### Adverse Event

#### Influenza vaccines (WHO position paper)

In terms of protective efficacy, the live influenza vaccines appear to be comparable with the TIVs (trivalent, inactivated influenza vaccines.) However, CAIV-T (cold-adapted influenza vaccine) is licensed only for healthy people aged 5-49 years, given reports of an increase in reactive airway disease in vaccinees <5 years of age and insufficiently documented protective efficacy in older people.

#### BCG

#### BCG vaccine (WHO position paper)

Unfortunately, the (BCG) vaccine does not fully meet the essential requirement of having a significant impact against the most common manifestation of TB, namely pulmonary disease. Despite the shortcomings of this vaccine, WHO continues to recommend that a single dose of BCG be given to neonates or as soon as possible after birth in countries with a high prevalence of TB.

#### BCG vaccine (WHO position paper)

Since severe adverse effects of BCG vaccination are extremely rare even in asymptomatic, HIV-positive infants, all healthy neonates should be BCG-vaccinated, even in areas endemic for HIV. However, where resources permit, long-term follow-up of BCG-vaccinated infants of known HIV-positive mothers is desirable for early treatment, should disseminated BCG disease occur in children with rapid development of immunodeficiency.

#### BCG vaccine (WHO position paper)

In cases where infants have been exposed to smear-positive pulmonary TB shortly after birth, BCG vaccination should be delayed until completion of 6 months of prophylactic isoniazid treatment.

#### BCG vaccine (WHO position paper)

Countries with a low burden of TB may choose to limit BCG vaccination to neonates and infants of recognized high-risk groups for the disease or to skin-testnegative older children. In some low-burden populations, BCG vaccination has been largely replaced by intensified case detection and supervised early treatment.

#### BCG vaccine (WHO position paper)

There is no proven benefit of repeated BCG vaccination against TB. This also applies to revaccination of BCG-vaccinated individuals who remain negative by subsequent tuberculin testing.
BCG vaccine (WHO position paper)

In the absence of a scar in children in high-burden countries, BCG vaccination is indicated.

BCG vaccine (WHO position paper)

In low-burden countries, good protection against primary TB may also be achieved following vaccination of skin-test-negative adults. BCG vaccination of skin-test-positive individuals, whether induced by environmental mycobacteria, Mtb or BCG does not improve immunity to TB.

BCG vaccine (WHO position paper)

Given the high risk of acquiring TB and the low risk of serious adverse events following BCG vaccination of HIV-exposed neonates, WHO maintains that, in HIV-infected areas, all neonates be given BCG. Older infants or children suspected of being HIV-infected should not be vaccinated if they have symptomatic disease or other evidence of immunosuppression.

Global Advisory Committee on Vaccine Safety, 34 December 2003

There are few population-based data on the effectiveness, or otherwise, of BCG vaccine in preventing severe tuberculosis in HIV-positive infants. Given the high prevalence of HIV and tuberculosis in certain countries and of the current development of new tuberculosis vaccines, some of which are based on BCG, GACVS advises no change in the current recommendations for BCG immunization of infants in countries with a high prevalence of tuberculosis and that population-based studies should be undertaken to determine the efficacy and safety of BCG and related vaccines in HIV-negative and HIV-positive children in countries with a high endemic rate of tuberculosis.

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

WHO recommends the following schedule for infants (Appendix 39_5).

State of the art of new vaccines: research and development

Since 1974, BCG vaccination has been included in the WHO Expanded Programme on Immunization (EPI)
**BCG vaccine (WHO position paper)**

BCG vaccination is indicated

- for all infants living in areas where TB is highly endemic (concerning HIV, see below);
- for infants and children at particular risk of TB exposure in otherwise low-endemic areas;
- for persons exposed to multidrug-resistant Mtb (impact not established.)

BCG vaccination is contraindicated

- for persons with impaired immunity symptomatic HIV infection, known or suspected congenital immunodeficiency, leukaemia, lymphoma or generalized malignant disease);
- for patients under immunosuppressive treatment (corticosteroids, alkylating agents, antimetabolites, radiation);
- in pregnancy.

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**Cholera**

**State of the art of new vaccines: research and development**

Although the whole-cell injectable vaccine (against cholera) is no longer recommended, it still is commercially available in some countries.

**State of the art of new vaccines: research and development**

Since 1999, WHO recommends the use of killed oral WC/rBS vaccine as a tool to prevent cholera in populations at risk of a cholera epidemic. Such high-risk populations may include, but are not limited to, refugees and urban slum residents.

**State of the art of new vaccines: research and development**

The Ty21a (typhoind) vaccine is . . . to be swallowed every other day for one week. It can be taken simultaneously with the attenuated CVD103-HgR V. cholerae vaccine.

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**Contraindications**

**BCG vaccine (WHO position paper)**

Given the high risk of acquiring TB and the low risk of serious adverse events following BCG vaccination of HIV-exposed neonates, WHO maintains that, in HIV-infected areas, all neonates be given BCG. Older infants or children suspected of being HIV-infected should not be vaccinated if they have symptomatic disease or other evidence of immunosuppression.
Yellow fever vaccine (WHO position paper)

Given the very rare, but potentially severe, adverse effects, YF (yellow fever) vaccine for travellers should be administered on strict indications only, particularly in the elderly. Restriction of YF vaccination to authorized centres is likely to promote the appropriate use of YF vaccine.

Global Advisory Committee on Vaccine Safety, 23 December 2004

GACVS reiterates that particular care should be taken that the (17D yellow fever) vaccine is received only by those travellers who are truly at risk of exposure to yellow fever. In addition, vaccine providers should give careful consideration to the risks and benefits for elderly travellers and should routinely enquire about a history of thymus disorder, irrespective of the age of the subject. Where a history of thymus disorder is reported, alternative prevention measures should be considered.

Global Advisory Committee on Vaccine Safety, 34 December 2003

(GACVS stated that) particular care should be taken that the (yellow fever) vaccine is received only by those travellers truly at risk for yellow fever exposure. Furthermore, care should be taken that routine yellow fever vaccination programmes are not jeopardized by riskbenefit ratios that may be inapplicable to the target populations in endemic countries.

Global Advisory Committee on Vaccine Safety, 34 December 2003

There are few population-based data on the effectiveness, or otherwise, of BCG vaccine in preventing severe tuberculosis in HIV-positive infants. Given the high prevalence of HIV and tuberculosis in certain countries and of the current development of new tuberculosis vaccines, some of which are based on BCG, GACVS advises no change in the current recommendations for BCG immunization of infants in countries with a high prevalence of tuberculosis and that population-based studies should be undertaken to determine the efficacy and safety of BCG and related vaccines in HIV-negative and HIV-positive children in countries with a high endemic rate of tuberculosis.
BCG vaccine (WHO position paper)

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- for persons exposed to multidrug-resistant Mtb (impact not established.)

BCG vaccination is contraindicated

- for persons with impaired immunity symptomatic HIV infection, known or suspected congenital immunodeficiency, leukaemia, lymphoma or generalized malignant disease);
- for patients under immunosuppressive treatment (corticosteroids, alkylating agents, antimetabolites, radiation);
- in pregnancy.

DPT

Diphtheria vaccine (WHO position paper)

The recommended schedule for vaccination against diphtheria varies considerably between countries. According to the WHO/EPI schedule, the primary series of DTwP- or DTaP-containing vaccines should be administered in 3 doses, starting as early as 6 weeks of age and given with a minimum interval of 4 weeks. Where resources permit, additional doses can be given after the completion of the primary series. Many national immunization programmes offer 1-2 booster doses, for example one at 2 years of age and a second at age 4-7 years.

Diphtheria vaccine (WHO position paper)

For previously un-immunized children aged 1-7 years, the recommended schedule (for diphtheria vaccine) is 2 doses 2 months apart, and a third dose after 6-12 months using DTwP or DTaP. The recommended schedule for primary immunizations of older children, adolescents and adults using the dT combination is 2 doses -months apart and a third dose after 6-12 months. People living in low-endemic or non-endemic areas should receive booster doses of DT approximately 10 years after completing the primary series and subsequently every 10 years throughout life. Special attention should be paid to immunizing health-care workers who may have occupational exposure to C. diphtheriae. Booster responses can still be elicited after intervals of 25-30 years, so repeat primary immunization is not required when boosters are delayed.

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

WHO recommends the following schedule for infants (Appendix 39_5).
Tetanus vaccine (WHO position paper)

See Appendix 83.18 for a summary table of immunizations with diphtheriatetanuspertussis (DTP) and diphtheria toxoid (Td) vaccines required to obtain long-term protection against tetanus.

Diphtheria

Diphtheria vaccine (WHO position paper)

According to WHO requirements, the potency of diphtheria vaccine used for the immunization of children shall be no less than 30 IU per single human dose. Vaccines of lower potency are used for immunization of children aged =7 years and adults. This reduction of diphtheria toxoid potency minimizes reactogenicity at the injection site but is still sufficient to provoke an antibody response in older children and adults.

Diphtheria vaccine (WHO position paper)

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Diphtheria vaccine (WHO position paper)

Unfortunately, diphtheria infection does not always confer protective immunity. Individuals recovering from the disease should therefore complete active immunization with diphtheria toxoid during convalescence.
Diphtheria vaccine (WHO position paper)

To compensate for the loss of natural boosting, industrialized countries should add childhood boosters of diphtheria toxoid to the primary immunization series of infancy. The optimal timing for and the number of such booster doses should be based on epidemiological surveillance as well as on immunological and programmatic considerations. Boosting at the age of 12 months, at school entry and just before leaving school are all possible options. In addition to these childhood immunizations, people living in low-endemic or non-endemic areas may require booster injections of diphtheria toxoid at about 10-year intervals to maintain life-long protection.

Diphtheria vaccine (WHO position paper)

To further promote immunity against diphtheria, diphtheria toxoid and tetanus toxoid rather than tetanus toxoid alone should be used when tetanus prophylaxis is needed following injuries.

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

In accordance with the recommendations in the previous position paper on diphtheria, use of diphtheriatetanus vaccine is preferable to single-antigen tetanus toxoid vaccine. In future, the inclusion of other antigens, e.g. pertussis or Haemophilus influenzae type b (Hib), in booster doses should be considered.

Tetanus vaccine (WHO position paper)

Vaccines containing DT are used for children aged <7 years and dT-containing vaccines for individuals aged =7 years.

Tetanus vaccine (WHO position paper)

As a rule, vaccine combinations containing diphtheria toxoid (D or d) and tetanus toxoid, rather than tetanus toxoid alone, should be used when immunization against tetanus is indicated.

Tetanus vaccine (WHO position paper)

Both TT and dT can be used at any time during pregnancy.

Tetanus vaccine (WHO position paper)

See Appendix 83_18 for a summary table of immunizations with diphtheriatetanuspertussis (DTP) and diphtheria toxoid (Td) vaccines required to obtain long-term protectiona against tetanus.
GACVS

Global Advisory Committee on Vaccine Safety, 23 December 2004

GACVS reiterates that particular care should be taken that the (17D yellow fever) vaccine is received only by those travellers who are truly at risk of exposure to yellow fever. In addition, vaccine providers should give careful consideration to the risks and benefits for elderly travellers and should routinely enquire about a history of thymus disorder, irrespective of the age of the subject. Where a history of thymus disorder is reported, alternative prevention measures should be considered.

Global Advisory Committee on Vaccine Safety, 34 December 2003

(GACVS stated that) particular care should be taken that the (yellow fever) vaccine is received only by those travellers truly at risk for yellow fever exposure. Furthermore, care should be taken that routine yellow fever vaccination programmes are not jeopardized by riskbenefit ratios that may be inapplicable to the target populations in endemic countries.

Global Advisory Committee on Vaccine Safety, 34 December 2003

There are few population-based data on the effectiveness, or otherwise, of BCG vaccine in preventing severe tuberculosis in HIV-positive infants. Given the high prevalence of HIV and tuberculosis in certain countries and of the current development of new tuberculosis vaccines, some of which are based on BCG, GACVS advises no change in the current recommendations for BCG immunization of infants in countries with a high prevalence of tuberculosis and that population-based studies should be undertaken to determine the efficacy and safety of BCG and related vaccines in HIV-negative and HIV-positive children in countries with a high endemic rate of tuberculosis.

General

Introducing hepatitis B vaccine into national immunization services

Prevention of perinatal HBV transmission should be considered depending on the epidemiology of HBV transmission in a particular country.

In order to prevent HBV transmission from mother to infant, the first dose of HepB vaccine needs to be given as soon as possible after birth (preferably within 24 hours). In countries where a high proportion of chronic infections is acquired perinatally (e.g. South-East Asia), a birth dose should be given to infants. It is usually most feasible to give HepB vaccine at birth when infants are born in hospitals. Efforts should also be made in these countries to give HepB vaccine as soon as possible after delivery to infants delivered at home. In countries where a lower proportion of chronic infections is acquired perinatally (e.g. Africa), the highest priority is to achieve high DTP3 and HepB3 vaccine coverage among infants. In these countries, use of a birth dose may also be considered after disease burden, cost-effectiveness, and feasibility are evaluated.
Introducing hepatitis B vaccine into national immunization services

Catch up vaccination of older persons should be considered depending on the epidemiology of HBV transmission in a particular country. (Note: The Vaccine Fund does not provide vaccine for catch-up immunization).

In countries with a high endemicity of chronic HBV infection (hepatitis B surface antigen [HBsAg] prevalence >8%), catch-up immunization is not usually recommended because most chronic infections are acquired among children <5 years of age, and thus, routine infant vaccination will rapidly reduce HBV transmission. In countries with lower endemicity of chronic HBV infection, a higher proportion of chronic infections may be acquired among older children, adolescents and adults; catch-up immunization for these groups may be considered.

Introducing hepatitis B vaccine into national immunization services

Monovalent HepB vaccines must be used to give the birth dose of HepB vaccine.
Combination vaccines that include HepB vaccine must not be used to give the birth dose of HepB vaccine because DTP and Hib vaccines are not recommended to be given at birth.
Combination vaccines can be given whenever all of the antigens in the vaccine are indicated.

Introducing hepatitis B vaccine into national immunization services

HepB vaccine schedules are very flexible; thus, there are multiple options for adding the vaccine to existing national immunization schedules without requiring additional visits for immunization. (See Appendix 20.5.)

Programmatically, it is usually easiest if the 3 doses of HepB vaccine are given at the same time as the 3 doses of DTP (Option I). This schedule will prevent infections acquired during early childhood, which account for most of the HBV-related disease burden in high endemic countries, and also will prevent infections acquired later in life. However, this schedule will not prevent perinatal HBV infections because it does not include a dose of HepB vaccine at birth. Two schedule options can be used to prevent perinatal HBV infections: a 3-dose schedule of monovalent HepB vaccine, with the 1st dose given at birth and the 2nd and 3rd doses given at the same time as the 1st and 3rd doses of DTP vaccine (Option II); or a 4-dose schedule in which a birth dose of monovalent HepB vaccine is followed by 3 doses of a combination vaccine, e.g. DTP HepB (Option III). The 3-dose schedule (Option II) is less expensive, but may be more complicated to administer, because infants receive different vaccines at the 2nd immunization visit than at the 1st and 3rd visits. The 4-dose schedule (Option III) may be easier to administer programmatically, but is more costly, and vaccine supply issues may make it unfeasible.
Introducing Haemophilus influenzae type b (Hib) conjugate vaccine into national immunization services

Combination vaccines that contain Hib conjugate vaccine:
can be used anytime all of the antigens in the vaccine are indicated by the schedule;
cannot be used before 6 weeks of age (e.g. for the birth dose of hepatitis B vaccine) because the immunogenicity of the DTP and Hib components will be reduced if given before this age.

Immunization of infants with Hib conjugate vaccine is usually accomplished by giving the vaccine at the same ages as DTP vaccine, either as a separate injection or in combination.

In general, infants should receive a primary dose schedule of 3 doses of Hib conjugate vaccine in the first year of life. Doses of Hib conjugate vaccine should be administered at least 4 weeks apart.

Children older than one year of age require only a single dose of Hib conjugate vaccine.

Booster doses of Hib conjugate vaccine may be given to children in the second year of life, but successful control of Hib disease does not require a booster dose.

Hib vaccine is indicated in children from the age of 6 weeks up to 18 months.

In general, the scheduling practices below are followed for Hib immunization:
- The first dose is given to children at six weeks of age or older.
- Three doses are given. Most Hib vaccines require three doses, and in the remainder of this document, a three-dose primary series will be considered routine. One conjugate is licensed for a two-dose primary series, but is not marketed widely.

In complex emergencies, immunization should include all children from 6 months through 14 years of age. At a minimum, children from 6 months through 4 years of age must be immunized. The choice of the ages covered will be influenced by vaccine availability, funding, human resources and local measles epidemiology.

Reducing measles mortality in emergencies (WHO/UNICEF Joint Statement)
Introduction of Haemophilus influenzae type b vaccine into immunization programmes

In most countries, the primary series of Hib immunizations protect children through their most susceptible period and thus, in general, a booster is not needed. Although boosters may be considered when Hib disease is a substantial problem for children older than 12 months, some countries do not use booster doses even under these circumstances because of the increased cost and administrative complexity.

BCG vaccine (WHO position paper)

Unfortunately, the (BCG) vaccine does not fully meet the essential requirement of having a significant impact against the most common manifestation of TB, namely pulmonary disease. Despite the shortcomings of this vaccine, WHO continues to recommend that a single dose of BCG be given to neonates or as soon as possible after birth in countries with a high prevalence of TB.

BCG vaccine (WHO position paper)

Since severe adverse effects of BCG vaccination are extremely rare even in asymptomatic, HIV-positive infants, all healthy neonates should be BCG-vaccinated, even in areas endemic for HIV. However, where resources permit, long-term follow-up of BCG-vaccinated infants of known HIV-positive mothers is desirable for early treatment, should disseminated BCG disease occur in children with rapid development of immunodeficiency.

BCG vaccine (WHO position paper)

In cases where infants have been exposed to smear-positive pulmonary TB shortly after birth, BCG vaccination should be delayed until completion of 6 months of prophylactic isoniazid treatment.

BCG vaccine (WHO position paper)

Countries with a low burden of TB may choose to limit BCG vaccination to neonates and infants of recognized high-risk groups for the disease or to skin-test-negative older children. In some low-burden populations, BCG vaccination has been largely replaced by intensified case detection and supervised early treatment.

BCG vaccine (WHO position paper)

There is no proven benefit of repeated BCG vaccination against TB. This also applies to revaccination of BCG-vaccinated individuals who remain negative by subsequent tuberculin testing.

BCG vaccine (WHO position paper)

In the absence of a scar in children in high-burden countries, BCG vaccination is indicated.
**BCG vaccine (WHO position paper)**

In low-burden countries, good protection against primary TB may also be achieved following vaccination of skin-test-negative adults. BCG vaccination of skin-test-positive individuals, whether induced by environmental mycobacteria, Mtb or BCG does not improve immunity to TB.

**BCG vaccine (WHO position paper)**

Given the high risk of acquiring TB and the low risk of serious adverse events following BCG vaccination of HIV-exposed neonates, WHO maintains that, in HIV-infected areas, all neonates be given BCG. Older infants or children suspected of being HIV-infected should not be vaccinated if they have symptomatic disease or other evidence of immunosuppression.

**Hepatitis A vaccines (WHO position paper)**

Currently, four inactivated vaccines against HAV are internationally available. All four vaccines are safe and effective, with long-lasting protection. None of the vaccines are licensed for children less than one year of age.

The (HAV) vaccines are given parenterally, as a two-dose series, 6-18 months apart. The dose of vaccine, vaccination schedule, ages for which the vaccine is licensed, and whether there is a paediatric and adult formulation varies from manufacturer to manufacturer.

**Hepatitis B vaccines (WHO position paper)**

(In countries where a high proportion of HBV infections are acquired perinatally, the first dose of hepatitis B vaccine should be given as soon as possible (<24 hours) after birth.

In countries where a lower proportion of HBV infections are acquired perinatally, the relative contribution of perinatal HBV infection to the overall disease burden, and the feasibility and cost-effectiveness of providing vaccination at birth, should be carefully considered before a decision is made on the optimal vaccination schedule.

**Hepatitis B vaccines (WHO position paper)**

(Hepatitis B vaccine catch-up) strategies targeted at older age groups or groups with risk factors for acquiring HBV infection should be considered as a supplement to routine infant vaccination in countries of intermediate or low hepatitis B endemicity. In such settings, a substantial proportion of the disease burden may be attributable to infections acquired by older children, adolescents and adults.

