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The Global Advisory Committee on Vaccine Safety (GACVS) was established in 1999 as an independent expert advisory body to the Director-General of the World Health Organization (WHO), as well as to WHO's collaborating centres and Member States, on policies and concerns related to the safety of vaccines. GACVS meets twice a year. The Forty-ninth meeting was held in hybrid mode on 27–28 November 2025.

The main objectives of the November 2025 GACVS meeting were to provide updates and to solicit feedback from the Committee on important vaccine safety and policy issues that had been identified since its meetings in November 2024 and May 2025.

COVID-19 current vaccine safety status and insights

Since 2021, GACVS has regularly reviewed the safety of COVID-19 vaccines, including through global pharmacovigilance data and dedicated reviews of myocarditis, pregnancy outcomes and other adverse events of special interest (AESI). The most recent updates reaffirmed that the benefits of vaccination outweigh the risks across all groups and advised continued monitoring for younger males and follow-up of persons who have reported vaccine-associated myocarditis.

Many individuals have received three or more doses of COVID-19 vaccine. Some adverse events – such as myocarditis – seem to occur mainly after the second dose of mRNA COVID- 19 vaccines. However, the outcomes were less severe in persons who developed myocarditis after vaccination compared to those unvaccinated and following infections, including SARS- CoV-2. Also, children under six months of age seem to be at higher risk of severe COVID-19 infection along with people over the age of 65 years. WHO has recommended continued vaccination for high-priority groups while acknowledging that gaps remain in the evidence on the safety of repeated dosing, long-term outcomes, and in subgroups such as children and pregnant women.

As of October 2025, for all COVID-19 vaccines, there were only 32 cases of perturbation of fetal development in EudraVigilance, of which most were reported with the original vaccine strains. An analysis of safety of protein-based COVID-19 vaccines by the Uppsala Monitoring Centre (UMC) showed that as of November 2025 there were almost 6 million reports for all COVID-19 vaccines in UMC's VigiBase. Of these, 16 548 reports concerned updated COVID-19 vaccine variants; among these were 5085 reports for updated protein-subunit vaccines. Around 17.4% of these were serious, and 50 reported a fatal outcome. Most reports were for the variant NVX CoV 2373 and most deaths were older vaccinees aged 75 years or more.

GACVS reviewed findings from the Scandinavian collaboration called SCOPE (**S**candinavian studies of **CO**vid-19 in **Pr**E**g**nancy). Findings showed no increased risk of adverse pregnancy, maternal or neonatal outcomes after mRNA COVID-19 vaccination in pregnancy in Denmark, Norway and Sweden. As of September 2025, the recommendation for vaccination in pregnancy was revised to apply only to specific high-risk groups.

A case-control study by SCOPE of all women with a miscarriage before 14 weeks and all women with a primary care-based confirmation of an ongoing pregnancy in the first trimester revealed no evidence of increased risk of early pregnancy loss after COVID-19

vaccination. A further investigation of COVID-19 infection and vaccination with mRNA vaccines during the first trimester of pregnancy and the risk of congenital anomalies, in a population-based cohort of 150 000 live-born infants in Denmark, Norway and Sweden, showed no increased risk of major congenital anomalies among infants whose mothers were vaccinated against COVID-19 during the first trimester.

A SCOPE investigation of the association between COVID-19 vaccination and several pregnancy outcomes among a cohort of almost 160 000 singleton pregnancies between January 2021 and 2022 in Norway and Sweden showed that vaccination against COVID-19 during pregnancy was not associated with any of the studied adverse pregnancy outcomes. In another SCOPE study of COVID-19 vaccination during pregnancy and the risk of severe postpartum haemorrhage, including more than 300 000 single-term deliveries in Denmark, Norway and Sweden, no evidence was found of an association between COVID-19 vaccination at any time during pregnancy and severe postpartum hemorrhage.

Finally, SCOPE investigated neonatal outcomes after COVID-19 vaccination with mRNA vaccine during pregnancy in a cohort of almost 200 000 infants in Norway and Sweden. Again, no increased odds were found of any adverse neonatal outcomes and neonatal mortality.

