

# CONSOLIDATED REGIONAL AND GLOBAL INFORMATION ON ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI) AND OTHER UPDATES

Fifty-second report

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## Dengue Vaccine

### Brazil (Anaphylaxis reports)

From 1 March 2023 to 12 August 2024, 3,404,877 doses of attenuated dengue vaccine were administered in Brazil. Of these, 2,630,892 (77.3%) were first doses and 773,985 (22.7%) were second doses. In the same period, 3,068 AEFI notifications were recorded, equivalent to 90.1 notifications per 100,000 doses administered. Of these, 227 (7.4%) corresponded to serious AEFI. One fatal outcome was recorded, which was evaluated and classified with causality C (coincident) by the Interinstitutional Pharmacovigilance Committee, concluding that the death was related to a pre-existing condition of severe cystic fibrosis.

A total of 501 cases of AEFI were reported (14.7 per 100,000 doses administered) with terms suggestive of hypersensitivity reactions and anaphylaxis. Of these, 388 (77,4%) were classified as immediate hypersensitivity and 113 (22,6%) as delayed hypersensitivity. Of the cases of immediate hypersensitivity, 124 (32.0%) were anaphylactic reactions (36.4 per million doses administered). No deaths from anaphylactic reactions have been reported to date. Of the cases of anaphylaxis following dengue vaccination, 117 cases (94.4%) occurred after the first dose, with a median age of 11 years (Q1: 10, Q3: 11.5) and 75 (60.5%) were female; Only five cases (10.5%) had a history of known allergies and 33 (26.6%) had comorbidities. The median time between vaccination and symptom onset was 25 minutes (range: 15-40 minutes), and in 43 cases (34.7%) symptoms began 15-30 minutes after vaccination.

Source: Departamento do Programa Nacional de Imunizações, Department of Health Surveillance and Environment, Ministry of Health. Informe: Monitoramento da segurança da vacina dengue atenuada, SE 9 de 2023 à SE 37 de 2024, Brasil. Updated 26 October 2024. Available from: https://www.gov.br/saude/pt-br/vacinacao/esavi/monitoramento-dos-eventos/2024/informe-monitoramento-da-seguranca-da-vacina-dengue-atenuada-se-9-2023-a-se-37-2024.pdf/view.

## COVID-19 Vaccines

### Colombia

In January, a descriptive study was published with the objective of analyzing the performance of the surveillance system for AEFIs related to COVID-19 vaccines in Colombia, using the pharmacovigilance indicators suggested by the World Health Organization in WHO pharmacovigilance indicators: a practical manual for the assessment of pharmacovigilance systems (2019).[1] Data were collected from the National Institute for Drug and Food Surveillance (INVIMA), the National Institute of Health (INS), the Ministry of Health and Social Protection (MSPS), and the Institute for the Assessment of Health Technologies (IETS), between February 2021 and September 2023. Structural, process, and impact indicators were evaluated.

**Process indicators**
Between 2021 and 2023, 84,223,063 doses were administered and 6,935 AEFIs were reported (73.54 per 100,000 doses). The notification rate increased from 1.88 in 2022 to 2.21 in 2023.

- 97.37% of AEFIs were not serious.
- Female:male ratio: 2:1, with higher incidence in 18-29 year-olds.
- Higher incidence after the second dose, except for AstraZeneca, which had more cases after the first dose (83.19 per 100,000 doses).
- 58.08% of severe AEFIs (945/1 627) had a causality analysis, 0.8% reviewed by the National Committee.

**Impact indicators**
Twenty-eight possible signals were identified, and four (14.29%) met the evaluation criteria.

The study had limitations in data collection, which required interviews with technical personnel. Although the PAHO indicators were useful, their sensitivity and specificity were not evaluated, so it is recommended that a weighting system be developed.

Source: Saza-Londoño W, Pinzón-Fajardo DY, Urrea-Duque MV, Pinzón-Niño EL, Sánchez-León EM, Urieles-Sierra KA, et al. Análisis del sistema de vigilancia de los ESAVI por vacunas contra la COVID-19 en Colombia, 2021-2023. Rev Panam Salud Publica, 2025:49;e2. https://doi.org/10.26633/RPSP.2025.2

[1] World Health Organization. (2019). WHO pharmacovigilance indicators: a practical manual for the assessment of pharmacovigilance systems. World Health Organization. https://www.who.int/publications/i/item/9789241508254.License: CC BY-NC-SA 3.0 IGO.

## COVID-19 Vaccines

### Epidemiology of Febrile Seizures During the COVID-19 Pandemic: A Canadian Immunization Monitoring Program-Active (IMPACT) Study

A descriptive observational study based on active surveillance data collected by the Canadian Immunization Monitoring Program Active (IMPACT) was published on 18 February. The study objective was to describe the epidemiology of febrile seizure in children and its possible association with viral infections and vaccination during periods when the Delta and Omicron variants of SARS-CoV-2 were circulating.

The population included children under 7 years of age who visited emergency services or were hospitalized in 12 IMPACT centers, representing approximately 50% of pediatric beds in Canada.

Febrile seizure was defined in children 0–<7 years old who visited an emergency service or were hospitalized at an IMPACT center with a measured temperature ≥38.0 °C and physician diagnosis of focal or generalized seizure, febrile seizure or status epilepticus (seizures lasting ≥30 minutes or multiple seizures without recovery in between).

