Advisory Committee on Immunization Practices (ACIP)
Centers for Disease Control and Prevention (CDC)
Influenza Immunization Workgroup
Terms of Reference
DRAFT: December 18, 2025

PURPOSE

This document defines the activities, membership, and administrative requirements associated with the establishment of an **Influenza Immunization Workgroup** under the Advisory Committee on Immunization Practices, Centers for Disease Control and Prevention (ACIP, CDC). ACIP utilizes subgroups of the Committee, known as Workgroups (WGs), to review relevant published and unpublished data, and clinical and scientific knowledge, and develop options for presentation to the full ACIP parent committee during its public meetings to facilitate discussion, deliberation and development of recommendations. ACIP WGs are intended to enhance the effectiveness of ACIP. The direction, focus, and pace of both ACIP and the individual WGs are guided by CDC and HHS policies and priorities, and by the need for expert input to inform development of CDC immunization policy. ACIP WGs serve a key **scientific role** in support of immunization recommendations. The Influenza Immunization WG has been specifically established to review data, as well as clinical and scientific knowledge on existing and developmental-stage influenza immunizations, to help develop influenza immunization policy options for ACIP consideration to formulate recommendations to the Director of the CDC.

For purposes of this document, "immunization" refers to vaccines and other antibody protective products to prevent disease, e.g., immunoglobulins.

BACKGROUND

Influenza is a disease caused by the influenza A and B viruses. There are other upper respiratory viruses and pathogens such as respiratory syncytial virus (RSV), rhinoviruses, mycoplasma, Sarbecoviruses, beta coronaviruses, and human metapneumoviruses that are associated with clinical signs and symptoms similar or identical to influenza. Both influenza viruses and these other pathogens contribute to the overall burden of influenza-like illness (ILI). For some patients, influenza and other ILI can be severe, causing significant morbidity and mortality, and are a frequent contributing cofactor to morbidity and mortality in some populations with additional risk factors. Currently, there are multiple vaccine manufacturers employing a wide range of manufacturing, formulation, and adjuvant technologies to produce influenza vaccines for the United States.

The specific virus components for the 2025–2026 season include:

An A/Victoria/4897/2022 (H1N1)pdm09-like virus (for egg-based vaccines) or an A/Wisconsin/67/2022 (H1N1)pdm09-like virus (for cell- or recombinant-based vaccines)

An A/Croatia/10136RV/2023 (H3N2)-like virus (for egg-based vaccines) or an A/District of Columbia/27/2023 (H3N2)-like virus (for cell- or recombinant-based vaccines)

A B/Austria/1359417/2021 (B/Victoria lineage)-like virus

For those manufacturing platforms employing either chick embryo or mammalian cell-based antigen production, the seed virus representing the annually selected influenza strain(s) requires adaptation from the circulating version infecting humans to support efficient reproduction in the relevant manufacturing platform supporting viral replication. In some cases, this adaptation may introduce partial antigenic mismatch relative to the parental human circulating viruses. For other platforms such as baculovirus-based manufacturing, it may be that this form of seed virus protein sequence drift relative to parental strain is minimized, but these platforms may yield antigens that diverge in critical glycosylation patterns relative to parental human circulating viruses. The significance, or lack thereof, of influenza antigens glycosylated with insect patterns rather than mammalian patterns is not well characterized.

New formulations, compositions, or technologies for use in influenza vaccines are actively being developed, with a specific emphasis on a universal influenza vaccine. These may require regulatory (by the appropriate entities) and ACIP safety and efficacy and/or effectiveness review in the foreseeable future.

According to the 21st Century Cures Act (PL 114-255), ACIP shall also, as appropriate, consider new vaccines or new indications at its next regularly scheduled meeting after licensure. If the Committee defers making a recommendation, it will provide an update on the status of its review. Additionally, ACIP shall make recommendations in a timely manner for vaccines that are designated as breakthrough interventions or could be used in a public health emergency.

The purpose of this WG is to review available data, as well as clinical and scientific knowledge, to support the development of vaccine and related product clinical use recommendations for ACIP parent committee consideration, which may then elect to advise the Director of the CDC concerning those recommendations.

