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WEBINAR
October 22, 2025
1:00 - 3:40 PM CEST
Replacing the monkey neurovirulence test: Challenges and opportunities for the future
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# *Yellow Fever Vaccine The Challenges of Neurovirulence Test*

*Carine Logvinoff,*

Virology Global Analytical Expert,

Analytical Sciences, sanofi

Marcy L'Etoile, France

# Background

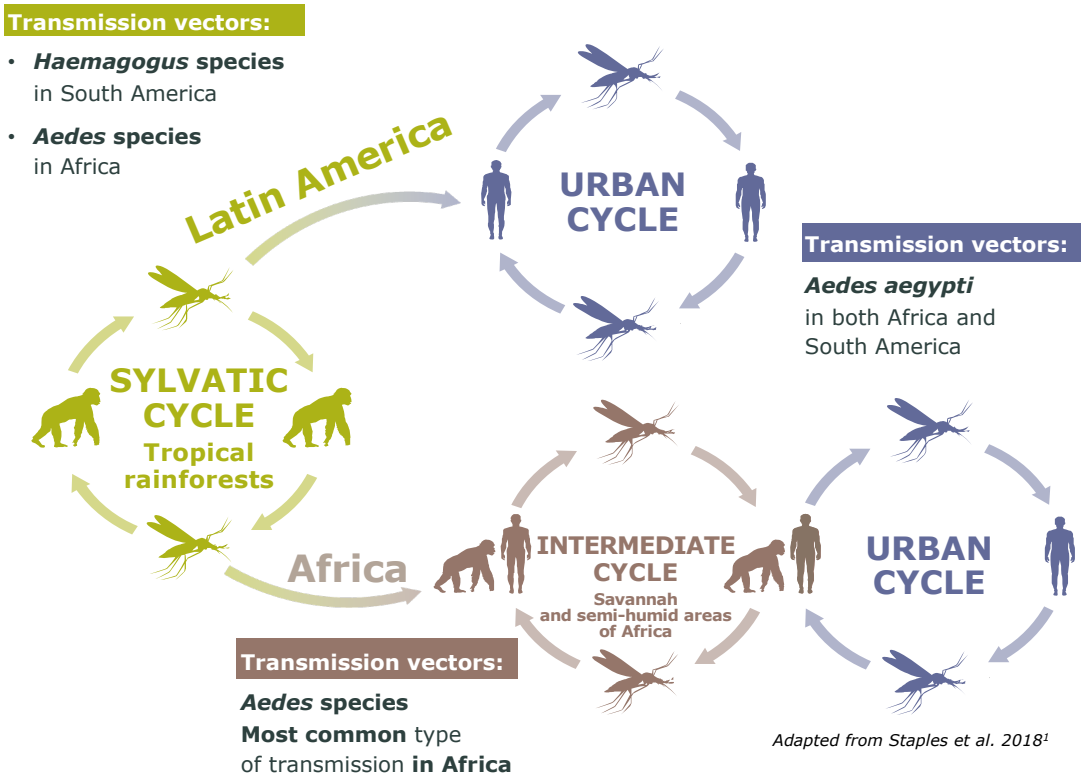
Yellow Fever is a viral disease that is transmitted to humans by the bites of infected mosquitoes

It is prone to epidemics , and is preventable with a vaccine

As of 2023, 34 countries in Africa and 13 countries in Central and South America are either endemic for, or have regions that are endemic for, yellow fever

**Vector:** *Haemagogus* and *Aedes* species(mostly)[1]

- Transmission after a blood meal from an infected animal/person[1]
- After ~10 days of incubation, YFV is secreted in saliva and transmissible to another host upon blood meal[1]



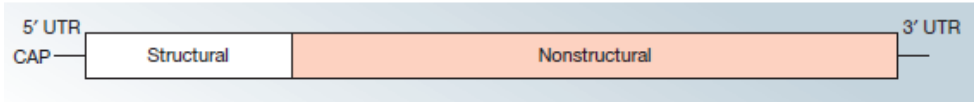

*Adapted from Staples et al. 2018[1]*

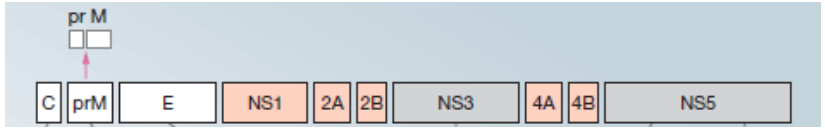
**1**. Staples JE et al. 2023 Plotkin's Vaccines, 8th edition, Chapter 64 Yellow Fever Vaccine pp:1251-1321.e19;

# Yellow Fever Virus

## The Prototype Member of the Flaviviridae (Latin flavus =“yellow”) Family of Viruses[1]

- YFV = Arbovirus of the flavivirus genus
- Wild-type virus : only one serotype (high genetic stability)
- 7 distinct genotypes: 5 in Africa & 2 in Latin America
- Small (50 nm), enveloped
- Viral Genome ( 10 862 nt) positive sens ssRNA
-




**The Yellow Fever Virus virion[2]**
(A) The immature (intracellular) and mature (extracellular) infectious virion and (B) arrangement of the E dimers

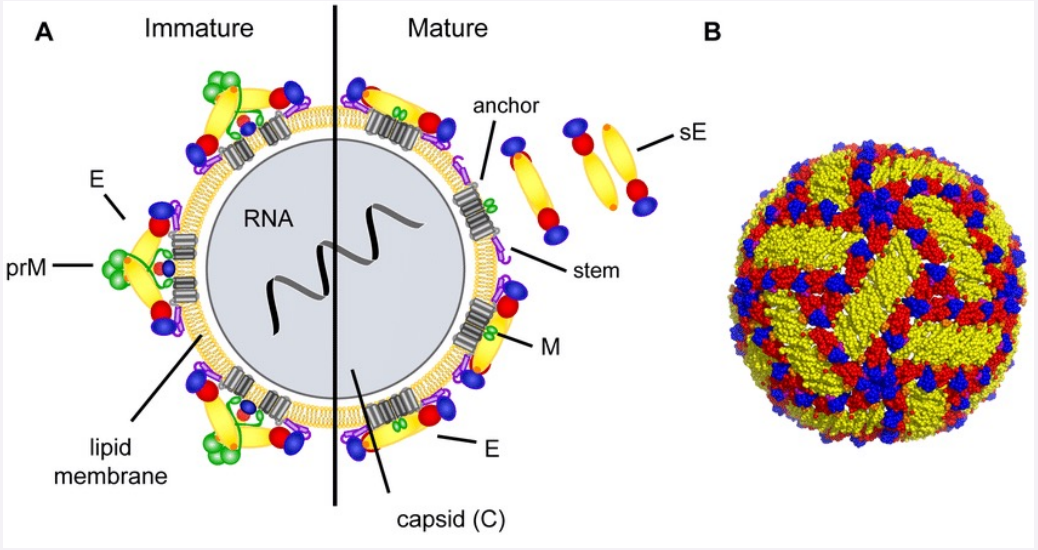



*Image From Vratskikh O, et al 2013[2]*

C: capsid; E: envelope protein E; M: monomer; prM: precursor of membrane; RNA: ribonucleic acid; sE: soluble form of Protein E; YFV: Yellow Fever virus.

**1.** Staples JE et al. 2023 Plotkin's Vaccines, 8th edition, Chapter 64 Yellow Fever Vaccine pp:1251-1321.e19; **2.** Vratskikh O, et al. 2013 PLoS Pathog 9(6): e1003458.

