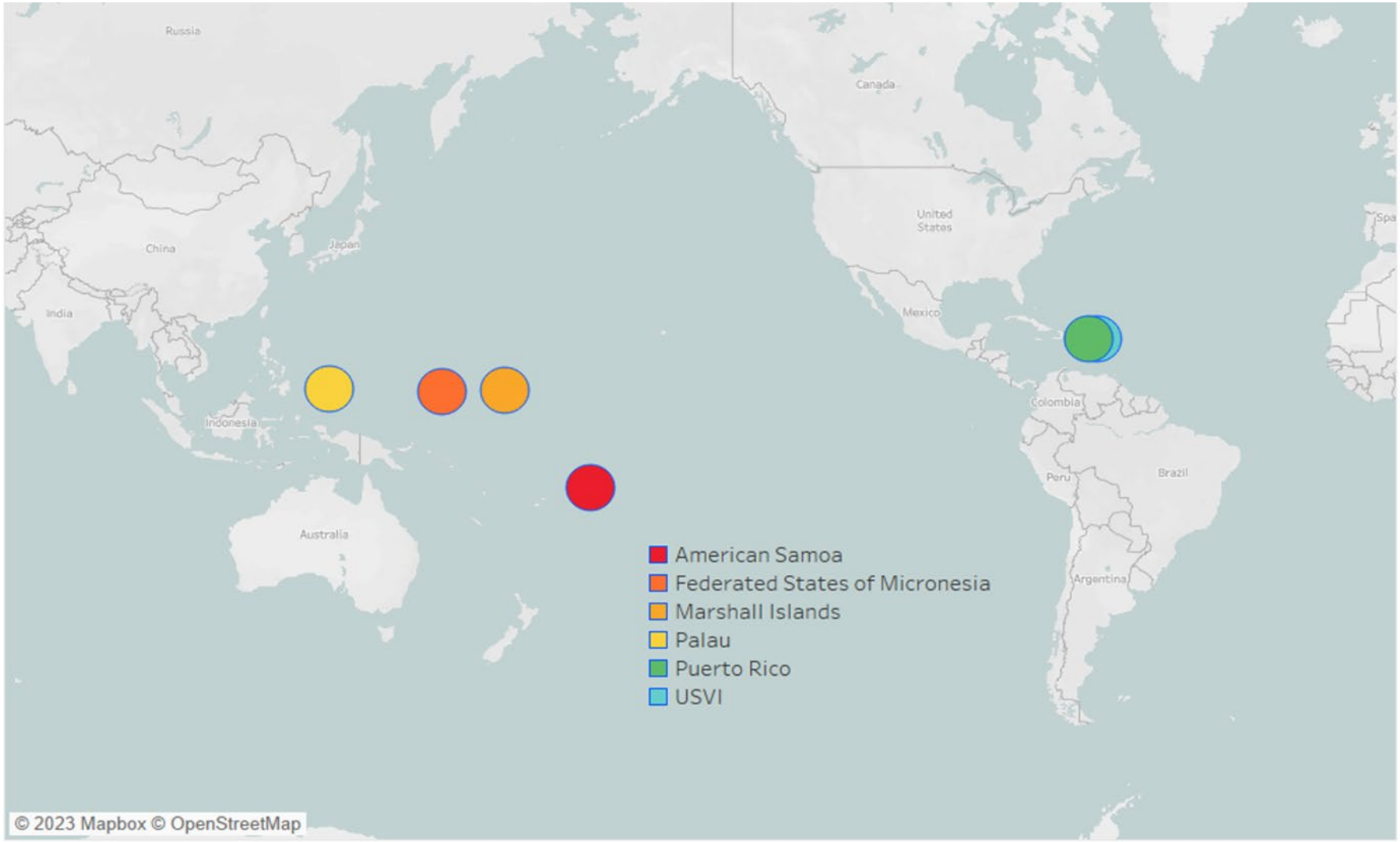
Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases

