Exploring Expert and Stakeholders Beliefs on the Role, Evolution, and Future of the Advisory Committee on Immunization Practices

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Abstract of Dissertation

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Background: The Advisory Committee on Immunization Practices (ACIP) provides guidance to and advises the Centers of Disease Control and Prevention (CDC) on the appropriate use of approved or authorized vaccines; this informs the United States immunization schedule. While public health has benefitted from the ACIP's processes in the sixty years since its establishment, evolution in vaccine science and implementation needs may be outpacing the historic role of expert committee.

Methods: In-depth interviews were conducted among experts who were well-versed in the procedural history and role of the ACIP, including former voting members, committee Chairpersons and CDC staff. Data were organized and qualitatively assessed in NVivo using thematic analysis.

Findings: Participants indicated that the ACIP's procedures would be applicable and effective for recommendation development of novel vaccines, but discussed others issues at play, such as cost and acceptable use. Because ACIP recommendations are linked to statutory cost-sharing applicable to preventive services benefits, scientific and clinical experts are essentially responsible for product coverage determinations. Participant feedback was leveraged for the proposal and development of 14 high-level recommendations to improve committee decision-making, prioritized by their likely impact and ease of implementation.

Conclusion: Findings from this analysis underscore the pivotal role the ACIP plays in shaping US vaccine policies, emphasizing the necessity for greater guidance in the midst of increasing and evolving immunizations that will significantly change future markets. Furthermore, findings highlight the complexities which result from authority delegated to a committee of scientific experts making recommendations that inform coverage determinations and influence access.

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I. Introduction

Since 1964, the Advisory Committee on Immunization Practices (ACIP or the Committee) has served as a technical advisory group that develops recommendations on how vaccines and other immunizations should be used to prevent illness and infection among the United States (US) population.[1–3] Given the burden and severity of infectious diseases, and the population-level impact effective prevention and control measures can have, the ACIP brings together relevant subject matter experts versed in topics such as but not limited to epidemiology, immunology, vaccinology, and implementation science to provide national guidance for the preservation and improvement of public health.[4] As vaccines become available (licensed or available under Emergence Use Authorization) and introduced within the US, the ACIP reviews relevant clinical trial data and scientific evidence to ensure that vaccines are not only safe and efficacious for use, but can be implemented into existing immunization programs without significant interruption or negative impact on provider use, patient access, or population health equity.[4,5]

In recent years, the number of vaccines and immunizations preparing for launch and entering the market has significantly increased.[6] Adding further to the confusion, the term "immunization" is used to describe the process and action of administering a vaccine. While sometimes used interchangeably, there are differences in how these products are actually defined (see Box).

A DEFINING MOMENT: VACCINES AND IMMUNIZATIONS

Recently, the attention and language around vaccination has changed. To date, no statutory or regulatory definition of vaccine or immunization exists for standardized use across the numerous governmental groups that participate in policymaking. As such, the terms are often used interchangeably, though, there can be notable differences. For the purposes of this research:

- ***Vaccines*** are defined as a preparation administered prophylactically to stimulate the body's immune response against diseases and prevent infection via active immunity (i.e., given before exposure to prevent infection and/or consequence),
- ***Immunizations*** are products administered orally, nasally, or through needle injections, which may protect against a disease but function via passive immunity.
    - Products that are immunizations, but not vaccines may include:
        - Monoclonal antibodies (mAbs): Laboratory-made proteins that mimic the immune system's ability to fight off harmful pathogens and can be passively infused for pre-exposure prophylaxis or treatment post-exposure.
        - Therapeutic immunizations: vaccines administered to persons who have already manifested signs and symptoms of infection by the targeted organism(s)

Innovations in research and development have led to many products building upon existing technologies with novel clinical features, paving the way for superior safety, efficacy, and duration of protection.[7] All vaccines and select immunizations have been reviewed by the ACIP, their data assessed using the same methodology and frameworks.[8] These processes include the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach and the Evidence to Recommendation (EtR) framework, both of which have previously been described in detail.[9–11] In application, these tools aim to establish a standardized methodology for evidence assessment and review of data, to support systematic use of that evidence to inform a decision for or against a recommendation of the product. The GRADE approach and EtR framework are applied for each new product assessed, creating a review timeline that takes place over

the course of at least three meetings, or generally one calendar year.[2] The large number of reviewed and recommended products to date highlights how the ACIP ("the Committee"), has applied the framework to create a roadmap to support its recommendation development process. Considering the pipeline of future vaccines and immunizations to be reviewed before market launch, this process requires critical planning and understanding of nuanced access considerations, namely the anticipated coverage pathways, safety monitoring, and implementation within existing immunization infrastructure.