In consideration of the evidence presented, GACVS members agreed the following:

- *Repeated-dose safety (including boosters with variant-containing vaccines)*: Current evidence remains reassuring, with no new safety signals recently identified.
- *Safety of protein-based vaccines:* While generally well tolerated, reported adverse events include a proportion of serious individual case safety reports (ICSRs) in the global database. Several potential signals (e.g. tinnitus, antibody-dependent enhancement, thrombosis) require further evaluation. Additional data collection and analysis are therefore recommended to strengthen the evidence base for these vaccines.
- *Long-term outcomes of known risks (e.g. myocarditis, pregnancy outcomes)*: Myocarditis continues to occur predominantly in younger adults, typically with mild-to- moderate severity and most frequently after the second dose. Longer follow-up studies are needed to define the long-term prognosis and risks of revaccination in affected individuals.
- *Subgroup-specific safety (children, young males, older adults, immunocompromised individuals, pregnant women)*: Evidence to date shows no harmful effects of mRNA COVID-19 vaccination during pregnancy, including no increase in congenital anomalies, adverse perinatal outcomes, or some post-natal complications. Some studies even suggest lower odds of intracranial haemorrhage, cerebral ischaemia and neonatal mortality among infants of vaccinated mothers.
- *Safety monitoring during the transition to endemic COVID-19 vaccination*: Continued vigilance is required, particularly regarding more recent variant-adapted vaccines which remain safe on the basis of current data. Enhanced monitoring of protein-based vaccines is important given the comparatively limited evidence and the presence of identified risks that warrant further investigation.

Updated criteria for WHO Vaccine Safety Net members

As a result of the spread of false and misleading information about the dangers of vaccines and immunization, including via the Internet, WHO established the Vaccine Safety Net (VSN) in 2003 to guide people to a global network of websites providing reliable information on vaccine safety. In May 2025, GACVS established a Working Group on Vaccine Safety Communication to advise on strategies and policies for developing the VSN initiative and to recommend updates to the VSN criteria, with a focus on encouraging more websites in low- and middle-income countries (LMICs) to apply for membership.

Among the websites in the VSN, 32% are from government organizations, 30% from private organizations, 17% from academia, and 14% from professional associations. There are also members from international organizations and community groups.

As of November 2025, the VSN included 118 websites in 50 countries in 41 languages. Although most of those sites are in high-income countries, the situation is slowly changing – of the 17 new members who joined the VSN during the last three years, 10 (59%) were from LMICs.

The original VSN membership criteria were published in 2022. The reasons for updating them in 2025 were that: 1) some mandatory requirements have been difficult to meet in LMICs; 2) some terms required clarification; 3) identical criteria applied to both government and nongovernmental websites although these sites differed in funding and how they manage editorial content; and 4) some LMICs lack the capacity to meet certain technical requirements. By making modifications, it is anticipated that VSN can improve access and participation while still maintaining high standards.

GACVS members reviewed each of the current and proposed VSN criteria, noting the rationale for each. In general, members were supportive of both the proposed screening and formal criteria, with some modifications. It was agreed

that there should be 7 screening, 26 mandatory and 14 desired criteria and that 6 criteria should be mandatory for nongovernmental websites and desired for government websites. Modification of wording was requested and GACVS members agreed to review the revised text, followed by final approval via email.

Vaccines and autism

GACVS reviewed the evidence on vaccines Autism Spectrum Disorder (ASD) repeatedly between 2002 and 2012, consistently concluding that there was no credible evidence to support a causal link between vaccines and autism. Recent United States vaccine policy developments have, however, renewed discussion regarding vaccine safety and autism. Consequently, the Forty-ninth meeting of GACVS considered two recent evidence reviews – one on vaccines and ASD and one on aluminium as a vaccine constituent and serious conditions. While considering both reviews, Committee members focused their discussion on vaccines and autism in order to give strong advice on the relationship between vaccines and ASD.

The first review by Daniels et al., which included peer-reviewed scientific literature published between January 2010 and August 2025, focused on two questions: 1) "What is the relationship between thimerosal-containing vaccines and ASD?" and 2) "What is the relationship between vaccines and ASD?"[1]

The findings for both research questions underscored that the most methodologically rigorous primary research studies do not support any causal association between vaccines, thimerosal- containing or otherwise, and ASD. GACVS members drew particular attention to the low strength of evidence and the high risk of bias in the studies claiming links between thiomersal and ASD.

The Committee also considered a Canadian review of articles that have assessed possible links between aluminium, which has been used in vaccines for almost a century, and systemic diseases such as ASD. That study concluded that available evidence does not support causal associations between aluminium-adjuvanted vaccines and chronic or systemic diseases such as ASD. The overall benefit–risk balance favours continued use of aluminium-adjuvanted vaccines.

GACVS members expressed agreement with the conclusions of the two systematic reviews and associated presentations. The GACVS members also noted that the recently published high quality Danish study[2] on aluminium adjuvants and vaccines is important as a large population-based study conducted in approximately 1.2 million children born in Denmark between 1997 and 2018. This study concluded that cumulative aluminum exposure from vaccination was not associated with increased rates of any of the disorders assessed, including ASD.