# Yellow Fever Disease Symptoms

## General Clinical Presentation[1–4]

**YF disease is often asymptomatic** or causes minimal symptoms

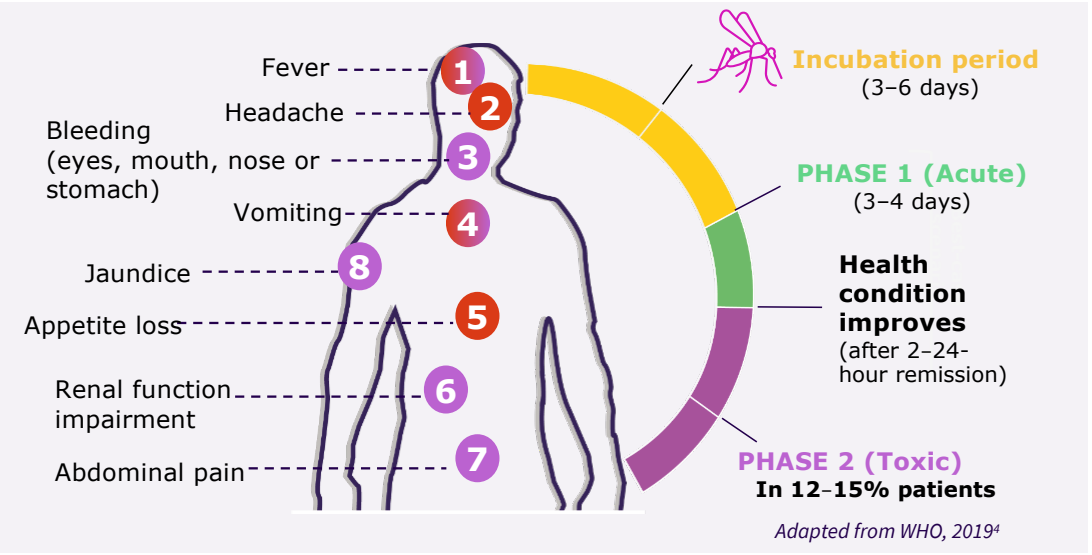
**The clinical spectrum of the YF disease is broad**: from subclinical infection to a potentially fatal hemorrhagic disease

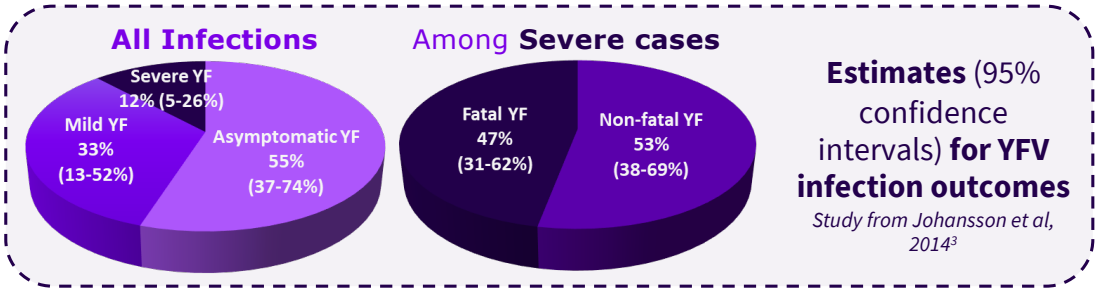
## Phase 1 (Acute Phase):

- For symptomatic cases, **incubation period = 3–6 days** followed by nonspecific symptoms: fever, chills, headache myalgia that disappear within **3–4 days**
- **Recovery after 2–24 hour remission** (most patients)

## Phase 2 (Toxic Phase):

- **Progression to serious form** in 12–15% of the patients[2,3]: jaundice, bleeding symptoms (e.g., mouth, nose, eyes or stomach [=black vomit]) shock and multisystem organ failure
- **Evolution to death:** 20–60% of the serious forms, within **7–10 days** after patient entered toxic phase[1-3,5]




YF: Yellow Fever; YFV: Yellow Fever virus.

**1.** CDC Yellow Book: Health Information for International Travel. Edition: 2026. Accessed July 2025. https://www.cdc.gov/yellow-book/hcp/travel-associated-infections-diseases/yellow-fever.html; **2.** WHO YF vaccine position paper 2013 Weekly Epidemiological Record, 88 (27): 269–83; **3.** Johansson MA, et al. Trans R Soc Trop Med Hyg. 2014 Aug;108(8):482-7; **4.** WHO. Yellow Fever Key Facts. Updated 31 May 2023. Accessed July 2025. https://www.who.int/en/news-room/fact-sheets/detail/yellow-fever; **5.** Monath TP & Vasconcelos PFC. J Clin Virol. 2015 Mar;64:160-73.

# Yellow Fever Disease Treatment & Prevention

**Treatment**

- **No specific treatment is available** for YF
- Only **supportive medical care** according to the severity of the disease, ranging from **symptomatic medications** to **hepatic transplant**[1]

**Prevention**

**Vector Control**[1]

- Prevention against mosquito bites
- Elimination of potential mosquito breeding sites
- Protection of reservoirs and water storage containers

