who-working-group.pdf.

WHO and partners have developed a *Global Vaccine Safety Blueprint*, which identifies the minimum capacity that all countries should have to monitor and address possible vaccine safety problems (see → Box 18). At a minimum, all countries should have the ability to conduct spontaneous reporting ("passive surveillance") of AEFI by health workers or community members using standard reporting forms; have reports of serious cases investigated with the help of a competent local AEFI expert review committee; and have an effective communications strategy to inform the public, address their concerns and correct misinformation.

BOX 18. Minimum country capacity for vaccine safety monitoring recommended by the WHO Global Vaccine Safety Blueprint

- A national dedicated vaccine pharmacovigilance capacity, with designated staff for this purpose, stable basic funding, clear mandates, well-defined structures and roles, and which collaborates with the WHO Programme for International Drug Monitoring;
- Encouragement of healthcare workers and others to report vaccine safety issues;
- A national reporting form for individual safety case reports;
- A national database or system for collating, managing and retrieving AEFI reports;
- A national AEFI expert review committee that is able to provide technical assistance on causality assessments of serious AEFI and clusters of AEFI so that unwanted risk can be managed; and
- A clear strategy for risk communications to prepare health professionals and the public about possible vaccine reactions, as well as a crisis communications plan in place to address possible vaccine safety crises.

Source: The Global Vaccine Safety Blueprint, found at: https://extranet.who.int/iris/restricted/bitstream/10665/70919/1/WHO_IVB_12.07_eng.pdf.

Countries that produce vaccines or are early adopters of newly available vaccines should also be able to conduct active AEFI surveillance, as well as epidemiological investigations when there is a concern about a possible association between a vaccine and a health problem. In active surveillance, an effort is made to find all AEFI through continuous, pre-planned systematic surveillance methods. It can include determining baseline (pre-vaccination) rates for these conditions, and actively seeking out possible cases through sentinel site or other prospective surveillance.

For example, in some countries that have introduced rotavirus vaccines, active surveillance is being conducted to measure the risk of intussusception (obstructed bowel syndrome).

WHO has developed a broad array of resources on vaccine safety for immunization programmes (see → Box 19). For up-to-date global reviews and assessments of the safety of specific vaccines, another important resource is WHO's website for the WHO Global Advisory Committee on Vaccine Safety (GACVS).[59] GACVS was established in 1999 to respond promptly, efficiently, and with scientific rigour to vaccine safety issues of potential global importance. The committee convenes regularly and routinely documents its reviews and statements regarding the safety of specific vaccines.

59 Information from the WHO Global Advisory Committee on Vaccine Safety may be found at: http://www.who.int/vaccine_safety/committee/en/.

BOX 19. WHO resources on vaccine safety for immunization programmes

- *The WHO Aide-mémoire on Safety of Vaccines Delivered through Mass Campaigns* may be found at: http://whqlibdoc.who.int/hq/2004/WHO_V&B_04.07_eng.pdf.
- *The Immunization Safety Surveillance Manual* developed by the WHO Western Pacific Regional Office may be found at: http://www.wpro.who.int/topics/immunization_safety/ImmunizationSafetySurveillance.pdf.
- *The WHO Manual on Post-Marketing Surveillance of Rotavirus Vaccine Safety* may be found at: http://whqlibdoc.who.int/hq/2009/WHO_IVB_09.01_eng.pdf.
- A list of AEFI core variables developed by WHO that are the basic minimum for AEFI data collection and surveillance may be found at http://www.who.int/vaccine_safety/news/AEFI_Core_Variables_2013.pdf?ua=1.
- A sample standard AEFI reporting form for national AEFI surveillance, based on the AEFI core variables may be found at: http://www.who.int/vaccine_safety/Reporting_form_for_adverse_events_following_immunization.pdf?ua=1.
- *The WHO Aide-mémoire for AEFI Investigation* may be found at: http://www.who.int/vaccine_safety/publications/AEFI_Investigation_Aide_Memoire.pdf?ua=1.
- *WHO User's Manual for Causality Assessment of an AEFI* may be found at: http://www.who.int/vaccine_safety/publications/gvs_aefi/en/index.html.
- *The WHO Aide-mémoire for Causality Assessment of an AEFI* may be found at: http://www.who.int/vaccine_safety/publications/aefi_aide_memoire/en/index.html.
- The WHO e-learning course on Vaccine Safety Basics may be found at: http://www.vaccine-safety-training.org/. The course provides simple on-line training on vaccine safety issues.
- The WHO Vaccine Pharmacovigilance Toolkit (VPvT) may be found at: http://vaccinepvtoolkit.org/.
- WHO information sheets on the reaction rates of specific vaccines are available as useful references when evaluating AEFIs or for preparing communication materials about specific vaccines and may be found at: http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/index.htm.
- WHO/CIOMS *Definition and application of terms for vaccine pharmacovigilance*, which includes a comprehensive list of AEFI-specific case definitions may be found at http://www.vaccine-safety-training.org/tl_files/vs/pdf/report-of-cioms-who-working-group.pdf).