In accordance with the ACIP Charter, the Influenza Immunization WG will prepare information for the ACIP parent committee members to enable them to:

- Advise on population groups and/or circumstances in which one or more influenza vaccines or related agents are recommended.
- Provide recommendations on contraindications and precautions for the use of influenza vaccines and related agents, and provide information on recognized adverse events.
- Provide recommendations that address the general use of influenza vaccines and immune-globulin preparations as a class of biologic agents, use of specific antibody products for prevention of influenza infection-related infectious diseases, and special situations or populations that may warrant modification of the routine recommendations.
- Support committee deliberations on the use of immunization to control disease, including consideration of disease epidemiology and burden of disease, immunization safety, immunization efficacy and effectiveness, the quality of evidence reviewed, economic analyses, and implementation issues.
- Revise or withdraw, as warranted, their recommendation(s) regarding a particular influenza immunization or related product as new information on disease epidemiology,

immunization effectiveness or safety, economic considerations, or other data that becomes available.
- Differentiate and provide differentiated data summaries regarding the use of specific influenza vaccines in various risk groups, and facilitate modified use recommendations as appropriate or necessary concerning specific influenza vaccines or related products and technologies.

The WG will also assist and support ACIP, in accordance with Section 1928 of the Social Security Act, [42 U.S.C. Section 1396s], to be able to establish and periodically review and, as appropriate, revise the list of immunizations for administration to children and adolescents eligible to receive immunizations through the Vaccines for Children Program, along with recommended schedules concerning the appropriate dose and dosing interval, and contraindications to administration of pediatric immunizations.

The WG will engage external subject matter experts, as needed, to support development of materials for presentation to the WG and/or parent committee for its deliberations.

TOPICS UNDER DISCUSSION BY THE WORKGROUP

In accordance with the ACIP Charter and in a multi-year effort, the Influenza Immunization WG members will work with expert consultants as appropriate and in accordance with FACA statutory requirements and policies, to prepare information for presentation to and deliberation by the parent ACIP committee in developing their recommendations. In particular, the following topics and related activities relevant to influenza immunization for effective control of influenza A and/or B-related disease in the civilian population of the United States will be considered as a framework for and/or undertaken by the Influenza WG in multi-year efforts:

1) Conduct and/or review risk-benefit and cost-benefit data for, and/or analyses of, existing and newly-licensed influenza vaccines, and their administration schedules, to inform the parent committee's deliberations on vaccine use recommendations according to age-group, major risk factors, and health status.
2) Identify critical gaps in existing scientific and clinical knowledge and CDC monitoring methods related to the safety, efficacy/effectiveness, immunogenicity, and long-term immune system impacts of influenza vaccines to inform the parent committee's deliberations on development of policy recommendations and to identify further analyses and research to be recommended to CDC for its consideration and CDC potential advice to other federal agencies and the scientific community to conduct.
3) Review and summarize data, clinical and scientific knowledge related to short and long-term adverse events associated with influenza vaccines to present to the parent committee for its deliberations in identifying precautions and contraindications recommendations.
4) Review and summarize data for presentation to the parent committee on the long-term immunological effects of repeated annual influenza vaccination as a function of risk group and strain variability or type (drift/shift).

DESCRIPTION of WORKGROUP ACTIVITIES

The following activities provide a framework for the Influenza Immunization WG multi-year efforts, which may involve data requests from the FDA and other federal agencies and private partners, for development of presentations to the parent ACIP for its deliberations as it develops recommendations to the CDC Director:

1. Review and summarize existing data including published and unpublished research and clinical knowledge related to the safety, effectiveness, and immunogenicity of influenza vaccines authorized or approved in the United States.
2. Summarize literature reviews of the epidemiology of influenza disease and infection.
3. Assess the benefit-risk balance for administration of influenza immunization products co-administered with other vaccinations.
4. Identify areas where additional data and research are needed to inform influenza immunization recommendations to be developed by ACIP.
5. Annually review and develop updates of U.S. seasonal influenza immunization policy recommendations.
6. Review and summarize the existing clinical and scientific information concerning the role of innate, adaptive innate, adaptive cellular, and adaptive humoral immune responses associated with different influenza vaccines, adjuvants, and correlates of protection associated with influenza vaccination.
7. Review and summarize the existing clinical and scientific information, and gaps in the existing knowledge, including from the FDA and other federal agencies, as well as academic studies, concerning the impact of repeated influenza vaccination including immunological effects such as immune imprinting, “original antigenic sin,” and related phenomena.
8. Review and summarize the existing clinical and scientific information, and identify and address gaps in the existing knowledge regarding both antigenic sequence mismatch, as well as glycosylation mismatch, in existing immunization products and their health impacts to inform immunization recommendations.
9. Review and summarize the existing scientific knowledge and gaps, regarding the cumulative short- and long-term impact of repeated annual seasonal influenza vaccination (including boosting in young children’s first season), including non-specific effects (e.g., IgG4 class switching, immune imprinting, viral evolution under leaky immunizations) to help inform immunization recommendations.
10. Examine the impact of Influenza A and B immunization on influenza and all-cause deaths, hospitalizations, and disability to inform immunization recommendations.
11. Analyze existing data and scientific knowledge regarding cardiovascular, thrombotic, neurological, immunological, and other serious adverse events potentially caused and averted by influenza immunization.
12. Review, analyze, and summarize available data concerning the safety and effectiveness of influenza immunization of the elderly, including the interaction between influenza vaccines and immunosenescence, and both innate and adaptive immunity.

13. Review and summarize available data, information, and gaps regarding long-term repeated Influenza vaccination effects from scientific literature and clinical experience associated with influenza immunization products and influenza infection to inform policy recommendations.
14. Map existing influenza immunization policies in countries around the world and how they compare to U.S. vaccine policy.
15. Analyze existing data and scientific knowledge related to the safety of influenza immunization during pregnancy, including both potential teratogenic effects and potential beneficial effects for the newborn.

MEMBERSHIP

Workgroup Leadership: The Influenza Immunization WG is chaired by one of the ACIP, CDC parent committee members appointed to serve as Special Government Employees. The Workgroup Lead (WGL) is a federal employee, identified by the Immediate Office of the Director in consultation with the appropriate CDC program. The WG Chair, in consultation with the WGL, ACIP CDC Designated Federal Official (DFO), determines the WG's membership and work priorities and deliverables to the full committee. The DFO may further assign some of the DFO-related roles and responsibilities, as appropriate, to the WGL.

Workgroup Membership: The Influenza Immunization WG is composed of experts who are appointed based on their professional, scientific, technical, or other expertise. They are experts who are regarded as an authority or a practitioner of unique competence and skill by other persons in their profession, or occupation. Upon request, HHS federal agencies named in the ACIP charter may also appoint members to serve on WGs. The Influenza Immunization WG will be composed of members from a variety of disciplines. The WG will engage with the following disciplines on WG activities:

- Public health science and practice;
- Public health policy development, analysis, and implementation, including development and execution of immunization programs for children and adults;
- Clinical and medical practice, and patient-care experience;
- Epidemiology;
- Molecular biology;
- Immunology;
- Virology;
- Diagnostics and correlates of protection;
- Drug and vaccine safety;
- Bioethics; and
- Consumer perspectives and/or social and community aspects of immunization programs

Due to the complexity and variability of the information to be gathered, additional external subject matter experts may also be invited to provide data and presentations to the WG and answer questions during Influenza Immunization WG meetings on an ad-hoc basis. Such

additional external subject matter experts will not be members of the WG and will not participate in any deliberations or WG discussions.

