



SANOFI

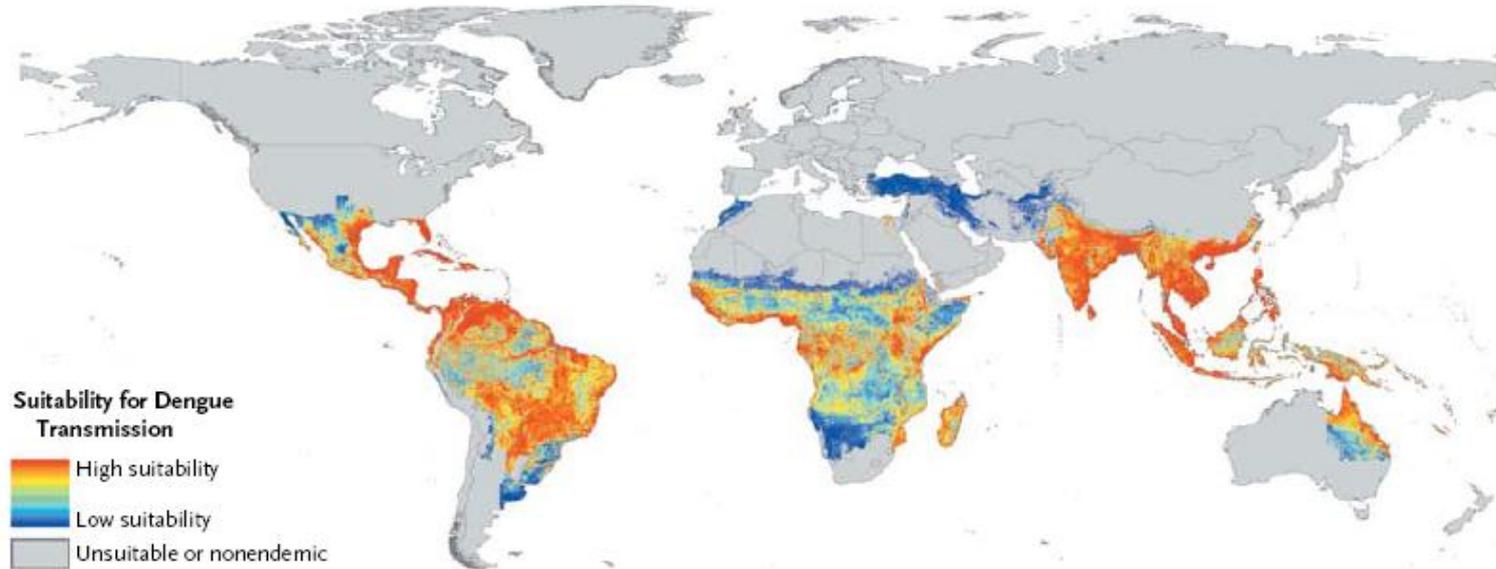
**Triple innovation dans le développement
du vaccin contre la dengue**