Although the Daniels et al. study used ASD as an outcome, GACVS members stressed there was no systematic characterization of the different elements of ASD. With the development of expanded diagnostic criteria (i.e. more inclusive of a clinical spectrum) and general awareness, there has been an increase in the incidence of autism diagnoses, but this may not necessarily reflect an increase in the incidence.

GACVS specifically noted that several studies reporting an association with vaccines or their ingredients had been conducted by the same small number of authors, had studied overlapping populations and had critical risk of bias and very low quality.

Although WHO had already issued a statement on the subject, GACVS members proposed drafting a statement on their assessment of their conclusions. GACVS members subsequently worked on a statement which has since been published.[3]

AEFMI causality assessment

The importance of causality assessment of Adverse Events Following Maternal Immunization (AEFMI) is increasing as several new maternal vaccines are expected to be introduced in the near future. At its May 2025 meeting, GACVS reviewed WHO's draft AEFMI causality assessment methodology. At its Forty-ninth meeting, GACVS noted that causality categories B1/B2 and C2 have been clarified and improvements made to ensure that the methodology can adequately handle complex maternal–fetal outcomes and timing considerations. The usability, security and workflow of the AEFMI software have also been improved.

[1] Davis R, Ring E, Deeks S. Geneva: World Health Organization; 2025 (https://cdn.who.int/media/docs/default-source/medicines/pharmacovigilance/rev1_vaccines-autism-and-asd-evidence-review-2010-2025_12-dec7ab84d63-5110-4b2c-9882-19651446b8cd.pdf).

[2] Andersson NW et al. Aluminum-adsorbed vaccines and chronic diseases in childhood: a nationwide cohort study. Annals of Internal Medicine. 2025;178(10) (https://www.acpjournals.org/doi/10.7326/ANNALS-25-00997).

[3] Statement of the WHO Global Advisory Committee on Vaccine Safety (GACVS) on vaccines and autism, 11 December 2025. Geneva: World Health Organization (https://www.who.int/news/item/11-12-2025- statement-gacvs-vaccines-autism).

A user manual and practical training materials are being developed to support pilot implementation, and an electronic tool is being developed on the basis of the Brighton Collaboration's GAIA case definitions to support standardized diagnosis assessment. GACVS also emphasized the need for communication strategies aimed at technical audiences and the general public to build confidence in maternal immunization.

The generic AEFMI software was developed in early 2025 and further enhanced following the May 2025 GACVS meeting. Outcome-specific investigation forms on antenatal bleeding, preterm birth and low birth weight were developed in collaboration with partner countries, a gestational hypertension investigation form is under way, and a separate investigation form for non-pregnancy outcomes is also available.

The first pilot of the AEFMI software was conducted in Egypt in July 2025 and the tools and software were modified. A second pilot in October 2025 showed that the revised forms were easier to complete, the investigation steps were clearer, and the training was satisfactory. Remaining challenges include limited Internet connectivity and the need to update the training.

WHO study on background rates of adverse events of special interest

Information on background rates AESI is useful in preparing for the introduction of a new vaccine (or medicine) or when an existing vaccine (or medicine) is introduced to a new population. However, many LMICs do not have these resources and may need directed studies to gather information on AESI background rates.

GACVS reviewed the WHO study on AESI background rates which includes selected AESIs for which monitoring is often recommended when new vaccines are introduced. Protocols have been developed for a selection of AESIs, namely: Guillain Barré syndrome (GBS),[4] thrombocytopenia[5] and neonatal outcomes (preterm birth, still birth, neonatal death, low birth weight).[6] The intention is to conduct a multi-site prospective cohort study in selected sentinel sites in LMICs, with primary objectives to estimate annual background rates of: 1) GBS in the general population and stratified by sex and age groups; 2) thrombocytopenia among children aged five months to less than 15 years; and 3) neonatal outcomes (preterm birth, stillbirth, neonatal death, low birth weight).

Generic training materials have been prepared in collaboration with the Paul-Ehrlich-Institut in Germany and sites have been identified in both countries. GACVS was informed of the training process.

Uganda and Zimbabwe are the two initial pilot countries in different stages of preparation. Uganda's National Drug Authority is implementing the studies of AESI background rates where screening of health facilities as study sites has been completed. Zimbabwe has agreed to use the three WHO protocols (locally adapted) for estimating background rates of each condition, with publication of the results and dissemination to stakeholders in the third and fourth quarters of 2027. Potential implementation challenges include project financing, statistical sample size calculation and statistical analysis.