In countries of high endemicity, large-scale routine vaccination of infants rapidly reduces the transmission of HBV. In these circumstances, catch-up vaccination of older children and adults has relatively little impact on chronic disease because most of them have already been infected.
Hepatitis B vaccines (WHO position paper)

In highly endemic areas, HBV is most commonly spread from mother to child at birth, or from person to person in early childhood. In countries with low HBV endemicity, sexual transmission and the use of contaminated needles, especially among injecting drug users, are the major routes of infection. However, perinatal transmission may account for 15% of HBV-related deaths, even in low-endemic areas.

Hepatitis B vaccines (WHO position paper)

When immunizing against HBV at birth, only monovalent hepatitis B vaccine should be used: the other antigens found in combination vaccines are currently not approved for use at birth (DTwP, DTaP, Hib, hepatitis A and IPV.)

Hepatitis B vaccines (WHO position paper)

The minimum recommended interval between (hepatitis B vaccine) doses is four weeks. Longer dose intervals may increase the final anti-HBs titres but not the seroconversion rates. More than 3 doses of the vaccine are not required, regardless of duration (>4 weeks) of the interval between them.

Hepatitis B vaccines (WHO position paper)

Recommended schedules for (hepatitis B) vaccination can be divided into those that include a birth-dose and those that do not. Schedules with a birth-dose call for the first vaccination at birth, followed by a second and third dose at the time of the first and third diphtheria/tetanus/pertussis (DTP) vaccination, respectively (see Appendix 55_9, column II.) Alternatively, a four-dose schedule may be used where the dose at birth is followed by three additional doses; these doses may be given either as monovalent vaccine or as a combination (e.g. with DTP and/or Hib) following the schedules commonly used for those vaccines (see Appendix 55_9, column III.) These schedules will prevent most perinatally acquired infection.

Hepatitis B vaccines (WHO position paper)

Some countries have chosen not to implement universal (hepatitis B) immunization and instead use comprehensive HBsAg screening of pregnant women with immunization of newborn infants born to HBsAg-positive women. This strategy is usually not feasible in developing countries with high prevalence of disease and may not be the most reliable and convenient option even in countries where HBsAg screening in pregnancy is well established.

Hepatitis B vaccines (WHO position paper)

When administered without the birth-dose, hepatitis B vaccine is usually given at the same time as DTP, either as a monovalent presentation or in combination with DTP and/or Hib vaccine (see Appendix 55_9, column I).
Hepatitis B vaccines (WHO position paper)

Countries that opt for schedules with a birth-dose (of hepatitis B vaccine) should vaccinate preterm infants at birth and subsequently enter the respective national hepatitis B vaccination schedule. However, if the birth weight is <2000 g, the vaccine dose at birth should not be counted towards the primary series, and three additional doses should be given.

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Hepatitis B vaccines (WHO position paper)

Immunocompromised children and adults can also benefit from vaccination (with hepatitis B vaccine.) However, the immune response may be reduced and additional injections of the vaccine may be required. Where possible, the anti-HBs antibody titres should be followed up after immunization of immunocompromised individuals.

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Hepatitis B vaccines (WHO position paper)

All children and adolescents aged less than 18 years and not previously vaccinated should receive the (hepatitis B) vaccine. Hepatitis B vaccination is also indicated for certain groups at high risk of contracting HBV infection, including persons with high-risk sexual behaviour, partners and household contacts of HBsAg-positive persons, injecting drug users, persons who frequently require blood or blood products, recipients of solid organ transplantation, those at occupational risk of HBV infection, including health care workers, as well as for international travellers to HBV-endemic countries.

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Hepatitis B vaccines (WHO position paper)

Temporary immunity may be obtained using hepatitis B immune globulin (HBIG) for post-exposure prophylaxis. HBIG prophylaxis may be indicated (i) for newborn infants whose mothers are HBsAg-positive, (ii) following percutaneous or mucous membrane exposure to HBsAg-positive blood or body fluids, (iii) following sexual exposure to an HBsAg-positive person, and (iv) to protect patients from recurrent HBV infection following liver transplantation. As a rule, HBIG should be used as an adjunct to hepatitis B vaccine. However, in full-term newborns, the protection against perinatally acquired infection achieved by immediate (<24 hours) hepatitis B vaccination is not significantly improved by the addition of HBIG.

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Hepatitis B vaccines (WHO position paper)

In countries of high disease endemicity (HBsAg prevalence >8%), HBV is mainly spread from mother to infant at birth or from child to child during early childhood (<5 years). In this epidemiological setting, schedules providing the first vaccine dose at birth are recommended.

page 262
Hepatitis B vaccines (WHO position paper)

Routine infant hepatitis B vaccination should also be given high priority in countries of intermediate or low HBV endemicity (HBsAg prevalence of >2-<8% or <2%, respectively) because, even in these settings, an important proportion of chronic infections are acquired through HBV transmission during early childhood.

Hepatitis B vaccines (WHO position paper)

Although HBsAg screening of all pregnant women and vaccination at birth only of infants born to HBsAg-positive mothers may be an option in areas with low HBV transmission, this strategy may be only partially effective, since women at highest risk of infection often fail to attend prenatal clinics.

Hepatitis B vaccines (WHO position paper)

Catch-up vaccination (with hepatitis B vaccine of older age groups, including adolescents and adults) should be considered only if the continuity of the infant vaccination programme can be ensured.

Influenza vaccines (WHO position paper)

Based on data from industrialized countries, and listed in order of priority, the following groups of individuals may be targeted for vaccination (against influenza) in order to reduce the incidence of severe illness and premature death.

1. Residents of long-term care facilities for elderly people and the disabled.
2. Elderly non-institutionalized individuals with chronic conditions such as pulmonary and cardiovascular illness, metabolic diseases including diabetes mellitus and renal dysfunction, and various types of immunosuppression, including people with acquired immunodeficiency syndrome (AIDS) and transplant recipients.
3. All adults and children aged >6 months with any of the conditions mentioned above.
4. Elderly individuals who are above a nationally defined age limit, irrespective of other risk factors. Although the appropriate age for general vaccination may be considerably lower in countries with poor living conditions, most countries define the age limit to be >65 years.
5. Other groups defined on the basis of national data and capacities, such as contacts of high-risk people, pregnant women, health-care workers and others with key functions in society, as well as children 6-23 months of age.

Influenza vaccines (WHO position paper)

In terms of protective efficacy, the live influenza vaccines appear to be comparable with the TIVs (trivalent, inactivated influenza vaccines.) However, CAIV-T (cold-adapted influenza vaccine) is licensed only for healthy people aged 5-49 years, given reports of an increase in reactive airway disease in vaccinees <5 years of age and insufficiently documented protective efficacy in older people.
Measles vaccines (WHO position paper)
Immunization against measles is recommended for all susceptible children and adults for whom measles vaccination is not contraindicated.

Measles vaccines (WHO position paper)
Asymptomatic HIV infection is an indication, not a contraindication, for measles vaccination. Ideally, the vaccine should be offered as early as possible in the course of HIV infection. In areas where measles is prevalent, or during outbreaks, individuals with early signs of HIV-induced immunosuppression may also be considered for vaccination.

Measles vaccines (WHO position paper)
The recommended age for measles vaccination depends on the local measles epidemiology as well as on programmatic considerations. In most developing countries, high attack rates and serious disease among infants necessitate early vaccination, usually at 9 months of age, despite the relatively low (80-85%) seroconversion rates following vaccination in this age group. Unless severely immunocompromised, HIV-infected infants should receive measles vaccine at 6 months of age, followed by an additional dose at 9 months.

Measles vaccines (WHO position paper)
In most industrialized countries, national health systems are consistently able to provide measles vaccine to a high proportion of infants, with a concomitant reduction in measles virus circulation. The probability of an infant being exposed to measles before his or her first birthday is low. It is therefore recommended that measles vaccination be deferred until a child is 12-15 months old, when seroconversion rates in excess of 90% may be expected.

Measles vaccines (WHO position paper)
In countries with measles elimination goals, a one-time only measles SIA (supplementary immunization activity) should be considered, targeting all children aged 9 months to 14 years, regardless of disease history or previous vaccination status. Efforts are also needed to target specific groups of young adults who may be at increased risk for measles infection, including military recruits, university students, health care workers, refugees and international travellers to measles-endemic areas.

Measles vaccines (WHO position paper)
Vitamin A supplementation has been shown to markedly reduce measles-associated mortality in developing countries and should always be given to measles patients in areas where vitamin A deficiency is prevalent.
Pneumococcal vaccines (WHO position paper)

Poor immunogenicity of polysaccharide (pneumococcal) vaccines in early childhood precludes the use of the 23-valent pneumococcal vaccine in the high-risk group of children under 2 years of age.

Pneumococcal vaccines (WHO position paper)

The duration of protection following immunization with the 23-valent polysaccharide vaccine is estimated at 5 years, or more, in healthy adults. However, the duration may be considerably shorter in some high-risk groups for pneumococcal disease. Revaccination using the polysaccharide vaccine is not routinely recommended.

(Page 116) Revaccination using the polysaccharide vaccine is not routinely recommended, but immunocompromised children who have received polysaccharide vaccine may be revaccinated after 3 years. The safety of three or more doses of the polysaccharide vaccine is not known.

Pneumococcal vaccines (WHO position paper)

A single dose of the 23-valent polysaccharide vaccine is recommended for selected groups above 2 years of age at increased risk of pneumococcal disease. These groups include the healthy elderly (over 65 years of age), particularly those living in institutions.

Pneumococcal vaccines (WHO position paper)

The polyvalent polysaccharide vaccine is recommended for selected groups above 2 years of age with increased risk of pneumococcal disease. Such groups include the healthy elderly (over 65 years old), particularly those living in institutions, patients suffering from chronic organ failure, diabetes, nephrotic syndrome and certain immunodeficiencies, particularly those with functional or anatomical asplenia.

Recent meta-analyses on the efficacy and effectiveness of the pneumococcal polysaccharide vaccine have raised doubts about the benefit of the vaccine in the elderly population. However, these vaccines continue to be recommended for this group based on evidence from observational studies that show a beneficial effect against pneumococcal disease associated with bacteraemia.

Rubella vaccines (WHO position paper)

Rubella vaccine is usually administered at age 12-15 months, but can also be administered to children as young as 9 months of age. In most countries, the vaccine is given as MR or MMR, and the age of administration is chosen based on the appropriate age for measles vaccination. It may also be administered to older children, adolescents, students, child care personnel, health care workers, military personnel and adult men in contact with women of childbearing age.
Yellow fever vaccine (WHO position paper)

YF (yellow fever) vaccine should be offered to all travellers to and from at-risk areas, unless they belong to the group of individuals for whom YF vaccination is contraindicated. There is currently insufficient scientific evidence to support a change in the International health regulations for travelers to endemic areas demanding proof of valid YF vaccination within the preceding ten years. However, in at-risk countries, vaccination resources should be directed to ensuring good primary vaccination coverage rather than to providing booster doses.

Yellow fever vaccine (WHO position paper)

All persons aged 9 months or older and living in YF (yellow fever) at-risk areas should receive YF vaccine. Highest priority should be given to those persons most likely to be exposed, such as forestry and agricultural workers, and to those living in villages or towns with a history of previous outbreaks. Immigrants to such regions from non-endemic areas should also be vaccinated against YF.

Travellers should be vaccinated at least 10 days before arrival in the at risk area.

Yellow fever vaccine (WHO position paper)

In countries at risk of YF (yellow fever), YF vaccine is recommended for use in all children aged at least 9-12 months of age. In addition, preventive vaccination of older children and adults is recommended in at risk areas. Vaccination for YF is also recommended for travellers aged above 9 months who plan to visit areas at risk for YF.

Yellow fever vaccine (WHO position paper)

According to the International health regulations and the WHO International certificate of vaccination, a booster dose of YF (yellow fever) vaccine is required every 10 years. However, in most cases, the duration of protection following the first dose of YF vaccine seems to be at least 30-35 years and possibly lifelong. For this reason, it has been proposed to limit vaccination against YF to a single dose. In order to clarify this matter, WHO organized a consultation with a group of YF experts in March 2003. This group reviewed relevant literature and available data and concluded that, at present, the evidence for protective immunity beyond 10 years was insufficient to justify a change in the current YF vaccination policy for international travellers. However, in at-risk countries, vaccination resources should be directed to ensuring good primary vaccination coverage rather than to providing booster doses. For the purposes of international travel, only YF vaccinations performed at nationally authorized YF vaccination sites and using WHO pre-qualified YF vaccines may be entered into the International Certificate of Vaccination.
Yellow fever vaccine (WHO position paper)

Given the very rare, but potentially severe, adverse effects, YF (yellow fever) vaccine for travellers should be administered on strict indications only, particularly in the elderly. Restriction of YF vaccination to authorized centres is likely to promote the appropriate use of YF vaccine.

Typhoid vaccines (WHO position paper)

Immunization of school-age children is recommended in areas where typhoid fever in these age groups is a significant public health problem, and particularly where antibiotic-resistant S. typhi strains are prevalent. In those settings immunization against typhoid fever will be required until socioeconomic improvements finally interrupt transmission of S. typhi. Where appropriate the use of typhoid vaccines should be harmonized with the administration of tetanus and diphtheria vaccines.

Typhoid vaccines (WHO position paper)

To maintain protection, revaccination (with the Vi polysaccharide vaccine) is recommended every 3 years.

Typhoid vaccines (WHO position paper)

Protection (provided by the Ty21a vaccine) is markedly influenced by the number of doses and their spacing. When the vaccine is given in 3 doses 2 days apart, protective immunity is achieved 7 days after the last dose. In endemic areas a booster dose is recommended every 3 years. Travellers from non-endemic to endemic regions are recommended a booster on a yearly basis. There are currently no field trial data to document the efficacy of this vaccine in children aged < 3 years.

Typhoid vaccines (WHO position paper)

The (Ty21a typhoid) vaccine is usually administrated orally as entericcoated capsules and is registered for use from 6 years of age.

A liquid formulation of the Ty21a (Ty21a typhoid) vaccine can be taken by children as young as 2 years and has proved more immunogenic than the capsular formulation.

Typhoid vaccines (WHO position paper)

Primary immunization with this (old inactivated whole-cell) parenteral (typhoid) vaccine consists of 2 doses given 4 weeks apart; a single booster dose is recommended every 3 years.
**Typhoid vaccines (WHO position paper)**

For the occasional small-scale vaccination in countries of low typhoid endemicity and for individual protection of short-term visitors to highly-endemic areas, either of the 2 modern (typhoid) vaccines is recommended. It should be noted, however, that the vaccines do not provide complete protection and should not replace hygiene precautions.

**Diphtheria vaccine (WHO position paper)**

According to WHO requirements, the potency of diphtheria vaccine used for the immunization of children shall be no less than 30 IU per single human dose. Vaccines of lower potency are used for immunization of children aged ≤7 years and adults. This reduction of diphtheria toxoid potency minimizes reactogenicity at the injection site but is still sufficient to provoke an antibody response in older children and adults.

**Diphtheria vaccine (WHO position paper)**

The recommended schedule for vaccination against diphtheria varies considerably between countries. According to the WHO/EPI schedule, the primary series of DTwP- or DTaP-containing vaccines should be administered in 3 doses, starting as early as 6 weeks of age and given with a minimum interval of 4 weeks. Where resources permit, additional doses can be given after the completion of the primary series. Many national immunization programmes offer 1-2 booster doses, for example one at 2 years of age and a second at age 4-7 years.

**Diphtheria vaccine (WHO position paper)**

For previously un-immunized children aged 1-7 years, the recommended schedule (for diphtheria vaccine) is 2 doses 2 months apart, and a third dose after 6-12 months using DTwP or DTaP. The recommended schedule for primary immunizations of older children, adolescents and adults using the dT combination is 2 doses 6-months apart and a third dose after 6-12 months. People living in low-endemic or non-endemic areas should receive booster doses of DT approximately 10 years after completing the primary series and subsequently every 10 years throughout life. Special attention should be paid to immunizing health-care workers who may have occupational exposure to C. diphtheriae. Booster responses can still be elicited after intervals of 25-30 years, so repeat primary immunization is not required when boosters are delayed.

**Diphtheria vaccine (WHO position paper)**

Unfortunately, diphtheria infection does not always confer protective immunity. Individuals recovering from the disease should therefore complete active immunization with diphtheria toxoid during convalescence.
Diphtheria vaccine (WHO position paper)

To compensate for the loss of natural boosting, industrialized countries should add childhood boosters of diphtheria toxoid to the primary immunization series of infancy. The optimal timing for and the number of such booster doses should be based on epidemiological surveillance as well as on immunological and programmatic considerations. Boosting at the age of 12 months, at school entry and just before leaving school are all possible options. In addition to these childhood immunizations, people living in low-endemic or non-endemic areas may require booster injections of diphtheria toxoid at about 10-year intervals to maintain life-long protection.

Diphtheria vaccine (WHO position paper)

To further promote immunity against diphtheria, diphtheria toxoid and tetanus toxoid rather than tetanus toxoid alone should be used when tetanus prophylaxis is needed following injuries.

WHO recommended standards for surveillance of selected vaccine-preventable diseases

If a child was unprotected (against neonatal tetanus at birth) the mother should receive a does of TT during the same visit and should be followed up with a subsequent TT dose if needed for protection. The same applies for mothers whose children were protected at birth but who remain eligible for another TT dose.

Global Advisory Committee on Vaccine Safety, 23 December 2004

GACVS reiterates that particular care should be taken that the (17D yellow fever) vaccine is received only by those travellers who are truly at risk of exposure to yellow fever. In addition, vaccine providers should give careful consideration to the risks and benefits for elderly travellers and should routinely enquire about a history of thymus disorder, irrespective of the age of the subject. Where a history of thymus disorder is reported, alternative prevention measures should be considered.

Global Advisory Committee on Vaccine Safety, 34 December 2003

(GACVS stated that) particular care should be taken that the (yellow fever) vaccine is received only by those travellers truly at risk for yellow fever exposure. Furthermore, care should be taken that routine yellow fever vaccination programmes are not jeopardized by riskbenefit ratios that may be inapplicable to the target populations in endemic countries.
Global Advisory Committee on Vaccine Safety, 34 December 2003

There are few population-based data on the effectiveness, or otherwise, of BCG vaccine in preventing severe tuberculosis in HIV-positive infants. Given the high prevalence of HIV and tuberculosis in certain countries and of the current development of new tuberculosis vaccines, some of which are based on BCG, GACVS advises no change in the current recommendations for BCG immunization of infants in countries with a high prevalence of tuberculosis and that population-based studies should be undertaken to determine the efficacy and safety of BCG and related vaccines in HIV-negative and HIV-positive children in countries with a high endemic rate of tuberculosis.

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 9-11 November 2005

(SAGE recognized) that immunization schedules in use today vary greatly around the world, and it is unlikely that a single, uniform immunization schedule would suit all countries. WHO should aim to provide countries with advice on the parameters to be considered when they select a schedule. There was unanimous support for a new review of the evidence base, and agreement that changes in schedule are not appropriate without strong evidence to demonstrate benefit.

SAGE recommended that a review of the issues surrounding the primary schedule, boosters and adolescent vaccination should be undertaken. This should incorporate disease control strategies, immunology, operational aspects of health services (not just vaccination services) and economics.

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

WHO recommends the following schedule for infants (Appendix 39_5).

Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents

In order to prevent perinatal HBV transmission the first dose of hepatitis B vaccine should be given as soon as possible after birth, preferably within 24 hours.
Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents

In all countries: Achieving a high level of completion of the hepatitis B vaccine series among all infants should be the highest priority. This has the greatest overall impact on the prevalence of chronic HBV infection in children, regardless of whether it is feasible to administer a birth dose.

In countries where a high proportion of chronic HBV infections is acquired perinatally (e.g. in south-east Asia): A birth dose should be given to infants who are delivered in hospitals when hepatitis B vaccine is introduced. Efforts should also be made in these countries to give hepatitis B vaccine as soon as possible after birth to infants delivered at home.

In countries where a lower proportion of chronic HBV infections is acquired perinatally (e.g. in Africa): The administration of a birth dose may be considered after evaluating:
- the relative contribution of perinatal HBV infections to the overall disease burden;
- the feasibility and cost-effectiveness of providing a birth dose.

Monovalent hepatitis B vaccine MUST BE USED for the birth dose. Combination vaccines that include hepatitis B vaccine MUST NOT BE USED to give the birth dose of hepatitis B vaccine because DTP and Hib vaccines should not be administered at birth. Either monovalent hepatitis B vaccine or combination vaccines may be used for later doses in the hepatitis B vaccine schedule. Combination vaccines can be given whenever all the antigens in the vaccines are indicated.

All infants aged under 1 year should receive a full series of hepatitis B vaccine. The need for catch-up immunization of older age groups and for targeted risk groups varies between countries.