Dr Rémy TEYSSOU
Senior Director Dengue Vaccine Program



Un enjeu mondial de santé publique

Epidémiologie et objectifs de l'OMS



Simmons CP, et al. N Engl J Med. 2012

Objectifs de l'OMS (NTD) pour 2015-2020

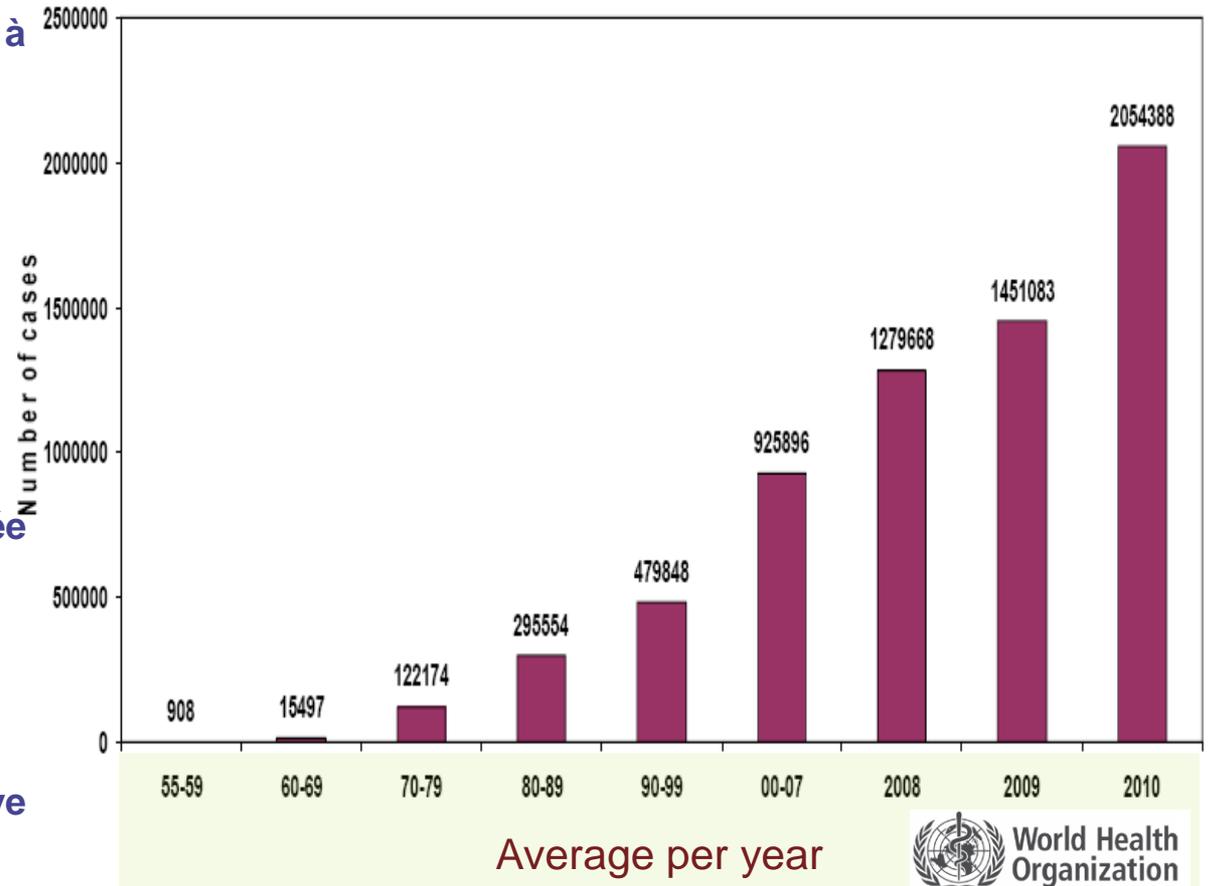
- Réduire de 50% la mortalité de la dengue d'ici 2020
- Réduire la morbidité de la maladie de 25% d'ici 2020
- Proposer une meilleure évaluation du poids épidémiologique de la maladie d'ici à 2015

World Health Organization. Report of the WHO strategic and Technical Advisory Group for Neglected Tropical Diseases, Geneva, Switzerland 24–25 April 2012. Available at http://www.who.int/neglected_diseases/NTD_STAG_Report_2012.pdf

Une maladie émergente sans solution

- 2.5 à 3.5 milliards de personnes vivant en zone à risque
- 230 millions de sujets infectés chaque année
- Plus de 500 000 cas sévères (90 % chez l'enfant de moins de 15 ans)
- 25 000 morts chaque année
- Un poids économique majeur
- Pas de solution thérapeutique ni préventive

