**Adverse Event**

**Immunization in practice: a practical resource guide for Health workers 2004 update** Module 2: The vaccines

(With yellow fever vaccine,) if a serious reaction does occur, health workers should report the problem to supervisors immediately.

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

Adverse events following YF (yellow fever) vaccination are usually minor, although hypersensitivity to vaccine components may occasionally occur, and very rare cases of viral encephalitis or multiple organ failures have been reported. The rare adverse events should not deter the appropriate use of this highly valuable vaccine.

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

Improved surveillance and reporting of any potential adverse event following (yellow fever) vaccination is recommended in order to correct any programmatic errors that may be involved and to facilitate improved understanding of the pathogenic mechanisms causing the recently described serious adverse events.

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

When promoting increased use of YF (yellow fever) vaccine in at risk areas, the outstanding safety and effectiveness profile, the long duration of protection and the cost-effectiveness of the 17D vaccine should continue to be emphasized. However, recent reports of severe, but very rare, vaccine-associated adverse events highlight the importance of careful post-licensure surveillance, even for well established vaccines. Enhanced surveillance of such events and careful molecular analyses of the 17D strains isolated from potential new cases as well as from the actual vaccine batches should contribute to the understanding of the pathogenetic mechanisms involved.

**BCG**

**Proper handling and reconstitution of vaccines avoids programme errors**

Reconstituted BCG, measles and yellow fever vaccines must be kept cooled and must be discarded after 6 hours after reconstitution.

**Proper handling and reconstitution of vaccines avoids programme errors**

It is no longer necessary to ship and store freeze-dried vaccines (measles, yellow fever and BCG) at 20C. Instead, they may be refrigerated at +2 to +8C.
Proper handling and reconstitution of vaccines avoids programme errors

WHO no longer recommends that freeze-dried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at 20°C. Storing them at 20°C is not harmful but is unnecessary and uses up valuable storage space in the deep-freeze. Instead, they should be kept in refrigeration and transported at +2 to +8°C.

Thermostability of vaccines

Reconstituted vaccines against measles, yellow fever and tuberculosis (BCG) are unstable vaccines; they should be used as soon as possible after reconstitution, be kept in an ice bath during the immunization session and should be discarded at the end of the session.

Getting started with vaccine vial monitors

Opened vials of measles, yellow fever, BCG and freeze-dried Hib vaccine cannot be used after an initial immunization session, (even if the VVM has not reached the discard point.). They must be discarded within six hours of reconstitution or at the end of the session, whichever comes first. The VVMs for these vaccines are attached to the vial caps and should be discarded when the vaccine is being reconstituted.

Immunization in practice: a practical resource guide for Health workers 2004 update Module 2: The vaccines

Typical immunization schedule for children (see Appendix 2_19.)

All infants should be immunized except in these three rare situations:
1. Anaphylaxis or a severe hypersensitivity reaction is an absolute contraindication to subsequent doses of a vaccine. Persons with a known allergy to a vaccine component should not be vaccinated.
2. Do not give BCG or yellow fever vaccine to an infant that exhibits the signs and symptoms of AIDS.

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO recommended vaccine storage conditions (Appendix 17_3).

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO no longer recommends that freezedried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at -20°C. Storing them at -20°C is not harmful but is unnecessary. Instead, these vaccines should be stored and transported at +2C to +8C.
All infants should be immunized except in these three rare situations:
1. Anaphylaxis or a severe hypersensitivity reaction is an absolute contraindication to subsequent doses of a vaccine. Persons with a known allergy to a vaccine component should not be vaccinated.
2. Do not give BCG or yellow fever vaccine to an infant who exhibits the signs and symptoms of AIDS (see Appendix 6_11A). Other vaccines should be given.
3. If a parent strongly objects to an immunization for a sick infant, do not give it. Ask the mother to come back when the infant is well.

The following are not contraindications. Infants with these conditions should be immunized (see Appendix 6_11B)

See Appendix 6_19 for chart entitled, "Administering vaccines to infants" BCG, DTP, DTP-HepB, HepB, measles, yellow fever, OPV"

The use of opened multi-dose vials of vaccine in subsequent immunization sessions (WHO Policy Statement)

The revised (multi-dose vial) policy does not change recommended procedures for handling vaccines that must be reconstituted, that is, BCG, measles, yellow fever, and some formulations of Hib vaccines. Once they are reconstituted, vials of these vaccines must be discarded at the end of each immunization session or at the end of six hours, whichever comes first.

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

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

Opened vials of measles, yellow fever and BCG vaccines MUST be discarded at the end of each immunization session or after 6 hours whichever comes first.
Temperature sensitivity of vaccines

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81_1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2oC and +8oC. All other vaccines should be stored between +2oC and +8oC at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.

Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e., at the national (central) and regional or provincial levels, OPV must be kept frozen between -15C and -25C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15C and -25C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2C and +8C. All other national immunization service vaccines should be stored between +2C and +8C at all levels of the cold chain.

Contraindications

Immunization in practice: a practical resource guide for Health workers 2004 update Module 2: The vaccines

All infants should be immunized except in these three rare situations:
1. Anaphylaxis or a severe hypersensitivity reaction is an absolute contraindication to subsequent doses of a vaccine. Persons with a known allergy to a vaccine component should not be vaccinated.
2. Do not give BCG or yellow fever vaccine to an infant that exhibits the signs and symptoms of AIDS.
Immunization in practice: a practical resource guide for Health workers 2004 update Module 6: Holding an immunization session

All infants should be immunized except in these three rare situations:
1. Anaphylaxis or a severe hypersensitivity reaction is an absolute contraindication to subsequent doses of a vaccine. Persons with a known allergy to a vaccine component should not be vaccinated.
2. Do not give BCG or yellow fever vaccine to an infant who exhibits the signs and symptoms of AIDS (see Appendix 6_11A). Other vaccines should be given.
3. If a parent strongly objects to an immunization for a sick infant, do not give it. Ask the mother to come back when the infant is well.

The following are not contraindications. Infants with these conditions should be immunized (see Appendix 6_11B)

Yellow fever vaccine (WHO position paper)

The (yellow fever) vaccine is contraindicated in children aged under 6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of YF virus transmission may be very high. It is also contraindicated for persons with severe allergy to egg and for severely immunocompromised persons. On theoretical grounds, the 17D vaccine is not recommended during pregnancy. However, pregnant women may be vaccinated during epidemics when the risk of YFV transmission may be very high.

Yellow fever vaccine (WHO position paper)

Contraindications against YF vaccination include age less than 6 months, severe hypersensitivity to egg antigens and severe immunodeficiency. Whereas it is relatively easy to avoid immunization of the first two categories, the principal contraindications against immunization during pregnancy and in severe immunodeficiency cause significant practical problems. Fortunately, the few published cases of congenital infection caused by 17D have not been associated with fetal abnormalities. Similarly, no adverse events occurred in a small study of HIV-infected children with low CD4+ counts who received the vaccine. These observations are important considering the likelihood that many pregnant women and HIV-positive individuals, including children, will be immunized inadvertently during large-scale immunization activities in at-risk countries.

For international travellers, where laboratory and other resources are available, YF (yellow fever) vaccination may be offered to asymptomatic HIV-infected persons with CD4+ counts above 200 cells/mm3 who require vaccination for unavoidable travel. Individual expert assessments are required before YF vaccination may be offered to persons taking highdose corticosteroids or antineoplastic drugs. If possible, tests should be performed to ensure that protective levels of neutralizing antibodies have been achieved, as primary vaccination failure is common in immunodeficient individuals.
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

Yellow fever vaccine is contraindicated for infants less than 6 months of age, immune-deficient persons and persons with egg allergy. The risk of disease should be weighed against the risk of vaccination in pregnant women and in persons with symptomatic HIV infection. These are important factors to consider before planning a mass preventive vaccination campaign.

Global Advisory Committee on Vaccine Safety, 34 December 2003

A critical and unresolved issue is the safety and efficacy of yellow fever vaccine in human subjects infected with immunodeficiency virus (HIV). It remains to be determined whether HIV-positive status materially affects seroconversion, the risk of invasion of the nervous system and of encephalopathy, the stage of HIV disease at which yellow fever vaccination should be contraindicated, and whether there are differences in the incidence of minor and major adverse effects in HIV-positive subjects.

Immunization in practice: a practical resource guide for Health workers 2004 update Module 2: The vaccines

Those who have a severe reaction (to yellow fever vaccine) should not receive additional doses.
**Temperature sensitivity of vaccines**

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81_1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15°C and -25°C. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15°C to -25°C if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2°C and +8°C. All other vaccines should be stored at between +2°C and +8°C at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.
**Diphtheria**

**Temperature sensitivity of vaccines**

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81.1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15°C and -25°C. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15°C to -25°C if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2°C and +8°C. All other vaccines should be stored at between +2°C and +8°C at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.