**Vaccination**[1–2]

**1 single dose** of vaccine needed

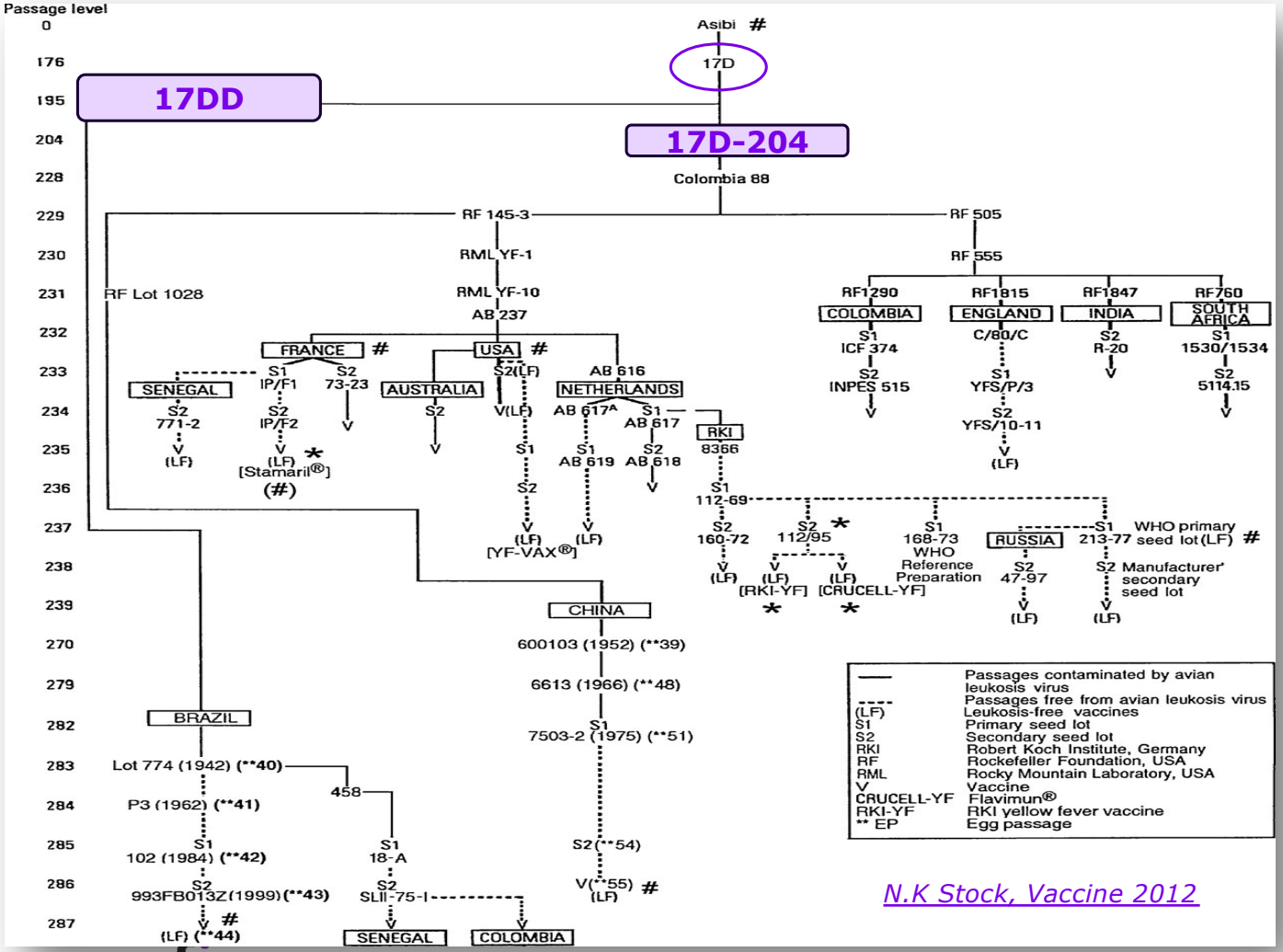
**No booster dose** recommended*

**Long protection, possibly life-long**

*Image from Microsoft 365 library (free of rigths)*

**1.** WHO. Yellow Fever Key Facts. Updated 31 May 2023. Accessed July 2025. https://www.who.int/en/news-room/fact-sheets/detail/yellow-fever;
**2.** WHO. Immunization, Vaccines and Biologicals. Yellow fever vaccines. Accessed July 2025. https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/yellow-fever.

# Yellow Fever 17D strain based Vaccines




*N.K Stock, Vaccine 2012*

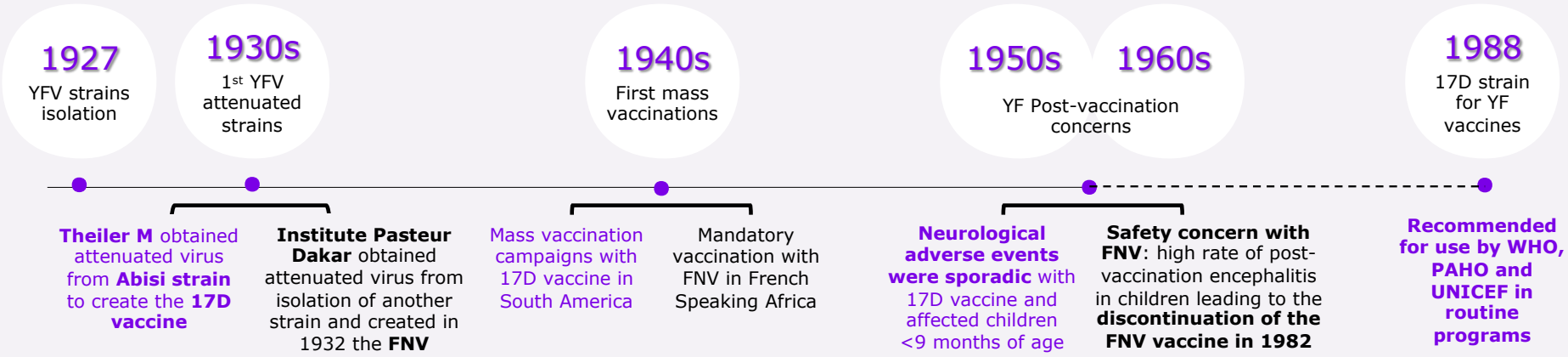
**6** **YF vaccine manufacturers** worldwide[1]

- All currently approved YF vaccines are :
  - live attenuated viral vaccines, originated from 2 sub-strains of 17D vaccine: 17DD and 17D-204[2]
  - produced in embryonated chicken eggs.

**4** **YF vaccines WHO prequalified**[1] to supply vaccines for EPI and mass vaccination campaigns during routine and outbreaks

# Yellow Fever is a Vaccine-Preventable Disease

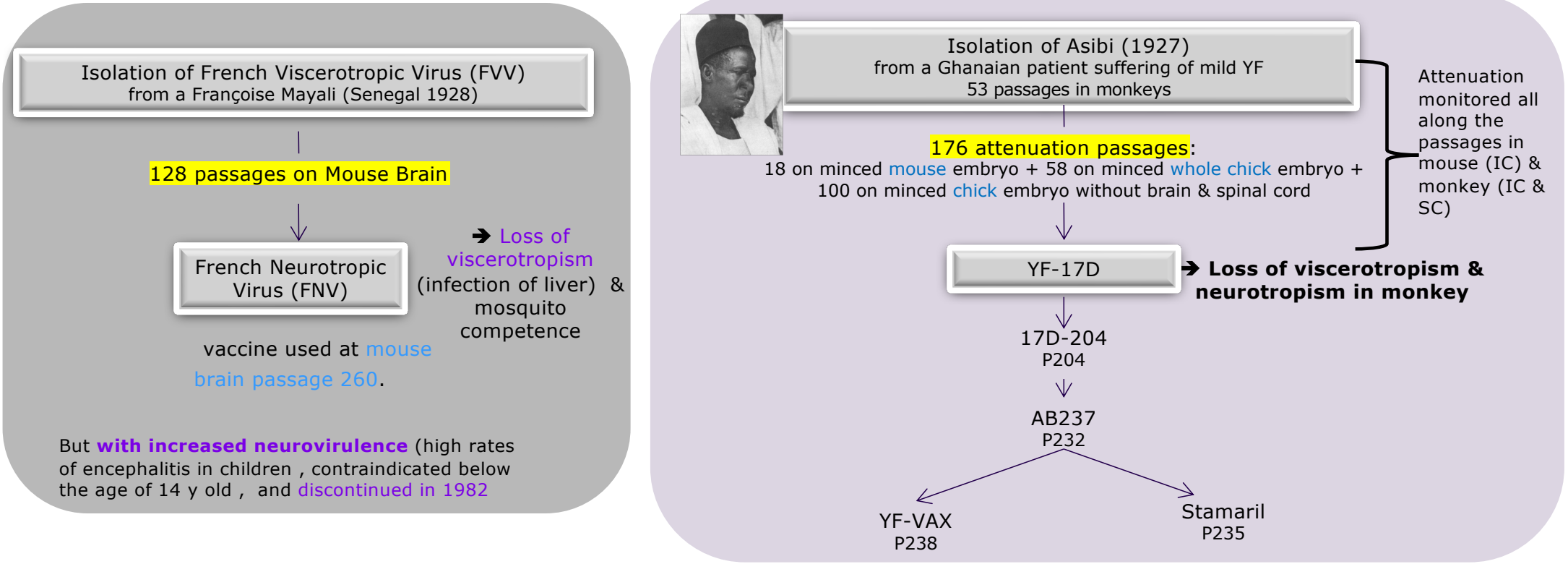
## History of Yellow Fever Vaccines (Main Steps)[1]




FNV: French Neurotropic Vaccine; IU: international unit; PAHO: Pan American Health Organization; WHO: World Health Organization; UNICEF: United Nations International Children's Emergency Fund;
YF: Yellow Fever; YFV: Yellow Fever virus.