Updates on Dengue Vaccines

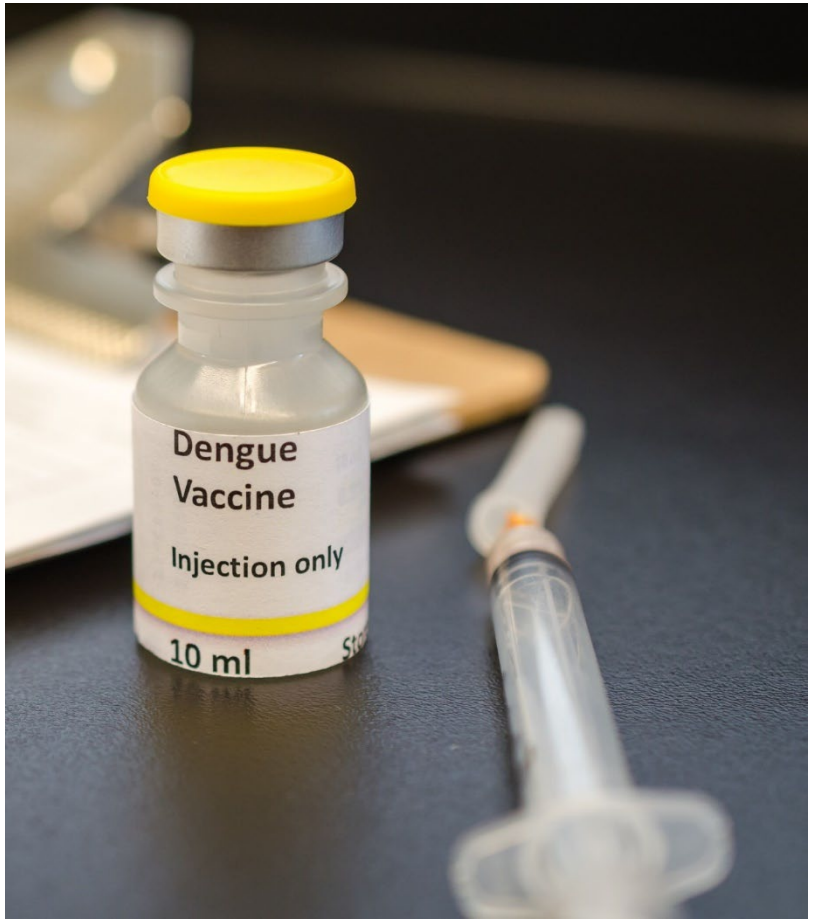
Wilbur Chen, MD

October 26, 2023

Dengue is endemic in 6 U.S. territories and freely associated states.



Dengvaxia™ ACIP Recommendation June 2021



Three doses of Dengvaxia are indicated for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3, and 4 in people 9–16 years old with:

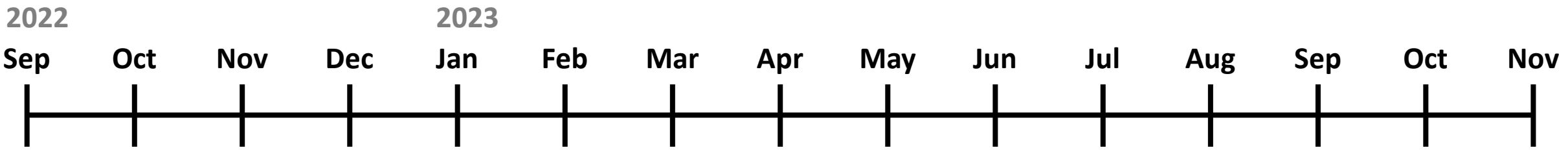
- laboratory confirmation of previous dengue virus infection

AND

- living in endemic areas.

Takeda Dengue Vaccine (TAK-003) has been under review by the FDA since Nov 2022

Dengue Workgroup presented to ACIP 3 times



- Dengue epidemiology
- Review of Sanofi dengue vaccine and ACIP recommendation

- Takeda dengue vaccine safety and efficacy presentation
- Workgroup summary and interpretation

- Policy questions
- Cost-effective (CE) analysis (CDC/Notre Dame)
- Comparison of CE models
- Partial EtR

- *Plan to present draft recommendations*

TAK-003 Efficacy*

Outcome: **Virologically Confirmed Dengue**

Overall VE

61.2% (56.0, 65.8%)

VE in Seropositives

64.2% (58.4, 69.2%)

VE in Seronegatives

53.5% (41.6–62.9%)

VE in Seropositives by Serotype		
DENV-1	**56.1%**	**(44.6, 65.2%)**
DENV-2	**80.4%**	**(73.1, 85.7%)**
DENV-3	**52.3%**	**(36.7, 64.0%)**
DENV-4	**70.6%**	**(39.9, 85.6%)**

VE in Seronegatives by Serotype		
DENV-1	**45.4%**	**(26.1, 59.7%)**
DENV-2	**88.1%**	**(78.6, 93.3%)**
DENV-3	-15.5%	(-108.2, 35.9%)
DENV-4	-105.6%	(-628.7, 42.0%)

*57 months after first dose, significant results **bolded.** Number for seropositive placebo participants 4,855 and vaccine 9,666; Seronegative placebo 1,832 and vaccine 3,714.