**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**

A critical and unresolved issue is the safety and efficacy of yellow fever vaccine in human subjects infected with immunodeficiency virus (HIV). It remains to be determined whether HIV-positive status materially affects seroconversion, the risk of invasion of the nervous system and of encephalopathy, the stage of HIV disease at which yellow fever vaccination should be contraindicated, and whether there are differences in the incidence of minor and major adverse effects in HIV-positive subjects.
### General

**Proper handling and reconstitution of vaccines avoids programme errors**

Reconstituted BCG, measles and yellow fever vaccines must be kept cooled and must be discarded after 6 hours after reconstitution.

**Proper handling and reconstitution of vaccines avoids programme errors**

It is no longer necessary to ship and store freeze-dried vaccines (measles, yellow fever and BCG) at 20°C. Instead, they may be refrigerated at +2 to +8°C.

**Proper handling and reconstitution of vaccines avoids programme errors**

WHO no longer recommends that freeze-dried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at 20°C. Storing them at 20°C is not harmful but is unnecessary and uses up valuable storage space in the deep-freeze. Instead, they should be kept in refrigeration and transported at +2 to +8°C.

#### Thermostability of vaccines

Reconstituted vaccines against measles, yellow fever and tuberculosis (BCG) are unstable vaccines; they should be used as soon as possible after reconstitution, be kept in a ice bath during the immunization session and should be discarded at the end of the session.

**Thermostability of vaccines**

Yellow fever vaccine can safely be stored at -20°C or +4°C for two years or more.

**Thermostability of vaccines**

WHO requirement for yellow fever vaccine stability stipulates that the vaccine should retain 1000 mouse LD50 or the equivalent in plaque-forming units (PFUs) per human dose, and that the mean titre loss should be less than 1 log10 after two weeks incubation at 37°C.

**Thermostability of vaccines**

Lyophilized yellow fever vaccine can be safely stored at -20°C or +4°C for two years.
Yellow Fever

Thermostability of vaccines

Yellow fever vaccine should be quickly administered after reconstitution (up to one hour). If the reconstituted vaccine is kept continuously in an ice bath, it can be used within one immunization session but must be discarded at the end of the session.

Getting started with vaccine vial monitors

Opened vials of measles, yellow fever, BCG and freeze-dried Hib vaccine cannot be used after an intial immunization session, (even if the VVM has not reached the discard point.). They must be discarded within six hours of reconstitution or at the end of the session, whichever comes first. The VVMs for these vaccines are attached to the vial caps and should be discarded when the vaccine is being reconstituted.

Immunization in practice: a practical resource guide for Health workers 2004 update Module 1: Target diseases

The main strategies to control yellow fever are based on a combination of immunization for protection against the disease and surveillance, and are outlined below.

Prevention:
- administering yellow fever vaccine as part of routine infant immunization;*
- preventing outbreaks in high-risk areas through mass campaigns;*
- control of Aedus aegypti in urban centres.

* Both these strategies should ensure a minimum coverage of at least 80%.

Control
- instituting a sensitive and reliable YF surveillance system including laboratory capacity to analyse samples and confirm suspected cases;
- emergency response to outbreaks through mass campaigns.

Immunization in practice: a practical resource guide for Health workers 2004 update Module 2: The vaccines

Administration summary: YF vaccine (see Appendix 2_17.)

(With yellow fever vaccine,) if a serious reaction does occur, health workers should report the problem to supervisors immediately.

Immunization in practice: a practical resource guide for Health workers 2004 update Module 2: The vaccines

Typical immunization schedule for children (see Appendix 2_19.)
All infants should be immunized except in these three rare situations:
1. Anaphylaxis or a severe hypersensitivity reaction is an absolute contraindication to subsequent doses of a vaccine. Persons with a known allergy to a vaccine component should not be vaccinated.
2. Do not give BCG or yellow fever vaccine to an infant that exhibits the signs and symptoms of AIDS.

The following are not contraindications. Infants with these conditions should be immunized (see Appendix 6_11B)

See Appendix 6_19 for chart entitled, "Administering vaccines to infants" BCG, DTP, DTP-HepB, HepB, measles, yellow fever, OPV"

Yellow fever vaccine (WHO position paper)

Adverse events following YF (yellow fever) vaccination are usually minor, although hypersensitivity to vaccine components may occasionally occur, and very rare cases of viral encephalitis or multiple organ failures have been reported. The rare adverse events should not deter the appropriate use of this highly valuable vaccine.
Yellow fever vaccine (WHO position paper)

In countries at risk for YF (yellow fever), the use of the 17D vaccine is the main strategy recommended to rapidly build up YF immunity in the population at large. This prevention strategy has two components. The first component is the inclusion of the 17D vaccine in national childhood immunization programmes.

The second component is the implementation of mass preventive vaccination campaigns to protect susceptible older age groups. In the event of limited resources, assessment of the degree of risk can help prioritize areas for mass preventive campaigns.

Yellow fever vaccine (WHO position paper)

During YF (yellow fever) epidemics, outbreak response vaccination campaigns should be carried out with minimum delay in order to limit the spread of the disease. The occurrence of an epidemic reflects incomplete implementation of prevention strategies, which therefore need to be strengthened following the outbreak. Appropriate measures to control Ae. Aegypti should accompany all efforts to improve immunization coverage.

Page 356: During YF outbreaks, mass immunization should be instituted at the earliest possible stage and according to locally defined priorities.

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)

The various clinical presentations of YF (yellow fever) may be mistaken for those of a number of other infectious diseases that occur in YF at-risk countries. This underscores the importance of having a sensitive, case-based YF surveillance system, supported by laboratory diagnostic facilities. The timely notification and investigation of patients with acute febrile illness and jaundice, with or without haemorrhagic manifestations, is recommended to increase the sensitivity of surveillance to detect the circulation of YF virus. The early detection of YF virus circulation would prompt timely implementation of outbreak response activities.
Yellow fever vaccine (WHO position paper)

Improved surveillance and reporting of any potential adverse event following (yellow fever) vaccination is recommended in order to correct any programmatic errors that may be involved and to facilitate improved understanding of the pathogenic mechanisms causing the recently described serious adverse events.

Yellow fever vaccine (WHO position paper)

Mechanisms should be found to provide incentives for manufacturers of YF (yellow fever) vaccine to sustain or increase their production capacity to ensure rapid delivery of sufficient quantities in the event of a major YF outbreak.

Yellow fever vaccine (WHO position paper)

In emergency situations, WHO, through its network of Collaborating Centres for Arboviruses and Haemorrhagic Fevers, can organize diagnostic assistance to affected countries.

Yellow fever vaccine (WHO position paper)

For convenience and improved coverage, the YF vaccine should be administered simultaneously with the measles vaccine at approximately 9-12 months of age, but in a separate syringe and at a different injection site.

The YF (yellow fever) vaccine is given as a single subcutaneous or intramuscular injection (0.5 ml per dose), although the subcutaneous route is preferred.

Yellow fever vaccine (WHO position paper)

According to current WHO requirements, a YF (yellow fever) vaccine that has been held at 37 C for 14 days must (i) maintain the minimal potency of >1000 MLD50 per dose and (ii) show a mean loss of titre <1 log 10 MLD50. These requirements necessitate the addition of stabilizers such as sorbitol and gelatin.

Yellow fever vaccine (WHO position paper)

Since there is no interference between YF (yellow fever) vaccine and other vaccines, YF vaccine may be administered simultaneously, but in different syringes and at different sites, with the following vaccines: measles, polio (oral polio vaccine), diphtheria-tetanus-pertussis, hepatitis B, hepatitis A, oral cholera and oral or parenteral typhoid. When not given simultaneously, live vaccines should be administered at least one month before or one month after the YF vaccination. This recommendation is based on the assumption that interferon released in response to the first vaccine may have a temporary inhibitory effect on other live virus vaccines.
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.

The (yellow fever) vaccine is contraindicated in children aged under 6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of YF virus transmission may be very high. It is also contraindicated for persons with severe allergy to egg and for severely immunocompromised persons. On theoretical grounds, the 17D vaccine is not recommended during pregnancy. However, pregnant women may be vaccinated during epidemics when the risk of YFV transmission may be very high.

In 1988, the joint United Nations Children's Fund/WHO Technical Group on Immunization in Africa recommended that countries at risk for YF (yellow fever) incorporate the 17D vaccine into their national immunization programme.

