ANNEX I

LIST OF THE NAMES, PHARMACEUTICAL FORMS, STRENGTHS OF THE MEDICINAL PRODUCTS, ROUTES OF ADMINISTRATION, MARKETING AUTHORISATION HOLDERS IN THE MEMBER STATES

Member State	Marketing Authorisation Holder	Name	Strength	Pharmaceutical Form	Route of administration
Austria	Sanofi Pasteur MSD SNC 8, rue Jonas Salk, 69007 Lyon, France Tel: 33 437284000 Fax: 33 437284400	STAMARIL	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Belgium	Sanofi Pasteur MSD SA Avenue Jules Bordet 13 1140 Brussels, Belgium Tel: 32 27269584 Fax: 32 27268584	STAMARIL PASTEUR	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Czech Republic	Aventis Pasteur SA 2, avenue Pont Pasteur 69007 Lyon, France Tel: 33 437370100 Fax: 33 437377737	STAMARIL PASTEUR	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Denmark	Sanofi Pasteur MSD SA Avenue Jules Bordet 13 1140 Brussels, Belgium Tel: 32 27269584 Fax: 32 27268584	STAMARIL	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Estonia	Aventis Pasteur SA 2, avenue Pont Pasteur 69007 Lyon, France Tel: 33 437370100 Fax: 33 437377737	STAMARIL	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Finland	Sanofi Pasteur MSD SA Avenue Jules Bordet 13 1140 Brussels, Belgium Tel: 32 27269584 Fax: 32 27268584	STAMARIL	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
France	Sanofi Pasteur MSD SNC 8, rue Jonas Salk 69007 Lyon, France Tel: 33 437284000 Fax: 33 437284400	STAMARIL	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use

Germany	Sanofi Pasteur MSD GmbH Paul-Ehrlich-Str. 1 69181 Leimen, Germany Tel: 49 62245940 Fax: 49 622459433	STAMARIL	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Hungary	Aventis Pasteur SA 2, avenue Pont Pasteur 69007 Lyon, France Tel: 33 437370100 Fax: 33 437377737	STAMARIL PASTEUR	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Ireland	Sanofi Pasteur MSD Ltd Belgard Road, Tallaght, Dublin 24, Ireland Tel: 35 314041688 Fax: 35 314041687	STAMARIL	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Italy	Sanofi Pasteur MSD SNC 8, rue Jonas Salk 69007 LYON – France Tel: 33 437284000 Fax: 33 437284400	STAMARIL PASTEUR	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Latvia	Aventis Pasteur SA 2, avenue Pont Pasteur 69007 LYON – France Tel: 33 437370100 Fax: 33 437377737	STAMARIL PASTEUR	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Lithuania	Aventis Pasteur SA 2, avenue Pont Pasteur 69007 Lyon, France Tel: 33 437370100 Fax: 33 437377737	STAMARIL PASTEUR	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Luxemburg	Sanofi Pasteur MSD SA Avenue Jules Bordet 13 B-1140 Bruxelles – Belgium Tel: 32 27269584 Fax: 32 27268584	STAMARIL PASTEUR	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use

Poland	Aventis Pasteur SA 2, avenue Pont Pasteur F-69007 LYON – France Tel: 33 437370100 Fax: 33 437377737	STAMARIL PASTEUR	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Portugal	Sanofi Pasteur MSD SNC 8, rue Jonas Salk 69007 Lyon, France Tel: 33 437284000 Fax: 33 437284400	STAMARIL	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Slovakia	Aventis Pasteur SA 2, avenue Pont Pasteur 69007 Lyon, France Tel: 33 437370100 Fax: 33 437377737	STAMARIL	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Spain	Sanofi Pasteur MSD SA Edificio Cuzco IV, Paseo de la Castellana, 141 28046 Madrid, Spain Tel: 34 913717800 Fax: 34 913717888	STAMARIL PASTEUR	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Sweden	Sanofi Pasteur MSD SA Avenue Jules Bordet 13 B-1140 Brussels, Belgium Tel: 32 27269584 Fax: 32 27268584	STAMARIL	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
The Netherlands	Sanofi-Pasteur MSD SA Avenue Jules Bordet 13 1140 Brussels, Belgium Tel: 32 27269584 Fax: 32 27268584	STAMARIL PASTEUR	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
United Kingdom	Sanofi Pasteur MSD Limited Mallards Reach, Bridge Road, Maidenhead Berkshire SL6 1QP, United Kingdom Tel: 44 1628785291 Fax: 44 1628588166	STAMARIL	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use

Iceland	Sanofi Pasteur MSD SA Avenue Jules Bordet 13 1140 Brussels, Belgium Tel: 32 27269584 Fax: 32 27268584	STAMARIL	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use
Norway	Sanofi Pasteur MSD SA Avenue Jules Bordet 13 1140 Brussels, Belgium Tel: 32 27269584 Fax: 32 27268584	STAMARIL	Not less than 1000 LD50 units	Powder and solvent for suspension for injection	Subcutaneous use (preferred) or intramuscular use

ANNEX II

SCIENTIFIC CONCLUSIONS AND GROUNDS FOR AMENDMENT OF THE SUMMARIES OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET PRESENTED BY THE EMEA

SCIENTIFIC CONCLUSIONS

OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF STAMARIL AND ASSOCIATED NAMES

Due to the fact that STAMARIL and associated names, powder and solvent for suspension for injection do not have the same Summary of Product Characteristics (SPC) in the various Member States in the European Union as a result of divergent national decisions, a harmonisation of the SPC for STAMARIL and associated names, throughout Europe has become necessary. While most sections of the SPC are affected, the MAH identifies two issues, each affecting several sections of the SPC, which would seem to have an important effect on the optimal use of the vaccine. These are:

1. Inconsistent recommendations on usage in children

- *Section 4.1 Indications*: Indicated in children from 6 months to 1 year depending on the country
- *Section 4.3 Contra-indications*: Contra-indicated for children under 4 months, under 9 months or under 1 year
- *Section 4.4 warnings*: Corresponding to 4.3, warnings for children between 6 to 9 months or for children less than 9 months.

2. Disparate information provided on viscerotropic disease, and associated risk factors in sections 4.4 Warning and 4.8 Undesirable effects:

- The wording used to describe warnings in the elderly population is divergent depending on the country.
- Warnings against vaccination in those with asymptomatic HIV infection.
- Warnings against vaccination in those with thymic disease.

3. Further discrepancies also exist between Member States regarding sections 4.2 Method of administration, 4.5 Interactions with other Medicinal Products and other forms of Interaction, 4.6 Pregnancy and lactation and 6.2 Incompatibilities

Sanofi Pasteur MSD on behalf of all the Marketing Authorisation Holders, (see Annex I of opinion) applied for harmonisation according to Article 30 of Directive 2001/83/EC, as amended, of their medicinal products STAMARIL and associated names. The pharmaceutical form (powder and solvent for suspension for injection) and the strength (each 0.5ml dose contains live yellow fever virus not less than 1000 LD50 units) are identical for all countries. However, since 2003, STAMARIL has been marketed under two different presentations in the EU (1 dose and 10 doses). The multi-dose presentation is licensed only in the Czech Republic, France and Latvia. Although the products in single and multi-dose presentations differ by the quantity of excipients in the finished product, the Applicant wishes to harmonize the SPCs for both presentations. A dossier and a proposal for SPC were submitted by the MAH on 30 August 2005.

1. Recommendations on usage in children

Very young age is associated with an increased risk of developing YEL-AND. Fourteen out of 26 reported cases occurred in infants below the age of 4 months, one case was reported at 7 months of age and one at 3 years of age. The remaining 9 cases of YEL-AND developed in adolescent and adults. More recent data on global outbreak control campaigns in Brazil demonstrate that approx. 8 Mio doses of vaccine were given to children below 1 year of age with no reporting of serious adverse events as YEL-AND. Up to the present, 110 Mio doses of STAMARIL have been administered during outbreak control campaigns in Africa and South America, whereof it was estimated that 10% of doses were used in children below 1 year of age. No case of neurological AE was reported after introduction of STAMARIL.

The EPI Global Advisory Group recommends that YF vaccine should be administered from the age of 6 months, but is more easily integrated in the EPI by administering YF together with measles vaccine at the age of 9 months.