Cas de dengue rapportés par l'OMS entre 1955 et 2010



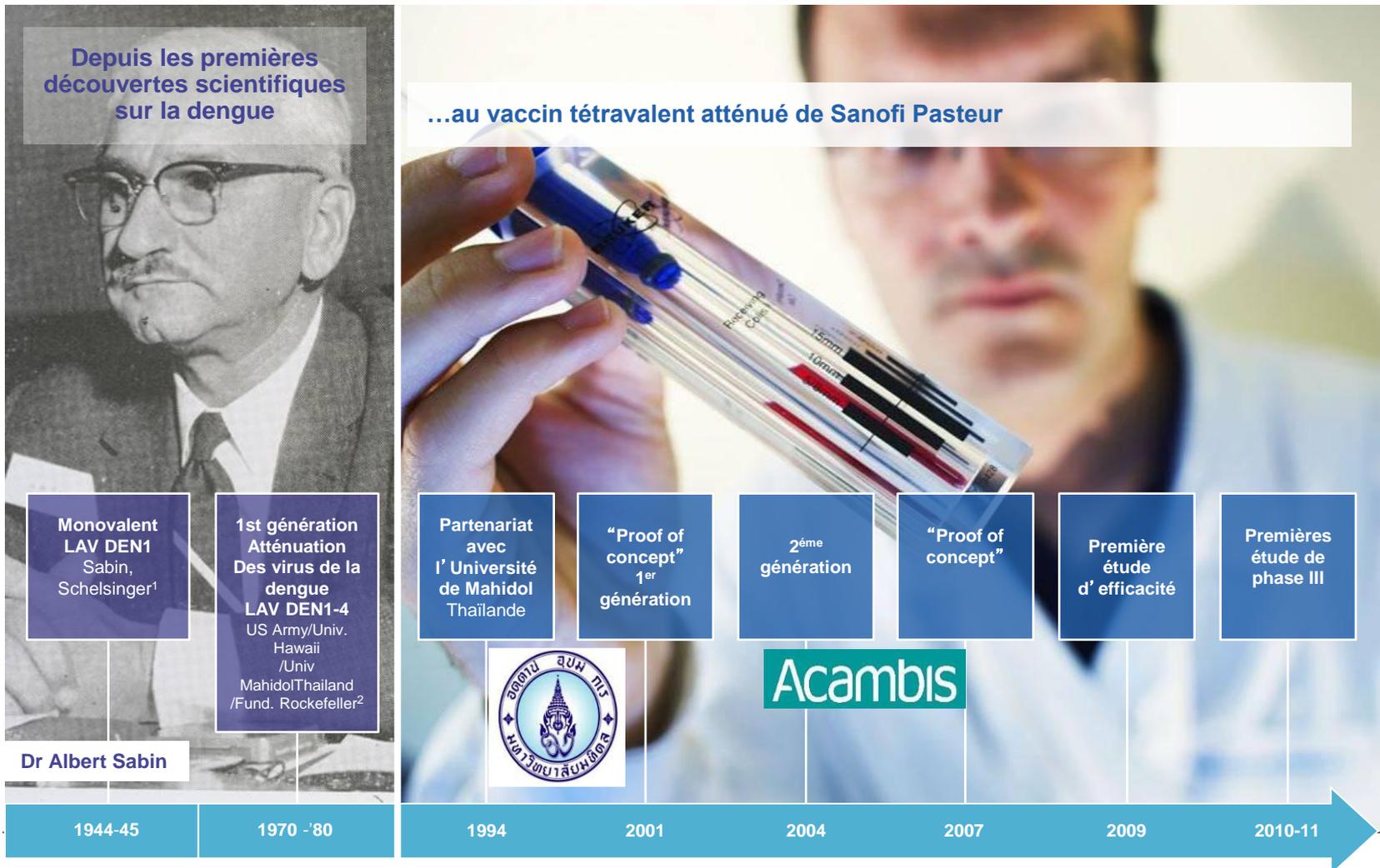
Beatty M Letson GW Margolis HS, Estimating the global burden of dengue., Am J Trop Med Hygiene 81, 5 :231 2009

Obstacles pour la recherche et le développement d'un vaccin contre la dengue

- **Pas de vaccin disponible malgré des efforts de recherche qui ont débuté il y a plus de 70 ans**

