FDA Briefing Document

Vaccines and Related Biological Products Advisory Committee Meeting
May 28, 2026

Selection of the 2026–2027 Formula for COVID-19 Vaccines

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1. Meeting Objective

On May 28, 2026, the Vaccines and Related Biological Products Advisory Committee (VRBPAC) will meet in open session to discuss and make recommendations on the selection of the 2026-2027 Formula for COVID-19 vaccines for use in the United States (U.S.).

2. Background

2.1 Previous VRBPAC Discussions and Vaccine Composition Recommendations

VRBPAC has met multiple times since 2022 to discuss and make recommendations on the selection of the strain compositions for COVID-19 vaccines. At the VRBPAC meeting on May 22, 2025, VRBPAC unanimously voted to recommend a monovalent JN.1-lineage vaccine composition for use in the U.S. beginning in the fall of 2025.

2.2 FDA Approved COVID-19 Vaccines

FDA has approved four COVID-19 vaccines.

COMIRNATY (2025–2026 Formula)

COMIRNATY (COVID-19 Vaccine, mRNA) manufactured by Pfizer-BioNTech is approved for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 65 years of age and older, or individuals 5 years through 64 years of age with at least one underlying condition that places them at high risk for severe outcomes from COVID-19. For additional information on dosing and schedule, please refer to the COMIRNATY USPI.

COMIRNATY (2025–2026 Formula) contains nucleoside-modified mRNA (modRNA) encoding the viral Spike (S) glycoprotein of the SARS-CoV-2 Omicron variant sublineage LP.8.1, formulated in lipid nanoparticles.

MNEXSPIKE (2025–2026 Formula)

MNEXSPIKE (COVID-19 Vaccine, mRNA) manufactured by Moderna is approved for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 65 years of age and older, or individuals 12 years through 64 years of age with at least one underlying condition that places them at high risk for severe outcomes from COVID-19. For additional information on dosing and schedule, please refer to the MNEXSPIKE USPI.

MNEXSPIKE (2025–2026 Formula) contains nucleoside-modified mRNA encoding the N-terminal domain (NTD) and receptor-binding domain (RBD) of the viral Spike (S) glycoprotein of the SARS-CoV-2 Omicron variant sublineage LP.8.1, encapsulated in lipid nanoparticles.

NUVAXOVID (2025–2026 Formula)

NUVAXOVID (Sanofi COVID-19 Vaccine, Adjuvanted) manufactured by Sanofi is approved for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 65 years of age and older, or individuals 12 years through 64 years of age

with at least one underlying condition that places them at high risk for severe outcomes from COVID-19. For additional information on dosing and schedule, please refer to the NUVAXOVID USPI.

NUVAXOVID (2025–2026 Formula) is a protein subunit vaccine. Each 0.5 mL dose contains 5 mcg of recombinant Spike (rS) protein nanoparticles derived from the SARS-CoV-2 Omicron variant lineage JN.1 and 50 mcg of Matrix-M adjuvant. The rS protein is produced using recombinant DNA technology in an insect cell line.

SPIKEVAX (2025–2026 Formula)

SPIKEVAX (COVID-19 Vaccine, mRNA) manufactured by Moderna is approved for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 65 years of age and older, or 6 months through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19. For additional information on dosing and schedule, please refer to the SPIKEVAX USPI.

SPIKEVAX (2025–2026 Formula) contains nucleoside-modified messenger RNA (mRNA), encoding the pre-fusion stabilized Spike glycoprotein (S) of the SARS-CoV-2 Omicron variant sublineage LP.8.1, encapsulated in lipid particles.

3. Considerations for a Periodic Updated Strain Composition of COVID-19 Vaccines

3.1 Current Effectiveness of U.S.-Authorized/Approved COVID-19 Vaccines (2025–2026 Formula) and Implications for the Selection of 2026–2027 Formula

Following the VRBPAC on May 22, 2025, FDA advised vaccine manufacturers that COVID-19 vaccines approved for use in the U.S. should be monovalent JN.1-lineage-based COVID-19 vaccines (2025–2026 Formula), preferentially using the LP.8.1 strain to provide a closer match to currently circulating SARS-CoV-2 viruses.