Programmatically, it is usually easiest if the three doses of hepatitis B vaccine are given at the same time as the three doses of DTP (See Appendix 36.9 for options for adding hepatitis B vaccine to childhood immunization schedules.)
Yellow fever vaccine (WHO position paper)

The (YF) vaccine is also widely used for the protection of travelers to YF-endemic areas.

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

(Considerations for hepatitis B vaccine schedule:)

A determination of the role of perinatal transmission (useful for birth dose considerations) can be made based on the overall seroprevalence of HBsAg, age-specific prevalence of HBsAg, and the prevalence of the HBeAg in pregnant women.

Combination products may not be used at birth; therefore, programmes including the birth dose will need to include monovalent HepB vaccine in the supply.

Hepatitis A vaccines (WHO position paper)

In developed countries with low endemicity of hepatitis A and with high rates of disease in specific high-risk populations, vaccination of those populations against hepatitis A may be recommended. The high-risk groups include injection-drug users, homosexual men, persons travelling to high-risk areas, and certain ethnic or religious groups. However, it should be noted that vaccination programmes targeting specific high-risk groups may have little impact on the overall national incidence of disease.

Mumps virus vaccines (WHO position paper)

If a large proportion of the population remains seronegative for mumps, care should be taken to vaccinate adults considered to be at special risk.

Mumps virus vaccines (WHO position paper)

Mumps vaccines are recommended for use in a 1-dose schedule, given at age 12-18 months.

(Page 355) Control of mumps can be achieved through high routine coverage with an effective mumps-containing vaccine administered at age 12-18 months.

Mumps virus vaccines (WHO position paper)

Due to its known low effectiveness, the Rubini-strain (mumps) vaccine should not be used in national immunization programmes. Persons previously immunized with the Rubini-strain vaccine should receive a dose of an effective mumps vaccine to ensure protection.
Mumps virus vaccines (WHO position paper)

A second (mumps) opportunity is not required in countries where coverage with the first dose is sufficiently high (i.e. > 95%). If a second opportunity is required, it could be administered through a second routine dose, or by implementing periodical catch-up campaigns. Finally, if an initial catch-up campaign is implemented, the target age group should be determined according to mumps susceptibility. In most unvaccinated populations, most children acquire mumps infections before the age of 10 years.

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

It was generally agreed (by SAGE members) that (for tetanus vaccine) there is no maximum interval between the primary series and a booster dose and that there is no need to re-start interrupted immunization schedules. Vaccination of school-age children would also help to sustain MNT (maternal and neonatal tetanus) elimination.

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

SAGE recommended the following (regarding tetanus immunization schedules):
A 5-dose childhood immunization schedule should be promoted. The primary series of 3 doses would be given in infancy, with a booster dose ideally at age 4-7 years and another booster dose in adolescence (e.g. at age 12-15 years). The exact timing of the booster doses should be flexible to take account of the most appropriate health service contacts in different countries and of integration with other vaccines and other interventions such as bednet distribution, vitamin A therapy and deworming. In some countries, these boosters could be given through school-based approaches, but efforts to reach those not attending school will be important. A sixth dose should be recommended for adults, for example in the first pregnancy or for military recruits.

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

In accordance with the recommendations in the previous position paper on diphtheria, use of diphtheriatetanus vaccine is preferable to single-antigen tetanus toxoid vaccine. In future, the inclusion of other antigens, e.g. pertussis or Haemophilus influenzae type b (Hib), in booster doses should be considered.

Tetanus vaccine (WHO position paper)

Vaccines containing DT are used for children aged <7 years and dT-containing vaccines for individuals aged ≥7 years.
**Tetanus vaccine (WHO position paper)**

As a rule, vaccine combinations containing diphtheria toxoid (D or d) and tetanus toxoid, rather than tetanus toxoid alone, should be used when immunization against tetanus is indicated.

**Tetanus vaccine (WHO position paper)**

A childhood tetanus immunization schedule of 5 doses is recommended. WHO recommends that the primary series of 3 doses should be given in infancy (aged <1 year). Where pertussis is of particular risk to young infants, DTP immunization should be started at age 6 weeks and 2 subsequent doses should be given at intervals of at least 4 weeks (e.g. at weeks 10 and 14). The exact timing of the booster doses should be flexible to take account of the most appropriate health service contacts in different countries. Ideally, a booster dose should be offered at age 4-7 years followed by another booster in adolescence, e.g. at age 12-15 years. Where a high percentage of children, including girls, attend school, school-based immunization programmes should be used where feasible to deliver the booster doses. Special efforts to reach school nonattenders will be needed.

In addition to the childhood vaccination programme, an extra tetanus toxoid-containing dose to adults will provide additional assurance of long-lasting, possibly lifelong protection. Therefore, a sixth dose should be recommended for adults, e.g. at the time of the first pregnancy or during military service. Those who receive their first tetanus vaccine doses as adolescents or adults require a total of only 5 appropriately spaced doses to obtain the same long-term protection.

**Tetanus vaccine (WHO position paper)**

Even after many years, an interrupted primary- or booster dose (tetanus vaccine) schedule should not be restarted; the schedule is simply continued with the next dose that is due.

**Tetanus vaccine (WHO position paper)**

The interval between the tetanus toxoid containing doses should be at least 4 weeks. Longer intervals may increase the magnitude and duration of the immune response, but should not be a reason to delay immunization.

**Tetanus vaccine (WHO position paper)**

Both TT and dT can be used at any time during pregnancy.
**Tetanus vaccine (WHO position paper)**

The high-risk approach to control neonatal tetanus should be part of the neonatal tetanus elimination strategy in countries where the elimination target (<1 case per 1000 live births at district level) has not yet been reached. This approach targets all women of childbearing age and consists of campaign-style immunization (supplementary immunization activities, or SIAs) with 3 doses of TT (or dT) with an interval of at least 4 weeks between doses 1 and 2, and of at least 6 months between doses 2 and 3. Promotion of clean deliveries is part of this approach. In addition to the 3 doses provided in the SIAs, 2 further boosters are needed to provide long-term protection to women with no documented receipt of tetanus toxoid-containing vaccines in childhood.

Although adequately immunized people should have sufficient protection against tetanus, treating physicians may give a dose of tetanus toxoid-containing vaccine in the case of an injury, in addition to other preventive measures. Depending on the severity of the injury and on the reliability of the history of previous tetanus vaccinations, the vaccine should be given if the last dose was administered more than 10 years ago (or 5 years in the case of severe injuries)*. The immunization schedule should be completed as soon as possible for those who have not received all doses of the basic schedule.

In addition, passive immunization using tetanus antitoxin, preferably of human origin, may be needed for prophylaxis (e.g. in cases of dirty wounds in incompletely immunized individuals). Such antitoxin is also essential in the treatment of tetanus cases and should be readily available in all countries. From page 200: While tetanus antitoxin should be readily available in all countries, its use cannot substitute for the need to achieve and sustain high tetanus vaccination coverage.


**Tetanus vaccine (WHO position paper)**

For previously non-immunized adolescents and adults, the recommended schedule is 2 (tetanus vaccine) doses administered at least 4 weeks apart followed by a third dose administered at least 6 months after the second, and subsequent boosters at least 1 year apart. Those who receive their first tetanus vaccine doses as adolescents or adults require a total of only 5 appropriately spaced doses to obtain long-term protection.
Tetanus vaccine (WHO position paper)

In countries where MNT remains a public health problem, pregnant women for whom reliable information on previous tetanus vaccinations is not available should receive at least 2 doses of tetanus toxoid-containing vaccine (normally dT) with an interval of at least 4 weeks between the doses. To ensure protection for a minimum of 5 years, a third dose should be given at least 6 months later. A fourth and fifth dose should be given at intervals of at least 1 year, e.g. during subsequent pregnancies, in order to ensure long-term protection. Pregnant women who have received only 3 doses of DTP in early infancy should receive 2 doses of a tetanus toxoid-containing vaccine with a minimal interval of 4 weeks. Those who received 4 doses of tetanus vaccine during their childhood need only 1 booster dose, which should be given at the first opportunity. In both scenarios, to provide protection throughout childbearing age, a sixth dose would be needed after at least 1 year.

Tetanus vaccine (WHO position paper)

See Appendix 83_18 for a summary table of immunizations with diphtheriatetanuspertussis (DTP) and diphtheria toxoid (Td) vaccines required to obtain long-term protection against tetanus.

State of the art of new vaccines: research and development

Although the whole-cell injectable vaccine (against cholera) is no longer recommended, it still is commercially available in some countries.

State of the art of new vaccines: research and development

Since 1999, WHO recommends the use of killed oral WC/rBS vaccine as a tool to prevent cholera in populations at risk of a cholera epidemic. Such high-risk populations may include, but are not limited to, refugees and urban slum residents.

State of the art of new vaccines: research and development

The Ty21a (typhoind) vaccine is . . . to be swallowed every other day for one week. It can be taken simultaneously with the attenuated CVD103-HgR V. cholerae vaccine.

State of the art of new vaccines: research and development

A trivalent live cold-adapted vaccine (Flumist) has been developed for intranasal spray delivery . . . The vaccine has been licensed in the USA for vaccination of persons from 5-49 years of age, in view of side effects in younger children (wheezing, nasal congestion) and absence of data in the elderly. The vaccine is safe, effective, and shows remarkable genetic stability, but it has to be kept at -18C.
State of the art of new vaccines: research and development

The polyvalent PS (polysaccharide) vaccine (against Streptococcus pneumoniae) is recommended for healthy people over 65 years of age, particularly those living in institutions. Randomized controlled trials in healthy elderly people in industrialized countries have, however, failed to show a beneficial effect of the vaccine, so that recommendation for its use in the elderly is based on data from observational studies showing a significant protective effect against invasive (bacteraemic) pneumococcal disease, but not pneumonia.

State of the art of new vaccines: research and development

Since 1974, BCG vaccination has been included in the WHO Expanded Programme on Immunization (EPI).

State of the art of new vaccines: research and development

This type of vaccine (inactivated rabies vaccine) is still unfortunately manufactured and used in South-East Asia, but the number of countries doing so has been decreasing during the past 10 years in accordance with the WHO recommendations to replace them by cell-cultured vaccines.

State of the art of new vaccines: research and development

It is well known that rabies PEP [post-exposure prophylaxis] with vaccine alone is not always sufficient, especially in cases of severe exposure (category 3) where concommitant passive immunization with rabies immunoglobulins (RIG) is strongly recommended.

WHO/UNICEF joint statement - Global plan for reducing measles mortality 2006-2010

A second opportunity for measles immunization is essential to ensure protection against measles.

WHO/UNICEF joint statement - Global plan for reducing measles mortality 2006-2010

In conflict or emergency areas, WHO and UNICEF have a commitment to ensure that, at a minimum, measles vaccine and vitamin A supplements are administered. (WHO/UNICEF joint statement: reducing measles mortality in emergencies, 2002.)
Consistent with WHO's position on new vaccines, PCV-7 (7-serotype conjugate pneumococcal vaccine) can be easily integrated into routine vaccination schedules, and it may be administered at the same time, though at a different site, as other vaccines in infant immunization programmes, including DTP, hepatitis B, Hib and polio vaccines. Routine immunization with PCV-7 should be initiated before the age of 6 months to maximize the benefits of the vaccine and may start as early as 6 weeks of age.

Clinical efficacy has been demonstrated in 2 schedules (for PCV-7, the 7-serotype conjugate pneumococcal vaccine): a 6-week, 10-week, 14-week schedule and a 2-month, 4-month, 6-month schedule, which was followed by a booster dose at 12-15 months of age. Further information on the cost effectiveness of other potential schedules (for example, using different numbers of doses or different intervals between doses, and with and without boosters) should be obtained. Other schedules (such as 2 doses in a primary series plus a booster dose) are being used in some countries, whose experiences may be important as GAVI-supported countries begin introducing PCV-7 or review its use. Although a late dose (around the first birthday) may be challenging operationally for GAVI-eligible countries, there may be suitable opportunities when a dose of PCV-7 could be given, such as at the same time as measles vaccination. Countries should evaluate this information once it is available and select the most appropriate schedule based on the anticipated impact, cost effectiveness and programmatic feasibility.

The ACPE (Advisory Committee on Polio Eradication) recommended that the risk of importation from polio-infected areas should be reduced further by ensuring all travellers from such areas are immunized, regardless of their age or immunization status; it proposed that a standing recommendation be established to this effect under the International Health Regulations (IHR) (2005).
Conclusions and recommendations from the meeting of the immunization Strategic Advisory Group of Experts (SAGE) - November 2006

SAGE accepted the proposal (of its working group on measles) to maintain the current recommendation for administration of the first dose of measles vaccine at 9 months in settings where the transmission is widespread and mortality is high. Where transmission has been substantially reduced (for example, following high quality nationwide SIAs), increasing the age from 9 months to 12 months represents a rational and desirable policy change. However, before implementing a change, policy-makers should review local data on the actual age at which infants receive measles vaccine, the coverage expected at 12 months compared with 9 months, age-specific measles incidence and review the immunogenicity and effectiveness of measles vaccine administered at 9 months compared with 12 months.

Conclusions and recommendations from the meeting of the immunization Strategic Advisory Group of Experts (SAGE) - November 2006

With respect to introducing a routine second dose of measles vaccine, SAGE emphasizes the principle that this should be considered only in settings where high coverage of the first dose has been achieved and sustained and where measles transmission has been reduced to a low level, indicating a well functioning routine immunization programme. Criteria that could be used to determine if the routine programme is strong enough and the coverage sufficiently high to benefit from a routine second dose require further analysis and consultation.

Conclusions and recommendations from the meeting of the immunization Strategic Advisory Group of Experts (SAGE) - November 2006

With respect to the optimal interval between SIAs (for measles), SAGE noted a number of examples where delays in conducting follow-up SIAs have led to large outbreaks (for example, in Brazil, Kenya and Uganda). SAGE agreed with the approach developed by the Regional Office for the Americas and adapted by the Technical Advisory Group on Measles in the African Region that follow-up SIAs should be conducted before the estimated number of susceptible children reaches the size of a birth cohort. This approach has been found to be programmatically useful and sufficiently accurate to prevent large outbreaks.

Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

The 23-valent (pneumococcal) vaccine is primarily designed for use in older children and adults who are at high risk for pneumococcal disease. It is not licensed for use in children aged <2 years.
Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

PCV-7 (7-valent polysaccharide-protein conjugate pneumococcal) vaccine is highly immunogenic in all age groups, but it is currently licensed for use only in children aged <5 years, including infants aged <12 months.

Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

Trials in several developing countries have demonstrated the efficacy of a 3-dose schedule for infants without a subsequent booster dose. This schedule is compatible with the schedules of national immunization programmes in many developing countries. The benefit of administering an additional dose in the second year of life requires further investigation in these settings. Similarly, consideration of alternative PCV-7 vaccination schedules - including delaying the administration of a third dose so it may be given along with measles vaccination or in the second year of life - should be guided by future research findings.

Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

When the vaccine is first introduced into routine childhood immunization programmes a single catch-up dose of PCV-7 may be given to previously unvaccinated children aged 12-24 months and to children aged 2-5 years who are at high risk.

(PAGE 98) - When the vaccine is initially introduced into childhood immunization programmes, a single catch-up dose of PCV-7 may be given to previously unvaccinated children aged 12-24 months and to children aged 2-5 years considered to be at high risk. It is not known whether re-vaccination is necessary later in life.

(PAGE 103) - When PCV-7 is first introduced into routine childhood immunization programmes, maximum individual and community-level protection can be achieved by also providing a single catch-up dose of the vaccine to previously unvaccinated children who are aged 12-24 months and to children aged 2-5 years who are considered to be at high risk.

Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

The primary series of PCV-7 consists of 3 intramuscular doses administered to infants at intervals of at least 4 weeks, starting at the age of 6 weeks or later.

Vaccination at the age of 6 weeks, 10 weeks and 14 weeks in infants in developing countries is as immunogenic as vaccination at 2 months, 4 months and 6 months in industrialized countries. A booster dose administered after 12 months of age may improve the immune response and may especially affect pneumococcal nasopharyngeal carriage. Some industrialized countries have adopted a schedule based on delivering 2 doses during infancy (for example, at 2 months and 4 months) and a third dose at 12-13 months.
Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

To maximize the benefits of the vaccine, routine immunization with PCV-7 should be initiated before 6 months of age and may start as early as 6 weeks of age.

Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

There are 2 schedules that have proven clinical efficacy: a 6 week10 week14 week series and a 2 month4 month6 month series; this latter series is followed by a booster dose at 1215 months of age.

Countries should evaluate information on impact and scheduling once it is available and select the most appropriate schedule based on anticipated impact, cost effectiveness and programmatic feasibility.

Rabies vaccines (WHO position paper)

Pre-exposure rabies vaccination requires IM doses of 1 ml or 0.5 ml, depending on the vaccine type, given on days 0, 7 and 28 (day 28 preferable, but administration may be advanced towards day 21 if time is limited).

Typhoid vaccines: WHO position paper

The Vi polysaccharide vaccine: The vaccine is licensed for individuals aged >2 years. Only 1 dose is required, and the vaccine confers protection 7 days after injection. To maintain protection, revaccination is recommended every 3 years. The Vi polysaccharide vaccine can be co-administered with other vaccines relevant for international travellers such as yellow fever and hepatitis A and with vaccines of the routine childhood immunization programmes.

23-valent pneumococcal polysaccharide vaccine (WHO position paper)

Primary immunization with PPV23 consists of a single intramuscular or subcutaneous dose. The intramuscular route may be preferred because of the lower rate of reactions at the injection site. The optimal timing, frequency and clinical effectiveness of additional doses of PPV23 are poorly defined, and national recommendations regarding revaccination vary. However, on the basis of the data on the duration of vaccine-induced protection, WHO suggests one single revaccination >5 years after a first vaccination.
**BCG vaccine (WHO position paper)**

BCG vaccination is indicated

- for all infants living in areas where TB is highly endemic (concerning HIV, see below);
- for infants and children at particular risk of TB exposure in otherwise low-endemic areas;
- for persons exposed to multidrug-resistant Mtb (impact not established.)

BCG vaccination is contraindicated

- for persons with impaired immunity symptomatic HIV infection, known or suspected congenital immunodeficiency, leukaemia, lymphoma or generalized malignant disease);
- for patients under immunsuppressive treatment (corticosteroids, alkylating agents, antimetabolites, radiation);
- in pregnancy.

**Weekly Epidimiological Record, No. 23 2010**

The primary series of 3 OPV vaccinations should be administered according to the schedules of national immunization programmes, for example at 6 weeks, 10 weeks, and 14 weeks, or at 2 months, 4 months, and 6 months. In addition, a birth dose should be given as soon as possible after birth when the potential for poliovirus importation is very high or high and the transmission potential is high or moderate. The interval between doses of OPV or IPV should be 4 weeks.

**Weekly Epidimiological Record, No. 23 2010**

IPV is given intramuscularly (preferably) or subcutaneously, and may be offered as a component of fixed combinations of vaccines. A primary series of 3 doses should be administered beginning at 2 months of age. If the primary series begins earlier (for example, with a 6-week, 10-week and 14-week schedule) then a booster dose should be administered after an interval of 6 months (for a 4-dose schedule). Where sequential IPV/OPV is used, WHO recommends that IPV be administered at 2 months of age (e.g. an IPV-OPV-OPV schedule) or at 2 months and 3-4 months of age (e.g. an IPV-IPV-OPV-OPV schedule); in both schedules IPV should be followed by at least 2 doses of OPV.

**Weekly Epidimiological Record, No. 23 2010**

Each dose in the primary series, whether IPV or OPV, should be separated by 4-8 weeks, depending on the risk of exposure to polio in early childhood. Both IPV and OPV may be administered simultaneously with other vaccines in national childhood immunization programmes.
**HIV/AIDS and immunosuppression**

**BCG vaccine (WHO position paper)**

Since severe adverse effects of BCG vaccination are extremely rare even in asymptomatic, HIV-positive infants, all healthy neonates should be BCG-vaccinated, even in areas endemic for HIV. However, where resources permit, long-term follow-up of BCG-vaccinated infants of known HIV-positive mothers is desirable for early treatment, should disseminated BCG disease occur in children with rapid development of immunodeficiency.

**BCG vaccine (WHO position paper)**

Given the high risk of acquiring TB and the low risk of serious adverse events following BCG vaccination of HIV-exposed neonates, WHO maintains that, in HIV-infected areas, all neonates be given BCG. Older infants or children suspected of being HIV-infected should not be vaccinated if they have symptomatic disease or other evidence of immunosuppression.