Similar to its adoption of tailored review frameworks, since its inception, the ACIP has shifted in its structure, process, and responsibilities to maintain its role in establishing immunization schedules and setting coverage standards for various markets. These changes have been shepherded by certain health policy reforms, including the establishment of the Vaccines for Children (VFC) program[12], and well as passage and enactment of the Affordable Care Act (ACA)[13] and the Inflation Reduction Act (IRA)[14], which have delegated various additional functions to the ACIP. Most critically, for immunizations reviewed and recommended for use by the ACIP, once adopted by the Director of the Centers for Disease Control and Prevention (CDC), those recommendations become federal policy and have the force of law as a coverage standard.[12–14] These policies, in an iterative fashion, have given the ACIP broad authority to establish the list of products recommended to be provided without cost-sharing through the VFC program and to develop recommendations for schedules which also must be covered by Medicaid, Medicare, and applicable commercial health plans without cost-sharing.

Because of the coverage implications associated with ACIP recommendations, vaccine manufacturers work to ensure products have certain characteristics and can demonstrate specific clinical benefit to support GRADE and EtR review. While the ACIP historically focused its recommendations on vaccines, over time the Committee has also developed recommendations for other products, including those that provide passive immunity[15], may be used post-exposure[16], or protect against manifestations of a latent infection later in life (See Box).[17] Applying the definitions above, ACIP's recommendations shifted over time from focusing solely on vaccines, given before

exposure to prevent infection, to also include other immunization and immune globulins. This shift is at the bedrock of this analysis and examination into the ACIP: given its role in establishing coverage and access standards for vaccines, there a growing interest in understanding whether other novel immunizations, such as monoclonal antibodies (passive immunity) or those that have therapeutic and preventive properties, should also be reviewed by the Committee and how precedence established from current-day decisions will have implications for shaping the future market.[18]

And while the ACIP has evolved to standardize and establish greater structure to its procedures, it still faces operational challenges and criticism from external stakeholders that should be prioritized for resolution ahead of the cascade of future products. The Committee demonstrated significant nimbleness and agility during the COVID-19 pandemic, increasing from 3 annual meetings to 17 in 2022 alone; however, its ability to swiftly review and make recommendations under regular conditions can often be hampered by the standard schedule of February, June and October meetings. Given the meeting cadence, populations that are more susceptible to or at risk of vaccine-preventable diseases may be left without covered access to regulatory approved products in the 3-4 months between meetings. These delays can have significant public health and health equity implications. Further, per the ACIP's charter, "the Committee shall consist of up to 19 (members), including the Chair."[4] These voting members hold external academic, research, and clinical positions while also each individually leading and participating in disease-specific ACIP work groups (WGs).[19] As a result of the finite number of members available to lead WGs, and the various products progressing through the stages of the pipeline at any given time, there is a set number of active WGs to review products. As previously noted, this limitation is an acute issue as research and development pipelines of vaccines and novel immunizations continue to grow. Most pressing, there is a lack of understanding for how novel immunizations will be managed by the ACIP, if reviewed by the Committee at all. Historically, these decisions have often been made well after a product has progressed through the development pipeline without explicit criteria, after manufacturers have made strategic business decisions. As one of many federal advisory committees expected to operate publicly and transparently, these issues can lead to strained relationships with immunization stakeholders, and potentially

impede crucial cooperative efforts inherent to the review process as well as mistrust of the Committee and its process.