The starting age for vaccination with YF vaccine is 9 months of age. The vaccine is contraindicated in children less than 6 months of age. However, in order to keep the possibility to vaccinate children between 6 and 9 months during outbreak situations a statement regarding this issue is implemented. The SPC is amended in section 4.1, 4.2, 4.3 and 4.4 in section 4.4. to reflect the lower age limit for vaccination with STAMARIL.

2. Information provided on viscerotropic disease, and associated risk factors in sections 4.4 Warning and 4.8 Undesirable effects:

- **The wording used to describe warnings in the elderly population.**

In elderly persons, yellow fever vaccines are associated with a higher frequency of significant AEs in the elderly and with a lower incidence of common non-serious side effects. The neutralizing antibody response is not reduced in healthy, elderly persons.

A warning for the use of the YF vaccine in persons 60 years and older is included in the SPC. In addition, the warning includes a clear statement that the benefit and risk of the YF vaccine should be carefully evaluated before considering the use of this vaccine.

- **Warnings vaccination in those with for asymptomatic HIV infection.**

Based on the available data from clinical studies investigating the safe administration of live attenuated vaccines (including YF vaccine) to HIV infected subjects, a universally accepted recommendation cannot be concluded. In addition, the absence of routine testing opportunities of the CD4 cell count in many countries and due to the fact that for adults the recommended CD4 cell count thresholds for the indication to vaccinate varies and may differ significantly when vaccinating infants and children, the proposal to focus on the distinction of symptomatic and asymptomatic HIV-infection is implemented in the SPC. Where accepted a locally established recommendation for a CD4 cell count threshold may be used additionally to support the decision whether the vaccination is indicated.

- **Warnings vaccination in those with for thymic disease.**

Taking into account that those with an impaired immune response due to congenital or acquired dysfunction or absence of the thymus could have a low immune response and so questionable protection from YF vaccination the warning statement regarding special populations is endorsed. The CHMP acknowledges that the contraindication for subjects with a history of thymus dysfunction or thymectomy is based on a small number of observations made during post-marketing surveillance of yellow fever vaccines.

3. Further discrepancies

- **4.2 Method of administration**

The recommendation to administer the yellow fever vaccine subcutaneously or intramuscularly was based on the standard of care at the time of the development of STAMARIL in the early 1980s. Following a review of published data the recommended route of administration of different yellow fever vaccines is subcutaneous.

Despite the fact that only limited data are available on the i.m. use of STAMARIL and no clinical studies were performed to demonstrate that both routes of administration are comparable most

European MS allow both, the s.c. and i.m. use due to routine vaccination practice. This is in line with the WHO recommendations.

- **4.2 Interactions with other Medicinal Products and other forms of Interaction**
- **6.2 Incompatibilities**

- *Co-administration with other vaccines*

The data on co-administration of STAMARIL with Vi polysaccharide, measles, HAV and Men A+C plain polysaccharide vaccines are limited. However, these studies did not show any major problems on co-administration and it must be acknowledged that some co-administrations have become common practise. In particular, concomitant administration of yellow fever and the first dose of measles vaccine in children aged around 9-12 months. Thus, STAMARIL may be administered at the same time as vaccines containing typhoid Vi capsular polysaccharide and/or inactivated hepatitis A virus (section 4.2). STAMARIL may be administered at the same time as measles vaccine if this is in accordance with official recommendations (section 4.2).

- *Mixing of STAMARIL with Vi or measles vaccine*

Although this practise is endorsed in some existing EU SPCs, the CHMP considers that the data are very limited. The limitations include the age of the studies, the nature of the population enrolled (e.g. only healthy young adults in some), the lack of details on vaccines, assays, safety and/or attention to GCP. Therefore, the assessor is reluctant to accept the findings. In addition, there would seem to be no reason to mix these vaccines before administration to EU residents and the CHMP does not find any endorsement for mixing in the recommendations of WHO. This is reflected in section 4.5 and 6.2 of the SPC.

- *Co-administration with immunoglobulin (IG)*

The interaction of immunoglobulin (IG) with YF vaccine was investigated in 160 healthy subjects in the US. IG with a neutralising antibody titer of ≥640 was administered 0-7 days before vaccination and in a control group 28-35 days after YF vaccination. The seroconversion rates were comparable in both groups (82 vs 83%) indicating that the administration of IG has no influence on the replication of the YF vaccine virus. Furthermore IGs sourced from European donors contain low or absent levels of YF neutralising antibody titers. Thus an interference of IG on the immune response to YF vaccine is not likely, and it is not necessary to include a statement on any potential interaction with IG in section 4.5.

- **4.6 Pregnancy and lactation**

Although data on a limited number of exposed pregnancies indicate no adverse effects of STAMARIL on pregnancy or the health of the foetus/newborn child no other relevant epidemiological, post marketing surveillance or literature data are available. No animal reproduction studies have been conducted with STAMARIL. The potential risk for human is unknown. STAMARIL should be given to pregnant women only when clearly needed (for example during an outbreak) and only after careful consideration of the potential risks and benefit (section 4.6)

Although the risk of transmitting vaccine virus via breast milk cannot be excluded in general no reports of adverse events or transmission of yellow fever vaccine virus from breastfeeding mothers to infants exist for the time being. In order to keep the possibility to vaccinate nursing mothers in outbreak situations or when travelling to high-risk areas vaccination of breastfeeding mothers is no longer a strict contraindication but should be avoided whenever possible. Thus it is recommended to vaccinate lactating mothers only in special situations as stated in section 4.6.

- **4.6 Undesirable effect**

The MAH conduct a review of the safety data obtained with the current formulation of STAMARIL in all clinical trials.

The clinical development of the yellow fever vaccine has been part of the development of a stabilized live attenuated yellow fever vaccine, derived from the working seed IP/F2, and the validation process of a new working seed, PV26. Altogether ten different clinical studies have been conducted and the safety data are summarised below:

Summary of the eight studies conducted between 1983 and 1988 for the development of a stabilized live attenuated yellow fever vaccine derived from the working seed IP/F2

Investigator	Year	Vaccine	# sub	Age (years)	Safety	Immune response
Fabiyi A	1983	STAMARIL	762	17-65	No SAE	100% SC (*)
Gentilini M	1984	STAMARIL	74	3-62	No SAE	Not tested
Georges AJ	1984	STAMARIL	209	1-5	No SAE	94% SC
Roche JC	1984	STAMARIL	45		No SAE	95.5% SC
Wolga J	1984	STAMARIL	49	16-71	No SAE	93.8% SC
		Amaril	146		No SAE	92.8% SC
Roche JC	1985	STAMARIL	115	19.8 [± 48 m]	No SAE	100% SN
		Amaril	143		No SAE	99.3% SN
Pivetaud JP	1986	STAMARIL	370	1-70	No SAE	Not tested
Roberts J	1988	STAMARIL	58	Adults	No SAE	100% SC
		Arilva	59		No SAE	100% SC

Abbreviations: # subj: number subjects; SC: seroconversion; SN: sero-neutralisation; No sAE: no serious AE; (*) tested in 322 subjects

Summary of the four studies conducted between 1987 and 1998 for the development of a stabilized live attenuated yellow fever vaccine derived from the new working seed PV26

Investigator	Year	Vaccine	# sub	Age (years)	Safety	Immune response
Goujon C	1987	STAMARIL	18	Adults	No SAE	100% SC (*)
Thabaut A	1988	Batch P5050	20	Adults	No SAE	100% SC
		Batch P5095	20		No SAE	96% SC
		Batch P5126	20		No SAE	76% SC
		Batch P5139	20		No SAE	50% SC
Muzellec	1989	Batch P5659	54	18-30	No SAE	100% SC
		Batch N5049	54		No SAE	100% SC
		Batch P5139	54		No SAE	100% SC
Zuckerman J	1997	STAMARIL	106	18-65	No SAE	100% SC
		Arilvax	105	18-69	No SAE	99% SC

Abbreviations: # subj: number subjects; in the studies by Thabaut and Muzellec different batches of STAMARIL were used; SC: se

During the clinical development of the stabilised live attenuated yellow fever vaccine, from the working seed lots IP/F2 and PV26, a total of 2,048 subjects were monitored for adverse events and a

total of 1,158 subjects also participated in an evaluation of the immune response. An overall seroconversion rate of 97% was calculated, including the low performance result of batch P5139 in the study by Thabaut and Meyran. When the same batch was used in another comparative double-blind randomized study, a 100% seroconversion rate observed in the 54 vaccinees. No serious adverse events have been reported in the study volunteers.

