Regional Consultation to standardize EPI schedule
in the Eastern Mediterranean Region of the World Health Organization

WHO EMRO, Cairo, 16-18 October 2006

Background: There is remarkable diversity in the Expanded Program Immunization (EPI) vaccination schedule among Member States in the Eastern Mediterranean Region of the World Health Organization. In May 2006, the Regional Technical Advisory Group for (RTAG) for EPI in the EMR reviewed vaccination schedules being used by Member States in the EMR and concluded that not all schedules were optimized for disease reduction among infants. In addition, the RTAG noted that many EPI programs did not extend their vaccination schedule beyond the first 12 months of life and wanted to provide guidance to Member States on expansion of the EPI schedule beyond the first 12 months of life in line with the Global VS strategy.

To ensure maximized benefits from the EPI program, the RTAG recommended that the regional office organize a consultation to advise Member States on a standardized EPI schedule in the region. The TORs for the consultation were to:

• Review vaccination schedules of all Member States.
• Review available data on optimal schedule for routine and new EPI vaccines
• Review vaccination schedules beyond the first year of life.
• Develop standardized schedule for EMRO region including recommended vaccines beyond the first year of life

The consultation was held in October 2006 with a panel of experts from WHO and various academic institutions (Appendix 1). This report summarizes the results of the consultation which was organized around the vaccination schedule at various stages of life (Appendices 2,3,4). The group agreed to some general principals related to the EPI schedule including:

a. beginning and completing the series as early in life as possible
b. choosing a schedule with maximal efficacy and fewest possible visits
c. selecting a schedule that was programmatically feasible to maximize coverage without impacting efficacy

INFANT IMMUNIZATION SCHEDULE

1. BCG
   a. Background
      TB is an important public health problem in the EMR. Most countries remain highly endemic. Currently, 20 countries provide BCG vaccine at birth or within the first 2 months of life. One country provides a second dose of BCG at 6 years of age.

      The signs and symptoms of TB vary significantly with age, the immune status of the patient and with stage of disease. In most patients, pulmonary disease is predominant but *Mycobacterium tuberculosis* (Mt) may affect any organ. Following inhalation of *Mt* bacterial growth in the alveoli initiates a local inflammatory response. In most patients, this primary asymptomatic infection is self-limiting and localized leaving the patient unaware of the infection. However,
Mtb may spread from the site of primary infection by lymph and blood to other parts of the body. In some instances, especially in young children, hematogenous spread may result in severe pulmonary disease including miliary TB and TB meningitis.

b. **Vaccine efficacy:**
BCG vaccine was first used in humans in 1921 and introduced in the WHO Expanded Program on Immunization in 1974. Current vaccine strains are derived from the original isolate of *M. bovis* developed by Calmette and Guerin in the early part of the last century. Numerous passages of the original strain has resulted in diversity of BCG strains showing phenotypic and genotypic differences. In order to prevent further deviation from the original BCG strain, lyophilized seed lots of vaccine strains have been maintained by WHO since 1956. A number of vaccine strains are available; the French Pasteur strain 1173 P2, the Danish strain 1331, the Glaxo strain 1077, and Tokyo strain 172 account for 90% of BCG utilization worldwide. No strain is demonstrably better than another and there is no global consensus on which strain is optimal for general use.

In countries with high TB disease burden, numerous studies have demonstrated that BCG vaccine provides protection against meningitis and disseminated TB in children (). These studies also indicate that BCG does not prevent the establishment of primary infection or reactivation of latent TB, the later condition being the main source of TB spread in a community. WHO recommends intradermal administration of vaccine in the deltoid region of the upper arm using a syringe and needle (). The number of bacilli per dose is vaccine-strain dependent, varying with bacillary virulence and the number of live bacilli. Newborn vaccines normally receive half the dose given to older children.

c. **Recommended schedule:**
Use of BCG vaccine was briefly discussed during the consultation and there was agreement to follow WHO recommendations for routine use in EPI. Available data on BCG vaccine indicate that vaccine effectiveness indicates that BCG should be administered as soon as possible after birth and before 1 month of age to provide maximum protection. There is no demonstrated benefit of giving BCG vaccine after 12 months of age or giving booster doses of vaccine ()

2. **DTP/OPV/Hib/Hep B (core schedule):**
a. **Background:**
There is remarkable diversity in the core schedule for DTP, OPV and Hib in the EMR (Figure 1). Generally, there was consensus that programs should attempt to Approximately half of the countries are using the WHO recommended schedule of 6,10 and 14 weeks for DTP vaccine; 9 countries are using a 2,4,6 month schedule. Eleven countries are using a combined DTP containing vaccine including 7 countries using pentavalent vaccine, 3 using DTP-Hib and 1 country using a DTP-Hep B combination vaccine. Seventeen countries provide a birth dose of OPV.
b. Vaccine efficacy