4.4

Assessing programme implementation and lessons learned: post-introduction evaluations

WHO recommends that all countries that have introduced a new vaccine conduct a post-introduction evaluation (PIE) six to 12 months following the introduction. The purposes of the assessment are to evaluate the impact of the vaccine introduction on the country's immunization programme and to rapidly identify problems needing correction that are the result of the introduction or that pre-existed it. The evaluation can not only lead to improvements in the implementation of the new vaccine and overall immunization programme, but can also provide valuable lessons for future vaccine introductions.

WHO has prepared a tool for conducting post-introduction evaluations, which includes questionnaires and checklists that countries can adapt.[60] The assessment, which can be carried out by a local team, takes place at all levels of the health system, down to the health facility level. It examines all key aspects of the programme, from pre-introduction planning to cold chain and logistics management, vaccine coverage, training, injection safety and waste management, communications, and disease and AEFI surveillance. Where possible, a PIE should be conducted in conjunction with other immunization evaluation activities, such as EPI reviews, to optimize the use of time and resources.

Many countries have used the results and recommendations from these evaluations to improve the implementation of the new vaccine introduction, as well as later vaccine introductions (see → Box 20).

60 This PIE tool may be found at: http://who.int/immunization/monitoring_surveillance/resources/PIE_tool/en/

BOX 20. How national immunization programmes have benefited from post-introduction evaluations

- In an East African country, a PIE conducted following the introduction of the pentavalent DTP-HepB-Hib vaccine raised the possibility that AEFI were under-reported. Based on recommendations from the PIE report and with technical support from international partners, the Ministry of Health enhanced the training of health workers to increase their awareness of the importance of AEFI monitoring and their skills in investigating and reporting AEFI, as part of on-going trainings in immunization.

- A PIE conducted in the former Yugoslav Republic of Macedonia following the introduction of HPV vaccine discovered an initial low coverage of the vaccination, due to concerns among parents and health professionals about the vaccine's safety. The programme used the recommendations of the PIE and experience from other countries to conduct additional communications campaigns. It also organized scientific conferences for medical practitioners on the topic. Within a year, coverage of all three doses of HPV had more than doubled – from 30% to 65%.

- A PIE conducted in Armenia following the introduction of DTP-HepB-Hib vaccine found that an active anti-vaccination movement was having a negative impact on the coverage of all routine vaccines, especially in urban areas. In response, the MOH conducted focus group studies to better understand the main factors influencing parents' decisions not to vaccinate their children and the factors behind the immunization safety concerns among medical professionals. The study findings were used to develop a communication strategy for the introduction of rotavirus vaccine.

Annexes

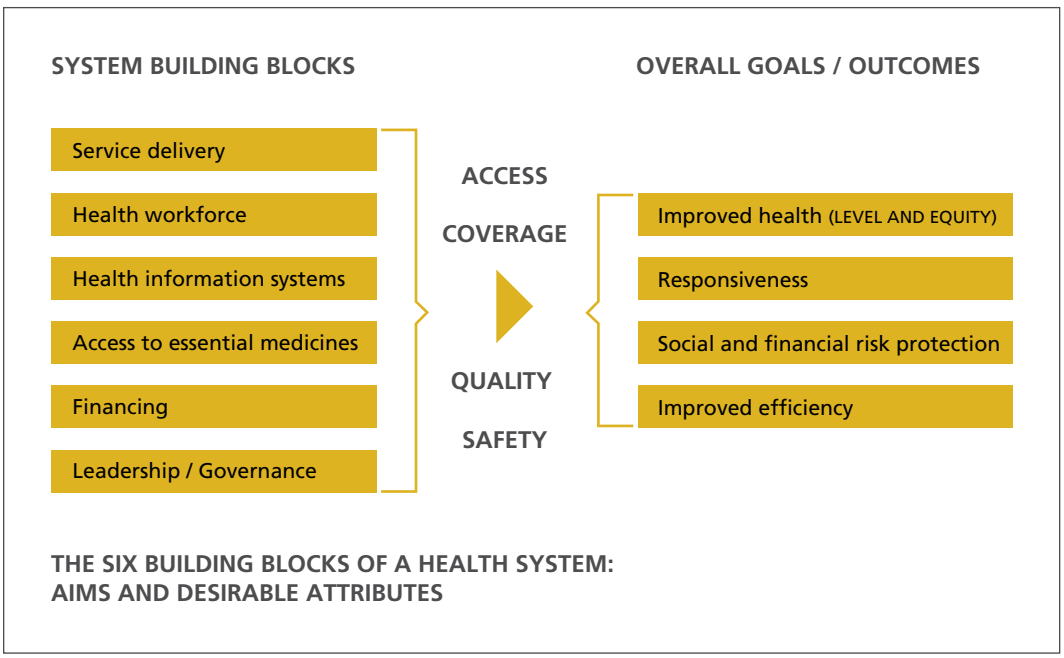
1–4

Annex 1.

