Statement on the antigen composition of COVID-19 vaccines

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Key points

- **Vaccination remains an important public health countermeasure against COVID-19. As per the WHO Director General's standing recommendations for COVID-19, Member States are recommended to continue to offer COVID-19 vaccination based on the recommendations of the WHO Strategic Advisory Group of Experts on Immunization (SAGE).**
- **SARS-CoV-2 continues to undergo sustained evolution since its emergence in humans, with important genetic and antigenic changes in the spike protein.**
- **The objective of an update to COVID-19 vaccine antigen composition is to enhance vaccine-induced immune responses to circulating SARS-CoV-2 variants.**
- **The WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) advises manufacturers that monovalent JN.1 or KP.2 vaccines remain appropriate vaccine antigens; monovalent LP.8.1 is a suitable alternative vaccine antigen.**
- **In accordance with WHO SAGE policy, vaccination should not be delayed in anticipation of access to vaccines with an updated composition.**

The WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) continues 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. Based on these evaluations, WHO advises vaccine manufacturers and regulatory authorities on the implications for future updates to COVID-19 vaccine antigen composition. In April 2024, the TAG-CO-VAC recommended the use of a monovalent JN.1 lineage vaccine antigen as one approach to induce enhanced neutralizing antibody responses to JN.1 and its descendent lineages. In December 2024, the TAG-CO-VAC advised retaining the use of a monovalent JN.1 lineage vaccine antigen. Multiple manufacturers (using mRNA, recombinant protein-based, and adenovirus-vectored platforms) have updated COVID-19 vaccine antigen composition to monovalent JN.1 lineage formulations (JN.1 or KP.2). Several of these vaccines have been approved for use by regulatory authorities and introduced into vaccination programmes in some countries during the second half of 2024. Previous statements from the TAG-CO-VAC can be found on the WHO website.

The TAG-CO-VAC reconvened on 6-7 May 2025 to review the genetic and antigenic evolution of SARS-CoV-2; immune responses to SARS-CoV-2 infection and/or COVID-19 vaccination; the performance of currently approved vaccines against circulating SARS-CoV-2 variants; and the implications for COVID-19 vaccine antigen composition.

Evidence reviewed

The published and unpublished evidence reviewed by the TAG-CO-VAC included: (1) SARS-CoV-2 genetic evolution with additional support from the WHO Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE); (2) Antigenic characterization of previous and emerging SARS-CoV-2 variants using virus neutralization tests with animal antisera and further analysis of antigenic relationships using antigenic cartography; (3) Immunogenicity data on the breadth of neutralizing antibody responses elicited by currently approved vaccine antigens against circulating SARS-CoV-2 variants using animal and human sera; (4) Preliminary immunogenicity data on immune responses following infection with circulating SARS-CoV-2 variants; (5) Available vaccine effectiveness (VE) estimates of currently approved vaccines during periods of JN.1 lineage circulation; and (6) Preliminary non-clinical and clinical immunogenicity data on the performance of candidate vaccines with updated antigens shared confidentially by vaccine manufacturers with TAG-CO-VAC. Further details on the data reviewed by the TAG-CO-VAC can be found in the accompanying data annex. Confidential data reviewed by the TAG-CO-VAC are not shown.