The efficacy of DTP vaccines has been the subject of considerable research since development of a combined vaccine in 1948. DTP vaccine contains core component of diphtheria and tetanus toxoid, and whole cell pertussis. Numerous studies have demonstrated good vaccine efficacy, however there has been a long history of concern about vaccine safety due to reactogenicity of the pertussis component. In 1996, less reactogenic acellular vaccines were licensed and introduced in many countries. Vaccine efficacy studies demonstrate all whole cell and acellular vaccines are more efficacious than placebo against pertussis. Whole cell vaccines have shown variable efficacy with a range from 37% to 92% (Jefferson T, Vaccine ‘03). The efficacy of one and two component acellular vaccines range from 67 to 70% compared with vaccines that have >= 3 components with an efficacy of 80-84%. Generally, vaccine efficacy studies do not warrant preferential use of acellular versus whole cell vaccines.

Early studies documented the minimum acceptable interval between doses is 1 month (4 weeks) (). Three doses of DTwP (or DTaP), and OPV (or IPV) are required to ensure optimal protection against these diseases in the first year of life (). Since 3 doses are also required for maximal protection against hep B and most formulations of Hib vaccine, many countries have developed schedules to offer simultaneous administration of these vaccines with DTP or use of combination vaccines containing these antigens.

Figure 1. DTP/OPV* Schedule in EMRO, 2005

* 17 countries are giving a birth dose of OPV
2 countries using IPV
Initiation of the post-neonatal vaccine series of DTP (and Hib) vaccines should begin by 6 weeks to 2 months of age to begin protecting infants as they enter a period of increasing risk for these vaccine preventable diseases. There is no additional benefit of giving a dose of these vaccines before 6 weeks of age. Administration of a birth dose of pertussis vaccine resulted in decreased antibody titers to pertussis toxin at 9 months of age (Baraff).

Several studies suggest that the optimal spacing between doses to maximize immune response for the core schedule is 2 months. Immunogenicity studies of DTaP-HBV-IPV+Hib vaccine in a schedule at 6,10, and 14 weeks of age demonstrated decreased response to the Hib component (anti-PRP) at 14 weeks of age (Figure 2). Numerous studies with hep B vaccine demonstrate that longer intervals between the 2nd and 3rd dose of vaccine result in higher antibody titer results. While schedules with minimal intervals (eg 6,10,14 weeks) have documented similar seroconversion rates compared to schedules with longer intervals, immunogenicity studies demonstrate reduction in geometric mean antibody titers among infants vaccinated with minimal intervals.

Figure 2. Percent of Infants with Protective Antibody at 14 Weeks of Age After HBV at Birth and 2 Doses of DTaP-HBV-IPV+Hib, at 6 & 10 Wks: Moldova

110

Percent SP

0 25 50 75 100

Anti-diphtheria Anti-tetanus Anti-HBs Anti-polio type 1 Anti-polio type 2 Anti-polio type 3 Anti-PRP
c. Recommended schedule Based on the ideal spacing between doses of at least 2 months for optimal immune response and the sub-optimal response to Hib when given at 10 and 14 weeks the consultative group recommended a core DTP schedule of 2, 4, 6 months of age.

3. Polio Vaccine

Consultation on EPI schedule, EMRO, October 2006, VPI/EMRO, 3/20/2008
a. **Background:**
The EMR has made considerable success in the global efforts to eradicate polio. However, polio remains endemic in two countries (Pakistan and Afghanistan) and several countries have experienced importation of disease since achieving eradication.

b. **Vaccine efficacy**
Development and use of polio vaccine highlights one of the most important scientific achievements of the 20th century. In the mid 1950s, an inactivated formulation of polio vaccine (Salk) vaccine was licensed and widely used in developed countries until the development of a live attenuated oral vaccine in the 1960s. This Sabin vaccine was quickly shown to be highly effective leading to substantial reductions in polio cases after vaccine licensure. Cuba was one of the first countries to document interruption of wild polio virus circulation through mass campaigns that were conducted in 1962. Wide scale use of OPV resulted in substantial disease reduction in developed countries followed by introduction into the national immunization programs of developing countries in the following decade. Three doses of OPV are highly effective in eliciting a protective immune response to polio virus infection. In controlled trials, 95% to 100% of infants develop antibodies to polio virus after 3 doses of polio vaccine.

c. **Recommendations**
Since there is considerable population movement between endemic and non-endemic countries throughout the region, recommendations for use of polio vaccine are on the premise that all countries are at high risk for importation of disease. To provide protection to polio as early in life as possible, a birth dose of polio vaccine is recommended followed by 3 doses of vaccine that should be given simultaneously with other infant vaccines (Appendix 2). To ensure long-term protection, booster doses are recommended at 18 months, and 4 to 6 years of age.