Examples of ways to strengthen immunization programmes and health systems during a new vaccine introduction

Suggestions on ways in which different aspects of an immunization programme and the overall health system can be improved in the process of planning an implementing a vaccine introduction may be seen in → Box A.1. below. This list is organized by the six building blocks of a health system shown in → Fig. A.1 of the WHO Health Systems Framework and is based on a body of research conducted in this area.[61]

FIG. A.1. The WHO Health Systems Framework



Source: WHO. *Everybody's Business: Strengthening Health Systems to Improve Health Outcomes* - WHO's *Framework for Action*. Geneva: World Health Organization, 2007.

61 See: Wang SA, Hyde TB, Mounier-Jack S, Brenzel L, Favin M, Gordon WS, Shearer JC, Mantel CF, Arora N, Durrheim D. New vaccine introductions: Assessing the impact and the opportunities for immunization and health systems strengthening. *Vaccine* 2013; 31 Supplement: B122-B128.http://dx.doi.org/10.1016/j.vaccine.2012.10.116

BOX A.1. Examples of opportunities during a new vaccine introduction to strengthen immunization and health systems

SERVICE DELIVERY

- Use the opportunity of the vaccine introduction to review and streamline, if necessary, the national immunization schedule and improve the timeliness of immunizations.

- Use the social mobilization campaigns for the new vaccine to promote:
  - Other vaccines and immunizations in general;
  - Other health interventions for the targeted disease or syndrome.

- Use the opportunity of a new vaccine that is in high demand and/or that targets new age groups to increase coverage for all EPI vaccines and other health services, especially to under-served populations.

HEALTH WORKFORCE

- Be sure that training for the new vaccine includes sufficient refresher training on immunization practices (as needed), based on findings from supervisory visits or an assessment of health worker knowledge, skills, beliefs and practices. Ensure that there is sufficient time and resources for this training.

- Include training in the provision and promotion of other interventions a) for coordinated health promotion,such as delivery of other newborn care interventions when HepB birth dose is given or delivery of other adolescent health services when HPV vaccine is given, and b) for coordinated disease prevention and control, such as for pneumonia and diarrhoea when administering Hib, pneumococcal and rotavirus vaccines.

- Ensure that supervision for the new vaccine is integrated with ongoing supervision for other immunization and health services and use the opportunity to increase the frequency of supervisory visits.

continued >>

HEALTH INFORMATION SYSTEMS

Programme monitoring:

- Use the vaccine introduction to improve immunization information systems and procedures in order to increase the overall accuracy and timeliness of EPI information – for example, by including training in data collection, analysis and monitoring (including calculating coverage, drop-out and wastage rates).

- Introduce the Post Introduction Evaluation (PIE) methodology to other health programmes as a possible model for evaluating other health interventions and services.

Disease surveillance: When planning surveillance against the disease targeted by the new vaccine, think about:

- What the main objectives are for conducting surveillance and design the system to meet these objectives.

- How disease surveillance capacity can be improved overall (e.g., new skills of laboratory workers, new testing equipment, enhancement or establishment of cancer registries).

- How surveillance for the new disease can build upon existing surveillance systems and programmes to increase efficiencies and save costs (for example, by adding the disease to existing sentinel site surveillance of other diseases).

Vaccine safety monitoring and reporting:

- Take the opportunity of the vaccine introduction to improve AEFI reporting forms and procedures.

- Explore opportunities to extend or improve adverse events monitoring of other health interventions (e.g., TB, malaria, HIV treatment) and to link AEFI surveillance with post-marketing surveillance for pharmaceuticals other than vaccines.

ACCESS TO ESSENTIAL MEDICINES (cold chain and logistics management)

- When expanding the cold chain to accommodate the new vaccine, replace old or substandard equipment with improved equipment at the same time, as funding permits.

- Plan an expansion of the cold chain and logistics system that will not only accommodate the vaccine being introduced, but also other vaccines that are likely to be introduced in the foreseeable future, as funding permits.

FINANCING AND LEADERSHIP/GOVERNANCE

Immunization and health system review:

- In preparation for the new vaccine introduction, conduct an assessment of the immunization programme that also identifies weak health system components as they affect the delivery of immunizations.
- Use available funding (such as from vaccine introduction or health system strengthening grants) to make improvements to areas identified in the assessment.

Planning and budgeting:

- EPI managers can use the opportunity of the vaccine introduction to participate more fully in the overall MOH budgeting process and to advocate for the immunization programme with MOH and MOF officials.
- Explore opportunities to introduce the multi-year planning process to other health programmes, such as by promoting the process within the MOH.

Decision-making:

- Use the experience of and lessons learned from NITAGs or other technical committees to introduce or improve evidence-based decision-making for other health programmes.

Regulation:

- Use the licensure process for the new vaccine to provide and strengthen the evidence base for the licensure of vaccines by the country's national regulatory agency (NRA).
- Use the experience with licensure of the new vaccine to improve the regulatory process for pharmaceuticals and other health commodities and to better align the regulatory processes for vaccines with that of other pharmaceuticals.

Annex 2.

