Adult Seasonal Combination Respiratory Vaccines: Policy Considerations

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Avalere
Part of Avalere Health

1201 New York Ave, NW
Washington, DC 20005

P | 202.207.1300
avalere.com

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Introduction

Combination vaccines provide protection against multiple diseases through one vaccination. Several combination vaccines are currently approved and recommended for pediatric use, including measles, mumps, and rubella (MMR) and diphtheria, tetanus, and acellular pertussis antigens (DTaP) vaccines. For adult use, there are only a few combination vaccines approved. Moreover, currently there are no approved combination vaccine that contain components that protect against seasonally circulating respiratory infections. As such, product approval, recommendation, coverage, and reimbursement pathways for adult combination respiratory vaccines are less established.

Multiple novel combination vaccines for adults 18+ are in development and expected to launch in the next decade, including products that provide protection against respiratory illnesses such as influenza, COVID-19, and respiratory syncytial virus (RSV). Stakeholders have noted the potential benefit of adult combination vaccines, including improved immunization rates, timely vaccination, reduced shipping/stocking costs, and reduced healthcare visits. As stakeholders prepare for the launch of new adult combination seasonal respiratory vaccines, they should consider key questions surrounding product approval, recommendation, coverage, and reimbursement pathways.

Overview

The systems and programs that currently facilitate patient access are focused on childhood vaccine coverage and payment models and are not designed with adult combination vaccines in mind. As such, there are open questions about how vaccine access systems may be modified to support access to these novel products. This paper discusses how current policies governing vaccine product approval, Advisory Committee on Immunization Practices (ACIP) recommendations, payer coverage, and provider payment could impact patient access to novel adult combination vaccines. The assessment focuses specifically on considerations for influenza-COVID-19 combination vaccines as there are multiple late-stage candidates in development expected to launch in the next several years. Many of the considerations discussed in this paper may also apply to other adult combination vaccines that could launch in the future.

To anticipate how systems may evolve to accommodate adult influenza/COVID-19 combination vaccines, Avalere considered questions in the following domains:

Respiratory Vaccine Strain Selection:

- What is the timing for the World Health Organization (WHO) and the Food and Drug Administration's (FDA) Vaccines Related Biological Products Advisory Committee (VRBPAC) to meet and publish recommendations for respiratory disease strain selection?

- Do current strain selection timing and processes differ between COVID-19 and influenza vaccines, and could any differences in timing influence product manufacturing and ACIP review?

ACIP Recommendation:

- How does ACIP currently review COVID-19 and influenza vaccines; how do these processes differ across respiratory disease work groups? How will ACIP approach review of a combination product?
- Does the timing for ACIP recommendations differ across COVID-19 and influenza?
- How might differences in timing impact payer coverage and provider payment?

Payer Coverage and Reimbursement:

- How do current requirements related to coverage and cost-sharing apply to adult combination products?
- Are there disparate standards for COVID-19 and influenza products, and if so, how will stakeholders apply these standards to a combined product?
- What are the implications for patient access?

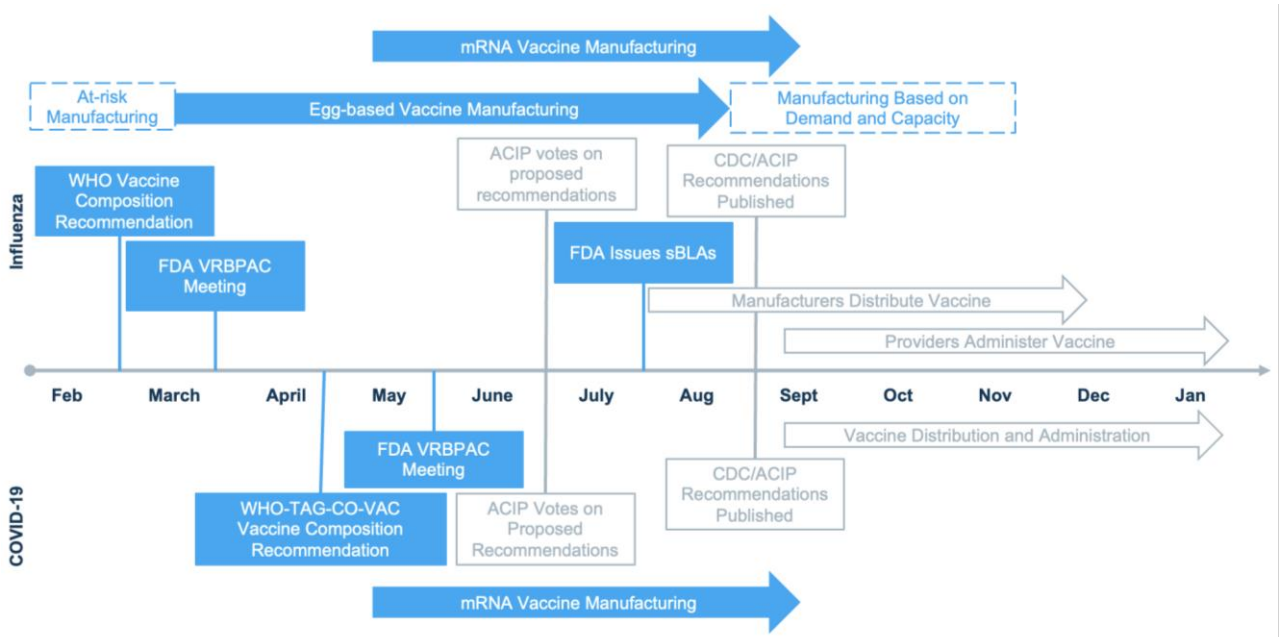
Policy Considerations to Advance Access to Adult Seasonal Respiratory Combination Vaccines