Unpublished data presented by Takeda to ACIP and ASTMH

TAK-003 Efficacy* Outcome: **Hospitalization**

Overall VE

84.1% (77.8, 88.6%)

VE in Seropositives

85.9% (78.7, 90.7%)

VE in Seronegatives

79.3% (63.5, 88.2%)

VE in Seropositives by Serotype

DENV-1	**66.8% (37.4, 82.3%)**
DENV-2	**95.8% (89.6, 98.3%)**
DENV-3	**74.0% (38.6, 89.0%)**
DENV-4	**100% (NE, NE)†**

†DENV-4 Placebo events: 3 TAK-003 events: 0

VE in Seronegatives by Serotype

DENV-1	**78.4%**	**(43.9, 91.7%)**
DENV-2	**100%**	**(NE, NE)§**
DENV-3	-87.9%	(-573.4, 47.6%)¶
DENV-4	100 %	(NE, NE)**

§DENV-2 Placebo events: 23 TAK-003 events: 0
¶DENV-3 Placebo events: 3 TAK-003 events: 11
**DENV-4 Placebo events: 1 TAK-003 events: 0

*57 months after first dose, significant results **bolded.** Number for seropositive placebo participants 4,855 and vaccine 9,666; Seronegative placebo 1,832 and vaccine 3,714.

Unpublished data presented by Takeda to ACIP and ASTMH

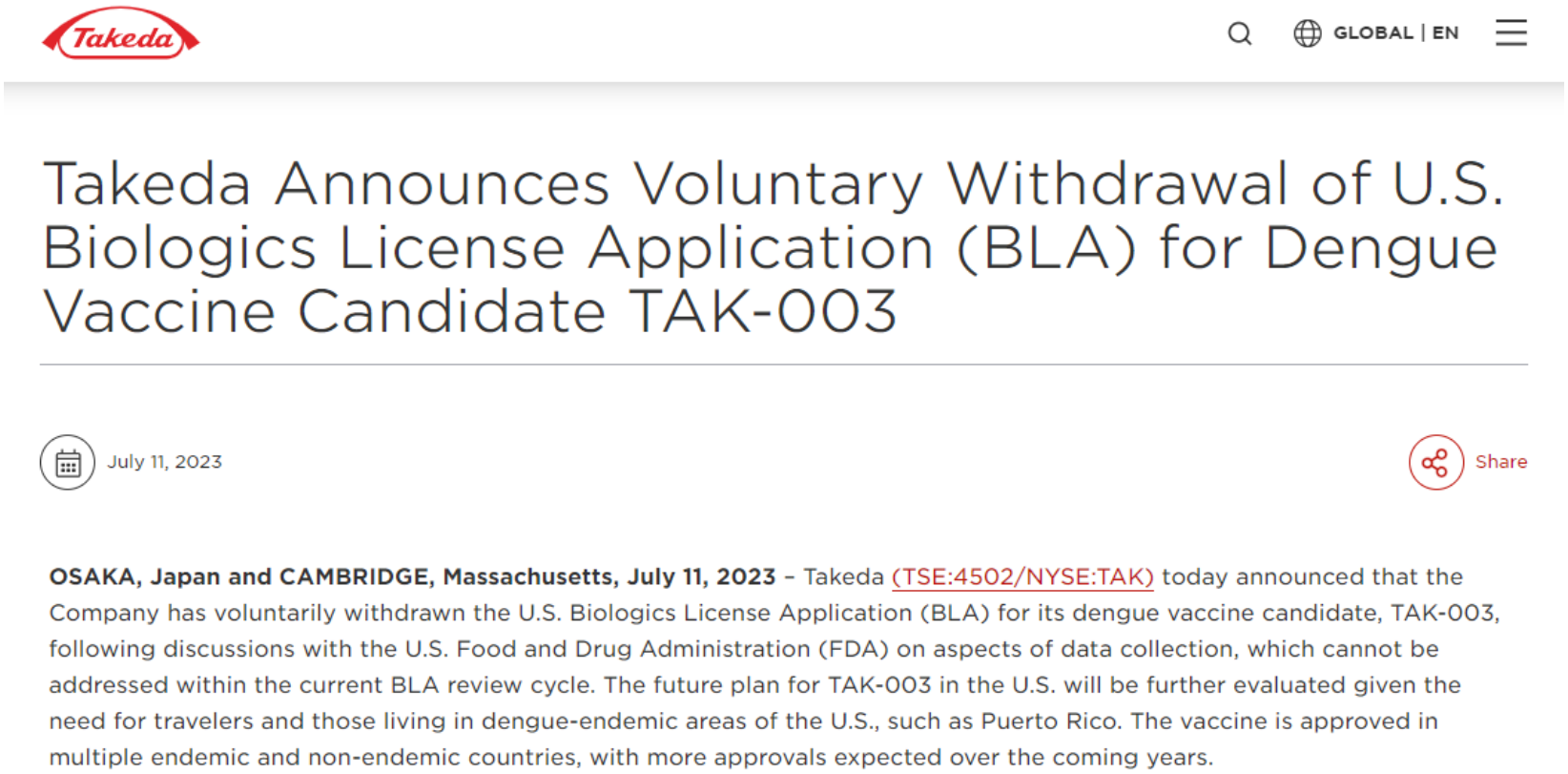
European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) issued positive opinion for TAK-003

