

Advances in TB mRNA Vaccine Development and Dengue Vaccine Implementation in Brazil

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TB Vaccine Pipeline

TB vaccine candidates in active clinical trials

Safety

Thp

Immunogenicity

Therapeutic

Prevention of Infection

Prevention of Disease

Prevention of Recurrence

There are 12 candidates in active clinical trials as of September 2024.

Platform

+8





People without Mtb infection -Mtb

People living with HIV

- People with Mtb infection +Mtb
- People with active TB disease aTBd
- People with MDR-TB MDR
- cTB People cured of active TB



WORKING GROUP ON **NEW TB VACCINES**



Last update: 2 September 2024

Adjuvant AS01 (GSK)

- Tuberculose: M72/AS01E
- Malaria: Mosquirix (RTS,S/AS01)
- VSR: Arexvy (RSVPreF3/AS01E)
- Hesper Zoster: Shingrix (HZ/su/AS01B)



IC = immunocompromised; MPL = 3-O-desacyl-4'-monophosphoryl lipid A; QS-21 = Quillaja saponaria Molina, fraction 21; RZV = recombinant zoster vaccine; VZV = varicella zoster virus Adapted from Yiu KH, HKMF 2024.

https://www.nature.com/articles/s41541-017-0027-3

Development of a New 100% Brazilian mRNA-Based Tuberculosis Vaccine



1. Overview of Study Objectives:

- Goal: Develop a Brazilian mRNA vaccine for TB with 3 targets (3 mRNA) to increase efficacy.

- Partnership: Collaboration between FIOCRUZ and Biomanguinhos, with financial support from the Ministry of Health and Open Philanthropy.

2. Key Milestones:

- Animal Studies: Conclusion by Q4 2025.
- Phase 1/2 Clinical Trials: Starting Q1 2026
- Phase 3 Clinical Trials: Expected to begin Q3 2027

3. Target Population:

- Participants include incarcerated individuals and their families across multiple Brazilian cities (e.g., Porto Alegre, São Paulo, Belo Horizonte).

4. Experimental Models:

- Three plasmid constructs with distinct mRNA sequences.
- Experimental testing on animals like BALB/c mice and guinea pigs for immunogenicity and protection efficacy.

5. Study Locations:

- Immunogenicity (Balb/C) and Toxicity (Rats): Biomanguinhos (Rio de Janeiro, Brazil).
- TB aerosol challenge (Guinea Pig): Colorado State University (USA)
- Phase 1/2 and 3: Brazil

Brazil – epidemiological context

Revista da Sociedade Brasileira de Medicina Tropical

Journal of the Brazilian Society of Tropical Medicine Vol.:57 | (e00203-2024) | 2024

Review Article

The greatest Dengue epidemic in Brazil: Surveillance, Prevention, and Control

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FIGURE 1: Dengue epidemics in Brazil between 2000 and 2024. The historical series shows probable cases of dengue/100,000 (gray) and probable deaths of dengue/100,000 inhabitants (red) recorded by month in each year. The small black bars indicate the probable cases of dengue/100,000 in January for each year. The longer black bar indicates the decades. The vertical dotted lines mark the first 4.5 years of each decade.

Key Elements Considered for Introducing Dengue Vaccination

Epidemiological Burden:

High incidence and prevalence of dengue cases. Significant morbidity and mortality rates.

Economic Impact:

Costs associated with healthcare and hospitalization. Economic burden due to loss of productivity.

Vaccine Efficacy and Safety:

Clinical trial results demonstrating efficacy across 4 serotypes Safety profile and side effect management, including sufficient follow-up time to assess antibodydependent enhancement.

Cost-Effectiveness:

Analysis comparing vaccination costs to treatment and outbreak management costs.

Public Health Infrastructure:

Capability to implement widespread vaccination programs. Cold chain and logistics for vaccine storage and distribution.

TAK-003 (TAKEDA)

Approval in The Brazilian Health Regulatory Agency (Anvisa)

- 02-March-2023
- Age: 4-60 years
- · Well tolerated and and has a good safety profile
- High efficacy to prevent diseases and hospitalization
- Risk Management Strategy: Continuous monitoring will be implemented to assess the efficacy and safety profiles against dengue serotypes 3 particularly in individuals who are seronegative

Incorporation of the TAK-003 into the Brazilian Immunization Program

National Commission for the Incorporation of Technologies into the Unified Health System DENGUE REPORT - DECEMBER 2023

Final Decision: "The CONITEC has endorsed the inclusion of the vaccine into the Brazilian Immunization Program with the recommendation to conducted effectiveness and safety studies in real-world settings, focusing on serotypes 3 and 4"

Source: 1. https://consultas.anvisa.gov.br/#/pareceres/q/?nomeProduto=QDENGA ; 2- https://www.gov.br/conitec/pt-br/midias/relatorios/2023/20231226_relatorio_871_vacina_dengue.pdf

