Mid-Level Management Course for EPI Managers

BLOCK IV: New vaccines

Module 12: New and under-utilized vaccine introduction

World Health Organization
REGIONAL OFFICE FOR Africa

Mid-Level Management Course for EPI Managers

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BLOCK IV: New vaccines

Module 12: New and under-utilized vaccine introduction

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Abbreviations and acronyms

AD	auto-disable (syringes)
AEFI	adverse events following immunization
DOR	drop-out rates
DTP/DPT	diphtheria-tetanus-pertussis-containing vaccine
EPI	Expanded Programme on Immunization
FIC	fully immunized child
GAPPD	Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea
Gavi	Global Alliance for Vaccines and Immunization
GVAP	Global Vaccine Action Plan (2011–2020)
HBcAg	hepatitis B core antigen
HBeAg	hepatitis B e antigen
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HepB	hepatitis B vaccine
Hib	*Haemophilus influenzae* type b vaccine
HMIS	health management information system
HPV	human papilloma virus/vaccine
HSCC	health sector coordinating committee
ICC	interagency coordinating committee
IEC	information, education and communication
LMIS	logistics management information system
MDVP	multi-dose vial policy (WHO)
MMR	measles, mumps, rubella vaccine
MOH	ministry of health
MR	measles and rubella vaccine
NESI	Network for Education and Support in Immunisation (Belgium)
NIP	national immunization programme
NITAG	national immunization technical advisory group
NRA	national regulatory authority
OPV	oral polio vaccine
PAHO	Pan American Health Organization
PCV	pneumococcal conjugate vaccine
Penta	pentavalent (vaccine with five antigens)

PIE	post-introduction evaluation
PSPQ_SC	Programmatic Suitability for Prequalification Standing (WHO)
RED/REC	Reaching Every District/Reaching Every Community
RI	routine immunization
RSPI	Regional Strategic Plan for Immunization (2014–2020)
SAGE	Strategic Advisory Group of Experts (WHO headquarters, Geneva)
SIA	supplementary immunization activity
VVM	vaccine vial monitor
UN	United Nations
UNICEF	United Nation Children's Fund
WHO	World Health Organization
YF	yellow fever

Glossary

Combination vaccine — A vaccine containing several antigens (e.g. DTP, DTP-HepB-Hib, MMR, etc.).

Intussusception — Invagination of one segment of gastro-intestinal tract into an adjacent and usually lower segment, resulting obstruction and strangulation of the invaginated portion.

New vaccine — In the context of this module, the new vaccine is a new antigen, a new combination vaccine or other vaccine product that is introduced into the immunization programme (e.g. HepB, Hib, pneumococcal conjugate, rotavirus, HPV vaccines or meningococcal meningitis A conjugate vaccine).

Post-introduction evaluation — A type of evaluation which usually takes place 6–12 months after the introduction of a new vaccine to evaluate implementation of the introduction, and its impact on various aspects of the immunization system in the country: accessibility by communities, level of adverse events of the vaccine, changes introduced in the new vaccination schedule, level of additional workload of health workers, whether available capacity of cold chain equipment is able to cope with new volumes, changes in disease occurrence captured by sentinel surveillance, etc.

Under-utilized vaccine — In the context of this module, this is an effective vaccine that is not sufficiently utilized through the routine immunization programme by countries at risk of infection, e.g. vaccine against yellow fever by countries that are in the yellow fever zone.

Vaccine — Biological product prepared from killed or attenuated (weakened) virus or bacteria or the toxins, used for vaccinating people to induce specific immunity against infectious diseases.

1. Introduction

1.1 Context

The Expanded Programme on Immunization (EPI) is a key global health programme. Its overall goal is to provide effective and quality immunization services to target populations. EPI programme managers and staff need to have sound technical and managerial capacities in order to achieve the programme's goals.

The immunization system comprises five key operations: service delivery, communication, logistics, vaccine supply and quality, and surveillance. It also consists of three support components: management, financing and capacity strengthening.

National immunization systems are constantly undergoing change, notably those related to the introduction of new vaccines and new technologies, and programme expansion to reach broader target populations beyond young children. The EPI programme also faces external changes related to administrative decentralization, health reforms, as well as the evolving context of public-private partnerships (PPPs) for health, among others.

To ensure the smooth implementation of immunization programmes, EPI programme staff have to manage these changes. This requires specific skills in problem-solving, setting priorities, decision-making, planning and managing human, financial and material resources as well as monitoring implementation, supervision and evaluation of services.

National immunization programmes (NIPs) operate within the context of national health systems, in alignment with global and regional strategies. For the current decade, 2011–2020, the key global immunization strategies are conveyed through the Global Vaccine Action Plan (2011–2020) (GVAP) and the African Regional Strategic Plan for Immunization (2014–2020) (RSPI).

These strategic plans call on countries to:

- improve immunization coverage beyond current levels;
- complete interruption of poliovirus transmission and ensure virus containment;[1]
- attain the elimination of measles and make progress in the elimination of rubella and congenital rubella syndrome;[2] and
- attain and maintain elimination/control of other vaccine-preventable diseases (VPDs).

The key approaches for implementation of the GVAP/RSPI include:

- implementation of the Reaching Every District/Reaching Every Community (RED/REC) approach and other locally tailored approaches and move from supply-driven to demand-driven immunization services;
- extending the benefits of new vaccines to all;
- establishing sustainable immunization financing mechanisms;
- integrating immunization into national health policies and plans;
- ensuring that interventions are quantified, costed and incorporated into the various components of national health systems;
- enhancing partnerships for immunization;
- improving monitoring and data quality;
- improving human and institutional capacities;
- improving vaccine safety and regulation; and
- promoting implementation research and innovation.

The RSPI promotes integration using immunization as a platform for a range of priority interventions or as a component of a package of key interventions. Immunization is a central part of initiatives for the elimination and eradication of VPDs, and of the integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD) by 2025.

It is understood that while implementing the above strategies, EPI managers will face numerous challenges and constraints that they need to resolve if the 2020 targets are to be met. Building national capacity in immunization service management at all levels of the health system is an essential foundation and key operational approach to achieving the goals of the global and regional strategic plans.

In view of this, the WHO Regional Office for Africa, in collaboration with key immunization partners such as the United Nations Children's Fund (UNICEF), United States Agency for International Development (Maternal and Child Survival Program) (USAID/MCSP), and the Network for Education and Support in Immunisation (NESI), have revised the Mid-Level Management Course for EPI Managers (MLM) training modules. These modules are complementary to other training materials including the Immunization in Practice (IIP) training manuals for health workers and the EPI/Integrated Management of Childhood Illnesses (IMCI) interactive training tool.

1 WHO, CDC and UNICEF (2012). Polio Eradication and Endgame Strategic Plan 2013-2018.
2 WHO (2012). Global Measles and Rubella Strategic Plan 2012-2020.

This module (12) titled *New and under-utilized vaccine introduction* forms Block IV: New vaccines.

1.2 Purpose of the module

The aim of this module is to introduce the key characteristics of the new and under-utilized vaccines and assist mid-level managers to identify issues that must be considered in planning for their introduction into NIPs.

1.3 Target audience

The module is intended for EPI managers at national and subnational levels, other programme managers involved with the introduction of new vaccines and teachers in health training institutions.

1.4 Learning objectives

At the end of the module, participants will be able to:
Explain the diseases targeted by new and under-utilized vaccines.

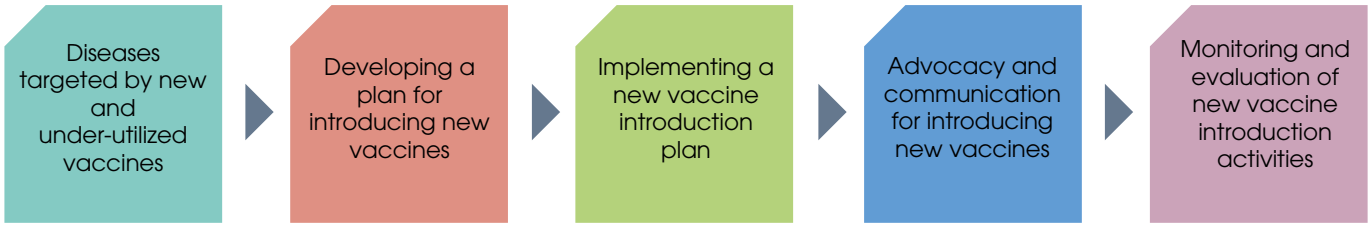
- Describe the basic epidemiology of the diseases targeted by new vaccines.
- Explain the basic information about the vaccines to be introduced.
- Develop a plan of action for the introduction of a new vaccine using the following sections:
  - conduct a situation analysis
  - formulate objectives and targets
  - determine operational strategies and activities
  - determine resource needs
  - revise immunization forms
  - estimate new vaccine requirements.
- Implement advocacy and communication for introducing a new vaccine including:
  - determining communication gaps related to introduction of new vaccines
  - identifying appropriate target groups for advocacy and communication
  - designing key messages for the target audiences.
- Implementing new vaccine introduction activities according to a plan.
- Monitoring and evaluation of new vaccine introduction activities through:
  - monitoring and supervising new vaccine introduction
  - conducting post-introduction evaluation (PIE).

1.5 Contents of the module

This module is comprised of several logically sequenced sections, shown below, on managing the introduction of new vaccines.

1.6 How to use this module

The chapters in this follow a logical sequence. Application exercises, role plays and case studies are provided to enable course participants to apply what they have learned. It is crucial for participants to understand from the beginning the implications of introducing new vaccines in the routine immunization (RI) programme. First, read the descriptive content of each section. The output of exercises, role plays, case studies and group work can then be discussed with colleagues and facilitators in group or plenary sessions.



2. Diseases targeted by new and under-utilized vaccines

2.1 Hepatitis B infection

Hepatitis B virus (HBV) infection is a major public health problem worldwide. Approximately 30% of the world's population, or about 2 billion people, have serological evidence of HBV infection. Of these, an estimated 350 million have chronic HBV infection, and at least 500 000 chronically infected people die each year from chronic liver disease, including cirrhosis and liver cancer. HBV is second only to tobacco as a known human carcinogen. In Africa, it is the first and second cause of human cancer among adult males and females, respectively.

Acute hepatitis B: After becoming infected, the incubation period is usually three to four months, with a range of six weeks to six months. The signs and symptoms usually last for several weeks, and may include loss of appetite, weakness, nausea, vomiting, abdominal pain, jaundice (yellow skin or yellow sclera of the eyes), dark urine, skin rashes and joint pains. The case fatality rate of acute hepatitis B is about 1.2%.

Chronic hepatitis B: Most of the disease manifestations associated with HBV infection are in people who are chronic carriers of the virus. Over many years, these chronically infected people eventually die of liver diseases such as cirrhosis and liver cancer.

The hepatitis B virus can be found in the blood and other body fluids of an infected person. It is spread either by skin puncture or mucous membrane contact with infected blood or body fluids. The primary routes of transmission are:

- from mother to baby (perinatal)
- from child to child
- through unsafe injections and blood transfusions
- through sexual contact.

Note: There are other types of hepatitis viruses – A, C, D and E. All hepatitis viruses can cause illness, but types A and B are the most common causes of hepatitis. In contrast to hepatitis B, hepatitis A is normally spread through contaminated food and water.

Vaccines are available only against hepatitis A and B. Hepatitis A vaccine is used for individual vaccination (e.g. for travellers) or for vaccination of some high-risk groups. Only hepatitis B vaccine (HepB) is used for childhood vaccination programmes.

Children should be immunized against hepatitis B as soon as possible starting at birth. It is safe and has been shown to be effective in preventing mother-to-child transmission of the virus. Infants and young children infected with hepatitis B seldom show signs and symptoms of acute infection, but 80–90% of infants infected during the first year of life and 30–50% of children infected between one and four years of age develop chronic conditions (only 2–5% of adults become chronically infected).

2.1.1 Hepatitis B vaccines

There are two types of hepatitis B vaccines: plasma derived and DNA recombinant. Plasma-derived vaccines are prepared with purified HBsAg from plasma of persons who are carriers of HBV infection. The DNA recombinant hepatitis B vaccine is a genetically engineered vaccine made by using HBsAg synthesized in yeast or mammalian cells into which the HBsAg gene has been inserted using plasmids. Both vaccines are equally safe and effective.

Hepatitis B vaccines are available as follows:

- Monovalent hepatitis B vaccine, which protects only against hepatitis B infections. This is the only formulation that can be used for giving a birth dose.
- Combination vaccines that include hepatitis B vaccine combined with Penta, Hib or both. When it is combined with only DTP (DTP-HepB), it is also known as quadrivalent (four-component) vaccine. When combined with both DTP and Hib (DTP-Hib), it is known as pentavalent (five-component) vaccine, which currently is the most widely used formulation in the African Region.

- Liquid monovalent hepatitis B vaccines are available in one-, two-, six-, and 10-dose vials; the DTP-HepB combination (quadrivalent vaccine) is available in 10-dose vials and, the pentavalent (DTP-HepB-Hib) vaccine is available as fully liquid or lyophilized (freeze-dried) Hib component in one-dose, two-dose and 10-dose vials.

2.2 *Haemophilus influenzae* type b (Hib) infection

Infections due to *Haemophilus influenzae* type b (Hib) are a major cause of morbidity and mortality in young children throughout the world. Six serotypes (a, b, c, d, e and f) are known to cause disease, but type b is responsible for more than 90% of the life-threatening Hib infections in children, particularly meningitis and pneumonia.

Other Hib infections include epiglottitis, septicaemia, septic arthritis, osteomyelitis, cellulitis and pericarditis. At least 450 000 children die each year due to this infection.

Hib bacteria are transmitted from child to child in droplets of saliva expelled when an infected child coughs or sneezes. Hib also spreads when children share toys and other things that they have put in their mouths. Transmission is increased when many children spend prolonged periods of time together in settings such as day-care centres or crèches. Hib disease is most common in children under five years of age; children 4–12 months are most at risk.

2.2.1 Hib vaccine

Hib vaccine is one of the new generations of vaccines known as conjugate vaccines. Conjugation is a process whereby part of the Hib bacterium is connected (conjugated) to certain proteins derived from toxoids of tetanus or diphtheria or diphtheria toxoid-like proteins, or a mix of proteins from another bacterium. With three doses, 90–99% of children vaccinated develop adequate protection against Hib infections.