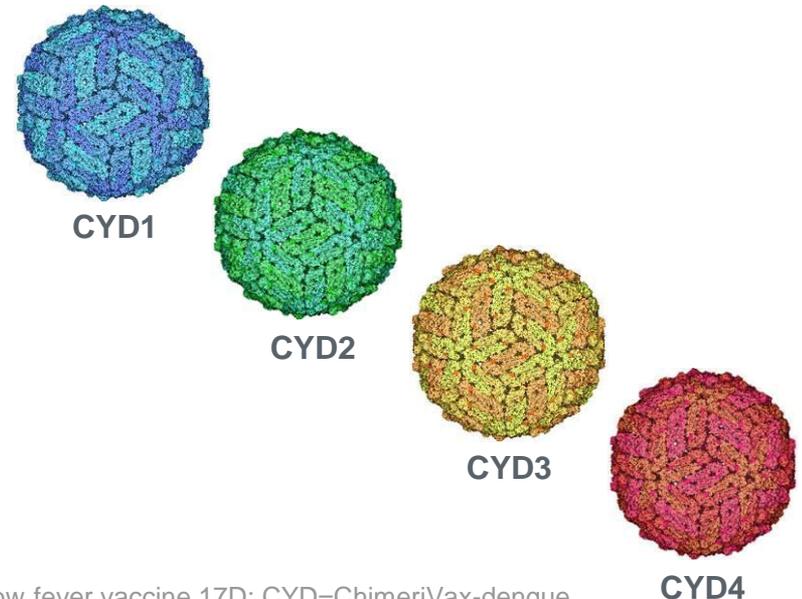
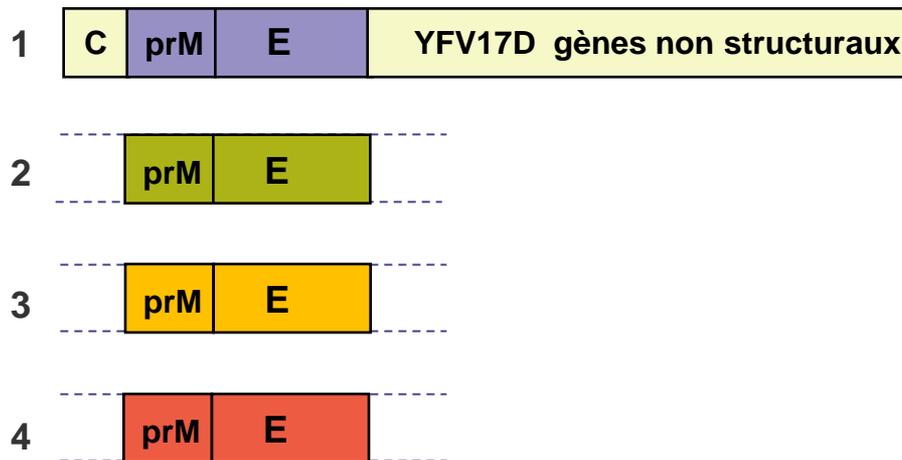
- **Principaux obstacles**
 - Pas de modèle animal
 - 4 sérotypes = 4 différents virus
 - **Vaccin multivalent**
 - Pas de corrélat de protection (seuil d'anticorps protecteur)
 - **Etudes d'efficacité clinique**
 - Industrialisation et production à large échelle

Le processus d'innovation en R&D est le résultat de collaborations entre Sanofi Pasteur et un réseau mondial de scientifiques (plus de 90 collaborations scientifiques nationales et internationales)



Première étape d'innovation : la construction d'un vaccin recombinant vivant atténué tétravalent