Regulatory Approval Process: Alignment of WHO and VRBPAC Strain Selection Timelines

Influenza and COVID-19 vaccines require periodic composition updates to reflect the most prevalent circulating virus strains. WHO and VRBPAC make annual recommendations on strain inclusion. Recommendation timeliness is critical, as manufacturers must produce and ship the vaccine ahead of each virus's season. While an earlier recommendation provides more time to prepare for the upcoming season, it can also result in less accurate recommendations if more virulent strains appear later in the season. Balancing timeliness with precision may be more consequential for combination vaccines because different respiratory diseases may have varying disease patterns and seasonal debut. Policymakers in both the US and globally have noted that appropriately accounting for these competing priorities is needed to develop a predictable timeline for the selection of disease strains.

COVID-19 and influenza strain selection timelines currently differ (Figure 1), and there may be opportunities for optimization while limiting disruption to the current system. For influenza, WHO typically selects Northern hemisphere strains in February and VRBPAC generally finalizes recommendations shortly thereafter. Current processes are designed to accommodate several existing manufacturing platforms (e.g., egg-based, cell-based), with the goal of facilitating production ahead of the influenza vaccine's seasonal start in July. In contrast, COVID-19 strain selection is newer, and the timeline is less established. For 2024, the WHO's Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) anticipates making a recommendation in April or May. Similar to the influenza process, VRBPAC often convenes shortly after WHO COVID-19 strain selection for vaccines licensed in the United States, which is anticipated to occur in May 2024.

Figure 1: Strain Selection and Recommendation Process Timeline for COVID-19 and Influenza Vaccines



Under the current process, strain selection for influenza would occur in March and COVID-19 in May. COVID-19 strain selection in May could complicate the production of influenza-COVID-19 combination vaccines ahead of the respiratory season, given the limited lead time. Moreover, the current influenza strain selection timeline may not account for mRNA platform efficiencies, which could allow for differentiated and potentially expedited manufacturing timelines following strain selection.