Considering the Committee's tenure and critical role in immunization access across applicable markets within the US, an evaluation of the ACIP's function, role, and reality is timely. Prompted by the 60th anniversary of the ACIP and the Committee's expanded jurisdiction to recommend "immune globulin preparations as a class of biologic agents [and the] use of specific antibody products for prevention of infectious diseases" for inclusion within the immunization schedule, this study adopted a qualitative approach to explore perceptions of ACIP's effectiveness as a federal advisory committee and opinions on its evolving role, responsibility and sustainability.[4] Primary research interviews served to build on the literature that has previously summarized ACIP action without the relevant context of in situ considerations and drivers of decision-making. While specific ACIP recommendation actions are well-documented[20,21] and certain considerations are shared, little literature exists to explain the inner workings of the Committee, its strengths and successes as well as its flaws and challenges. This analysis of in-depth expert interviews sought to collect stakeholder input on ACIP's current role, authority, and scope for recommendation development of future novel immunizations, in an effort to proactively identify what procedural changes may be needed for future policymaking. In addition to the overall evaluation of the ACIP, participants shared focused insights into previous experiences, understanding of ACIP and CDC operations, and additional perceptions and concerns of the future of the Committee. While the ACIP has a historied past, its future is dependent on the US landscape of vaccine policy, which is constantly evolving; any research and evaluation of the Committee must be considered in the context of the federal government, presidential administrations, and the general public. Recommendations developed, and changes made, have the ability to impact public perception, which is extremely influential in the overall sentiment towards and uptake of vaccines. Given the often-polarized public perception of immunizations, continuous quality improvement to mitigate concerns and increase clarity and communication to encourage vaccination can have significant and valuable public health impacts.

II. Methods

Research Objective

As part of a continuation of research focused on the ACIP, the purpose of this project is to assess whether the ACIP has been able to effectively maintain its role as the immunization technical advisory group within the US. Specifically, this work aimed to collect expert opinions on how the ACIP has functioned, and whether the ACIP should be the recommending body to review and appraise evidence on future vaccines and immunizations. Semi-structured interviews aimed to explore whether the ACIP's current approach is fitting and appropriately transparent to support and sustain stakeholder buy-in needed for effective implementation of an ACIP recommendation. Transparency in decision-making has been demonstrated to significantly increase confidence in new vaccine policies and research processes, both pre- and post- the COVID-19 pandemic.[22,23] Leveraging findings and various consensus statements from participants on the Committee's approach and review practices, recommendations for modifications and policies were also developed to encourage evolution, streamline decision-making, and positively increase public perception in the ACIP's process. The George Washington University Institutional Review Board (IRB) approved the study protocol and exempted the research from further Human Subjects Research review (Appendix 1; FWA: 00005945; IRB:00000169; Project NCR235215).

Recruitment

An initial outreach list of interview subjects was developed following review of former ACIP voting member rosters, WG membership, meeting participation and through inquiries with members of the research committee. Additional subjects were identified via an analysis of relevant literature authorship, pulled from a previously-supported literature review analysis.[24] Candidates with varying backgrounds and levels of ACIP involvement were approached in order to collect and reflect an array of viewpoints from individuals most experienced with the Committee. Recruitment for these individuals included outreach via email. Initial solicitation emails were sent to a targeted, convenient sample of 25 individuals explaining the request for interview participation, outlining the broad topics to be discussed and the extent of participation expected. Recruitment emails also

solicited recommendations or referrals to additional contacts knowledgeable of the content and willing/able to participate. In total, sixteen interviews were organized and facilitated: meetings occurred virtually via secured and recorded Microsoft Teams or Zoom video calls. To ensure confidentiality, interviews were conducted in private settings, and records (written and audio/visual) were encrypted and secured – as dictated by George Washington University Institutional Review Board protocol.

Data Collection

Interviews were semi-structured and aimed to elicit participants' perceptions of the ACIP, including historical insights and experiences from time served on or supporting the Committee in addition to sentiments and opinions on more recent ACIP activities. To facilitate the semi-structured format, an interview guide was developed and used to ensure consistency in data collection throughout the multiple interviews. Tailored versions of the interview guide were shared accordingly, based on participant backgrounds, in advance of interviews, together with consent materials and additional participation information to provide context of discussions and outline research objectives (Appendices 1-3). Interviews lasted roughly 60 minutes and were audio recorded with consent.