October 2023

- EU-M4all: parallel review for EU and participating dengue endemic countries globally

- TAK-003 vaccine approved in multiple countries
  - EU, UK, Brazil, Argentina, Indonesia, & Thailand

On July 11, Takeda voluntarily withdrew TAK-003 from FDA review.



Takeda

GLOBAL | EN

Takeda Announces Voluntary Withdrawal of U.S. Biologics License Application (BLA) for Dengue Vaccine Candidate TAK-003

July 11, 2023

Share

OSAKA, Japan and CAMBRIDGE, Massachusetts, July 11, 2023 – Takeda (TSE:4502/NYSE:TAK) today announced that the Company has voluntarily withdrawn the U.S. Biologics License Application (BLA) for its dengue vaccine candidate, TAK-003, following discussions with the U.S. Food and Drug Administration (FDA) on aspects of data collection, which cannot be addressed within the current BLA review cycle. The future plan for TAK-003 in the U.S. will be further evaluated given the need for travelers and those living in dengue-endemic areas of the U.S., such as Puerto Rico. The vaccine is approved in multiple endemic and non-endemic countries, with more approvals expected over the coming years.

https://www.takeda.com/newsroom/statements/2023/takeda-announces-voluntary-withdrawal-of-US-biologics-license-application-for-dengue-vaccine-candidate-TAK-003/

WHO SAGE Recommendations for TAK-003

Sept 25, 2023

- Consider for introduction in settings with **high dengue disease burden** and **high transmission intensity**
- SAGE recommended the vaccine be introduced to children aged **6 to 16 years** of age.
  - Within that age range, the vaccine should be introduced about **1-2 years prior to the age-specific peak incidence of dengue-related hospitalizations.**
  - The vaccine should be administered in a 2-dose schedule with a 3-month interval between doses.

Future Dengue Vaccine Work

- Dengue workgroup will be paused until TAK-003 is re-submitted to FDA or a new vaccine submitted for approval

ACIP Dengue Vaccines Workgroup

ACIP Members

Wilbur Chen (Chair)

Kathy Poehling

Beth Bell

Veronica McNally

CDC Co-Lead

Gabriela Paz-Bailey

Laura Adams

Ex Officio Members

Kaitlyn Morabito (NIH)

Ralph LeBlanc (FDA)

Ihid Carneiro Leao (FDA)

Kirk Prutzman (FDA)

Srihari Seshadri (DOD)

Liaison Representatives

Elizabeth Barnett (AAP)

Rob Schechter (AIM)

Consultants

Edwin Asturias

Robert Atmar

Alan Barrett

Iris Cardona

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Cindy Weinbaum

Rita Helfand