Daily hospital admissions and emergency room visit lists were screened for febrile seizure cases meeting the case definition by trained nurse monitors using standard terms, complemented by searches using the ICD-10 coding system. The Brighton Collaboration case definition (BCCD) for generalized seizure was applied, determining levels of diagnostic certainty based on clinical documentation. Cases of reported focal seizure were excluded.

Between 1 August 2021 and 31 December 2022, 3,367 cases of febrile seizure were reported, 649 (19.3%) of them requiring hospitalization. Of the total cases, 156 (5%) had laboratory-confirmed acute SARS-CoV-2 infection, 363 (11%) had non-SARS-CoV-2 infection, and 107 (3%) occurred as AEFIs (vaccinated within 15 days before presentation). Of the 107 cases of febrile seizures that met the reporting interval for an AEFI, 71 were temporally associated with the MMRV (measles, mumps, rubella, and varicella) vaccine (66.4%); followed by DTaP-containing vaccines (diphtheria, tetanus, and acellular pertussis), with 13 cases (12.1%); and MMR (measles, mumps, and rubella), with eight cases (7.5%). The remaining 15 cases (14%) included events linked to other vaccines or unspecified situations, including 14 cases (13.1%) with laboratory-confirmed SARS-CoV-2 or other viral agent (such as influenza or enterorhinovirus), and five cases presenting within 3 days of COVID-19 vaccination, none of which required hospitalization or had confirmed infection.

In general, febrile seizures were more frequently associated with infections than with vaccination. The median age was 1.8 years and most were male (57.7%). Eighty-one percent of cases occurred during the Omicron period. A significant proportion of generalized seizure cases met the BCCD, especially among those hospitalized.

The authors conclude that febrile seizures were more frequently associated with infection than vaccination. Febrile seizure continues to be a major cause of medical attention in young children, particularly during periods of high viral circulation. The authors highlight the importance of its surveillance as an adverse event of special interest in the context of the introduction of new pediatric vaccines.

Source: Top, Karina et al. Epidemiology of febrile seizures during the COVID-19 pandemic: a Canadian immunization monitoring program-active (IMPACT) STUDY. The Pediatric Infectious Disease Journal ():10.1097/INF.0000000000004759, February 18, 2025. | DOI: 10.1097/INF.0000000000004759

## Respiratory Syncytial Virus (RSV) Vaccine

### Efficacy, immunogenicity, and safety of a maternal RSV vaccine (RSVPreF3-Mat): Final results of phase 3 trial

In January, the final results of a phase 3 clinical trial evaluating the efficacy, immunogenicity, and safety of a maternal RSV prefusion F protein-based vaccine (RSVPreF3-Mat) were published.

The study was conducted in 24 countries of different income levels, with pregnant women aged 18-49 years with singleton and uncomplicated pregnancies at 24-34 weeks' gestation at the time of vaccination. Participants were randomized 2:1 to receive one dose of RSVPreF3-Mat (n=3,557) or placebo (n=1,771).

The objectives of the study were to:

1. Assess the efficacy of RSVPreF3-Mat vaccine in the prevention of:
    - Any medically assessed RSV-associated lower respiratory tract disease (MA-RSV-LRTD) in infants until 6 months post-birth.
    - Severe MA-RSV-LRTD in infants until 6 months post-birth.
    - Hospitalization for RSV in infants up to 6 months post-birth.

2. Assess the immunogenicity of RSVPreF3-Mat by measuring:
    - RSV-A neutralization titers in mothers and infants.
    - Efficacy of transplacental transfer of antibodies.
    - Persistence of antibodies in infants up to 6 months post-birth.

3. Evaluate the safety of RSVPreF3-Mat, including:
    - Adverse events in mothers up to 6 months postpartum.
    - Adverse events in infants up to 12 months post-birth.
    - Incidence of preterm birth in the vaccine group compared to the placebo group.

The results showed that the vaccine had an efficacy of 65.5% (95% CI; 37.5%-82.0%) in the prevention of any MA-RSV-LRTD, increasing to 69.0% (95%CI; 33.0%-87.6%) in cases of severe disease.

A reduction of 50.1% (95%CI;-3.6%-75.8%) in RSV hospitalizations was also observed, the latter figure having a wide confidence interval.

The protection conferred by the vaccine decreased over time and showed differences according to region: in high-income countries, efficacy reached 75.9% (95% CI;46.1%-91.5%), while in low- and middle-income countries it was 47.8%(95% CI;-25. 8%-77.3%).

Immunogenicity results showed that the vaccine induced a strong response in mothers, allowing efficient transplacental transfer of antibodies that persisted in infants until at least 6 months post-birth.

An increased risk of preterm birth was identified in the vaccinated group (6.8%) compared to the placebo group (4.9%), leading to discontinuation of enrollment and vaccination in the trial. Despite this, subsequent analysis showed no other safety signals of concern, and adverse events were similar in both groups.

The authors conclude that the study findings suggest that maternal vaccination with RSVPreF3-Mat could be an effective tool to reduce the risk of severe RSV in infants. The rate of preterm births created uncertainty about the safety of the intervention. As a result, vaccine development was interrupted. Further research is required to evaluate the benefit-risk ratio of maternal immunization against RSV.