Data Analysis

Participants represented backgrounds that varied in academic/institutional research, clinical practice, governmental positions, and market expertise. While various current members were contacted for interest in participation, current voting and work group members declined due to confidentiality and potential conflict of interest concerns. Interviews were automatically transcribed using Otter.ai and transcriptions were manually verified for accuracy by the author (EA). Thematic analysis was conducted with key themes derived from the interviews as the main units of analysis using NVivo 13 (QSR International, Burlington, MA). Conceptual categories were created inductively (i.e., codes and themes were developed based upon interview feedback and data) and concepts belonging to similar dimensions were grouped together. These conceptual categories, or themes, were updated in an iterative manner and revised until no new properties,

dimensions or relationships emerged during analysis. Coding for data was performed primarily by the author (EA) with a representative sample (30%) also coded by a research assistant for consistency (AG). The coding scheme was discussed and validated collectively by both researchers (EA and AG). Independent, dual coding of a subset of the interviews was performed, and data discrepancies were resolved by discussion. The final coding structure contained 6 multi-dimensional ACIP-related themes (sets) for a total of 76 nodes/code. The coding structure is available in full upon request. Key quotes and interview excerpts illustrate findings, although the analysis ultimately drew from the entirety of the dataset. Participant responses were analyzed both qualitatively and quantitatively, and descriptive thresholds were applied in synthesis to illustrate consensus on commonly discussed topics: few (≤3 individuals); several (4-6 individuals); many (7-9 individuals); most (10-15 individuals); and all (16 individuals/all participants).

III. Findings

Sixteen individuals holding a variety of leadership roles in ACIP recommendation development and vaccine policymaking, programming, implementation and practice participated in interviews. Participants included members representing both public and private entities, as well as past ACIP chairs and executive secretaries, including (non-mutually exclusive): 8 former voting members, 7 liaison members, 12 work group members, 3 federal employees, 2 biopharmaceutical industry/manufacturer employees, and 7 individuals actively monitoring and engaging with the ACIP on behalf of the vaccine industry and relevant medical societies. Given participant backgrounds and convenient sampling of external experts, it is important to note interviewees' baseline perceptions and opinions of the ACIP are likely to be more positive than a population that may have otherwise consisted of less informed stakeholders. Considering previous participation and engagement with the Committee, individuals included within the final interview sample may be less likely to question the fundamental role, remit, or purpose of the ACIP.

Themes

While interviews were structured to focus on: 1) current vaccine policy environment and ACIP recommendation development; 2) recent regulatory and policy evolution and reform; 3) future receptivity to evolution and reform; and 4) evidence generation and review methods for future product needs, thematic analysis derived six primary themes (Table 1).

Table 1. Analytic Themes and Codes

Theme	Codes
ACIP as an Organization Now	- The Role of the ACIP - External Perceptions of Committee (e.g., Visibility and Transparency) - Committee And Meeting Structure - Role Of the CDC And ACIP Leadership (Executive Secretary) - Role Of Other Committees and Regulatory Bodies
Decision-Making	- Decision-Making Frameworks - Facilitators/Barriers to Good Decision-Making - Preferential Decision-Making - Decision-Making Impact on Market Shaping - Vaccine Program Implementation
The Role of Cost-Effectiveness	- ACIP Cost-Based Decision-Making (e.g., Health Economics, Cost-Effectiveness Analysis) - Impact Of Cost in Recommendation Decision - Financial Implications
External/Environmental Factors on ACIP	- Broader Social and Political Context - External Agency Influence on ACIP - Reputation and Credibility Risks - Public Understanding and Vaccine Confidence
Defining and Designating Vaccines	- Future Vaccines and Immunization - Diseases And Pathogens - Vaccine Definition - Parties Responsible for Defining and Designation - Implications By Product
ACIP In the Future	- Future Decision-Making for New Products - Increased Public Sharing of Process/Decision-Making - Outstanding Issues Ahead of the ACIP

ACIP as an Organization Now

Overall, interviewee sentiment of the ACIP was positive, and most interviewees affirmed the critical need for a policymaking body. All participants acknowledged the significant and critical role of the ACIP, emphasizing the amount of work and effort required to convene public and work group meetings, review evidence, and develop evidence-based recommendations. One participant specifically felt that,

> *"of all the activities of the CDC, the ACIP has the largest direct impact on the health of the U.S. population… once it makes its recommendations, certainly, it reconstitutes itself as the advisory committee to the Vaccines for Children's program, and its recommendations become public policy. And for the Vaccines for Children's program, Congress must find money to support those recommendations…I don't know of any other circumstance where the US Congress has given an external group of experts both appropriation authority and authority to set or expand the limits of a benefits program like this*."