**Hepatitis B vaccines (WHO position paper)**

Immunocompromised children and adults can also benefit from vaccination (with hepatitis B vaccine.) However, the immune response may be reduced and additional injections of the vaccine may be required. Where possible, the anti-HBs antibody titres should be followed up after immunization of immunocompromised individuals.

**Influenza vaccines (WHO position paper)**

Based on data from industrialized countries, and listed in order of priority, the following groups of individuals may be targeted for vaccination (against influenza) in order to reduce the incidence of severe illness and premature death.

1. Residents of long-term care facilities for elderly people and the disabled.
2. Elderly non-institutionalized individuals with chronic conditions such as pulmonary and cardiovascular illness, metabolic diseases including diabetes mellitus and renal dysfunction, and various types of immunosuppression, including people with acquired immunodeficiency syndrome (AIDS) and transplant recipients.
3. All adults and children aged >6 months with any of the conditions mentioned above.
4. Elderly individuals who are above a nationally defined age limit, irrespective of other risk factors. Although the appropriate age for general vaccination may be considerably lower in countries with poor living conditions, most countries define the age limit to be >65 years.
5. Other groups defined on the basis of national data and capacities, such as contacts of high-risk people, pregnant women, health-care workers and others with key functions in society, as well as children 6-23 months of age.
Measles vaccines (WHO position paper)

Asymptomatic HIV infection is an indication, not a contraindication, for measles vaccination. Ideally, the vaccine should be offered as early as possible in the course of HIV infection. In areas where measles is prevalent, or during outbreaks, individuals with early signs of HIV-induced immunosuppression may also be considered for vaccination.

Measles vaccines (WHO position paper)

The recommended age for measles vaccination depends on the local measles epidemiology as well as on programmatic considerations. In most developing countries, high attack rates and serious disease among infants necessitate early vaccination, usually at 9 months of age, despite the relatively low (80-85%) seroconversion rates following vaccination in this age group. Unless severely immunocompromised, HIV-infected infants should receive measles vaccine at 6 months of age, followed by an additional dose at 9 months.

Pneumococcal vaccines (WHO position paper)

The duration of protection following immunization with the 23-valent polysaccharide vaccine is estimated at 5 years, or more, in healthy adults. However, the duration may be considerably shorter in some high-risk groups for pneumococcal disease. Revaccination using the polysaccharide vaccine is not routinely recommended.

(Page 116) Revaccination using the polysaccharide vaccine is not routinely recommended, but immunocompromised children who have received polysaccharide vaccine may be revaccinated after 3 years. The safety of three or more doses of the polysaccharide vaccine is not known.

Global Advisory Committee on Vaccine Safety, 34 December 2003

There are few population-based data on the effectiveness, or otherwise, of BCG vaccine in preventing severe tuberculosis in HIV-positive infants. Given the high prevalence of HIV and tuberculosis in certain countries and of the current development of new tuberculosis vaccines, some of which are based on BCG, GACVS advises no change in the current recommendations for BCG immunization of infants in countries with a high prevalence of tuberculosis and that population-based studies should be undertaken to determine the efficacy and safety of BCG and related vaccines in HIV-negative and HIV-positive children in countries with a high endemic rate of tuberculosis.
BCG vaccine (WHO position paper)

BCG vaccination is indicated

- for all infants living in areas where TB is highly endemic (concerning HIV, see below);
- for infants and children at particular risk of TB exposure in otherwise low-endemic areas;
- for persons exposed to multidrug-resistant Mtb (impact not established.)

BCG vaccination is contraindicated

- for persons with impaired immunity symptomatic HIV infection, known or suspected congenital immunodeficiency, leukaemia, lymphoma or generalized malignant disease);
- for patients under immunosuppressive treatment (corticosteroids, alkylating agents, antimetabolites, radiation);
- in pregnancy.

Hepatitis A

Hepatitis A vaccines (WHO position paper)

Currently, four inactivated vaccines against HAV are internationally available. All four vaccines are safe and effective, with long-lasting protection. None of the vaccines are licensed for children less than one year of age.

The (HAV) vaccines are given parenterally, as a two-dose series, 6-18 months apart. The dose of vaccine, vaccination schedule, ages for which the vaccine is licensed, and whether there is a paediatric and adult formulation varies from manufacturer to manufacturer.

Hepatitis A vaccines (WHO position paper)

In developed countries with low endemicity of hepatitis A and with high rates of disease in specific high-risk populations, vaccination of those populations against hepatitis A may be recommended. The high-risk groups include injection-drug users, homosexual men, persons travelling to high-risk areas, and certain ethnic or religious groups. However, it should be noted that vaccination programmes targeting specific high-risk groups may have little impact on the overall national incidence of disease.
Hepatitis B

Introducing hepatitis B vaccine into national immunization services

Prevention of perinatal HBV transmission should be considered depending on the epidemiology of HBV transmission in a particular country.

In order to prevent HBV transmission from mother to infant, the first dose of HepB vaccine needs to be given as soon as possible after birth (preferably within 24 hours). In countries where a high proportion of chronic infections is acquired perinatally (e.g. South-East Asia), a birth dose should be given to infants. It is usually most feasible to give HepB vaccine at birth when infants are born in hospitals. Efforts should also be made in these countries to give HepB vaccine as soon as possible after delivery to infants delivered at home. In countries where a lower proportion of chronic infections is acquired perinatally (e.g. Africa), the highest priority is to achieve high DTP3 and HepB3 vaccine coverage among infants. In these countries, use of a birth dose may also be considered after disease burden, cost-effectiveness, and feasibility are evaluated.

Catch up vaccination of older persons should be considered depending on the epidemiology of HBV transmission in a particular country. (Note: The Vaccine Fund does not provide vaccine for catch-up immunization).

In countries with a high endemicity of chronic HBV infection (hepatitis B surface antigen [HBsAg] prevalence >8%), catch-up immunization is not usually recommended because most chronic infections are acquired among children <5 years of age, and thus, routine infant vaccination will rapidly reduce HBV transmission. In countries with lower endemicity of chronic HBV infection, a higher proportion of chronic infections may be acquired among older children, adolescents and adults; catch-up immunization for these groups may be considered.

Monovalent HepB vaccines must be used to give the birth dose of HepB vaccine. Combination vaccines that include HepB vaccine must not be used to give the birth dose of HepB vaccine because DTP and Hib vaccines are not recommended to be given at birth. Combination vaccines can be given whenever all of the antigens in the vaccine are indicated.
Introducing hepatitis B vaccine into national immunization services

HepB vaccine schedules are very flexible; thus, there are multiple options for adding the vaccine to existing national immunization schedules without requiring additional visits for immunization. (See Appendix 20_5.)

Programmatically, it is usually easiest if the 3 doses of HepB vaccine are given at the same time as the 3 doses of DTP (Option I). This schedule will prevent infections acquired during early childhood, which account for most of the HBV-related disease burden in high endemic countries, and also will prevent infections acquired later in life. However, this schedule will not prevent perinatal HBV infections because it does not include a dose of HepB vaccine at birth. Two schedule options can be used to prevent perinatal HBV infections: a 3-dose schedule of monovalent HepB vaccine, with the 1st dose given at birth and the 2nd and 3rd doses given at the same time as the 1st and 3rd doses of DTP vaccine (Option II); or a 4-dose schedule in which a birth dose of monovalent HepB vaccine is followed by 3 doses of a combination vaccine, e.g. DTP HepB (Option III).

The 3-dose schedule (Option II) is less expensive, but may be more complicated to administer, because infants receive different vaccines at the 2nd immunization visit than at the 1st and 3rd visits. The 4-dose schedule (Option III) may be easier to administer programmatically, but is more costly, and vaccine supply issues may make it unfeasible.

Hepatitis B vaccines (WHO position paper)

In countries where a high proportion of HBV infections are acquired perinatally, the first dose of hepatitis B vaccine should be given as soon as possible (<24 hours) after birth.

In countries where a lower proportion of HBV infections are acquired perinatally, the relative contribution of perinatal HBV infection to the overall disease burden, and the feasibility and cost-effectiveness of providing vaccination at birth, should be carefully considered before a decision is made on the optimal vaccination schedule.

Hepatitis B vaccines (WHO position paper)

(Hepatitis B vaccine catch-up) strategies targeted at older age groups or groups with risk factors for acquiring HBV infection should be considered as a supplement to routine infant vaccination in countries of intermediate or low hepatitis B endemicity. In such settings, a substantial proportion of the disease burden may be attributable to infections acquired by older children, adolescents and adults.

In countries of high endemicity, large-scale routine vaccination of infants rapidly reduces the transmission of HBV. In these circumstances, catch-up vaccination of older children and adults has relatively little impact on chronic disease because most of them have already been infected.
Hepatitis B vaccines (WHO position paper)

In highly endemic areas, HBV is most commonly spread from mother to child at birth, or from person to person in early childhood. In countries with low HBV endemicity, sexual transmission and the use of contaminated needles, especially among injecting drug users, are the major routes of infection. However, perinatal transmission may account for 15% of HBV-related deaths, even in low-endemic areas.

Hepatitis B vaccines (WHO position paper)

When immunizing against HBV at birth, only monovalent hepatitis B vaccine should be used: the other antigens found in combination vaccines are currently not approved for use at birth (DTwP, DTaP, Hib, hepatitis A and IPV.)

Hepatitis B vaccines (WHO position paper)

The minimum recommended interval between (hepatitis B vaccine) doses is four weeks. Longer dose intervals may increase the final anti-HBs titres but not the seroconversion rates. More than 3 doses of the vaccine are not required, regardless of duration (>4 weeks) of the interval between them.

Hepatitis B vaccines (WHO position paper)

Recommended schedules for (hepatitis B) vaccination can be divided into those that include a birth-dose and those that do not. Schedules with a birth-dose call for the first vaccination at birth, followed by a second and third dose at the time of the first and third diphtheria/tetanus/pertussis (DTP) vaccination, respectively (see Appendix 55_9, column II.) Alternatively, a four-dose schedule may be used where the dose at birth is followed by three additional doses; these doses may be given either as monovalent vaccine or as a combination (e.g. with DTP and/or Hib) following the schedules commonly used for those vaccines (see Appendix 55_9, column III.) These schedules will prevent most perinatally acquired infection.

Hepatitis B vaccines (WHO position paper)

Some countries have chosen not to implement universal (hepatitis B) immunization and instead use comprehensive HBsAg screening of pregnant women with immunization of newborn infants born to HBsAg-positive women. This strategy is usually not feasible in developing countries with high prevalence of disease and may not be the most reliable and convenient option even in countries where HBsAg screening in pregnancy is well established.

Hepatitis B vaccines (WHO position paper)

When administered without the birth-dose, hepatitis B vaccine is usually given at the same time as DTP, either as a monovalent presentation or in combination with DTP and/or Hib vaccine (see Appendix 55_9, column I).
Hepatitis B vaccines (WHO position paper)

Countries that opt for schedules with a birth-dose (of hepatitis B vaccine) should vaccinate preterm infants at birth and subsequently enter the respective national hepatitis B vaccination schedule. However, if the birth weight is <2000 g, the vaccine dose at birth should not be counted towards the primary series, and three additional doses should be given.

Hepatitis B vaccines (WHO position paper)

Immunocompromised children and adults can also benefit from vaccination (with hepatitis B vaccine.) However, the immune response may be reduced and additional injections of the vaccine may be required. Where possible, the anti-HBs antibody titres should be followed up after immunization of immunocompromised individuals.

Hepatitis B vaccines (WHO position paper)

All children and adolescents aged less than 18 years and not previously vaccinated should receive the (hepatitis B) vaccine. Hepatitis B vaccination is also indicated for certain groups at high risk of contracting HBV infection, including persons with high-risk sexual behaviour, partners and household contacts of HBsAg-positive persons, injecting drug users, persons who frequently require blood or blood products, recipients of solid organ transplantation, those at occupational risk of HBV infection, including health care workers, as well as for international travellers to HBV-endemic countries.

Hepatitis B vaccines (WHO position paper)

Temporary immunity may be obtained using hepatitis B immune globulin (HBIG) for post-exposure prophylaxis. HBIG prophylaxis may be indicated (i) for newborn infants whose mothers are HBsAg-positive, (ii) following percutaneous or mucous membrane exposure to HBsAg-positive blood or body fluids, (iii) following sexual exposure to an HBsAg-positive person, and (iv) to protect patients from recurrent HBV infection following liver transplantation. As a rule, HBIG should be used as an adjunct to hepatitis B vaccine. However, in full-term newborns, the protection against perinatally acquired infection achieved by immediate (<24 hours) hepatitis B vaccination is not significantly improved by the addition of HBIG.

Hepatitis B vaccines (WHO position paper)

In countries of high disease endemicity (HBsAg prevalence >8%), HBV is mainly spread from mother to infant at birth or from child to child during early childhood (<5 years). In this epidemiological setting, schedules providing the first vaccine dose at birth are recommended.
Hepatitis B vaccines (WHO position paper)

Routine infant hepatitis B vaccination should also be given high priority in countries of intermediate or low HBV endemicity (HBsAg prevalence of >2-<8% or <2%, respectively) because, even in these settings, an important proportion of chronic infections are acquired through HBV transmission during early childhood.

Hepatitis B vaccines (WHO position paper)

Although HBsAg screening of all pregnant women and vaccination at birth only of infants born to HBsAg-positive mothers may be an option in areas with low HBV transmission, this strategy may be only partially effective, since women at highest risk of infection often fail to attend prenatal clinics.

Hepatitis B vaccines (WHO position paper)

Catch-up vaccination (with hepatitis B vaccine of older age groups, including adolescents and adults) should be considered only if the continuity of the infant vaccination programme can be ensured.

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

WHO recommends the following schedule for infants (Appendix 39_5).

Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents

In order to prevent perinatal HBV transmission the first dose of hepatitis B vaccine should be given as soon as possible after birth, preferably within 24 hours.
Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents

In all countries: Achieving a high level of completion of the hepatitis B vaccine series among all infants should be the highest priority. This has the greatest overall impact on the prevalence of chronic HBV infection in children, regardless of whether it is feasible to administer a birth dose.

In countries where a high proportion of chronic HBV infections is acquired perinatally (e.g. in south-east Asia): A birth dose should be given to infants who are delivered in hospitals when hepatitis B vaccine is introduced. Efforts should also be made in these countries to give hepatitis B vaccine as soon as possible after birth to infants delivered at home.

In countries where a lower proportion of chronic HBV infections is acquired perinatally (e.g. in Africa): The administration of a birth dose may be considered after evaluating:
- the relative contribution of perinatal HBV infections to the overall disease burden;
- the feasibility and cost-effectiveness of providing a birth dose.

Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents

Monovalent hepatitis B vaccine MUST BE USED for the birth dose. Combination vaccines that include hepatitis B vaccine MUST NOT BE USED to give the birth dose of hepatitis B vaccine because DTP and Hib vaccines should not be administered at birth.

Either monovalent hepatitis B vaccine or combination vaccines may be used for later doses in the hepatitis B vaccine schedule. Combination vaccines can be given whenever all the antigens in the vaccines are indicated.

Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents

All infants aged under 1 year should receive a full series of hepatitis B vaccine. The need for catch-up immunization of older age groups and for targeted risk groups varies between countries.

Programmatically, it is usually easiest if the three doses of hepatitis B vaccine are given at the same time as the three doses of DTP (See Appendix 36_9 for options for adding hepatitis B vaccine to childhood immunization schedules.)
Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

(Considerations for hepatitis B vaccine schedule:)

A determination of the role of perinatal transmission (useful for birth dose considerations) can be made based on the overall seroprevalence of HBsAg, age-specific prevalence of HBsAg, and the prevalence of the HBeAg in pregnant women.

Combination products may not be used at birth; therefore, programmes including the birth dose will need to include monovalent HepB vaccine in the supply.

### Hib

Introducing Haemophilus influenzae type b (Hib) conjugate vaccine into national immunization services

Combination vaccines that contain Hib conjugate vaccine:
- can be used anytime all of the antigens in the vaccine are indicated by the schedule;
- cannot be used before 6 weeks of age (e.g. for the birth dose of hepatitis B vaccine) because the immunogenicity of the DTP and Hib components will be reduced if given before this age.

Introducing Haemophilus influenzae type b (Hib) conjugate vaccine into national immunization services

Immunization of infants with Hib conjugate vaccine is usually accomplished by giving the vaccine at the same ages as DTP vaccine, either as a separate injection or in combination.

In general, infants should receive a primary dose schedule of 3 doses of Hib conjugate vaccine in the first year of life. Doses of Hib conjugate vaccine should be administered at least 4 weeks apart.

Children older than one year of age require only a single dose of Hib conjugate vaccine.

Introducing Haemophilus influenzae type b (Hib) conjugate vaccine into national immunization services

Booster doses of Hib conjugate vaccine may be given to children in the second year of life, but successful control of Hib disease does not require a booster dose.

Introduction of Haemophilus influenzae type b vaccine into immunization programmes

Hib vaccine is indicated in children from the age of 6 weeks up to 18 months.
Introduction of Haemophilus influenzae type b vaccine into immunization programmes

In general, the scheduling practices below are followed for Hib immunization:
- The first dose is given to children at six weeks of age or older.
- Three doses are given. Most Hib vaccines require three doses, and in the remainder of this document, a three-dose primary series will be considered routine. One conjugate is licensed for a two-dose primary series, but is not marketed widely.

Introduction of Haemophilus influenzae type b vaccine into immunization programmes

In most countries, the primary series of Hib immunizations protect children through their most susceptible period and thus, in general, a booster is not needed. Although boosters may be considered when Hib disease is a substantial problem for children older than 12 months, some countries do not use booster doses even under these circumstances because of the increased cost and administrative complexity.

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

WHO recommends the following schedule for infants (Appendix 39_5).

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

In accordance with the recommendations in the previous position paper on diphtheria, use of diphtheriatetanus vaccine is preferable to single-antigen tetanus toxoid vaccine. In future, the inclusion of other antigens, e.g. pertussis or Haemophilus influenzae type b (Hib), in booster doses should be considered.
Influenza vaccines (WHO position paper)

Based on data from industrialized countries, and listed in order of priority, the following groups of individuals may be targeted for vaccination (against influenza) in order to reduce the incidence of severe illness and premature death.

1. Residents of long-term care facilities for elderly people and the disabled.
2. Elderly non-institutionalized individuals with chronic conditions such as pulmonary and cardiovascular illness, metabolic diseases including diabetes mellitus and renal dysfunction, and various types of immunosuppression, including people with acquired immunodeficiency syndrome (AIDS) and transplant recipients.
3. All adults and children aged >6 months with any of the conditions mentioned above.
4. Elderly individuals who are above a nationally defined age limit, irrespective of other risk factors. Although the appropriate age for general vaccination may be considerably lower in countries with poor living conditions, most countries define the age limit to be >65 years.
5. Other groups defined on the basis of national data and capacities, such as contacts of high-risk people, pregnant women, health-care workers and others with key functions in society, as well as children 6-23 months of age.

In terms of protective efficacy, the live influenza vaccines appear to be comparable with the TIVs (trivalent, inactivated influenza vaccines.) However, CAIV-T (cold-adapted influenza vaccine) is licensed only for healthy people aged 5-49 years, given reports of an increase in reactive airway disease in vaccinees <5 years of age and insufficiently documented protective efficacy in older people.

State of the art of new vaccines: research and development

A trivalent live cold-adapted vaccine (Flumist) has been developed for intranasal spray delivery . . . The vaccine has been licensed in the USA for vaccination of persons from 5-49 years of age, in view of side effects in younger children (wheezing, nasal congestion) and absence of data in the elderly. The vaccine is safe, effective, and shows remarkable genetic stability, but it has to be kept at -18°C.
## MMR

**Rubella vaccines (WHO position paper)**

Rubella vaccine is usually administered at age 12-15 months, but can also be administered to children as young as 9 months of age. In most countries, the vaccine is given as MR or MMR, and the age of administration is chosen based on the appropriate age for measles vaccination. It may also be administered to older children, adolescents, students, child care personnel, health care workers, military personnel and adult men in contact with women of childbearing age.

![Wer 2000, vol. 75, 20, pp 161-169](page 166)

## Measles


In complex emergencies, immunization should include all children from 6 months through 14 years of age. At a minimum, children from 6 months through 4 years of age must be immunized. The choice of the ages covered will be influenced by vaccine availability, funding, human resources and local measles epidemiology.

![Wer 2004, vol. 79, 14, pp 130-142](page 3)

**Measles vaccines (WHO position paper)**

Immunization against measles is recommended for all susceptible children and adults for whom measles vaccination is not contraindicated.

![Wer 2004, vol. 79, 14, pp 130-142](page 131)

**Measles vaccines (WHO position paper)**

Asymptomatic HIV infection is an indication, not a contraindication, for measles vaccination. Ideally, the vaccine should be offered as early as possible in the course of HIV infection. In areas where measles is prevalent, or during outbreaks, individuals with early signs of HIV-induced immunosuppression may also be considered for vaccination.