Additional information on economic and financial issues

Types of cost estimates for economic and financial analyses

When determining how to estimate the costs of the new vaccine, it is important to distinguish between different types of costs in order to decide which are appropriate for the specific analysis to be conducted (see → Fig. A.2.). These include the following:

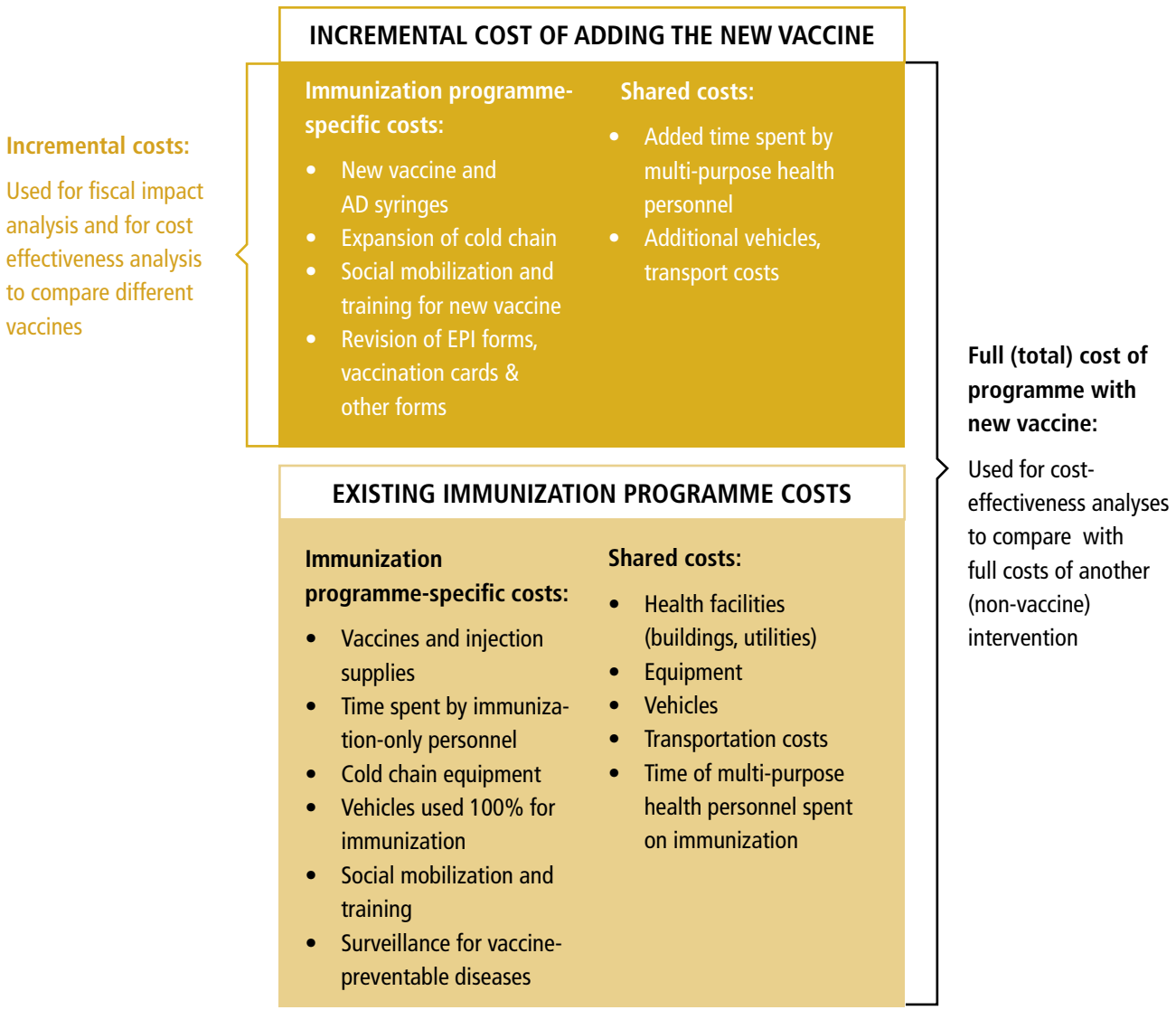
- **Full vs. incremental (or added) costs:** An analysis of incremental costs estimates only the costs of adding the new vaccine to the existing immunization programme. In contrast, an analysis of full costs looks at **all** of the resources being used by the programme, with the addition of the new vaccine. For budget impact analyses or to compare the cost-effectiveness of the new vaccine with that of other vaccines, only an estimate of incremental costs is needed. For example, to decide whether to first introduce rotavirus vaccine or pneumococcal vaccine would require an incremental cost analysis as part of a cost-effectiveness analysis. Full costs of the programme with the new vaccine must be estimated when comparing the cost-effectiveness of the enhanced immunization programme with that of another (non-vaccine) health intervention, such as comparing HPV vaccination with a cervical cancer screening programme.