Hib vaccines are available as follows:

- Liquid Hib+DTP, which comes in either single- or 10-dose vials.
- Lyophilized Hib vaccine that the user reconstitutes with liquid DTP (to make tetravalent).
- Lyophilized Hib vaccine that the user reconstitutes with liquid DTP-HepB (to make Pentavalent).
- Lyophilized DTP-HepB-Hib, which comes in multi-dose or single-dose vials.
- Monovalent liquid Hib vaccine as single- or 10-dose vials.
- Lyophilized (freeze-dried) Hib vaccine, comes only as a single-dose vial, vaccinator reconstitutes with saline diluent.

2.3 Yellow fever infection

Yellow fever (YF) occurs in tropical and subtropical regions of Africa and the Americas. It is a major public health concern in at least 33 African and 13 Latin American countries. An estimated 200 000 cases and 30 000 deaths are attributable to yellow fever annually, most of them in sub-Saharan Africa. In the 33 endemic countries of Africa, estimated combined populations of more than 610 million are considered to be at risk for yellow fever, among which more than 219 million live in urban settings.

Yellow fever is a viral haemorrhagic fever transmitted by mosquitoes infected with the yellow fever virus. The disease is untreatable and the case fatality rate in severe cases can exceed 50%. Clinical response to infection with YF virus ranges from mild, undifferentiated fever to severe illness resulting in death from either liver or kidney failure or from the consequences of severe bleeding episodes. A single infection confers lifelong immunity. Therefore, the pattern of the disease occurrence consists of recurrent outbreaks with intervals of several years in areas where susceptible human pool is accumulated and maintained.

There are two modes of transmission of the virus: the sylvatic or forest cycle and the urban cycle. Transmission begins when the vector (*Aedes africanus* in Africa, several species of mosquito of the genus *Haemagogus* in South America) feeds upon non-human primates infected with the yellow fever virus. Infected *Aedes africanus* then feed upon humans travelling through the forest. The greatest risk for an epidemic occurs when viraemic humans return to urban areas and are fed upon by domestic vector mosquitoes, *Aedes aegypti*, (present in urban areas of both Africa and Latin America), which then transmit the virus to other humans, thus forming the urban cycle.

2.3.1 Yellow fever vaccine

Yellow fever vaccine is the most successful live attenuated vaccine known to science. The 17D vaccine is safe and highly effective, protecting more than 95% of those vaccinated with a single dose. Antibodies appear from 7–10 days after vaccination. A single dose of yellow fever vaccine is sufficient to confer sustained lifelong protective immunity against yellow fever disease. The yellow fever vaccine comes in 2-, 5-, 10- and 20-dose vials.

WHO recommends the incorporation of yellow fever vaccine into routine EPI to be done at the time of the visit for the first measles vaccine (at 9–12 months of age), thus avoiding the need for an extra visit. In addition to RI, in areas where epidemics are known to have occurred or in the face of impending outbreaks of the disease, mass campaigns have been conducted successfully.

2.4 Pneumococcal infection

Pneumococcal disease is a major cause of child illness and death. Of the estimated 1.6 million annual deaths due to pneumococcal disease globally, approximately 826 000 occur in children under the age of five. Deaths are primarily the result of pneumonia, sepsis or meningitis, and occur mainly in the developing world, where access to curative care is limited.

Pneumococcus (also known as *Streptococcus pneumoniae*) is a bacterium that causes a group of diseases called "pneumococcal disease". These include severe diseases and complications such as pneumonia, meningitis, bacteraemia, and milder diseases such as middle ear infection (otitis media), sinusitis and bronchitis. Pneumococcus is classified into serotypes, denoted by numbers and letters (e.g. 18C, 23F, etc.). There are over 90 known serotypes and the prevalence of different serotypes varies by regions of the world.

Pneumococcus is transmitted through the following ways:

- Droplet spread from a patient or healthy carrier or contact with surfaces contaminated with their secretions.
- Direct contact with respiratory secretions from patients or healthy carriers, who may transmit the pneumococci on their fingers, handkerchiefs, cloths and objects (e.g. toys).

Pneumococcus may then spread to the blood stream causing bacteraemia (presence of bacteria in the blood) and then infect distant organs and tissues such as the meninges (lining of the brain) causing meningitis, the lung causing pneumonia, or can spread to adjoining sites causing otitis media (ear infections) or sinusitis (sinus infections). Children under five years of age (especially those under two years of age) and the elderly are most at risk of developing and dying from pneumococcal disease. Apart from young age and old age, other risk factors for pneumonia include HIV infection, influenza virus infection, overcrowding, indoor air pollution, and, for infants, lack of breast feeding and incomplete immunization (e.g. measles, Hib and pertussis).

2.4.1 Pneumococcal vaccines

Safe and effective vaccines now exist to protect against many (but not all) strains of pneumococcal disease. Pneumococcal vaccines protect against severe forms of pneumococcal disease and complications, such as meningitis, pneumonia and bacteraemia. The immunity induced by the vaccine is specific and will not protect against these conditions if they are caused by agents other than pneumococcus or other strains of pneumococcus that are not contained in the vaccine.

In 2009, the seven-valent pneumococcal conjugate vaccine (PCV7) was prequalified by WHO. This vaccine contains seven serotypes that account for 50% or more of invasive disease among children below five years old in most countries, but does not contain serotypes that are also prevalent in developing countries.

The 10-valent pneumococcal vaccine (PCV10) was prequalified in 2010 for the one-dose and two-dose vial presentations, with a condition that the two-dose preservative-free liquid presentation undergoes a study to monitor potential adverse events following immunization (AEFI) in a Gavi-eligible country. PCV 10 includes the seven serotypes in PCV7 as well as serotypes 1, 5 and 7F. The approval from WHO indicated that as a two-dose presentation of a preservative-free liquid vaccine had not previously been used in United Nations (UN) supported immunization programmes, formal post-introduction monitoring was therefore initiated and the prequalification status would be reviewed after receipt of interim and final reports. Interim data from Ethiopia and Kenya have been received and reviewed. Taking into account that risk-benefit estimates of using this presentation in high disease burden countries show that the benefits outweigh the potential risks associated with the presentation; the two-dose presentation of Synflorix™ remains prequalified. The presentation is considered suitable for supply through the UN to further countries.

Each country considering introduction of this vaccine presentation will need to ensure its programmatic readiness to do so. Each country will also need to ensure the monitoring of its correct use and implementation of any corrective training needed. To mitigate against potential programmatic risk countries should ensure that they:

- Understand the benefits and potential contamination risks of the two-dose unpreserved presentation and understand the need for special training to enhance immunization worker practices.
- Conduct post-introduction evaluations to determine levels of health-care worker knowledge and compliance with the correct handling of the vaccine; and implement corrective training if needed.

The 13-valent pneumococcal vaccine (PCV13) was prequalified in 2010 as a single-dose vial. PCV13 includes the 10 serotypes of PCV10 and serotypes 3, 6A and 19A.

Several candidate vaccines based on pneumococcal common protein antigens are in pre-clinical or early clinical development. These may be used as "standalone" vaccines or incorporated into combinations with pneumococcal conjugate vaccines.

2.5 Rotavirus infection

Rotavirus infections are responsible for approximately 527 000 deaths each year globally. 80% of all rotavirus-related deaths occur in South Asia and sub-Saharan Africa. Diarrhoea is a significant cause of deaths among children under five years in sub-Saharan Africa (as a result of severe dehydration) and about half of the burden of severe diarrhoeal disease associated deaths is due to rotavirus. Rotavirus is estimated to be responsible for over one third of deaths caused by diarrhoeal diseases, especially in children aged between six months and two years.

Virtually all children in developing countries are infected with rotavirus in their first two years of life, but many are asymptomatic and most cases are mild. Rotavirus accounts for 24–40% of hospitalized children with acute diarrhoeal disease in Africa. Hospital-based surveillance data from the WHO African Region East and Southern Africa countries indicate that rotavirus diarrhoeal disease accounts for an estimated 30% in Ethiopia, 41% in Kenya, 39% in the United Republic of Tanzania, 29% in Zimbabwe, 39% in Uganda, 35% Zambia, 33% in Mauritius and 33% in South Africa among the children admitted with severe diarrhoeal diseases.

The high incidence and attack rates of rotavirus in both developing and developed countries indicate that other preventive measures, such as improved water and sanitation and hygienic conditions, have not significantly reduced the transmission of the virus, and thus vaccination is the most promising method to control the disease.

2.5.1 Rotavirus vaccine

In 2009, WHO's Strategic Advisory Group of Experts (SAGE) on immunization recommended the inclusion of rotavirus vaccination of infants into all NIPs, particularly in countries where diarrhoeal deaths account for more than 10% of mortality among children aged under five years.

Two pre-qualified rotavirus vaccines are currently available, one with two-dose schedule (Rotarix) and the other one with a three-dose schedule (RotaTeq).

The initial WHO recommendation for rotavirus vaccines was that both vaccines were not to be administered to children before 12 weeks of age for the first dose and beyond 24 (Rotarix) or 32 (RotaTeq) weeks of age for completing the series due to possible risk of intussusception which may occur in infants' gastro-intestinal tract (see Glossary).

Following a review of new evidence on the age-specific burden of rotavirus disease and deaths, timeliness of vaccination, and the safety and effectiveness of different immunization schedules, WHO continues to recommend that the first dose of rotavirus vaccine be administered as soon as possible after six weeks of age, along with vaccination against diphtheria-tetanus-pertussis (DTP), to ensure induction of protection prior to natural rotavirus infection.

Although early immunization is still favoured, age restrictions on the first and last dose of rotavirus vaccines may have prevented vaccination of many vulnerable children in settings where the DTP doses are given late (i.e. after 15 weeks for DTP1 after 32 weeks for DTP2 or DTP3).

By allowing infants to receive rotavirus vaccine together with DTP regardless of the recommended time of DTP vaccination in the existing national schedules, programmes will be able to reach children who were previously excluded from the benefits of rotavirus vaccines. However, vaccination of children aged over 24 months with rotavirus vaccine is not recommended due to the typical age distribution of rotavirus gastroenteritis.

Table 2.1 Rotavirus vaccines

Characteristics of rotavirus vaccines	Type of rotavirus vaccines	
	Rotarix (GSK Bio)	**RotaTeq (Merck)**
Origin	Human monovalent	Bovine pentavalent
Strain	G1P[8]	G1, G2, G3, G4P[8] and G6P[7]
Vaccine course	2 doses – oral	3 doses – oral
Schedule	With Penta1 and Penta2	With Penta1, Penta2 and Penta3
Age restrictions for administration of the vaccine	None but WHO now recommends timely administration of each dose accompanied by measures to ensure high vaccination coverage	
Presentation	Lyophilized, reconstituted or liquid	Liquid
Intussusception risk	No association observed	No association observed
WHO pre-qualification	Yes, in 2007	Yes, in 2008

2.6 Human papilloma virus infection

Persistent infection with human papilloma virus (HPV) of common "high-risk" types (e.g. 16, 18) causes about 70% of cervical cancer cases. Cervical cancer resulted in 274 000 deaths worldwide in 2008, of which about 85% or more occurred in developing countries. High-risk HPV types are also associated with other anogenital and head and neck cancers.

HPV of common "low risk" types (e.g. 6 and 11) cause anogenital warts in sexually active populations and respiratory papillomatosis in infants which result in substantial morbidity and health-care costs for women, men and infants.

Genital types of HPV are sexually transmitted. They are highly transmissible; peak infection incidence occurs soon after sexual debut. Infection is generally asymptomatic and frequently clears spontaneously, but some infections persist.

2.6.1 Human papilloma virus vaccine

There are currently two HPV vaccines widely marketed internationally: quadrivalent and bivalent vaccines. Both vaccines were WHO-prequalified in 2009. WHO recommends that HPV vaccination should be introduced into NIPs where prevention of cervical cancer and other HPV-related diseases is a public health priority; vaccine introduction is programmatically feasible, and financially sustainable; and the cost-effectiveness aspects have been duly considered. The primary target population for HPV vaccine is likely to be girls 9–14 years old.

Cervarix™ is a preservative-free vaccine available in one- and two-dose vials. For the two-dose presentation it was indicated that a two-dose preservative-free liquid presentation was a novel presentation for UN supported EPI programmes and that supply of this presentation of the product through UN procurement agencies would not be expected before revision of the WHO policy statement on the use of opened multi-dose vials of vaccine in subsequent immunization sessions (multi-dose vial policy – MDVP). Revision of the MDVP was finalized in 2014. The WHO Programmatic Suitability for Prequalification Standing Committee (PSPQ_SC) reviewed the two-dose Cervarix™ presentation and took into account experience gained with two-dose Synflorix and that risk-benefit estimates of using this presentation in high disease burden countries show that the benefits outweigh the potential risks associated with the presentation.

The two-dose presentation of Cervarix™ remains prequalified and the presentation is considered suitable for supply through UN agencies. Experience with two-dose Synflorix indicated that special attention to training of health-care staff will be required for the proper use of the Cervarix™ two-dose presentation. Specific pre-introduction measures are required to assure programmatic readiness is achieved prior to introduction. Post-introduction evaluations (PIEs) and corrective training actions, where needed, are required to assure appropriate continued use of this presentation.

The quadrivalent vaccine prevents the most common high and low risk types of HPV (16, 18, 6 and 11) while the bivalent vaccine prevents infection with high risk types 16 and 18. Although the duration of protection is not yet known, there is evidence of protection for five to eight years after vaccination.

As of December 2014, the U.S. Food and Drug Administration approved Merck's 9-valent HPV vaccine (GARDASIL 9®) which includes the additional five HPV types 31, 33, 45, 52 and 58 compared with the quadrivalent vaccine. The 9-valent vaccine is currently undergoing WHO review for prequalification.

2.7 Epidemic meningitis

In the "African meningitis belt", a region that extends from Ethiopia in the east to Senegal in the west, group A meningococcal disease has posed a recurrent threat to public health for at least 100 years. Major group A epidemics occur at intervals of 7–14 years and particularly affect children and young adults. When epidemic meningococcal disease occurs, annual incidence rates can reach 1000 cases per 100 000 population (1%) and it commands public health attention and calls for a large scale public health response.

The case fatality rate of meningococcal disease is 5–25% and among survivors there is also considerable morbidity, including persistent neurological sequealae.

In recent years, group W135 meningococcal have caused outbreaks in this region (as well as in Saudi Arabia), whereas several Western countries have experienced outbreaks of group C strains. Chemoprophylactic measures are in general insufficient for the control of this disease.

2.7.1 Meningococcal vaccines

Currently two types of meningococcal vaccines are available in the market: polysaccharide and conjugate vaccines. While both group A and C polysaccharide vaccines are effective when used in age group two years and above, they are not immunogenic in children below two years of age. The polysaccharide vaccines do not affect individual nasopharyngeal carriage and thus do not confer herd immunity.