![Wer 2004, vol. 79, 14, pp 130-142](page 131)

**Measles vaccines (WHO position paper)**

The recommended age for measles vaccination depends on the local measles epidemiology as well as on programmatic considerations. In most developing countries, high attack rates and serious disease among infants necessitate early vaccination, usually at 9 months of age, despite the relatively low (80-85%) seroconversion rates following vaccination in this age group. Unless severely immunocompromised, HIV-infected infants should receive measles vaccine at 6 months of age, followed by an additional dose at 9 months.
Measles vaccines (WHO position paper)

In most industrialized countries, national health systems are consistently able to provide measles vaccine to a high proportion of infants, with a concomitant reduction in measles virus circulation. The probability of an infant being exposed to measles before his or her first birthday is low. It is therefore recommended that measles vaccination be deferred until a child is 12-15 months old, when seroconversion rates in excess of 90% may be expected.

Measles vaccines (WHO position paper)

In countries with measles elimination goals, a one-time only measles SIA (supplementary immunization activity) should be considered, targeting all children aged 9 months to 14 years, regardless of disease history or previous vaccination status. Efforts are also needed to target specific groups of young adults who may be at increased risk for measles infection, including military recruits, university students, health care workers, refugees and international travellers to measles-endemic areas.

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

WHO recommends the following schedule for infants (Appendix 39_5).

WHO/UNICEF joint statement - Global plan for reducing measles mortality 2006-2010

A second opportunity for measles immunization is essential to ensure protection against measles.

WHO/UNICEF joint statement - Global plan for reducing measles mortality 2006-2010

In conflict or emergency areas, WHO and UNICEF have a commitment to ensure that, at a minimum, measles vaccine and vitamin A supplements are administered. (WHO/UNICEF joint statement: reducing measles mortality in emergencies, 2002.)
SAGE accepted the proposal (of its working group on measles) to maintain the current recommendation for administration of the first dose of measles vaccine at 9 months in settings where the transmission is widespread and mortality is high. Where transmission has been substantially reduced (for example, following high quality nationwide SIAs), increasing the age from 9 months to 12 months represents a rational and desirable policy change. However, before implementing a change, policy-makers should review local data on the actual age at which infants receive measles vaccine, the coverage expected at 12 months compared with 9 months, age-specific measles incidence and review the immunogenicity and effectiveness of measles vaccine administered at 9 months compared with 12 months.

With respect to introducing a routine second dose of measles vaccine, SAGE emphasizes the principle that this should be considered only in settings where high coverage of the first dose has been achieved and sustained and where measles transmission has been reduced to a low level, indicating a well functioning routine immunization programme. Criteria that could be used to determine if the routine programme is strong enough and the coverage sufficiently high to benefit from a routine second dose require further analysis and consultation.

With respect to the optimal interval between SIAs (for measles), SAGE noted a number of examples where delays in conducting follow-up SIAs have led to large outbreaks (for example, in Brazil, Kenya and Uganda). SAGE agreed with the approach developed by the Regional Office for the Americas and adapted by the Technical Advisory Group on Measles in the African Region that follow-up SIAs should be conducted before the estimated number of susceptible children reaches the size of a birth cohort. This approach has been found to be programmatically useful and sufficiently accurate to prevent large outbreaks.

**Mumps**

*Mumps virus vaccines (WHO position paper)*

If a large proportion of the population remains seronegative for mumps, care should be taken to vaccinate adults considered to be at special risk.
Mumps virus vaccines (WHO position paper)

Mumps vaccines are recommended for use in a 1-dose schedule, given at age 12-18 months.

(Page 355) Control of mumps can be achieved through high routine coverage with an effective mumps-containing vaccine administered at age 12-18 months.

Mumps virus vaccines (WHO position paper)

Due to its known low effectiveness, the Rubini-strain (mumps) vaccine should not be used in national immunization programmes. Persons previously immunized with the Rubini-strain vaccine should receive a dose of an effective mumps vaccine to ensure protection.

Mumps virus vaccines (WHO position paper)

A second (mumps) opportunity is not required in countries where coverage with the first dose is sufficiently high (i.e. > 95%). If a second opportunity is required, it could be administered through a second routine dose, or by implementing periodical catch-up campaigns. Finally, if an initial catch-up campaign is implemented, the target age group should be determined according to mumps susceptibility. In most unvaccinated populations, most children acquire mumps infections before the age of 10 years.

Outbreak Control

Measles vaccines (WHO position paper)

Asymptomatic HIV infection is an indication, not a contraindication, for measles vaccination. Ideally, the vaccine should be offered as early as possible in the course of HIV infection. In areas where measles is prevalent, or during outbreaks, individuals with early signs of HIV-induced immunosuppression may also be considered for vaccination.

Conclusions and recommendations from the meeting of the immunization Strategic Advisory Group of Experts (SAGE) - November 2006

The ACPE (Advisory Committee on Polio Eradication) recommended that the risk of importation from polio-infected areas should be reduced further by ensuring all travellers from such areas are immunized, regardless of their age or immunization status; it proposed that a standing recommendation be established to this effect under the International Health Regulations (IHR) (2005).
Pentavalent

Introducing hepatitis B vaccine into national immunization services

Monovalent HepB vaccines must be used to give the birth dose of HepB vaccine. Combination vaccines that include HepB vaccine must not be used to give the birth dose of HepB vaccine because DTP and Hib vaccines are not recommended to be given at birth. Combination vaccines can be given whenever all of the antigens in the vaccine are indicated.

Introducing Haemophilus influenzae type b (Hib) conjugate vaccine into national immunization services

Combination vaccines that contain Hib conjugate vaccine:
- can be used anytime all of the antigens in the vaccine are indicated by the schedule;
- cannot be used before 6 weeks of age (e.g. for the birth dose of hepatitis B vaccine) because the immunogenicity of the DTP and Hib components will be reduced if given before this age.

Hepatitis B vaccines (WHO position paper)

When immunizing against HBV at birth, only monovalent hepatitis B vaccine should be used: the other antigens found in combination vaccines are currently not approved for use at birth (DTwP, DTaP, Hib, hepatitis A and IPV.)

Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents

Monovalent hepatitis B vaccine MUST BE USED for the birth dose. Combination vaccines that include hepatitis B vaccine MUST NOT BE USED to give the birth dose of hepatitis B vaccine because DTP and Hib vaccines should not be administered at birth. Either monovalent hepatitis B vaccine or combination vaccines may be used for later doses in the hepatitis B vaccine schedule. Combination vaccines can be given whenever all the antigens in the vaccines are indicated.

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

(Considerations for hepatitis B vaccine schedule:)

A determination of the role of perinatal transmission (useful for birth dose considerations) can be made based on the overall seroprevalence of HBsAg, age-specific prevalence of HBsAg, and the prevalence of the HBeAg in pregnant women. Combination products may not be used at birth; therefore, programmes including the birth dose will need to include monovalent HepB vaccine in the supply.
Pertussis

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

In accordance with the recommendations in the previous position paper on diphtheria, use of diphtheriatetanus vaccine is preferable to single-antigen tetanus toxoid vaccine. In future, the inclusion of other antigens, e.g. pertussis or Haemophilus influenzae type b (Hib), in booster doses should be considered.

Pneumococcal

Pneumococcal vaccines (WHO position paper)

(P)oor immunogenicity of polysaccharide (pneumococcal) vaccines in early childhood precludes the use of the 23-valent pneumococcal vaccine in the high-risk group of children under 2 years of age.

Pneumococcal vaccines (WHO position paper)

The duration of protection following immunization with the 23-valent polysaccharide vaccine is estimated at 5 years, or more, in healthy adults. However, the duration may be considerably shorter in some high-risk groups for pneumococcal disease. Revaccination using the polysaccharide vaccine is not routinely recommended.

(Page 116) Revaccination using the polysaccharide vaccine is not routinely recommended, but immunocompromised children who have received polysaccharide vaccine may be revaccinated after 3 years. The safety of three or more doses of the polysaccharide vaccine is not known.

Pneumococcal vaccines (WHO position paper)

A single dose of the 23-valent polysaccharide vaccine is recommended for selected groups above 2 years of age at increased risk of pneumococcal disease. These groups include the healthy elderly (over 65 years of age), particularly those living in institutions.
Pneumococcal vaccines (WHO position paper)

The polyvalent polysaccharide vaccine is recommended for selected groups above 2 years of age with increased risk of pneumococcal disease. Such groups include the healthy elderly (over 65 years old), particularly those living in institutions, patients suffering from chronic organ failure, diabetes, nephrotic syndrome and certain immunodeficiencies, particularly those with functional or anatomical asplenia.

Recent meta-analyses on the efficacy and effectiveness of the pneumococcal polysaccharide vaccine have raised doubts about the benefit of the vaccine in the elderly population. However, these vaccines continue to be recommended for this group based on evidence from observational studies that show a beneficial effect against pneumococcal disease associated with bacteraemia.

State of the art of new vaccines: research and development

The polyvalent PS (polysaccharide) vaccine (against Streptococcus pneumoniae) is recommended for healthy people over 65 years of age, particularly those living in institutions. Randomized controlled trials in healthy elderly people in industrialized countries have, however, failed to show a beneficial effect of the vaccine, so that recommendation for its use in the elderly is based on data from observational studies showing a significant protective effect against invasive (bacteraemic) pneumococcal disease, but not pneumonia.

Conclusions and recommendations from the meeting of the immunization Strategic Advisory Group of Experts (SAGE) - November 2006

Consistent with WHO’s position on new vaccines, PCV-7 (7-serotype conjugate pneumococcal vaccine) can be easily integrated into routine vaccination schedules, and it may be administered at the same time, though at a different site, as other vaccines in infant immunization programmes, including DTP, hepatitis B, Hib and polio vaccines. Routine immunization with PCV-7 should be initiated before the age of 6 months to maximize the benefits of the vaccine and may start as early as 6 weeks of age.
Conclusions and recommendations from the meeting of the immunization Strategic Advisory Group of Experts (SAGE) - November 2006

Clinical efficacy has been demonstrated in 2 schedules (for PCV-7, the 7-serotype conjugate pneumococcal vaccine): a 6-week, 10-week, 14-week schedule and a 2-month, 4-month, 6-month schedule, which was followed by a booster dose at 12-15 months of age. Further information on the cost effectiveness of other potential schedules (for example, using different numbers of doses or different intervals between doses, and with and without boosters) should be obtained. Other schedules (such as 2 doses in a primary series plus a booster dose) are being used in some countries, whose experiences may be important as GAVI-supported countries begin introducing PCV-7 or review its use. Although a late dose (around the first birthday) may be challenging operationally for GAVI-eligible countries, there may be suitable opportunities when a dose of PCV-7 could be given, such as at the same time as measles vaccination. Countries should evaluate this information once it is available and select the most appropriate schedule based on the anticipated impact, cost effectiveness and programmatic feasibility.

Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

The 23-valent (pneumococcal) vaccine is primarily designed for use in older children and adults who are at high risk for pneumococcal disease. It is not licensed for use in children aged <2 years.

Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

PCV-7 (7-valent polysaccharide-protein conjugate pneumococcal) vaccine is highly immunogenic in all age groups, but it is currently licensed for use only in children aged <5 years, including infants aged <12 months.

Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

Trials in several developing countries have demonstrated the efficacy of a 3-dose schedule for infants without a subsequent booster dose. This schedule is compatible with the schedules of national immunization programmes in many developing countries. The benefit of administering an additional dose in the second year of life requires further investigation in these settings. Similarly, consideration of alternative PCV-7 vaccination schedules - including delaying the administration of a third dose so it may be given along with measles vaccination or in the second year of life - should be guided by future research findings.
**Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)**

When the vaccine is first introduced into routine childhood immunization programmes a single catch-up dose of PCV-7 may be given to previously unvaccinated children aged 12-24 months and to children aged 2-5 years who are at high risk.

(Page 98) - When the vaccine is initially introduced into childhood immunization programmes, a single catch-up dose of PCV-7 may be given to previously unvaccinated children aged 12-24 months and to children aged 2-5 years considered to be at high risk. It is not known whether re-vaccination is necessary later in life.

(Page 103) - When PCV-7 is first introduced into routine childhood immunization programmes, maximum individual and community-level protection can be achieved by also providing a single catch-up dose of the vaccine to previously unvaccinated children who are aged 12-24 months and to children aged 2-5 years who are considered to be at high risk.

**Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)**

The primary series of PCV-7 consists of 3 intramuscular doses administered to infants at intervals of at least 4 weeks, starting at the age of 6 weeks or later.

Vaccination at the age of 6 weeks, 10 weeks and 14 weeks in infants in developing countries is as immunogenic as vaccination at 2 months, 4 months and 6 months in industrialized countries. A booster dose administered after 12 months of age may improve the immune response and may especially affect pneumococcal nasopharyngeal carriage. Some industrialized countries have adopted a schedule based on delivering 2 doses during infancy (for example, at 2 months and 4 months) and a third dose at 12-13 months.

**Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)**

To maximize the benefits of the vaccine, routine immunization with PCV-7 should be initiated before 6 months of age and may start as early as 6 weeks of age.

**Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)**

There are 2 schedules that have proven clinical efficacy: a 6 week10 week14 week series and a 2 month4 month6 month series; this latter series is followed by a booster dose at 1215 months of age.

Countries should evaluate information on impact and scheduling once it is available and select the most appropriate schedule based on anticipated impact, cost effectiveness and programmatic feasibility.
Primary immunization with PPV23 consists of a single intramuscular or subcutaneous dose. The intramuscular route may be preferred because of the lower rate of reactions at the injection site. The optimal timing, frequency and clinical effectiveness of additional doses of PPV23 are poorly defined, and national recommendations regarding revaccination vary. However, on the basis of the data on the duration of vaccine-induced protection, WHO suggests one single revaccination >5 years after a first vaccination.

**Introducing hepatitis B vaccine into national immunization services**

Prevention of perinatal HBV transmission should be considered depending on the epidemiology of HBV transmission in a particular country.

In order to prevent HBV transmission from mother to infant, the first dose of HepB vaccine needs to be given as soon as possible after birth (preferably within 24 hours). In countries where a high proportion of chronic infections is acquired perinatally (e.g. South-East Asia), a birth dose should be given to infants. It is usually most feasible to give HepB vaccine at birth when infants are born in hospitals. Efforts should also be made in these countries to give HepB vaccine as soon as possible after delivery to infants delivered at home. In countries where a lower proportion of chronic infections is acquired perinatally (e.g. Africa), the highest priority is to achieve high DTP3 and HepB3 vaccine coverage among infants. In these countries, use of a birth dose may also be considered after disease burden, cost-effectiveness, and feasibility are evaluated.

In countries with a high endemicity of chronic HBV infection (hepatitis B surface antigen [HBsAg] prevalence >8%), catch-up immunization is not usually recommended because most chronic infections are acquired among children <5 years of age, and thus, routine infant vaccination will rapidly reduce HBV transmission. In countries with lower endemicity of chronic HBV infection, a higher proportion of chronic infections may be acquired among older children, adolescents and adults; catch-up immunization for these groups may be considered.
Introducing hepatitis B vaccine into national immunization services

Monovalent HepB vaccines must be used to give the birth dose of HepB vaccine. Combination vaccines that include HepB vaccine must not be used to give the birth dose of HepB vaccine because DTP and Hib vaccines are not recommended to be given at birth. Combination vaccines can be given whenever all of the antigens in the vaccine are indicated.

Introducing hepatitis B vaccine into national immunization services

HepB vaccine schedules are very flexible; thus, there are multiple options for adding the vaccine to existing national immunization schedules without requiring additional visits for immunization. (See Appendix 20_5.)

Programmatically, it is usually easiest if the 3 doses of HepB vaccine are given at the same time as the 3 doses of DTP (Option I). This schedule will prevent infections acquired during early childhood, which account for most of the HBV-related disease burden in high endemic countries, and also will prevent infections acquired later in life. However, this schedule will not prevent perinatal HBV infections because it does not include a dose of HepB vaccine at birth. Two schedule options can be used to prevent perinatal HBV infections: a 3-dose schedule of monovalent HepB vaccine, with the 1st dose given at birth and the 2nd and 3rd doses given at the same time as the 1st and 3rd doses of DTP vaccine (Option II); or a 4-dose schedule in which a birth dose of monovalent HepB vaccine is followed by 3 doses of a combination vaccine, e.g. DTP HepB (Option III).

The 3-dose schedule (Option II) is less expensive, but may be more complicated to administer, because infants receive different vaccines at the 2nd immunization visit than at the 1st and 3rd visits. The 4-dose schedule (Option III) may be easier to administer programmatically, but is more costly, and vaccine supply issues may make it unfeasible.

Introducing Haemophilus influenzae type b (Hib) conjugate vaccine into national immunization services

Combination vaccines that contain Hib conjugate vaccine:
- can be used anytime all of the antigens in the vaccine are indicated by the schedule;
- cannot be used before 6 weeks of age (e.g. for the birth dose of hepatitis B vaccine) because the immunogenicity of the DTP and Hib components will be reduced if given before this age.

Immunization of infants with Hib conjugate vaccine is usually accomplished by giving the vaccine at the same ages as DTP vaccine, either as a separate injection or in combination.

In general, infants should receive a primary dose schedule of 3 doses of Hib conjugate vaccine in the first year of life. Doses of Hib conjugate vaccine should be administered at least 4 weeks apart. Children older than one year of age require only a single dose of Hib conjugate vaccine.
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<td>Introducing Haemophilus influenzae type b (Hib) conjugate vaccine into national immunization services</td>
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<tr>
<td>Booster doses of Hib conjugate vaccine may be given to children in the second year of life, but successful control of Hib disease does not require a booster dose.</td>
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<td>Introduction of Haemophilus influenzae type b vaccine into immunization programmes</td>
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<td>Hib vaccine is indicated in children from the age of 6 weeks up to 18 months.</td>
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<td>Introduction of Haemophilus influenzae type b vaccine into immunization programmes</td>
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<td>In general, the scheduling practices below are followed for Hib immunization:</td>
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<tr>
<td>- The first dose is given to children at six weeks of age or older.</td>
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<tr>
<td>- Three doses are given. Most Hib vaccines require three doses, and in the remainder of this document, a three-dose primary series will be considered routine. One conjugate is licensed for a two-dose primary series, but is not marketed widely.</td>
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<tr>
<td>Reducing measles mortality in emergencies (WHO/UNICEF Joint Statement)</td>
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<tr>
<td>In complex emergencies, immunization should include all children from 6 months through 14 years of age. At a minimum, children from 6 months through 4 years of age must be immunized. The choice of the ages covered will be influenced by vaccine availability, funding, human resources and local measles epidemiology.</td>
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<td>Introduction of Haemophilus influenzae type b vaccine into immunization programmes</td>
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<td>In most countries, the primary series of Hib immunizations protect children through their most susceptible period and thus, in general, a booster is not needed. Although boosters may be considered when Hib disease is a substantial problem for children older than 12 months, some countries do not use booster doses even under these circumstances because of the increased cost and administrative complexity.</td>
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<td>BCG vaccine (WHO position paper)</td>
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<tr>
<td>Unfortunately, the (BCG) vaccine does not fully meet the essential requirement of having a significant impact against the most common manifestation of TB, namely pulmonary disease. Despite the shortcomings of this vaccine, WHO continues to recommend that a single dose of BCG be given to neonates or as soon as possible after birth in countries with a high prevalence of TB.</td>
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</table>
BCG vaccine (WHO position paper)

Since severe adverse effects of BCG vaccination are extremely rare even in asymptomatic, HIV-positive infants, all healthy neonates should be BCG-vaccinated, even in areas endemic for HIV. However, where resources permit, long-term follow-up of BCG-vaccinated infants of known HIV-positive mothers is desirable for early treatment, should disseminated BCG disease occur in children with rapid development of immunodeficiency.

BCG vaccine (WHO position paper)

In cases where infants have been exposed to smear-positive pulmonary TB shortly after birth, BCG vaccination should be delayed until completion of 6 months of prophylactic isoniazid treatment.

BCG vaccine (WHO position paper)

Countries with a low burden of TB may choose to limit BCG vaccination to neonates and infants of recognized high-risk groups for the disease or to skin-test-negative older children. In some low-burden populations, BCG vaccination has been largely replaced by intensified case detection and supervised early treatment.

BCG vaccine (WHO position paper)

There is no proven benefit of repeated BCG vaccination against TB. This also applies to revaccination of BCG-vaccinated individuals who remain negative by subsequent tuberculin testing.