A few reports describing the effectiveness of the COVID-19 vaccines (2025–2026) have recently become available:

- One study estimated early vaccine effectiveness (VE) of the BNT162b2 LP.8.1-adapted vaccine against emergency department/urgent care (ED/UC) and outpatient visits in the U.S. Veterans Affairs Healthcare System [1]. The LP.8.1 vaccine was effective during the early 2025–2026 respiratory virus season, with a VE of 57% (95% CI 39%–70%) against ED/UC visits and 54% (95% CI 15%–75%) against outpatient visits at approximately 4 weeks postvaccination.
- Results from an interim 2025/2026 LP.8.1 VE study from the Canadian Sentinel Practitioner Surveillance Network found that the LP.8.1 vaccine approximately halved the medically attended COVID-19 risk [2].
- A third study, using a registry-based cohort study of adults 65 years of age and older in Denmark, found that the LP.8.1-adapted vaccine provided good protection over a 4-month period against COVID-19 hospitalization and death [3].

Observational data from prior years indicates an inverse relationship between the time since vaccination and vaccine effectiveness, and that better matching of the vaccine to circulating strains is associated with improved neutralizing antibody titers. SARS-CoV-2 continues to evolve incrementally (drift-like) into distinct sublineages by acquiring additional mutations (see section 3.2). Since May 2025, JN.1-lineage virus variants NB.1.8.1 and XFG emerged from distinct recombinant sublineages of JN.1 with a growth advantage over the previously dominant LP.8.1 virus variant [4]. Data from some recent studies using sera following immunization indicated that LP.8.1 vaccination increased neutralization titers against LP.8.1, as well as more recent virus variants including NB.1.8.1 and XFG, but the neutralization titers were modestly reduced compared with the homologous LP.8.1 strain [5]. Updating the current formula of COVID-19 vaccines to more closely match currently circulating JN.1-lineage viruses may be beneficial.