4. **Measles, mumps and rubella vaccines:**
   a. **Background**
   All countries provide measles vaccine in their EPI program. The RTAG has made previous recommendations for use of measles vaccine including routine use of a 2 dose schedule and providing the first dose of vaccine at 12 months of age (for countries with low levels of measles virus transmission). Despite these recommendations, twelve countries, including many that achieved low levels of transmission, provide the first dose of vaccine at 9 months of age (Figure 3). Twenty programs provide 2 doses of measles vaccine including 19 countries that have a 2 dose schedule and 1 country that use periodic supplementary immunization campaigns to provide the second dose of measles vaccine. Fifteen countries are using a combined MMR vaccine including 8 countries that are giving 2 doses of MMR, 6 countries that are giving a single dose of MMR for the second dose of measles and 1 country that is using a dose schedule of MR followed by MMR.
b. Measles Vaccine efficacy

Measles vaccines were first developed after isolation and propagation of measles virus in tissue culture in 1954. The Edmonston strain, named after the patient from whom the virus was isolated, was initially used for many of the vaccines developed worldwide. The Moraten and Schwarz strains were derived from the Edmonston strains in the 1960s and have become the predominant used in vaccine preparations worldwide. The immune to measles vaccination is similar in almost aspects to that noted after natural infection.

A number of host factors may be responsible for primary vaccine failure including the presence of maternal antibody. Passively acquired maternal antibody may neutralize vaccine virus before a complete immune response develops. Early in the clinical evaluation of measles vaccines, it was recognized that maternal antibody interfered with seroconversion and the only 60 to 70% of infants < 9 months of age seroconverted after measles vaccine. Thus, vaccines were licensed to be given at 9 months of age in the early 1960s. Experience with vaccine given at 9 months of age also demonstrated accumulation of susceptibles over time occurrence of outbreaks among vaccinated cohorts and controlled trials demonstrated 86% of infants seroconverted at 9 months of age compared to 97% of infants who were vaccinated at 12 months of age (1).

The age of measles vaccination must balance 1) the earliest age at which high rates of seroconversion can be achieved and 2) the age group with the greatest
risk of severe infection and death. Since children < 1 year of age are at high risk of complications and death due to measles virus infection, early vaccination is indicated in settings with high rates of disease transmission in these age groups.

c. Mumps vaccine efficacy

Shortly after isolation of mumps virus, attempts were made to develop attenuated vaccines. There are several vaccine strains used worldwide. Generally vaccine efficacy studies demonstrate high seroprotection (>95% protection) after a single dose of mumps vaccine in controlled trials. However, field efficacy studies have demonstrated somewhat lower levels of protection. More recently, studies on long-term protection suggest decreased efficacy over time.

Due to frequent outbreaks among countries that introduced MMR vaccine, the EMR regional office conducted a consultation on use of mumps vaccine in the EMR in 2005. During this consultation, the experience mumps vaccine among Member States revealed was reviewed. Several countries using a single dose schedule of MMR vaccine in their EPI program experienced outbreaks among vaccinated cohorts ~ 10-15 years post-vaccine introduction (Figure 4). The most recent outbreak with > 10,000 cases was reported from the West Bank in Palestine.

![Figure 4. Mumps in UAE 1988-2003](image_url)

Recent outbreaks in the US and England are similar to the experience in the EMR suggesting that countries will experience a significant accumulation of susceptible populations and outbreaks after introduction of a single dose of mumps vaccine.
d. Rubella vaccine efficacy
Several rubella vaccines were developed after isolation of virus in tissue culture. Generally, vaccine efficacy studies demonstrate that all currently licensed strains are highly efficacious after a single dose of rubella vaccine. Rubella vaccine is administered with measles vaccine in all member states.

e. Recommended schedule
The expert panel recommended 2 doses of measles vaccine. The recommended age for measles vaccination depends on the local measles epidemiology as well as on programmatic considerations. Due to well-documented evidence of improved immune response, the first dose of measles should be given at 12 months of life. In countries with high attack rates and serious disease among infants early vaccination at 9 months of age is recommended. The second dose of measles should be provided as early in life as possible with a recommended schedule at 18 months of life. However, program managers may choose to offer the second dose of measles vaccine at 4-6 years of age if higher coverage can be achieved through school-based immunization programs.