# Isolation of YF Vaccine Strains & Attenuation

From Asibi Strain (1927) to 17D Vaccine Strains



# Test in NonHuman Primates Description

Each new YF vaccine seed lot is to be tested for neurotropism, viscerotropism and immunogenicity in nonhuman primate (NHP)

World Health Organization

**Recommendations to assure the quality, safety and efficacy of live attenuated yellow fever vaccines**

**Tests in nonhuman primates of new virus master and working seeds**

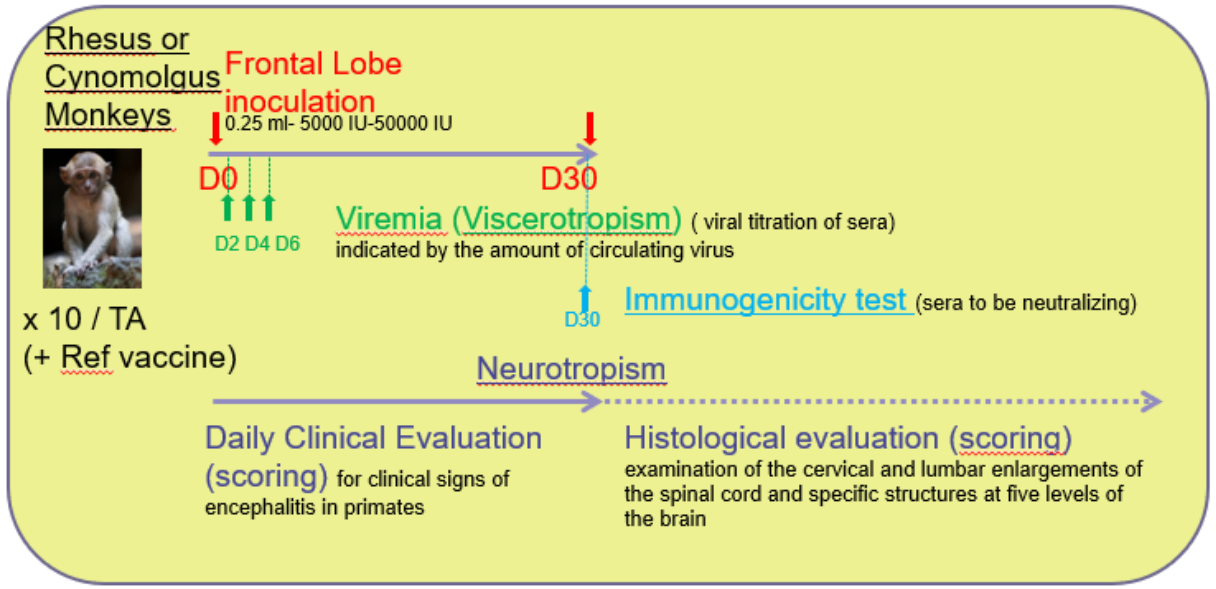
Each virus master and working seed lot should be tested for viscerotropism, immunogenicity and neurotropism, in a group of 10 test monkeys. Animals that

01/2019:0537

**YELLOW FEVER VACCINE (LIVE)**

Vaccinum febris flavae vivum

**Tests in monkeys.** Each master and working seed lot complies with the following tests in monkeys for viraemia (viscerotropism), immunogenicity and neurotropism.



# Tests in Nonhuman Primates Evolution

1937

1942

1945

Requirement for Test in NonHuman Primates

1958

1976

WHO TRS 594

Annex 1

REQUIREMENTS FOR YELLOW FEVER VACCINE [a]

(Requirements for Biological Substances No. 3)
(Revised 1975)

1987

1998

WHO TRS 872

Annex 2
**Requirements for yellow fever vaccine**
(Requirements for Biological Substances No. 3, revised 1995)

THE AMERICAN JOURNAL OF HYGIENE

VOL. 36 SEPTEMBER, 1942 NO. 2

ENCEPHALITIS IN MAN FOLLOWING VACCINATION WITH 17 D YELLOW FEVER VIRUS [1]

By

JOHN P. FOX, EDWIN H. LENNETTE, CAIO MANSO, AND JACY R. SOUZA AGUIAR

(Received for publication June 26th, 1942)

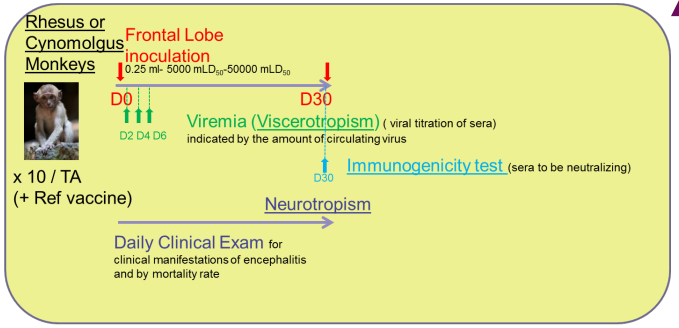
Cases of encephalitis in Brazil in 1941
Studies in Monkey using IC inoculation

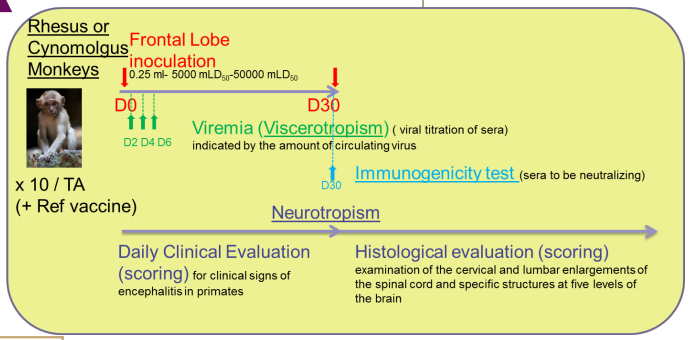
THE EFFECT OF PROLONGED CULTIVATION IN VITRO UPON THE PATHOGENICITY OF YELLOW FEVER VIRUS

By MAX THEILER, M.R.C.S., L.R.C.P., AND HUGH H. SMITH, M.D.

*(From the Laboratories of the International Health Division, The Rockefeller Foundation, New York)*

(Received for publication, March 18, 1937)




*Journal of Biological Standardization* (1987) 15, 305–313

The monkey safety test for neurovirulence of yellow fever vaccines: the utility of quantitative clinical evaluation and histological examination*

*Inessa S. Levenbook,†§ Linda J. Pelleu,‡ and Bennett L. Elisberg†*

# Tests in Nonhuman Primates Evolution

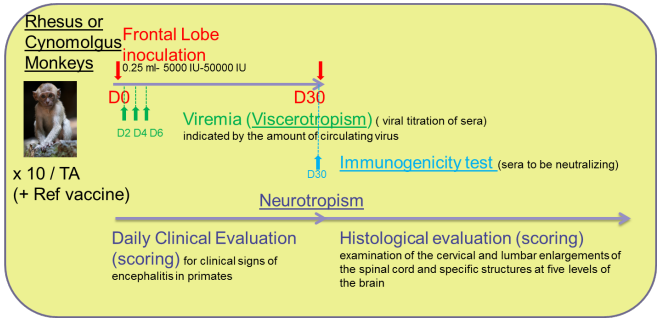
## 2012

WHO TRS 978

**Annex 5**

**Recommendations to assure the quality, safety and efficacy of live attenuated yellow fever vaccines**

Replacement of Annex 2 of WHO Technical Report Series, No. 872 and of the Amendment to that annex in WHO Technical Report Series, No. 964 (2012)




1: rough coat, not eating;
2: high-pitched voice, inactive, slow moving;
3: shaky movements, tremors, incoordination, limb weakness;
4: inability to stand, limb paralysis or death.