When promoting increased use of YF (yellow fever) vaccine in at risk areas, the outstanding safety and effectiveness profile, the long duration of protection and the cost-effectiveness of the 17D vaccine should continue to be emphasized. However, recent reports of severe, but very rare, vaccine-associated adverse events highlight the importance of careful post-licensure surveillance, even for well established vaccines. Enhanced surveillance of such events and careful molecular analyses of the 17D strains isolated from potential new cases as well as from the actual vaccine batches should contribute to the understanding of the pathogenetic mechanisms involved.

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)

Contraindications against YF vaccination include age less than 6 months, severe hypersensitivity to egg antigens and severe immunodeficiency. Whereas it is relatively easy to avoid immunization of the first two categories, the principal contraindications against immunization during pregnancy and in severe immunodeficiency cause significant practical problems. Fortunately, the few published cases of congenital infection caused by 17D have not been associated with fetal abnormalities. Similarly, no adverse events occurred in a small study of HIV-infected children with low CD4+ counts who received the vaccine. These observations are important considering the likelihood that many pregnant women and HIV-positive individuals, including children, will be immunized inadvertently during large-scale immunization activities in at-risk countries.

For international travellers, where laboratory and other resources are available, YF (yellow fever) vaccination may be offered to asymptomatic HIV-infected persons with CD4+ counts above 200 cells/mm3 who require vaccination for unavoidable travel. Individual expert assessments are required before YF vaccination may be offered to persons taking high-dose corticosteroids or antineoplastic drugs. If possible, tests should be performed to ensure that protective levels of neutralizing antibodies have been achieved, as primary vaccination failure is common in immunodeficient individuals.

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.
Yellow fever vaccine (WHO position paper)

Concerned international organizations have agreed to build up an emergency stockpile of YF (yellow fever) vaccine that should be retained for outbreak response in Africa and South America. A stockpile of 6 million doses is now reserved for this purpose.

Yellow fever vaccine (WHO position paper)

To avoid devastating outbreaks of YF (yellow fever) in the future, YF vaccine must be fully introduced into well functioning childhood vaccination programmes. In addition, childhood vaccination should be combined with pre-emptive YF vaccination campaigns in at-risk areas, and in urban areas control efforts directed against Ae. aegypti should be increased. In areas of predominantly jungle-type transmission, YF vaccination of persons belonging to the high-risk groups is strongly recommended.

Yellow fever vaccine (WHO position paper)

WHO recognizes the urgent need for improved surveillance of YF (yellow fever) in at-risk countries. There is therefore an urgent need for rapid laboratory confirmation of diagnosis in clinically suspected cases. WHO recommends extended use of the filter-paper method for blood collection because it improves safety of the procedure and simplifies both collection and transportation of the samples. Dried blood on filter-paper allows testing for PCR products as well as for YF virus-specific IgM.

WHO recommended standards for surveillance of selected vaccine-preventable diseases

Yellow fever surveillance is therefore critical for monitoring the incidence of the disease and allowing the prediction and early detection of outbreaks and the monitoring of control measures. Case-reporting of yellow fever is universally required by the International Health Regulations.
Yellow Fever

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

Recommended types of surveillance for yellow fever:
1) Routine monthly reporting of aggregated data on suspected and confirmed cases form the peripheral level to the intermediate and central levels.
2) Designated reporting sites at all levels should report at a specified frequency (e.g. weekly or monthly) even if there are zero cases (often referred to as zero reporting).
3) Immediate reporting of suspected cases from the peripheral level to the intermediate and central levels.
4) All suspected cases and outbreaks should be investigated immediately and blood samples should be collected for laboratory confirmation.
5) Case-based surveillance should be implemented in countries identified by WHO as being at risk for yellow fever. Specimens should be collected to confirm epidemics as rapidly as possible. Priority should then be given to collecting specimens from new or neighbouring areas (other than the areas where epidemics are already confirmed).

Note: The international Health Regulations require all yellow fever cases to be reported to WHO within 24 hours of detection.

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

Opportunities should be seized to integrate yellow fever surveillance with other surveillance efforts that share similar objectives and strategies (e.g. joint laboratory training on measles and yellow fever diagnosis.)

**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 risk-benefit ratios that may be inapplicable to the target populations in endemic countries.

**The use of opened multi-dose vials of vaccine in subsequent immunization sessions (WHO Policy Statement)**

The revised (multi-dose vial) policy does not change recommended procedures for handling vaccines that must be reconstituted, that is, BCG, measles, yellow fever, and some formulations of Hib vaccines. Once they are reconstituted, vials of these vaccines must be discarded at the end of each immunization session or at the end of six hours, whichever comes first.
Yellow Fever

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 is contraindicated for infants less than 6 months of age, immune-deficient persons and persons with egg allergy. The risk of disease should be weighed against the risk of vaccination in pregnant women and in persons with symptomatic HIV infection. These are important factors to consider before planning a mass preventive vaccination campaign.

Yellow fever vaccine (WHO position paper)

In countries at risk for YF, this vaccine is recommended for individual and outbreak prevention as well as outbreak control. At risk for yellow fever is defined as areas where evidence for presence of the virus has been demonstrated and where ecological factors can support yellow fever virus transmission to man.

Yellow fever vaccine (WHO position paper)

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

Yellow fever vaccine (WHO position paper)

The lyophilized (YF) vaccine requires proper storage under cold-chain conditions, and reconstituted vaccine must be kept on ice and used within six hours.

Immunization in practice: a practical resource guide for Health workers 2004 update Module 6: Holding an immunization session

Opened vials of measles, yellow fever and BCG vaccines MUST be discarded at the end of each immunization session or after 6 hours whichever comes first.

Global Advisory Committee on Vaccine Safety, 34 December 2003

A critical and unresolved issue is the safety and efficacy of yellow fever vaccine in human subjects infected with immunodeficiency virus (HIV). It remains to be determined whether HIV-positive status materially affects seroconversion, the risk of invasion of the nervous system and of encephalopathy, the stage of HIV disease at which yellow fever vaccination should be contraindicated, and whether there are differences in the incidence of minor and major adverse effects in HIV-positive subjects.
Temperature sensitivity of vaccines

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81_1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or provincial level, OPV must be kept frozen between -15°C and -25°C. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15°C to -25°C if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2°C and +8°C. All other vaccines should be stored at between +2°C and +8°C at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.

Temperature sensitivity of vaccines

Regardless of stability of a reconstituted vaccine (including yellow fever), because of the risk of contamination, such products should be kept cold after reconstitution and discarded at the end of a 6-hour immunization session.

Temperature sensitivity of vaccines

Yellow fever vaccine should be quickly administered after reconstitution, maintained at 2-8°C, and discarded at the end of the session, not only to preserve potency, but to minimize risk of contamination of this lyophilized vaccine once reconstituted.

Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15°C and -25°C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15°C and -25°C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2°C and +8°C. All other national immunization service vaccines should be stored between +2°C and +8°C at all levels of the cold chain.

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

Another challenge for (yellow fever vaccine) introduction is maintaining high vaccination coverage, as at least 80% of the infants need to be vaccinated for effective disease control.
It is essential that only the diluent supplied with the (yellow fever) vaccine be used.

Reconstituted (yellow fever) vaccine must be kept at 2°C - 8°C and discarded after six hours or at the end of the immunization session, whichever comes first.

Those who have a severe reaction (to yellow fever vaccine) should not receive additional doses.

For yellow fever:
_ All suspected cases and outbreaks should be investigated immediately and blood samples should be collected for laboratory confirmation.
_ Case-based surveillance should be implemented in countries identified by WHO as being at risk for yellow fever. Specimens should be collected to confirm epidemics as rapidly as possible. Priority should then be given to collecting specimens from new or neighbouring areas (other than the areas where epidemics are already confirmed).

The (yellow fever) vaccine is contraindicated in children aged under 6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of YF virus transmission may be very high.

Yellow fever vaccine is recommended as part of the routine national immunization programme in countries where the disease is endemic.

(Yellow fever vaccines) meeting the WHO stability guidelines show a minimum mouse potency titer (or an equivalent potency in PFU) of greater than 1000 units after exposure to 37°C for 14 days, and their loss in potency during this exposure is less than 1 log10.
HIV/AIDS and immunosuppression

Immunization in practice: a practical resource guide for Health workers 2004 update Module 2: The vaccines

All infants should be immunized except in these three rare situations:
1. Anaphylaxis or a severe hypersensitivity reaction is an absolute contraindication to subsequent doses of a vaccine. Persons with a known allergy to a vaccine component should not be vaccinated.
2. Do not give BCG or yellow fever vaccine to an infant that exhibits the signs and symptoms of AIDS.