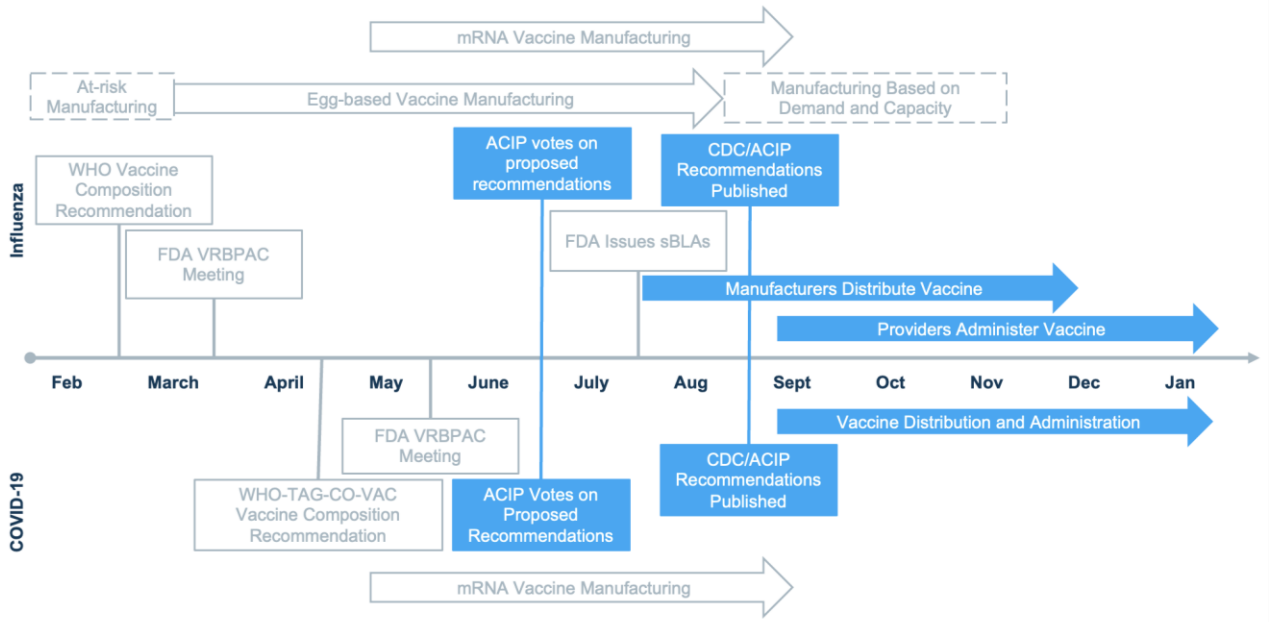
Policymakers should consider whether current strain selection procedures for each vaccine type continues to be most appropriate and whether a more streamlined approach via a single regulatory review timeline based on vaccine type (e.g., combination vaccines vs. single antigen

vaccines) or platform (e.g., mRNA vs. egg-based vs. recombinant) may be more efficient. For example, completing the strain selection and regulatory review process for both vaccine types at one time closer to the respiratory season may result in efficiencies. Alternatively, by maintaining the two-meeting March-May timeline, regulators could consider review of mRNA influenza products during the later meeting, given potentially shorter manufacturing timelines. As regulatory approval directly influences the window for which ACIP can begin recommendation development, both scenarios would support simpler clinical review and downstream access.

Alignment of ACIP Reccomendations

After regulatory approval, ACIP reviews and develops recommendations for the use of a vaccine, influencing payer coverage and provider behavior. Just as the regulatory review timelines for influenza and COVID-19 vary, so do ACIP recommendations and timelines. Currently divergent recommendations and timelines may complicate the patient accessibility.

Figure 2: ACIP Recommendation Process Timeline for COVID-19 and Influenza Vaccines



ACIP convenes Work Groups (WG) to review products based on disease area, including but not limited to influenza, COVID-19, and RSV vaccines. Given the novelty of combination adult vaccines, together the Centers for Disease Control and Prevention (CDC) and ACIP will need to decide whether to establish a new Adult Combination Vaccine WG or to use existing WGs for these purposes. A new WG could allow for the development of recommendations specific to combination vaccines, such as aligning the immunization schedules. For example, when multiple pediatric combination vaccines were launched and recommended, ACIP established a new WG to lead this work. In contrast, if ACIP relies on existing WGs and leverages established processes, this may serve to ensure that recommendations are developed and aligned with

historical guidelines. ACIP procedural documentation suggests an appropriate WG would need to be established 18–24 months prior to launch. Since combination vaccines are anticipated to launched in less than 18 months, it appears likely that in the short term any upcoming combination respiratory vaccine will be reviewed by existing WGs.

While relying on existing WGs removes certain logistical challenges, ACIP may still need to establish novel ways of working and collaborating. Most notably, COVID-19 and influenza vaccines currently have differing recommendations for use. ACIP would need to procedurally define how multiple WGs may assess and compare evidence for decision-making with regard to the Evidence to Recommendation (EtR) framework. Generally, only WG members are privy to early data and closed-door discussions, and they are discouraged from sharing information outside of public meetings. As such, ACIP will need to develop ways of working and communication guidance for different WGs reviewing the same combination product to anticipate how those WGs will build consensus for EtR appraisal.

Whether CDC pursues a single versus multiple WG model will ultimately impact recommendation development timing for component vaccines as ACIP recommendations for COVID-19 and influenza vaccines are made at different times in the year. Influenza recommendations are finalized and voted upon in June and COVID-19 vaccines were most recently recommended in September. At the February 2024 ACIP meeting, the committee discussed the benefits and drawbacks of modifying the COVID-19 recommendation timeline, including shifting from the fall to the summer to better align with influenza vaccines. While it appears that the COVID-19 WG and the CDC both support a June timeline, if the September recommendation timeline were maintained, it is unclear as to whether a combination vaccine would be covered by the start of the influenza season (i.e., July), potentially delaying payer coverage until late in the respiratory season. As the CDC considers the recommendation timeline for respiratory vaccines in the 2024-25 season, stakeholders should take into consideration how combination vaccines may be recommended in future seasons before establishing any new precedent.