BCG vaccine (WHO position paper)

In the absence of a scar in children in high-burden countries, BCG vaccination is indicated.

BCG vaccine (WHO position paper)

In low-burden countries, good protection against primary TB may also be achieved following vaccination of skin-test-negative adults. BCG vaccination of skin-test-positive individuals, whether induced by environmental mycobacteria, Mtb or BCG does not improve immunity to TB.

BCG vaccine (WHO position paper)

Given the high risk of acquiring TB and the low risk of serious adverse events following BCG vaccination of HIV-exposed neonates, WHO maintains that, in HIV-infected areas, all neonates be given BCG. Older infants or children suspected of being HIV-infected should not be vaccinated if they have symptomatic disease or other evidence of immunosuppression.
Hepatitis A vaccines (WHO position paper)
Currently, four inactivated vaccines against HAV are internationally available. All four vaccines are safe and effective, with long-lasting protection. None of the vaccines are licensed for children less than one year of age.

The (HAV) vaccines are given parenterally, as a two-dose series, 6-18 months apart. The dose of vaccine, vaccination schedule, ages for which the vaccine is licensed, and whether there is a paediatric and adult formulation varies from manufacturer to manufacturer.

Hepatitis B vaccines (WHO position paper)
In countries where a high proportion of HBV infections are acquired perinatally, the first dose of hepatitis B vaccine should be given as soon as possible (<24 hours) after birth.

In countries where a lower proportion of HBV infections are acquired perinatally, the relative contribution of perinatal HBV infection to the overall disease burden, and the feasibility and cost-effectiveness of providing vaccination at birth, should be carefully considered before a decision is made on the optimal vaccination schedule.

Hepatitis B vaccines (WHO position paper)
(Hepatitis B vaccine catch-up) strategies targeted at older age groups or groups with risk factors for acquiring HBV infection should be considered as a supplement to routine infant vaccination in countries of intermediate or low hepatitis B endemicity. In such settings, a substantial proportion of the disease burden may be attributable to infections acquired by older children, adolescents and adults.

In countries of high endemicity, large-scale routine vaccination of infants rapidly reduces the transmission of HBV. In these circumstances, catch-up vaccination of older children and adults has relatively little impact on chronic disease because most of them have already been infected.

Hepatitis B vaccines (WHO position paper)
In highly endemic areas, HBV is most commonly spread from mother to child at birth, or from person to person in early childhood. In countries with low HBV endemicity, sexual transmission and the use of contaminated needles, especially among injecting drug users, are the major routes of infection. However, perinatal transmission may account for 15% of HBV-related deaths, even in low-endemic areas.

Hepatitis B vaccines (WHO position paper)
When immunizing against HBV at birth, only monovalent hepatitis B vaccine should be used: the other antigens found in combination vaccines are currently not approved for use at birth (DTwP, DTaP, Hib, hepatitis A and IPV.)
Hepatitis B vaccines (WHO position paper)

The minimum recommended interval between (hepatitis B vaccine) doses is four weeks. Longer dose intervals may increase the final anti-HBs titres but not the seroconversion rates. More than 3 doses of the vaccine are not required, regardless of duration (> 4 weeks) of the interval between them.

Hepatitis B vaccines (WHO position paper)

Recommended schedules for (hepatitis B) vaccination can be divided into those that include a birth-dose and those that do not. Schedules with a birth-dose call for the first vaccination at birth, followed by a second and third dose at the time of the first and third diphtheria/tetanus/pertussis (DTP) vaccination, respectively (see Appendix 55_9, column II.) Alternatively, a four-dose schedule may be used where the dose at birth is followed by three additional doses; these doses may be given either as monovalent vaccine or as a combination (e.g. with DTP and/or Hib) following the schedules commonly used for those vaccines (see Appendix 55_9, column III.) These schedules will prevent most perinatally acquired infection.

Hepatitis B vaccines (WHO position paper)

Some countries have chosen not to implement universal (hepatitis B) immunization and instead use comprehensive HBsAg screening of pregnant women with immunization of newborn infants born to HBsAg-positive women. This strategy is usually not feasible in developing countries with high prevalence of disease and may not be the most reliable and convenient option even in countries where HBsAg screening in pregnancy is well established.

Hepatitis B vaccines (WHO position paper)

When administered without the birth-dose, hepatitis B vaccine is usually given at the same time as DTP, either as a monovalent presentation or in combination with DTP and/or Hib vaccine (see Appendix 55_9, column I).

Hepatitis B vaccines (WHO position paper)

Countries that opt for schedules with a birth-dose (of hepatitis B vaccine) should vaccinate preterm infants at birth and subsequently enter the respective national hepatitis B vaccination schedule. However, if the birth weight is < 2000 g, the vaccine dose at birth should not be counted towards the primary series, and three additional doses should be given.

Hepatitis B vaccines (WHO position paper)

Immunocompromised children and adults can also benefit from vaccination (with hepatitis B vaccine.) However, the immune response may be reduced and additional injections of the vaccine may be required. Where possible, the anti-HBs antibody titres should be followed up after immunization of immunocompromised individuals.
**Hepatitis B vaccines (WHO position paper)**

All children and adolescents aged less than 18 years and not previously vaccinated should receive the (hepatitis B) vaccine. Hepatitis B vaccination is also indicated for certain groups at high risk of contracting HBV infection, including persons with high-risk sexual behaviour, partners and household contacts of HBsAg-positive persons, injecting drug users, persons who frequently require blood or blood products, recipients of solid organ transplantation, those at occupational risk of HBV infection, including health care workers, as well as for international travellers to HBV-endemic countries.

**Hepatitis B vaccines (WHO position paper)**

Temporary immunity may be obtained using hepatitis B immune globulin (HBIG) for post-exposure prophylaxis. HBIG prophylaxis may be indicated (i) for newborn infants whose mothers are HBsAg-positive, (ii) following percutaneous or mucous membrane exposure to HBsAg-positive blood or body fluids, (iii) following sexual exposure to an HBsAg-positive person, and (iv) to protect patients from recurrent HBV infection following liver transplantation. As a rule, HBIG should be used as an adjunct to hepatitis B vaccine. However, in full-term newborns, the protection against perinatally acquired infection achieved by immediate (<24 hours) hepatitis B vaccination is not significantly improved by the addition of HBIG.

**Hepatitis B vaccines (WHO position paper)**

In countries of high disease endemicity (HBsAg prevalence >8%), HBV is mainly spread from mother to infant at birth or from child to child during early childhood (<5 years). In this epidemiological setting, schedules providing the first vaccine dose at birth are recommended.

**Hepatitis B vaccines (WHO position paper)**

Routine infant hepatitis B vaccination should also be given high priority in countries of intermediate or low HBV endemicity (HBsAg prevalence of >2-<8% or <2%, respectively) because, even in these settings, an important proportion of chronic infections are acquired through HBV transmission during early childhood.

**Hepatitis B vaccines (WHO position paper)**

Although HBsAg screening of all pregnant women and vaccination at birth only of infants born to HBsAg-positive mothers may be an option in areas with low HBV transmission, this strategy may be only partially effective, since women at highest risk of infection often fail to attend prenatal clinics.

**Hepatitis B vaccines (WHO position paper)**

Catch-up vaccination (with hepatitis B vaccine of older age groups, including adolescents and adults) should be considered only if the continuity of the infant vaccination programme can be ensured.
Influenza vaccines (WHO position paper)

Based on data from industrialized countries, and listed in order of priority, the following groups of individuals may be targeted for vaccination (against influenza) in order to reduce the incidence of severe illness and premature death.

1. Residents of long-term care facilities for elderly people and the disabled.
2. Elderly non-institutionalized individuals with chronic conditions such as pulmonary and cardiovascular illness, metabolic diseases including diabetes mellitus and renal dysfunction, and various types of immunosuppression, including people with acquired immunodeficiency syndrome (AIDS) and transplant recipients.
3. All adults and children aged >6 months with any of the conditions mentioned above.
4. Elderly individuals who are above a nationally defined age limit, irrespective of other risk factors. Although the appropriate age for general vaccination may be considerably lower in countries with poor living conditions, most countries define the age limit to be >65 years.
5. Other groups defined on the basis of national data and capacities, such as contacts of high-risk people, pregnant women, health-care workers and others with key functions in society, as well as children 6-23 months of age.

Influenza vaccines (WHO position paper)

In terms of protective efficacy, the live influenza vaccines appear to be comparable with the TIVs (trivalent, inactivated influenza vaccines.) However, CAIV-T (cold-adapted influenza vaccine) is licensed only for healthy people aged 5-49 years, given reports of an increase in reactive airway disease in vaccinees <5 years of age and insufficiently documented protective efficacy in older people.

Measles vaccines (WHO position paper)

Immunization against measles is recommended for all susceptible children and adults for whom measles vaccination is not contraindicated.

Measles vaccines (WHO position paper)

Asymptomatic HIV infection is an indication, not a contraindication, for measles vaccination. Ideally, the vaccine should be offered as early as possible in the course of HIV infection. In areas where measles is prevalent, or during outbreaks, individuals with early signs of HIV-induced immunosuppression may also be considered for vaccination.
Measles vaccines (WHO position paper)

The recommended age for measles vaccination depends on the local measles epidemiology as well as on programmatic considerations. In most developing countries, high attack rates and serious disease among infants necessitate early vaccination, usually at 9 months of age, despite the relatively low (80-85%) seroconversion rates following vaccination in this age group. Unless severely immunocompromised, HIV-infected infants should receive measles vaccine at 6 months of age, followed by an additional dose at 9 months.

Measles vaccines (WHO position paper)

In most industrialized countries, national health systems are consistently able to provide measles vaccine to a high proportion of infants, with a concomitant reduction in measles virus circulation. The probability of an infant being exposed to measles before his or her first birthday is low. It is therefore recommended that measles vaccination be deferred until a child is 12-15 months old, when seroconversion rates in excess of 90% may be expected.

Measles vaccines (WHO position paper)

In countries with measles elimination goals, a one-time only measles SIA (supplementary immunization activity) should be considered, targeting all children aged 9 months to 14 years, regardless of disease history or previous vaccination status. Efforts are also needed to target specific groups of young adults who may be at increased risk for measles infection, including military recruits, university students, health care workers, refugees and international travellers to measles-endemic areas.

Measles vaccines (WHO position paper)

Vitamin A supplementation has been shown to markedly reduce measles-associated mortality in developing countries and should always be given to measles patients in areas where vitamin A deficiency is prevalent.

Pneumococcal vaccines (WHO position paper)

(Poor immunogenicity of polysaccharide (pneumococcal) vaccines in early childhood precludes the use of the 23-valent pneumococcal vaccine in the high-risk group of children under 2 years of age.)
**Pneumococcal vaccines (WHO position paper)**

The duration of protection following immunization with the 23-valent polysaccharide vaccine is estimated at 5 years, or more, in healthy adults. However, the duration may be considerably shorter in some high-risk groups for pneumococcal disease. Revaccination using the polysaccharide vaccine is not routinely recommended.

(Page 116) Revaccination using the polysaccharide vaccine is not routinely recommended, but immunocompromised children who have received polysaccharide vaccine may be revaccinated after 3 years. The safety of three or more doses of the polysaccharide vaccine is not known.

**Pneumococcal vaccines (WHO position paper)**

A single dose of the 23-valent polysaccharide vaccine is recommended for selected groups above 2 years of age at increased risk of pneumococcal disease. These groups include the healthy elderly (over 65 years of age), particularly those living in institutions.

**Pneumococcal vaccines (WHO position paper)**

The polyvalent polysaccharide vaccine is recommended for selected groups above 2 years of age with increased risk of pneumococcal disease. Such groups include the healthy elderly (over 65 years old), particularly those living in institutions, patients suffering from chronic organ failure, diabetes, nephrotic syndrome and certain immunodeficiencies, particularly those with functional or anatomical asplenia.

Recent meta-analyses on the efficacy and effectiveness of the pneumococcal polysaccharide vaccine have raised doubts about the benefit of the vaccine in the elderly population. However, these vaccines continue to be recommended for this group based on evidence from observational studies that show a beneficial effect against pneumococcal disease associated with bacteraemia.

**Rubella vaccines (WHO position paper)**

Rubella vaccine is usually administered at age 12-15 months, but can also be administered to children as young as 9 months of age. In most countries, the vaccine is given as MR or MMR, and the age of administration is chosen based on the appropriate age for measles vaccination. It may also be administered to older children, adolescents, students, child care personnel, health care workers, military personnel and adult men in contact with women of childbearing age.
Yellow fever vaccine (WHO position paper)

YF (yellow fever) vaccine should be offered to all travellers to and from at-risk areas, unless they belong to the group of individuals for whom YF vaccination is contraindicated. There is currently insufficient scientific evidence to support a change in the International health regulations for travelers to endemic areas demanding proof of valid YF vaccination within the preceding ten years. However, in at-risk countries, vaccination resources should be directed to ensuring good primary vaccination coverage rather than to providing booster doses.

Yellow fever vaccine (WHO position paper)

All persons aged 9 months or older and living in YF (yellow fever) at-risk areas should receive YF vaccine. Highest priority should be given to those persons most likely to be exposed, such as forestry and agricultural workers, and to those living in villages or towns with a history of previous outbreaks. Immigrants to such regions from non-endemic areas should also be vaccinated against YF.

Travellers should be vaccinated at least 10 days before arrival in the at risk area.

Yellow fever vaccine (WHO position paper)

In countries at risk of YF (yellow fever), YF vaccine is recommended for use in all children aged at least 9-12 months of age. In addition, preventive vaccination of older children and adults is recommended in at risk areas. Vaccination for YF is also recommended for travellers aged above 9 months who plan to visit areas at risk for YF.

Yellow fever vaccine (WHO position paper)

According to the International health regulations and the WHO International certificate of vaccination, a booster dose of YF (yellow fever) vaccine is required every 10 years. However, in most cases, the duration of protection following the first dose of YF vaccine seems to be at least 30-35 years and possibly lifelong. For this reason, it has been proposed to limit vaccination against YF to a single dose. In order to clarify this matter, WHO organized a consultation with a group of YF experts in March 2003. This group reviewed relevant literature and available data and concluded that, at present, the evidence for protective immunity beyond 10 years was insufficient to justify a change in the current YF vaccination policy for international travellers. However, in at-risk countries, vaccination resources should be directed to ensuring good primary vaccination coverage rather than to providing booster doses. For the purposes of international travel, only YF vaccinations performed at nationally authorized YF vaccination sites and using WHO pre-qualified YF vaccines may be entered into the International Certificate of Vaccination.
Yellow fever vaccine (WHO position paper)

Given the very rare, but potentially severe, adverse effects, YF (yellow fever) vaccine for travellers should be administered on strict indications only, particularly in the elderly. Restriction of YF vaccination to authorized centres is likely to promote the appropriate use of YF vaccine.

Typhoid vaccines (WHO position paper)

Immunization of school-age children is recommended in areas where typhoid fever in these age groups is a significant public health problem, and particularly where antibiotic-resistant S. typhi strains are prevalent. In those settings immunization against typhoid fever will be required until socioeconomic improvements finally interrupt transmission of S. typhi. Where appropriate the use of typhoid vaccines should be harmonized with the administration of tetanus and diphtheria vaccines.

Typhoid vaccines (WHO position paper)

To maintain protection, revaccination (with the Vi polysaccharide vaccine) is recommended every 3 years.

Typhoid vaccines (WHO position paper)

Protection (provided by the Ty21a vaccine) is markedly influenced by the number of doses and their spacing. When the vaccine is given in 3 doses 2 days apart, protective immunity is achieved 7 days after the last dose. In endemic areas a booster dose is recommended every 3 years. Travellers from non-endemic to endemic regions are recommended a booster on a yearly basis. There are currently no field trial data to document the efficacy of this vaccine in children aged < 3 years.

Typhoid vaccines (WHO position paper)

The (Ty21a typhoid) vaccine is usually administrated orally as entericcoated capsules and is registered for use from 6 years of age.

A liquid formulation of the Ty21a (Ty21a typhoid) vaccine can be taken by children as young as 2 years and has proved more immunogenic than the capsular formulation.

Typhoid vaccines (WHO position paper)

Primary immunization with this (old inactivated whole-cell) parenteral (typhoid) vaccine consists of 2 doses given 4 weeks apart; a single booster dose is recommended every 3 years.
Typhoid vaccines (WHO position paper)

For the occasional small-scale vaccination in countries of low typhoid endemicity and for individual protection of short-term visitors to highly-endemic areas, either of the 2 modern (typhoid) vaccines is recommended. It should be noted, however, that the vaccines do not provide complete protection and should not replace hygiene precautions.

Diphtheria vaccine (WHO position paper)

(A)ccording to WHO requirements, the potency of diphtheria vaccine used for the immunization of children shall be no less than 30 IU per single human dose. Vaccines of lower potency are used for immunization of children aged =7 years and adults. This reduction of diphtheria toxoid potency minimizes reactogenicity at the injection site but is still sufficient to provoke an antibody response in older children and adults.

Diphtheria vaccine (WHO position paper)

The recommended schedule for vaccination against diphtheria varies considerably between countries. According to the WHO/EPI schedule, the primary series of DTwP- or DTaP-containing vaccines should be administered in 3 doses, starting as early as 6 weeks of age and given with a minimum interval of 4 weeks. Where resources permit, additional doses can be given after the completion of the primary series. Many national immunization programmes offer 1-2 booster doses, for example one at 2 years of age and a second at age 4-7 years.

Diphtheria vaccine (WHO position paper)

For previously un-immunized children aged 1-7 years, the recommended schedule (for diphtheria vaccine) is 2 doses 2 months apart, and a third dose after 6-12 months using DTwP or DTaP. The recommended schedule for primary immunizations of older children, adolescents and adults using the dT combination is 2 doses -months apart and a third dose after 6-12 months. People living in low-endemic or non-endemic areas should receive booster doses of DT approximately 10 years after completing the primary series and subsequently every 10 years throughout life. Special attention should be paid to immunizing health-care workers who may have occupational exposure to C. diphtheriae. Booster responses can still be elicited after intervals of 25-30 years, so repeat primary immunization is not required when boosters are delayed.

Diphtheria vaccine (WHO position paper)

Unfortunately, diphtheria infection does not always confer protective immunity. Individuals recovering from the disease should therefore complete active immunization with diphtheria toxoid during convalescence.
Diphtheria vaccine (WHO position paper)

To compensate for the loss of natural boosting, industrialized countries should add childhood boosters of diphtheria toxoid to the primary immunization series of infancy. The optimal timing for and the number of such booster doses should be based on epidemiological surveillance as well as on immunological and programmatic considerations. Boosting at the age of 12 months, at school entry and just before leaving school are all possible options. In addition to these childhood immunizations, people living in low-endemic or non-endemic areas may require booster injections of diphtheria toxoid at about 10-year intervals to maintain life-long protection.

Diphtheria vaccine (WHO position paper)

To further promote immunity against diphtheria, diphtheria toxoid and tetanus toxoid rather than tetanus toxoid alone should be used when tetanus prophylaxis is needed following injuries.

WHO recommended standards for surveillance of selected vaccine-preventable diseases

If a child was unprotected (against neonatal tetanus at birth) the mother should receive a dose of TT during the same visit and should be followed up with a subsequent TT dose if needed for protection. The same applies for mothers whose children were protected at birth but who remain eligible for another TT dose.

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

WHO recommends the following schedule for infants (Appendix 39_5).

Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents

In order to prevent perinatal HBV transmission the first dose of hepatitis B vaccine should be given as soon as possible after birth, preferably within 24 hours.
Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents

In all countries: Achieving a high level of completion of the hepatitis B vaccine series among all infants should be the highest priority. This has the greatest overall impact on the prevalence of chronic HBV infection in children, regardless of whether it is feasible to administer a birth dose.

In countries where a high proportion of chronic HBV infections is acquired perinatally (e.g. in south-east Asia): A birth dose should be given to infants who are delivered in hospitals when hepatitis B vaccine is introduced. Efforts should also be made in these countries to give hepatitis B vaccine as soon as possible after birth to infants delivered at home.

In countries where a lower proportion of chronic HBV infections is acquired perinatally (e.g. in Africa): The administration of a birth dose may be considered after evaluating:
- the relative contribution of perinatal HBV infections to the overall disease burden;
- the feasibility and cost-effectiveness of providing a birth dose.

Monovalent hepatitis B vaccine MUST BE USED for the birth dose. Combination vaccines that include hepatitis B vaccine MUST NOT BE USED to give the birth dose of hepatitis B vaccine because DTP and Hib vaccines should not be administered at birth.

Either monovalent hepatitis B vaccine or combination vaccines may be used for later doses in the hepatitis B vaccine schedule. Combination vaccines can be given whenever all the antigens in the vaccines are indicated.