A low-cost conjugate group A meningococcal vaccine (MenAfriVac) was developed, and if introduced in well planned programmes, will prevent the epidemics of group A meningococcal disease. The recently introduced meningococcal group C conjugate vaccines have also proved to be safe and efficacious in all age groups including infants, and are easily adapted to the timing of routine childhood immunization services.

As with Hib and pneumococcal conjugate vaccines, group A, C, Y and W135 meningococcal polysaccharides have been chemically conjugated to carrier proteins.

Conjugate vaccines induce a T cell-dependent response, resulting in an improved immune response in infants and young children and a priming of immunologic memory leading to a booster response to subsequent doses.

These vaccines are expected to provide long-lasting immunity even when given as a series in infancy, and to enhance herd immunity by decreasing nasopharyngeal carriage and thus transmission of the causing bacteria.

Two double-blind randomized controlled studies of monovalent MenA conjugate vaccine have been conducted in Ghana and Mali that show that both formulations of MenA conjugate vaccine are immunogenic in a one-dose schedule for those aged 9–24 months or in a two-dose schedule for those aged 3–9 months.

The two licensed formulations are:

- **MenAfriVac:** 10 µg of purified MenA polysaccharide antigen conjugated with tetanus toxoid (PsA-TT) per dose for use in those aged 1–29 years.
- **MenAfriVac:** 5 µg of PsA-TT per dose for use in infants and children aged 3–24 months.

Duration of protection beyond 27 months after the final dose is unknown. The reactogenicity profile of MenA conjugate vaccine given concomitantly with routinely administered vaccines was shown to be similar to that of the concomitantly given routine vaccines alone, with a comparable safety profile. Both clinical studies provide evidence that the two MenAfriVac formulations were well tolerated and safe.

2.8 Poliomyelitis

Polio is a highly infectious disease caused by a virus. It invades the nervous system, and can cause total paralysis in a matter of hours. The virus is transmitted by person-to-person spread mainly through the faecal-oral route or, less frequently, by a common vehicle (e.g. contaminated water or food) and multiplies in the intestine. Initial symptoms are fever, fatigue, headache, vomiting, and stiffness in the neck and pain in the limbs. One in 200 infections leads to irreversible paralysis (usually in the legs). Among those paralysed, 5% to 10% die when their breathing muscles become immobilized. Polio mainly affects children under five years of age.

Polio cases have decreased by over 99% since 1988, from an estimated 350 000 cases in more than 125 endemic

countries to 306 cases in 2014, in only three endemic countries. Of the three strains of wild poliovirus (WPV) type 1, type 2, and type 3, WPV2 was eradicated in 1999 and no new cases of WPV3 were notified since November 2012. Since 2014, total WPV cases are at the lowest ever level since the beginning of global polio eradication initiative.

2.8.1 Polio vaccines

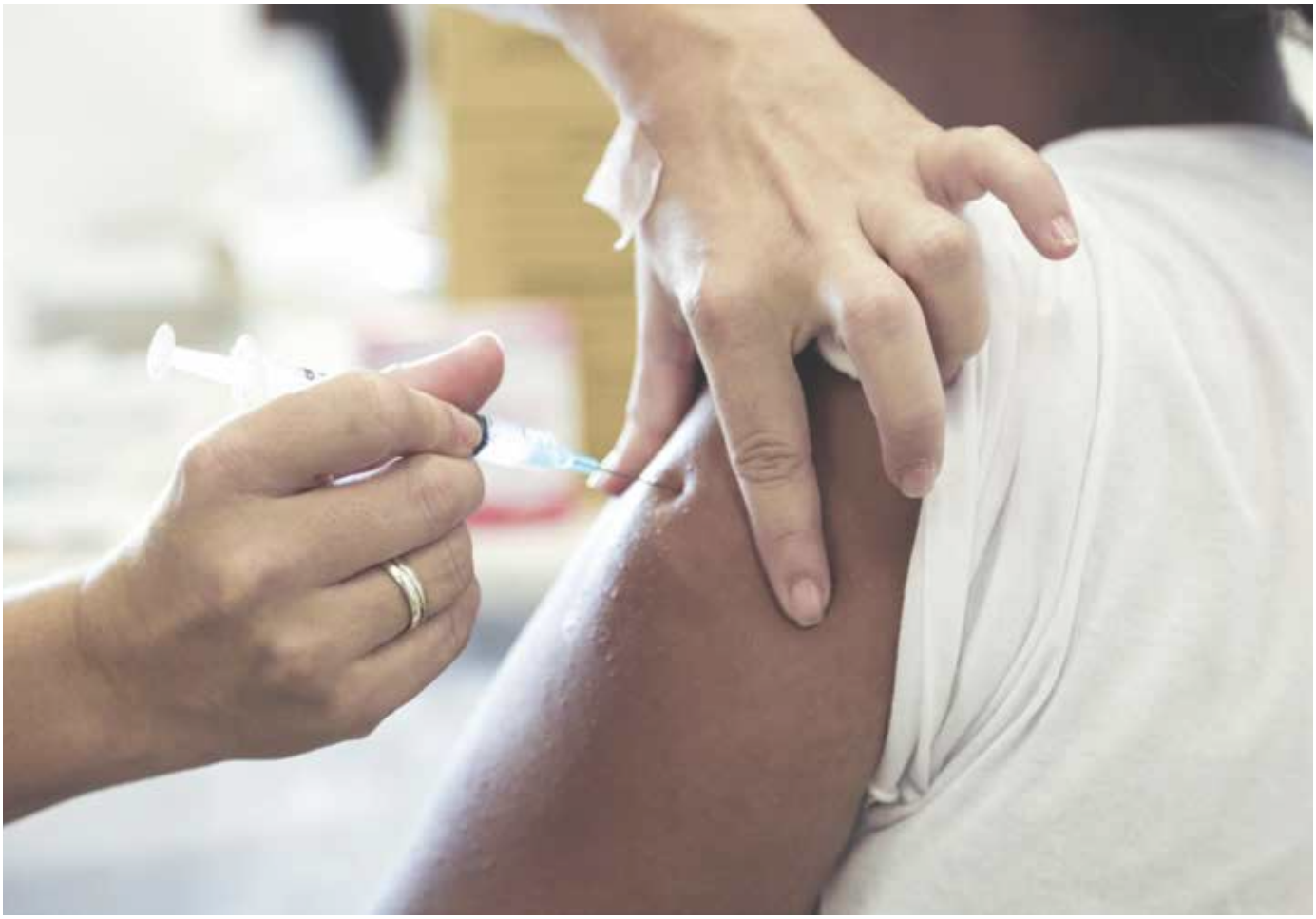
Polio prevention involves immunization with live oral polio vaccine (OPV). The EPI schedule for RI is comprised of four doses. The first dose is given at birth. The other three doses are given with Penta vaccine at 6-10-14 weeks of age. A dose includes two drops of the vaccine given into the mouth (orally). OPV is recommended by EPI for the eradication of polio. It is cheap, easy to give, highly effective and safe.

In May 2008, in line with guidance from the SAGE, the World Health Assembly endorsed the principle of synchronized OPV cessation globally. Recognizing that WPV2 was eradicated in 1999 and that more than 90% of the circulating vaccine derived polio virus (cVDPV) cases in recent years were caused by the vaccine-derived type 2 strain, in 2012 the SAGE further recommended the withdrawal of OPV2 as the first step towards complete withdrawal of all oral polio vaccines.

To safeguard against the withdrawal of the type 2 serotype, in November 2012 the SAGE recommended that at least one dose of inactivated polio vaccine (IPV) be introduced into all RI programmes prior to the switch from three-valent oral polio vaccine (tOPV) to bivalent oral polio vaccine (bOPV). The IPV dose is expected to:

- Prevent paralytic polio in individuals exposed to a cVDPV type 2 or WPV2.
- Improve the immunological response to monovalent oral polio vaccine (mOPV) type 2 if required to be given in response to a WPV2 or cVDPV2 outbreak after tOPV cessation.
- Reduce transmission of cVDPV type 2 or WPV2 should either be introduced after tOPV cessation.
- Boost immunity to WPV1 and WPV3 in vaccine recipients, which may further accelerate WPV eradication.

From 2015, all countries using OPV started introducing one dose of injectable IPV into the RI schedule at 14 weeks or 4 months, together with bOPV. This is part of the Polio Endgame Strategy that involves changing the polio vaccines used in both RI and supplementary immunization activities (SIAs)



Exercise 1

In this self-assessment exercise put "T" or "F" (true or false) against the following statements. When you have completed the exercise, ask your facilitator to provide the correct answers and compare them with yours. For every correct answer score 1; if wrong put a 0. Total your score and if less than 18 read the above section again.

Statements	True (T)/ false (F)	Score
1. Infants and children, when infected with hepatitis B virus, have much higher chances of becoming chronically infected than adults.		
2. Giving a birth dose is important to reduce perinatal transmission of hepatitis B virus.		
3. Hib infection is responsible for at least 90% of *Haemophilus influenzae* infections in children.		
4. Keeping children in day care reduces chances of Hib infection.		
5. With three doses of Hib vaccine, 90–99% children develop adequate protection against Hib infections.		
6. Yellow fever is seen only in sub-Saharan Africa.		
7. Recovery from yellow fever confers lifelong immunity.		
8. For routine immunization, it is best to administer yellow fever vaccine at the same time as measles vaccine.		
9. In terms of childhood mortality, pneumococcal disease has the highest burden when compared with mortality from other diseases that can be prevented with available new vaccines.		
10. PCVs were developed because the polysaccharide vaccines had too many side-effects.		
11. Both PCV10 and PCV13 protect against most of the pneumococcal serotypes causing severe pneumococcal disease in developing countries.		
12. Rotavirus disease manifests itself mainly as diarrhoea, but it causes also one fifth of pneumonias in under fives in developing countries.		
13. Rotavirus infections are rare in industrialized countries and if developing countries succeed in improving hygiene and sanitation the infection will cease to be a major health problem.		
14. Two rotavirus vaccines have been prequalified by the WHO and are currently available; one with a two-dose schedule (Rotarix) and one with a three-dose schedule (RotaTeq).		
15. The schedule for the oral rotavirus vaccines is with Penta1 and 2 for Rotarix and with Penta1, 2 and 3 for RotaTeq; catch-up vaccination is recommended for infants up to one year.		
16. WHO has prequalified two HPV vaccines: a quadrivalent (against g/types 16, 18, 6, 11) and a bivalent (against g/types 16, 18); both vaccines will prevent around 70% of cervical cancers worldwide.		
17. As the HPV vaccines target the prevention of HPV infection, which is a sexually transmitted infection, girls and boys should be vaccinated once they have become sexually active.		
18. Many industrialized countries have already introduced HPV vaccination mainly in young adolescent girls (10–14 years old) through the school health system.		
19. The African "meningitis belt" is characterized by regular epidemic meningitis outbreaks, most of which are due to serogroup A meningococcal disease.		
20. A low-cost conjugate group A meningococcal vaccine (MenAfriVac), if introduced in well planned programmes, will prevent the epidemics by group A meningococcal disease.		
Total score for correct answers		

3. Developing a plan for introducing new vaccines

3.1 Decision-making process for introduction of new vaccines

The introduction of a new vaccine into the routine childhood immunization schedule requires proper planning which should include all the components of the immunization system with special emphasis on the following areas:

- Advance communication and advocacy activities to prepare population, involve decision-makers and provide advance information to health workers about introduction of a new vaccine.
- Training of health personnel on specifics related to vaccine properties, administration routes, target population groups, expected changes in current immunization schedule, etc.
- Availability of adequate storage capacity of vaccines and other supplies, and whether there will be a need to expand cold chain storing capacity, ordering vaccines, monitoring vaccine use and wastage, estimated vaccine coverage.

The vaccine introduction can 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 introduction of a new vaccine is a perfect opportunity to strengthen the RI processes such as micro-planning, upgrading the cold chain, logistics system and vaccine management, disease surveillance, improved monitoring of and evaluation of programme performance etc. which contribute to better functioning of the overall immunization programme. 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.

It is important to have a systematic and transparent process for making a decision about introducing a vaccine into the NIP. Also critical is that key stakeholders both in and outside 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. 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.

In line with this, more and more countries are recognizing the need to establish a NITAG to make recommendations to the government about the NIP, based on a rigorous review of the evidence. NITAGs consist of national experts in a broad range of disciplines who are capable of analysing 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.

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, so as to secure their buy-in and assistance in planning and implementing the new vaccine introduction.

In addition, interagency 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.

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 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 RI 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.
- **Vaccine choice.** The choice or preference of vaccine, formulation and presentation, in consideration of the costs, storage requirements, and training needs for each product.

There are several related technical and policy steps to be considered by the government, before taking the decision to introduce a new vaccine, as shown in Figure 3.1.

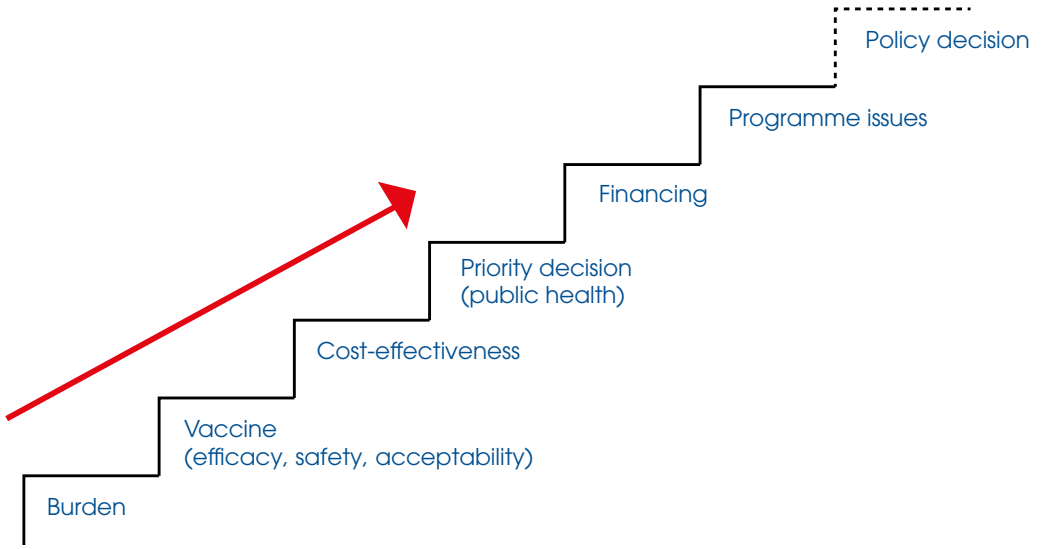
The key issues to be considered before deciding to introduce a vaccine (see Figure 3.2) include:

- 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 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 capacity/strength 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.