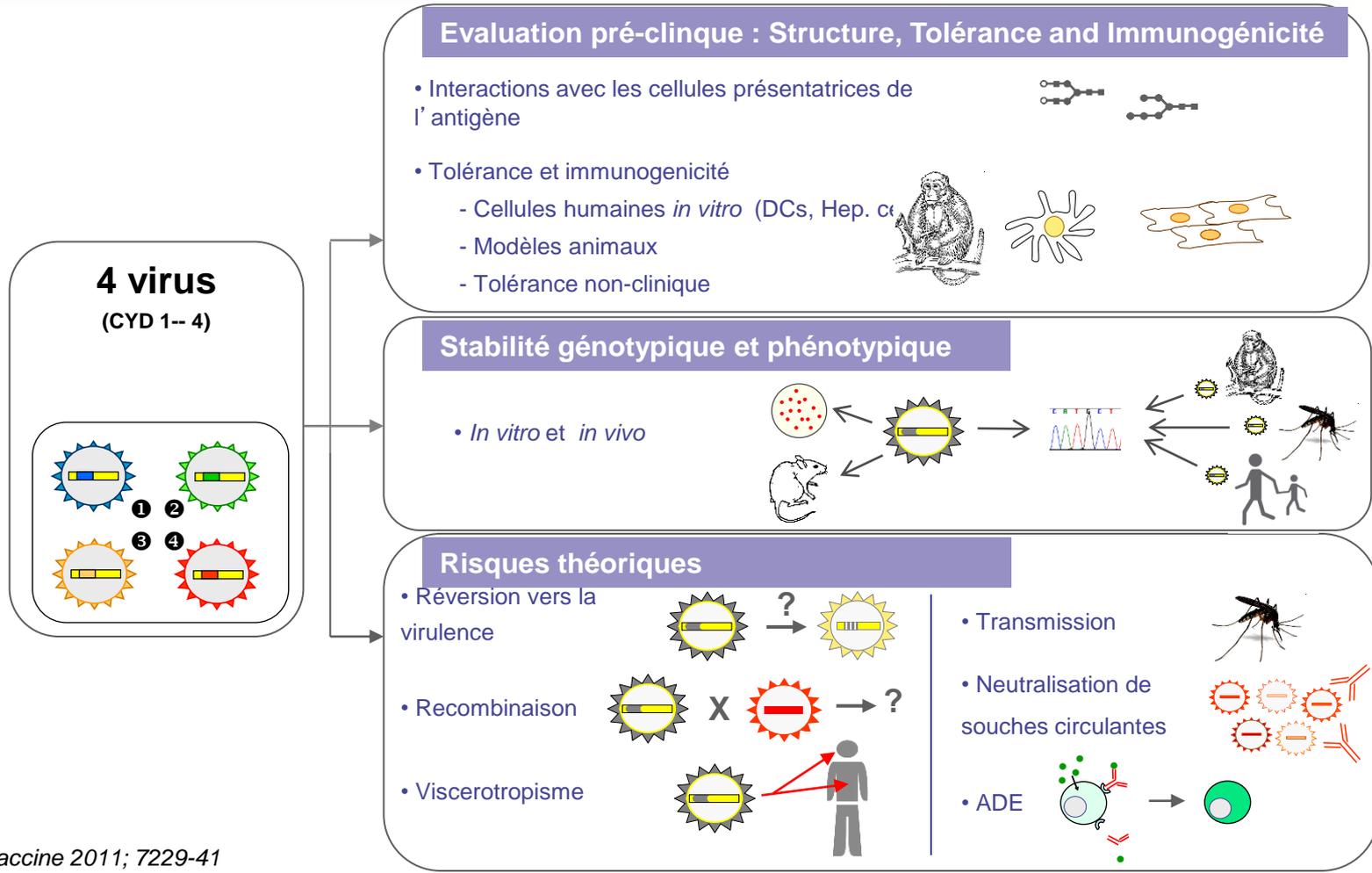
- Le génome de la souche vaccinale YF-17D a été modifié
 - Substitution des gènes codant pour les protéines d'enveloppe (PrM – E)
 - Insertion des gènes correspondant du virus de la Dengue
- Quatre souches recombinantes ont été construites, une pour chaque sérotype



LAV=live attenuated vaccine; YF-17D=yellow fever vaccine 17D; CYD=ChimeriVax-dengue
4. Guy B, et al. *Vaccine* 2011;29:7229-7241