For countries that have introduced a combined MMR vaccine, the group recommended a 2 dose schedule beginning at 12 months of age with the second dose at 18 months.

5. Hep B vaccine:
a. Background
Hepatitis B virus infection is a leading cause of deaths caused by vaccine preventable diseases worldwide. The adverse outcomes of HBV infection occur among patients who develop chronic HBV infection. It is estimated that 15-25% of persons with chronic HBV infection develop chronic liver disease and/or hepatocellular carcinoma during their lifetime. Thus, the goal of hep B immunization program is to reduce the prevalence of chronic HBV infection among cohorts of children targeted for immunization.

The risk of developing chronic HBV infection varies with age and is highest (~90%) among infants who are infected at birth. Serologic studies indicate ~ 2% to 7% of pregnant women in the EMR have serologic evidence of chronic HBV infection through detection of hepatitis B surface antigen. Infants born to HBsAg-positive women are at high risk of HBV infection at birth. Prevention of perinatal HBV transmission is a high priority for programs that have introduced hep B vaccine into their childhood immunization schedule. Even in countries where the prevalence of chronic HBV infection among pregnant women is low, it is estimated that 25% of chronic infections are acquired through perinatal HBV transmission. In many countries, the prevalence of HBsAg among pregnant women varies considerably by geographic region with some areas having high prevalence and others a low prevalence. In addition, many countries in the EMR have large immigrant populations from countries with high prevalence of HBsAg among women of childbearing age.

Overall, 21 countries have introduced hep B vaccine into their EPI program. Due to low routine coverage, Somalia has not yet introduced hep B vaccine into their EPI program. To prevent perinatal HBV transmission, ten countries provide a birth dose of hep B vaccine. Most countries have elected to provide hep B
vaccine simultaneously with DTP including four countries that are using a combined hep B, DTP, Hib (pentavalent vaccine). One country provides regular booster doses of vaccine.

b. **Vaccine efficacy**
Three doses of hep B vaccine is highly efficacious in preventing HBV infection. Perinatal HBV transmission can be prevented through administration of the first dose of hep B vaccine within the first 24 hours of life with completion of the series by 6 months of age. There are 2 principal strategies to prevent perinatal HBV transmission including screening of pregnant women for HBsAg and providing prophylaxis to infants born to HBsAg-positive women. This is a challenging strategy, particularly ensuring all pregnant women are screened and that screening results are available to providers caring for infants. To ensure that all infants are protected, many countries have elected to provide a birth dose of hep B vaccine to all infants with follow-up doses through the routine EPI schedule.

c. **Recommended schedule**
To protect all infants from perinatal HBV transmission and provide protection in life as early as possible, a birth dose of hep B vaccine is recommended for all infants. Follow-up doses are recommended at 2 and 6 months of age. EPI programs using a 3-dose schedule with a combined hep B vaccine can provide 4 doses (including the birth dose) as part of the routine schedule. Long-term studies suggest that protection after hep B immunization is long-lasting; there are no recommendations to provide a booster dose of hep B vaccine.

**CATCH-UP IMMUNIZATION SCHEDULE**

6. **Background**
The panel of experts made recommendations for catch-up immunization of children who do receive vaccine according to the recommended schedule (Appendix 3). These recommendations were based on accelerated schedules to provide protection as quickly as possible.

a. **Recommended schedule**
The catch-up schedule was based on the minimum intervals between doses, the minimum age for the first dose of vaccine, and indications for vaccination based on age of the recipient.

**IMMUNIZATION SCHEDULE AFTER 12 MONTHS OF LIFE**
The panel of experts recommended development of a routine vaccination visits at 18 months, 4 to 6 years, 11 to 12 years of age and adults at various ages of life.

7. **Diphtheria, Pertussis, and Tetanus**
   a. **Background**
   Long-term protection and antibody kinetic studies indicate the need for booster doses to provide long-term protection against diphtheria, pertussis, and tetanus. The best evidence supporting the need of diphtheria booster doses are the large scale outbreaks among older age groups that have occurred in countries that do not provide booster doses beyond the first 12 months of life. Protection from the primary series appears to be long-lasting but not life-long (Table 1).
Immunity to tetanus has been the subject of considerable research since vaccine introduction. After a primary immunization series antibody titers decrease over time requiring booster doses to maintain protective levels of antibody (Figure 5). A recent review by the WHO expert panel for immunization recommended a lifelong schedule of 5 doses. The primary series of 3 doses of DTP3 (DTwP or DTaP) should be given in infancy (age <1 year), with a booster dose of a tetanus toxoid-containing vaccine ideally at age 4-7 years and another booster in adolescence, e.g. at age 12-15 years.