Optimal vaccine introduction into a NIP that strengthens health systems benefits from:

- A strong country-led, evidence-based decision-making, planning and prioritization process that is accountable and coordinated with other components of the health system.
- A well-performing or improving and responsive immunization programme.
- Seizing the opportunity to achieve:
  - well trained and motivated health force;
  - quality education and communication about the new vaccine or 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; and
  - resource, performance and management accountability.

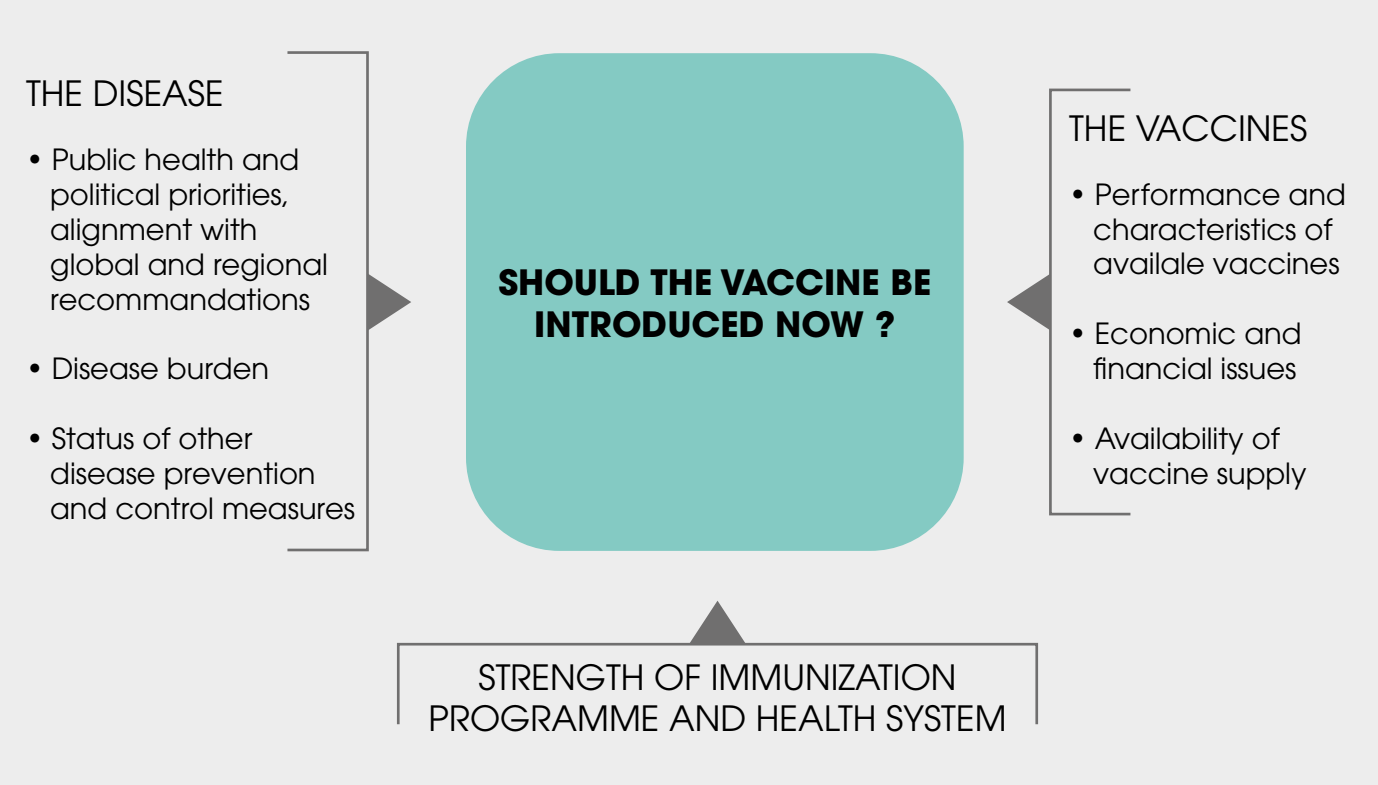
Figure 3.1 Steps in decision-making in the introduction of a new vaccine



- 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.
- Sufficient allocation of human and financial resources to introduce the new vaccine and sustain its use without adversely affecting other programmes and services.
- A safe and efficacious vaccine that is appropriate for local use and is available with an uninterrupted, sufficient supply.

The following sections suggest how to proceed in planning for the introduction of new vaccines into immunization programmes.

Figure 3.2 Key issues to consider before deciding to introduce a vaccine



3.2 Conduct a situation analysis

When considering the introduction of new vaccines, an assessment should be made to determine the strengths and weaknesses of the RI services and how to use the introduction of new vaccines as an opportunity to improve routine services. Specifically, the assessment should focus on the following:

- **Cold chain issues:** Assess the storage capacity of vaccine cold stores and dry stores for needles, syringes and safety boxes. Determine what policies and procedures need to be put in place to prevent freezing of freeze-sensitive vaccines.
- **Injection safety:** Is there an injection safety plan? If yes, does the plan include the management of waste and what steps have been taken to implement the plan? If your country is not already using auto-disable (AD) syringes for all immunization injections, what plans does it have to do so? Are there provisions for adequate supplies of appropriate injection equipment: ordered or available?
- **Vaccine wastage:** Is there a system in place to monitor vaccine wastage? If yes, what is the current DTP-HepB-Hib wastage rate? If not, what policies and procedures need to be put in place to ensure that vaccine wastage is carefully monitored and is at minimum level?
- **EPI forms and records:** When will EPI forms and records be revised to accommodate the new vaccines?
- **Health worker training:** How will health workers be trained? What training materials are available and which ones will need to be revised or developed? What is the timetable for training?
- **Communication:** The immunization communication component in the plan should be comprehensive, addressing all aspects of the new vaccine introduction. Communication needs to be integrated in the planning from the beginning in order to ensure necessary funds for new materials, training, monitoring and operations to ensure quality interventions in support of new vaccine introduction. The communication strategy should be appropriate to the characteristics of the new vaccines or technologies and should be included in the introduction plans as well as the timelines for preparation, launch, implementation, and monitoring (including the pre- and post-introduction evaluations).

3.3 Formulate objectives and targets

The objectives of the new vaccine introduction plan, to a large extent, will depend on the findings of the assessment. The analysis will further determine the specific strategy that should be adopted for introduction of new vaccines. 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 broken down cold chain equipment to be repaired;
- all relevant health management information system (HMIS) forms, including immunization cards, updated to include the new vaccine;
- training of health workers in health facilities providing immunization services conducted; and
- advocacy, information, education and communication (IEC) activities started.

Some examples of intermediate term objectives might be:

- improved AEFI monitoring;
- improved supportive supervision; and
- improved data management and utilization.

Long-term objectives may be:

- contributing to the reduction in morbidity and mortality of the children (as a result of successful social mobilization and delivery of the new vaccine particularly when integrated approaches are implemented such as the Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD); and
- successful delivery of integrated disease prevention and control services to populations that have traditionally been hard to reach.

Depending on your country's specific situation, you can choose from a number of operational strategy options for the introduction of new vaccines.

3.4 Determine operational strategies and activities

3.4.1 Simultaneous or phased introduction

There are different options for new vaccine introduction.

Simultaneous nationwide roll-out: 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.

Phased-in introduction to gradually cover the entire country: This 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 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).
- 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.
- Introduction in geographically-targeted areas.

3.4.2 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 NIP. 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.

However, the simultaneous introduction of vaccines may require a sharp increase in the NIP 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 RI programmes and add complexity to the planning and implementation of a vaccine introduction.

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 them and the budgetary requirements of a multiple vaccine introduction.

3.4.3 Optimal schedule for routine immunization

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

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

The new vaccine schedule may be flexible depending on the vaccine formulation you select to introduce (monovalent or combination vaccine). A number of options are available for adding new vaccines to the existing national immunization schedule without requiring mothers to make additional visits for vaccinations. Tables 3.1 and 3.2 show examples of how new vaccines can be added to existing childhood immunization schedules. The tables summarize the recommendations for vaccine administration found in WHO position papers, which are published in the Weekly Epidemiological Record (WER). Its purpose is to assist planners to develop an appropriate immunization schedule. Health-care workers should refer to their national immunization schedules. While vaccines are universally recommended, some children may have contraindications to particular vaccines.

Vaccines can generally be co-administered (i.e. more than one vaccine given at different sites during the same visit). Recommendations that explicitly endorse co-administration are indicated in the table, however, the lack of an explicit co-administration recommendation does not imply that the vaccine cannot be co-administered; further, there are no recommendations against co-administration.

Table 3.1 Summary of WHO position papers – recommended routine immunizations for children

(updated March 2017)

Table 2: Summary of WHO Position Papers - Recommended Routine Immunizations for Children

Antigen		Age of 1st Dose	Doses in Primary Series	Interval Between Doses			Booster Dose	Considerations (see footnotes for details)
				1st to 2nd	2nd to 3rd	3rd to 4th		
Recommendations for all children								
BCG [1]		As soon as possible after birth	1					Exceptions HIV
Hepatitis B [2]	**Option 1**	As soon as possible after birth (<24h)	3	4 weeks (min) with DTP1	4 weeks (min) with DTP3			Premature and low birth weight Co-administration and combination vaccine High risk groups
	Option 2	As soon as possible after birth (<24h)	4	4 weeks (min) with DTP1	4 weeks (min) with DTP2	4 weeks (min),with DTP3		
Polio [3]	**bOPV + IPV**	6 weeks (see footnote for birth dose)	4 (IPV dose to be given with bOPV dose from 14 weeks)	4 weeks (min) with DTP2	4 weeks (min) with DTP3			bOPV birth dose Transmission and importation risk criteria
	IPV / bOPV Sequential	8 weeks (IPV 1st)	1-2 IPV 2 bOPV	4-8 weeks	4-8 weeks	4-8 weeks		
	IPV	8 weeks	3	4-8 weeks	4-8 weeks		(see footnote)	IPV booster needed for early schedule (i.e. first dose given <8 weeks)
DTP-containing vaccine [4]		6 weeks (min)	3	4 weeks (min) - 8 weeks	4 weeks (min) - 8 weeks		3 Boosters 12-23 months (DTP-containing vaccine); 4-7 years (Td); and 9-15 yrs (Td)	Delayed/ interrupted schedule Combination vaccine; maternal immunization
***Haemophilus influenzae* type b** [5]	**Option 1**	6 weeks (min) 59 months (max)	3	4 weeks (min) with DTP2	4 weeks (min) with DTP3		(see footnote)	Single dose if >12 months of age Not recommended for children > 5 yrs Delayed/ interrupted schedule Co-administration and combination vaccine
	Option 2		2-3	8 weeks (min) if only 2 doses 4 weeks (min) if 3 doses	4 weeks (min) if 3 doses		At least 6 months (min) after last dose	
Pneumococcal (Conjugate) [6]	**Option 1**	6 weeks (min)	3	4 weeks (min)	4 weeks		(see footnote)	Vaccine options Initiate before 6 months of age Co-administration HIV+ and preterm neonates booster
	Option 2	6 weeks (min)	2	8 weeks (min)			9-15 months	
Rotavirus [7]	**Rotarix**	6 weeks (min) with DTP1	2	4 weeks (min) with DTP2				Vaccine options Not recommended if > 24 months old
	Rota Teq	6 weeks (min) with DTP1	3	4 weeks (min) - 10 weeks with DTP2	4 weeks (min) with DTP3			
Measles [8]		9 or 12 months (6 months min, see footnote)	2	4 weeks (min) (see footnote)				Combination vaccine; HIV early vaccination; Pregnancy
Rubella [9]		9 or 12 months with measles containing vaccine	1					Achieve and sustain 80% coverage Combination vaccine and Co-administration; Pregnancy
HPV [10]		As soon as possible from 9 years of age (females only)	2	6 months (min 5 months)				Target 9-14 year old girls; Multi-age cohort vaccination; Pregnancy Older age ≥ 15 years 3 doses HIV and immunocompromised

Refer to http://www.who.int/immunization/documents/positionpapers/ for table & position paper updates.

This table summarizes the WHO vaccination recommendations for children.The ages/intervals cited are for the development of country specific schedules and are not for health workers.

National schedules should be based on local epidemiologic, programmatic, resource & policy considerations. While vaccines are universally recommended, some children may have contraindications to particular vaccines.

Table 3.2 Summary of WHO position papers – recommended routine immunizations for children in specific high-risk areas or high-risk groups

Table 2: Summary of WHO Position Papers - Recommended Routine Immunizations for Children (updated March 2017)

Antigen		Age of 1st Dose	Doses in Primary Series	Interval Between Doses			Booster Dose	Considerations (see footnotes for details)
				1st to 2nd	2nd to 3rd	3rd to 4th		
Recommendations for children residing in certain regions								
Japanese Encephalitis [11]	**Inactivated Vero cell-derived**	6 month	2 generally	4 weeks (generally)				Vaccine options and manufacturer's recommendations; Pregnancy; Immunocompromised
	Live attentuated	8 months	1					
	Live recombinant	9 months	1					
Yellow Fever [12]		9-12 months with measles containing vaccine	1					
Tick-Borne Encephalitis [13]		≥ 1 yr FSME-Immun and Encepur ≥ 3 yrs TBE_Moscow and EnceVir	3	1-3 months FSME-Immun and Encepur 1-7 months TBE-Moscow and EnceVir	5-12 months FSME-Immun and Encepur 12 months TBE-Moscow and EnceVir		At least 1 Every 3 years (see notes)	Definition of high-risk Vaccine options Timing of booster
Recommendations for children in some high-risk populations								
Typhoid [14]	**Vi PS**	2 years (min)	1				Every 3 years	Definition of high risk
	Ty21a	Capsules 5 years (min) (see footnote)	3 or 4 (see footnote)	1 day	1 day	1 day	Every 3-7 years	Definition of high risk
Cholera [15]	**Dukoral (WC-rBS)**	2 years (min)	3 (2-5 years) 2 (≥6 years)	≥ 7 days (min) < 6 weeks (max)	≥ 7 days (min) < 6 weeks (max)		Every 6 months Every 2 years	Minimum age Definition of high risk
	Shanchol and mORCVAX	1 year (min)	2	14 days			After 2 years	
Meningococcal [16]	**MenA conjugate**	9-18 months (5µg)	1					Definition of high risk; Vaccine options; 2 doses if < 9 months with 8 week interval
	MenC conjugate	2-11 months	2	8 weeks			After 1 year	Definition of high risk; Vaccine options
		≥12 months	1					
	Quadrivalent conjugate	9-23 months	2	12 weeks				Definition of high risk; Vaccine options
		≥2 years	1					
Hepatitis A [17]		1 year	At least 1					Level of endemicity; Vaccine options; Definition of high risk groups
Rabies [18]		As required	3	7 days	14-21 days		(see footnote)	Definition of high risk, booster
Dengue (CYD-TDV) [19]		9 years (min)	3	6 months	6 months			Seroprevalence
Recommendations for children receiving vaccinations from immunization programmes with certain characteristics								
Mumps [20]		12-18 months with measles containing vaccine	2	1 month (min) to school entry				Coverage criteria > 80%; Combo vaccine
Seasonal influenza (inactivated tri- and qudri-valent) [21]		6 months (min)	2 (<9 years) 1 (≥ 9 years)	4 weeks			Revaccinate annually: 1 dose only (see footnotes)	Priority risk groups, especially pregnant women Lower dosage for children 6-35 months
Varicella[22]		12-18 months	1-2	4 weeks to 3 months per manufacturer recommendations				Achieve & sustain ≥ 80% coverage Pregnancy Co-admin with other live vaccines

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Each country's needs will differ depending on their situation. Below, a number of options are proposed from which countries could select the best option for their situation.