Payer Coverage and Reimbursement

Coverage and Reimbursement for Combination Vaccine Products

Policies governing vaccine coverage and reimbursement for single-antigen vaccines will be applied to adult combination products, and payers across markets will be required to cover and reimburse these products without cost sharing per ACIP's recommendation. However, specific requirements related to the timing of coverage, as well as when providers can be reimbursed, varies across COVID-19 and influenza vaccines. As a result, stakeholders may need to determine whether existing coverage and reimbursement policies will need to be modified to accommodate combination influenza-COVID-19 vaccines.

Across markets, payers typically design policies to cover and reimburse only the current season's vaccines. Influenza vaccine products typically expire on June 30 of each year, meaning the current vaccine can be used from July 1 through June 30. For Medicare Part B and many state Medicaid programs, coverage of the seasonal influenza vaccine spans August 1 through July 31 of the following year. In contrast, COVID-19 vaccines do not have consistent expiration dates and vary based on product. As such, payers have not established coverage policies restricting their use between seasons. Given that influenza vaccines have an established coverage window, it is unclear whether an influenza-COVID-19 combination vaccine would also only be covered from August 1 to July 31, or whether a different coverage window would apply for combination vaccines.

Medicare coverage for vaccine types differs, complicating coverage for future combination vaccines. For example, influenza and COVID-19 vaccines are covered by Part B, while RSV vaccines are covered under Part D; it is unclear what coverage would look like for an influenza-RSV or influenza-COVID-19-RSV combination vaccine. An influenza-COVID-19 combination vaccine is more straightforward: both individual vaccines are covered under Part B, so a combination vaccine would likely also be covered under the program.

While Part B coverage for an influenza-COVID-19 combination vaccine is probable, different processes to activate provider reimbursement for COVID-19 and influenza vaccines introduce potential concerns. For influenza vaccines, Medicare retroactively reimburses providers for products administered between August 1 and October 1, after the release of the average sales price (ASP)/average wholesale price (AWP) file in October. In contrast, COVID-19 vaccines are reimbursed immediately after they are covered, since the Centers for Medicare and Medicaid Services (CMS) often perform ad hoc additions to the ASP/AWP file. CMS may need to provide clarity to providers on when payment is anticipated for combination influenza-COVID-19 vaccines.

In the commercial market, payers are required to cover COVID-19 vaccines immediately after FDA approval. This differs from the timeline for influenza vaccines, which must be covered by the beginning of the plan year that begins at least one year after the date the CDC adopts the ACIP recommendation. Since an influenza/COVID-19 combination vaccine may be the first combination vaccine containing a COVID-19 component, it is unclear which coverage standard will apply. If the current standard for influenza vaccines is applied, commercial payers may have a year or longer before they are required to cover newly recommended products, potentially delaying patient access for the initial season.

There are also outstanding questions as to how uninsured individuals may access COVID-19-containing combination vaccines. While the CDC's Bridge Access program currently provides free doses to the uninsured, it is expected to sunset at the end of 2024. While there are other adult safety net programs (e.g., Section 317) that could provide some doses, funding is limited, impacting access for uninsured adults.

Table 1: Vaccine Coverage Reimbursement Timelines for New COVID-19 and Influenza Vaccines

Market	Coverage and Reimbursement Timeline	
	Influenza	COVID-19
Medicare Part B	Coverage is initiated on August 1 and reimbursement is retroactively established on October 1	Coverage and reimbursement are established immediately following FDA approval and ACIP recommendation
Commercial	Coverage and reimbursement are often established after CDC Morbidity and Mortality Weekly Report publication; plans have up to one year and the beginning of a plan year after the publication of an ACIP recommendation to implement	Coverage and reimbursement must be established immediately after FDA approval for annual reformulations
Medicaid	Depending on state policy, coverage and reimbursement are either established per Medicare or commercial market timelines	Coverage and reimbursement are expected to be established directly following FDA approval and ACIP recommendation (there is a lag while the formularies are updated)
Uninsured	No-cost vaccines are largely not available	No-cost vaccines are available through the CDC Bridge Program until December 31, 2024, after which access is not guaranteed

Reimbursement for Combination Vaccine Administration

Payment for immunization administration to an adult may vary based on whether the vaccine is a combination or single antigen for adults. This discrepancy arises due to the structure of the Current Procedural Terminology (CPT) codes, specifically 90471–9047, 90480 for commercial and Medicaid markets, and the Level II Healthcare Common Procedure Coding System (HCPCS) codes, G0008–G0010, used in Medicare. These codes lack the granularity to differentiate reimbursement based on the number of vaccine components, and only allow

providers to report administration of a vaccine, without specifying whether the vaccine was a combination vaccine. In contrast, CPT codes commonly used for child/adolescent immunizations (90460–90461) are designed to facilitate reporting, billing, and payment for each component within a combination vaccine.