Numerous studies have documented the need for booster doses of pertussis vaccine. Immunity from whole-cell pertussis vaccines declines 6-10 yrs after vaccination highlighting the need for booster doses at school-entry and early adolescence.

Table 1. Persistence of Diphtheria Antitoxin Antibodies >0.01 Au/mL by Years after 3 Dose Primary Series Without Booster Doses

<table>
<thead>
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<th>1-2</th>
<th>5-7</th>
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</table>

b. Recommendations
To provide protection as early in life as possible and maintain high levels of protective antibody to tetanus, the panel recommended booster doses of DTP at 18 months and 4 to 6 years of age. Countries using DT at school entry are encouraged to switch to DTP to provide long-term protection for pertussis.

8. Hib vaccine
Background
The need for booster doses of Hib vaccine has been the subject of considerable study and debate. Studies in the UK have documented a increase in rates of Hib disease among children 1 to 4 years of age who do not receive a booster dose of vaccine (Figure 6). However, there was a concomitant change in the EPI schedule with introduction of acellular pertussis vaccine co-incident with documented increase in Hib diseases. It has been repeatedly observed that mixing Haemophilus influenzae type b (Hib) conjugate vaccines with acellular pertussis-containing vaccines (diphtheria-tetanus-acellular pertussis [DTPa]) results in a reduced magnitude of the anti-polyriboseribitolphosphate antibody response compared to that obtained when Hib vaccines were administered separately and not mixed. Thus, the need for booster doses may be related to the type and formulation of Hib vaccine provided to infants. The epidemiology of Hib disease suggests that disease is rare/absent among normal children > 5 years of age. Antibody kinetic studies indicate that a single booster dose of Hib vaccine at 18 months of life will provide long-term protection beyond the age of 5 years.

Figure 5. Response to Immunisation – Profile of Antitoxin Levels Following Either 2,3,4 Months or 2,4,6 Months

9. ADOLESCENT IMMUNIZATIONS

a. Background
There are several reasons to justify the establishment of an adolescent immunization visit in the EMR. Many EPI programs have not provided booster doses of tetanus and diphtheria vaccines in early childhood. In addition, many children may have received only a single dose of measles or mumps vaccines. There are a few countries where hepatitis B vaccine has recently been introduced into the EPI program and older children have not received any doses of vaccine. Screening of children at the age of 11 to 12 years during an adolescent immunization visit provides an opportunity to vaccinate those children who were not fully immunized and accelerate control of these diseases.

b. Recommendations

Adolescent immunization visit
To ensure that all adolescents are protected from vaccine preventable diseases, the panel recommended the establishment of an adolescent immunization visit at 11 to 12 years of age. During this visit, vaccine histories should be reviewed. Children who have not received routine EPI vaccines should receive catch-up vaccines according the schedule outlined in Appendix 4.

Tetanus and diphtheria
Adolescents and adults with uncertain histories of a complete vaccination history with diphtheria, and tetanus toxoid containing vaccines should be given 3 doses of Td. Administer the first 2 doses at least 4 weeks apart and the third dose 6-12
months after the second doses. Adolescents and adults who have completed a primary series and whose last vaccination was > 10 years previously should be given a booster dose of vaccine. If a woman is pregnant and received the last Td > 10 years previously, administer the Td in the second or third trimester; if the person received the last Td < 10 years, administer Tdap during the post-partum period (see below).

**Pertussis vaccination:** The experience of many countries indicates that waning immunity from childhood immunization creates susceptibility and pertussis disease in adults. The use of Tdap has been limited due high cost and limited supplies. If available, Tdap should replace a single dose of Td for adults aged < 65 years who have not previously received a dose of Tdap (either in a primary series, as a booster, or for wound management). A one-time administration of Tdap with an interval as short as 2 years from previous Td vaccination is recommended for post-partum women, close contacts of infants < 12 months of age, and all health care workers with direct patient contact.

**Rubella:** Programs that have included rubella vaccine into their EPI schedule should ensure that all adolescents have received at least 1 dose of rubella vaccine and women of childbearing age are immune to rubella. If susceptibility profiles suggest susceptibility among WCBA, efforts should be made to provide 1 dose of rubella vaccine. Vaccine should be offered at any opportunity including pre-marital health visits, pre-employment health visits, school and university-based vaccination programs, routine health care visits, or through supplementary immunization activities. Pregnant women should not be vaccinated with rubella vaccine but can be offered vaccine in the post-partum period.