- **Immunization programme-specific vs. shared costs:** Immunization programme-specific costs are the value of resources that are used solely for the immunization programme, such as vaccines, injection supplies, and the salaries of vaccinators and other EPI-only health workers. Shared costs are estimates of the resources used by the immunization programme that are shared with other programmes, such as nurses and other multi-purpose health workers, space and utilities of health facilities where immunization services are provided, and vehicles used to provide outreach health services including immunization. When conducting a fiscal impact analysis, a country may want to consider only the programme-specific costs, if they assume that adding the new vaccine will not require additional building space, the hiring of more health workers, buying more vehicles, and so forth; that is, there is excess capacity at present. On the other hand, if these shared resources are already constrained, the programme

may reach the tipping point at which additional shared health workers, equipment, health facility space and so on are needed. If so, these additional shared resources should be included in the budget impact analysis. Shared costs are always included in cost-effectiveness analyses.

- **Financial vs. economic costs**: Financial costs are actual expenditures that show up on budgets, while economic costs are the value of all resources involved in a programme or intervention, whether or not they result in actual expenditures and regardless of who pays for them. For example, the use of volunteers is an economic cost but not a financial cost, since it doesn't result in actual budgetary expenditures. Analyses of fiscal or budgetary impact and sustainability are based on financial costs, while cost-effectiveness analyses are based on economic costs.

FIG. A.2. Types of costs for economic and financial analyses of new vaccine introductions



Strategies for improving financial sustainability of immunization programmes

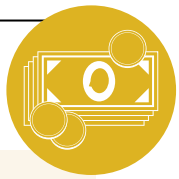
Countries can mobilize new resources by increasing national or local government funding or by obtaining new donor support or loans from development banks. A number of countries have used funds freed through debt relief for Heavily Indebted Poor Countries (HIPC) or as part of Poverty Reduction Strategies to increase funding for immunization.[62] Still others have been successful in increasing both donor and government funding commitments by establishing sector-wide approaches (SWaPs), in which donor and government funding is pooled together to help the country implement its national health plan. In this vein, several international partners, including the GAVI Alliance and the World Bank, are encouraging countries to develop Health System Funding Platforms (HSFPs), in which funding from different donors for health systems strengthening are pooled together to support national health plans.

Some countries have found innovative ways to finance immunization, including earmarking funds from national lotteries, establishing a national health trust fund, or imposing taxes on luxury goods or products harmful to health, such as tobacco or alcohol.[63] What's critical for financial sustainability is that governments demonstrate a long-term commitment to financing the immunization programme and continuously increase that commitment over time.

Strategies to increase the reliability of funding include establishing an immunization line item in the MoH budget – which has been shown to result in increased government budget allocations for immunization,[64] and obtaining long-term commitments from donors. Improving immunization programme efficiencies to reduce costs can range from reducing vaccine wastage to reducing dropout rates between doses; improving immunization coverage; and finding ways to reduce vaccine procurement costs while ensuring quality, such as by purchasing through UNICEF or another pooled procurement mechanism.

62 Information and resources on debt relief and immunization financing can be found at: www.who.int/immunization/programmes_systems/financing/analyses/debt_relief/en.
63 See the Immunization Financing Toolkit, prepared by the World Bank, for more information at: www.who.int/immunization/programmes_systems/financing/tools/en/.
64 Lydon P, Beyai PL, Chaudhri I, Cakmak N, Satoulou A, Dumolard L. Government financing for health and specific national budget lines: the case of vaccines and immunization. *Vaccine* 2008; 26:6727-34.

BOX A.2. Examples of strategies to increase financial sustainability for immunization programmes



Mobilizing additional resources:

- Increased funding from the central government through:
  - Funds freed up through debt relief
  - Poverty Reduction Strategies Paper funding
- Pooled donor and government funding, e.g., through Sector-wide Approaches (SWaPs)
- Social insurance (e.g. "mutuelles" in francophone Africa) or national health insurance programmes
- Local government funding (e.g., local taxes)
- Increased donor funding (new donors and/or increased funding from existing donors)
- Development loans
- New tax revenues earmarked for immunization (taxes on luxury goods, "sin taxes" on alcohol and tobacco, funds earmarked from national lotteries)
- National health trust fund

Increasing reliability of funding:

- Establish immunization or EPI line item in MOH budget and in Mid-Term Expenditure Frameworks (MTEFs)
- Obtain long-term government and donor commitments
- Improve financial management for quicker disbursement of funds
- Negotiate better prices and select appropriate products and presentation

Improving programme efficiencies:

- Reduce vaccine wastage
- Reduce drop-out rates and increase immunization coverage
- Improve vaccine and cold chain management
- Integrate immunization services with other health interventions

Source: Kamara L, Milstien JB, Patyna M, Lydon P, Levin A, Brenzel L. Strategies for financial sustainability of immunization programs: a review of the strategies from 50 immunization program financial sustainability plans. Vaccine 2008; 26(51):6717-26.

Annex 3.