A total of 453 subjects received either the non-stabilised yellow fever vaccine or a competitive yellow fever vaccine and the seroconversion rate and adverse event profile was similar.

The final wording of section 4.8. (see attached SPC) was agreed upon this analysis.

GROUNDS FOR AMENDMENT OF THE SUMMARIES OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

Based on the documentation submitted by the MAH and the scientific discussion within the Committee, the CHMP considered that the benefit/risk ratio of STAMARIL and associated names is favourable for use relating to:

Active immunisation against yellow fever in persons from 9 months of age:

- Travelling to, passing through or living in an endemic area,
- Travelling to any country that requires an International Certificate of Vaccination for entry (which may or may not depend on the previous itinerary).
- Handling potentially infectious materials (*e.g.* laboratory personnel).

The divergences identified at the start of the referral have been resolved.

GROUNDS FOR AMENDMENTS OF THE SUMMARIES OF PRODUCTS CHARACTERISTICS

Whereas,

- the scope of the referral was the harmonisation of the Summaries of Products Characteristics,
- the Summary of Products Characteristic proposed by the Marketing Authorisation Holders has been assessed based on the documentation submitted and the scientific discussion within the Committee,

the CHMP has recommended the amendment of the Marketing Authorisations for which the Summary of Product Characteristics, Labelling and Package Leaflet is set out in Annex III of the CHMP Opinion for STAMARIL and associated names (see Annex I of the opinion).

ANNEX III

SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

Note: This SPC, labelling and package leaflet is the version that was annexed to the Commission Decision on this Article 30 referral for yellow fever vaccine (live) containing medicinal products. The text was valid at that time.

After the Commission Decision, the Member State competent authorities will update the product information as required. Therefore, this SPC, labelling and package leaflet may not necessarily represent the current text.

SUMMARY OF PRODUCT CHARACTERISTICS

SINGLE DOSE PRESENTATION

1. NAME OF THE MEDICINAL PRODUCT

STAMARIL (or local trade name)
Powder and solvent for suspension for injection.
Yellow fever vaccine (Live).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (0.5 ml) contains:

Yellow fever virus[1] 17 D-204 strain (live, attenuated) …….not less than 1000 LD_{50} units[2]

[1] produced in specified pathogen-free chick embryos
[2] The statistically determined lethal dose in 50% of animals tested

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for suspension for injection.

Before reconstitution, the powder is beige to orange beige; the solvent is clear and colourless.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

STAMARIL is indicated for active immunization against yellow fever in persons:

- travelling to, passing through or living in an endemic area,
- travelling to any country that requires an International Certificate of Vaccination for entry (which may or may not depend on the previous itinerary).
- handling potentially infectious materials (*e.g.* laboratory personnel).

See sections 4.2, 4.3 and 4.4 regarding the minimum age for vaccination of children under special circumstances and guidance for vaccination of other specific patient populations.

In order to comply with vaccine regulations and to be officially recognised, yellow fever vaccines must be administered in an approved World Health Organization (WHO) vaccination centre and registered on an International Certificate of Vaccination. This certificate is valid for 10 years from the 10th day after vaccination and immediately after re-vaccination.

4.2 Posology and method of administration

Posology:
Primary vaccination
Adults and children aged 9 months and over: A single dose of 0.5 ml of reconstituted vaccine.

Children under 9 months of age: The vaccine must not be given to children less than 6 months old (see section 4.3). Vaccination against yellow fever is not usually recommended in children aged from

6 months up to 9 months except in specific circumstances and in accordance with available official recommendations (see section 4.4), in which case the dose is the same as in older children and adults.

The vaccine should be given at least 10 days before entering an endemic area since protective immunity may not be achieved until at least this time has elapsed.

Elderly
The dose is the same as for adults. However due to a higher risk of yellow fever vaccine-associated severe and potentially fatal disease in persons from 60 years of age, the vaccine should only be given when it is considered that there is a considerable and unavoidable risk of acquiring yellow fever infection (see sections 4.4 and 4.8).

Re-vaccination:
Re-vaccination with one dose of 0.5 ml is recommended every 10 years in persons considered to be at risk of exposure.
International Health Regulations require re-vaccination, using the same dose as for primary vaccination, at intervals of 10 years in order to retain a valid certificate.

Method of administration:

It is preferable that the vaccine is injected by the subcutaneous route

Intramuscular injection may be performed if this is in accordance with applicable official recommendations.
For intramuscular use the recommended injection sites are the anterolateral aspect of the thigh in the infants and toddlers (6 months up to 2 years of age) and the deltoid muscle in older children and adults.

DO NOT INJECT INTRAVASCULARLY

See section 6.6. for instructions on reconstitution

4.3 Contraindications

- Hypersensitivity reaction to eggs, chicken proteins or to any component of STAMARIL
- Serious hypersensitivity reactions (*e.g.*, anaphylaxis) after a previous dose of any yellow fever vaccine.
- Immunosuppression, whether congenital, idiopathic or as a result of treatment with systemic steroids (greater than the standard dose of topical or inhaled steroids), radiotherapy or cytotoxic drugs.
- History of thymus dysfunction (including thymoma, thymectomy)
- Symptomatic HIV infection
- Asymptomatic HIV infection when accompanied by evidence of impaired immune function (see section 4.4).
- Age less than 6 months (see sections 4.2 and 4.4).
- Current severe febrile illness.

4.4 Special warnings and precautions for use

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of anaphylaxis or other severe hypersensitivity reaction following administration of the vaccine.

STAMARIL should be administered only to persons who are/will be at risk of infection with yellow fever virus or who must be vaccinated to comply with international health regulations. Before

considering administration of yellow fever vaccine, care should be taken to identify those who might be at increased risk of adverse reactions following vaccination (see section 4.3 and below).

Yellow fever vaccine associated neurotropic disease
Very rarely, yellow fever vaccine-associated neurotropic disease (YEL-AND) has been reported following vaccination, with sequelae or with fatal outcome in some cases (see section 4.8). Clinical features have appeared within one month of vaccination and include high fever with headache that may progress to include one or more of the following: confusion, encephalitis/encephalopathy, meningitis, focal neurological deficits, or Guillain Barré syndrome. To date, those affected have been primary vaccinees. The risk appears to be higher in those aged over 60 years, although cases have been also reported in younger persons.

Yellow fever vaccine-associated viscerotropic disease
Very rarely, yellow fever vaccine-associated viscerotropic disease (YEL-AVD) resembling fulminant infection by wild-type virus has been reported following vaccination (see section 4.8). The clinical presentation may include fever, fatigue, myalgia, headache, hypotension, progressing to one or more of metabolic acidosis, muscle and liver cytolysis, lymphocytopenia and thrombocytopenia, renal failure and respiratory failure. The mortality rate has been around 60%. To date, all cases of YEL-AVD have been in primary vaccinees with onset within 10 days of vaccination. The risk appears to be higher in those aged over 60 years although cases have also been reported in younger persons. Disease of the thymus gland has also been recognised as a potential risk factor (see section 4.3 and section 4.8).

Immunosuppressed persons
STAMARIL must not be administered to immunosuppressed persons (see section 4.3).
If the immunosuppression is temporary, vaccination should be delayed until the immune function has recovered. In patients who have received systemic corticosteroids for 14 days or more, it is advisable to delay vaccination until at least one month after completing the course.

HIV infection
STAMARIL must not be administrated to persons with symptomatic HIV infection or with asymptomatic HIV infection when accompanied by evidence of impaired immune function (see section 4.3). However, there are insufficient data at present to determine the immunological parameters that might differentiate persons who could be safely vaccinated and who might mount a protective immune response from those in whom vaccination could be both hazardous and ineffective. Therefore, if an asymptomatic HIV-infected person cannot avoid travel to an endemic area available official guidance should be taken into account when considering the potential risks and benefits of vaccination.

Children born to HIV positive mothers
Children aged at least 6 months (see sections 4.2 and 4.3 and below) may be vaccinated if it is confirmed that they are not infected with HIV.
HIV infected children aged at least 6 months who are potentially in need of protection against yellow fever should be referred to a specialist paediatric team for advice on whether or not to vaccinate.