**Measles:** Adolescents who have not received 2 doses of measles vaccine should be vaccinated. In countries where epidemiologic data suggest susceptibility among adults, strategies should be developed to provide a single dose of measles vaccine.

**Mumps:** Programs that have included mumps vaccine into their EPI program should ensure that adolescents are vaccinated with 2 doses of mumps vaccine. In countries where epidemiologic data suggest susceptibility among adults, strategies should be developed to provide a single dose of mumps vaccine.

**Hepatitis B:** Countries that have included hep B vaccine into their EPI program should consider catch-up vaccination of adolescents who have not been previously vaccinated. In countries where local epidemiologic data exists, hep B vaccine should offered to high risk groups. Special efforts should be made to vaccinate health care professionals prior to training in a clinical setting.

10. **ADULT IMMUNIZATION**
   
   **a. Background:**
   
   Adult immunization programs are not well-established in the EMR. While the epidemiology of many vaccine preventable diseases in adults has not been well-characterized in the EMR, studies in the EURO and PAHO regions have documented substantial morbidity and mortality associated with seasonal influenza and invasive pneumococcal disease. Other diseases of concern include influenza, hepatitis B virus infection and meningococcal disease among high risk groups. Seasonal influenza can cause substantial morbidity and mortality among persons with asthma, chronic metabolic disease, diabetes mellitus, renal dysfunction, hemoglobinopathies or immunosuppression caused either by medication or HIV infection. Several studies have documented high frequency of needlestick injuries and HBV infection among health care workers in the EMR.
b. **Recommendations**

**Influenza:** Persons with the following chronic medical conditions should be offered influenza vaccine annually: cardiovascular and pulmonary disease including asthma, chronic metabolic disease, diabetes mellitus, renal dysfunction, hemoglobinopathies or immunosuppression caused either by medication or HIV infection. Persons with any condition that compromise respiratory function should also be vaccinated including persons with spinal cord injuries, cognitive dysfunction, and neuromuscular disorders. Other groups recommended for immunization include health care workers, and employees in long-term care facilities, residents of long-term care facilities, persons likely to transmit influenza to persons at high risk of severe disease and anyone who wants to receive influenza vaccine.

**Pneumococcal polysaccharide vaccine:** *Medical indications:* chronic disorders of the pulmonary system excluding asthma; cardiovascular diseases, diabetes mellitus, chronic liver disease, chronic renal failure or nephritic syndrome, functional or anatomic asplenia; immunosuppressive conditions (eg HIV infection, leukemia, lymphoma, multiple myeloma, Hodgkin disease, generalized malignancy, or organ/bone marrow transplant recipient). For persons > 65 years, one-time revaccination if they were vaccinated > 5 years previously and were aged < 65 at the time of primary vaccination. Other groups recommended to receive pneumococcal vaccine include residents of long-term care facilities and nursing homes. High risk groups and persons > 65 should be revaccinated every 5 years.

**Meningococcal polysaccharide vaccine:** Vaccination with quadrivalent meningitis vaccine (MPSV4) is required by the government of Saudi Arabia for all travelers to Mecca during the annual Hajj. Other groups recommended for vaccination vary by country and may include students living in dormitory housing, military recruits and persons living in the meningitis belt. Revaccination may be indicated after 5 years.

**Inactivated polio vaccine:** Adults at high risk of exposure to wild polio virus (eg laboratory workers) should be vaccinated with IPV
Appendix 1

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### Appendix 2
WHO EASTERN MEDITERRANEAN REGION

#### Recommended Early Childhood Immunization Schedule, 2007

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Birth</th>
<th>2 months</th>
<th>4 months</th>
<th>6 months</th>
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</table>

1. Age at vaccination: Age refers to the number of completed months of age, for example 2 months means the end of 2 months (~8 weeks)
2. BCG vaccine:
   - At birth: as soon as possible after birth within 1 month to provide maximum protection.
   - BCG is of no demonstrated benefit after 12 months of age. Use of BCG vaccine above the age of 12 months and booster doses should be stopped.
   - At a certain level of TB prevalence in the country, BCG immunization is not recommended (see vaccine position paper on TB control)
3. DTP vaccination schedule:
   - DTP vaccine: refers to DTwP or DTaP or DTwP/DTaP containing combo vaccines
   - Countries currently having other schedule and unable to switch immediately to the afore mentioned schedule, might continue temporarily-following their current schedule provided that the first dose is not given before the age of 6 weeks and that a 4 weeks minimum interval between the successive doses is respected.
   - Booster doses: 2 booster doses are needed during this period of life (the 1st to boost immunity against tetanus and the second against Pertussis). However, if there is budget limitation and inability of providing the 2 doses, at least 1 dose should be provided (the timing will depend on the country programme feasibility.)
· Countries currently providing booster DT vaccine at school entry (4-6 years) should switch to DTP to enhance protection against Pertussis.