Summary of available evidence

- **There are persistent and increasing gaps in the reporting of cases, hospitalizations and deaths, from WHO Member States, making epidemiological trends difficult to infer. Nonetheless, in 2025, SARS-CoV-2 continues to circulate globally, causing severe disease, post COVID-19 condition, and death. The majority of COVID-19 deaths continue to occur in individuals aged 65 years and older and those with coexisting conditions. Some countries have reported an increase in incidence of COVID-19-related hospitalizations and deaths among children under 1 year of age, as compared to young adults, although this group still accounts for a small proportion of total COVID-19 hospitalizations and deaths.**
- **As of May 2025, currently circulating SARS-CoV-2 variants are derived from JN.1. The weekly proportion of Variant Under Monitoring (VUM) LP.8.1 among all SARS-CoV-2 sequences submitted to GISAID continues to increase. The weekly proportion of JN.1 (Variant of Interest, VOI) is slowly increasing, largely due to increases in LF.7 and its descendent variants, while all other VUMs (KP.3, KP.3.1.1, XEC, and LB.1) are declining.**
- **Several JN.1 derived variants have independently evolved changes in the spike protein at epitopes known to be targeted by neutralizing antibodies.**
- **Published and unpublished data using antisera from naïve hamsters infected with JN.1, KP.2, KP.3.1.1, XEC or LP.8.1 or mice immunized with mRNA vaccine antigens JN.1, KP.2 or KP.3 showed that JN.1, KP.2, KP.3.1.1, XEC, and LP.8.1 are antigenically closely related to each other (approximately 1 antigenic unit in cartographic analysis, which corresponds to a two-fold-difference in neutralization).**
- **In published and unpublished data from humans, vaccination with monovalent JN.1 or KP.2 antigens significantly increased neutralizing antibody titers against all JN.1 descendent lineages tested:**
  - **Analysis of pre- and post-vaccination sera from JN.1 lineage (i.e. JN.1 or KP.2) immunized individuals demonstrated significant rises in neutralization of JN.1 and its descendent lineages, including KP.3.1.1, XEC, LF.7.2.1, and LP.8.1.**

    - Neutralization titers against LP.8.1 were generally modestly lower (2-fold reduction) than those against the homologous JN.1 or KP.2 antigen.
- Contemporary vaccine effectiveness (VE) estimates are relative (rVE), rather than absolute (comparing vaccinated to unvaccinated individuals), and demonstrate the added or incremental protection of recent vaccination over and above pre-existing infection- and vaccine-derived immunity. Monovalent JN.1 or KP.2 COVID-19 vaccines were introduced into some vaccination programmes in the second half of 2024. There are only a few studies estimating rVE for the monovalent JN.1 or KP.2 mRNA COVID-19 vaccines during periods of JN.1 descendent lineage circulation. Both vaccines demonstrated additional protection—relative to pre-existing immunity—against symptomatic and severe COVID-19 during the first three to four months after vaccination.
- Data shared confidentially with the TAG-CO-VAC by vaccine manufacturers showed that:
    - Immunization of naïve mice, as well as of mice previously immunized with SARS-CoV-2 variants, with monovalent JN.1 or KP.2 vaccines resulted in high neutralizing antibody titers against JN.1 and its derivatives including KP.2, KP.3.1.1, XEC, LP.8.1, and LF.7.2. However, neutralization titers against LP.8.1 were typically lower than those against the homologous immunizing antigen.
    - Immunization of naïve mice, as well as of mice previously immunized with SARS-CoV-2 variants, with monovalent LP.8.1 vaccine candidates elicited high neutralizing antibody titers against the homologous antigen. Cross-neutralizing antibody titers elicited against other JN.1 lineage variants including JN.1, KP.2, KP.3, KP.3.1.1, XEC, and LF.7.2 were similar or modestly higher than those elicited by JN.1 or KP.2 antigens.
    - In humans, vaccination with monovalent JN.1 or KP.2 antigens resulted in robust neutralizing antibody responses to JN.1 and descendent variants, including KP.3.1.1, XEC, LP.8.1, and LF.7.2.
    - As in non-clinical data, analysis of pre- and post-vaccination sera from JN.1 or KP.2 immunized individuals showed some variation in neutralizing antibody titers against LP.8.1 and LF.7.2 across different studies. In most instances, they were similar or lower than those against the homologous JN.1 or KP.2 antigens.