		Detalhe do Produto: QDENG	A		
Nome da Empresa Detentora do Registro	TAKEDA PHARMA LTDA.	CNPJ	60.397.775/0001-74	Autorização	1.00.639-8
Processo	25351.389376/2021-36	Categoria Regulatória	Biológico	Data do registro	02/03/2023
Nome Comercial	QDENGA	Registro	106390307	Vencimento do registro	03/2033
Princípio Ativo	VACINA DENGUE 1, 2, 3 E 4	(ATENUADA)	Medicamento de referência	¥	
Classe Terapêutica	VACINAS			ATC	
Parecer Público	Acesse aqui			Bulário Eletrônico	Acesse aqui



Dengue Vaccine campaign

• Total dose in 2024: 6.571.334

 521 from 5570 Municipalities of Brazil (9%) Urban areas with populations over 100,000 (Higher burden of the disease)
High dengue incidence over the past decade (Higher soroprevalence)
Predominant dengue serotype 2 in 2024 (TAK-003 has a High efficacy in seronegative patients)
Highest number of cases in 2023/2024 (EW-27/2023 to EW-02/2024).

• **Target Age Group:** 10-14 years old Higher risk for hospitalization Vaccines are offered at community level in the basic health unit

• Total dose in 2025: 9.100.000

NOTA TÉCNICA Nº 7/2024-CGFAM/DPNI/SVSA/MS NOTA TÉCNICA Nº 8/2024-CGICI/DPNI/SVSA/MS

Zé Gotinha - Symbol of the Brazilian Immunization

Program

Anaphylaxis

Table 1

Description of Adverse Events Following Immunization (AEFI) cases by hypersensitivity diagnoses related to the attenuated tetravalent dengue vaccine, March 1, 2023, to March 11, 2024, Brazil. (Total doses administered: 380,358).

Diagnoses	n	Notification rate per million doses administered
Hypersensitivity reactions	95	249.8
Late Hypersensitivity	10	26.3
Immediate		
Hypersensitivity		
Non-Anaphylaxis	61	160.4
Anaphylaxis*	24	63.1
Anaphylactic Shock	3	7.9

 * Anaphylaxis was defined according to the criteria of the Brighton Collaboration and WAO: World Allergy Organization.

Table 2

Description of an aphylaxis cases reported for the attenuated tetravalent dengue vaccine, March 1, 2023, to March 11, 2024, Brazil. (N = 24).

Variables	n	%
Gender		
Female	13	54.2
Male	11	45.8
Age (years)		
Median in years (range)	10.5	(4–38)
Co-administered vaccines		
No	20	83.3
Yes	4	16.7
Outcome*		
Recovery without sequelae	11	45.8
Under observation	8	33.3
Not specified	5	20.8
History of previous allergy		
No	3	12,5
Yes	2	8,3
Not specified	19	79.2
Onset of symptoms time		
Median in minutes (range)	28.5	(3-160)
≤15 min	10	41.7
16 to 30 min	5	20,8
> 30 min	9	37.5
Brighton certainty level [†]		
Level 1	12	50.0
Level 2	0	-
Level 3	12	50.0
Use of adrenaline		
Yes	11	45.8
No	13	54.2

*As documented in the notification within Brazil's AEFI information system. [†]Level 1 of Brighton represents the highest level of diagnostic certainty that a reported case is indeed a case of anaphylaxis; levels 2 and 3 are progressively lower levels of diagnostic certainty.

https://doi.org/10.1016/j.vaccine.2024.126407

Anaphylaxis

- Type I hypersensitivity reaction (mediated by IgE antibodies)
 - Multisystem involvement
 - Variable clinical spectrum
 - Potentially fatal
 - Rapid onset and progression
- Estimated incidence of postvaccination anaphylaxis
 - Vaccination in general: 1 per 100,000 to 1 per 1,000,000 doses administered
 - Vaccine Safety Datalink (VSD-CDC) study: 0.13 per 100.000 doses administered

Incidence rate of anaphylaxis (A) per applied dose (DA) 100,000 doses in Brazil

Vaccine	DA	Α	Rate per 100,000
Seasonal influenza			
vaccine	135.344.321	3	0.002
Measles vaccine	357.271	1	0.28
DTP vaccine	10.157.454	0	-
Meningococcal C vaccine	14.826.616	3	0.02
Pneumococcal 23 vaccine	654.479	1	0.46
SCR vaccine	16.845.804	1	0.0059
Yellow fever vaccine	16.833.464	1	0.0059
AstraZeneca/Fiocruz			
vaccine	117.597.423	21	0.018
Coronavac-			
Sinovac/Butantan vaccine	76.235.510	14	0.018
Pfizer (Comirnaty) vaccine	153.684.896	15	0.01
Covid-19 - Janssen-Cilag			
vaccine	22.049.722	1	0.004
Pfizer (Comirnaty)			
pediatric vaccine	13.102.289	4	0.031

McNeil et. al. Allergy Clin Immunol, 2016

Obrigado Gracias Thank you

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