MEETINGS, ADMINISTRATION, and TIMELINES

1. Administrative Oversight: The WGL will work with the WG Chair to arrange meetings, document meeting proceedings, and report to the ACIP on the Influenza Immunization WG's activities and findings.
2. Meeting frequency and location: The Influenza Immunization WG will meet on an as needed basis as determined by the WG Chair and WGL. All Influenza Immunization WG meetings are convened virtually via teleconference.
3. Meeting structure: In addition to the WGL, at least two ACIP parent committee members (one of whom serves as the Influenza Immunization WG Chair) must be present at each meeting for a quorum. An agenda, relevant publications, and background documents will be circulated as read-ahead material before each meeting.
4. Conflicts of Interest: WG members will complete an ACIP WG Agreement and Conflict of Interest Certification process before participation on the WG. The WGL will screen for conflict of interest declarations and share any conflicts with the ACIP Secretariat. The ACIP Secretariat/DFO, in collaboration with WGL will work with the Office of Business Initiatives (OSBI) ethics officials and the Office of General Counsel (OGC), as needed, to resolve any conflicts that the WGL identified. WG members will consent to abide by several guiding principles and disclose interests (e.g., employment, special interests, grants, or contracts) that a reasonable person could view as conflicts or potential conflicts of interest with their Influenza Immunization WG participation. Members will also disclose any potential conflicts of interest before each meeting. If an Influenza Immunization WG member indicates a potential or actual conflict of interest to the WGL, the WGL or designee will forward any conflicts to the DFO to determine whether the individual must recuse themselves from participating in WG discussions that implicate such a conflict-of-interest concern. If needed, the DFO will engage OSBI and OGC to assist with making COI determination.
5. Confidentiality: The discussions by the Influenza Immunization WG may include information that is unpublished, protected, privileged, proprietary, or confidential. WG deliberations, including policy options under consideration by the WG, are also considered confidential. Information of this nature must not be disseminated, distributed, or copied to, and/or described or discussed with, persons not authorized to receive such information. When these types of information are distributed, the person/s presenting will identify the information as such, so all members are duly informed; and written materials shall be clearly marked as such. Unlike ACIP parent committee meetings, which are open to the public, Influenza Immunization WG teleconferences are not subject to the open meeting requirements of the Federal Advisory Committee Act or the GSA Final Rule; data presented during these meetings/teleconferences are often proprietary and should not be distributed to people other than approved Influenza Immunization WG members.
6. CDC Staff Involvement: CDC staff do not serve as members of the Influenza Immunization WG but may provide administrative support and technical expertise to ACIP WGs, bringing subject matter expertise and current professional focus in areas relevant to the goals of the Influenza Immunization WG. Consultation or informational presentations by CDC staff will be transparent and evident to minimize the risk of, or the appearance of, undue influence that would

compromise the independence of the WG. The DFO, and WGL of Influenza Immunization WG, in consultation with the Chair of the Influenza Immunization WG, will monitor the interaction between the WG and the agency staff to ensure that the WG activities and work products are appropriate and that there is not undue influence by the CDC or by any special interest group on the activities or work products of the WG.

7. Timelines: ACIP WGs are established when needed and terminated once the activities and work products stated in the terms of reference have been completed and the WG's charge has been fulfilled.
8. Workgroup Meeting Summaries: Meeting minutes will be created to capture the information gathered during each Influenza Immunization WG meeting and teleconference.
9. Workgroup findings: The Influenza Immunization WG will present findings (briefing documents, background materials, and presentations) to ACIP parent committee for consideration and deliberation in a public meeting. Final versions of all slides presented at the ACIP parent committee meeting will be posted on the ACIP website following the meeting and included in the committee's official records.
10. Workgroup Record Keeping: All CDC FACA committees, subcommittees, and WGs are subject to the Federal Records Act. All records will be uploaded to the Federal Advisory Committee Management Portal. The summary report and other WG documents will become part of the ACIP's official records as required by GENERAL RECORDS SCHEDULE 6.2: Federal Advisory Committee Records.

RECORDKEEPING and REPORTING

The WG Chair and/or WGL will present findings/outcomes/observations to the ACIP parent committee for discussion, deliberations, further development of recommendations, and vote in an open public forum. Approved ACIP recommendations adopted by the CDC Director will be posted on CDC's ACIP website and also published in the Morbidity and Mortality Weekly Report (MMWR). In addition, approved ACIP recommendations will be included in the ACIP meeting minutes and annual report.