4. OPV:
   · The birth dose is highly recommended for endemic countries and those with high risk of importation.
   · Endemic countries and those with high risk of importation should consider using the 12 months contact to provide an additional dose of OPV.

5. HepB vaccine
   · Birth dose: Mono-valent HepB vaccine should be given as soon as possible after birth, maximum within 24 hours.
   · To ensure early protection in life, the 3-dose series should be completed by 6 months of age.
   · For countries that are using HepB containing combo vaccine, they can provide additional dose of HepB with DTP2.

6. Hib vaccine
   · Booster dose (4th dose) of Hib vaccine is recommended if local epidemiological data support its importance. Available information suggests that a 4th dose of Hib vaccine should be considered in countries using DTaP-Hib vaccine and/or using accelerated schedule (with 4 weeks interval between the first three doses).

7. New vaccines:
   · This recommended vaccination schedule will be periodically revised to accommodate any new vaccine, once the vaccine is available and recommended for use by WHO.
   · the epidemiological information on disease burden is available and information on the optimum schedule of the vaccine is available and affordable.

8. MMR:
   · Countries that have not been able to reduce measles transmission among infants should provide the first dose of measles vaccine at 9 months of age.
   · Countries providing only one dose of rubella vaccine should give it with the first dose of measles.
   · Countries with a mumps elimination goal should provide two doses before the age of 6 years.
   · Second measles dose should be preferably given during the second year of life; however it can be delayed to 4-6 years for programmatic reasons (higher coverage)
Appendix 3
WHO EASTERN MEDITERRANEAN REGION
Recommended immunization schedule
for children who start late or who are more than 1 month behind

The table below gives catch-up schedules and minimum intervals between doses for children who have delayed immunization. There is no need to restart a vaccine series regardless of the time that has elapsed between doses. Use the chart appropriate for the child's age.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Minimum age for dose 1</th>
<th>Minimum Interval Between Doses</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dose 1 to Dose 2</td>
<td>Dose 2 to Dose 3</td>
<td>Dose 3 to Dose 4</td>
</tr>
<tr>
<td>BCG¹</td>
<td>Birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diphtheria, Tetanus, Pertussis</td>
<td>6 weeks</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>6 months</td>
<td>6 months²</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>6 weeks</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B³</td>
<td>Birth</td>
<td>4 weeks</td>
<td>8 weeks</td>
<td>(and 16 weeks after first dose)</td>
<td></td>
</tr>
<tr>
<td>Measles, Mumps, Rubella</td>
<td>12 months</td>
<td>4 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus Influenzae b⁴</td>
<td>6 weeks</td>
<td># 4 weeks: if first dose given at age &lt; 12 months. # No further dose needed if first dose given at age &gt;= 12 months</td>
<td># 4 weeks: if current age &lt; 12 months. # 8 weeks (as final dose) if current age &gt; 12 months and second dose at age &lt;12 months. # No further dose needed if previous dose at age &gt;= 12 months</td>
<td>8 weeks (as final dose). This dose only necessary for aged 12 months-5 years who received 3 doses before age 12 months</td>
<td></td>
</tr>
</tbody>
</table>

1. BCG: administer one dose to all children of less than 12 month of age that have not received a previous dose.
2. DTP: the 5th dose is not necessary if the 4th dose was administered after the 4th birthday.
3. HepB: Administer the 3-dose series to all children and adolescents < 19 years of age if they were not previously vaccinated.
4. Hib vaccine is not generally recommended for children aged >= 5 years.
## Appendix 4

### WHO EASTERN MEDITERRANEAN REGION

**Recommended Vaccination Schedule for Adolescents and Adults**

### Adolescent and Adult Immunization Table

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age in years</th>
<th>11-12 Years</th>
<th>15-49</th>
<th>50-64</th>
<th>&gt; 65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetanus/diphtheria, pertussis (Td, Tdap)</td>
<td>Td</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rubella*</td>
<td>Check vaccination status and refer to catch-up schedule for children who have not received primary series</td>
<td>WCBA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mumps*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hep B'</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza*</td>
<td>High risk groups (1 dose annually)</td>
<td>1 dose annually</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal polysaccharide vaccine*</td>
<td>High risk groups (1 dose every five years)</td>
<td>1 dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal vaccine*</td>
<td>High risk groups (1 dose five years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPV*</td>
<td>High risk groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. **Adolescent immunization visit**: Countries are encouraged to establish an adolescent immunization visit between the ages of 10 to 12 years to provide an opportunity to ensure that adolescents are protected from vaccine preventable diseases.