Deuxième étape d'innovation :

Caractérisation complète des souches vaccinales, impliquant la virologie, l'immunologie et la biologie moléculaire en partenariat avec des équipes internationales



Un développement industriel innovant localisé en France pour face à un problème mondial

Bâtiment A 100 : Principe actif



Bâtiment A 300 : Contrôle Qualité



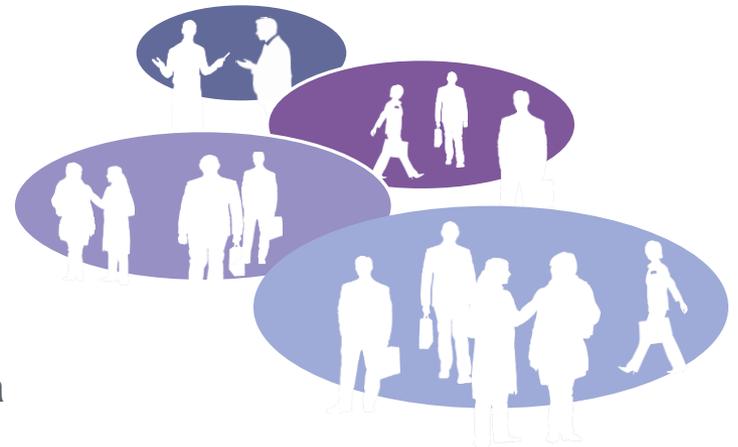
Bâtiment A 900 : Utilités



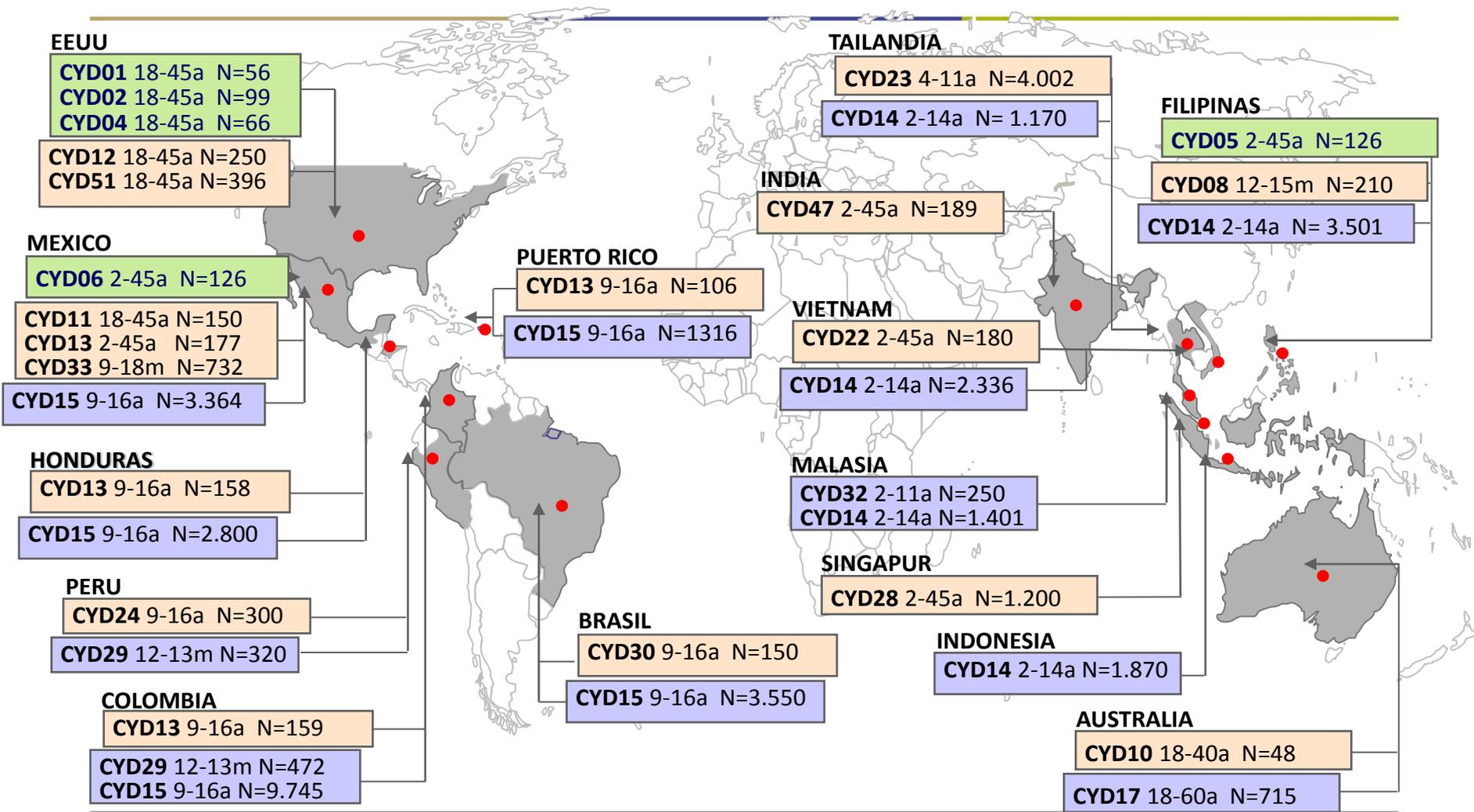
- 300 millions d'€ d'investissement en France (Neuville-sur-Saône), avant les résultats d'efficacité
- Reconversion d'un site industriel
- 175 professionnels impliqués
- Capacité de 100 millions de doses à partir de 2016