GACVS expressed concern about the reliance on hospital records, which may not capture community-level events, leading to underreporting. If demographic data cannot be accessed in a particular location, then that site cannot be included in the study. Members emphasized that even a relatively small number of cases could still be valuable, provided there is confidence that they are representative of the broader population under study. Also, while training materials are aligned with Brighton Collaboration standards, variability in interpretation remains a challenge.

GACVs recommended:

- Implementation should be focused on sites where patient records and demographic information can be accessed and validated, ensuring data quality and representativeness.
- Partnerships (e.g. with the African Academy of Neurology [AFAN] or international agencies such as the Institute for Health Metrics and Evaluation) should be explored to improve case detection and diagnostic accuracy.

Safety of chikungunya vaccines in older persons

GACVS was updated on the review of the safety profile of EMA-approved chikungunya vaccines by the EMA's Pharmacovigilance Risk Assessment Committee (PRAC), and on the ongoing /planned safety monitoring of Ixchiq in older populations.

[4] Protocol on estimation of Guillain-Barré syndrome background rates in general population in low- and middle-income countries. Geneva: World Health Organization; 2025 (https://www.who.int/publications/i/item/9789240108240).

[5] Protocol on estimation of thrombocytopenia background rates in children aged 5 months to <15 years in low- and middle-income countries. Geneva: World Health Organization; 2025 (https://www.who.int/publications/i/item/9789240111882).

[6] Estimation of background rates of adverse events of special interest in neonatal outcomes: preterm births, stillbirths, neonatal deaths and low birthweight. Geneva: World Health Organization; 2025 (https://iris.who.int/bitstreams/1c658cd3-e693-4c47-b570-6844c4bef274/download).

In May 2025, cases of serious adverse events (SAEs), some fatal, were received by the French regulatory authority after the start of a vaccination campaign with Ixchiq in La Réunion, an overseas department of France (and therefore within the European Union/EU). Because the SAEs mostly affected older persons, a preliminary restriction on the use of Ixchiq in people of 65 years and older was implemented by the PRAC.

According to data presented in May 2025, 12 767 doses of Ixchiq were administered cumulatively in La Réunion/EU, with 10 417 doses going to people aged over 65 years. In post-marketing data from November 2023 to May 2025, 72 cases of adverse events were identified, of which 28 were serious (including seven with conditions indicating immune suppression). Fifteen of the post-marketing cases reported hospitalization. The AESI were chiefly neurological and cardiac events. In three of the SAEs, fatal outcome was reported.

Although PRAC members concluded that elderly people seem to be more at risk for SAEs, they also felt that older persons would benefit most from vaccination due to the higher risks of hospitalization and of fatal outcome after infection with chikungunya. Consequently, Ixchiq may be used in elderly people after individual benefit–risk analysis if there is a relevant risk of chikungunya infection.

The risk management plan for Ixchiq was updated, noting an increased risk for SAEs in individuals ≥65 years of age with chronic medical conditions. Safety in persons aged 12–64 years with clinical conditions associated with impaired or dysregulated immune responses is now added to the summary of safety concerns as missing information.

The safety profile of Vimkunya vaccine shows no important identified or potential risks but points to lack of information on use during pregnancy and breastfeeding. Consequently, a pregnancy registry is to be established to evaluate pregnancy outcomes in women immunized with Vimkunya up to 14 days before conception or at any time during pregnancy. Current decisions to administer Vimkunya during pregnancy should consider the individual's risk of exposure to wild-type chikungunya virus, gestational age and risks to the fetus or neonate. Some 18 000 doses of Vimkuya have so far been distributed.

GACVS members noted that many adverse effects observed after Ixchiq administration were neurology-related and that SAE reporting after administration of chikungunya vaccine seems similar to that following administration of yellow fever vaccine. When adverse events took place with the yellow fever vaccine it was found that the vaccine was secreted in breastmilk.

GACVS noted that the reactions observed would normally be more likely in younger patients than in older ones. The higher occurrence of SAEs in the elderly might be due to immunosuppression in the elderly population and the fact that this is a live-attenuated vaccine.

GACVS members were informed that SAGE had formed a working group on these vaccines which would meet to discuss chikungunya outbreaks and infections through to June 2026.[7] Members noted that the PRAC decided that the vaccine could be used in elderly persons because, although older people are more prone to have serious side-effects, the benefit in this population is highest. Therefore, the overall benefit–risk balance remains positive.