Immunization in practice: a practical resource guide for Health workers 2004 update Module 6: Holding an immunization session

All infants should be immunized except in these three rare situations:
1. Anaphylaxis or a severe hypersensitivity reaction is an absolute contraindication to subsequent doses of a vaccine. Persons with a known allergy to a vaccine component should not be vaccinated.
2. Do not give BCG or yellow fever vaccine to an infant who exhibits the signs and symptoms of AIDS (see Appendix 6_11A). Other vaccines should be given.
3. If a parent strongly objects to an immunization for a sick infant, do not give it. Ask the mother to come back when the infant is well.

The following are not contraindications. Infants with these conditions should be immunized (see Appendix 6_11B)

Yellow fever vaccine (WHO position paper)

The (yellow fever) vaccine is contraindicated in children aged under 6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of YF virus transmission may be very high. It is also contraindicated for persons with severe allergy to egg and for severely immunocompromised persons. On theoretical grounds, the 17D vaccine is not recommended during pregnancy. However, pregnant women may be vaccinated during epidemics when the risk of YFV transmission may be very high.
Yellow fever vaccine (WHO position paper)

Contraindications against YF vaccination include age less than 6 months, severe hypersensitivity to egg antigens and severe immunodeficiency. Whereas it is relatively easy to avoid immunization of the first two categories, the principal contraindications against immunization during pregnancy and in severe immunodeficiency cause significant practical problems. Fortunately, the few published cases of congenital infection caused by 17D have not been associated with fetal abnormalities. Similarly, no adverse events occurred in a small study of HIV-infected children with low CD4+ counts who received the vaccine. These observations are important considering the likelihood that many pregnant women and HIV-positive individuals, including children, will be immunized inadvertently during large-scale immunization activities in at-risk countries.

For international travellers, where laboratory and other resources are available, YF (yellow fever) vaccination may be offered to asymptomatic HIV-infected persons with CD4+ counts above 200 cells/mm³ who require vaccination for unavoidable travel. Individual expert assessments are required before YF vaccination may be offered to persons taking high dose corticosteroids or antineoplastic drugs. If possible, tests should be performed to ensure that protective levels of neutralizing antibodies have been achieved, as primary vaccination failure is common in immunodeficient individuals.

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

Yellow fever vaccine is contraindicated for infants less than 6 months of age, immune-deficient persons and persons with egg allergy. The risk of disease should be weighed against the risk of vaccination in pregnant women and in persons with symptomatic HIV infection. These are important factors to consider before planning a mass preventive vaccination campaign.

Global Advisory Committee on Vaccine Safety, 34 December 2003

A critical and unresolved issue is the safety and efficacy of yellow fever vaccine in human subjects infected with immunodeficiency virus (HIV). It remains to be determined whether HIV-positive status materially affects seroconversion, the risk of invasion of the nervous system and of encephalopathy, the stage of HIV disease at which yellow fever vaccination should be contraindicated, and whether there are differences in the incidence of minor and major adverse effects in HIV-positive subjects.

Hepatitis B

Immunization in practice: a practical resource guide for Health workers 2004 update Module 2: The vaccines

Typical immunization schedule for children (see Appendix 2_19.)
WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO recommended vaccine storage conditions (Appendix 17.3).

Immunization in practice: a practical resource guide for Health workers 2004 update Module 6: Holding an immunization session

See Appendix 6.19 for chart entitled, "Administering vaccines to infants" BCG, DTP, DTP-HepB, HepB, measles, yellow fever, OPV"

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

WHO recommends the following schedule for infants (Appendix 39.5).

Temperature sensitivity of vaccines

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81.1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15°C and -25°C. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15°C to -25°C if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2°C and +8°C. All other vaccines should be stored at between +2°C and +8°C at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.

Hib

Proper handling and reconstitution of vaccines avoids programme errors

WHO no longer recommends that freeze-dried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at 20°C. Storing them at 20°C is not harmful but is unnecessary and uses up valuable storage space in the deep-freeze. Instead, they should be kept in refrigeration and transported at +2 to +8°C.

Getting started with vaccine vial monitors

Opened vials of measles, yellow fever, BCG and freeze-dried Hib vaccine cannot be used after an initial immunization session, (even if the VVM has not reached the discard point.). They must be discarded within six hours of reconstitution or at the end of the session, whichever comes first. The VMs for these vaccines are attached to the vial caps and should be discarded when the vaccine is being reconstituted.
Immunization in practice: a practical resource guide for Health workers 2004 update Module 2: The vaccines

Typical immunization schedule for children (see Appendix 2_19.)

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO recommended vaccine storage conditions (Appendix 17_3).

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO no longer recommends that freeze-dried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at -20C. Storing them at -20C is not harmful but is unnecessary. Instead, these vaccines should be stored and transported at +2C to +8C.

The use of opened multi-dose vials of vaccine in subsequent immunization sessions (WHO Policy Statement)

The revised (multi-dose vial) policy does not change recommended procedures for handling vaccines that must be reconstituted, that is, BCG, measles, yellow fever, and some formulations of Hib vaccines. Once they are reconstituted, vials of these vaccines must be discarded at the end of each immunization session or at the end of six hours, whichever comes first.

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

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

Temperature sensitivity of vaccines

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81_1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.
Immunization Coverage

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

Another challenge for (yellow fever vaccine) introduction is maintaining high vaccination coverage, as at least 80% of the infants need to be vaccinated for effective disease control.

MMR

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO recommended vaccine storage conditions (Appendix 17_3).

Temperature sensitivity of vaccines

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81_1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15°C and -25°C. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15°C to -25°C if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2°C and +8°C. All other vaccines should be stored at between +2°C and +8°C at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.

Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15°C and -25°C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15°C and -25°C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2°C and +8°C. All other national immunization service vaccines should be stored between +2°C and +8°C at all levels of the cold chain.
# Measles

## Proper handling and reconstitution of vaccines avoids programme errors

Reconstituted BCG, measles and yellow fever vaccines must be kept cooled and must be discarded after 6 hours after reconstitution.

### Proper handling and reconstitution of vaccines avoids programme errors

It is no longer necessary to ship and store freeze-dried vaccines (measles, yellow fever and BCG) at 20°C. Instead, they may be refrigerated at +2 to +8°C.

### Proper handling and reconstitution of vaccines avoids programme errors

WHO no longer recommends that freeze-dried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at 20°C. Storing them at 20°C is not harmful but is unnecessary and uses up valuable storage space in the deep-freeze. Instead, they should be kept in refrigeration and transported at +2 to +8°C.

## Thermostability of vaccines

Reconstituted vaccines against measles, yellow fever and tuberculosis (BCG) are unstable vaccines; they should be used as soon as possible after reconstitution, be kept in a ice bath during the immunization session and should be discarded at the end of the session.

### Getting started with vaccine vial monitors

Opened vials of measles, yellow fever, BCG and freeze-dried Hib vaccine cannot be used after an initial immunization session (even if the VVM has not reached the discard point). They must be discarded within six hours of reconstitution or at the end of the session, whichever comes first. The VVMs for these vaccines are attached to the vial caps and should be discarded when the vaccine is being reconstituted.

## Immunization in practice: a practical resource guide for Health workers 2004 update Module 2: The vaccines

Typical immunization schedule for children (see Appendix 2_19.)

## WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO recommended vaccine storage conditions (Appendix 17_3).
WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO no longer recommends that freezedried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at -20°C. Storing them at -20°C is not harmful but is unnecessary. Instead, these vaccines should be stored and transported at +2°C to +8°C.

Immunization in practice: a practical resource guide for Health workers 2004 update Module 6: Holding an immunization session

See Appendix 6 for chart entitled, "Administering vaccines to infants" BCG, DTP, DTP-HepB, HepB, measles, yellow fever, OPV"

The use of opened multi-dose vials of vaccine in subsequent immunization sessions (WHO Policy Statement)

The revised (multi-dose vial) policy does not change recommended procedures for handling vaccines that must be reconstituted, that is, BCG, measles, yellow fever, and some formulations of Hib vaccines. Once they are reconstituted, vials of these vaccines must be discarded at the end of each immunization session or at the end of six hours, whichever comes first.

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

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

Immunization in practice: a practical resource guide for Health workers 2004 update Module 6: Holding an immunization session

Opened vials of measles, yellow fever and BCG vaccines MUST be discarded at the end of each immunization session or after 6 hours whichever comes first.