Age
Children aged 6 to 9 months
STAMARIL must not be administered to children before the age of 6 months (see section 4.3). Children aged from 6 months up to 9 months should only be vaccinated under special circumstances (e.g. during major outbreaks) and on the basis of current official advice.

Persons aged 60 years and older
Some serious and potentially fatal adverse reactions (including systemic and neurological reactions persisting more than 48 hours, YEL-AVD and YEL-AND) appear to occur at higher frequencies after the age of 60 years. Therefore, the vaccine should only be given to those who have a considerable risk of acquiring yellow fever (see above and section 4.8).

Because intramuscular injection can cause injection site haematoma, STAMARIL should not be given by the intramuscular route to persons with any bleeding disorder, such as haemophilia or thrombocytopenia, or to persons on anticoagulant therapy. The subcutaneous route of administration should be used instead.

Patients with rare hereditary problems of fructose intolerance should not take this vaccine.

4.5 Interaction with other medicinal products and other forms of interaction

STAMARIL must not be mixed with any other vaccine or medicinal product in the same syringe.
If there is a need to administer another injectable vaccine(s) at the same time as STAMARIL each vaccine should be injected into a separate site (and preferably a separate limb).
STAMARIL may be administered at the same time as measles vaccine if this is in accordance with official recommendations.
STAMARIL may be administered at the same time as vaccines containing typhoid Vi capsular polysaccharide and/or inactivated hepatitis A virus.

STAMARIL must not be administered to persons who are receiving immunosuppressant therapy (***e.g.***, cytotoxic agents, systemic steroids, greater than standard dose of topical or inhaled steroids or other agents). See section 4.3.

4.6 Pregnancy and lactation

Pregnancy
No animal reproduction studies have been conducted with STAMARIL and the potential risk for humans is unknown. Data on a limited number of exposed pregnancies indicate no adverse effects of STAMARIL on pregnancy or the health of the fetus/newborn child. Nevertheless, STAMARIL should be given to pregnant women only when clearly needed and only after careful consideration of the potential risks and benefits.

Lactation
It is not known if the live attenuated yellow fever virus is excreted in animal or human breast milk. Although there have been no reports of transmission of vaccine viruses from breastfeeding mothers to infants STAMARIL should not be given to nursing mothers unless this cannot be avoided.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive or use machine have been performed.

4.8 Undesirable effects

Data from clinical studies
Across clinical studies, the most common adverse reactions occurring after vaccine administration were local reactions, reported in approximately 16% of subjects.

The following adverse events are from one clinical study in which 106 healthy adult subjects received STAMARIL. .
The adverse events are ranked under headings of frequency, using the following convention:
- Very common: ≥ 10%
- Common: : ≥ 1% and ≤ 10%
- Uncommon: : ≥ 0.1% and ≤ 1%

Nervous system disorders
Very common: Headache

Gastro-intestinal system disorders
Common: Nausea, Diarrhoea, Vomiting
Uncommon: Abdominal pain

Musculo-skeletal and connective tissue disorders
Common: Myalgia
Uncommon: Arthralgia

General disorders and administration site conditions
Very common: Local reactions (including pain, redness, haematoma, induration, swelling)
Common: Pyrexia, Asthenia

Data from post-marketing experience
The following additional adverse events have been reported during post marketing experience with STAMARIL. They are based on spontaneous reporting therefore the frequencies are unknown.

Blood and lymphatic system disorders
Lymphadenopathy

Immune system disorders
Anaphylaxis, angioedema.

Nervous system disorders
Cases of neurotropic disease (known as YEL-AND), some of which have had a fatal outcome, have been reported following yellow fever vaccination (see section 4.4). YEL-AND may manifest as high fever with headache that may progress to include one or more of confusion, lethargy, encephalitis, encephalopathy and meningitis (see section 4.4).
Other neurological signs and symptoms have been reported and include convulsion, Guillain-Barré syndrome and focal neurological deficits.

Skin and subcutaneous tissue disorders
Rash, Urticaria

General disorders and administration site conditions
Cases of viscerotropic disease (known as YEL-AVD and formerly described as "Febrile Multiple Organ-System Failure") have been reported following yellow fever vaccination some of which have been fatal (see section 4.4). YEL-AVD may manifest as fever, fatigue, myalgia, headache and hypotension progressing to one or more of metabolic acidosis, muscle and liver cytolysis, lymphocytopenia and thrombocytopenia, renal and respiratory failure.

Additional information on special population
Congenital or acquired immunodeficiency has been identified as a risk factor for neurotropic disease (See sections 4.3 and 4.4).
Age of more than 60 years (see section 4.4) has been identified as a risk factor for YEL-AVD and YEL-AND. A medical history of thymic disease (see sections 4.3 and 4.4) has been identified as a risk factor for YEL-AVD.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Yellow Fever Vaccine (Live)
ATC code: J07B L1

STAMARIL is a live attenuated yellow fever virus vaccine. As with other live attenuated viral vaccines, there is a sub-clinical infection in healthy recipients that results in the production of specific B and T cells and the appearance of specific circulating antibody.
Protective immunity appears from about 10 days after injection. Although International Health Regulations require re-vaccination at intervals of 10 years in order to retain a valid certificate, some degree of immunity likely persists for more than 10 years.

5.2 Pharmacokinetic properties

No pharmacokinetic studies have been performed.

5.3 Preclinical safety data

Pre-clinical data reveal no special hazard for humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder:
Lactose
Sorbitol E420
L-histidine hydrochloride
L-alanine
Sodium chloride
Potassium chloride
Disodium phosphate
Monopotassium phosphate
Calcium chloride
Magnesium sulphate

Solvent:
Sodium chloride
Water for injections.

6.2 Incompatibilities

This vaccine must not be mixed with other medicinal products.

6.3 Shelf life

3 years.
After reconstitution, the medicinal product must be used immediately.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.

For storage conditions of the reconstituted medicinal product, see section 6.3

6.5 Nature and contents of container

Powder in vial (type I glass), with stopper (chlorobutyl) and aluminium flip-off cap + 0.5 ml of solvent in pre-filled syringe (type I glass), with a plunger-stopper (chlorobromobutyl), attached needle and needle-shield (natural rubber or polyisoprene) or tip-cap (chlorobromobutyl) – pack size of 1, 10 or 20.

The following presentations may not be registered depending on the country. Their implementation will be reviewed nationally.
Powder in vial (type I glass), with stopper (chlorobutyl) and aluminium flip-off cap + 0.5 ml of solvent in pre-filled syringe (type I glass), with a plunger-stopper (chlorobromobutyl), without attached needle and tip-cap (chlorobromobutyl) – pack size of 1, 10 or 20.

Powder in vial (type I glass), with stopper (chlorobutyl) and aluminium flip-off cap + 0.5 ml of solvent in pre-filled syringe (type I glass), with a plunger-stopper (chlorobromobutyl), without attached needle and tip cap (chlorobromobutyl) with 1 or 2 separate needles attached in the blister– pack size of 1 and 10.

Not all pack sizes or presentations may be marketed.

6.6 Special precautions for disposal

For syringe without attached needle only: After removing the syringe tip cap, the needle should be firmly placed on the tip of the syringe and secured by rotating a quarter of a turn (90°).
The powder is reconstituted by adding the solvent provided in the pre-filled syringe to the vial. The vial is shaken and, after complete dissolution, the suspension obtained is withdrawn into this same syringe for injection.
Before administration, the reconstituted vaccine should be shaken vigorously.
Use immediately after reconstitution.
After reconstitution with the sodium chloride solution provided STAMARIL is a beige to pink beige suspension for injection.
Contact with disinfectants is to be avoided since they may inactivate the virus.

Any unused product or waste material should be disposed of, preferably by heat inactivation or incineration, in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

SUMMARY OF PRODUCT CHARACTERISTICS

MULTIDOSE PRESENTATION

This presentation is not applicable in all countries. The SPC will be completed nationally

1. NAME OF THE MEDICINAL PRODUCT

STAMARIL (or local trade name)
Powder and solvent for suspension for injection.
Yellow fever vaccine (Live).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (0.5 ml) contains:

Yellow fever virus[1] 17 D-204 strain (live, attenuated) …….not less than 1000 LD_{50} units[2]

[1] produced in specified pathogen-free chick embryos
[2] The statistically determined lethal dose in 50% of animals tested

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for suspension for injection.