Création de la “ Dengue Company” en Septembre 2011

- Equipe intégrée, transversale et multifonctionnelle, réunie derrière le leadership de Guillaume Leroy, avec une ambition définie: “faire de la dengue la prochaine maladie prévenue par la vaccination”
- Missions
 - Consolider et mettre en place toutes les activités nécessaires au développement, à l’enregistrement, à la production et au lancement du vaccin dans les pays endémiques et non endémiques



23 essais cliniques (Phase I to III) initiés et coordonnés par le département R&D à Lyon



La première étude d'efficacité : une étape importante

THE WALL STREET JOURNAL

HEALTH INDUSTRY | Updated September 11, 2012, 12:16 a.m. ET

Dengue Vaccine Test Encourages Scientists

LONDON—Results from an early test of a dengue vaccine suggest it isn't ideal, but scientists say the study is still encouraging news in the global fight against the disease known as "break-bone fever."

There is currently no treatment or vaccine for dengue, which causes symptoms including fever, severe joint pain, headache and bleeding. The mosquito-borne disease infects up to 100 million people world-wide every year, mostly in Asia, Africa and Latin America.

JORNAL DO BRASIL

Ciência e Tecnologia

Vacina se mostra parcialmente efetiva contra três tipos de dengue

Uma vacina testada por pesquisadores da Tailândia e da França conseguiu imunizar parcialmente (entre 60 e 90%) contra três dos quatro vírus que causam a dengue.

substância
estudantes
1333, um p

Dengue vaccine likely to be available by 2015

60%-90% Protection Rate Against 3 Main Virus Strains

Scientists claim breakthrough on first vaccine against dengue

Kounteya Sinha | CNN

New Delhi: The world's first effective vaccine against dengue could be available by 2015.

DEADLY DISEASE
Of the 220 million people infected annually, two million—mostly kids—develop dengue.

GM mosquito that kills own species
US and UK scientists have developed a strain of genetically modified...

DENGUE UN VACCIN SE PROFILE

Première lueur d'espoir dans le combat contre la dengue: un vaccin se profile pour tous les continents.



Dengue vaccine to be a reality by '15

WHO says over 2.5 billion people—over 40% of the world's population—are now at risk from dengue. The UN body currently estimates there may be 50-100 million dengue cases.