Temperature sensitivity of vaccines

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15°C and -25°C. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15°C to -25°C if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2°C and +8°C. All other vaccines should be stored at between +2°C and +8°C at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.
Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15°C and -25°C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15°C and -25°C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2°C and +8°C. All other national immunization service vaccines should be stored between +2°C and +8°C at all levels of the cold chain.

Meningococcal

Temperature sensitivity of vaccines

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81_1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15°C and -25°C. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15°C to -25°C if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2°C and +8°C. All other vaccines should be stored at between +2°C and +8°C at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.

Mumps

Temperature sensitivity of vaccines

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81_1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15°C and -25°C. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15°C to -25°C if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2°C and +8°C. All other vaccines should be stored at between +2°C and +8°C at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.
New Vaccines

Yellow fever vaccine (WHO position paper)

In 1988, the joint United Nations Children's Fund/WHO Technical Group on Immunization in Africa recommended that countries at risk for YF (yellow fever) incorporate the 17D vaccine into their national immunization programme.

Immunization in practice: a practical resource guide for Health workers 2004 update Module 2: The vaccines

Yellow fever vaccine is recommended as part of the routine national immunization programme in countries where the disease is endemic.

Open Vials

Getting started with vaccine vial monitors

Opened vials of measles, yellow fever, BCG and freeze-dried Hib vaccine cannot be used after an initial immunization session, (even if the VVM has not reached the discard point.). They must be discarded within six hours of reconstitution or at the end of the session, whichever comes first. The VVMs for these vaccines are attached to the vial caps and should be discarded when the vaccine is being reconstituted.

The use of opened multi-dose vials of vaccine in subsequent immunization sessions (WHO Policy Statement)

The revised (multi-dose vial) policy does not change recommended procedures for handling vaccines that must be reconstituted, that is, BCG, measles, yellow fever, and some formulations of Hib vaccines. Once they are reconstituted, vials of these vaccines must be discarded at the end of each immunization session or at the end of six hours, whichever comes first.

Immunization in practice: a practical resource guide for Health workers 2004 update Module 6: Holding an immunization session

Opened vials of measles, yellow fever and BCG vaccines MUST be discarded at the end of each immunization session or after 6 hours whichever comes first.
Outbreak Control

Yellow fever vaccine (WHO position paper)

During YF (yellow fever) epidemics, outbreak response vaccination campaigns should be carried out with minimum delay in order to limit the spread of the disease. The occurrence of an epidemic reflects incomplete implementation of prevention strategies, which therefore need to be strengthened following the outbreak. Appropriate measures to control Ae. Aegypti should accompany all efforts to improve immunization coverage.

Page 356: During YF outbreaks, mass immunization should be instituted at the earliest possible stage and according to locally defined priorities.

Yellow fever vaccine (WHO position paper)

The (yellow fever) vaccine is contraindicated in children aged under 6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of YF virus transmission may be very high. It is also contraindicated for persons with severe allergy to egg and for severely immunocompromised persons. On theoretical grounds, the 17D vaccine is not recommended during pregnancy. However, pregnant women may be vaccinated during epidemics when the risk of YFV transmission may be very high.

Yellow fever vaccine (WHO position paper)

In countries at risk for YF, this vaccine is recommended for individual and outbreak prevention as well as outbreak control. At risk for yellow fever is defined as areas where evidence for presence of the virus has been demonstrated and where ecological factors can support yellow fever virus transmission to man.

WHO recommended standards for surveillance of selected vaccine-preventable diseases

For yellow fever:
- All suspected cases and outbreaks should be investigated immediately and blood samples should be collected for laboratory confirmation.
- Case-based surveillance should be implemented in countries identified by WHO as being at risk for yellow fever. Specimens should be collected to confirm epidemics as rapidly as possible. Priority should then be given to collecting specimens from new or neighbouring areas (other than the areas where epidemics are already confirmed).

Yellow fever vaccine (WHO position paper)

The (yellow fever) vaccine is contraindicated in children aged under 6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of YF virus transmission may be very high.
Pentavalent

Temperature sensitivity of vaccines

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81_1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15°C and -25°C. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15°C to -25°C if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2°C and +8°C. All other vaccines should be stored at between +2°C and +8°C at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.

Policy

Proper handling and reconstitution of vaccines avoids programme errors

Reconstituted BCG, measles and yellow fever vaccines must be kept cooled and must be discarded after 6 hours after reconstitution.

Proper handling and reconstitution of vaccines avoids programme errors

It is no longer necessary to ship and store freeze-dried vaccines (measles, yellow fever and BCG) at 20°C. Instead, they may be refrigerated at +2 to +8°C.

Proper handling and reconstitution of vaccines avoids programme errors

WHO no longer recommends that freeze-dried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at 20°C. Storing them at 20°C is not harmful but is unnecessary and uses up valuable storage space in the deep-freeze. Instead, they should be kept in refrigeration and transported at +2 to +8°C.

Thermostability of vaccines

Reconstituted vaccines against measles, yellow fever and tuberculosis (BCG) are unstable vaccines; they should be used as soon as possible after reconstitution, be kept in a ice bath during the immunization session and should be discarded at the end of the session.
Thermostability of vaccines

WHO requirement for yellow fever vaccine stability stipulates that the vaccine should retain 1000 mouse LD50 or the equivalent in plaque-forming units (PFUs) per human dose, and that the mean titre loss should be less than 1 log10 after two weeks incubation at 37C.

Thermostability of vaccines

Lyophilized yellow fever vaccine can be safely stored at -20C or +4C for two years.

Thermostability of vaccines

Yellow fever vaccine should be quickly administered after reconstitution (up to one hour). If the reconstituted vaccine is kept continuously in an ice bath, it can be used within one immunization session but must be discarded at the end of the session.

Getting started with vaccine vial monitors

Opened vials of measles, yellow fever, BCG and freeze-dried Hib vaccine cannot be used after an initial immunization session, (even if the VVM has not reached the discard point.). They must be discarded within six hours of reconstitution or at the end of the session, whichever comes first. The VVMs for these vaccines are attached to the vial caps and should be discarded when the vaccine is being reconstituted.

Immunization in practice: a practical resource guide for Health workers 2004 update Module 1: Target diseases

The main strategies to control yellow fever are based on a combination of immunization for protection against the disease and surveillance, and are outlined below.

Prevention:
- administering yellow fever vaccine as part of routine infant immunization;*
- preventing outbreaks in high-risk areas through mass campaigns;*
- control of Aedus aegypti in urban centres.
* Both these strategies should ensure a minimum coverage of at least 80%.

Control
- instituting a sensitive and reliable YF surveillance system including laboratory capacity to analyse samples and confirm suspected cases;
- emergency response to outbreaks through mass campaigns.

Immunization in practice: a practical resource guide for Health workers 2004 update Module 2: The vaccines

Administration summary: YF vaccine (see Appendix 2.17.)
With yellow fever vaccine, if a serious reaction does occur, health workers should report the problem to supervisors immediately.

Typical immunization schedule for children (see Appendix 2_19.)

All infants should be immunized except in these three rare situations:
1. Anaphylaxis or a severe hypersensitivity reaction is an absolute contraindication to subsequent doses of a vaccine. Persons with a known allergy to a vaccine component should not be vaccinated.
2. Do not give BCG or yellow fever vaccine to an infant that exhibits the signs and symptoms of AIDS.

WHO no longer recommends that freezedried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at -20C. Storing them at -20C is not harmful but is unnecessary. Instead, these vaccines should be stored and transported at +2C to +8C.

All infants should be immunized except in these three rare situations:
1. Anaphylaxis or a severe hypersensitivity reaction is an absolute contraindication to subsequent doses of a vaccine. Persons with a known allergy to a vaccine component should not be vaccinated.
2. Do not give BCG or yellow fever vaccine to an infant who exhibits the signs and symptoms of AIDS (see Appendix 6_11A). Other vaccines should be given.
3. If a parent strongly objects to an immunization for a sick infant, do not give it. Ask the mother to come back when the infant is well.

The following are not contraindications. Infants with these conditions should be immunized (see Appendix 6_11B)
Yellow Fever

Yellow fever vaccine (WHO position paper)

Adverse events following YF (yellow fever) vaccination are usually minor, although hypersensitivity to vaccine components may occasionally occur, and very rare cases of viral encephalitis or multiple organ failures have been reported. The rare adverse events should not deter the appropriate use of this highly valuable vaccine.

Yellow fever vaccine (WHO position paper)

In countries at risk for YF (yellow fever), the use of the 17D vaccine is the main strategy recommended to rapidly build up YF immunity in the population at large. This prevention strategy has two components. The first component is the inclusion of the 17D vaccine in national childhood immunization programmes.