All infants aged under 1 year should receive a full series of hepatitis B vaccine. The need for catch-up immunization of older age groups and for targeted risk groups varies between countries.

Programmatically, it is usually easiest if the three doses of hepatitis B vaccine are given at the same time as the three doses of DTP (See Appendix 36_9 for options for adding hepatitis B vaccine to childhood immunization schedules.)
### Yellow fever vaccine (WHO position paper)

The (YF) vaccine is also widely used for the protection of travelers to YF-endemic areas.

### Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

(Considerations for hepatitis B vaccine schedule:)

A determination of the role of perinatal transmission (useful for birth dose considerations) can be made based on the overall seroprevalence of HBsAg, age-specific prevalence of HBsAg, and the prevalence of the HBeAg in pregnant women.

Combination products may not be used at birth; therefore, programmes including the birth dose will need to include monovalent HepB vaccine in the supply.

### Hepatitis A vaccines (WHO position paper)

In developed countries with low endemicity of hepatitis A and with high rates of disease in specific high-risk populations, vaccination of those populations against hepatitis A may be recommended. The high-risk groups include injection-drug users, homosexual men, persons travelling to high-risk areas, and certain ethnic or religious groups. However, it should be noted that vaccination programmes targeting specific high-risk groups may have little impact on the overall national incidence of disease.

### Mumps virus vaccines (WHO position paper)

If a large proportion of the population remains seronegative for mumps, care should be taken to vaccinate adults considered to be at special risk.

### Mumps virus vaccines (WHO position paper)

Mumps vaccines are recommended for use in a 1-dose schedule, given at age 12-18 months.

(Page 355) Control of mumps can be achieved through high routine coverage with an effective mumps-containing vaccine administered at age 12-18 months.

### Mumps virus vaccines (WHO position paper)

Due to its known low effectiveness, the Rubini-strain (mumps) vaccine should not be used in national immunization programmes. Persons previously immunized with the Rubini-strain vaccine should receive a dose of an effective mumps vaccine to ensure protection.
**Mumps virus vaccines (WHO position paper)**

A second (mumps) opportunity is not required in countries where coverage with the first dose is sufficiently high (i.e. > 95%). If a second opportunity is required, it could be administered through a second routine dose, or by implementing periodical catch-up campaigns. Finally, if an initial catch-up campaign is implemented, the target age group should be determined according to mumps susceptibility. In most unvaccinated populations, most children acquire mumps infections before the age of 10 years.

**Tetanus vaccine (WHO position paper)**

Vaccines containing DT are used for children aged <7 years and dT-containing vaccines for individuals aged ≥7 years.

**Tetanus vaccine (WHO position paper)**

As a rule, vaccine combinations containing diphtheria toxoid (D or d) and tetanus toxoid, rather than tetanus toxoid alone, should be used when immunization against tetanus is indicated.

**Tetanus vaccine (WHO position paper)**

A childhood tetanus immunization schedule of 5 doses is recommended. WHO recommends that the primary series of 3 doses should be given in infancy (aged <1 year). Where pertussis is of particular risk to young infants, DTP immunization should be started at age 6 weeks and 2 subsequent doses should be given at intervals of at least 4 weeks (e.g. at weeks 10 and 14). The exact timing of the booster doses should be flexible to take account of the most appropriate health service contacts in different countries. Ideally, a booster dose should be offered at age 4-7 years followed by another booster in adolescence, e.g. at age 12-15 years. Where a high percentage of children, including girls, attend school, school-based immunization programmes should be used where feasible to deliver the booster doses. Special efforts to reach school nonattenders will be needed.

In addition to the childhood vaccination programme, an extra tetanus toxoid-containing dose to adults will provide additional assurance of long-lasting, possibly lifelong protection. Therefore, a sixth dose should be recommended for adults, e.g. at the time of the first pregnancy or during military service. Those who receive their first tetanus vaccine doses as adolescents or adults require a total of only 5 appropriately spaced doses to obtain the same long-term protection.

**Tetanus vaccine (WHO position paper)**

Even after many years, an interrupted primary- or booster dose (tetanus vaccine) schedule should not be restarted; the schedule is simply continued with the next dose that is due.

**Tetanus vaccine (WHO position paper)**

Both TT and dT can be used at any time during pregnancy.
Tetanus vaccine  (WHO position paper)

The high-risk approach to control neonatal tetanus should be part of the neonatal tetanus elimination strategy in countries where the elimination target (<1 case per 1000 live births at district level) has not yet been reached. This approach targets all women of childbearing age and consists of campaign-style immunization (supplementary immunization activities, or SIAs) with 3 doses of TT (or dT) with an interval of at least 4 weeks between doses 1 and 2, and of at least 6 months between doses 2 and 3. Promotion of clean deliveries is part of this approach. In addition to the 3 doses provided in the SIAs, 2 further boosters are needed to provide long-term protection to women with no documented receipt of tetanus toxoid-containing vaccines in childhood.

Tetanus vaccine  (WHO position paper)

Although adequately immunized people should have sufficient protection against tetanus, treating physicians may give a dose of tetanus toxoid-containing vaccine in the case of an injury, in addition to other preventive measures. Depending on the severity of the injury and on the reliability of the history of previous tetanus vaccinations, the vaccine should be given if the last dose was administered more than 10 years ago (or 5 years in the case of severe injuries)*. The immunization schedule should be completed as soon as possible for those who have not received all doses of the basic schedule.

In addition, passive immunization using tetanus antitoxin, preferably of human origin, may be needed for prophylaxis (e.g. in cases of dirty wounds in incompletely immunized individuals). Such antitoxin is also essential in the treatment of tetanus cases and should be readily available in all countries. From page 200: While tetanus antitoxin should be readily available in all countries, its use cannot substitute for the need to achieve and sustain high tetanus vaccination coverage.


Tetanus vaccine  (WHO position paper)

For previously non-immunized adolescents and adults, the recommended schedule is 2 (tetanus vaccine) doses administered at least 4 weeks apart followed by a third dose administered at least 6 months after the second, and subsequent boosters at least 1 year apart. Those who receive their first tetanus vaccine doses as adolescents or adults require a total of only 5 appropriately spaced doses to obtain long-term protection.
Tetanus vaccine  (WHO position paper)

In countries where MNT remains a public health problem, pregnant women for whom reliable information on previous tetanus vaccinations is not available should receive at least 2 doses of tetanus toxoid-containing vaccine (normally dT) with an interval of at least 4 weeks between the doses. To ensure protection for a minimum of 5 years, a third dose should be given at least 6 months later. A fourth and fifth dose should be given at intervals of at least 1 year, e.g. during subsequent pregnancies, in order to ensure long-term protection. Pregnant women who have received only 3 doses of DTP in early infancy should receive 2 doses of a tetanus toxoid-containing vaccine with a minimal interval of 4 weeks. Those who received 4 doses of tetanus vaccine during their childhood need only 1 booster dose, which should be given at the first opportunity. In both scenarios, to provide protection throughout childbearing age, a sixth dose would be needed after at least 1 year.

Tetanus vaccine  (WHO position paper)

See Appendix 83_18 for a summary table of immunizations with diphtheriatetanuspertussis (DTP) and diphtheria toxoid (Td) vaccines required to obtain long-term protection against tetanus.

State of the art of new vaccines: research and development

Although the whole-cell injectable vaccine (against cholera) is no longer recommended, it still is commercially available in some countries.

State of the art of new vaccines: research and development

Since 1999, WHO recommends the use of killed oral WC/rBS vaccine as a tool to prevent cholera in populations at risk of a cholera epidemic. Such high-risk populations may include, but are not limited to, refugees and urban slum residents.

State of the art of new vaccines: research and development

The Ty21a (typhoind) vaccine is . . . to be swallowed every other day for one week. It can be taken simultaneously with the attenuated CVD103-HgR V. cholerae vaccine.

State of the art of new vaccines: research and development

A trivalent live cold-adapted vaccine (Flumist) has been developed for intranasal spray delivery . . . The vaccine has been licensed in the USA for vaccination of persons from 5-49 years of age, in view of side effects in younger children (wheezing, nasal congestion) and absence of data in the elderly. The vaccine is safe, effective, and shows remarkable genetic stability, but it has to be kept at -18C.
State of the art of new vaccines: research and development

The polyvalent PS (polysaccharide) vaccine (against Streptococcus pneumoniae) is recommended for healthy people over 65 years of age, particularly those living in institutions. Randomized controlled trials in healthy elderly people in industrialized countries have, however, failed to show a beneficial effect of the vaccine, so that recommendation for its use in the elderly is based on data from observational studies showing a significant protective effect against invasive (bacteraemic) pneumococcal disease, but not pneumonia.

State of the art of new vaccines: research and development

Since 1974, BCG vaccination has been included in the WHO Expanded Programme on Immunization (EPI).

State of the art of new vaccines: research and development

This type of vaccine (inactivated rabies vaccine) is still unfortunately manufactured and used in South-East Asia, but the number of countries doing so has been decreasing during the past 10 years in accordance with the WHO recommendations to replace them by cell-cultured vaccines.

State of the art of new vaccines: research and development

It is well known that rabies PEP [post-exposure prophylaxis] with vaccine alone is not always sufficient, especially in cases of severe exposure (category 3) where concomitant passive immunization with rabies immunoglobulins (RIG) is strongly recommended.

WHO/UNICEF joint statement - Global plan for reducing measles mortality 2006-2010

A second opportunity for measles immunization is essential to ensure protection against measles.

WHO/UNICEF joint statement - Global plan for reducing measles mortality 2006-2010

In conflict or emergency areas, WHO and UNICEF have a commitment to ensure that, at a minimum, measles vaccine and vitamin A supplements are administered. (WHO/UNICEF joint statement: reducing measles mortality in emergencies, 2002.)

Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

The 23-valent (pneumococcal) vaccine is primarily designed for use in older children and adults who are at high risk for pneumococcal disease. It is not licensed for use in children aged <2 years.
Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

PCV-7 (7-valent polysaccharideprotein conjugate pneumococcal) vaccine is highly immunogenic in all age groups, but it is currently licensed for use only in children aged <5 years, including infants aged <12 months.

Trials in several developing countries have demonstrated the efficacy of a 3-dose schedule for infants without a subsequent booster dose. This schedule is compatible with the schedules of national immunization programmes in many developing countries. The benefit of administering an additional dose in the second year of life requires further investigation in these settings. Similarly, consideration of alternative PCV-7 vaccination schedules - including delaying the administration of a third dose so it may be given along with measles vaccination or in the second year of life - should be guided by future research findings.

When the vaccine is first introduced into routine childhood immunization programmes a single catch-up dose of PCV-7 may be given to previously unvaccinated children aged 12-24 months and to children aged 2-5 years who are at high risk.

The primary series of PCV-7 consists of 3 intramuscular doses administered to infants at intervals of at least 4 weeks, starting at the age of 6 weeks or later.

Vaccination at the age of 6 weeks, 10 weeks and 14 weeks in infants in developing countries is as immunogenic as vaccination at 2 months, 4 months and 6 months in industrialized countries. A booster dose administered after 12 months of age may improve the immune response and may especially affect pneumococcal nasopharyngeal carriage. Some industrialized countries have adopted a schedule based on delivering 2 doses during infancy (for example, at 2 months and 4 months) and a third dose at 12-13 months.
Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

To maximize the benefits of the vaccine, routine immunization with PCV-7 should be initiated before 6 months of age and may start as early as 6 weeks of age.

There are 2 schedules that have proven clinical efficacy: a 6 week10 week14 week series and a 2 month4 month6 month series; this latter series is followed by a booster dose at 1215 months of age.

Countries should evaluate information on impact and scheduling once it is available and select the most appropriate schedule based on anticipated impact, cost effectiveness and programmatic feasibility.

Rabies vaccines (WHO position paper)

Pre-exposure rabies vaccination requires IM doses of 1 ml or 0.5 ml, depending on the vaccine type, given on days 0, 7 and 28 (day 28 preferable, but administration may be advanced towards day 21 if time is limited).

23-valent pneumococcal polysaccharide vaccine (WHO position paper)

Primary immunization with PPV23 consists of a single intramuscular or subcutaneous dose. The intramuscular route may be preferred because of the lower rate of reactions at the injection site. The optimal timing, frequency and clinical effectiveness of additional doses of PPV23 are poorly defined, and national recommendations regarding revaccination vary. However, on the basis of the data on the duration of vaccine-induced protection, WHO suggests one single revaccination >5 years after a first vaccination.
BCG vaccine (WHO position paper)

BCG vaccination is indicated

- for all infants living in areas where TB is highly endemic (concerning HIV, see below);
- for infants and children at particular risk of TB exposure in otherwise low-endemic areas;
- for persons exposed to multidrug-resistant Mtb (impact not established.)

BCG vaccination is contraindicated

- for persons with impaired immunity symptomatic HIV infection, known or suspected congenital immunodeficiency, leukaemia, lymphoma or generalized malignant disease);
- for patients under immnosuppressive treatment (corticosteroids, alkylating agents, antimetabolites, radiation);
- in pregnancy.

Polio

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

WHO recommends the following schedule for infants (Appendix 39_5).

Conclusions and recommendations from the meeting of the immunization Strategic Advisory Group of Experts (SAGE) - November 2006

The ACPE (Advisory Committee on Polio Eradication) recommended that the risk of importation from polio-infected areas should be reduced further by ensuring all travellers from such areas are immunized, regardless of their age or immunization status; it proposed that a standing recommendation be established to this effect under the International Health Regulations (IHR) (2005).

Weekly Epidemiological Record, No. 23 2010

The primary series of 3 OPV vaccinations should be administered according to the schedules of national immunization programmes, for example at 6 weeks, 10 weeks, and 14 weeks, or at 2 months, 4 months, and 6 months. In addition, a birth dose should be given as soon as possible after birth when the potential for poliovirus importation is very high or high and the transmission potential is high or moderate. The interval between doses of OPV or IPV should be 4 weeks.
IPV is given intramuscularly (preferably) or subcutaneously, and may be offered as a component of fixed combinations of vaccines. A primary series of 3 doses should be administered beginning at 2 months of age. If the primary series begins earlier (for example, with a 6-week, 10-week and 14-week schedule) then a booster dose should be administered after an interval of 6 months (for a 4-dose schedule). Where sequential IPV/OPV is used, WHO recommends that IPV be administered at 2 months of age (e.g. an IPV-OPV-OPV schedule) or at 2 months and 3-4 months of age (e.g. an IPV-IPV-OPV-OPV schedule); in both schedules IPV should be followed by at least 2 doses of OPV.

Each dose in the primary series, whether IPV or OPV, should be separated by 4-8 weeks, depending on the risk of exposure to polio in early childhood. Both IPV and OPV may be administered simultaneously with other vaccines in national childhood immunization programmes.

**Pregnant Women**

**Influenza vaccines (WHO position paper)**

Based on data from industrialized countries, and listed in order of priority, the following groups of individuals may be targeted for vaccination (against influenza) in order to reduce the incidence of severe illness and premature death.

1. Residents of long-term care facilities for elderly people and the disabled.
2. Elderly non-institutionalized individuals with chronic conditions such as pulmonary and cardiovascular illness, metabolic diseases including diabetes mellitus and renal dysfunction, and various types of immunosuppression, including people with acquired immunodeficiency syndrome (AIDS) and transplant recipients.
3. All adults and children aged >6 months with any of the conditions mentioned above.
4. Elderly individuals who are above a nationally defined age limit, irrespective of other risk factors. Although the appropriate age for general vaccination may be considerably lower in countries with poor living conditions, most countries define the age limit to be >65 years.
5. Other groups defined on the basis of national data and capacities, such as contacts of high-risk people, pregnant women, health-care workers and others with key functions in society, as well as children 6-23 months of age.

**Tetanus vaccine (WHO position paper)**

Both TT and dT can be used at any time during pregnancy.
Tetanus vaccine (WHO position paper)

In countries where MNT remains a public health problem, pregnant women for whom reliable information on previous tetanus vaccinations is not available should receive at least 2 doses of tetanus toxoid-containing vaccine (normally dT) with an interval of at least 4 weeks between the doses. To ensure protection for a minimum of 5 years, a third dose should be given at least 6 months later. A fourth and fifth dose should be given at intervals of at least 1 year, e.g. during subsequent pregnancies, in order to ensure long-term protection. Pregnant women who have received only 3 doses of DTP in early infancy should receive 2 doses of a tetanus toxoid-containing vaccine with a minimal interval of 4 weeks. Those who received 4 doses of tetanus vaccine during their childhood need only 1 booster dose, which should be given at the first opportunity. In both scenarios, to provide protection throughout childbearing age, a sixth dose would be needed after at least 1 year.

BCG vaccine (WHO position paper)

BCG vaccination is indicated

- for all infants living in areas where TB is highly endemic (concerning HIV, see below);
- for infants and children at particular risk of TB exposure in otherwise low-endemic areas;
- for persons exposed to multidrug-resistant Mtb (impact not established.)

BCG vaccination is contraindicated

- for persons with impaired immunity symptomatic HIV infection, known or suspected congenital immunodeficiency, leukaemia, lymphoma or generalized malignant disease);
- for patients under immunosuppressive treatment (corticosteroids, alkylating agents, antimetabolites, radiation);
- in pregnancy.

Program Management

Yellow fever vaccine (WHO position paper)

YF (yellow fever) vaccine should be offered to all travellers to and from at-risk areas, unless they belong to the group of individuals for whom YF vaccination is contraindicated. There is currently insufficient scientific evidence to support a change in the International health regulations for travelers to endemic areas demanding proof of valid YF vaccination within the preceding ten years. However, in at-risk countries, vaccination resources should be directed to ensuring good primary vaccination coverage rather than to providing booster doses.
Yellow fever vaccine (WHO position paper)

Given the very rare, but potentially severe, adverse effects, YF (yellow fever) vaccine for travellers should be administered on strict indications only, particularly in the elderly. Restriction of YF vaccination to authorized centres is likely to promote the appropriate use of YF vaccine.

WHO/UNICEF joint statement - Global plan for reducing measles mortality 2006-2010

In conflict or emergency areas, WHO and UNICEF have a commitment to ensure that, at a minimum, measles vaccine and vitamin A supplements are administered. (WHO/UNICEF joint statement: reducing measles mortality in emergencies, 2002.)

Rabies

State of the art of new vaccines: research and development

This type of vaccine (inactivated rabies vaccine) is still unfortunately manufactured and used in South-East Asia, but the number of countries doing so has been decreasing during the past 10 years in accordance with the WHO recommendations to replace them by cell-cultured vaccines.

Rabies vaccines (WHO position paper)

Pre-exposure rabies vaccination requires IM doses of 1 ml or 0.5 ml, depending on the vaccine type, given on days 0, 7 and 28 (day 28 preferable, but administration may be advanced towards day 21 if time is limited).
Research

Global Advisory Committee on Vaccine Safety, 34 December 2003

There are few population-based data on the effectiveness, or otherwise, of BCG vaccine in preventing severe tuberculosis in HIV-positive infants. Given the high prevalence of HIV and tuberculosis in certain countries and of the current development of new tuberculosis vaccines, some of which are based on BCG, GACVS advises no change in the current recommendations for BCG immunization of infants in countries with a high prevalence of tuberculosis and that population-based studies should be undertaken to determine the efficacy and safety of BCG and related vaccines in HIV-negative and HIV-positive children in countries with a high endemic rate of tuberculosis.

State of the art of new vaccines: research and development

Although the whole-cell injectable vaccine (against cholera) is no longer recommended, it still is commercially available in some countries.

Conclusions and recommendations from the meeting of the immunization Strategic Advisory Group of Experts (SAGE) - November 2006

Clinical efficacy has been demonstrated in 2 schedules (for PCV-7, the 7-serotype conjugate pneumococcal vaccine): a 6-week, 10-week, 14-week schedule and a 2-month, 4-month, 6-month schedule, which was followed by a booster dose at 12-15 months of age. Further information on the cost effectiveness of other potential schedules (for example, using different numbers of doses or different intervals between doses, and with and without boosters) should be obtained. Other schedules (such as 2 doses in a primary series plus a booster dose) are being used in some countries, whose experiences may be important as GAVI-supported countries begin introducing PCV-7 or review its use. Although a late dose (around the first birthday) may be challenging operationally for GAVI-eligible countries, there may be suitable opportunities when a dose of PCV-7 could be given, such as at the same time as measles vaccination. Countries should evaluate this information once it is available and select the most appropriate schedule based on the anticipated impact, cost effectiveness and programmatic feasibility.