Source: Banooni P, Gonik B, Epalza C, Reyes O, Madhi SA, Gomez-Go GD, et al. Efficacy, Immunogenicity, and Safety of an Investigational Maternal Respiratory Syncytial Virus Prefusion F Protein-Based Vaccine. Clin Infect Dis. 2025 Jan 29;80(1):1-10. doi:10.1093/cid/ciaf033.

## Dengue Vaccine

### Immunogenicity, safety, and efficacy of a tetravalent dengue vaccine in children and adolescents: an analysis by age group.

On 15 January, an exploratory analysis was published evaluating the immunogenicity, safety, and efficacy of a live-attenuated tetravalent dengue vaccine (TAK-003) in a randomized, placebo-controlled, phase 3 study (DEN-301, NCT02747927) of 20 099 participants (vaccine group, n=13,401); placebo group, n=6698) aged 4-16 years, stratified by age (4-5 years, 6-11 years, and 12-16 years) and endemic region (Asia or Latin America). Participants were randomly assigned in a 2:1 ratio to receive two doses of TAK-003 or placebo, administered three months apart.

Participants (or their parents/guardians) were contacted at least weekly to monitor for fever and possible dengue cases, which were confirmed by serotype-specific RT-PCR. Hospitalization and case management followed local clinical protocols.

The objectives of the study were to:

1. Assess the efficacy of TAK-003 in the prevention of virologically confirmed dengue (VCD) and hospitalized VCD from the first dose to 57 months after vaccination.
2. Assess immunogenicity in terms of geometric mean titers (GMT) of serotype-specific neutralizing antibodies and seropositivity rates.
3. Assess safety, including solicited and unsolicited adverse events, serious adverse events (SAEs), and discontinuations and deaths related to adverse events.

The results were as follows:

1.1 Vaccine efficacy (VE) against VCD by age group:

- 43.5% (CI 95%: 25.3% - 57.3%) in children 4-5 years of age
- 63.5% (CI 95%: 56.9% - 69.1%) in children 6-11 years of age
- 67.7% (CI 95%: 57.8% - 75.2%) in adolescents 12-16 years of age

1.2 Efficacy against hospitalized DVC:

- 63.8% (CI 95%: 21.1% - 83.4%) in children 4-5 years of age
- 85.1% (CI 95%: 77.1% - 90.3%) in children 6-11 years of age

2. Immunogenicity

- Geometric mean titers (GMTs) remained elevated for all four serotypes up to ~4 years post-vaccination, with no significant differences between age groups.
- In seronegative participants, there were no clear differences in post-vaccination GMTs between age groups, although some decline in antibody was observed over time, especially against DENV-2.
- In HIV-positive participants, GMTs were highest in older age groups and lowest at 4-5 years. Despite the post-vaccination decline, GMTs remained above placebo levels throughout the study.
- Tetravalent seropositivity rates were high one month after the second dose and maintained through month 51, with higher rates in baseline seropositive participants.

3. Safety results:

- There were no significant differences in adverse events between age groups, nor in serological status. Serious adverse events were reported in 4.7%-6.9% of participants, the most common being gastrointestinal disorders, infections, and injuries.
- There were no deaths in the 4-5 year-old group; 11 deaths in the 6-11 year-old group; and 12 deaths in the 12-16 year-old group. None were considered vaccine-related.

The authors concluded that TAK-003 would be effective in preventing dengue in children and adolescents aged 4-16 years in endemic regions. Efficacy was lower in the 4-5 year-old group, possibly due to serotype distribution, small sample size, and vaccine efficacy by serotype, all of which should be considered in benefit-risk evaluations in this age group.

Source: Source: Borja-Tabora C, et al. Immunogenicity, Safety, and Efficacy of a Tetravalent Dengue Vaccine in Children and Adolescents: An Analysis by Age Group. Clin Infect Dis. 2025 Feb 5;80(1):199-206. doi: 10.1093/cid/ciae369.

## Ebola Virus and Sudan Virus Vaccine

### Safety and immunogenicity of a bivalent Ebola virus and Sudan virus ChAdOx1 vectored vaccine in adults in the UK: an open-label, non-randomized, first-in-human, phase 1 clinical trial.

On 5 February, a phase 1 study was published, evaluating the safety and immunogenicity of a non-replicating single-adenoviral vaccine (ChAdOx1 biEBOV) encoding both Ebola virus and Sudan virus glycoproteins, these two species being the main Orthoebolavirus species responsible for most Ebola disease outbreaks and cases.

This open-label, non-randomized, dose-escalation clinical trial was conducted in Oxford, UK, between 11 November 2021 and 7 April 2022. Twenty-six healthy volunteers between 18 and 55 years of age, without significant comorbidities or previous exposure to adenoviral vaccines, were divided into three groups according to the dose administered: low ($5 \times 10^9$ viral particles (pv)), medium ($2.5 \times 10^{10}$ pv) and high ($5 \times 10^{10}$ pv), all administered intramuscularly. Subsequently, the protocol was amended to administer a second dose to a subgroup of the high-dose group 12 weeks after the first dose.

Primary outcome measures included solicited adverse events (monitored in a predefined manner) and unsolicited adverse events (reported without being specifically requested), changes in laboratory measures, and serious events or events of special interest; Secondary outcome measures involved analysis of the humoral and cellular immune response against the glycoproteins of both viruses.

The results showed that 65% of the participants reported local adverse events and that 88% reported systemic events after the first dose and 71% after the second dose.