The second component is the implementation of mass preventive vaccination campaigns to protect susceptible older age groups. In the event of limited resources, assessment of the degree of risk can help prioritize areas for mass preventive campaigns.

Yellow fever vaccine (WHO position paper)

During YF (yellow fever) epidemics, outbreak response vaccination campaigns should be carried out with minimum delay in order to limit the spread of the disease. The occurrence of an epidemic reflects incomplete implementation of prevention strategies, which therefore need to be strengthened following the outbreak. Appropriate measures to control Ae. Aegypti should accompany all efforts to improve immunization coverage.

Page 356: During YF outbreaks, mass immunization should be instituted at the earliest possible stage and according to locally defined priorities.

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)

The various clinical presentations of YF (yellow fever) may be mistaken for those of a number of other infectious diseases that occur in YF at-risk countries. This underscores the importance of having a sensitive, case-based YF surveillance system, supported by laboratory diagnostic facilities. The timely notification and investigation of patients with acute febrile illness and jaundice, with or without haemorrhagic manifestations, is recommended to increase the sensitivity of surveillance to detect the circulation of YF virus. The early detection of YF virus circulation would prompt timely implementation of outbreak response activities.

Yellow fever vaccine (WHO position paper)

Improved surveillance and reporting of any potential adverse event following (yellow fever) vaccination is recommended in order to correct any programmatic errors that may be involved and to facilitate improved understanding of the pathogenic mechanisms causing the recently described serious adverse events.

Yellow fever vaccine (WHO position paper)

Mechanisms should be found to provide incentives for manufacturers of YF (yellow fever) vaccine to sustain or increase their production capacity to ensure rapid delivery of sufficient quantities in the event of a major YF outbreak.

Yellow fever vaccine (WHO position paper)

In emergency situations, WHO, through its network of Collaborating Centres for Arboviruses and Haemorrhagic Fevers, can organize diagnostic assistance to affected countries.

Yellow fever vaccine (WHO position paper)

For convenience and improved coverage, the YF vaccine should be administered simultaneously with the measles vaccine at approximately 9-12 months of age, but in a separate syringe and at a different injection site.

The YF (yellow fever) vaccine is given as a single subcutaneous or intramuscular injection (0.5 ml per dose), although the subcutaneous route is preferred.

Yellow fever vaccine (WHO position paper)

According to current WHO requirements, a YF (yellow fever) vaccine that has been held at 37 C for 14 days must (i) maintain the minimal potency of >1000 MLD50 per dose and (ii) show a mean loss of titre <1 log 10 MLD50. These requirements necessitate the addition of stabilizers such as sorbitol and gelatin.
Yellow fever vaccine (WHO position paper)

Since there is no interference between YF (yellow fever) vaccine and other vaccines, YF vaccine may be administered simultaneously, but in different syringes and at different sites, with the following vaccines: measles, polio (oral polio vaccine), diphtheria-tetanus-pertussis, hepatitis B, hepatitis A, oral cholera and oral or parenteral typhoid. When not given simultaneously, live vaccines should be administered at least one month before or one month after the YF vaccination. This recommendation is based on the assumption that interferon released in response to the first vaccine may have a temporary inhibitory effect on other live virus vaccines.

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)

The (yellow fever) vaccine is contraindicated in children aged under 6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of YF virus transmission may be very high. It is also contraindicated for persons with severe allergy to egg and for severely immunocompromised persons. On theoretical grounds, the 17D vaccine is not recommended during pregnancy. However, pregnant women may be vaccinated during epidemics when the risk of YFV transmission may be very high.

Yellow fever vaccine (WHO position paper)

In 1988, the joint United Nations Children's Fund/WHO Technical Group on Immunization in Africa recommended that countries at risk for YF (yellow fever) incorporate the 17D vaccine into their national immunization programme.

Yellow fever vaccine (WHO position paper)

When promoting increased use of YF (yellow fever) vaccine in at risk areas, the outstanding safety and effectiveness profile, the long duration of protection and the cost-effectiveness of the 17D vaccine should continue to be emphasized. However, recent reports of severe, but very rare, vaccine-associated adverse events highlight the importance of careful post-licensure surveillance, even for well established vaccines. Enhanced surveillance of such events and careful molecular analyses of the 17D strains isolated from potential new cases as well as from the actual vaccine batches should contribute to the understanding of the pathogenetic mechanisms involved.
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)

Contraindications against YF vaccination include age less than 6 months, severe hypersensitivity to egg antigens and severe immunodeficiency. Whereas it is relatively easy to avoid immunization of the first two categories, the principal contraindications against immunization during pregnancy and in severe immunodeficiency cause significant practical problems. Fortunately, the few published cases of congenital infection caused by 17D have not been associated with fetal abnormalities. Similarly, no adverse events occurred in a small study of HIV-infected children with low CD4+ counts who received the vaccine. These observations are important considering the likelihood that many pregnant women and HIV-positive individuals, including children, will be immunized inadvertently during large-scale immunization activities in at-risk countries.

For international travellers, where laboratory and other resources are available, YF (yellow fever) vaccination may be offered to asymptomatic HIV-infected persons with CD4+ counts above 200 cells/mm3 who require vaccination for unavoidable travel. Individual expert assessments are required before YF vaccination may be offered to persons taking high-dose corticosteroids or antineoplastic drugs. If possible, tests should be performed to ensure that protective levels of neutralizing antibodies have been achieved, as primary vaccination failure is common in immunodeficient individuals.

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.

Yellow fever vaccine (WHO position paper)

Concerned international organizations have agreed to build up an emergency stockpile of YF (yellow fever) vaccine that should be retained for outbreak response in Africa and South America. A stockpile of 6 million doses is now reserved for this purpose.

Yellow fever vaccine (WHO position paper)

To avoid devastating outbreaks of YF (yellow fever) in the future, YF vaccine must be fully introduced into well functioning childhood vaccination programmes. In addition, childhood vaccination should be combined with pre-emptive YF vaccination campaigns in atrisk areas, and in urban areas control efforts directed against Ae. aegypti should be increased. In areas of predominantly jungle-type transmission, YF vaccination of persons belonging to the high-risk groups is strongly recommended.

Yellow fever vaccine (WHO position paper)

WHO recognizes the urgent need for improved surveillance of YF (yellow fever) in at-risk countries. There is therefore an urgent need for rapid laboratory confirmation of diagnosis in clinically suspected cases. WHO recommends extended use of the filter-paper method for blood collection because it improves safety of the procedure and simplifies both collection and transportation of the samples. Dried blood on filter-paper allows testing for PCR products as well as for YF virus-specific IgM.

WHO recommended standards for surveillance of selected vaccine-preventable diseases

Yellow fever surveillance is therefore critical for monitoring the incidence of the disease and allowing the prediction and early detection of outbreaks and the monitoring of control measures. Case-reporting of yellow fever is universally required by the International Health Regulations.
WHO recommended standards for surveillance of selected vaccine-preventable diseases

Recommended types of surveillance for yellow fever:
1) Routine monthly reporting of aggregated data on suspected and confirmed cases form the peripheral level to the intermediate and central levels.
2) Designated reporting sites at all levels should report at a specified frequency (e.g. weekly or monthly) even if there are zero cases (often referred to as zero reporting).
3) Immediate reporting of suspected cases from the peripheral level to the intermediate and central levels.
4) All suspected cases and outbreaks should be investigated immediately and blood samples should be collected for laboratory confirmation.
5) Case-based surveillance should be implemented in countries identified by WHO as being at risk for yellow fever. Specimens should be collected to confirm epidemics as rapidly as possible. Priority should then be given to collecting specimens from new or neighbouring areas (other than the areas where epidemics are already confirmed).
Note: The international Health Regulations require all yellow fever cases to be reported to WHO within 24 hours of detection.

WHO recommended standards for surveillance of selected vaccine-preventable diseases

Opportunities should be seized to integrate yellow fever surveillance with other surveillance efforts that share similar objectives and strategies (e.g. joint laboratory training on measles and yellow fever diagnosis.)

The use of opened multi-dose vials of vaccine in subsequent immunization sessions (WHO Policy Statement)

The revised (multi-dose vial) policy does not change recommended procedures for handling vaccines that must be reconstituted, that is, BCG, measles, yellow fever, and some formulations of Hib vaccines. Once they are reconstituted, vials of these vaccines must be discarded at the end of each immunization session or at the end of six hours, whichever comes first.