Option I: Programmatically, it is usually easiest if the three doses of HepB and Hib vaccines are given as a combined formulation in Penta-HepB-Hib vaccine and yellow fever vaccine is given with measles vaccine. This schedule will prevent infections acquired during early childhood, which account for most of the HepB as well as Hib-related disease burden in high-endemic countries, and also will prevent infections acquired later in life. It is also useful in countries where significant births occur outside health facilities. This schedule, however, will not prevent perinatal HepB infections because it does not include a dose of HepB vaccine at birth.

In addition, PCV can be given at the same visit with pentavalent vaccine at 6, 10 and 14 weeks of age; rotavirus vaccine can be given within the same schedule or as a two-dose schedule at 6 and 10 weeks of age depending on the type of vaccine (Rotateq or Rotarix respectively). The recommended target for HPV vaccine is 9–14-year-old girls, while 1–29-year-olds are targeted for meningococcal A vaccine (in preventive campaigns).

Due to significant damage to new born babies by rubella infection more and more countries are planning to shift to measles-rubella (MR) vaccine which will be easily incorporated in current childhood EPI schedules.

Option II: A four-dose schedule in which a birth dose of monovalent HepB vaccine is followed by three doses of a combination vaccine (Penta-HepB-Hib). This option is more costly, and vaccine supply issues may make it less convenient.

The two options above include yellow fever vaccine given at the same time as measles vaccine. The HPV vaccine will, however, require new service delivery platforms to reach adolescent populations as ages are expanded beyond the traditional EPI vaccines schedule.

3.4.4 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-age 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.

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. 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 versus 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 Tool (C4P).

3.4.5 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 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 require a package of interventions, including the promotion and use of oral rehydration salts 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 introduction of Hib, pneumococcal and rotavirus vaccines in developing countries thus provides an excellent opportunity to 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 GAPPD.

Similarly, the introduction of HPV vaccine provides two important opportunities to implement integrated approaches towards disease control and health promotion:

- In developing comprehensive national strategies for the prevention and control of cervical cancer, including cervical cancer screening, treatment and palliative care.
- In providing 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 described in the WHO guidance note "Comprehensive cervical cancer prevention and control: A healthier future for girls and women" (WHO, 2013).

Note: 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.

3.4.6 Selecting the vaccine, presentation and formulation

The characteristics of vaccine products can have a profound impact on immunization programme and costs. The immunization programme should assess the available options for formulation (e.g. combination versus monovalent, lyophilized versus liquid) and presentation (e.g. vial versus pre-filled syringe for injectable vaccines, squeeze tube versus 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 sound decision-making. Rather, an analysis of all the costs, and the advantages and disadvantages of introducing a specific product into the immunization programme should be considered.

Table 3.3 Characteristics of new vaccines

Vaccine	Characteristics	Route of inoculation[a]	Formulation, presentation	Handling procedures	Storage temperature
DPT-HepB-Hib (pentavalent vaccine or Penta)	Hib conjugated vaccine, HepB vaccine DPT (see above)	IM	Liquid; multi-dose/ single-dose vial	Never freeze	+2°C to +8°C
Hib	Conjugated vaccine	IM	Lyophilized or liquid; multi-dose/single-dose vial	Diluents should be refrigerated before mixing with vaccine; Hib liquid vaccine should never be frozen	+2°C to +8°C
HepB	Recombinant vaccine	IM	Liquid; multi-dose/single-dose	Never freeze	+2°C to +8°C
Inactivated polio vaccine (IPV)[b]	Inactivated vaccine	IM	Liquid; prefilled syringes/ multi-dose vial	Never freeze	+2°C to +8°C
Yellow fever	Live attenuated virus vaccine	SC	Lyophilized with diluents; multi-dose/single-dose	Avoid exposure to sunlight; diluent should be refrigerated before mixing with vaccine but never be frozen	+2°C to +8°C or (-20°C)
Rotavirus	Live attenuated virus vaccine	Oral	Lyophilized with diluents or liquid; single-dose plastic tube or applicator	Avoid exposure to sunlight, prefilled syringe and lyophilized vaccine should be refrigerated but never be frozen	+2°C to +8°C
Measles mumps rubella (MMR)	Live attenuated virus vaccine	SC	Lyophilized with diluents; multi-dose/single-dose	Avoid exposure to sunlight; diluents should be refrigerated before mixing with vaccine but never be frozen	+2°C to +8°C or (-20°C)
Measles rubella (MR)	Live attenuated virus vaccine	SC	Lyophilized with diluents; single-dose/ multi-dose	Avoid exposure to sunlight; diluents should be refrigerated prior to mixing with vaccine but never be frozen	+2°C to +8°C or (-20°C)
Pneumococcal	Conjugated vaccine	IM	Liquid; multi-dose/ single-dose prefilled syringes	Never freeze	+2°C to +8°C
Hepatitis B	Live attenuated virus vaccine	IM	Liquid, single-/multi-dose	Never freeze	+2°C to +8°C
Meningococcal A	Conjugated vaccine and polysaccharide	IM	Lyophilized with diluents; multi-dose vial	Diluents should be refrigerated before mixing with vaccine but never be frozen	+2°C to +8°C
Human rabies –Vero cell	Inactivated vaccine	IM	Lyophilized with diluents	Never freeze	+2°C to +8°C
Influenza[c]	Live attenuated virus vaccine	Intranasal	Prefilled syringes	Avoid thawing/freezing	+2°C to +8°C
Influenza[c]	Inactivated vaccine	IM	Multi-dose vial or prefilled syringes	Never freeze	+2°C to +8°C
Human papilloma virus	Recombinant vaccine	IM	Liquid; single and multi-dose vial	Never freeze	+2°C to +8°C

Notes: a: ID – intradermal; IM – intramuscular, SC – subcutaneous.
b: Inactivated IPV vaccine is a trivalent formulation, types 1, 2 and 3.
c: Seasonal influenza vaccine, both inactivated and live attenuated formulations contain a trivalent mix, which may change from year to year.

Temperature sensitivity of selected vaccines: Figure 3.3 illustrates the relative temperature sensitivity across antigens as the same type of vaccine from different manufacturers may have different vaccine vial monitors (VVMs).

3.4.7 Factors influencing the choice of vaccine formulation

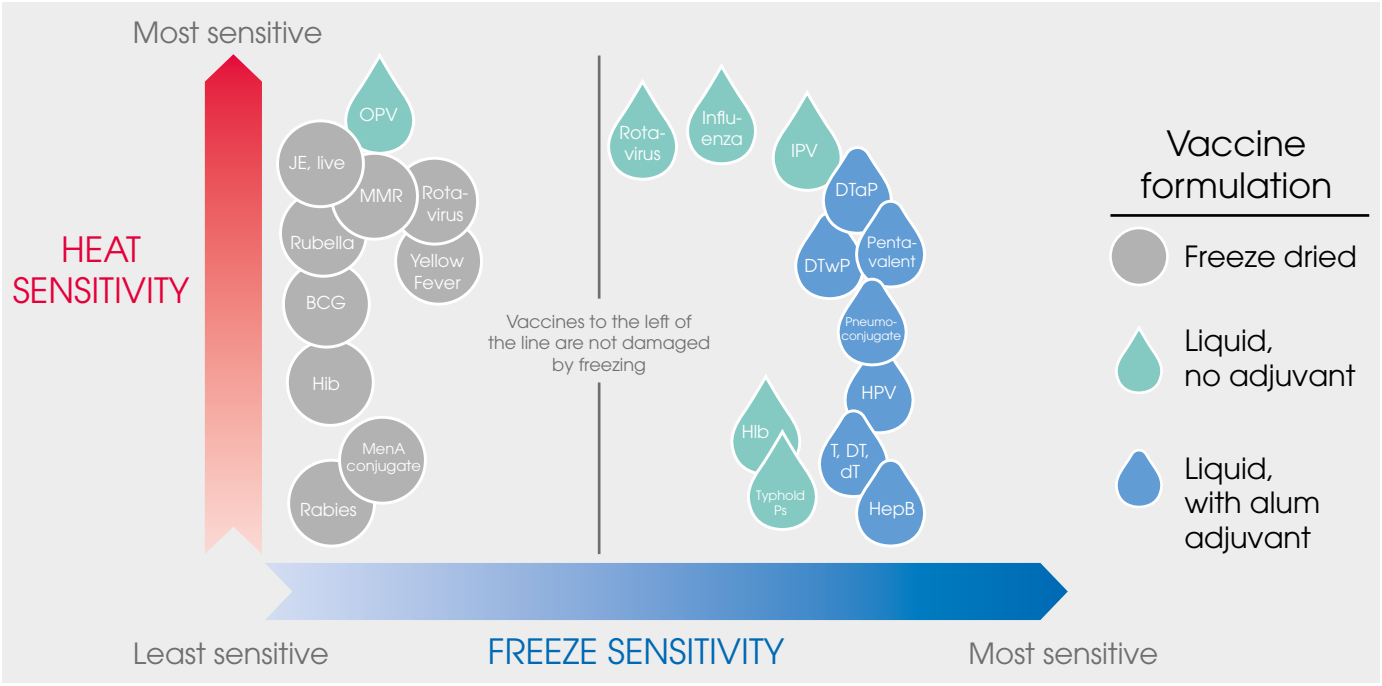
Safety: Product formulations and presentations should be selected that are least likely to result in programmatic errors and that correspond with the training levels and capacities of the health workers providing immunizations. Use of combination vaccines (e.g. DPT-HepB-Hib vaccine) may offer certain programme advantages such as a reduced number of injections required per visit, the number of needles and syringes is reduced for administration and waste disposal and a decrease in the amount of space required for cold chain and dry storage facilities and transportation requirements.

Ease of use: In some situations, the time required to prepare a vaccine is critical, such as during campaigns with long queues 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 AD devices.

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.

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 above, 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 VVM assigned to the product, as it indicates the number of days of stability of the vaccine at 37°C, e.g. a product with a VVM2 is stable for two days at 37°C. This information can be found on the product insert or, for all WHO pre-qualified vaccines, on the WHO website for pre-qualified vaccines. If power outages are frequent or if the vaccine will be used for outreach activities, a more heat-stable vaccine will be preferable.

Figure 3.3 Temperature sensitivity of selected vaccines



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 least freeze sensitive should be selected, if available. The following aspects in selection should be considered:

- flexibility in adding the vaccine to the national immunization schedule
- impact on cold chain capacity
- number of injections per visit
- accine supply security and cost.

3.4.8 Assuring quality and procurement of vaccine and injection supplies

The establishment of international norms and standards for vaccines: WHO's Expert Committee on Biological Standardization 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.

WHO pre-qualification of vaccines: All vaccines procured through the United Nations Children's Fund (UNICEF) (which can include Gavi-supported vaccines), the Pan American Health Organization (PAHO) Revolving Fund and other UN 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 prequalified 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. 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 NIP be WHO pre-qualified.

National regulatory authorities: A 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 NRAs need to perform, depending on the source of the vaccines (see Table 3.4).

Table 3.4 Required functions of national regulatory authorities by source of vaccine

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

*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:

- Issue marketing authorizations and licences for the vaccines, manufacturers and distributors, based on a published set of licensure requirements.
- Conduct post-marketing surveillance, including monitoring of 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.
- Provide 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.
- Regulatory oversight of clinical trials held in the country.

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.

3.4.9 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. Countries can also procure vaccines and safe injection supplies through UNICEF, the PAHO Revolving Fund (for countries in the Americas) or other subregional pooled procurement mechanisms, such as the Gulf Cooperation Council group purchasing programme.

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

Some 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 NIP is ready to introduce the new vaccine, and in selecting the specific product and presentation. 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 RI sessions or in campaigns.

3.4.11 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 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 AD syringes and safety boxes.

The WHO EPI Logistics Forecasting Tool is an Excel tool designed to help NIPs 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. The tool is populated with automatically updated information on volume, transport requirements, amount of waste generated and storage costs for all WHO pre-qualified 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 NIP 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 should include 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.

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. Such strategies have included:

- Shortening the interval between vaccine deliveries from the supplier. For example, if vaccines are received every six months (but no shorter) the volume of vaccine required per shipment will reduce.

- 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 national and provincial levels will be lower. However, this will incur additional transportation costs (for drivers' salaries and per diems, fuel, vehicle maintenance) that must be taken into account.

3.4.12 Updating the logistics management information system

The logistics management information system (or stock management system) (LMIS) 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 – i.e. 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 NIP to trace individual vaccines or batches, in case there are suspected 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 of computerized stock records for vaccines and injection equipment
- vaccine wastage reports
- temperature monitoring and alarm systems (upgrading from instant readers to temperature recorders).

3.4.13 Eligibility for vaccination

When a new vaccine is introduced or is replacing an old vaccine (e.g. pentavalent replacing DTP or IPV replacing OPV), health workers 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 programme 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.

For example, it is recommended that yellow fever vaccine be given at the same time as measles vaccine (9–12 months of age in most countries). However, in case of an outbreak situation, the yellow fever vaccine should be given to all susceptible individuals (depending on the epidemiology of the outbreak) in the population starting from six months of age.

3.5 Determine resource needs

While the addition of a new vaccine can and should be used to strengthen national immunization services, it imposes additional resource requirements, which are important to recognize and budget for from the onset.

