17 May 2025
EMA/166854/2025
Emergency Task Force
European Medicines Agency

EMA recommendation to update the antigenic composition of authorised COVID-19 vaccines for 2025-2026

The European Medicines Agency (EMA) is providing a recommendation to change the antigenic composition of authorised COVID-19 vaccines for use during the 2025-2026 vaccination campaign.

The composition of vaccines against COVID-19 has changed four times since first approval in 2020. SARS-CoV-2, like any RNA virus that infects humans, is prone to accumulating mutations in its genome during replication in the human host. New SARS-CoV-2 variants continue to arise driven by immune evasion and viral fitness.

A large body of evidence is now available to anticipate that, even if COVID-19 vaccines remain effective at preventing severe disease and death caused by new emerging variants, protection tends to decrease as the virus evolves into more antigenically distant variants. Studies have shown that matching the content of vaccines to the circulating viruses improves protection against the disease. For these reasons, COVID-19 vaccine composition has been updated since the virus established itself in humans.

It is of note that since the emergence of the JN.1 family the virus has kept its evolution restricted to closely related strains. Between the end of 2024 and the beginning of 2025, SARS-CoV-2 variant XEC emerged and became dominant (still accounted for 50% of sequences in Europe in February). Progressively since February 2025, however, LP.8.1's spread began increasing at a faster rate than other variants and it is now showing the largest prevalence globally. This strain has already become dominant in different parts of the world such as the US and is now spreading in Europe as well. Both XEC and LP.8.1 variants belong to the BA.2.86 family of Omicron subvariants, which is antigenically distant from the XBB family circulating in 2023 and from previously circulating variants. XEC is a recombinant variant that derives from the JN.1 descendent lineages KS.1.1 and KP.3.3, with the earliest sample collected on 26 June 2024. LP.8.1 derives from the JN.1 descendent lineage KP.1.1.3, with the earliest sample collected on 1 July 2024. LP.8.1.1 or other subvariants might become the predominant strains within the LP.8.1 lineage.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands

Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

As compared to XEC, LP.8.1 has six spike mutations, which has been shown to enhance binding affinity to the receptor. As a consequence, LP.8.1 might possess the greatest growth advantage and increased transmissibility among other variants. Additionally, LP.8.1 was shown to exhibit strong humoral immune evasion.

Other JN.1 sublineages that are emerging include MC.10.1, NP.1 and LF.7 and its descendants such as LF.7.7.2 and LF.7.2.1, which have rapidly spread in some regions of the world. However, even if LF.7.2.1 is the most immune-evasive variant, similarly to MC.10.1 and NP.1, they show restricted growth advantage as compared to LP.8.1[1].

Based on this evidence, the LP.8.1 variant appears the best trade-off in terms of evolutionary fitness.

The EMA's Emergency Task Force (ETF) has consulted with marketing authorisation holders for COVID-19 vaccines, international regulators and the WHO. In the course of these consultations, the following evidence was evaluated:

- real world evidence on the effectiveness of vaccines containing JN.1 and KP.2
- surveillance data on virus epidemiology and evolution
- animal and human studies on cross-neutralisation elicited by JN.1 and KP.2 vaccines against emerging variants, including antigenic cartography
- animal studies of KP.3.1.1-, XEC-, LF.7 and LP.8.1-adapted vaccine candidates, including both primary and boosting settings.

Overall, these data have provided insight into the protection afforded by the approved JN.1 and KP.2 vaccines and newer candidate vaccines against current and emerging strains and lineages. Preliminary vaccine effectiveness estimates indicate relevant protection against outcome of severe disease as expected[2], with no apparent difference in level of protection between JN1 and KP.2 vaccines[3]. Data from a Danish Nationwide Register-based Cohort Study show high effectiveness against hospitalisation and death for the authorised mRNA vaccines carrying JN.1[4]. Similar trends are emerging from studies conducted by public health authorities in the UK[5].

Existing vaccines showed cross-neutralization on all tested JN.1 sub-variants, with however the greatest reduction (2-3 fold) in titers against the most recently emerging strains such as XEC, LF.7.2.1 and LP.8.1, suggesting some immune evasion. In certain cases, KP.2 appears to provide a small advantage over JN.1 in terms of breadth of neutralising antibody responses. Both LF.7 and LP.8.1 experimental vaccines provide as expected robust neutralisation of the homologous strain and emerging viruses belonging to the JN.1 family. Despite some differences, the clinical relevance of which is difficult to anticipate, the available evidence indicates that the 3 variant vaccines most widely tested at this point in time, JN.1, KP.2 and LP.8.1, are broadly comparable in their ability to cross-neutralise the known emerging variants including the most immune evading LF.7 and related descendants.

[1] Virological and antigenic characteristics of SARS-CoV-2 variants LF.7.2.1, NP.1, and LP.8.1 - The Lancet Infectious Diseases
[2] Early effectiveness of the BNT162b2 KP.2 vaccine against COVID-19 in the US Veterans Affairs Healthcare System | medRxiv
[3] BNT162b2 JN.1-adapted vaccine effective against COVID-19 hospitalization | Multidisciplinary | MIMS Thailand
[4] Effectiveness of the BNT162b2 and mRNA-1273 JN.1-adapted Vaccines Against COVID-19-associated Hospitalisation and Death: a Danish Nationwide Register-based Cohort Study by Christian Holm Hansen, Ria Lassauniere, Morten Rasmussen, Ida Rask Moustsen-Helms, Palle Valentiner-Branth :: SSRN
[5] Epidemiology of COVID-19 in England: January 2020 to December 2024 - GOV.UK

Recommendations and considerations to Marketing Authorisation Holders regarding updates to vaccine composition

The ETF is of the opinion that:

- Adapting vaccines to target the LP.8.1 variant of the JN.1 family of Omicron subvariants is preferentially recommended to ensure cross-reactivity against current dominant and emerging strains. Vaccine compositions targeting other JN.1 descendants could be considered if there is adequate justification.
- Approvals can be based on manufacturing/quality and non-clinical data, provided that data with prior vaccines of different composition support predictability of clinical immunogenicity and reactogenicity.
- Vaccines targeting JN.1 or KP.2 strains could still be considered for the vaccination campaigns in 2025 until updated LP.8.1 vaccines become available.

This ETF position is intended to provide guidance to marketing authorisation holders (MAHs) of EU-authorised COVID-19 vaccines on the next steps to update vaccine composition for the upcoming winter season. For investigational vaccines with compositions that do not meet the most recent recommendations regarding antigen content, applicants should discuss with EMA the strategy for obtaining marketing authorisation and amending the vaccine composition before marketing in the EU.

Post-authorisation collection of effectiveness and clinical immunogenicity data will be needed to support future decisions on vaccine updates and vaccination campaigns strategies.

Revision of product information for the strain change variation

Marketing authorisation holders of authorised COVID-19 vaccines should discuss revision of the product information with the EMA. Changes should be kept to a minimum to ensure a rapid assessment timetable and should focus on the antigenic composition and any important editorial improvements.

Marketing authorisation holders should also consider conducting a comprehensive review of the Product Information for COVID-19 vaccines, aiming at simplification. The exact content of the dossier and timing of this submission after the update of the vaccine composition can be discussed with EMA in due course.

The Committee for Medicinal Products for Human Use (CHMP) will reach a final decision on the variation and changes to the product information on conclusion of the assessment of the data submitted.