Qdenga® vaccine

Qdenga® (or TAK-003) is a live-attenuated tetravalent dengue vaccine containing attenuated strains of dengue virus serotypes 1–4. The vaccine is approved in the EU for adults, adolescents and children from 4 years of age. Cumulative exposure is some 18 million doses globally. GACVS previously reviewed the safety of Qdenga® in May 2023, May 2024 and November 2024. The objective in November 2025 was to provide GACVS members with an update on progress of the roll-out and safety aspects of Qdenga®. GACVS therefore held discussions with representatives of the Paul-Ehrlich-Institute, Germany, the Secretariat of Health and Environmental Surveillance, Brazil, the Brazilian Health Regulatory Agency (ANVISA), and the Pan American Health Organization (PAHO).

GACVS emphasized the importance of addressing remaining knowledge gaps, particularly a safety signal for anaphylaxis. In addition, GACVS noted there are limited data on Qdenga® and pregnancy, the potential for vaccine-associated enhanced disease (VAED) should be investigated, and it is important to consider subgroups such as children under 6 years, immunocompromised persons, and co-administration or interactions with other vaccines.

Young people aged between 10 and 14 years were the focus of the Qdenga® public vaccination campaign in Brazil. The roll-out of the campaign coincided with a period of higher dengue incidence. The probable number of cases fell from 446 885 in 2024 to an estimated 98 983 in 2025 (up to October 2025). The number of severe cases and cases with warning signs in this population was 1788, with 19 probable deaths from dengue among young people in 2025.

[7] SAGE Working Group on Chikungunya vaccines. Geneva: World Health Organization; 2025 (https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/working- groups/chikungunya).

Vaccination was implemented in 2752 of 5570 priority municipalities. The number of doses administered in the public campaign has been 6 564 940 since February 2024. Of these, 4 470 156 were given as the first dose and 2 094 784 as the second dose, corresponding to coverage levels of 44.1% for the first dose and 22.4% for the second.

During the initial year of the vaccination campaign, the observed rates of anaphylaxis were significantly higher than expected. These rates declined but stayed above 10 cases per million doses – an incidence higher than observed with other routine immunization campaigns. However, no case progressed to death due to post-vaccination anaphylaxis following dengue immunization.

GACVS members expressed concern at the high drop-out rate after the first dose. While regular vaccine programmes for young people in Brazil are carried out in schools, the health authorities were concerned that the risk of cases of anaphylaxis in schools could jeopardize the whole vaccination programme. Hence, young people had to visit health-care units voluntarily for vaccination with Qdenga®.

Qdenga® vaccine received marketing authorization in Brazil in March 2023 and was integrated into the National Immunization Programme in February 2024. Shortly after this, a signal for anaphylaxis was identified. In 2025, ANVISA mandated additional regulatory measures and reclassified anaphylaxis as an "important identified risk" within the risk management plan. Quality assurance investigations by the manufacturer concluded that there was no evidence of procedural deviations or atypical events contributing to the reported adverse reactions. In 2025, the manufacturer (Takeda) entered a research partnership with the University of São Paulo and the Ministry of Health to implement a research protocol exploring the mechanisms of anaphylaxis.

In addition to Brazil, Argentina began using Qdenga® in the public sector in 2024. Colombia approved the vaccine in 2023 but so far it is being used only in the private sector. In November 2024, Qdenga® was introduced by Peru and in March 2025 by Honduras. Brazil has the highest number of administered doses. PAHO has developed regional guidance on safety monitoring for the dengue vaccine.[8]

In November 2024, GACVS recommended seeking evidence on the effectiveness and risk of VAED. It was reported in November 2025 that two protocols are being drafted to evaluate the effectiveness of dengue vaccines and the risk and molecular and immunological mechanisms of VAED in the Americas. GACVS members agreed that difficulties in distinguishing between wild dengue virus and VAED need to be explored further.

GACVS members were pleased that the number of anaphylaxis reactions had fallen in Brazil. The Ministry of Health was encouraged to continue to work with the manufacturer on this issue. If the vaccine is shown to be allergenic, the manufacturer should make every effort to reduce the allergenicity. Nevertheless, it was acknowledged that it is a difficult situation, since an increase in the anaphylaxis events could derail the entire immunization programme.

GACVS recommended:

- post-marketing surveillance for anaphylaxis should continue to document the ongoing reporting rate and to inform programmatic and risk–benefit decisions on the vaccine.
- a pregnancy registry should be established for follow-up of women who are accidentally vaccinated during pregnancy to identify any adverse events in the mother, fetus and neonate. ■

[8] Regional guidelines for dengue vaccine safety surveillance, QDENGA - TAK-003. Washington (DC): Pan American Health Organization; 2025 (https://iris.paho.org/items/541da4eb-395c-4731-a001-07e94a63f64c).

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