3.5.1 Budgeting for new vaccine introduction

Capital and recurrent costs related to the introduction of new vaccines should be estimated and included in the annual immunization budget. Additional capital costs might include investment in cold chain equipment. Recurrent costs include vaccines, AD syringes and needles, training, safe disposal of waste, advocacy/social mobilization, monitoring, supervision and evaluation of the impact of immunization.

3.5.2 Injection equipment

The injection equipment for new vaccines is the same type as that for all other EPI vaccines (except for BCG): 0.5 ml AD syringes are recommended, 2 ml standard disposable syringes for reconstitution and safety boxes.

3.5.3 Cold chain issues

Adding new vaccine to the national immunization schedule will require a thorough assessment of cold chain storage capacity and cold chain procedures at all administrative levels. The impact of adding new vaccines on cold chain storage capacity will vary depending on:

- **Use of monovalent versus combination vaccine:** The use of combination vaccines is likely to have less impact on cold chain storage capacity. For example, storage requirements for multi-dose vials of DPT-HepB vaccine are the same as for vials of Penta vaccine.

- **The vaccine storage and shipping volumes:** WHO standard storage volumes for Penta vaccine are 2.5 cm^3 per dose in 20-dose vials (3.0 cm^3 per dose in 10-dose vials); and the total storage volume for other EPI vaccines (BCG, Penta, measles, OPV and TT) is about 11.0 cm^3 per dose. For comparison, storage volumes for hepatitis B vaccines supplied through UNICEF are shown in Table 3.5.
- **Use of single- versus multi-dose vials:** Use of single-dose vials will increase the need for storage space. For example, if single-dose vials were used instead of 10-dose vials, a three-to-four-fold increase in storage and transport space would be necessary.

Table 3.5 Maximum recommended packed volume per vaccine dose

Vaccine	Source	(cm^3/dose)	Doses per vial packed volume
BCG freeze-dried	WHO	10 or 20	1.2
DPT-HepB	GSK	10	3.0
DPT-HepB-Hib	GSK	2	11.0
DPT-Hib freeze-dried	Aventis Pasteur	10	7.5
DPT-HepB-Hib	GSK	10	5.3
Hib freeze-dried	GSK	1	13
Hib freeze-dried	GSK	2	6
Hib liquid	Chiron	10	12
HepB	GSK	1	9.7
HepB	GSK	2	4.8
HepB	Merck	6	4.5
HepB	GSK	10	4.0
HepB (UNIJECT)	Bio Farma	1	12.0
Measles freeze-dried	Aventis Pasteur	1	26.1
Measles freeze-dried	Serum Institute India	2	13.1
Measles freeze-dried	Serum Institute India	5	5.2
Measles freeze-dried	WHO	10	3.0
Oral polio	WHO	10	2.0
Oral polio	WHO	20	1.1
DT, DTP, TT	WHO	10	3.0
DT, DTP, TT	WHO	20	2.5
Yellow fever	IPVE	2	7.2
Yellow fever	IPVE	5	6.5
Yellow fever	Aventis Pasteur	10	2.5
Yellow fever	Aventis Pasteur	20	1.5
PCV10	GSK	2	4.8
PCV13	Pfizer	1	12.0
Rotavirus (Rotarix liquid)	GSK	1	17.1
Rotavirus (Rotarix)	GSK	1	156.0
Rotavirus (RotaTeq liquid)	Merck	1	46.5
HPV (Cervarix™)	GSK	1	9.7
HPV (Cervarix™)	GSK	2	4.8
HPV (Gardasil)	Merck	1	15.0
MenAfriVac	Serum Institute India	10	2.6

Exercise 2

For all groups.
The Republic of Vaccineland has a total population of 10 million inhabitants with an under-one population of 400 000. The current Penta3 vaccination coverage is 50% and you hope to achieve 75% coverage by the end of first year after the introduction of new vaccines. Your Penta wastage rate is estimated at 30%. The Penta currently used in the programme comes in a 10-dose vial. You plan to introduce the pentavalent vaccine (DTP-HepB-Hib) in 10-dose vials. The nationwide introduction is planned to start at the beginning of January next year (after six months from now).
Using the above information, calculate:

- The vaccine needed (DTP-HepB-Hib) for the first year of introduction.
- The number of AD syringes needed for the pentavalent vaccine.
- The number of safety boxes needed for safe disposal of syringes and needles.

3.6 Revise immunization forms

An important element of integrating new vaccines into NIPs is that EPI forms, personal vaccination records, reporting forms, databases and training materials must be reviewed and revised to accommodate the new vaccines. Depending on the quantity of these materials in stock at the time of introduction, countries may decide to continue the use of the old forms/records and insert the new vaccine manually until all are used up.

3.7 Estimate new vaccine requirements

The method of estimating vaccine requirement for new vaccines is the same as those for other childhood vaccines such as Penta (see Module 8: Vaccine management). See the following example:

Step 1: If your annual target for immunization is 500 000 children under one year and if you are ordering DPT-HepB-Hib (pentavalent) vaccine in 10-dose vials, the following formula is applied:

Number of infants x Number of doses (500 000 x 3) = 1 500 000 doses

Step 2: The buffer stock quantity needs to be added. Usually this is estimated to be 25–50% of your total requirement and it is done only once, with your first order. Therefore, the total vaccine requirement is:

1 500 000 x 0.25 + 1 500 000 = (375 000 + 1 500 000) = 1 875 000 doses.

Step 3: You also need to take in consideration your wastage rate. Suppose your wastage is known to be 20% for your Penta. To estimate the quantity of vaccine needed to adjust for the wastage, first calculate the wastage factor: 100/100-20 = 1.25. Next, the total number of vaccine calculated in step 2 should be multiplied by the wastage factor: 1 875 000 x 1.25 = 2 343 750 doses. This is the total number of doses of the DPT-HepB-Hib vaccine that is needed for the year. The number of vials needed is calculated by dividing the total doses by the vial size (10 in this case). Therefore, number of vials needed is:

2 343 750/10 = 234 374 vials

Step 4: The projected coverage should also be taken into account. For example, if you judge that the best that you can do is attain only 85% coverage, then you need only 85% of the total doses estimated above:

2 343 750 x 0.85 = 1 992 187 doses of vaccines

Exercise 3

For all groups.
You are the EPI manager of the Republic of Vaccineland. Your government has decided to introduce a new vaccine (PCV) into the RI programme. You have been asked to develop an introduction plan. The last programme review took place five years ago, and below is the basic information from the review.

Service delivery

- The national DTP3 coverage was 60%, but in half of rural districts the coverage was <50%.
- Outreach services were irregular and infrequent in remote districts.
- Standard disposable needles and syringes were used for all vaccination injections. 80% of staff reported needle sticks injuries in the previous 12 months.
- 75% of injections observed were done with sterile needles.
- 50% of health facilities burned and buried used injection materials, 25% disposed of used materials in opened dumpsites, and other 25% used incinerators to dispose of used injection materials.

Logistics

- The EPI review also revealed that 98% of health facilities had a refrigerator; 85% of the refrigerators were in good working condition and almost all the refrigerators were used for vaccine storage only.
- The average age of the refrigerators was 7.5 years.
- The overall strengths of the cold chain remain somewhat questionable, but the system had sufficient capacity for at least one additional vaccine.

Vaccine management

- Findings of the review showed that stock management was very poor at all levels.
- Based on the consumption rate, the estimated quantity of measles vaccine in the country was adequate for 40 months, but the vaccine would expire in 12 months.
- There were sufficient supplies of all other vaccines for 8–25 months.
- 50% of rural health facilities reported at least two DTP stock-outs in the previous six months, each lasting for about four weeks.
- Vaccine wastage rate for DTP (10-dose vial) was estimated at 40%. Vaccine wastage was not monitored routinely.
- Open vial policy was not implemented in many health facilities and outreach sites.

The MOH and the ICC are in support of the introduction. They have requested you to come up with a realistic plan for the introduction of the new vaccine.

Task 1: Explain the process followed by the country for the decision to introduce the new vaccine.

Task 2: Outline the key activities you will undertake to develop a realistic introduction plan.

Task 3: If you choose to do a situation analysis, list the components of EPI you would give special attention to and provide reasons for your choice.

Task 4: Form small working groups to prepare various components of the plan and present the consolidated plan to the plenary session.

4. Implementing a new vaccine introduction plan

As mentioned in the previous section, the introduction of a new vaccine into the NIP should be used as an opportunity to strengthen existing RI services. When a new vaccine is introduced, plans should be made regarding specific immunization service components that need to be improved and measurable indicators should be established to monitor progress towards strengthening them. Key issues that need to be addressed as countries introduce new vaccines are outlined in this section.

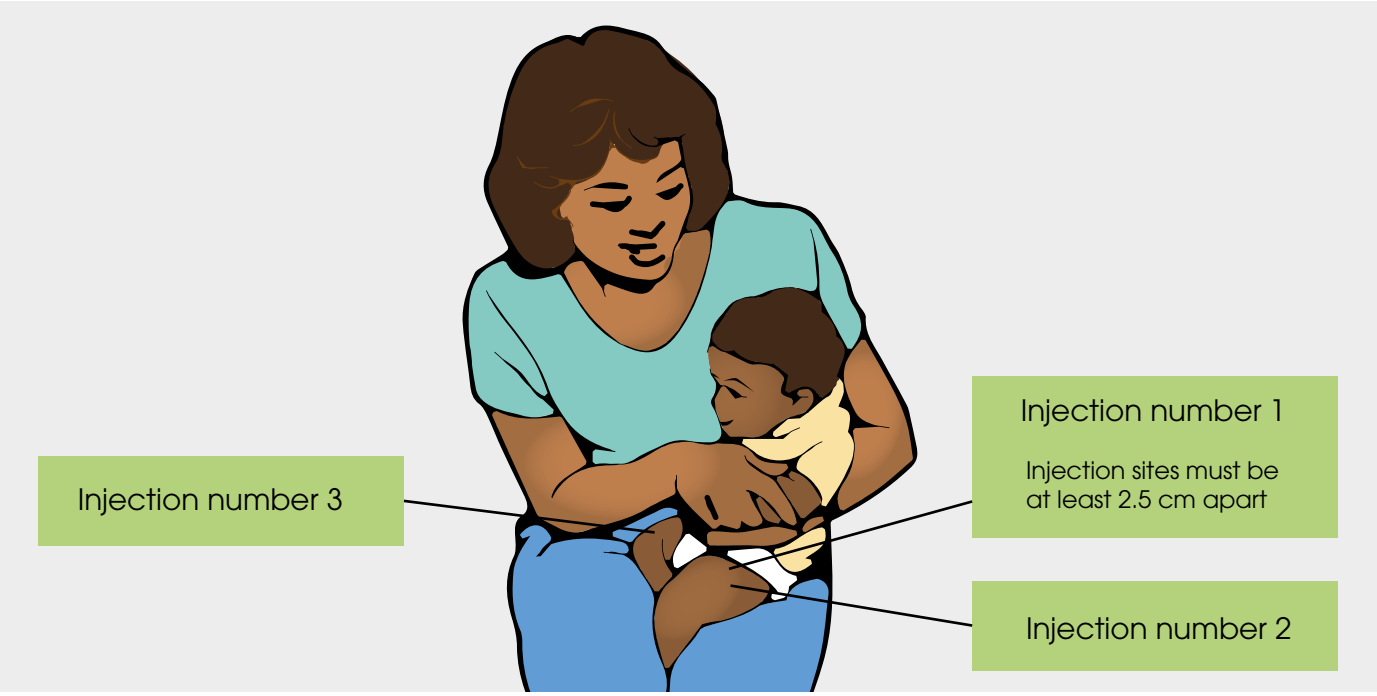
4.1 WHO opened multi-dose vial policy (revised in 2014)

All opened WHO-prequalified multi-dose vials of vaccines should be discarded at the end of the immunization session, or within six hours of opening, whichever comes first, unless the vaccine meets all four of the criteria listed below. If the vaccine meets the four criteria, the opened vial can be kept and used for up to 28 days after opening. The criteria are as follows:

1. The vaccine is currently prequalified by WHO.
2. The vaccine is approved for use for up to 28 days after opening the vial, as determined by WHO.
3. The expiry date of the vaccine has not passed.
4. The vaccine vial has been, and will continue to be, stored at WHO- or manufacturer-recommended temperatures; furthermore, the vaccine vial monitor, if one is attached, is visible on the vaccine label and is not past its discard point, and the vaccine has not been damaged by freezing.

For vaccines that are not prequalified by WHO, independent determinations on preservative efficacy, sterility, presentation and stability may not have been made by a functional NRA Consequently, this could mean that the vaccine does not meet WHO requirements on safety and efficacy, which form the minimum recommended standard for keeping multi-dose vaccine vials opened for more than six hours. Therefore, WHO recommends using non-WHO-prequalified vaccines as soon as possible after opening, and respecting the time limit for using opened vials as indicated by the manufacturer's instructions in the package insert. If this information is not indicated in the package insert, WHO recommends discarding all non-WHO-prequalified vaccine products within six hours after opening or at the end of the immunization session, whichever comes first.

Figure 4.1 Injection sites for multiple injections



4.2 Vaccine administration

Pentavalent (DPT-HepB-Hib), PCV, MenAfriVac, HPV vaccines are given by intramuscular injection in the anterolateral aspect of the thigh (infants) or deltoid muscle (older children). These vaccines can be given safely at the same time as other vaccines (e.g. DTP-HepB-Hib can be given with PCV, rotavirus, measles, OPV and yellow fever vaccines). If two injectable vaccines are given on the same day, it is preferable to give them in different limbs/arms. Measles and yellow fever vaccines are administered subcutaneously. Rotavirus vaccine is administered orally (refer to Table 3.3).

The following practices should be avoided when administering injectable vaccines:

- These vaccines SHOULD NOT be administered into the buttock because of the risk of injury to the sciatic nerve. In addition, this route of administration has been associated with decreased hepatitis B vaccine immunogenicity, presumably because of mistaken or accidental subcutaneous injection or injection into deep fat tissue.
- These vaccines SHOULD NOT be administered intradermally because this route of administration does not produce an adequate antibody response in children.
- These vaccines SHOULD NOT be mixed in the same syringe with other vaccines unless specifically recommended by the manufacturer.

Note: The standard paediatric dose for all these vaccines is 0.5 ml (rotavirus vaccine comes in 1 dose per vial of 1 ml).

4.3 Precautions to prevent freezing of vaccine

- Some vaccines including DTP, hepatitis B, Hib, PCV and rotavirus vaccines, are destroyed or inactivated by freezing. Therefore, storage and shipping procedures to prevent freezing of these vaccines should be assessed at all levels of the cold chain.