Instructions and Template for a New Vaccine Introduction Plan

Instructions for using the template:

This is a generic template to guide countries in developing a practical plan for introducing a new vaccine. This template is intended to provide suggestions for key areas to be considered, and as such, may be missing some items relevant to a particular country or to a particular vaccine introduction, or equally may contain some items that are not relevant. Each country and vaccine introduction will have different characteristics and requirements, and thus each country's introduction plan will need to be adjusted accordingly. The overall recommended length for this plan is 10-25 pages.

The introduction plan should build on plans, strategies and activities outlined in the country's own broader strategic plans, such as the National Immunization Plan, National Health Plan or Comprehensive Multi-Year Plan. Additionally, countries may want to consider developing an introduction plan for lower administrative levels in the country that translates goals and activities articulated at the national level into ones more relevant at the sub-national level.

Section numbers in footnotes refer to sections of the main document, "*Principles and Consideration for Adding a Vaccine to a National Immunization Programme.*"

New Vaccine Introduction Plan Template

Executive Summary

Summarize key aspects of the introduction plan, such as:

- Justification, goals, and objectives (short-, intermediate- and long-term) of the new vaccine introduction, with reference to the National Health (or Immunization) Plan or the Comprehensive Multi-Year Plan, as well as expected impacts on the immunization programme and health system
- The vaccine and presentation to be introduced, the specific target populations, introduction strategy (phased or nation-wide implementation), and delivery strategies
- Coordination mechanisms and key partnerships for overseeing the introduction
- Opportunities provided by the new vaccine introduction to improve the immunization programme and health system (e.g., such as key issues and weaknesses to be addressed by the vaccine introduction)
- Major activities of the introduction (e.g., expanding health worker capacity, reaching the hard-to-reach with social mobilization, improving the cold chain and logistics system, etc.)
- Costs and financing of the short- and intermediate-term vaccine introduction activities and the associated operational costs
- Sources of funding and the contribution of the Government

1. Background and Country Context

- Brief background information about the country (e.g., geography, population size, health status of children)
- Brief background on the national immunization programme, such as:
    - Goals, plans and vaccines in the current immunization programme
    - Programme performance and achievements (e.g., trends in coverage rates, accelerated disease control efforts) disaggregated by sex, geography and wealth quintile, as possible
    - Past experience with new vaccine introductions and lessons learned, key findings from a recent EPI review, post-introduction evaluation, EVM assessment or other analyses and how identified issues and recommendations are being addressed by the programme

- Recent improvements made to the immunization programme and health systems that will facilitate introduction of the new vaccine (e.g., increase in cold chain capacity)

- Burden of the targeted disease in the country (e.g., summary of local data or regional or global estimates of disease burden, estimates of the economic burden of the disease)
- Decision-making process regarding the new vaccine introduction, such as the decision-making body involved (e.g., NITAG, special task force), types of evidence reviewed and rationale for the decision (e.g., contribution to national and/or global disease prevention and health goals; cost, affordability and cost-effectiveness of the vaccination vs. other prevention and control measures), involvement of stakeholders and experts from different agencies and sectors of society, government review and approval process (e.g., HSCC, ICC, other health departments)

2. Goals, objectives and expected impact and challenges of the vaccine introduction

- Goals, objectives and targets (e.g., short-, intermediate- and long-term), and alignment with regional and/or global timelines (if applicable)
- Expected impact of the vaccine (e.g., on disease incidence and mortality; on equity related to gender, wealth and geography, etc.; on the overall immunization programme and health system)
- Major challenges and risks of the new vaccine introduction (e.g., programmatic, financial, cultural/societal), and the country's ability to address them
- An equity analysis (gender, wealth, geography) and suggested actions to overcome any equity-related barriers

3. Strategies and policies for introducing the vaccine into the national immunization programme

- Choice of vaccine product to be introduced and rationale (including availability and acceptance of alternative presentations or products, if relevant)[65]
- Target ages and populations, eligibility for routine vaccination and for catch-up vaccination, if any; size and locations of the target population[66]
- Updated immunization schedule with the new vaccine (including booster doses, if relevant) and any schedule changes for the other routine vaccines[67]
- Delivery strategies to be used, including how to overcome barriers to reach new and hard-to-reach populations, the possible role of other sectors (e.g., education), etc.[68]

- Opportunities for integrating activities related to delivery of the new vaccine with other health interventions[69]
- Phased or nation-wide introduction and planned month of national introduction or time table for a phased introduction[70]

4. Resources, costs, financing, and sustainability

- Overall trend of country immunization financing, including government funding, private sector, and donor funding, as applicable
- Identification of key immunization programme and health system needs for the vaccine introduction, such as human resources (e.g., addressing number, distribution, turnover, and skills of vaccinators, nurses, logisticians, supervisors, delivery truck drivers, etc.), equipment, systems, etc.
- Estimated cost of adding the new vaccine to the immunization programme, including non-vaccine operational costs and plans for financing the additional costs of the new vaccine
- Overview of the comprehensive multi-year plan (cMYP), highlighting any funding shortfalls and plans to address these, and potential impact of such programme funding gaps on the vaccine introduction

5. Strategies and activities for the vaccine introduction, including opportunities to improve the immunization programme and overall health system during the introduction[71]