All events were mild or moderate, with no serious effects or serious adverse reactions, although one case of transient thrombocytopenia and mild lymphopenia was identified in one participant. In the high-dose group, a single $5 \times 10^{10}$ pv dose elicited seropositivity to Ebola virus in 100% of participants and seropositivity to Sudan virus in 86%, with an enhanced antibody response after the second dose.

The authors conclude that the ChAdOx1 biEBOV vaccine would be safe, well tolerated, and able to induce a robust immune response, especially with a two-dose schedule.

Source: Jenkin D et al. Safety and immunogenicity of a bivalent Ebola virus and Sudan virus ChAdOx1 vectored vaccine in adults in the UK: an open-label, non-randomised, first-in-human, phase 1 clinical trial. Lancet Microbe. 2025 Feb 5:101022. doi: 10.1016/j.lanmic.2024.101022. Epub ahead of print. PMID: 39922207.

## Herpes Zoster Vaccine

### Surveillance on the coverage of herpes zoster vaccine and post-marketing adverse events in Jiangsu province, China

On 19 January, a retrospective observational study conducted in Jiangsu province, China, was published with the objective of analyzing herpes zoster (HZ) vaccination coverage in older adults and the incidence of adverse events following immunization (AEFI).

The analysis included vaccination data for the year 2023 in persons aged 50 years and older, and AEFI reports from 2020 to 2023, collected through the Jiangsu province vaccination management system and China's national AEFI information management system.

The results showed a low coverage rate (0.19%); about 20% of those vaccinated (12 821 persons) did not complete the two-dose schedule.

Between 2020 and 2021, a total of 17 863 doses of the vaccine were administered, and 43 AEFIs were reported, for a reporting rate of 240.7 per 100,000 doses. During 2022-2023, 107 858 doses were administered and 217 AEFIs were reported, for a reporting rate of 201.2 per 100,000 doses.

The majority of AEFIs were mild and common; in over 55% of cases they occurred within 30 minutes post-vaccination. The most frequent symptoms were fever, allergic eruptions, drowsiness, and reactions such as redness and induration at the injection site. Only 1.5% corresponded to rare reactions and 0.4% to coincidental events.

The authors conclude that, despite the favorable safety profile of the vaccine, its low coverage indicates the need to conduct further active surveillance and promote vaccination in this population.

Source: Xiang Sun et al. Surveillance on the coverage of herpes zoster vaccine and post-marketing adverse events in Jiangsu province, China, Human Vaccines & Immunotherapeutics, 21:1, 2449714, DOI: 10.1080/21645515.2025.2449714

## Meningococcal Vaccines

### Safety and immunogenicity of a pentavalent meningococcal conjugate vaccine targeting serogroups A, C, W, Y, and X when co-administered with routine childhood vaccines at ages 9 months and 15 months in Mali.

On 11 March, a double-blind, randomized, controlled, non-inferiority, phase 3 trial was published, assessing the safety and immunogenicity of a pentavalent meningococcal conjugate vaccine (NmCV-5) targeting serogroups A, C, Y, W, and X. This was compared with an already licensed quadrivalent conjugate vaccine (MenACWY-TT) when co-administered with routine childhood vaccines.

The study was conducted at the *Centre pour le Développement des Vaccins*, in Bamako, Mali. A total of 1325 children between 9 and 11 months of age, who had completed their childhood Expanded Program on Immunization (EPI) vaccination schedule, participated. The study was conducted between March 2022 and February 2023.

Participants were randomly assigned to receive a meningococcal vaccine at 9 or 15 months of age. In each age group, children were again randomized (2:1) to receive either NmCV-5 or MenACWY-TT. The vaccines were co-administered with other routine vaccines (measles-rubella and yellow fever at 9 months, or a second dose of measles-rubella at 15 months). Parents and investigators were masked to meningococcal vaccine assignments.

The main objective was to compare the proportion of children who achieved a seroprotective response with serum bactericidal antibody titers ≥1:8 at 28 days post-vaccination. A predefined non-inferiority margin of -10% was used. In this study, it was established that the NmCV-5 vaccine was considered non-inferior if its efficacy was no more than 10% lower than that of MenACWY-TT. Safety was assessed for 6 months post-vaccination.

In the 9-month-old group, 373 children received NmCV-5 and 191 received MenACWY-TT. In the 15-month age group, 367 received NmCV-5 and 182 received MenACWY-TT. The differences in seroprotection ratio between NmCV-5 and MenACWY-TT (compared to the worst result of MenACWY-TT) were as follows:

- At age 9 months :
  - Serogroup A: 0.0% (CI 95%: -1.0 to 2.0)
  - Serogroup C: -0.5% (-2.3 to 1.9)
  - Serogroup W: -3.0% (-6.3 to 0.8)
  - Serogroup Y: -3.0% (-5.4 to -0.4)
  - Serogroup X: +2.3% (0.3 to 4.7)

- At age 15 months:
  - Serogroup A: +0.8% (-0.6 to 3.7)
  - Serogroup C: -0.8% (-3.3 to 2.5)
  - Serogroup W: +0.3% (-1.8 to 3.5)
  - Serogroup Y: +1.4% (-0.6 to 4.8)

- Serogroup X: +1.9% (0.0 to 4.4)

In all cases, the NmCV-5 vaccine was non-inferior to MenACWY-TT, meeting the main study criterion. In terms of safety, six serious adverse events were recorded, but none were considered to be vaccine-related.