## 2018

Manufacturer Study highlighting **variability of clinical scoring**

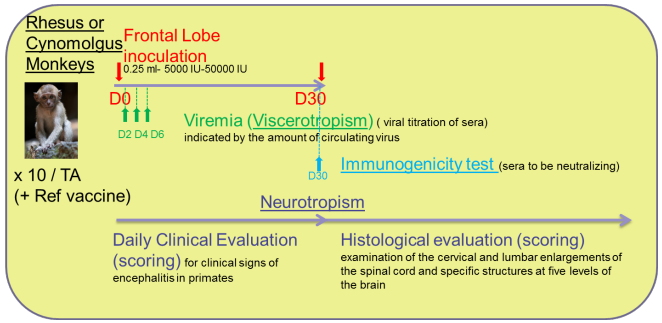
## 2022

WHO Technical Report Series 1039

**Annex 2**

**Recommendations to assure the quality, safety and efficacy of live attenuated yellow fever vaccines**

Amendment to Annex 5 of WHO Technical Report Series, No. 978

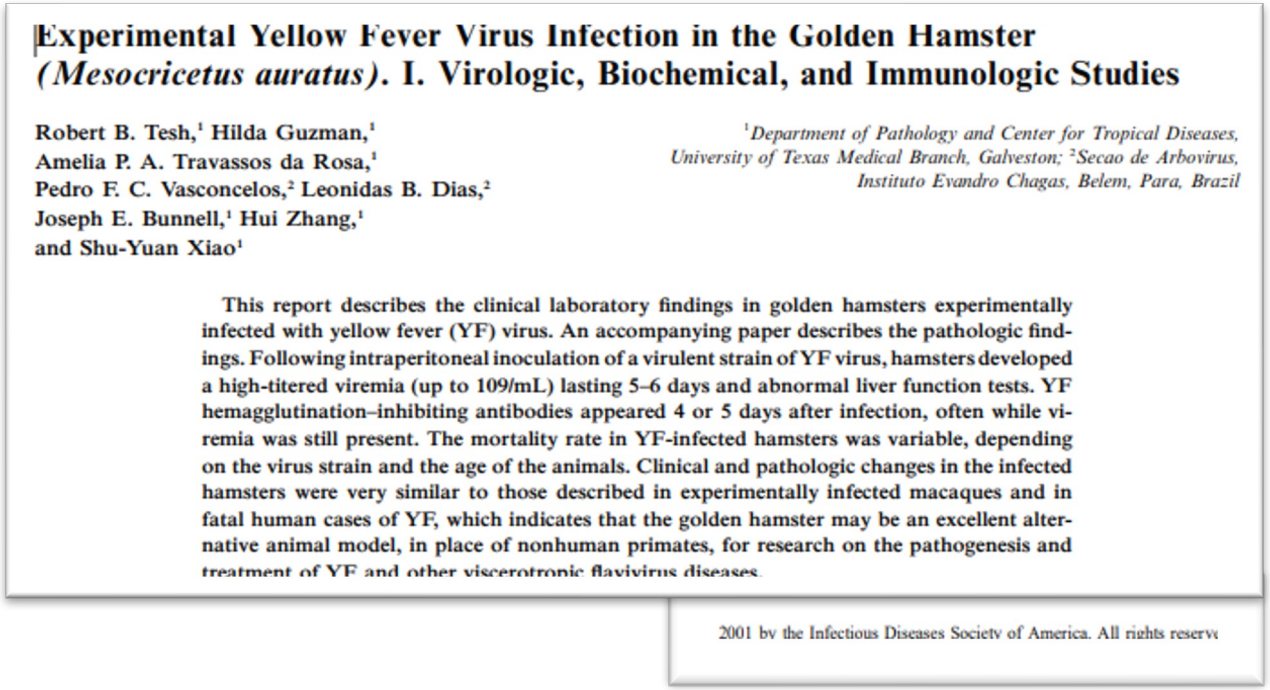



*Due to the **intrinsic variability of the clinical scoring** in the Monkey model **as evidenced with 2011 and 2018 tests** , the poor accuracy of clinical scoring in non-human primates , along with the use of in-house reference preparation with very low residual neurovirulence , **may increase the risk of failing virus seeds lots that are sufficiently attenuated** for vaccine production*

*"It is acknowledged that the clinical evaluation may be imprecise "*

# Alternatives to NHP test ? ...with smaller animal

## Hamster



**Experimental Yellow Fever Virus Infection in the Golden Hamster (*Mesocricetus auratus*). I. Virologic, Biochemical, and Immunologic Studies**

Robert B. Tesh,[1] Hilda Guzman,[1] Amelia P. A. Travassos da Rosa,[1] Pedro F. C. Vasconcelos,[2] Leonidas B. Dias,[2] Joseph E. Bunnell,[1] Hui Zhang,[1] and Shu-Yuan Xiao[1]

[1]*Department of Pathology and Center for Tropical Diseases, University of Texas Medical Branch, Galveston;* [2]*Secao de Arbovirus, Instituto Evandro Chagas, Belem, Para, Brazil*

This report describes the clinical laboratory findings in golden hamsters experimentally infected with yellow fever (YF) virus. An accompanying paper describes the pathologic findings. Following intraperitoneal inoculation of a virulent strain of YF virus, hamsters developed a high-titered viremia (up to 109/mL) lasting 5–6 days and abnormal liver function tests. YF hemagglutination–inhibiting antibodies appeared 4 or 5 days after infection, often while viremia was still present. The mortality rate in YF-infected hamsters was variable, depending on the virus strain and the age of the animals. Clinical and pathologic changes in the infected hamsters were very similar to those described in experimentally infected macaques and in fatal human cases of YF, which indicates that the golden hamster may be an excellent alternative animal model, in place of nonhuman primates, for research on the pathogenesis and treatment of YF and other viscerotropic flavivirus diseases.

