MODEL INSERT
YELLOW FEVER VACCINE

DESCRIPTION
An attenuated live virus vaccine containing freeze-dried attenuated virus from the 17D strain produced in SPF eggs.

<table>
<thead>
<tr>
<th>COMPOSITION</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>YF</td>
<td>XXX LD50</td>
</tr>
<tr>
<td>Nature / amount of excipient</td>
<td>XX mg/ml</td>
</tr>
<tr>
<td>Nature / amount of stabilizer</td>
<td>XX mg/ml</td>
</tr>
<tr>
<td>Nature and amount of residual antibiotic</td>
<td>XX µg/ml</td>
</tr>
</tbody>
</table>

Diluent composition

ADMINISTRATION
The vaccine is for the active immunization of adults and children from the age of 9 months against yellow fever. A 0.5 ml dose of vaccine should be administered intramuscularly preferably. The lyophilizate must be reconstituted by adding the entire content of the supplied container of diluent to the vaccine vial. The vaccine pellet should be completely dissolved in the diluent. Following reconstitution, the vaccine should be inspected visually for any foreign particulate matter prior to administration. If observed, the vaccine must be discarded.

A sterile needle and sterile syringe must be used for the reconstitution of the vaccine and for each injection.

Because of sensitivity to ultraviolet light, the vaccine must be protected from sunlight. Once the vaccine has been reconstituted, it should be used the same day (preferably immediately but by no means beyond six hours after reconstitution), and only then if the vial has been maintained between +2°C and +8°C and protected from sunlight (if not used immediately after reconstitution, the vaccine should be kept in the vaccine carrier or refrigerator at 2°C to 8°C). Any opened vials remaining at the end of an immunization session (within six [6] hours of reconstitution) should be discarded. The vaccine vial monitor for this type of vaccine is attached to the vial cap and should be discarded when the vaccine is being reconstituted.

The diluent supplied by the manufacturer is specially designed for use with this vaccine. Only this diluent may be used to reconstitute the vaccine. Do not use diluents from other types of vaccine or from other manufacturers. Water for injection may NOT be used for this purpose. Using an incorrect diluent may result in damage to the vaccine and/or serious reactions to those receiving the vaccine. Diluent must not be frozen but must be cooled between +2°C and +8°C before reconstitution. The vaccine should not be reconstituted with another vaccine.

Revised, December 2005
IMMUNIZATION SCHEDULE
The yellow fever vaccine should be administered simultaneously with measles vaccine at approximately 9-12 months of age but in a separate syringe and at a different injection site. Yellow fever vaccine can also be given safely and effectively at the same visit as DT, Td, TT, polio (OPV and IPV), hepatitis B, and *Haemophilus influenzae* type b vaccines and vitamin A supplementation.
In countries where yellow fever poses a risk for children, the vaccine is given as soon as possible after 6 months (180 days) of age. A single dose of vaccine provides protection for at least 30 years, and probably for life in most recipients. When administered for purposes of the International Certificate of Vaccination, a dose of yellow fever vaccine is valid for a period of 10 years, starting 10 days after the date of immunization.

SIDE EFFECTS
Mild systemic reactions such as headaches, myalgia, low-grade fevers, and malaise occur during the first few days after vaccination in 10-30% of vaccines.

Serious adverse reactions are extremely rare. Immediate hypersensitivity reactions characterized by rash, urticaria, or asthma occur in less than one in one million persons, and principally among those with a history of egg allergy. Generally, persons who can eat eggs or egg products may receive the vaccine. If vaccination of an individual with a questionable history of egg hypersensitivity is considered essential because of high risk of exposure, an intradermal test dose may be administered under close medical supervision.

At least 26 patients with post-vaccinal encephalitis have been reported to WHO in over 400 million doses of 17D Yellow Fever vaccine given world-wide since 1945. Of the 26 cases, 16 were in infants aged less than 7 months. WHO recommends that the vaccine not be given to children under 6 months of age. Recent data suggest a higher risk of YF vaccine-associated neurotropic disease (including encephalitis as well as other neurological conditions) in vaccinees older than 60 years compared to younger subjects.

The risk of YF vaccine-associated viscerotropic disease has been recognized since 2001 and appears to be limited to the first immunization against YF. In addition, the elderly seem more susceptible than the YF-vaccinated population at large. While, there is currently limited knowledge of the risk factors for viscerotropic disease, age above 60 years has been found to be a risk factor. Available data also suggest that thymus disease or thymic dysfunction is a potential risk factor. The risk for viscerotropic disease is currently estimated to range between 1 case per 10 million doses to 1 per 200,000,300 000 million doses overall and up to 1 case per 40,000-50,000 doses for vaccines above 60 years of age.

CONTRAINDICATIONS
The vaccine is contraindicated in children aged under 6 months and is not recommended for those aged 6 to 8 months, except during epidemics when the risk of YF virus transmission may be very high and the risk of disease would outweigh the small theoretical safety risk from immunization. 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, there is no evidence that vaccination of pregnant

Revised, December 2005
women is associated with abnormal effects on the fetus. Pregnant women may be vaccinated during epidemics when the risk of YF virus transmission can be very high.

Particular care should be taken that, when administered for travel purposes, the vaccine is only administered to persons travelling to at-risk countries who therefore are truly at risk for wild yellow fever virus infection. In addition, because of the current limited knowledge about the factors predisposing to risk of both viscerotropic and neurotropic disease following YF vaccination, and the prediction of subjects at risk, it is essential that vaccination providers carefully consider the benefits and risks of vaccination for elderly travellers. Vaccination providers should also enquire about a history of thymus disorder or dysfunction (including myasthenia gravis, thymoma, thymectomy, or DiGeorge syndrome), irrespective of age, before administering yellow fever vaccine. If travel plans cannot be altered to avoid yellow fever-endemic areas, people with a history of thymus disease should consider alternative means of yellow fever prevention, including use of insect repellents, containing N,N-diethyl-metatoluamide (DEET) and permethrin, and other behaviours to reduce mosquito bites.

**Immune deficiency**

Yellow Fever vaccine can be given to asymptomatic HIV-infected patients, but should not be given to symptomatic HIV-infected persons. This advice may be modified if the risk from yellow fever infection is greater than from the theoretical risk of the vaccine.

**STORAGE**

The vaccine should be transported and stored at +2°C to +8°C. The vials of vaccine and the diluents should be stored and transported together.

**PRESENTATION**

The vaccine comes in vials of ... doses.
The Vaccine Vial Monitors (VVMs) are on the cap of ……(specify vaccine) supplied through ………(specify supplier or manufacturer). The colour dot which appears on the label of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.