2. **Tetanus and diphtheria vaccination**: Adolescents and adults with uncertain histories of a complete vaccination history with diphtheria, and tetanus toxoid containing vaccines should be given 3 doses of Td. Administer the first 2 doses at least 4 weeks apart and the third dose 6-12 months after the second doses. Adolescents and adults who have completed a primary series and whose last vaccination was > 10 years previously should be given a booster dose of vaccine. If a woman is pregnant and received the last Td > 10 years previously, administer the Td in the second or third trimester; if the person received the last Td < 10 years, administer Tdap during the post-partum period (see below).

3. **Pertussis vaccination**: The experience of many countries indicates that waning immunity from childhood immunization creates susceptibility and pertussis disease in adults. The use of Tdap has been limited due high cost and limited supplies. If available, Tdap should replace a single dose of Td for adults aged < 65 years who have not previously received a dose of Tdap (either in a primary series, as a booster, or for wound management). A one-time administration of Tdap with an interval as short as 2 years from previous Td vaccination is recommended for post-partum women, close contacts of infants < 12 months of age, and all health care workers with direct patient contact.
4. **Rubella**: Programs that have included rubella vaccine into their EPI schedule should ensure that all adolescents have received at least 1 dose of rubella vaccine and women of childbearing age are immune to rubella. If susceptibility profiles suggest susceptibility among WCBA, efforts should be made to provide 1 dose of rubella vaccine. Vaccine should be offered at any opportunity including pre-marital health visits, pre-employment health visits, school and university-based vaccination programs, routine health care visits, or through supplementary immunization activities. Pregnant women should not be vaccinated with rubella vaccine but can be offered vaccine in the post-partum period.

5. **Measles**: Adolescents who have not received 2 doses of measles vaccine should be vaccinated. In countries where epidemiologic data suggest susceptibility among adults, strategies should be developed to provide a single dose of measles vaccine.

6. **Mumps**: Programs that have included mumps vaccine into their EPI program should ensure that adolescents are vaccinated with 2 doses of mumps vaccine. In countries where epidemiologic data suggest susceptibility among adults, strategies should be developed to provide a single dose of mumps vaccine.

7. **Hepatitis B**: Countries that have included hep B vaccine into their EPI program should consider catch-up vaccination of adolescents who have not been previously vaccinated. In countries where local epidemiologic data exists, hep B vaccine should be offered to high risk groups. Special efforts should be made to vaccinate health care professionals prior to training in a clinical setting.

8. **Influenza**: Medical indications: Persons with the following chronic medical conditions should be offered influenza vaccine annually: cardiovascular and pulmonary disease including asthma, chronic metabolic disease, diabetes mellitus, renal dysfunction, hemoglobinopathies or immunosuppression caused either by medication or HIV infection. Persons with any condition that compromise respiratory function should also be vaccinated including persons with spinal cord injuries, cognitive dysfunction, and neuromuscular disorders. Other groups recommended for immunization include health care workers, and employees in long-term care facilities, residents of long-term care facilities, persons likely to transmit influenza to persons at high risk of severe disease and anyone who wants to receive influenza vaccine.

9. **Pneumococcal polysaccharide vaccine**: Medical indications: chronic disorders of the pulmonary system excluding asthma; cardiovascular diseases, diabetes mellitus, chronic liver disease, chronic renal failure or nephritic syndrome, functional or anatomic asplenia; immunosuppressive conditions (eg HIV infection, leukemia, lymphoma, multiple myeloma, Hodgkin disease, generalized malignancy, or organ/bone marrow transplant recipient). For persons > 65 years, one-time revaccination if they were vaccinated > 5 years previously and were aged < 65 at the time of primary vaccination. Other groups recommended to receive pneumococcal vaccine include residents of long-term care facilities and nursing homes. High risk groups and persons > 65 should be revaccinated every 5 years.

10. **Meningococcal polysaccharide vaccine**: Vaccination with quadrivalent meningitis vaccine (MPSV4) is required by the government of Saudi Arabia for all travelers to
Mecca during the annual Hajj. Other groups recommended for vaccination vary by country and may include students living in dormitory housing, military recruits and persons living in the meningitis belt. Revaccination may be indicated after 5 years.

11. **Inactivated polio vaccine:** Adults at high risk of exposure to wild polio virus (eg laboratory workers) should be vaccinated with IPV.