Before reconstitution, the powder is beige to orange beige; the solvent is clear and colourless.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

STAMARIL is indicated for active immunization against yellow fever in persons:

- travelling to, passing through or living in an endemic area,
- travelling to any country that requires an International Certificate of Vaccination for entry (which may or may not depend on the previous itinerary).
- handling potentially infectious materials (*e.g.* laboratory personnel).

See sections 4.2, 4.3 and 4.4 regarding the minimum age for vaccination of children under special circumstances and guidance for vaccination of other specific patient populations.

In order to comply with vaccine regulations and to be officially recognised, yellow fever vaccines must be administered in an approved World Health Organization (WHO) vaccination centre and registered on an International Certificate of Vaccination. This certificate is valid for 10 years from the 10th day after vaccination and immediately after re-vaccination.

4.2 Posology and method of administration

Posology:
Primary vaccination
Adults and children aged 9 months and over: A single dose of 0.5 ml of reconstituted vaccine.

Children under 9 months of age: The vaccine must not be given to children less than 6 months old (see section 4.3). Vaccination against yellow fever is not usually recommended in children aged from

6 months up to 9 months except in specific circumstances and in accordance with available official recommendations (see section 4.4), in which case the dose is the same as in older children and adults.

The vaccine should be given at least 10 days before entering an endemic area since protective immunity may not be achieved until at least this time has elapsed.

Elderly
The dose is the same as for adults. However due to a higher risk of yellow fever vaccine-associated severe and potentially fatal disease in persons from 60 years of age, the vaccine should only be given when it is considered that there is a considerable and unavoidable risk of acquiring yellow fever infection (see sections 4.4 and 4.8).

Re-vaccination:
Re-vaccination with one dose of 0.5 ml is recommended every 10 years in persons considered to be at risk of exposure.
International Health Regulations require re-vaccination, using the same dose as for primary vaccination, at intervals of 10 years in order to retain a valid certificate.

Method of administration:

It is preferable that the vaccine is injected by the subcutaneous route

Intramuscular injection may be performed if this is in accordance with applicable official recommendations.
For intramuscular use the recommended injection sites are the anterolateral aspect of the thigh in the infants and toddlers (6 months up to 2 years of age) and the deltoid muscle in older children and adults.

DO NOT INJECT INTRAVASCULARLY

See section 6.6. for instructions on reconstitution

4.3 Contraindications

- Hypersensitivity reaction to eggs, chicken proteins or to any component of STAMARIL
- Serious hypersensitivity reactions (*e.g.*, anaphylaxis) after a previous dose of any yellow fever vaccine.
- Immunosuppression, whether congenital, idiopathic or as a result of treatment with systemic steroids (greater than the standard dose of topical or inhaled steroids), radiotherapy or cytotoxic drugs.
- History of thymus dysfunction (including thymoma, thymectomy)
- Symptomatic HIV infection
- Asymptomatic HIV infection when accompanied by evidence of impaired immune function (see section 4.4).
- Age less than 6 months (see sections 4.2 and 4.4).
- Current severe febrile illness.

4.4 Special warnings and precautions for use

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of anaphylaxis or other severe hypersensitivity reaction following administration of the vaccine.

STAMARIL should be administered only to persons who are/will be at risk of infection with yellow fever virus or who must be vaccinated to comply with international health regulations. Before

considering administration of yellow fever vaccine, care should be taken to identify those who might be at increased risk of adverse reactions following vaccination (see section 4.3 and below).

Yellow fever vaccine associated neurotropic disease
Very rarely, yellow fever vaccine-associated neurotropic disease (YEL-AND) has been reported following vaccination, with sequelae or with fatal outcome in some cases (see section 4.8). Clinical features have appeared within one month of vaccination and include high fever with headache that may progress to include one or more of the following: confusion, encephalitis/encephalopathy, meningitis, focal neurological deficits, or Guillain Barré syndrome. To date, those affected have been primary vaccinees. The risk appears to be higher in those aged over 60 years, although cases have been also reported in younger persons.

Yellow fever vaccine-associated viscerotropic disease
Very rarely, yellow fever vaccine-associated viscerotropic disease (YEL-AVD) resembling fulminant infection by wild-type virus has been reported following vaccination (see section 4.8). The clinical presentation may include fever, fatigue, myalgia, headache, hypotension, progressing to one or more of metabolic acidosis, muscle and liver cytolysis, lymphocytopenia and thrombocytopenia, renal failure and respiratory failure. The mortality rate has been around 60%. To date, all cases of YEL-AVD have been in primary vaccinees with onset within 10 days of vaccination. The risk appears to be higher in those aged over 60 years although cases have also been reported in younger persons. Disease of the thymus gland has also been recognised as a potential risk factor (see section 4.3 and section 4.8).

Immunosuppressed persons
STAMARIL must not be administered to immunosuppressed persons (see section 4.3).
If the immunosuppression is temporary, vaccination should be delayed until the immune function has recovered. In patients who have received systemic corticosteroids for 14 days or more, it is advisable to delay vaccination until at least one month after completing the course.

HIV infection
STAMARIL must not be administrated to persons with symptomatic HIV infection or with asymptomatic HIV infection when accompanied by evidence of impaired immune function (see section 4.3). However, there are insufficient data at present to determine the immunological parameters that might differentiate persons who could be safely vaccinated and who might mount a protective immune response from those in whom vaccination could be both hazardous and ineffective. Therefore, if an asymptomatic HIV-infected person cannot avoid travel to an endemic area available official guidance should be taken into account when considering the potential risks and benefits of vaccination.

Children born to HIV positive mothers
Children aged at least 6 months (see sections 4.2 and 4.3 and below) may be vaccinated if it is confirmed that they are not infected with HIV.
HIV infected children aged at least 6 months who are potentially in need of protection against yellow fever should be referred to a specialist paediatric team for advice on whether or not to vaccinate.

Age
Children aged 6 to 9 months
STAMARIL must not be administered to children before the age of 6 months (see section 4.3). Children aged from 6 months up to 9 months should only be vaccinated under special circumstances (e.g. during major outbreaks) and on the basis of current official advice.

Persons aged 60 years and older
Some serious and potentially fatal adverse reactions (including systemic and neurological reactions persisting more than 48 hours, YEL-AVD and YEL-AND) appear to occur at higher frequencies after the age of 60 years. Therefore, the vaccine should only be given to those who have a considerable risk of acquiring yellow fever (see above and section 4.8).

Because intramuscular injection can cause injection site haematoma, STAMARIL should not be given by the intramuscular route to persons with any bleeding disorder, such as haemophilia or thrombocytopenia, or to persons on anticoagulant therapy. The subcutaneous route of administration should be used instead.

Patients with rare hereditary problems of fructose intolerance should not take this vaccine.

4.5 Interaction with other medicinal products and other forms of interaction

STAMARIL must not be mixed with any other vaccine or medicinal product in the same syringe.
If there is a need to administer another injectable vaccine(s) at the same time as STAMARIL each vaccine should be injected into a separate site (and preferably a separate limb).
STAMARIL may be administered at the same time as measles vaccine if this is in accordance with official recommendations.
STAMARIL may be administered at the same time as vaccines containing typhoid Vi capsular polysaccharide and/or inactivated hepatitis A virus.

STAMARIL must not be administered to persons who are receiving immunosuppressant therapy (***e.g.***, cytotoxic agents, systemic steroids, greater than standard dose of topical or inhaled steroids or other agents). See section 4.3.

4.6 Pregnancy and lactation

Pregnancy
No animal reproduction studies have been conducted with STAMARIL and the potential risk for humans is unknown. Data on a limited number of exposed pregnancies indicate no adverse effects of STAMARIL on pregnancy or the health of the fetus/newborn child. Nevertheless, STAMARIL should be given to pregnant women only when clearly needed and only after careful consideration of the potential risks and benefits.

Lactation
It is not known if the live attenuated yellow fever virus is excreted in animal or human breast milk. Although there have been no reports of transmission of vaccine viruses from breastfeeding mothers to infants STAMARIL should not be given to nursing mothers unless this cannot be avoided.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive or use machine have been performed.