Scientists are set to release a major dengue vaccine trial in 2015, with a goal to have a vaccine available by 2015. The study will involve 4000 children in Thailand.

Early test suggests dengue vaccine possible

LONDON (AP) — Results from an early test of a dengue vaccine suggest it isn't ideal, but scientists say the study is still encouraging news in the global fight against the disease known as "break-bone fever."

There is currently no treatment or vaccine for dengue, which causes symptoms including fever, severe joint pain and bleeding. The mosquito-borne disease infects up to 100 million people worldwide in Asia, Africa and Latin America.

Sanofi's dengue vaccine trials show optimistic results

BY JACOB P. KOSHY & VIDYA KRISHNAN

NEW DELHI

Scientists have reported "optimistic" results from preliminary human trials conducted to develop a vaccine for dengue fever, according to the forthcoming issue of *Lancet* medical journal.

The vaccine (76 cases or 2.8% of the vaccine group) and placebo groups (58 cases or 4.4% of the control group), secondary tests showed the vaccine was effective against DENV 1, 3 and 4 (in the range of 60-90%), with only DENV 2 appearing to be resistant to the vaccine's effects.

The Malaysian Times

Dengue fever : Vaccine trial raises a muted cheer

PARIS: A prototype vaccine for dengue matched up the best success yet against the disease but failed to protect against all its viral strains, researchers said on Tuesday.

In rural Thailand who were badly exposed had no side effects but only worked from over, but the most reason is "a safe researchers said in more than 100 children."

Dengue still retains its deadly

Vaccine's overall efficacy in a recent trial is 'lower than expected'

The just concluded Phase IIB (proof-of-concept) dengue vaccine trial against all the four virus types (serotypes) that cause dengue has not only shown an unexpectedly low efficacy of 30.2 per cent but has also challenged many well-established hypotheses and ideas.

The trial was conducted in about 4,000 children in the age group 4 and 11 in Thailand.



La Jornada en línea

INICIO POLÍTICA ECONOMÍA MUNDO ESTADOS CAPITAL SOCIEDAD Y JUSTICIA CIENCIAS CULTURA ESPECTÁCULOS DEPORTES

Hallan vacuna eficaz contra el dengue

Bangkok: Investigadores de Tailandia y Francia han hallado una nueva vacuna contra el virus del dengue, con una eficacia de un 30 por ciento, según la publicación especializada "The Lancet".

Los resultados provienen de un estudio realizado con 4.000 niños tailandeses en edad escolar, cerca de Bangkok. Los niños son especialmente susceptibles de contraer el virus.



New vaccine for dengue victims

OUR CORRESPONDENT KOLKATA

A new vaccine spells hope for the fear of dengue, the deadly vector-borne disease caused by three virus types. The live attenuated vaccine is to be administered in three doses over the course of a year, with a six-month gap between doses.

The study which led to the discovery of the vaccine was conducted among 4,002 children aged from 4 to 11 in Muang district of Ratchaburi province in Thailand under the patronage of the Thai ministry of public health. The vaccine showed efficacy of 61.2 per cent against dengue virus 1, 81.3 per cent against dengue virus 3 and 90 per cent against dengue virus 4. Dengue virus 2, which is the most common, was not included in the vaccine; studies continue to find a solution to that.

found to protect a large group of children from clinical diseases caused by dengue viruses. This brings hope to millions of parents whose children are at risk of dengue.

Dengue is a threat to nearly three billion people and a health priority in many countries of Asia and Latin America. Though the disease is expanding geographically, there is high mortality in many people and a health priority in many countries of Asia and Latin America. Though the disease is expanding geographically, there is high mortality in many people and a health priority in many countries of Asia and Latin America.





Après 20 ans d'efforts continus, Sanofi Pasteur a démontré grâce à une approche innovante qu'un vaccin contre la dengue est possible.

Sanofi Pasteur est aujourd'hui un leader scientifique mondial dans la recherche et la lutte contre la dengue

Sanofi Pasteur a investi dans un site de production à Neuville, pour faire face à un enjeu international de santé publique