Unless this discrepancy is addressed, the current immunization administration code structure would likely allow lower provider reimbursement for administering a combination vaccine than if they administered each component vaccine separately (Table 2). This creates uncertainty and disincentivizes providers from administering adult combination vaccines.

Table 2: Illustrative Example of Adult Immunization Administration Reimbursement for a Combination Influenza-COVID-19 Vaccine vs. Separate COVID-19 and Influenza Vaccines

	Commercial / Medicaid		Medicare	
	HCPCS Codes	Payment	HCPCS Codes	Payment*
Influenza/COVID-19 Combination Vaccine	90471	$20.64	TBD	$32.57
Single Antigen COVID-19 and Influenza Vaccines Administered in Same Visit	90480 + 90471	$60.64	90480 + G0008	$72.57

*Based on 2024 National Physician Fee Schedule after the adjustments in the Consolidated Appropriations Act, 2024 and Medicare program payment rates and assumes enhanced COVID-19 vaccine payment rate is retained.

In response to similar payment concerns related to the launch of pediatric combination vaccines in the mid-2000s, the American Medical Association's CPT Panel adopted the current pediatric multi-component immunization administration codes (90460 and 90461). Before this adjustment, provider reimbursement was based on the number of vaccines administered rather than the components, which incentivized providers to prioritize administering multiple single-antigen vaccines over a combination vaccine in order to maximize payment. If stakeholders have similar concerns about incentives to administer adult combination vaccines, they could consider implementing a similar payment approach as the pediatric vaccine market or developing a Level II HCPC code that is mapped to a higher reimbursement rate in Medicare.

Looking Ahead

With several adult combination vaccines in the pipeline and nearing launch, stakeholders will need to assess how current vaccine approval, recommendation, coverage, and reimbursement

processes may need to be adapted to support patient access (Table 3). To that end, it is likely that policymakers will contemplate changes and/or clarifications to strain selection process, ACIP procedures, CPT codes, and coverage/payment timelines in the near future. Manufacturers, providers, healthcare plans, and other stakeholders should assess the impact of potential changes and consider proactive policy engagement to optimize adult combination vaccine access.

Table 3: Summary of Access Considerations for Combination Influenza-COVID-19 Vaccines and Key Stakeholders

Issue Area	Considerations	Key Stakeholders
Strain Selection Timeline	• Stakeholders will need to consider how to approach strain selection for combination vaccines, as current influenza and COVID-19 processes vary • Balancing strain selection timeliness with precision may be more consequential for combination vaccines due to differences in disease patterns and seasonal debut • Stakeholders may explore streamlined approaches, e.g., a single review timeline based on vaccine type or platform	• WHO, TAG-CO-VAC • FDA, VRBPAC
ACIP Review	• ACIP will need to decide whether to form a new Adult Combination Vaccine WG or rely on existing WGs • If relying on existing WGs, ACIP may need to establish new approaches to working and collaboration when two or more WGs are reviewing the same combination product • ACIP and other stakeholders will also need to consider recommendation timing; a later recommendation for either component could impact payer coverage and patient access	• CDC, ACIP
Product Coverage and Reimbursement	• Clarity is needed to understand if influenza/COVID-19 combination vaccine coverage will be limited to a certain window/season	• Commercial insurers • CMS • CCIIO

	• While Part B coverage is likely, CMS may need to clarify when product payment is anticipated • CMS' Center for Consumer Information and Insurance Oversight (CCIIO) may need to clarify whether commercial market coverage timelines for COVID-19 vaccines applies to combination products • CDC and other stakeholders may need to assess strategies to provide access for uninsured adults	• Medicaid agencies • Managed care organizations • CDC
Payment for Administration	• Stakeholders may consider changes to facilitate multi-component billing for combination vaccines	• AMA, CPT Editorial Panel • CMS • Providers

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Contact Us

Avalere
Part of Avalere Health
1201 New York Ave, NW
Washington, DC 20005
202.207.1300
avalere.com