4.8 Undesirable effects

Data from clinical studies
Across clinical studies, the most common adverse reactions occurring after vaccine administration were local reactions, reported in approximately 16% of subjects.

The following adverse events are from one clinical study in which 106 healthy adult subjects received STAMARIL. .
The adverse events are ranked under headings of frequency, using the following convention:
- Very common: ≥ 10%
- Common: : ≥ 1% and ≤ 10%
- Uncommon: : ≥ 0.1% and ≤ 1%

Nervous system disorders
Very common: Headache

Gastro-intestinal system disorders
Common: Nausea, Diarrhoea, Vomiting
Uncommon: Abdominal pain

Musculo-skeletal and connective tissue disorders
Common: Myalgia
Uncommon: Arthralgia

General disorders and administration site conditions
Very common: Local reactions (including pain, redness, haematoma, induration, swelling)
Common: Pyrexia, Asthenia

Data from post-marketing experience
The following additional adverse events have been reported during post marketing experience with STAMARIL. They are based on spontaneous reporting therefore the frequencies are unknown.

Blood and lymphatic system disorders
Lymphadenopathy

Immune system disorders
Anaphylaxis, angioedema.

Nervous system disorders
Cases of neurotropic disease (known as YEL-AND), some of which have had a fatal outcome, have been reported following yellow fever vaccination (see section 4.4). YEL-AND may manifest as high fever with headache that may progress to include one or more of confusion, lethargy, encephalitis, encephalopathy and meningitis (see section 4.4).
Other neurological signs and symptoms have been reported and include convulsion, Guillain-Barré syndrome and focal neurological deficits.

Skin and subcutaneous tissue disorders
Rash, Urticaria

General disorders and administration site conditions
Cases of viscerotropic disease (known as YEL-AVD and formerly described as "Febrile Multiple Organ-System Failure") have been reported following yellow fever vaccination some of which have been fatal (see section 4.4). YEL-AVD may manifest as fever, fatigue, myalgia, headache and hypotension progressing to one or more of metabolic acidosis, muscle and liver cytolysis, lymphocytopenia and thrombocytopenia, renal and respiratory failure.

Additional information on special population
Congenital or acquired immunodeficiency has been identified as a risk factor for neurotropic disease (See sections 4.3 and 4.4).
Age of more than 60 years (see section 4.4) has been identified as a risk factor for YEL-AVD and YEL-AND. A medical history of thymic disease (see sections 4.3 and 4.4) has been identified as a risk factor for YEL-AVD.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Yellow Fever Vaccine (Live)
ATC code: J07B L1

STAMARIL is a live attenuated yellow fever virus vaccine. As with other live attenuated viral vaccines, there is a sub-clinical infection in healthy recipients that results in the production of specific B and T cells and the appearance of specific circulating antibody.
Protective immunity appears from about 10 days after injection. Although International Health Regulations require re-vaccination at intervals of 10 years in order to retain a valid certificate, some degree of immunity likely persists for more than 10 years.

5.2 Pharmacokinetic properties

No pharmacokinetic studies have been performed.

5.3 Preclinical safety data

Pre-clinical data reveal no special hazard for humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder:
Lactose
Sorbitol E420
L-histidine hydrochloride
L-alanine
Sodium chloride
Potassium chloride
Disodium phosphate
Monopotassium phosphate
Calcium chloride
Magnesium sulphate

Solvent:
Sodium chloride
Water for injections.

6.2 Incompatibilities

This vaccine must not be mixed with other medicinal products.

6.3 Shelf life

3 years.
After reconstitution, the product must be kept in a refrigerator (2°C - 8°C) and must be used within 6 hours.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.

For storage conditions of the reconstituted medicinal product, see section 6.3

6.5 Nature and contents of container

Powder (10 doses) in vial (type I glass), with a stopper (chlorobutyl) + 5 ml of solvent in a vial (type I glass), with a stopper (chlorobutyl)– Pack size of 1, 10 or 20.

Not all pack sizes or presentations may be marketed.

6.6 Special precautions for disposal

The powder is reconstituted in its container with a small quantity of sodium chloride 9 mg/ml (0.9%) solution for injection.
The vial is shaken and after dissolution, the suspension obtained is withdrawn and added to the remaining solution. Before administration, the reconstituted vaccine is vigorously shaken.
For each vaccination 0.5 ml is withdrawn.
The reconstitution and withdrawal of vaccine should be performed under aseptic conditions.
After reconstitution STAMARIL is a beige to pink beige suspension for injection.

Contact with disinfectant is to be avoided since they may inactivate the virus.

Any unused product or waste material should be disposed of, preferably by heat inactivation or incineration, in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

LABELLING AND PACKAGE LEAFLET

LABELLING

SINGLE DOSE PRESENTATION

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

STAMARIL - Carton for Vial 0.5 ml and syringe – Box of 1 – 10 - 20

1. NAME OF THE MEDICINAL PRODUCT

STAMARIL (or invented name)
Powder and solvent for suspension for injection
Yellow fever vaccine (Live).

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml) contains:

Yellow fever virus[1] 17 D-204 strain (live, attenuated) …….not less than 1000 LD_{50} units[2]

[1] produced in specified pathogen-free chick embryos
[2]The statistically determined lethal dose in 50% of animals tested

3. LIST OF EXCIPIENTS

Powder: lactose, sorbitol, L-histidine hydrochloride, L-alanine, sodium chloride, potassium chloride, disodium phosphate, monopotassium phosphate, calcium chloride, magnesium sulphate
Solvent: sodium chloride (0.4%), water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for suspension for injection
This pack contains 1 single dose vial + 1 pre-filled syringe
This pack contains 10 single dose vials + 10 pre-filled syringes
This pack contains 20 single dose vials + 20 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous or Intramuscular use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C – 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

12. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

<[To be completed nationally]>
Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

STAMARIL - Carton for Vial 0.5 ml and syringe without needle with 1 separated needle – box of 1 – 10

1. NAME OF THE MEDICINAL PRODUCT

STAMARIL (or local trade name)
Powder and solvent for suspension for injection.
Yellow fever vaccine (Live).

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml) contains:

Yellow fever virus[1] 17 D-204 strain (live, attenuated) …….not less than 1000 LD_{50} units[2]

[1] produced in specified pathogen-free chick embryos
[2]The statistically determined lethal dose in 50% of animals tested

3. LIST OF EXCIPIENTS

Powder: lactose, sorbitol, L-histidine hydrochloride, L-alanine, sodium chloride, potassium chloride, disodium phosphate, monopotassium phosphate, calcium chloride, magnesium sulphate
Solvent: sodium chloride (0.4%), water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for suspension for injection.
This pack contains 1 single dose vial + 1 pre-filled syringe with 1 separated needle
This pack contains 10 single dose vials + 10 pre-filled syringes with 10 separated needle

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous or intramuscular use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C – 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

12. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

<[To be completed nationally]>
Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON <THE OUTER PACKAGING

STAMARIL - Carton for Vial 0.5 ml and syringe without needle with 2 separated needles – box of 1 – 10

1. NAME OF THE MEDICINAL PRODUCT

STAMARIL (or local trade name)
Powder and solvent for suspension for injection .
Yellow fever vaccine (Live).

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml) contains:

Yellow fever virus[1] 17 D-204 strain (live, attenuated) …….not less than 1000 LD_{50} units[2]

[1] produced in specified pathogen-free chick embryos
[2]The statistically determined lethal dose in 50% of animals tested

3. LIST OF EXCIPIENTS

Powder: lactose, sorbitol, L-histidine hydrochloride, L-alanine, sodium chloride, potassium chloride, disodium phosphate, monopotassium phosphate, calcium chloride, magnesium sulphate
Solvent: sodium chloride (0.4%), water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for suspension for injection
This pack contains 1 single dose vial + 1 pre-filled syringe with 2 separated needles
This pack contains 10 single dose vials + 10 pre-filled syringes with 20 separated needles

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous of intramuscular use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C – 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

12. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

<[To be completed nationally]>
Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

STAMARIL - Carton for Vial 0.5 ml and syringe without needle – box of 1, 10

1. NAME OF THE MEDICINAL PRODUCT

STAMARIL (or local trade name)
Powder and solvent for suspension for injection .
Yellow fever vaccine (Live).