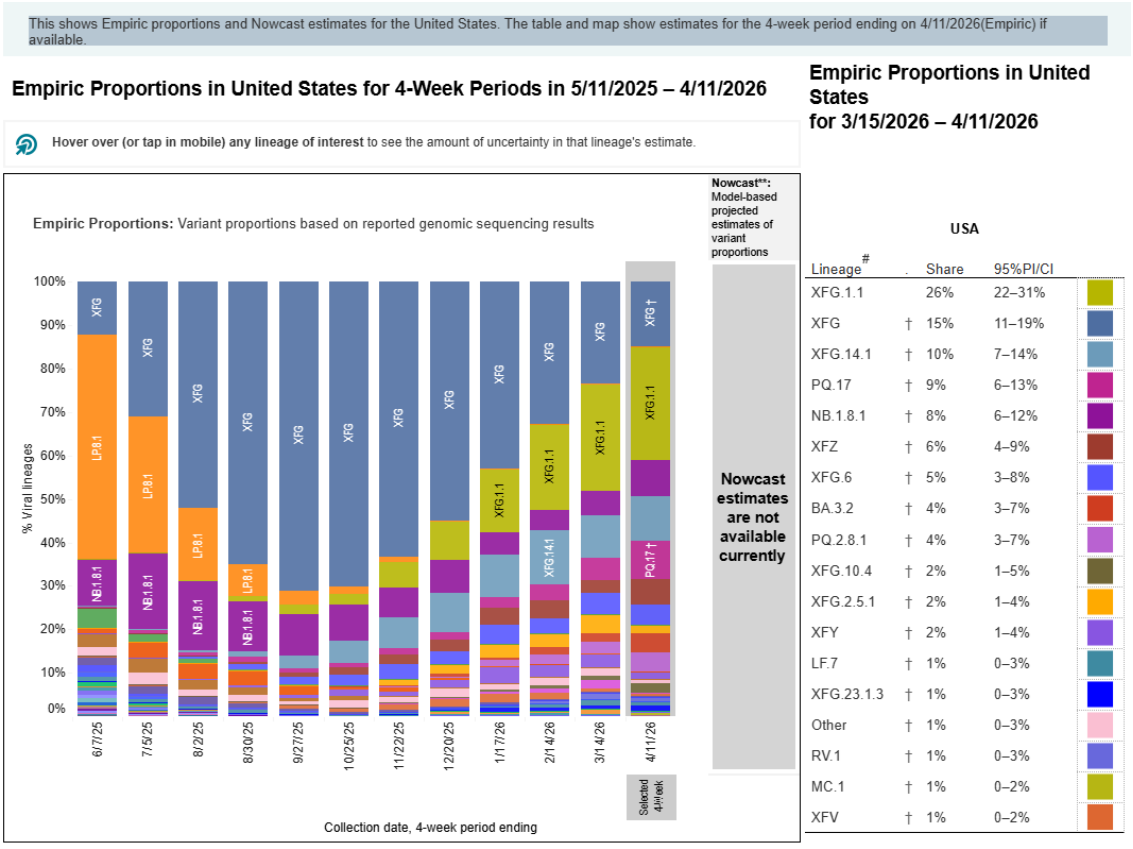
3.2 Virus Evolution

SARS-CoV-2 has continued to evolve rapidly since it emerged in 2019, driven by selection pressures that balance intrinsic viral fitness with the ability to evade pre-existing immunity. Early in the pandemic, the D614G substitution and subsequent emergence of the Alpha variant were associated with increased fitness and transmissibility [6]. As population immunity increased through infections and vaccinations, variants with mutations that conferred immune escape gained an increasing selective advantage. Variants can emerge through gradual accumulation of mutations within an existing lineage, producing drift variants with incremental genetic and antigenic changes. Recombination between co-infecting variants can also introduce new combinations of mutations, ranging from small changes to larger genetic shifts. In saltational evolution, many accumulated mutations are first detected together, potentially giving rise to a distinct evolutionary branch. SARS-CoV-2 evolution has often been marked by successive global sweeps of highly fit variants. Predicting which variant will become dominant is challenging because variant success depends on the interplay among antigenic distance, immune escape, intrinsic fitness, and the immune history of the population.

More than six years after its emergence, SARS-CoV-2 is evolving against an increasingly heterogeneous immune landscape shaped by varied histories of prior infection, COVID-19 vaccination, and waning immunity after both. This heterogenous immunity likely contributes to the increasing complexity in the composition of currently circulating variants globally and in the U.S. Omicron JN.1 descendants remain prominent and have diversified into multiple lineages, including LP.8.1, XFG, NB.1.8.1, and LF.7, with additional drift variants emerging within these lineages [7, 8]. Following 22 May 2025 VRBPAC discussion, FDA advised the manufacturers of the approved COVID-19 vaccines that to more closely match currently circulating SARS-CoV-2 viruses, the COVID-19 vaccines for use in the U.S. beginning in fall 2025 should be monovalent JN.1-lineage-based COVID-19 vaccines (2025–2026 Formula), preferentially using the LP.8.1 strain [9]. At the time of this writing, XFG variants remain dominant in the U.S. and globally, though NB.1.8.1 variants are increasing in prevalence domestically [7, 8].

In November 2024, the highly divergent BA.3.2 saltation variant, derived from a minor Omicron BA.3 variant that briefly circulated in 2022, was first identified in South Africa [10]. It has since spread globally in a slow and stochastic manner, without displacing JN.1 lineage variants. BA.3.2 has more than 70 substitutions and deletions in the Spike glycoprotein relative to JN.1 descendent variants, as well as deletions in ORF7a, ORF7b, and ORF8 accessory genes [11]. The functional consequences of the accessory gene deletions are currently unknown. BA.3.2 detection in Africa was limited and followed by detections in the Netherlands and Germany in April 2025 [11]. After October 2025, BA.3.2 began to spread more efficiently in Australia and Europe, reaching a prevalence of approximately 30% in some European countries [12]. More recently, it has been increasing in Italy, Spain, and Korea, and currently represents a minor variant in the U.S. Available phenotypic data suggest that this limited expansion is consistent with reduced intrinsic fitness, including weaker ACE2 binding, lower infectivity, lower fusogenicity, and modest replication capacity relative to LP.8.1, NB.1.8.1, and XFG, despite substantial antigenic drift and antibody escape [13].