The authors concluded that a single dose of NmCV-5 vaccine, co-administered with routine childhood vaccines, would be safe and elicited an immune response not inferior to that of the licensed quadrivalent vaccine. This finding would support the use of NmCV-5 to extend protection against multiple serogroups, including serogroup X, particularly in high-incidence regions.

Source: Diallo, Fatoumata et al. Safety and immunogenicity of a pentavalent meningococcal conjugate vaccine targeting serogroups A, C, W, Y, and X when co-administered with routine childhood vaccines at ages 9 months and 15 months in Mali: a single-centre, double-blind, randomised, controlled, phase 3, non-inferiority trial. The Lancet, Volume 405, Issue 10484, 1069 - 1080

## COVID-19 Vaccines

### WHO recommendations on the antigen composition of COVID-19 vaccines

On 23 December 2024, the WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) updated its recommendations, which are summarized below.

- Given the breadth of immune responses demonstrated by monovalent JN.1 lineage vaccines against circulating variants, TAG-CO-VAC recommends maintaining the current antigen composition of COVID-19 vaccines: a monovalent JN.1 lineage variant (NextStrain: 24A, GenBank: PP298019, GISAID: EPI_ISL_18872762).

- Other approaches that demonstrate broad and robust neutralizing antibody responses against currently circulating JN.1 descendent lineage variants could also be considered.

The TAG-CO-VAC will continue to closely monitor the genetic and antigenic evolution of SARS-CoV-2 variants, immune responses to SARS-CoV-2 infection and COVID-19 vaccination, and the performance of COVID-19 vaccines against circulating variants. The TAG-CO-VAC will reconvene in six months to evaluate the antigenic composition of COVID-19 vaccines.

For more information, see: https://www.who.int/news/item/23-12-2024-statement-on-the-antigen-composition-of-covid-19-vaccines

### Statement by the WHO Technical Advisory Group on COVID-19 Vaccine Composition

On 25 March, WHO released a statement from the Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC), updating guidance to the scientific community and vaccine manufacturers on what data should be generated prior to the next decision-making meeting, in May 2025.

TAG-CO-VAC will review data on the genetic evolution of SARS-CoV-2 and the antigenic characteristics of previous and current circulating variants; estimates of the effectiveness of currently approved COVID-19 vaccines; animal and human studies demonstrating the breadth and durability of immune responses elicited by currently authorized vaccines, as well as candidate vaccines in development, among other data.

Additional information is available at: https://www.who.int/news/item/25-03-2025-types-of-data-requested-to-inform-may-2025-covid-19-vaccine-antigen-composition-deliberations

## Dengue Vaccine

### The Brazilian Health Regulatory Agency reports on the evaluation of the single-dose dengue vaccine.

On 21 January, the Brazilian Health Regulatory Agency (ANVISA) reported progress in the evaluation of the single-dose dengue vaccine being developed by the Butantan Institute of Brazil.

ANVISA authorized the continuous submission of documentation by the manufacturer, this being the step prior to application for official registration. This procedure was established by the working group created to monitor and carry out ANVISA's actions to combat the dengue health emergency.

Initially, the Butantan Institute presented administrative documents and general information on clinical and non-clinical studies. The second deliverable consisted of information on the package insert and labeling (information for patients and health professionals), pharmacovigilance data, risk management plan, clinical overview, benefit-risk analysis report, and reports on relevant controlled clinical studies. The third set of information, submitted in December 2024, included updates on some documents delivered in previous packages, as well as new documents (quality summaries and non-clinical and clinical data) in common technical document (CTD) format.

ANVISA estimates that the review process will take about 90 days from the date of the last data submission.

Additional information is available at: https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2025/atualizacao-sobre-analise-da-vacina-de-dose-unica-contra-dengue

## Chikungunya Vaccine

### The European Medicines Agency authorizes a new chikungunya vaccine for adults and adolescents from 12 years of age

On 31 May, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) recommended granting a marketing authorization in the European Union (EU) for Vimkunya, a chikungunya vaccine. The first EU vaccine to protect adolescents aged 12 years and older against chikungunya, Vimkunya is also indicated for adults and is administered in a single dose.

The recommendation was based largely on data from two placebo-controlled studies. Study 1 evaluated the immunogenicity and safety of the vaccine in 3,258 people aged 12 to 64 years; study 2 evaluated 413 older adults. Immune response was evaluated in 3,355 participants (2748 with Vimkunya and 607 with placebo). Eight days after vaccination, the difference in seroresponse rates between those vaccinated with Vimkunya and those receiving placebo in

study 1 was 46.1%. This rose to 96% at day 15, 96.6% at day 22, and 84% at day 183. In Study 2, the difference in seroresponse rates was 79.5% at day 15, 86.2% at day 22, and 74.4% at day 183.

The licensee will conduct a post-authorization efficacy study to confirm the effectiveness of Vimkunya in preventing chikungunya in adolescents and adults.

The safety profile of Vimkunya is based on pooled data from five clinical studies with 3522 participants with a 6-month follow-up. The most common side effects reported were tiredness, headache, muscle pain, and pain at the injection site.