This is the core of the Introduction Plan. It should include all activities that need to take place to prepare for a smooth vaccine introduction. It should incorporate activities that address the issues, challenges and weaknesses of the existing immunization programme that were identified in previous reviews and assessments (mentioned in → Section 1 above). Suggested areas to address include:

5.1 Coordinating and monitoring the preparation and implementation of the vaccine introduction

- Groups that will coordinate and oversee the introduction (e.g., steering committee or ICC, technical sub-committees to plan and monitor different aspects of the introduction), and persons to be included on these committees

65 See Sections 2.3.1 and 3.3 of the main document.
66 See Sections 3.2.3 and 3.2.4.
67 See Section 3.2.3.
68 See Section 3.2.5.
69 See Section 3.2.6.
70 See Section 3.2.1.
71 See Section 3.1.2.

- How the various committees will function (e.g., frequency of meetings, chairpersons and secretariat, to whom they report, etc.)
- Partnerships for the introduction, including sectors and types of organizations to be involved (e.g., education, civil society, medical associations) and how they will participate in the planning and implementation of the vaccine introduction

5.2 Planning for procurement and distribution of vaccine[72]

- National licensure status of the selected vaccine, or process and timeframe for licensure
- Forecasted vaccine needs, including estimated size of the target population by year and estimated number of doses and injection supplies required per year (taking into account any catch-up vaccinations in the first year of introduction, or in subsequent years)
- Procurement procedures, such as likely source(s) of vaccine and the procurement process
- Shipping and distribution, including customs regulations and requirements that may affect timing of vaccine deliveries; and planned frequency of vaccine deliveries to regions, districts, and health facilities

5.3 Expanding or upgrading cold chain, logistics, and vaccine management[73]

- Current cold chain capacity at different levels of the system and source of these data; additional requirements at various levels for cold storage, transportation and equipment to accommodate the new vaccine; how any gaps will be filled
- Current status of the vaccine stock management system, including recent assessments, key issues (e.g., freeze monitoring), and any planned improvements
- Plans to increase supervision for vaccine management as part of the vaccine introduction

5.4 Planning for increased waste management and injection safety needs to accommodate the new vaccine[74]

- Current waste management capacity and practices, injection safety practices and their adequacy; changes needed to accommodate additional volume of wastage due to new vaccine, and plans for upgrading the waste management system

5.5 Revising health and immunization management information/data collection forms and systems[75]

- Revisions to be made to the various HMIS forms and systems to add the new vaccine
- Other innovations or modifications to be made to the forms, Child Health or Vaccination cards or Booklets or information systems in order to improve data quality or to align with government data requirements and to take advantage of the new vaccine introduction
- Coordination with the persons or departments responsible for revising, printing and distributing the various forms or improving the information system, and the estimated timeline

5.6 Planning for the monitoring and evaluation of the new vaccine introduction

- Monitoring the vaccine introduction and programme performance (e.g., plans for monitoring short-, intermediate-, and long-term targets and objectives); including monitoring coverage of the new vaccine[76]
- Planning and implementing pre- and post-introduction assessments using available tools (e.g., → Annex 4, New Vaccine Introduction Checklist, and the WHO New Vaccine Post-Introduction Evaluation (PIE) Tool)
- Updating or enhancing AEFI surveillance and reporting (e.g., current national AEFI monitoring policy and practices and planned improvements)[77]
- Supportive supervision and pre- and post-introduction monitoring, including plans for supervision activities before, during and after the introduction of the new vaccine (e.g., pre-introduction visits to assess readiness for introduction; immediate post-introduction monitoring visits; post-introduction evaluation or EPI review, etc.)[78]
- Measuring the impact of the new vaccine (e.g., description of any current disease surveillance plans for monitoring vaccine impact, and timeframe)[79]

5.7 Training of health workers and other professionals involved in vaccination[80]

- Types and numbers of personnel who provide or assist with vaccination and need to be trained; results of any recent assessments of health worker skills and knowledge

72 See Sections 3.4 and 3.5.
73 See Section 3.5.
74 See Section 3.6.
75 See Sections 3.9.
76 See Sections 3.1, 4.1, 4.3, and 4.4.
77 See Section 4.3
78 See Sections 3.7.2 and 4.4.
79 See Section 4.2.
80 See Section 3.7.