Figure 1 [Variants and Genomic Surveillance | Covid | CDC]



In summary, SARS-CoV-2 evolution has shifted from a pattern dominated by periodic global sweeps of highly fit variants to a more complex landscape marked by diversification within JN.1-descendant lineages and persistent co-circulation of genetically and antigenically distinct evolutionary branches. Assessing these trajectories

has also become more uncertain as virologic surveillance, sequencing volume, and timely sequence deposition into public databases have declined.

3.3 Antigenic Characterization of SARS-CoV-2 Variants and Population Immunity

Diverse and repeated SARS-CoV-2 antigenic exposures from successive variant infections and variant-updated COVID-19 immunizations have created a complex and heterogeneous immune landscape. This accumulated immunity has reduced severe COVID-19 outcomes [1, 3, 14], but protection varies by age, immune status, underlying medical conditions, exposure history, and time since last exposure. COVID-19 vaccination remains an important tool for enhancing protection, particularly in people at increased risk of severe disease [15].

The variant composition of COVID-19 vaccines and the recipient's pre-existing immunity together shape antibody responses after vaccination [16]. In immunologically naïve or less-exposed individuals, including some infants and young children, responses may be more strongly directed toward immunodominant epitopes in the vaccine antigen [17, 18]. In previously exposed individuals, variant-updated vaccination may recall immune memory responses to conserved regions in Spike that are shared with earlier variants while also inducing responses to new regions present in the updated antigen [19-21]. As a result, additional doses can broaden neutralization across antigenically related variants, although the magnitude and breadth of response depend on several factors, including antigenic distance, variant exposure history, and time since previous exposures.

Available data support substantial cross-reactivity among JN.1-descendant variants [5, 22-24]. Antigenic mapping places JN.1, KP.2, KP.3.1.1, XEC, and LP.8.1 in a closely related cluster, and vaccines containing JN.1 and LP.8.1 antigens elicited broadly cross-reactive neutralizing antibody responses against related JN.1-derived variants. Studies comparing XFG, NB.1.8.1, and BA.3.2 similarly show greater antigenic relatedness among JN.1-descendant lineages than between those lineages and BA.3.2. In contrast, antigenic maps place BA.3.2.1 and BA.3.2.2 apart from the JN.1/XFG/NB.1.8.1 cluster and show low BA.3.2 titers after multiple exposures to many non-BA.3.2 antigens. Together, these findings indicate substantial antigenic divergence of BA.3.2 from recent vaccine antigens and circulating JN.1-descendant variants. Residual low-level cross-neutralization observed in sera from adults may reflect broader cumulative exposure histories rather than close antigenic relatedness.

Age-stratified sequence analyses of some datasets revealed a higher proportion of BA.3.2 sequences from pediatric subjects compared with non-BA.3.2 sequences, consistent with the hypothesis that limited or divergent prior antigenic exposures may reduce cross-neutralizing antibody responses to BA.3.2 in children[12, 25]. This signal needs further evaluation because age-stratified sequence data can be affected by surveillance and reporting practices. Whether age-related immune histories influence susceptibility, or whether BA.3.2 could acquire compensatory mutations that improve fitness while preserving immune escape, remain relevant considerations for vaccine-

strain deliberations. So far, BA.3.2 has not been linked to higher rates of hospitalization or death.

3.4 Global Alignment of COVID-19 Vaccine Strain Composition

The continued evolution of SARS-CoV-2, the unpredictable emergence and spread of virus variants, and the diversity of vaccine manufacturers and complexities in vaccine supply present challenges for a globally coordinated recommendation for periodically updating COVID-19 vaccines. Global public health agencies and vaccine regulators have had ongoing discussions throughout the year to address the issue of periodically updating COVID-19 vaccines to align the criteria for selection and the recommendations for updating COVID-19 vaccines, when possible.