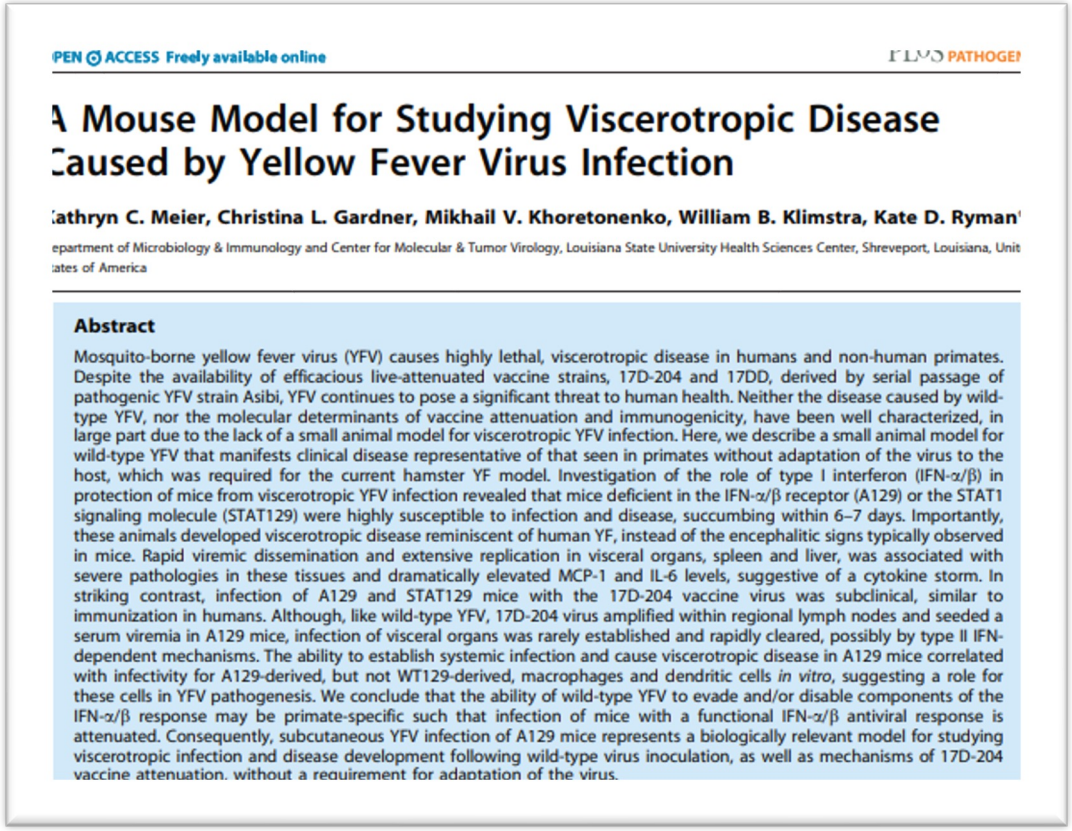


Hamster model that shows viscerotropic disease

However, most wild-type strains (which need to be adapted to hamsters) and viruses from YEL-AVD cases do not show viscerotropic disease in this model.

# Alternatives to NHP test ? ...with smaller animal

## Mouse



PEN ACCESS Freely available online PLoS PATHOGEN

# A Mouse Model for Studying Viscerotropic Disease Caused by Yellow Fever Virus Infection

Kathryn C. Meier, Christina L. Gardner, Mikhail V. Khoretonenko, William B. Klimstra, Kate D. Ryman

Department of Microbiology & Immunology and Center for Molecular & Tumor Virology, Louisiana State University Health Sciences Center, Shreveport, Louisiana, United States of America

**Abstract**

Mosquito-borne yellow fever virus (YFV) causes highly lethal, viscerotropic disease in humans and non-human primates. Despite the availability of efficacious live-attenuated vaccine strains, 17D-204 and 17DD, derived by serial passage of pathogenic YFV strain Asibi, YFV continues to pose a significant threat to human health. Neither the disease caused by wild-type YFV, nor the molecular determinants of vaccine attenuation and immunogenicity, have been well characterized, in large part due to the lack of a small animal model for viscerotropic YFV infection. Here, we describe a small animal model for wild-type YFV that manifests clinical disease representative of that seen in primates without adaptation of the virus to the host, which was required for the current hamster YF model. Investigation of the role of type I interferon (IFN-α/β) in protection of mice from viscerotropic YFV infection revealed that mice deficient in the IFN-α/β receptor (A129) or the STAT1 signaling molecule (STAT129) were highly susceptible to infection and disease, succumbing within 6–7 days. Importantly, these animals developed viscerotropic disease reminiscent of human YF, instead of the encephalitic signs typically observed in mice. Rapid viremic dissemination and extensive replication in visceral organs, spleen and liver, was associated with severe pathologies in these tissues and dramatically elevated MCP-1 and IL-6 levels, suggestive of a cytokine storm. In striking contrast, infection of A129 and STAT129 mice with the 17D-204 vaccine virus was subclinical, similar to immunization in humans. Although, like wild-type YFV, 17D-204 virus amplified within regional lymph nodes and seeded a serum viremia in A129 mice, infection of visceral organs was rarely established and rapidly cleared, possibly by type II IFN-dependent mechanisms. The ability to establish systemic infection and cause viscerotropic disease in A129 mice correlated with infectivity for A129-derived, but not WT129-derived, macrophages and dendritic cells *in vitro*, suggesting a role for these cells in YFV pathogenesis. We conclude that the ability of wild-type YFV to evade and/or disable components of the IFN-α/β response may be primate-specific such that infection of mice with a functional IFN-α/β antiviral response is attenuated. Consequently, subcutaneous YFV infection of A129 mice represents a biologically relevant model for studying viscerotropic infection and disease development following wild-type virus inoculation, as well as mechanisms of 17D-204 vaccine attenuation, without a requirement for adaptation of the virus.

PLoS Pathog. 2009 Oct;5(10):e1000614. doi: 10.1371/journal.ppat.1000614. Epub 2009 Oct 9.

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BIOLOGICALS

Biologicals 33 (2005) 131–144

www.elsevier.com/locate/biologicals

# Safety testing for neurovirulence of novel live, attenuated flavivirus vaccines: Infant mice provide an accurate surrogate for the test in monkeys

Thomas P. Monath [a,*], Gwendolyn A. Myers [a], Robert A. Beck [a], Michael Knauber [a], Kelly Scappaticci [a], Thad Pullano [a], W. Tad Archambault [b], John Catalan [a], Chuck Miller [a], Zhen-Xi Zhang [a], Sunheang Shin [a], Konstantin Pugachev [a], Ken Draper [c], Inessa S. Levenbook [d], Farshad Guirakhoo [a]

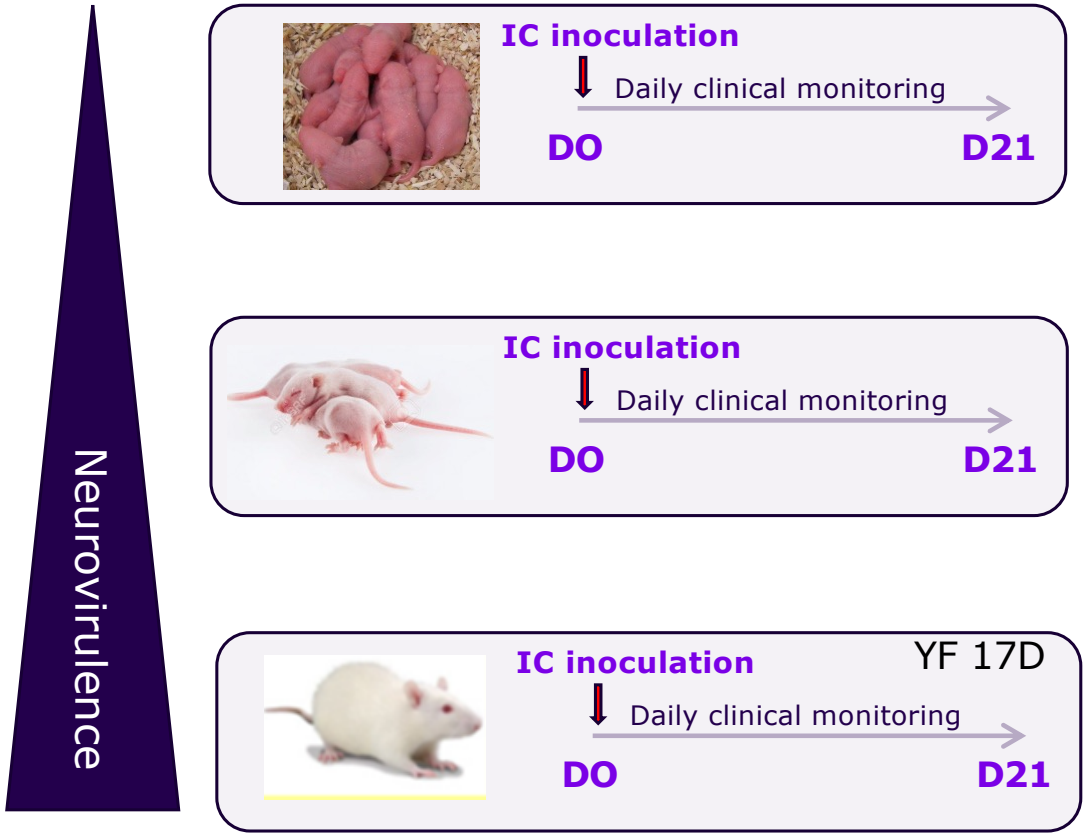
[a] *Acambis Inc., 38 Sidney Street, Cambridge, MA 02139, USA*
[b] *Virtu Stat, Ltd., North Wales, PA, USA*
[c] *Sierra Division of Charles River Laboratories Inc., Sparks, NV, USA*
[d] *Private consultant, Albany, NY, USA*