- At each level of vaccine distribution, ice packs should be kept at room temperature for 5 to 10 minutes (until beads of water are present on the ice packs) before putting them in the vaccine carrier or cold box.

- A barrier of insulating material should be placed between the ice packs and the vaccine, both along the sides of the container and over the top.

- These precautions should be taken at all levels of the cold chain, and they are particularly important at higher levels, where chest freezers are capable of freezing ice packs to -20°C, and where greater numbers of vials could be affected.

- Freeze watch indicators should be included in all international and, ideally, in all in-country vaccine shipments.

4.3.1 The shake test

If it is suspected that pentavalent or PCV vaccines were frozen, you need to conduct a shake test as follows:

1. Prepare a frozen control sample: Take a vial of vaccine of the same type and batch number as the vaccine you want to test, and from the same manufacturer. Freeze the vial until the contents are solid, (at least 10 hours at -10°C) and then let it thaw. This vial is the control sample. Mark the vial clearly so that it is easily identifiable and will not be used by mistake.

2. Choose a test sample: Take a vial(s) of vaccine from the batch(es) that you suspect has been frozen. This is the test sample.

3. Shake the control and test samples: Hold the control sample and the test sample together in one hand and shake vigorously for 10–15 seconds.

4. Allow to rest: Leave both vials to rest.

5. Compare the vials: View both vials against the light to compare the sedimentation rate. If the test sample shows a much slower sedimentation rate than the control sample, the test sample has most probably **NOT BEEN FROZEN** and can be used. If the sedimentation rate is similar and the test sample contains flakes, the vial has probably been damaged by freezing and **SHOULD NOT BE USED**. Note that some vials have large labels which conceal the vial contents. This makes it difficult to see the sedimentation process. In such cases, turn the sample and reference vials upside down and observe sedimentation taking place in the neck of the vial.

6. If the test procedure indicates that the test sample has been damaged by freezing, you should notify your supervisor immediately. Standard operating procedures should then be followed to ensure that all damaged vaccine is identified and that none of this damaged vaccine is distributed to the intermediate stores or vaccinators.

4.4 Contraindications

The new vaccines, whether in combination or monovalent form, are very safe. However, there are few contraindications that health workers need to be aware of, namely:

- history of evolving neurologic disease;
- history of convulsions immediately following previous administration of a particular antigen;
- a child with symptomatic HIV infection should not be given yellow fever vaccine (also BCG); and
- a child with asymptomatic HIV infection should not be given BCG vaccine as following vaccination they can develop generalized BCG infection.

4.5 Adverse events following immunization (AEFI)

An AEFI is a medical incident that takes place after an immunization and is believed to be caused by the immunization. Although modern vaccines are safe, no vaccine is entirely without risk. After immunization, some people experience reactions ranging from mild local reactions to life-threatening illnesses. In some cases, these reactions are caused by the vaccine; in others, they are caused by an error in the administration of the vaccine; and in others, there is no causal relationship. The causes of AEFIs can be categorized as follows:

1. Nature of the vaccine: This refers to the vaccine's properties or an individual body's reaction to the vaccine itself. Typical non-significant reactions to vaccines include fever which subsides after some time, redness or swelling at the injection site, and rash. Carers should be reassured that they are not serious and need no special treatment. A child can be given paracetamol to reduce the fever. If, however, pus appears at the site of the injection a week or more after the injection, the caregiver should report to the nearest health facility. In rare cases, however, convulsions may happen associated with an elevated fever. This is a rare complication and mostly associated with the pertussis component of the DPT-HepB-Hib vaccine. These transient signs/symptoms usually start within one day after the vaccine is given (except abscesses) and last from one to three days. When given at the same time as DTP, the rate of fever is no higher than when Penta alone is given. Administration of hepatitis B vaccine soon after birth has not been associated with an increased rate of elevated fever.

2. Programme errors: an error in handling, reconstitution or administration of the vaccine. A programme or programmatic error is usually person-based rather than vaccine. Programme errors, which can be prevented, are usually the cause of an AEFI. Now that mass campaigns may include injectable vaccines such as pentavalent vaccine, measles or meningococcal vaccine, additional precautions must be taken to ensure that the campaigns are conducted safely and adverse events are kept to a minimum. An abscess at the vaccination site is the most frequent AEFI episode appearing a week or more after the injection. It can generally be prevented through proper staff training and an adequate supply and proper use of safe injection equipment. A regular supervision will greatly contribute to the reduction of this unwanted phenomenon.

3. Coincidental: When there is no causal association between the immunization and the medical condition of the child or woman. The latter just coincides with immunization. Children in the immunization age group may have symptoms unrelated to immunization due to common infections at the time of vaccination. Sometimes illness appears to be more frequent following vaccination due to parental concern or more intense observation after immunization.

4. Unknown cause: Sometimes the cause of AEFI remains undiscovered. With increased quality of investigations, most of the unknown causes probably will be classified in one of the above three categories.

All immunization programmes should monitor at least the following AEFIs:

- all injection site abscesses;
- all cases of lymphadenitis;
- all deaths that are thought by health workers, or the public, to be related to immunization; and
- all cases requiring hospitalization that are thought by health workers, or the public, to be related to immunization.

These categories of AEFIs are sometimes called trigger events because their presence stimulates or triggers a response. For the credibility of immunization services introducing new vaccines, the EPI manager must ensure that AEFI detection, investigation and analysis lead to action. Actions include: treatment of the affected person/s, correction of programme errors if any, communication with the community, and research.

Side-effects do not constitute contraindications for vaccination, including administration of new vaccines!!

All serious AEFI suspected to be associated with any vaccination should be reported to the EPI supervisor and then to the EPI Unit at the MOH by filling out the appropriate AEFI form. When applicable, a full-scale investigation should be instituted (refer to Module 9: *Immunization safety*).

Policies and procedures should be instituted to monitor AEFIs.

4.6 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 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. 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 (WHO, 2014).

4.7 Training health workers for introduction of new vaccines

Health-care providers are responsible for handling and administering the vaccine. In addition, they are a major source of information about new vaccines for parents and the general public. To fulfil this role, health workers must be trained to assume that role.

4.7.1 Issues to consider for training programmes

- **Timing:** What is the most appropriate time to train personnel to achieve the best results (months before the introduction, weeks before, continue training during the introduction)? Timing may differ for the various target groups.
- **Training materials:** All EPI training materials should be updated as soon as possible to include information about the disease being targeted and new vaccines.
- **Pre-service training:** It is a long-term investment to update the curricula of training institutions by including information on new vaccines.
- **Opportunities for training:** Every opportunity should be used to train and retrain health-care staff. Possible training opportunities include distribution of supplements to EPI training manuals, regular staff meetings, in-service training workshops and distribution of newsletters and professional journals.

4.7.2 Target groups and key areas of emphasis in the training for new vaccine introduction

Target groups and topics to be covered when conducting training activities prior or during introduction of new vaccines include the following:

Target groups for training	Topics to be covered during training
EPI staff and focal points at central and subnational level	Modes of transmission of the target diseases and who is at risk of becoming infected (the target groups for immunization) Efficacy of the new vaccines Limitations of the vaccines (some new vaccines need injection of several doses to build up a solid protection against the diseases, some vaccine offer protection against only one cause of a syndrome and will not for example prevent all causes of diarrhoea or pneumonia) How to use the introduction of the new vaccines to strengthen the national RI programme Monitoring and evaluation methods regarding the introduction of new vaccines in the programme
Logisticians/logistic officers	How to handle the vaccines, vaccine wastage, cold chain requirements, implementation of the opened vial policy etc.
Health personnel at central, regional, provincial, district and health facility levels	The vaccination schedule, including the importance of administering the complete vaccine series to provide long-term protection How to administer vaccines: recording and reporting requirements Side-effects and safety of the vaccine Safe injection practices How to address and communicate with communities and, specifically, mothers about the new vaccines How to address misconceptions about the new vaccines
Researchers and trainers in training and research institutions	Information on new vaccines Efficacy of the new vaccines Role of sentinel surveillance in monitoring vaccine efficacy and programme impact
National regulatory authority officials	New vaccines, their properties and licensure by WHO/UNICEF
Community health workers, traditional birth attendants	How to address and communicate with communities and, specifically, mothers about the new vaccines How to address misconceptions about the new vaccines
General public	General knowledge on disease burden targeted for immunization with new vaccines Vaccines as life-saving products for children and other target groups

4.8 Research and development

The last century was, in many respects, the century of treatment, resulting in dramatic reductions in morbidity and mortality, with the discovery and use of antibiotics as one of the biggest agents of change in health. This century promises to be the century of vaccines, with the potential to eradicate, eliminate or control a number of serious, life-threatening or debilitating infectious diseases, and with immunization at the core of preventive strategies.

The GVAP has been approved by WHO Member States to guide their efforts in reaching the "Decade of Vaccines" goals; one of them specifically calling countries and their partners to "develop and introduce new and improved vaccines and technologies". Based on this goal, the GVAP reiterates existing goals and proposes six strategic objectives:

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.

The last objective is the one that is closely related to the content of this module. This objective will lead to improved institutional and technical capacity to manufacture vaccines and/or carry out related clinical trials and operational and organizational research. Other areas of innovative research under this objective will include:

- Identification of mechanisms of protection and pathogenesis.
- Well-defined and novel antigenic targets for development of new vaccines.
- Development of bio-processing, formulation, manufacturing and delivery technologies for new and improved vaccines.
- Development of disease-burden and cost-effectiveness data for in-country decision-making.

5. Advocacy and communication for introducing new vaccines

When a new idea is being introduced, it may bring an element of uncertainty and some degree of resistance. The situation analysis may have identified factors that relate to uncertainties at individual, family, community and country level. These should then be used to plan appropriate communication input. Refer to Module 3: *Communication and community involvement for immunization programmes* for details.

5.1 Assessing communication gaps

When introducing new vaccines, many communication gaps may need to be addressed. Such gaps may include lack of knowledge about:

- the new vaccine – its effectiveness and safety
- the diseases that can be prevented by the vaccine
- how the vaccine is administered
- potential AEFI and their management.

5.2 Targeting communication messages

Once the communication gaps are identified, it is necessary to define the target groups towards whom the communication activities will be directed. Not all the groups need to receive the same information. Careful targeting of essential messages will have a greater impact than providing multiple messages to everyone. There follow some messages specifically targeted for certain groups.

5.2.1 Decision-makers (ministries of health/finance/economic affairs, political leaders at different levels)

Inform them about the cost, safety and benefits to the country by having this vaccine in the NIP, as well as the intended geographic/administrative area coverage. Make use of available information/research on the economic burden of non-vaccination in the advocacy messages.

Key messages:

- The available vaccine is safe and effective and is in use in many other countries.
- The introduction of a new vaccine is an opportunity to strengthen national EPI.
- The new vaccines are costly compared with present EPI vaccines. However, the diseases prevented and lives saved far outweigh the cost of the vaccines.
- National funding is of major importance to sustain the availability and benefits of new vaccines in the long-term, as childhood immunization is an investment for the future.
- Introduction of new vaccines will enhance the image of the government.
- New vaccine introduction will contribute to reducing under-five deaths and achieve SDG 3.

Exercise 4

Working individually, list at least three major communication gaps related to new vaccine introduction that may be relevant in your area.
1.
2.
3.

Make a plan for filling those gaps. Use the following format for presentation:

Communication gaps	Planned activities	Indicators	Timeline	Responsible person	Projected budget	Remarks

5.2.2 Health workers, medical professional societies/ organizations)

Communication should centre on the diseases that can be prevented and the effectiveness and safety of the new vaccines. The proper management and care of the new vaccines in the EPI system should be highlighted. Other information to relay is the target group for immunization (dose, injection site, reconstitution techniques etc.), and potential AEFI with and their management. Other preventive measures at household level such as breastfeeding, nutrition and hygiene (for pneumococcal and rotavirus infections) and the importance of completion of the vaccination schedule to reduce drop-out rates (DOR) should be covered.

Key messages:

- More antigens can be delivered with fewer injections with the combination vaccines.
- Some vaccines offer protection against only one cause of a syndrome and will not prevent all causes of diarrhoea or pneumonia.
- Freezing is the most important cold chain issue. Never freeze or use freezed pentavalent and pneumococcal vaccines.
- The new vaccines, either as monovalent or in combination, do not cause more adverse events than traditional vaccines.
- The schedule of the new vaccines can easily be fitted within existing routine EPI schedules.
- Injection safety and injection waste management are important parts of EPI.
- Introduction of a new vaccine is an opportunity to strengthen routine programmes.

5.2.3 Parents/caregivers and the public (NGOs, community level social networks)

Communication should centre on the advantages of giving another injection at the same visit, efficacy and safety of the new vaccines and the new target diseases burden for children and the family.

Key messages:

- Pneumococcal and Hib infections cause dangerous diseases that can kill many children through infection of the lungs (pneumonia) or the brain (meningitis).
- Hepatitis B infection in childhood kills people later in adult life.
- In yellow fever endemic countries, many who are not vaccinated are at risk of dying from the disease.
- Rotavirus is a major cause of severe diarrhoea which can be prevented by vaccination.
- HPV vaccine can prevent against cervical cancer.
- Combination vaccines give more protection to children without additional injections or an extra visit to the health clinic.
- The new vaccines are effective and safe and are used in many countries globally.

5.2.4 Media personnel

Communications aimed at the media should focus on the advantages and safety aspects of the new vaccines, their use in other countries of the region and world and the reasons why the vaccine is being introduced in the country. It should cover the steps the health system is taking to ensure that no undue adverse events occur, especially due to programme errors. The role of the media in raising awareness on the benefits of the new vaccines should be emphasized.

Key messages:

- Pneumonia, meningitis, diarrhoea, cervical cancer, chronic liver disease and liver cancer are major public health problems, of which a large fraction can be prevented by vaccines.
- With the introduction of combination vaccines, there is opportunity now to provide more protection without additional injections.
- New technologies such as AD syringes are introduced to enhance injection safety.
- The new vaccines are safe and effective.
- Although these vaccines are called new, they have been in use in industrialized countries for decades.
- Due to their cost, most developing countries could not afford to introduce them until now.
- Yellow fever vaccine, though widely available, is still under-utilized.
- Along with vaccination, other preventive measures to be observed at household level should be implemented such as nutrition, breastfeeding and hygiene.