- Training plan with strategy (e.g., cascade training), numbers and types of people to be trained at national and district levels, duration and content of training at each level, materials to be developed or updated for training the trainers and health workers
- Plans for monitoring and evaluation of the training

5.8 Planning and conducting social mobilization, communications and advocacy activities[81]

- Considerations for handling and obtaining informed consent for vaccination, if required
- Description of any community assessments of Knowledge, Attitude, Practice and Behaviour (KAPB), focus group discussions or formative research for the disease or vaccine that have or will take place and how the findings will inform the messages and strategies for information, education, communication, and training
- Advocacy plans to sensitize opinion leaders and the media at national, regional, and district levels regarding the introduction and benefits of the new vaccine and to obtain their active support
- Development of a communication strategy and a crisis communication plan

Suggested Annexes:

1. New Vaccine Introduction Checklist and New Vaccine Introduction Activity List & Timeline (see → Annex 4 of this document for templates)
2. Budget (see → example of budget and resource table below)

81 See Section 3.8.

Sample budget and resource table for vaccine introduction activities

Activity	Total Cost	Government Support	Name	Amount	Non-Government Support	Total Support Secured	Shortfall in Support	Comment
Programme management & coordination								
Planning & preparation								
Social mobilization, IEC & advocacy								
Training & meetings								
Materials production and data management								
Human resources and incentives								
Cold chain equipment								
Transport for implementation & supervision								
Immunization session supplies								
Waste management								
Surveillance & monitoring								
Post-introduction evaluation								
Technical assistance								
Other (specify)								
Total								

Annex 4.

Instructions for a New Vaccine Introduction Checklist, Activity List, & Timeline

Purpose of the New Vaccine Introduction (NVI) Checklist, Activity List & Timeline

In order to ensure that all steps to guarantee a successful introduction of the new vaccine(s) are planned and budgeted for, that roles and responsibilities are clear, and that a clear timeline is in place, countries are encouraged to use the New Vaccine Introduction (NVI) Checklist to develop a New Vaccine Introduction Activity List & Timeline that reflects the country situation, and to regularly monitor and review these planning tools at planning and review meetings to oversee the vaccine introduction.

WHO has developed a generic template to guide countries in developing their own NVI checklists, activity lists, and timelines. The template is intended to provide suggestions for key areas to be addressed, and as such, may be missing some items relevant to a particular country or to a particular vaccine introduction, or equally may contain some items that are not relevant. The NVI checklist, activity list, and timelines for each country will need to be adjusted accordingly. The template is in Excel format and may be found at the following URL: www.who.int/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines/).

Instructions for use of these templates:

→ Fig. A.3 depicts the sequence of using the templates in Annexes 3 and 4 to plan the new vaccine introduction. Using the main document "*Principles and Considerations for Adding a Vaccine to a National Immunization Programme*" and building on national discussions (by the NITAG, NRA, and national immunization programme) that took place and which led to the decision for vaccine introduction, the country should develop a national New Vaccine Introduction (NVI) Plan (see template in → Annex 3).

Fig. A.3. Sequence of New Vaccine Planning Steps

A country should review its national New Vaccine Introduction Plan and then systematically consider the goals, objectives, and key needs for the vaccine introduction, with the help of the WHO template NVI Checklist (see → Fig. A.4 which is the first worksheet, "NVI Checklist," of the Excel file, located at the URL listed above). The Excel file allows the country to make modifications or additions and to tailor the NVI Checklist according to country requirements.

FIG. A.4. Screenshot of New Vaccine Introduction (NVI) Checklist worksheet

Annex 4: New Vaccine Introduction Checklist

Country:	Country X
New Vaccine:	Vaccine X
Planned Introduction Date:	Date X

Theme	Timeline (months before intro)	Issue	Lead Agency	Activity/Action to be taken	Deadline
Programme objectives/targets	12	**Setting Short, Intermediate and Long-Term Goals:** If the short, intermediate and long-term goals of the introduction have not been set to contribute to global, regional and/or national health goals, what actions need to be taken to ensure this?			
t population and delivery strategy	10	**Establishing the Target Population:** If the new vaccine is for older age groups, or for age groups outside the traditional infant target population, and the size and location of the target population has not been established, what steps need to be taken to establish this information? (Including involving actors not traditionally involved in EPI, e.g. Ministry of Education.)			
	10	**Establishing the Target Population:** If target population is "new", what steps need to be taken to identify this population and to cost delivery strategy options?			
	10	**Delivery Strategy:** If the identification of ways of reaching children not located at the primary vaccine delivery site has not			

The questions in the NVI Checklist worksheet will help to establish the status of key programmatic requirements prior to introduction, to clarify gaps, and to identify the activities that need to be carried forward from the first worksheet into the second worksheet, "NVI Activity List & Timeline" (see → Fig. A.5 which is the second worksheet of the Excel file). The NVI Activity List & Timeline can be easily monitored on one sheet by the National Steering Committee or the National Technical Sub-Committees established to oversee the introduction of the new vaccine. The timelines should be regularly reviewed and updated as necessary in line with changing plans and priorities.

Fig. A.5. Screenshot of New Vaccine Introduction (NVI) Activity List & Timeline worksheet

Annex 4: New Vaccine Introduction Activity List & Timeline

Instructions: Copy from the checklist only the activities that require action.

Country:	Country X
New Vaccine:	Vaccine X
Planned Introduction Date:	Date X

Theme	Lead Agency	Activity/Action to be taken	Deadline	Status	Jan	Feb	Mar	Apr	May
Programme objectives/ targets									
Target population and delivery strategy									
Policy									
Financial considerations									
Situational Analysis									
National Coordination Mechanism									
Vaccine procurement & distribution									
Cold chain & logistics									
ste gement jection fety									

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