Additional information is available at: https://www.ema.europa.eu/en/news/new-chikungunya-vaccine-adolescents-12-adults

## Influenza Vaccine

### WHO recommendations announced for influenza vaccine composition for the 2025–2026 Northern Hemisphere influenza season

On 28 September, the World Health Organization (WHO) announced its recommendations for the composition of influenza vaccines for the 2025-2026 influenza season in the northern hemisphere:

- **Egg-based vaccines**
  - an A/Victoria/4897/2022 (H1N1)pdm09-like virus
  - an A/Croatia/10136RV/2023 (H3N2)-like virus
  - a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

- **Cell culture-, recombinant protein- or nucleic acid-based vaccines**
  - an A/Wisconsin/67/2022 (H1N1)pdm09-like virus
  - an A/District of Columbia/27/2023 (H3N2)-like virus
  - a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

- **Quadrivalent vaccines:** The recommendation for the B/Yamagata lineage component of quadrivalent influenza vaccines remains unchanged from previous recommendations:
  - a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

https://www.who.int/news/item/28-02-2025-recommendations-announced-for-influenza-vaccine-composition-for-the-2025-2026-southern-hemisphere-influenza-season

## Pneumococcal Vaccine

### EMA recommends authorization of Capvaxive, a pneumococcal polysaccharide conjugate vaccine (21-valent)

On 30 January, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) recommended marketing authorization for Capvaxive, a pneumococcal polysaccharide conjugate vaccine (21-valent) to prevent invasive disease and pneumonia caused by *Streptococcus pneumoniae* in persons 18 years of age and older.

Capvaxive will be available as a solution for injection in a prefilled syringe. The most common side effects of Capvaxive are pain at the injection site, fatigue, headache, and myalgia.

For more information, see:
https://www.ema.europa.eu/en/medicines/human/EPAR/capvaxive

## Yellow Fever Vaccine

### Chile's Public Health Institute updates contraindications and precautions for use of yellow fever vaccine

In January 2025, Chile's Institute of Public Health (ISP) announced new measures aimed at minimizing the risks of AEFI associated with the yellow fever vaccine.

The updated recommendations emphasize the need for caution in immunosuppressed persons and in adults over 60 years of age, due to the risk of serious diseases caused by the live attenuated virus contained in this vaccine.

The information was disseminated through the ISP's Pharmacovigilance Bulletin in order to enhance safe administration of this vaccine to vulnerable populations.

Additional information is available at: https://www.ispch.cl/wp-content/uploads/2025/01/BoletinFV2502-13012025A.pdf

## Vaccine Safety

### Summary of the report of the 4th joint meeting of the WHO Global Advisory Committee on Vaccine Safety (GACVS) and the Advisory Committee on Safety of Medicinal Products, 12-14 November 2024

The meeting addressed specific topics on vaccine safety, pharmacovigilance issues common to vaccines and medicines, and topics specific to medicines safety. The following is a brief summary of the presentations and recommendations from the vaccine-specific sessions.

- **Safety of the novel oral polio vaccine type 2 (nOPV2):** On 18 July 2024, the GACVS nOPV2 subcommittee met to review safety data from 10 March 2021 to 16 December 2023. A summary of the subcommittee's conclusions and recommendations was presented to GACVS. The subcommittee concluded from data from 35 countries, representing over 1 billion administered doses of nOPV2, that there was no evidence of any clusters or patterns of adverse event reports, either temporally or geographically, that would give rise to any unexpected safety concerns.

  GACVS recommended continued strong surveillance and reporting of AEFI, including emergencies related to circulating vaccine-derived poliovirus type 2 (cVDPV2).

- **Safety of Qdenga® (TAK-003) vaccine:** The Safety Committee recommended continued active surveillance for anaphylaxis, hypersensitivity, and other adverse events associated with Qdenga® in Brazil and in other regions where it is used. It also suggested supporting immunological studies by the manufacturer to identify possible triggers and immunological mechanisms (such as mast cell and basophil degranulation), as well as risk factors and biomarkers. It urged clear communication of risks to families and healthcare workers, training for healthcare workers in recognizing and managing anaphylaxis, and encouragement of routine reporting of adverse events to databases such as VigiBase. It recommended extending the post-vaccination observation time to allow for timely attention to severe reactions, and suggested that regulatory authorities collaborate with the manufacturer to review manufacturing and allergenicity issues. Emphasis was also placed on the importance of monitoring the clinical and epidemiological characteristics of dengue in vaccinated persons, especially to assess the risk of vaccine-associated enhanced disease (VAED), and of integrating vaccination information into national arbovirus surveillance and pharmacovigilance systems.

  The need to provide complete clinical information on severe cases and deaths following vaccination was emphasized, especially in the 30 days post-vaccination, including diagnosis to differentiate between vaccine and wild-type virus infections.

- **Safety of maternal vaccination against respiratory syncytial virus (RSV):** The maternal bivalent prefusion F RSV vaccine, RSVPreF (Abrysvo®, Pfizer) is authorized for use in more than 40 countries with different recommendations according to gestational age. The committees reviewed data from a placebo-controlled phase-3 clinical trial, in which a safety

signal related to preterm birth was detected. Although the rate was higher in vaccinated women, it was not statistically significant. There were geographic variations, with higher relative risks in Argentina and South Africa (statistically significant only in the latter). No imbalance was observed in high-income countries.