Exercise 5

Role play on dealing with rumours.
A country has introduced a new vaccine. An article has appeared in a local newspaper claiming that the new vaccine is actually a new product in development that is now being tested on children in that country. Following this article, all sorts of rumours start going around about the recently introduced vaccine, despite extensive communication efforts carried out at all vaccination centres. The national radio aired daily spot messages about the vaccine for one week before and after the initiative was launched: at least one TV spot was made and broadcast. A poster (unfortunately in English only) was made and widely distributed; immunization slogans and information about the new vaccine were printed on T-shirts and distributed. UNICEF contributed US$ 40 000 to support the government's communication campaign.

The minister of health is concerned and has convened a meeting of the key stakeholders to discuss this issue further. The following officials attended this meeting:

- Minister of health
- Director of health services
- WHO representative
- UNICEF representative
- National EPI programme manager
- National cold chain and logistics manager.

Task 1: Identify potential negative impact of the above article on the vaccination campaign in which a new vaccine has been used.

Task 2: Detail a coherent strategy and plan to combat such rumours to ensure a smooth continuum of the ongoing campaign and continued political commitment towards EPI.

Task 3: List possible strategies to prevent the occurrence of such rumours in the future.

Task 4: Discuss how to address rumours at the community level.

5.3 Conducting advocacy and communication activities

The introduction of new vaccines and technologies can provide an opportunity to improve overall services and re-motivate health staff as well as build public demand for RI. The communication strategy should be appropriate to the characteristics of the new vaccines or technologies and should be included in the introduction plans as well as the timelines for preparation, launch, implementation and monitoring (including the pre- and post-introduction evaluations). There is the need to develop and test basic messages for the public based on target audience analysis in order to assure them that the immunization service is now improved because it offers protection against more diseases. In addition, the messages should emphasize that these vaccines are highly effective and have only minor side-effects. Many of the new vaccines are linked with existing RI schedules to ensure that children receive more protection early in life.

Health workers need to understand the details regarding the new vaccines and corresponding diseases, so that they are convinced of the new vaccines' importance and can respond knowledgeably to questions from the public.

The plan for communication activities should include:

- Advocacy and communication targets/ participants.
- A timeframe for the proposed activities.
- Responsible persons for carrying out the various tasks.
- Tools and materials (posters, flip charts, radio/ TV spots etc.).
- Budgetary and other resource requirements.
- Indicators for monitoring communication component (refer to Module 3: *Communication and community involvement for immunization programmes*).

Every effort should be made to launch new vaccines successfully in a way that boosts demand and utilization of RI services.

6. Monitoring and evaluation of new vaccine introduction activities

6.1 Monitoring vaccine coverage

Monitoring new vaccine coverage should be incorporated into the routine EPI monitoring system as soon as the vaccine is introduced. Preparations for new vaccine introduction should include updating of monitoring tools before introduction of the new vaccines. With the addition of a new vaccine to the routine childhood vaccination schedule, a fully immunized child (FIC) will now be defined as a child under one year of age with all doses of the new and the traditional EPI vaccines.

Programme managers should monitor new vaccine coverage closely, especially during the first few years after introduction, to ensure that coverage levels of new and traditional vaccines are comparable. Vaccination coverage can be monitored using both routine service statistics and special coverage surveys. For calculation of coverage rates of any new vaccines use the following formula:

[Number of doses administered/Number of children under 1 year of age] x 100 = Vaccination coverage (%)

6.2 Monitoring vaccine wastage

Since most new vaccines are more expensive than the traditional EPI vaccines, it is important to monitor the wastage of these vaccines and to develop and implement strategies to reduce wastage. Strategies to reduce wastage include:

- Careful planning of vaccine ordering and distribution (calculations need to be made of requirements for single- and multi-dose vial at each level).
- Implementation of WHO's opened vial policy. This policy does not apply to the current PCV two-dose vaccine which comes without preservative. Therefore, an opened vial of that vaccine must be discarded at the end of the vaccination session or six hours after opening or whichever comes first.
- Appropriate use of single- and multi-dose vials (vaccine vial size should be considered for different set-ups).
- Careful maintenance of the cold chain. Maintenance should be carried out at all levels to prevent wastage due to cold chain failure. A cold chain technician should be engaged at central, provincial and district levels.

6.3 Coverage surveys

Vaccine coverage surveys are important to validate coverage estimates based on service statistics and to provide additional information needed to assess and improve programme performance. These can be done using WHO methodology on immunization cluster surveys (see Module 17: *Conducting immunization coverage survey* and the revised *WHO Vaccination coverage cluster surveys: Reference manual*).

6.4 Drop-out rates

Drop-out rates (DOR) greatly affect vaccination coverage and should be monitored routinely. At health facility and district levels drop-out rates for the new vaccines can be monitored using the monitoring chart (see Module 5: *Increasing immunization coverage*). The calculation for dropout between the first and last doses (such as Penta1 and Penta3) should be done for traditional and new vaccines. The following formula is used to calculate the drop-out rate:

[Penta1 - Penta3/Penta1] x 100 = % DOR

If new vaccines are to be administered according to the same schedule (such as PCV or rotavirus vaccine with pentavalent vaccine), their drop-out rates should be comparable. If the difference is more than 5% then an investigation should be initiated.

6.5 Post-introduction evaluation

WHO recommends that all countries which have introduced a new vaccine should evaluate the programmatic impact on their vaccination system. A post-introduction evaluation (PIE) tool was designed to assist immunization managers in countries that have introduced a new or under-utilized vaccine to provide a systematic method for evaluating the implementation of the introduction, and its impact on the existing immunization system. The PIE is normally conducted 6–12 months following the new vaccine introduction. The PIE will allow early identification and correction of problems associated with the introduction of the new vaccine. The experience gained in the process of PEI can be used in future when the country decides to introduce another new vaccine into the child immunization schedule.

The PIE is conducted by using questionnaires, checklists, observation of practices and desk review of reports and various recording forms. The evaluation covers all levels of the health system associated with reception, storing, distributing and administration of the new vaccine (from central level to health facility level). Specifically, data are collected on 10 principal areas:

1. Planning an introduction
2. Coverage by new vaccines, drop-out rates, recording and reporting procedures
3. Cold chain management
4. Vaccine management, distribution and logistics
5. Monitoring and supervision systems
6. Training and knowledge of health workers about new vaccines
7. Vaccine safety and waste management
8. Adverse events following immunization
9. Vaccine wastage rates
10. Advocacy, communication and acceptance by communities.

A reference manual for conducting PIE is available (New Vaccine Post-Introduction Evaluation (PIE) Tool, WHO).

6.6 Measuring the impact of new and under-utilized vaccines introduction

6.6.1 Impact of hepatitis B immunization programmes

Since the main disease burden of HBV infection takes place much later in life, it is difficult to measure it in children. However, in addition to vaccine coverage, the most reliable way to measure the impact of hepatitis B immunization programme is to conduct seroprevalence studies among young children. In particular, the prevalence of total HBV infections (anti-HepBc or anti-HepBs) and chronic HBV infection (HBsAg) in unimmunized age cohorts (e.g. among school children) can be measured in an operational area before programme implementation.

For comparison, similar information can be collected on fully and partially immunized children in the same age group after hepatitis B vaccine is introduced. If age-specific seroprevalence data are not available from children before the programme is implemented, a study can be conducted to compare the prevalence of HBV infection among older unvaccinated children with the prevalence of infection among younger children born after the programme was introduced. Because passively transferred maternal antibodies can be detected up to 12–15 months of age the lower age limit for seroprevalence studies should be two years.

6.6.2 Impact of Hib vaccination

The best method of evaluating the impact of Hib vaccination is to set up a sentinel surveillance system that can measure the number of cases of Hib meningitis. If possible, the surveillance would be in place one to two years prior to vaccine introduction to obtain baseline rates of the disease. For this, a laboratory where Hib bacteria can be cultured is necessary. If such a laboratory already exists, using the WHO Rapid Assessment Tool, a baseline rate of Hib meningitis can be estimated. In subsequent years, following the introduction of Hib vaccine, the rate of Hib meningitis can be compared with the baseline data to assess the impact of Hib vaccination.

6.6.3 Impact of yellow fever vaccination

Surveillance to capture the number of yellow fever cases and deaths should form the basis of evaluating the impact of yellow fever vaccination.

6.6.4 Impact of pneumococcal and rotavirus vaccination

Sentinel laboratory-based surveillance to monitor the trends in pneumococcal and rotavirus disease burden are useful for evaluation of the impact of vaccination.

6.6.5 Impact of human papilloma virus vaccination

Countries should consider establishing sentinel surveillance to monitor the impact of vaccination on the prevalence of HPV types, the incidence of cervical abnormalities and precancerous lesions, the incidence of and mortality from invasive cancer, and the incidence of ano-genital warts. However, measuring the impact of vaccination on precancerous lesions and cervical cancer will require monitoring for decades.

6.6.7 Impact of meningococcal A vaccination

Implementation of mass immunization campaigns has contributed to control of major group A and C epidemics throughout the world. However, in many areas additional work is needed to develop the surveillance and response

capacity necessary for early identification of outbreaks and immunization of population at risk rapidly enough to yield maximum impact from the intervention. According to the current mode of delivery – campaigns involving 1–29-year-old groups with one dose of vaccine, will provide protection for at least 10 years. Based on experience gained from other conjugate vaccines (e.g. Hib), the meningococcal conjugate vaccines may be expected to provide high level of protection following completion of the three-dose course in infants.

Exercise 6 – Case study

At the end of the exercise participants should have discussed and evaluated the options for introducing new vaccines. The participants are divided into four groups.

OPTION 1: The desire of the authorities to introduce the new vaccine is so strong that they have decided to cover the entire country from the first year with new vaccines.

Task for Group 1 – discuss:
Advantages and disadvantages of nationwide introduction of new vaccines.
Which new vaccines to consider as a priority for introduction?
Resources needed for introduction and their source.

Task for Group 2 – discuss:
Steps to be taken to initiate the introduction.
Logistical requirements for introduction.
Changes in communication strategies to maximize community participation and support for introduction.

OPTION 2: Authorities have reservations regarding the nationwide introduction of new vaccines and push for phased introduction of new vaccines starting with some regions of the country.

Task for Group 3 – discuss:
Advantages and disadvantages of a phased introduction of new vaccines.
Priority activities for phase 1.
Activities for other phases to complete the introduction of targeted vaccines.

Task for Group 4 – discuss:
Develop indicators for monitoring and evaluation of the introduction process for Option 1 and Option 2.

Task 5: In turn, each of the four groups should discuss the strengths and weaknesses of each option and show their comparative advantages. In a plenary session groups should make their presentations of their findings from considering the two different options.

6.6.8 Measuring progress regarding the sixth strategic objective of GVAP

The sixth strategic objective of GVAP ("Country, regional and global research and development innovations maximize the benefits of immunization") is closely related to the content of this module. This objective will lead to improved institutional and technical capacity to manufacture vaccines and/or carry out related clinical trials and operational and organizational research. Other areas of innovative research under this objective include:

- Identification of mechanisms of protection and pathogenesis.
- Well-defined and novel antigenic targets for development of new vaccines.
- Development of bio-processing, formulation, manufacturing and delivery technologies for new and improved vaccines.
- Development of disease-burden and cost-effectiveness data for in-country decision-making.

The implementation of the GVAP strategic objectives will be closely monitored using specific indicators for each of them. For measuring progress specifically regarding the sixth strategic objective, the five indicators in Table 6.1 will be used.

Table 6.1 Indicators for measuring GVAP's sixth strategic objective

Indicator	Content	Operational definition
Indicator 6.1	Progress towards development of HIV, TB and malaria vaccines	Number of HIV, TB and malaria vaccine clinical trials assessing clinical efficacy completed and with results reported
Indicator 6.2	Progress towards a universal influenza vaccine	Number of influenza clinical trials assessing clinically the breadth of protection completed and reported
Indicator 6.3	Progress towards institutional and technical capacity carry out vaccine clinical trials	Number of countries per WHO region having reported conduct of a vaccine clinical trials that meet quality standards
Indicator 6.4	Vaccines that have either been re-licensed or licensed for use in a controlled-temperature chain at temperatures above the traditional +2°C to +8°C range	Number of vaccines re-licensed or licensed
Indicator 6.5	Number of vaccine delivery technologies (devices and equipment) that have received WHO pre-qualification against the 2010 baseline	Four categories of equipment would be tracked: • refrigerators and freezers • cold boxes and vaccine carriers • coolant packs • temperature monitoring devices

Exercise 7 – Sixth strategic objective of GVAP

For all groups.
Review your background document on GVAP. Discuss in the group the sixth strategic objective on research and development of innovations and review the list of indicators for measuring progress. Answer to the following question:
What is actually being or can be done in the countries of your group regarding each specific indicator?
Present your deliberations to the plenary using the table below.

Indicators	What is being done?	What else can be done?
1. Progress towards development of HIV, TB and malaria vaccines		
2. Progress towards a universal influenza vaccine		
3. Progress towards institutional and technical capacity carry out vaccine clinical trials		
4. Vaccines that have either been re-licensed or licensed for use in a controlled-temperature chain at temperatures above the traditional +2°C to +8°C range		
5. Number of vaccine delivery technologies (devices and equipment) that have received WHO pre-qualification against the 2010 baseline		

Recommended reading

WHO (2008). Implementing the Reaching Every District approach: A guide for district health management teams. Regional Office for Africa: World Health Organization. Available at: http://www.who.int/immunization/programmes_systems/service_delivery/AFRO-RED_Aug2008.pdf (accessed 5 December 2016).

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WHO – Immunization, Vaccines and Biologicals (Cervical Cancer Prevention and Control Costing Tool – C4P):
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WHO – Immunization, Vaccines and Biologicals (EPI Logistics Forecasting Tool):
http://www.who.int/immunization/programmes_systems/supply_chain/resources/tools/en/index4.html

WHO – Immunization, Vaccines and Biologicals (Immunization coverage):
http://www.who.int/immunization/monitoring_surveillance/routine/coverage/en/index2.html

WHO – Immunization, Vaccines and Biologicals (New Vaccine Post-Introduction Evaluation (PIE) Tool):
http://apps.who.int/iris/bitstream/10665/70436/1/WHO_IVB_10.03_eng.pdf

WHO – Immunization, Vaccines and Biologicals (School Vaccination Readiness Assessment Tool):
http://apps.who.int/iris/bitstream/10665/90566/1/WHO_IVB_13.02_eng.pdf?ua=1&ua=1

WHO – Immunization, Vaccines and Biologicals (Working to increase vaccine price transparency):
http://www.who.int/vaccines-diseases/epitraining

World Health Organization

REGIONAL OFFICE FOR Africa

http://www.afro.who.int/