Received 8 March 2005; accepted 30 March 2005

**Abstract**

Current requirements for control of live viral vaccines, including yellow fever 17D, produced from potentially neurotropic wild type viruses include tests for neurovirulence in nonhuman primates. We have used yellow fever 17D virus as a live vector for nove flavivirus vaccines (designated ChimeriVax™) against dengue, Japanese encephalitis (JE), and West Nile (WN) viruses. For contro of these vaccines, it would be preferable to substitute a test in mice for the test in a higher species (monkeys). In this study, w compare the neurovirulence of ChimeriVax™ vaccine candidates in suckling mice inoculated by the intracerebral (IC) route witl graded doses of the test article or yellow fever 17D vaccine as a reference control. Mortality ratio and survival distribution are th outcome measures. The monkey safety test is performed as described for control of yellow fever vaccines [World Healtl Organization. Tech Rep Ser, WHO, Geneva; 1997]. In both mice and monkeys, all chimeric vaccines were significantly les neurovirulent than yellow fever 17D vaccine. The test in suckling mice discriminated between strains of two different vaccine (ChimeriVax™-JE and ChimeriVax™-DEN1) differing by a single amino acid change, and was more sensitive for detecting virulenc differences than the test in monkeys. The results indicate that the suckling mouse test is simple to perform, highly sensitive and, witl appropriate validation, could complement or possibly even replace the neurovirulence component of the monkey safety test. The tes in infant mice is particularly useful as a means of demonstrating biological consistency across seed virus and vaccine lots.

# Neurovirulence Test in Mice



# Alternatives to NHP test ? ...with smaller animal

Vaccine 40 (2022) 5641–5650

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

## Phenotypic and genetic characterization of a next generation live-attenuated yellow fever vaccine candidate

Raphael Esson [a], Emanuel Rodrigues De Sousa [a], Loic Benair [a], Nicolas Devard [a], Damien Soulet [a], Audrey Gillet [a], Isabelle Bassard [a], Stephanie Falque [a], Audrey Chareyre [a], Morgane Marmin [a], Yves Girerd-Chambaz [b], Carine Logvinoff [a,*], Martha Erika Navarro Sanchez [a,*]

[a] Analytical Sciences, Sanofi, Marcy l'Etoile, France
[b] Research and External Innovation, Sanofi, Marcy l'Etoile, France

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YF-VAX

ABSTRACT

We assessed the genetic and phenotypic characteristics of a yellow fever vaccine candidate, which was cloned from a YF-VAX substrain selected for growth in Vero cells (vYF-247), during the manufacturing process from the master seed lot (MSL) and working seed lot (WSL) through to the drug substance (DS) stage. There were nine minor nucleotide variants observed from the MSL to the DS stage, of which five led to amino acid changes. The variant positions were, however, not known risks for any virulence modification. vYF-247 exhibits a homogenous plaque size profile (as expected for a cloned vaccine candidate) composed of small plaques (<1 mm) that remained consistent throughout the manufacturing process. In addition, there was no change in the viral replication rate. Of note, the DS sequences across the two manufacturing campaigns (2018 and 2019) were very similar suggesting a high batch-to-batch consistency. All MSL, WSL and DS batches exhibited similar neurovirulence profiles in mice and had a more attenuated neurovirulence phenotype than the YF-VAX (egg-based vaccine) comparator. Overall, the neurovirulence phenotype of vYF-247 does not change from MSL, WSL to DS. These data collectively support the safety and genetic stability of vYF-247 during the production process.


**IC inoculation**

Daily clinical monitoring

**DO** **D21**

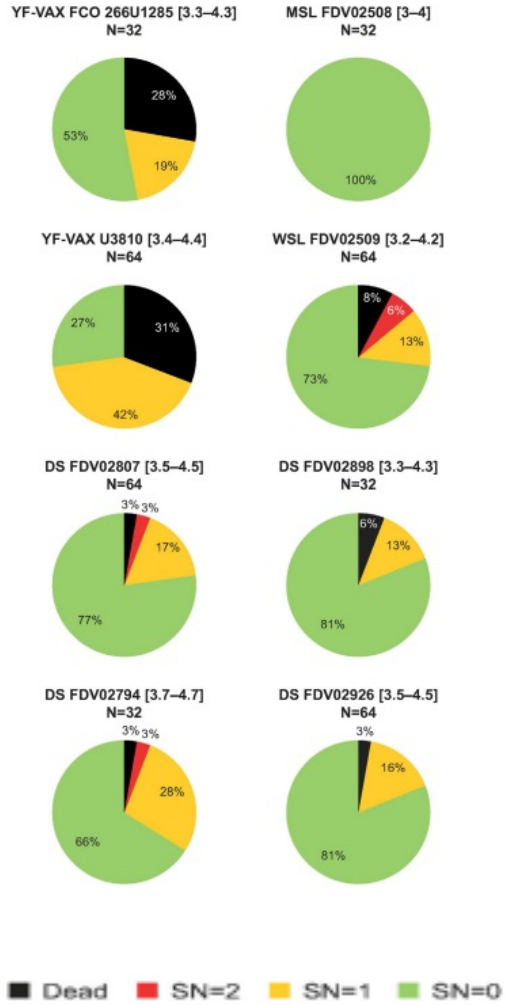


**Fig. 4.** Ne
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# Neurovirulence Test in Mice &

Neurovirulence

**IC inoculation**

Daily clinical monitoring

**DO** **D21**

**IC inoculation**

Daily clinical monitoring

**DO** **D21**

**IC inoculation** vYF-247

Daily clinical monitoring

**DO** **D21**

**IC inoculation** YF 17D

Daily clinical monitoring

**DO** **D21**

3R

Replace Reduce Refine

*IN VITRO ALTERNATIVE ?*

*In cellulo ?*

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Biologicals

journal homepage: www.elsevier.com/locate/biologicals

Innovative *in cellulo* method as an alternative to *in vivo* neurovirulence test for the characterization and quality control of human live Yellow Fever virus vaccines: A pilot study

Anaelle da Costa[a,b,1], Christophe Prehaud[a,1], Cecile Khou[c], Nathalie Pardigon[c], Aure Saulnier[b], Nolwenn Nougarede[b], Monique Lafon[a,*]