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml) contains:

Yellow fever virus[1] 17 D-204 strain (live, attenuated) …….not less than 1000 LD_{50} units[2]

[1] produced in specified pathogen-free chick embryos
[2]The statistically determined lethal dose in 50% of animals tested

3. LIST OF EXCIPIENTS

Powder: lactose, sorbitol, L-histidine hydrochloride, L-alanine, sodium chloride, potassium chloride, disodium phosphate, monopotassium phosphate, calcium chloride, magnesium sulphate
Solvent: sodium chloride (0.4%), water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for suspension for injection.
This pack contains 1 single dose vial + 1 pre-filled syringe without needle
This pack contains 10 single dose vials + 10 pre-filled syringes without needle

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous of intramuscular use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C – 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

12. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

<[To be completed nationally]>
Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

STAMARIL – Vial single dose

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

STAMARIL (or local trade name)
Powder and solvent for suspension for injection.
Yellow fever vaccine (Live).

2. METHOD OF ADMINISTRATION

SC or IM use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Pre-filled syringe of solvent 4 mg/ml (0.4 %)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Solvent for STAMARIL
Sodium chloride 0.4% solution for injection

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose

6. OTHER

LABELLING

MULTIDOSE PRESENTATION

This presentation is not applicable in all countries. The labelling will be completed nationally

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

STAMARIL - Carton for Vial 5 ml and vial – Box of 10 – will be completed nationally

1. NAME OF THE MEDICINAL PRODUCT

STAMARIL (or local trade name)
Powder and solvent for suspension for injection
Yellow fever vaccine (Live).

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml) contains:

Yellow fever virus[1] 17 D-204 strain (live, attenuated) …….not less than 1000 LD_{50} units[2]

[1] produced in specified pathogen-free chick embryos
[2]The statistically determined lethal dose in 50% of animals tested

3. LIST OF EXCIPIENTS

Powder: lactose, sorbitol, L-histidine hydrochloride, L-alanine, sodium chloride, potassium chloride, disodium phosphate, monopotassium phosphate, calcium chloride, magnesium sulphate.
Solvent: sodium chloride (0.9%), water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for suspension for injection.
This pack contains 10 multi dose vials + 10 vials.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous or Intramuscular use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C – 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

12. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

<[To be completed nationally]>
Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

STAMARIL – Vial multi dose will be completed nationally

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

STAMARIL (or local trade name)
powder and solvent for suspension for injection in vial.
Yellow fever vaccine (Live).

2. METHOD OF ADMINISTRATION

SC or IM use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 doses.

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial of solvent 9 mg/ml (0.9 %) will be completed nationally

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Solvent for STAMARIL
Sodium chloride 0.9% solution for injection

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 doses

6. OTHER

PACKAGE LEAFLET

SINGLE DOSE PRESENTATION

PACKAGE LEAFLET: INFORMATION FOR THE USER

STAMARIL, Powder and solvent for suspension for injection
Yellow fever vaccine (Live).

Read all of this leaflet carefully before you/your child are vaccinated.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This vaccine has been prescribed for you. Do not pass it on to others.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What STAMARIL is and what it is used for
2. Before you use STAMARIL
3. How to use STAMARIL
4. Possible side effects
5. How to store STAMARIL
6. Further information

1. WHAT STAMARIL IS AND WHAT IT IS USED FOR

STAMARIL is an injectable vaccine against a serious infectious disease called yellow fever.
Yellow fever occurs in certain areas of the world and is spread to man through the bites of infected mosquitoes.
STAMARIL is intended to be given to:
- Persons who are travelling to, passing through or living in an area where yellow fever occurs,
- Persons travelling to any country that requires an International Certificate of vaccination for entry (Which may or may not depend on the countries previously visited during the same trip).
- Persons who may handle infectious materials such as laboratory workers.

To obtain a valid vaccination certificate against yellow fever it is necessary to be vaccinated in an approved vaccination centre so that an International Certificate of Vaccination can be issued. This certificate is valid from 10 days until 10 years after the first dose of vaccine. Certificates issued after booster doses (see section 3 below) are valid immediately after the injection.

2. BEFORE YOU USE STAMARIL

To make sure that STAMARIL is suitable for you or your child it is important to tell the doctor or nurse if any of the points below apply to the person receiving the vaccine. If there is anything you do not understand, ask the doctor or nurse to explain.

Do not use STAMARIL

The following questions apply to the person who is to receive the vaccine regardless of age:
- If you are allergic (hypersensitive) to eggs, chicken proteins or any of the components of STAMARIL , or if you have experienced a serious reaction after a previous dose of any yellow fever vaccine.
- If you have been told that you have poor immunity to infections for any reason, such as due to illness or due to medical treatments that may weaken your immune system (for example corticoids or chemotherapy)
- If you have a history of problems with your thymus gland or have had your thymus gland removed for any reason
- If you are infected by the HIV virus and have active symptoms due to the infection

- If you are infected by the HIV virus and your laboratory results show that your immune system is not working very well. . Your doctor will advise you if you can still have STAMARIL based on the results of your blood tests.
- If you have an infection with a fever. Vaccination should be postponed until after you have recovered.
- Please note that STAMARIL must not be given to children aged less than 6 months.

Take special care with STAMARIL
- If you are more than 60 years old. Persons aged over 60 years appear to run an increased risk of certain types of severe but rare reactions to yellow fever vaccines that include effects on the brain and nerves or an illness that resembles yellow fever itself, with widespread symptoms affecting most body systems. Therefore persons aged over 60 years are usually only given yellow fever vaccine if they are going to run a considerable and unavoidable risk of infection with the virus.
- If your child is aged 6 to 9 months. STAMARIL may be given to children aged between 6 and 9 months only in special situations and on the basis of current official advice.
- If you are infected by the HIV virus but do not have active symptoms due to the infection your doctor will advise you if you can have STAMARIL based on the results of laboratory tests.
- If your child is infected with the HIV (AIDS) virus the doctor may need to do special tests and to obtain special advice before advising you if the child can receive STAMARIL.
- If you have any bleeding disorder (such as haemophilia or low level of platelets) or are taking any medicines that stop the blood clotting normally. You can still be given STAMARIL provided that it is injected under the skin and not into muscle (see section 3).

Taking other medicines
Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.
If you have recently been receiving any treatment which may have weakened your immune system, vaccination against yellow fever should be postponed until your laboratory results show that your immune system has recovered. Your doctor will advise you when it is safe for you to be vaccinated.

STAMARIL can be given at the same time as measles vaccine or vaccines against typhoid (those containing the Vi capsular polysaccharide) and/or hepatitis A. .

Pregnancy and breastfeeding
Females who are pregnant, think they might be pregnant or who are breastfeeding a child are not usually given STAMARIL unless this cannot be avoided.
Your doctor or nurse can advise you on whether it is essential that you are vaccinated while pregnant or breastfeeding.

Important information about some of the ingredients of STAMARIL
STAMARIL contains a small amount of sorbitol. The vaccine should not be given to people who have fructose intolerance.

3. HOW TO USE STAMARIL

Initial (first) dose of yellow fever vaccine
STAMARIL should be given at least 10 days before putting yourself at any risk of infection because the vaccine may not provide good protection before the 10^{th} day.
Adults (including the elderly) and children from 6 months of age should be given a single dose of 0.5 millilitres.
Booster doses
If you are still thought to be at risk of infection with yellow fever (e.g. you still travel to or are living in areas where yellow fever can be caught or could be infected through your work) a booster dose with 0.5 millilitres of vaccine is recommended every 10 years.

STAMARIL should usually be given as an injection just underneath the skin.
Alternatively, it can be given as an injection into muscle if that is in the official recommendations for the area in which you live. Your doctor or nurse will take care that STAMARIL is not injected into a blood vessel.

If you have any further questions on the use of this vaccine, ask your doctor.

4. POSSIBLE SIDE EFFECTS

Like all medicines, STAMARIL can cause side effects, although not everybody gets them.

The most common side effects (in more than 1 in 10 adults vaccinated) seen in a clinical trial were problems around the injection site (such as redness, bruising, pain or discomfort, swelling or appearance of a hard lump) and headache.
Other side effects that occured in more than one in a hundred people vaccinated in a trial were feeling or being sick, diarrhoea, muscle pains, fever and weakness.
Side effects that occurred in more than one in a thousand people were painful joints and stomach pains.