- **Safety of vaccination against RSV in older adults:** There are two licensed RSV vaccines for older adults: Abrysvo® and Arexvy® (GSK), which is not indicated for pregnant women. People over 65 years of age in the USA showed a 2-3 times increased risk of Guillain-Barré syndrome (GBS) after vaccination, although the absolute risk was low (less than 10 cases per million).

  Pfizer has planned four post-authorization safety studies on maternal vaccination with Abrysvo® (one in the EU and three in the U.S.) to evaluate birth outcomes and GBS, as well as its safety in high-risk groups such as immunocompromised pregnant women. These studies will continue until 2032.

  A study is also planned in four African countries, starting in 2025, to assess preterm births and low birth weight. It was recommended that local baseline rates be established to properly interpret safety data. Co-administration with other vaccines (such as influenza and COVID-19) and the importance of monitoring associated adverse events were also discussed.

- **Safety of malaria vaccines:** WHO recommends two vaccines to prevent *Plasmodium falciparum* malaria in children: RTS,S and R21/Matrix-M, currently used in 15 African countries.

  The RTS,S vaccine has demonstrated a favorable safety profile in clinical trials and during 46 months of the malaria vaccine implementation program (MVIP). No relevant safety signals or differences in mortality by sex were identified. Adverse effects were similar to the control group, with low incidence of febrile convulsions.

  The R21/Matrix-M vaccine has also shown an acceptable safety profile in several clinical trials. In the VAC078 trial, six serious, possible vaccine-related events (febrile convulsions) were reported, but with no associated deaths. In post-marketing surveillance in 12 African countries, few serious vaccine-related events were reported, although there are challenges, such as low reporting quality and limited resources.

  The Committee recommended strengthening post-marketing surveillance, allocating resources to investigate and assess causality, calculating adverse event rates, documenting programmatic errors, continuing to monitor clinical studies, including new populations in research, and ensuring a robust R21-PMS-01 study design.

- **Safety of mpox vaccines**: In September 2024, GACVS reviewed the available safety data, noting that the post-marketing data were consistent with those from previous clinical trials and showed favorable safety profiles in adults, but recommended close monitoring to detect safety signals.

WHO presented updates on the use and monitoring of vaccines in 13 affected African countries. The African Vaccine Regulatory Forum (AVAREF) assessed MVA-BN for emergency use. It concluded that, although the vaccine has great potential, robust data are lacking in key populations such as infants, children, pregnant women, and immunocompromised individuals, requiring continued surveillance.

Due to limited data in African populations during initial deployment, it was recommended that data collection be integrated with the vaccination process and surveillance systems be strengthened.

WHO developed a cohort event monitoring protocol to estimate:

- Incidence of AEFI in vaccinated persons.
- Frequency of common local and systemic reactions.

GACVS recommended the following:

- Support countries in identifying challenges and bottlenecks in safety surveillance.
- Ensure high-quality data, especially for off-label use (children, pregnant women, immunocompromised persons).
- Present data along with coverage information (rates in exposed populations).
- Actively use the WHO protocol to detect possible safety signals.
- Share data in a timely manner to enable pooling of safety data to facilitate rapid detection of risk signals.
- Expand the use of electronic tools to improve AEFI reporting.
  Strengthen specific risk communication on vaccine safety and keep communities informed.

- **Safety monitoring of medicines and vaccines in pregnant women and neonates**: The Committees were briefed on recent efforts to improve data quality and harmonize data collection for safety monitoring of medicines and vaccines in pregnant and breastfeeding women and neonates. This includes the results of a pilot study of the WHO minimum maternal and newborn health data sets (mMNHDS).

  The Committees discussed the importance of harmonizing the definitions and methods used in monitoring maternal and newborn health, as well as the use and improvement of existing data sources, such as electronic clinical records and pregnancy exposure registries. It was recommended that the mMNHDS be enhanced by developing an implementation strategy, including the mMNHDS in health registries, creating training materials for health professionals and data managers, and actively promoting its dissemination and use (both the core set and the catalogue data set).

Source: Weekly epidemiological record Relevé épidémiologique hebdomadaire 7 MARCH 2025, 100th YEAR / 7 MARS 2025, 100e ANNÉE No 10, 2025, 100, 75-86 http://www.who.int/wer

## WHO pharmacovigilance activities

In issue No. 10-2025 of the Weekly epidemiological record, on 7 March, WHO published information on pharmacovigilance activities, as summarized below.

- **"Smart" pharmacovigilance strategy:** WHO launched the Smart Safety Surveillance (3S) concepts in 2017 to guide regulators and immunization programs in resource-limited countries in the construction of pharmacovigilance systems.

  The Global Smart Pharmacovigilance Strategy builds on prior work done between WHO and countries to apply the 3S concepts of simplicity, speed, and sustainability, and on their application by the African Union during the COVID-19 pandemic.

  Its aim is to develop sustainable pharmacovigilance systems in all Member States through four principles: 1) leveraging previous efforts, infrastructure, and lessons learned; (2) adopting a risk-based approach and prioritization; 3) work-sharing and reliance; and 4) strengthening regulatory systems.

- **Monitoring new AESIs: harmonization of the AESI X case definition:** WHO is carrying out a collaborative project between the Safety Platform for Emergency Vaccines and the Brighton Collaboration, funded by the Coalition for Epidemic Preparedness Innovations, to develop a process for the rapid development of new case definitions for adverse events of special interest (AESI) ("AESI-X") in emerging safety signals.