Overall, the currently approved monovalent JN.1 or KP.2 vaccines continue to elicit broadly cross-reactive immune responses to circulating JN.1-derived variants. LP.8.1 as a vaccine antigen offers similar or modestly increased cross-reactive antibody responses to circulating JN.1-derived variants, as compared to monovalent JN.1 or KP.2 vaccines. Mathematical modeling indicates that an increase in neutralizing antibody titers may translate into an improvement in vaccine effectiveness and duration of protection.

The TAG-CO-VAC acknowledges several limitations of available data:

- There are persistent and increasing gaps in the reporting of cases, hospitalizations and deaths, from WHO Member States, as well as in genetic/genomic surveillance of SARS-CoV-2 globally, including low numbers of samples sequenced and limited geographic diversity. The TAG-CO-VAC strongly supports the ongoing work of the WHO Coronavirus Network (CoViNet) and the Global Influenza Surveillance and Response System (GISRS) to address this information gap.
- The timing, specific mutations and antigenic characteristics of emerging and future variants are difficult to predict, and the potential public health impact of these variants remain unknown. There are JN.1-derived variants and long branch saltation variants that are currently detected in low or very low proportions, and which will continue to be monitored and/or characterized. The TAG-CO-VAC strongly supports the ongoing work of the TAG-VE.
- Although neutralizing antibody titers have been shown to be important correlates of protection from SARS-CoV-2 infection and of estimates of vaccine effectiveness, there are multiple components of immune protection elicited by infection and/or vaccination. Data on the immune responses following JN.1 descendent lineage infection or monovalent JN.1 or KP.2 vaccination are largely restricted to neutralizing antibodies. Data and interpretation of other aspects of the immune response, including cellular immunity, are limited.
- Immunogenicity data against currently circulating SARS-CoV-2 variants are not available for all COVID-19 vaccines.
- Estimates of rVE against recently circulating JN.1 variants are limited in terms of the number of studies, geographic diversity, vaccine platforms evaluated, populations assessed, duration of follow-up, and contemporary comparisons of vaccines with different antigen composition.

Recommendations for COVID-19 vaccine antigen composition

Monovalent JN.1 (NextStrain: 24A, GenBank: PP298019, GISAID: EPI_ISL_18872762) or KP.2 vaccines remain appropriate for ongoing use; monovalent LP.8.1 (NextStrain: 25A; GenBank: PV074550.1; GISAID: EPI_ISL_19467828) is a suitable alternative vaccine antigen.

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

As per the WHO Director General's standing recommendations for COVID-19, Member States are recommended to continue to offer COVID-19 vaccination based on the recommendations of the WHO SAGE. Vaccination should not be delayed in anticipation of access to vaccines with an updated composition.

Further data requested

Given the limitations of the evidence upon which the recommendations above are derived and the anticipated continued evolution of the virus, the TAG-CO-VAC strongly encourages generation of the following data (in addition to the types of data outlined in March 2025):

- Immune responses and clinical endpoints (i.e. VE and/or comparator rates of infection and severe disease) in varied human populations who receive currently approved COVID-19 vaccines against emerging SARS-CoV-2 variants, across different vaccine platforms.
- Strengthened epidemiological and virological surveillance, as per the Standing Recommendations for COVID-19 in accordance with the International Health Regulations (2005), to determine if emerging variants are antigenically distinct and able to displace circulating variants.
- Strengthened epidemiological surveillance to characterize disease severity in immunologically naïve and/ or immature individuals (i.e. birth cohorts).
- Clinical evaluation of relevant new vaccine antigens derived from more recent SARS-CoV-2 variants.

As previously stated, the TAG-CO-VAC continues to encourage the further development of vaccines that may improve protection against infection and reduce transmission of SARS-CoV-2.

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 also continue to reconvene every six months, or as needed, to evaluate the implications for COVID-19 vaccine antigen composition. At each meeting, recommendations to either maintain current vaccine composition or to consider updates will be issued. Prior to each meeting, the TAG-CO-VAC will publish an update to the statement on the types of data requested to inform COVID-19 vaccine antigen composition deliberations.