[a] Institut Pasteur, CNRS UMR 3569, Unité de Neuroimmunologie Virale, 25 Rue du Dr Roux, 75724, Paris Cedex 15, France
[b] Sanofi Pasteur, Plateforme de Caractérisation Immunologique et Microbiologique, Département Analytique de la R&D, 1541 Avenue Marcel Mérieux, 69280, Marcy l'Etoile, France
[c] Institut Pasteur, Unité de Recherche et d'Expertise Environnement et Risques Infectieux, Groupe Arbovirus, 25 Rue du Dr Roux, 75724, Paris Cedex 15, France

*Sequencing ?*

MAJOR ARTICLE

Comparison of the Live Attenuated Yellow Fever Vaccine 17D-204 Strain to Its Virulent Parental Strain Asibi by Deep Sequencing

Andrew Beck,[1,2] Robert B. Tesh,[1,2] Thomas G. Wood,[3] Steven G. Widen,[3] Kate D. Ryman,[4] and Alan D. T. Barrett[1,2]

[1]Department of Pathology, [2]Sealy Center for Vaccine Development, and [3]Molecular Genomics Core Facility, University of Texas Medical Branch,

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# From Asibi Strain (1927) to 17D Vaccine Strains : Attenuation

Amino acid differences and nucleotide differences in the 3′ non-coding region between wild-type Asibi virus and attenuated 17D vaccines

| Nucleotide | Gene | Amino acid[a] | Asibi | 17D-204, 17D-213 and 17DD vaccine viruses |
|---|---|---|---|---|
| 854 | *M* | 36 | Leu | Phe |
| 1127 | *E* | 52 | Gly | Arg |
| 1482 | | 170 | Ala | Val |
| 1491 | | 173 | Thr | Ile |
| 1572 | | 200 | Lys | Thr |
| 1870 | | 299 | Met | Ile |
| 1887 | | 305 | Ser | Phe |
| 2112 | | 380 | Thr | Arg |
| 2193 | | 407 | Ala | Val |
| 3371 | *NS1* | 307 | Ile | Val |
| 3860 | *NS2A* | 118 | Met | Val |
| 4007 | | 167 | Thr | Ala |
| 4022 | | 172 | Thr | Ala |
| 4056 | | 183 | Ser | Phe |
| 4505 | *NS2B* | 109 | Ile | Leu |
| 6023 | *NS3* | 485 | Asp | Asn |
| 6876 | *NS4A* | 146 | Val | Ala |
| 7171 | *NS4B* | 95 | Ile | Met |
| 10 142 | *NS5* | 836 | Glu | Lys |
| 10 338 | | 900 | Pro | Leu |
| 10 367 | *(3′ NCR)* | — | U | C |
| 10 418 | | — | U | C |
| 10 800 | | — | G | A |
| 10 847 | | — | A | C |

[a] The 20 amino acids and 4 nucleotide changes in the 3′ non-coding region identified in this table are conserved in any vaccine virus derived from the 17D strain.

WHO TRS 978 Annex 5

Science. 1985 Aug 23;229(4715):726-33. doi: 10.1126/science.4023707.

**Nucleotide sequence of yellow fever virus: implications for flavivirus gene expression and evolution**

C M Rice, E M Lenches, S R Eddy, S J Shin, R L Sheets, J H Strauss

PMID: 4023707 DOI: 10.1126/science.4023707

Rice CM *et al.* Science 1985

MAJOR ARTICLE

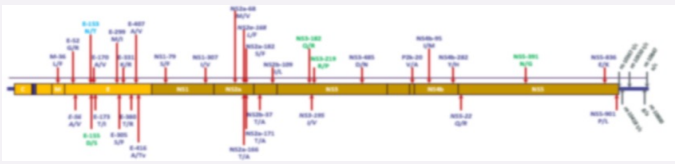
**Comparison of the Live Attenuated Yellow Fever Vaccine 17D-204 Strain to Its Virulent Parental Strain Asibi by Deep Sequencing**

**Andrew Beck,[1,2] Robert B. Tesh,[1,2] Thomas G. Wood,[3] Steven G. Widen,[3] Kate D. Ryman,[4] and Alan D. T. Barrett[1,2]**

[1]Department of Pathology, [2]Sealy Center for Vaccine Development, and [3]Molecular Genomics Core Facility, University of Texas Medical Branch, Galveston; and [4]Center for Vaccine Research, University of Pittsburgh, Pennsylvania

Beck *et al.* JID 2014

Attenuation-related mutations are shared all along the genome
YF-17D attenuation is based on >49 mutations inducing 24 AA changes



Role of each individual mutation in attenuation is not known

Relative quasispecies structure is a plausible correlate of attenuation for live viral vaccines

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# Alternative to NHP Test

In the absence of clear understanding of 17D attenuation , relevance of *in cellulo* approach as an alternative to NHP test might be challenged

Considering the sequence data alone might appear difficult since

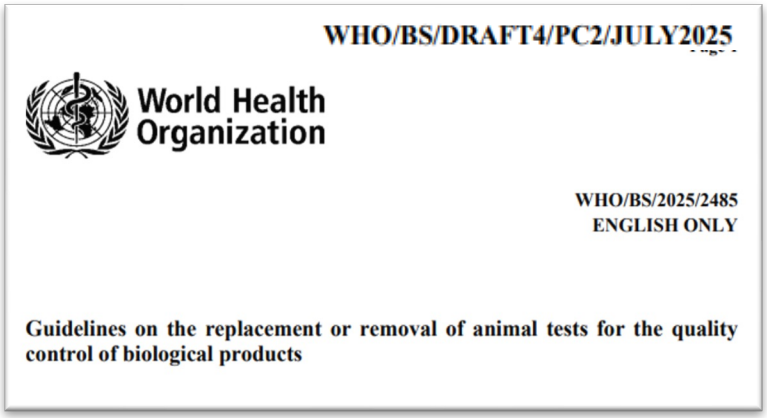
-the importance of each attenuation-related mutation within the overall attenuation is unknown

- the interaction between mutations within the overall attenuation is unknown

In depth sequencing data should be considered within an overall characterization package, assessing genetic and phenotypic characteristics of the viral population

=> To demonstrate the consistency of the viral population (genetically and phenotypically) with previously qualified material ( such as a reference lot) rather than systematically performing NHP test

# Sequencing as an Alternative to NHP test



WHO/BS/DRAFT4/PC2/JULY2025

World Health Organization

WHO/BS/2025/2485
ENGLISH ONLY

Guidelines on the replacement or removal of animal tests for the quality control of biological products

*"Although the precise mechanism and genetic basis of neurovirulence of yellow fever viruses are poorly understood,* ***the level of residual neurovirulence of an attenuated virus is determined by the viral genome sequence****.*

*As a result, validated molecular methods are suitable alternatives to in vivo neurovirulence tests for the control of yellow fever virus seed lots."*

*Leveraging Previous NHP Test results & Consistency of Sequences*

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# Conclusion on Yellow Fever  Vaccines - Test in NHP

Yellow Fever vaccines are very succesful live attenuated vaccines

single dose, high and early immune response , long lasting protection , good safety profile

But test in NHP is  currently still required for new seed Lot

While the relevance of an alternative *in vitro* model might be difficult to demonstrate , the **consistency of *the genetic and phenotypic characteristics*** of the viral vaccine with previously established material should be considered as an alternative to neurovirulence test

# THANK YOU

Carine Logvinoff is a Sanofi employee and may hold shares and/or stock options in the company

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