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

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

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

Yellow fever vaccine is contraindicated for infants less than 6 months of age, immune-deficient persons and persons with egg allergy. The risk of disease should be weighed against the risk of vaccination in pregnant women and in persons with symptomatic HIV infection. These are important factors to consider before planning a mass preventive vaccination campaign.
Yellow fever vaccine (WHO position paper)

In countries at risk for YF, this vaccine is recommended for individual and outbreak prevention as well as outbreak control. At risk for yellow fever is defined as areas where evidence for presence of the virus has been demonstrated and where ecological factors can support yellow fever virus transmission to man.

Yellow fever vaccine (WHO position paper)

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

Yellow fever vaccine (WHO position paper)

The lyophilized (YF) vaccine requires proper storage under cold-chain conditions, and reconstituted vaccine must be kept on ice and used within six hours.

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Opened vials of measles, yellow fever and BCG vaccines MUST be discarded at the end of each immunization session or after 6 hours whichever comes first.

Temperature sensitivity of vaccines

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81_1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.

Temperature sensitivity of vaccines

Regardless of stability of a reconstituted vaccine (including yellow fever), because of the risk of contamination, such products should be kept cold after reconstitution and discarded at the end of a 6-hour immunization session.
Temperature sensitivity of vaccines

Yellow fever vaccine should be quickly administered after reconstitution, maintained at 2-8°C, and discarded at the end of the session, not only to preserve potency, but to minimize risk of contamination of this lyophilized vaccine once reconstituted.

Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15°C and -25°C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15°C and -25°C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2°C and +8°C. All other national immunization service vaccines should be stored between +2°C and +8°C at all levels of the cold chain.

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

Another challenge for (yellow fever vaccine) introduction is maintaining high vaccination coverage, as at least 80% of the infants need to be vaccinated for effective disease control.

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It is essential that only the diluent supplied with the (yellow fever) vaccine be used.

Reconstituted (yellow fever) vaccine must be kept at 2°C - 8°C and discarded after six hours or at the end of the immunization session, whichever comes first.

Those who have a severe reaction (to yellow fever vaccine) should not receive additional doses.
**Yellow Fever**

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

For yellow fever:
- All suspected cases and outbreaks should be investigated immediately and blood samples should be collected for laboratory confirmation.
- Case-based surveillance should be implemented in countries identified by WHO as being at risk for yellow fever. Specimens should be collected to confirm epidemics as rapidly as possible. Priority should then be given to collecting specimens from new or neighbouring areas (other than the areas where epidemics are already confirmed).

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

The (yellow fever) vaccine is contraindicated in children aged under 6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of YF virus transmission may be very high.

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Yellow fever vaccine is recommended as part of the routine national immunization programme in countries where the disease is endemic.

**Temperature sensitivity of vaccines**

(Yellow fever vaccines) meeting the WHO stability guidelines show a minimum mouse potency titer (or an equivalent potency in PFU) of greater than 1000 units after exposure to 37°C for 14 days, and their loss in potency during this exposure is less than 1 log10.

**Polio**

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Typical immunization schedule for children (see Appendix 2_19.)

**WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4**

WHO recommended vaccine storage conditions (Appendix 17_3).
Immunization in practice: a practical resource guide for Health workers 2004 update Module 6: Holding an immunization session

See Appendix 6_19 for chart entitled, "Administering vaccines to infants" BCG, DTP, DTP-HepB, HepB, measles, yellow fever, OPV"

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

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

Temperature sensitivity of vaccines

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81_1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.

Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15C and -25C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15C and -25C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2C and +8C. All other national immunization service vaccines should be stored between +2C and +8C at all levels of the cold chain.
Pregnant Women

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

The (yellow fever) vaccine is contraindicated in children aged under 6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of YF virus transmission may be very high. It is also contraindicated for persons with severe allergy to egg and for severely immunocompromised persons. On theoretical grounds, the 17D vaccine is not recommended during pregnancy. However, pregnant women may be vaccinated during epidemics when the risk of YFV transmission may be very high.

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

Contraindications against YF vaccination include age less than 6 months, severe hypersensitivity to egg antigens and severe immunodeficiency. Whereas it is relatively easy to avoid immunization of the first two categories, the principal contraindications against immunization during pregnancy and in severe immunodeficiency cause significant practical problems. Fortunately, the few published cases of congenital infection caused by 17D have not been associated with fetal abnormalities. Similarly, no adverse events occurred in a small study of HIV-infected children with low CD4+ counts who received the vaccine. These observations are important considering the likelihood that many pregnant women and HIV-positive individuals, including children, will be immunized inadvertently during large-scale immunization activities in at-risk countries.

For international travellers, where laboratory and other resources are available, YF (yellow fever) vaccination may be offered to asymptomatic HIV-infected persons with CD4+ counts above 200 cells/mm3 who require vaccination for unavoidable travel. Individual expert assessments are required before YF vaccination may be offered to persons taking high-dose corticosteroids or antineoplastic drugs. If possible, tests should be performed to ensure that protective levels of neutralizing antibodies have been achieved, as primary vaccination failure is common in immunodeficient individuals.

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

Yellow fever vaccine is contraindicated for infants less than 6 months of age, immune-deficient persons and persons with egg allergy. The risk of disease should be weighed against the risk of vaccination in pregnant women and in persons with symptomatic HIV infection. These are important factors to consider before planning a mass preventive vaccination campaign.
**Procurement**

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

Mechanisms should be found to provide incentives for manufacturers of YF (yellow fever) vaccine to sustain or increase their production capacity to ensure rapid delivery of sufficient quantities in the event of a major YF outbreak.

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

Concerned international organizations have agreed to build up an emergency stockpile of YF (yellow fever) vaccine that should be retained for outbreak response in Africa and South America. A stockpile of 6 million doses is now reserved for this purpose.

**Program Management**

**Immunization in practice: a practical resource guide for Health workers 2004 update Module 1: Target diseases**

The main strategies to control yellow fever are based on a combination of immunization for protection against the disease and surveillance, and are outlined below.

**Prevention:**
- administering yellow fever vaccine as part of routine infant immunization;
- preventing outbreaks in high-risk areas through mass campaigns;
- control of Aedus aegypti in urban centres.

* Both these strategies should ensure a minimum coverage of at least 80%.

**Control**
- instituting a sensitive and reliable YF surveillance system including laboratory capacity to analyse samples and confirm suspected cases;
- emergency response to outbreaks through mass campaigns.

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

In countries at risk for YF (yellow fever), the use of the 17D vaccine is the main strategy recommended to rapidly build up YF immunity in the population at large. This prevention strategy has two components. The first component is the inclusion of the 17D vaccine in national childhood immunization programmes.

The second component is the implementation of mass preventive vaccination campaigns to protect susceptible older age groups. In the event of limited resources, assessment of the degree of risk can help prioritize areas for mass preventive campaigns.
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.

Yellow fever vaccine (WHO position paper)

To avoid devastating outbreaks of YF (yellow fever) in the future, YF vaccine must be fully introduced into well functioning childhood vaccination programmes. In addition, childhood vaccination should be combined with pre-emptive YF vaccination campaigns in at-risk areas, and in urban areas control efforts directed against Ae. aegypti should be increased. In areas of predominantly jungle-type transmission, YF vaccination of persons belonging to the high-risk groups is strongly recommended.

Rubella

Temperature sensitivity of vaccines

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81_1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.

Schedule

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Typical immunization schedule for children (see Appendix 2_19.)
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.

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.

Tetanus

Temperature sensitivity of vaccines

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81.1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.
Travellers

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.
Contraindications against YF vaccination include age less than 6 months, severe hypersensitivity to egg antigens and severe immunodeficiency. Whereas it is relatively easy to avoid immunization of the first two categories, the principal contraindications against immunization during pregnancy and in severe immunodeficiency cause significant practical problems. Fortunately, the few published cases of congenital infection caused by 17D have not been associated with fetal abnormalities. Similarly, no adverse events occurred in a small study of HIV-infected children with low CD4+ counts who received the vaccine. These observations are important considering the likelihood that many pregnant women and HIV-positive individuals, including children, will be immunized inadvertently during large-scale immunization activities in at-risk countries.

For international travellers, where laboratory and other resources are available, YF (yellow fever) vaccination may be offered to asymptomatic HIV-infected persons with CD4+ counts above 200 cells/mm3 who require vaccination for unavoidable travel. Individual expert assessments are required before YF vaccination may be offered to persons taking high-dose corticosteroids or antineoplastic drugs. If possible, tests should be performed to ensure that protective levels of neutralizing antibodies have been achieved, as primary vaccination failure is common in immunodeficient individuals.

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.

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.