Rubella

Rubella vaccines (WHO position paper)

Rubella vaccine is usually administered at age 12-15 months, but can also be administered to children as young as 9 months of age. In most countries, the vaccine is given as MR or MMR, and the age of administration is chosen based on the appropriate age for measles vaccination. It may also be administered to older children, adolescents, students, child care personnel, health care workers, military personnel and adult men in contact with women of childbearing age.
**SAGE - recommend to WHO**

**Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 9-11 November 2005**

(SAGE recognized) that immunization schedules in use today vary greatly around the world, and it is unlikely that a single, uniform immunization schedule would suit all countries. WHO should aim to provide countries with advice on the parameters to be considered when they select a schedule. There was unanimous support for a new review of the evidence base, and agreement that changes in schedule are not appropriate without strong evidence to demonstrate benefit.

SAGE recommended that a review of the issues surrounding the primary schedule, boosters and adolescent vaccination should be undertaken. This should incorporate disease control strategies, immunology, operational aspects of health services (not just vaccination services) and economics.

**Conclusions and recommendations from the meeting of the immunization Strategic Advisory Group of Experts (SAGE) - November 2006**

The ACPE (Advisory Committee on Polio Eradication) recommended that the risk of importation from polio-infected areas should be reduced further by ensuring all travellers from such areas are immunized, regardless of their age or immunization status; it proposed that a standing recommendation be established to this effect under the International Health Regulations (IHR) (2005).

## Tetanus

**Diphtheria vaccine (WHO position paper)**

To further promote immunity against diphtheria, diphtheria toxoid and tetanus toxoid rather than tetanus toxoid alone should be used when tetanus prophylaxis is needed following injuries.

**WHO recommended standards for surveillance of selected vaccine-preventable diseases**

If a child was unprotected (against neonatal tetanus at birth) the mother should receive a does of TT during the same visit and should be followed up with a subsequent TT dose if needed for protection. The same applies for mothers whose children were protected at birth but who remain eligible for another TT dose.

**Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006**

It was generally agreed (by SAGE members) that (for tetanus vaccine) there is no maximum interval between the primary series and a booster dose and that there is no need to re-start interrupted immunization schedules. Vaccination of school-age children would also help to sustain MNT (maternal and neonatal tetanus) elimination.
Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

SAGE recommended the following (regarding tetanus immunization schedules):

A 5-dose childhood immunization schedule should be promoted. The primary series of 3 doses would be given in infancy, with a booster dose ideally at age 4-7 years and another booster dose in adolescence (e.g. at age 12-15 years). The exact timing of the booster doses should be flexible to take account of the most appropriate health service contacts in different countries and of integration with other vaccines and other interventions such as bednet distribution, vitamin A therapy and deworming. In some countries, these boosters could be given through school-based approaches, but efforts to reach those not attending school will be important. A sixth dose should be recommended for adults, for example in the first pregnancy or for military recruits.

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

In accordance with the recommendations in the previous position paper on diphtheria, use of diphtheriatetanus vaccine is preferable to single-antigen tetanus toxoid vaccine. In future, the inclusion of other antigens, e.g. pertussis or Haemophilus influenzae type b (Hib), in booster doses should be considered.

Tetanus vaccine (WHO position paper)

Vaccines containing DT are used for children aged <7 years and dT-containing vaccines for individuals aged =7 years.

Tetanus vaccine (WHO position paper)

As a rule, vaccine combinations containing diphtheria toxoid (D or d) and tetanus toxoid, rather than tetanus toxoid alone, should be used when immunization against tetanus is indicated.
Tetanus vaccine  (WHO position paper)

A childhood tetanus immunization schedule of 5 doses is recommended. WHO recommends that the primary series of 3 doses should be given in infancy (aged <1 year). Where pertussis is of particular risk to young infants, DTP immunization should be started at age 6 weeks and 2 subsequent doses should be given at intervals of at least 4 weeks (e.g. at weeks 10 and 14). The exact timing of the booster doses should be flexible to take account of the most appropriate health service contacts in different countries. Ideally, a booster dose should be offered at age 4-7 years followed by another booster in adolescence, e.g. at age 12-15 years. Where a high percentage of children, including girls, attend school, school-based immunization programmes should be used where feasible to deliver the booster doses. Special efforts to reach school nonattenders will be needed.

In addition to the childhood vaccination programme, an extra tetanus toxoid-containing dose to adults will provide additional assurance of long-lasting, possibly lifelong protection. Therefore, a sixth dose should be recommended for adults, e.g. at the time of the first pregnancy or during military service. Those who receive their first tetanus vaccine doses as adolescents or adults require a total of only 5 appropriately spaced doses to obtain the same long-term protection.

Tetanus vaccine  (WHO position paper)

Even after many years, an interrupted primary- or boosterdose (tetanus vaccine) schedule should not be restarted; the schedule is simply continued with the next dose that is due.

Tetanus vaccine  (WHO position paper)

The interval between the tetanus toxoid-containing doses should be at least 4 weeks. Longer intervals may increase the magnitude and duration of the immune response, but should not be a reason to delay immunization.

Tetanus vaccine  (WHO position paper)

Both TT and dT can be used at any time during pregnancy.

Tetanus vaccine  (WHO position paper)

The high-risk approach to control neonatal tetanus should be part of the neonatal tetanus elimination strategy in countries where the elimination target (<1 case per 1000 live births at district level) has not yet been reached. This approach targets all women of childbearing age and consists of campaign-style immunization (supplementary immunization activities, or SIAs) with 3 doses of TT (or dT) with an interval of at least 4 weeks between doses 1 and 2, and of at least 6 months between doses 2 and 3. Promotion of clean deliveries is part of this approach. In addition to the 3 doses provided in the SIAs, 2 further boosters are needed to provide long-term protection to women with no documented receipt of tetanus toxoid-containing vaccines in childhood.
Tetanus vaccine (WHO position paper)

Although adequately immunized people should have sufficient protection against tetanus, treating physicians may give a dose of tetanus toxoid-containing vaccine in the case of an injury, in addition to other preventive measures. Depending on the severity of the injury and on the reliability of the history of previous tetanus vaccinations, the vaccine should be given if the last dose was administered more than 10 years ago (or 5 years in the case of severe injuries)*. The immunization schedule should be completed as soon as possible for those who have not received all doses of the basic schedule.

In addition, passive immunization using tetanus antitoxin, preferably of human origin, may be needed for prophylaxis (e.g. in cases of dirty wounds in incompletely immunized individuals). Such antitoxin is also essential in the treatment of tetanus cases and should be readily available in all countries. From page 200: While tetanus antitoxin should be readily available in all countries, its use cannot substitute for the need to achieve and sustain high tetanus vaccination coverage.


Tetanus vaccine (WHO position paper)

For previously non-immunized adolescents and adults, the recommended schedule is 2 (tetanus vaccine) doses administered at least 4 weeks apart followed by a third dose administered at least 6 months after the second, and subsequent boosters at least 1 year apart. Those who receive their first tetanus vaccine doses as adolescents or adults require a total of only 5 appropriately spaced doses to obtain long-term protection.

Tetanus vaccine (WHO position paper)

In countries where MNT remains a public health problem, pregnant women for whom reliable information on previous tetanus vaccinations is not available should receive at least 2 doses of tetanus toxoid-containing vaccine (normally dT) with an interval of at least 4 weeks between the doses. To ensure protection for a minimum of 5 years, a third dose should be given at least 6 months later. A fourth and fifth dose should be given at intervals of at least 1 year, e.g. during subsequent pregnancies, in order to ensure long-term protection. Pregnant women who have received only 3 doses of DTP in early infancy should receive 2 doses of a tetanus toxoid-containing vaccine with a minimal interval of 4 weeks. Those who received 4 doses of tetanus vaccine during their childhood need only 1 booster dose, which should be given at the first opportunity. In both scenarios, to provide protection throughout childbearing age, a sixth dose would be needed after at least 1 year.
**Tetanus vaccine (WHO position paper)**

See Appendix 83.18 for a summary table of immunizations with diphtheriatetanuspertussis (DTP) and diphtheria toxoid (Td) vaccines required to obtain long-term protection against tetanus.

**Travellers**

**Hepatitis B vaccines (WHO position paper)**

All children and adolescents aged less than 18 years and not previously vaccinated should receive the (hepatitis B) vaccine. Hepatitis B vaccination is also indicated for certain groups at high risk of contracting HBV infection, including persons with high-risk sexual behaviour, partners and household contacts of HBsAg-positive persons, injecting drug users, persons who frequently require blood or blood products, recipients of solid organ transplantation, those at occupational risk of HBV infection, including health care workers, as well as for international travellers to HBV-endemic countries.

**Measles vaccines (WHO position paper)**

In countries with measles elimination goals, a one-time only measles SIA (supplementary immunization activity) should be considered, targeting all children aged 9 months to 14 years, regardless of disease history or previous vaccination status. Efforts are also needed to target specific groups of young adults who may be at increased risk for measles infection, including military recruits, university students, health care workers, refugees and international travellers to measles-endemic areas.

**Yellow fever vaccine (WHO position paper)**

YF (yellow fever) vaccine should be offered to all travellers to and from at-risk areas, unless they belong to the group of individuals for whom YF vaccination is contraindicated. There is currently insufficient scientific evidence to support a change in the International health regulations for travelers to endemic areas demanding proof of valid YF vaccination within the preceding ten years. However, in at-risk countries, vaccination resources should be directed to ensuring good primary vaccination coverage rather than to providing booster doses.

**Yellow fever vaccine (WHO position paper)**

All persons aged 9 months or older and living in YF (yellow fever) at-risk areas should receive YF vaccine. Highest priority should be given to those persons most likely to be exposed, such as forestry and agricultural workers, and to those living in villages or towns with a history of previous outbreaks. Immigrants to such regions from non-endemic areas should also be vaccinated against YF.

Travellers should be vaccinated at least 10 days before arrival in the at-risk area.
Yellow fever vaccine (WHO position paper)

In countries at risk of YF (yellow fever), YF vaccine is recommended for use in all children aged at least 9-12 months of age. In addition, preventive vaccination of older children and adults is recommended in at risk areas. Vaccination for YF is also recommended for travellers aged above 9 months who plan to visit areas at risk for YF.

Yellow fever vaccine (WHO position paper)

According to the International health regulations and the WHO International certificate of vaccination, a booster dose of YF (yellow fever) vaccine is required every 10 years. However, in most cases, the duration of protection following the first dose of YF vaccine seems to be at least 30-35 years and possibly lifelong. For this reason, it has been proposed to limit vaccination against YF to a single dose. In order to clarify this matter, WHO organized a consultation with a group of YF experts in March 2003. This group reviewed relevant literature and available data and concluded that, at present, the evidence for protective immunity beyond 10 years was insufficient to justify a change in the current YF vaccination policy for international travellers. However, in at-risk countries, vaccination resources should be directed to ensuring good primary vaccination coverage rather than to providing booster doses. For the purposes of international travel, only YF vaccinations performed at nationally authorized YF vaccination sites and using WHO pre-qualified YF vaccines may be entered into the International Certificate of Vaccination.

Yellow fever vaccine (WHO position paper)

Given the very rare, but potentially severe, adverse effects, YF (yellow fever) vaccine for travellers should be administered on strict indications only, particularly in the elderly. Restriction of YF vaccination to authorized centres is likely to promote the appropriate use of YF vaccine.

Typhoid vaccines (WHO position paper)

Protection (provided by the Ty21a vaccine) is markedly influenced by the number of doses and their spacing. When the vaccine is given in 3 doses 2 days apart, protective immunity is achieved 7 days after the last dose. In endemic areas a booster dose is recommended every 3 years. Travellers from non-endemic to endemic regions are recommended a booster on a yearly basis. There are currently no field trial data to document the efficacy of this vaccine in children aged < 3 years.

Typhoid vaccines (WHO position paper)

For the occasional small-scale vaccination in countries of low typhoid endemicity and for individual protection of short-term visitors to highly-endemic areas, either of the 2 modern (typhoid) vaccines is recommended. It should be noted, however, that the vaccines do not provide complete protection and should not replace hygiene precautions.
Global Advisory Committee on Vaccine Safety, 23 December 2004

GACVS reiterates that particular care should be taken that the (17D yellow fever) vaccine is received only by those travellers who are truly at risk of exposure to yellow fever. In addition, vaccine providers should give careful consideration to the risks and benefits for elderly travellers and should routinely enquire about a history of thymus disorder, irrespective of the age of the subject. Where a history of thymus disorder is reported, alternative prevention measures should be considered.

Yellow fever vaccine (WHO position paper)

The (YF) vaccine is also widely used for the protection of travelers to YF-endemic areas.

Hepatitis A vaccines (WHO position paper)

In developed countries with low endemicity of hepatitis A and with high rates of disease in specific high-risk populations, vaccination of those populations against hepatitis A may be recommended. The high-risk groups include injection-drug users, homosexual men, persons travelling to high-risk areas, and certain ethnic or religious groups. However, it should be noted that vaccination programmes targeting specific high-risk groups may have little impact on the overall national incidence of disease.

Conclusions and recommendations from the meeting of the immunization Strategic Advisory Group of Experts (SAGE) - November 2006

The ACPE (Advisory Committee on Polio Eradication) recommended that the risk of importation from polio-infected areas should be reduced further by ensuring all travellers from such areas are immunized, regardless of their age or immunization status; it proposed that a standing recommendation be established to this effect under the International Health Regulations (IHR) (2005).

Typhoid

Typhoid vaccines (WHO position paper)

Immunization of school-age children is recommended in areas where typhoid fever in these age groups is a significant public health problem, and particularly where antibiotic-resistant S. typhi strains are prevalent. In those settings immunization against typhoid fever will be required until socioeconomic improvements finally interrupt transmission of S. typhi. Where appropriate the use of typhoid vaccines should be harmonized with the administration of tetanus and diphtheria vaccines.

Typhoid vaccines (WHO position paper)

To maintain protection, revaccination (with the Vi polysaccharide vaccine) is recommended every 3 years.
**Typhoid vaccines (WHO position paper)**

Protection (provided by the Ty21a vaccine) is markedly influenced by the number of doses and their spacing. When the vaccine is given in 3 doses 2 days apart, protective immunity is achieved 7 days after the last dose. In endemic areas a booster dose is recommended every 3 years. Travellers from non-endemic to endemic regions are recommended a booster on a yearly basis. There are currently no field trial data to document the efficacy of this vaccine in children aged < 3 years.

**Typhoid vaccines (WHO position paper)**

The (Ty21a typhoid) vaccine is usually administrated orally as entericoated capsules and is registered for use from 6 years of age.

A liquid formulation of the Ty21a (Ty21a typhoid) vaccine can be taken by children as young as 2 years and has proved more immunogenic than the capsular formulation.

**Typhoid vaccines (WHO position paper)**

Primary immunization with this (old inactivated whole-cell) parenteral (typhoid) vaccine consists of 2 doses given 4 weeks apart; a single booster dose is recommended every 3 years.

**Typhoid vaccines (WHO position paper)**

For the occasional small-scale vaccination in countries of low typhoid endemicity and for individual protection of short-term visitors to highly-endemic areas, either of the 2 modern (typhoid) vaccines is recommended. It should be noted, however, that the vaccines do not provide complete protection and should not replace hygiene precautions.

**State of the art of new vaccines: research and development**

The Ty21a (typhoind) vaccine is . . . to be swallowed every other day for one week. It can be taken simultaneously with the attenuated CVD103-HgR V. cholerae vaccine.

**Typhoid vaccines: WHO position paper**

The Vi polysaccharide vaccine: The vaccine is licensed for individuals aged >2 years. Only 1 dose is required, and the vaccine confers protection 7 days after injection. To maintain protection, revaccination is recommended every 3 years. The Vi polysaccharide vaccine can be co-administered with other vaccines relevant for international travellers such as yellow fever and hepatitis A and with vaccines of the routine childhood immunization programmes.
Vaccine Administration

Typhoid vaccines (WHO position paper)

The (Ty21a typhoid) vaccine is usually administrated orally as entericcoated capsules and is registered for use from 6 years of age.

A liquid formulation of the Ty21a (Ty21a typhoid) vaccine can be taken by children as young as 2 years and has proved more immunogenic than the capsular formulation.

Conclusions and recommendations from the meeting of the immunization Strategic Advisory Group of Experts (SAGE) - November 2006

Consistent with WHO's position on new vaccines, PCV-7 (7-serotype conjugate pneumococcal vaccine) can be easily integrated into routine vaccination schedules, and it may be administered at the same time, though at a different site, as other vaccines in infant immunization programmes, including DTP, hepatitis B, Hib and polio vaccines. Routine immunization with PCV-7 should be initiated before the age of 6 months to maximize the benefits of the vaccine and may start as early as 6 weeks of age.

23-valent pneumococcal polysaccharide vaccine (WHO position paper)

Primary immunization with PPV23 consists of a single intramuscular or subcutaneous dose. The intramuscular route may be preferred because of the lower rate of reactions at the injection site. The optimal timing, frequency and clinical effectiveness of additional doses of PPV23 are poorly defined, and national recommendations regarding revaccination vary. However, on the basis of the data on the duration of vaccine-induced protection, WHO suggests one single revaccination >5 years after a first vaccination.

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Vaccine Handling

State of the art of new vaccines: research and development

A trivalent live cold-adapted vaccine (Flumist) has been developed for intranasal spray delivery . . . The vaccine has been licensed in the USA for vaccination of persons from 5-49 years of age, in view of side effects in younger children (wheezing, nasal congestion) and absence of data in the elderly. The vaccine is safe, effective, and shows remarkable genetic stability, but it has to be kept at -18°C.
**Vaccine Quality**

**Mumps virus vaccines (WHO position paper)**

Due to its known low effectiveness, the Rubini-strain (mumps) vaccine should not be used in national immunization programmes. Persons previously immunized with the Rubini-strain vaccine should receive a dose of an effective mumps vaccine to ensure protection.

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**Vitamin A**

**Measles vaccines (WHO position paper)**

Vitamin A supplementation has been shown to markedly reduce measles-associated mortality in developing countries and should always be given to measles patients in areas where vitamin A deficiency is prevalent.

WER 2004, vol. 79, 14, pp 130-142
page 134

**WHO/UNICEF joint statement - Global plan for reducing measles mortality 2006-2010**

In conflict or emergency areas, WHO and UNICEF have a commitment to ensure that, at a minimum, measles vaccine and vitamin A supplements are administered. (WHO/UNICEF joint statement: reducing measles mortality in emergencies, 2002.)

WHO/IVB/05.11
page 3

**Yellow Fever**

**Yellow fever vaccine (WHO position paper)**

YF (yellow fever) vaccine should be offered to all travellers to and from at-risk areas, unless they belong to the group of individuals for whom YF vaccination is contraindicated. There is currently insufficient scientific evidence to support a change in the International health regulations for travelers to endemic areas demanding proof of valid YF vaccination within the preceding ten years. However, in at-risk countries, vaccination resources should be directed to ensuring good primary vaccination coverage rather than to providing booster doses.

WER 2003, vol. 78, 40, pp 349-359
page 350

**Yellow fever vaccine (WHO position paper)**

All persons aged 9 months or older and living in YF (yellow fever) at-risk areas should receive YF vaccine. Highest priority should be given to those persons most likely to be exposed, such as forestry and agricultural workers, and to those living in villages or towns with a history of previous outbreaks. Immigrants to such regions from non-endemic areas should also be vaccinated against YF.

Travellers should be vaccinated at least 10 days before arrival in the at risk area.

WER 2003, vol. 78, 40, pp 349-359
page 356
Yellow fever vaccine (WHO position paper)

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Yellow fever vaccine (WHO position paper)

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Yellow fever vaccine (WHO position paper)

Given the very rare, but potentially severe, adverse effects, YF (yellow fever) vaccine for travellers should be administered on strict indications only, particularly in the elderly. Restriction of YF vaccination to authorized centres is likely to promote the appropriate use of YF vaccine.

Global Advisory Committee on Vaccine Safety, 23 December 2004

GACVS reiterates that particular care should be taken that the (17D yellow fever) vaccine is received only by those travellers who are truly at risk of exposure to yellow fever. In addition, vaccine providers should give careful consideration to the risks and benefits for elderly travellers and should routinely enquire about a history of thymus disorder, irrespective of the age of the subject. Where a history of thymus disorder is reported, alternative prevention measures should be considered.

Global Advisory Committee on Vaccine Safety, 34 December 2003

(GACVS stated that) particular care should be taken that the (yellow fever) vaccine is received only by those travellers truly at risk for yellow fever exposure. Furthermore, care should be taken that routine yellow fever vaccination programmes are not jeopardized by riskbenefit ratios that may be inapplicable to the target populations in endemic countries.
Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

WHO recommends the following schedule for infants (Appendix 39_5).

Yellow fever vaccine (WHO position paper)

The (YF) vaccine is also widely used for the protection of travelers to YF-endemic areas.