  Usually, development of new case definitions takes about 18 months. The objective of this project is to create consensus around the rapid development of global case definitions for new AESI-X.

Source: WHO. Weekly epidemiological record. Weekly epidemiologic report.
7 MARCH 2025, No 10, 2025, 100, 75-86, available at http://www.who.int/wer.

# Influenza Vaccine

## WHO prequalifies trivalent influenza vaccine developed in Russia

On 5 March, WHO prequalified a trivalent seasonal influenza vaccine developed by the Saint Petersburg Scientific Research Institute of Vaccines and Serums of the Russian Federation, with Cuba's Center for State Control of Quality of Medicines (CECMED) as the regulatory authority of reference.

This vaccine is based on fractionated viruses, inactivated with beta-propiolactone. It is produced in chicken embryos and complies with WHO recommendations for the 2024 season in the southern hemisphere.

Additional information is available at: https://extranet.who.int/prequal/vaccines/p/influenza-seasonal-trivalent

## Respiratory Syncytial Virus (RSV) Vaccine

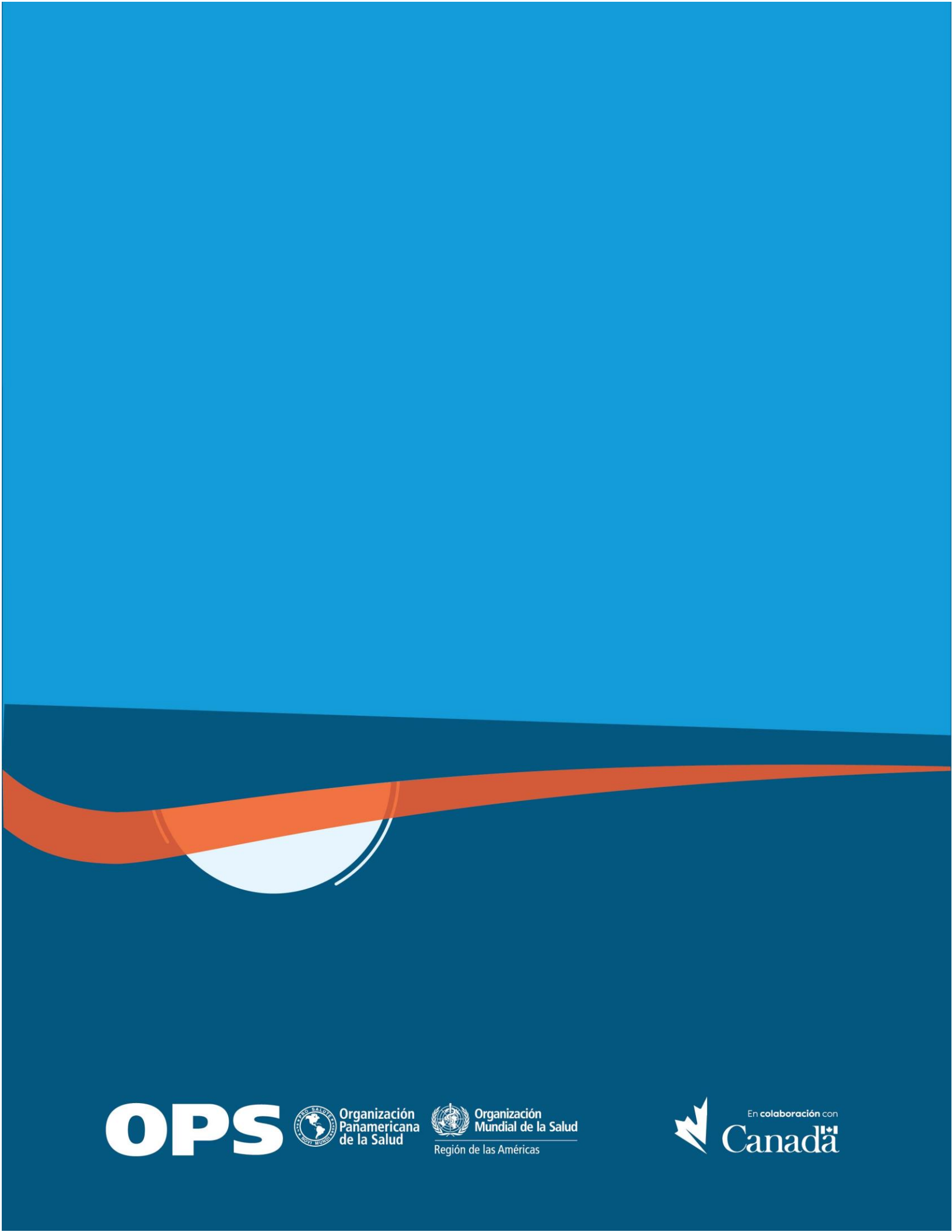
### WHO prequalifies first maternal respiratory syncytial virus vaccine

On 12 March, WHO prequalified the first maternal respiratory syncytial virus (RSV) vaccine. Its trade name is ABRYSVO® and it is manufactured by Pfizer, with the EMA as the regulatory authority of reference.

This prequalified maternal vaccine aims to prevent RSV-associated disease in infants during the first six months of life by transferring antibodies during gestation.

Additional information is available at: https://www.who.int/news/item/19-03-2025-who-prequalifies-first-maternal-respiratory-syncytial-virus-vaccine

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