Yellow fever vaccine (WHO position paper)

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

VPD Surveillance

Yellow fever vaccine (WHO position paper)

The various clinical presentations of YF (yellow fever) may be mistaken for those of a number of other infectious diseases that occur in YF at-risk countries. This underscores the importance of having a sensitive, case-based YF surveillance system, supported by laboratory diagnostic facilities. The timely notification and investigation of patients with acute febrile illness and jaundice, with or without haemorrhagic manifestations, is recommended to increase the sensitivity of surveillance to detect the circulation of YF virus. The early detection of YF virus circulation would prompt timely implementation of outbreak response activities.

Yellow fever vaccine (WHO position paper)

In emergency situations, WHO, through its network of Collaborating Centres for Arboviruses and Haemorrhagic Fevers, can organize diagnostic assistance to affected countries.

Yellow fever vaccine (WHO position paper)

When promoting increased use of YF (yellow fever) vaccine in at risk areas, the outstanding safety and effectiveness profile, the long duration of protection and the cost-effectiveness of the 17D vaccine should continue to be emphasized. However, recent reports of severe, but very rare, vaccine-associated adverse events highlight the importance of careful post-licensure surveillance, even for well established vaccines. Enhanced surveillance of such events and careful molecular analyses of the 17D strains isolated from potential new cases as well as from the actual vaccine batches should contribute to the understanding of the pathogenetic mechanisms involved.
Yellow fever vaccine (WHO position paper)

WHO recognizes the urgent need for improved surveillance of YF (yellow fever) in at-risk countries. There is therefore an urgent need for rapid laboratory confirmation of diagnosis in clinically suspected cases. WHO recommends extended use of the filter-paper method for blood collection because it improves safety of the procedure and simplifies both collection and transportation of the samples. Dried blood on filter-paper allows testing for PCR products as well as for YF virus-specific IgM.

WHO recommended standards for surveillance of selected vaccine-preventable diseases

Yellow fever surveillance is therefore critical for monitoring the incidence of the disease and allowing the prediction and early detection of outbreaks and the monitoring of control measures. Case-reporting of yellow fever is universally required by the International Health Regulations.

WHO recommended standards for surveillance of selected vaccine-preventable diseases

Recommended types of surveillance for yellow fever:
1) Routine monthly reporting of aggregated data on suspected and confirmed cases form the peripheral level to the intermediate and central levels.
2) Designated reporting sites at all levels should report at a specified frequency (e.g. weekly or monthly) even if there are zero cases (often referred to as zero reporting).
3) Immediate reporting of suspected cases from the peripheral level to the intermediate and central levels.
4) All suspected cases and outbreaks should be investigated immediately and blood samples should be collected for laboratory confirmation.
5) Case-based surveillance should be implemented in countries identified by WHO as being at risk for yellow fever. Specimens should be collected to confirm epidemics as rapidly as possible. Priority should then be given to collecting specimens from new or neighbouring areas (other than the areas where epidemics are already confirmed).

Note: The international Health Regulations require all yellow fever cases to be reported to WHO within 24 hours of detection.

WHO recommended standards for surveillance of selected vaccine-preventable diseases

Opportunities should be seized to integrate yellow fever surveillance with other surveillance efforts that share similar objectives and strategies (e.g. joint laboratory training on measles and yellow fever diagnosis.)
WHO recommended standards for surveillance of selected vaccine-preventable diseases

For yellow fever:
- All suspected cases and outbreaks should be investigated immediately and blood samples should be collected for laboratory confirmation.
- Case-based surveillance should be implemented in countries identified by WHO as being at risk for yellow fever. Specimens should be collected to confirm epidemics as rapidly as possible. Priority should then be given to collecting specimens from new or neighbouring areas (other than the areas where epidemics are already confirmed).

Vaccine Administration

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Administration summary: YF vaccine (see Appendix 2_17.)

Immunization in practice: a practical resource guide for Health workers 2004 update Module 6: Holding an immunization session

See Appendix 6_19 for chart entitled, "Administering vaccines to infants" BCG, DTP, DTP-HepB, HepB, measles, yellow fever, OPV"

Yellow fever vaccine (WHO position paper)

For convenience and improved coverage, the YF vaccine should be administered simultaneously with the measles vaccine at approximately 9-12 months of age, but in a separate syringe and at a different injection site.

The YF (yellow fever) vaccine is given as a single subcutaneous or intramuscular injection (0.5 ml per dose), although the subcutaneous route is preferred.

Yellow fever vaccine (WHO position paper)

Since there is no interference between YF (yellow fever) vaccine and other vaccines, YF vaccine may be administered simultaneously, but in different syringes and at different sites, with the following vaccines: measles, polio (oral polio vaccine), diphtheria-tetanus-pertussis, hepatitis B, hepatitis A, oral cholera and oral or parenteral typhoid. When not given simultaneously, live vaccines should be administered at least one month before or one month after the YF vaccination. This recommendation is based on the assumption that interferon released in response to the first vaccine may have a temporary inhibitory effect on other live virus vaccines.
Vaccine Handling

Proper handling and reconstitution of vaccines avoids programme errors

Reconstituted BCG, measles and yellow fever vaccines must be kept cooled and must be discarded after 6 hours after reconstitution.

Proper handling and reconstitution of vaccines avoids programme errors

It is no longer necessary to ship and store freeze-dried vaccines (measles, yellow fever and BCG) at 20C. Instead, they may be refrigerated at +2 to +8C.

Proper handling and reconstitution of vaccines avoids programme errors

WHO no longer recommends that freeze-dried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at 20C. Storing them at 20C is not harmful but is unnecessary and uses up valuable storage space in the deep-freeze. Instead, they should be kept in refrigeration and transported at +2 to +8C.

Thermostability of vaccines

Reconstituted vaccines against measles, yellow fever and tuberculosis (BCG) are unstable vaccines; they should be used as soon as possible after reconstitution, be kept in a ice bath during the immunization session and should be discarded at the end of the session.

Thermostability of vaccines

Yellow fever vaccine can safely be stored at -20C or +4C for two years or more.

Thermostability of vaccines

Lyophilized yellow fever vaccine can be safely stored at -20C or +4C for two years.

Thermostability of vaccines

Yellow fever vaccine should be quickly administered after reconstitution (up to one hour). If the reconstituted vaccine is kept continuously in an ice bath, it can be used within one immunization session but must be discarded at the end of the session.

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO recommended vaccine storage conditions (Appendix 17_3).
**WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4**

WHO no longer recommends that freezedried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at -20C. Storing them at -20C is not harmful but is unnecessary. Instead, these vaccines should be stored and transported at +2C to +8C.

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

The lyophilized (YF) vaccine requires proper storage under cold-chain conditions, and reconstituted vaccine must be kept on ice and used within six hours.

**Temperature sensitivity of vaccines**

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81_1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.

**Temperature sensitivity of vaccines**

Regardless of stability of a reconstituted vaccine (including yellow fever), because of the risk of contamination, such products should be kept cold after reconstitution and discarded at the end of a 6-hour immunization session.

**Temperature sensitivity of vaccines**

Yellow fever vaccine should be quickly administered after reconstitution, maintained at 2-8C, and discarded at the end of the session, not only to preserve potency, but to minimize risk of contamination of this lyophilized vaccine once reconstituted.
Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15C and -25C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15C and -25C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2C and +8C. All other national immunization service vaccines should be stored between +2C and +8C at all levels of the cold chain.

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It is essential that only the diluent supplied with the (yellow fever) vaccine be used.

Reconstituted (yellow fever) vaccine must be kept at 2C - 8C and discarded after six hours or at the end of the immunization session, whichever comes first.

Vaccine Quality

Thermostability of vaccines

WHO requirement for yellow fever vaccine stability stipulates that the vaccine should retain 1000 mouse LD50 or the equivalent in plaque-forming units (PFUs) per human dose, and that the mean titre loss should be less than 1 log10 after two weeks incubation at 37C.

Yellow fever vaccine (WHO position paper)

According to current WHO requirements, a YF (yellow fever) vaccine that has been held at 37 C for 14 days must (i) maintain the minimal potency of >1000 MLD50 per dose and (ii) show a mean loss of titre <1 log 10 MLD50. These requirements necessitate the addition of stabilizers such as sorbitol and gelatin.

Temperature sensitivity of vaccines

(Yellow fever vaccines) meeting the WHO stability guidelines show a minimum mouse potency titer (or an equivalent potency in PFU) of greater than 1000 units after exposure to 37C for 14 days, and their loss in potency during this exposure is less than 1 log10.
Temperature sensitivity of vaccines

(Yellow fever vaccines) meeting the WHO stability guidelines show a minimum mouse potency titer (or an equivalent potency in PFU) of greater than 1000 units after exposure to 37°C for 14 days, and their loss in potency during this exposure is less than 1 log10.