The World Health Organization (WHO) has established the Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) to review and assess the public health implications of emerging SARS-CoV-2 variants of concern (VOCs) on the performance of COVID-19 vaccines and to provide global recommendations on proposed modifications to COVID-19 vaccine antigen composition. Recently, TAG-CO-VAC recommended LP.8.1 as the vaccine antigen in a monovalent COVID-19 vaccine but noted that other antigens such as XFG or NB.1.8.1 could also be used [26].

4. Options for Selection of Strains for COVID-19 Vaccines (2026–2027 Formula)

4.1 Summary of the Approach and the Data Reviewed for the Vaccine Strain Composition Recommendation Formula

In previous discussions with VRBPAC, FDA described the proposed evidentiary basis that would be used to determine the need for updating the strain composition of COVID-19 vaccines for use in the U.S. In preparation for the May 2026 VRBPAC discussion, FDA reviewed various types of data, engaged with key partners generating such data including vaccine manufacturers and other U.S. government agencies and reviewed the discussions and recommendations put forth by other regulatory groups and public health agencies.

The relevant data reviewed included:

- Virus surveillance and genomic analyses to identify emerging new virus variants. As described in section 3.2, the SARS-CoV-2 LP.8.1 virus previously dominant and recommended for the 2025–2026 vaccine formula has been replaced by other emerging JN.1-lineage virus variants (e.g., XFG).
- Antigenic characterization of viruses to identify antigenically distinct variant viruses. As described in section 3.3, recent SARS-CoV-2 subvariants such as XFG have additional amino acid changes relative to previously circulating SARS-CoV-2 JN.1-like variants, suggesting continued evolution and increasing antigenic drift from the components of currently authorized or approved COVID-19 vaccines.

- Postvaccination human serology studies to evaluate antibody responses generated by current vaccines against more recently circulating JN.1 sublineage virus variants. Data will be presented at the VRBPAC meeting by vaccine manufacturers.
- Nonclinical immunogenicity studies to evaluate immune responses generated by new candidate vaccines expressing or containing updated variant Spike components against antigenically distinct circulating virus variants. Data will be presented at the VRBPAC meeting by vaccine manufacturers.

4.2 Manufacturing Considerations

Recommendations for updating the strain composition of COVID-19 vaccines must consider the time needed for manufacturers to implement and deliver an updated COVID-19 vaccine formula. The timelines likely differ for different manufacturing technologies and are also affected by manufacturing experience and the availability and capacity of manufacturing facilities. All licensed manufacturers have indicated that they are prepared to produce an XFG vaccine for COVID-19 vaccines (2026–2027 Formula).

4.3 Summary of Considerations for Selection of Strain(s) for Inclusion in 2026–2027 Formula for COVID-19 Vaccines

As noted in section 3.2, while most current circulating SARS-CoV-2 variants continue to be derived from the JN.1 virus variant that appeared in late 2023, this SARS-CoV-2 lineage continues to evolve. The LP.8.1 subvariant that was dominant in 2025 has now been replaced by other JN.1-lineage virus variants. Because of the continuing virus antigenic drift, a review and discussion regarding the need for a strain composition update for COVID-19 vaccines is warranted.

5. VRBPAC Meeting Topics

On May 28, 2026, VRBPAC will meet in open session to discuss and make recommendations on the selection of the 2026–2027 Formula for COVID-19 vaccines for use in the U.S. The committee will be asked to discuss available evidence on recent and currently circulating SARS-CoV-2 variants, including data from:

- Virus surveillance and genomic analyses
- Antigenic characterization analyses
- Vaccine effectiveness and clinical immunogenicity studies of current U.S.-authorized/approved COVID-19 vaccines
- Nonclinical immunogenicity studies of candidate vaccines expressing or containing updated Spike antigens

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