Other side effects that have sometimes been reported during routine use of STAMARIL have included:
- Swollen glands
- Serious allergic reactions that could include rash, itching or hives on the skin, swelling of the face, lips, tongue or other parts of the body, difficulty swallowing or breathing and loss of consciousness.
- Symptoms affecting the brain and nerves that have occurred within one month after vaccination and have sometimes been fatal. These include high fever with headache and confusion, lethargy, stiff neck, and inflammation of brain and nerve tissues. Sometimes fits, loss of movement in part or all of the body or more localised difficulties with movement or feeling have been seen.
- Symptoms that can resemble infection with the yellow fever virus that usually appear within 10 days after vaccination and may have a fatal outcome. It generally begins with feeling tired, fever, headache, muscle pain and sometimes low blood pressure. It may then go on to a severe muscle and liver disorder, drops in numbers of some types of blood cells resulting in unusual bruising or bleeding and increased risk of infections, and loss of normal functioning of the kidneys and lungs.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, nurse or pharmacist.

5. HOW TO STORE STAMARIL

Keep out of the reach and sight of children.
Do not use STAMARIL after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C – 8°C). Do not freeze.
Keep the vial and syringe in the outer carton in order to protect from light.
Use immediately after reconstitution.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What STAMARIL contains

The active ingredient in the vaccine is Yellow fever virus of the 17 D-204 strain (grown in hens eggs) that is live but has been weakened so that it does not cause yellow fever in healthy persons. Each dose of half a millilitre contains not less than 1000 LD_{50} units of the virus, which is a measure of the actions of the virus in animals.

The other ingredients are:
Powder: lactose, sorbitol, L-histidine hydrochloride, L-alanine, sodium chloride, potassium chloride, disodium phosphate, monopotassium phosphate, calcium chloride, magnesium sulphate.
Solvent: sodium chloride and water for injections.

What STAMARIL looks like and contents of the pack

The vaccine is a powder for suspension for injection contained in a single dose vial. Before use, the beige to orange beige powder is mixed with the sodium chloride solvent provided in a syringe to make a beige to pink beige suspension.

STAMARIL is available in packs of 1, 10 and 20 with or without needles. Not all pack sizes or presentations may be marketed.

Marketing Authorisation Holder

<[To be completed nationally]> *[This section is not to be harmonised]*

Manufacturer
Sanofi Pasteur SA –
2 avenue Pont Pasteur 69007 – Lyon – France

This medicinal product is authorised in the Member States of the EEA under the following names:

<{Name of the Member State}> <{Name of the medicinal product}>
<{Name of the Member State}> <{Name of the medicinal product}>

<[See Annex I - To be completed nationally]> *[For referral procedures, as appropriate]*

This leaflet was last approved in {MM/YYYY}.

<[To be completed nationally]>

Detailed information on this medicine is available on the web site of {name of MA/Agency}.

PACKAGE LEAFLET

MULTIDOSE PRESENTATION

This presentation is not applicable in all countries. The package leaflet will be completed nationally

PACKAGE LEAFLET: INFORMATION FOR THE USER

STAMARIL, Powder and solvent for suspension for injection
Yellow fever vaccine (Live).

Read all of this leaflet carefully before you/your child are vaccinated.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This vaccine has been prescribed for you. Do not pass it on to others.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What STAMARIL is and what it is used for
2. Before you use STAMARIL
3. How to use STAMARIL
4. Possible side effects
6. How to store STAMARIL
6. Further information

1. WHAT STAMARIL IS AND WHAT IT IS USED FOR

STAMARIL is an injectable vaccine against a serious infectious disease called yellow fever.
Yellow fever occurs in certain areas of the world and is spread to man through the bites of infected mosquitoes.
STAMARIL is intended to be given to:
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- Persons who may handle infectious materials such as laboratory workers.

To obtain a valid vaccination certificate against yellow fever it is necessary to be vaccinated in an approved vaccination centre so that an International Certificate of Vaccination can be issued. This certificate is valid from 10 days until 10 years after the first dose of vaccine. Certificates issued after booster doses (see section 3 below) are valid immediately after the injection.

2. BEFORE YOU USE STAMARIL

To make sure that STAMARIL is suitable for you or your child it is important to tell the doctor or nurse if any of the points below apply to the person receiving the vaccine. If there is anything you do not understand, ask the doctor or nurse to explain.

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- If you have been told that you have poor immunity to infections for any reason, such as due to illness or due to medical treatments that may weaken your immune system (for example corticoids or chemotherapy)
- If you have a history of problems with your thymus gland or have had your thymus gland removed for any reason
- If you are infected by the HIV virus and have active symptoms due to the infection

- If you are infected by the HIV virus and your laboratory results show that your immune system is not working very well. . Your doctor will advise you if you can still have STAMARIL based on the results of your blood tests.
- If you have an infection with a fever. Vaccination should be postponed until after you have recovered.
- Please note that STAMARIL must not be given to children aged less than 6 months.

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STAMARIL should usually be given as an injection just underneath the skin.
Alternatively, it can be given as an injection into muscle if that is in the official recommendations for the area in which you live. Your doctor or nurse will take care that STAMARIL is not injected into a blood vessel.

If you have any further questions on the use of this vaccine, ask your doctor.

4. POSSIBLE SIDE EFFECTS

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The most common side effects (in more than 1 in 10 adults vaccinated) seen in a clinical trial were problems around the injection site (such as redness, bruising, pain or discomfort, swelling or appearance of a hard lump) and headache.
Other side effects that occured in more than one in a hundred people vaccinated in a trial were feeling or being sick, diarrhoea, muscle pains, fever and weakness.
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- Swollen glands
- Serious allergic reactions that could include rash, itching or hives on the skin, swelling of the face, lips, tongue or other parts of the body, difficulty swallowing or breathing and loss of consciousness.
- Symptoms affecting the brain and nerves that have occurred within one month after vaccination and have sometimes been fatal. These include high fever with headache and confusion, lethargy, stiff neck, and inflammation of brain and nerve tissues. Sometimes fits, loss of movement in part or all of the body or more localised difficulties with movement or feeling have been seen.
- Symptoms that can resemble infection with the yellow fever virus that usually appear within 10 days after vaccination and may have a fatal outcome. It generally begins with feeling tired, fever, headache, muscle pain and sometimes low blood pressure. It may then go on to a severe muscle and liver disorder, drops in numbers of some types of blood cells resulting in unusual bruising or bleeding and increased risk of infections, and loss of normal functioning of the kidneys and lungs.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, nurse or pharmacist.

5. HOW TO STORE STAMARIL

Keep out of the reach and sight of children.
Do not use STAMARIL after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C – 8°C). Do not freeze.
Keep the vials of powder and solvent in the outer carton in order to protect from light.
After reconstitution, the product must be used within 6 hours.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What STAMARIL contains

The active ingredient in the vaccine is Yellow fever virus of the 17 D-204 strain (grown in hens eggs) that is live but has been weakened so that it does not cause yellow fever in healthy persons. Each dose of half a millilitre contains not less than 1000 LD_{50} units of the virus, which is a measure of the actions of the virus in animals.

The other ingredients are:
Powder: lactose, sorbitol, L-histidine hydrochloride, L-alanine, sodium chloride, potassium chloride, disodium phosphate, monopotassium phosphate, calcium chloride, magnesium sulphate.
Solvent: sodium chloride and water for injections.

What STAMARIL looks like and contents of the pack

The vaccine is a powder for suspension for injection contained in a 10 doses vial. Before use, the beige to orange beige powder is mixed with the sodium chloride solvent provided in a vial to make a beige to pink beige suspension.

STAMARIL is available in packs of 10.

Marketing Authorisation Holder

<*[*To be completed nationally*]*> *[This section is not to be harmonised.]*

Manufacturer
Sanofi Pasteur SA –
2 avenue Pont Pasteur 69007 – Lyon – France

This medicinal product is authorised in the Member States of the EEA under the following names:

<{Name of the Member State}> <{Name of the medicinal product}>
<{Name of the Member State}> <{Name of the medicinal product}>

<[See Annex I - To be completed nationally]> *[For referral procedures, as appropriate]*

This leaflet was last approved in {MM/YYYY}.

<[To be completed nationally]>

Detailed information on this medicine is available on the web site of {name of MA/Agency}