Several others noted the ACIP's work as an independent advisory body is critically important and should be even more visible to everyone. Increased visibility could occur with a return to public, in-person meetings, as opposed to virtual only for non-voting participants, as quickly recommended by most participants. This is because the Committee's significance extends beyond just the US, as several participants commented. Specifically, one participant indicated that "*ACIP is an extraordinary resource for the US and for the world. It's become the model of the national immunization technical advisory groups (NITAGs) that countries have established. It does a lot of training for other countries' experts about how to set something up and provides the evidence accessible to others for their policymaking*."

However, while there was mostly high regard for the role of the Committee, many participants suggested that the perception of the ACIP has deteriorated amongst experts, industry, and the general public. Participants acknowledged shifts in attitudes towards and views of the Committee in the wake of the COVID-19 pandemic. Specifically, one participant noted that "*ACIP is dysfunctional at best. It's largely being externally viewed as a rubber stamp. And many industry leaders have questioned why do we even need an ACIP?"* The conceptual theme that the ACIP may or may not serve as some rubber stamp

body for decision-making came up in many interviews. This theory, that the ACIP serves as an official yet powerless body for policymaking, was referenced in comparing its role to that of the Vaccines and Related Biologic Products Advisory Committee (VRBPAC), an advisory body of the Food and Drug Administration (FDA), the FDA itself, and the CDC. A matrix of these organizations (Figure 1) highlights their critical relationships as well as their differences and is explored further below. Still, many participants did not find the two vaccine-specific advisory committees to be duplicative in nature, regardless of the perceived influence or dynamic remit. While VRBPAC discussions may often evolve or stray into vaccine use, the objective questions that are posed to VRBPAC by the FDA are not intended to inform or better understand more programmatic considerations.[25]

Uniquely, the idea that the ACIP simply authorizes decisions influenced or driven by others, namely the CDC, without proper consideration, was dismissed by many but not all participants, with one suggesting "*the ACIP is not the committee that [is] just going to rubber stamp something or ignore a whole set of issues that are just relevant to people getting the vaccine. It is absolutely going to have those hard conversations."* Irrespective of dissenting opinions, participants noted the critical importance of having an advisory committee with this purpose, highlighting the need for greater recognition of ACIP's work, because, "*the fact that no one knows about it is kind of a problem. People need to understand that their health is being protected by this group. This group is taking it very seriously, and they're not going to recommend a vaccine if it's not safe, efficacious or needed.*" The ACIP's review process and decision-making efforts were prudent even prior to the COVID-19 pandemic, as some available and approved vaccines received narrower recommendations due to concerns of safety and benefit/risk ratio (e.g., Lyme[26] and meningococcal[27] vaccines). Still, the commitment or compulsion to recommend all available and approved vaccines has been particularly questioned post-COVID-19, given growing vaccine hesitancy and decreased acceptance and uptake. Most recently, the ACIP's 2024 decision to not recommend respiratory syncytial virus (RSV) vaccines for adults 18-59 years at risk of severe disease, though FDA-approved products are available, serves as a contemporary example that the committee does not automatically recommend all FDA-approved vaccines, particularly in circumstances of insufficient evidence and especially in a post-COVID era.[28,29]

Decision-Making

Given the perceived importance of the Committee among all participants, ACIP's role in recommendation development and decision-making, specifically its ability to serve as the principal vaccine market shaper was a common discussion theme, cited as a key impact by several participants. Though most participants did not emphasize this point, it is important to reiterate that while ACIP advises and makes recommendations to the government, it is ultimately with CDC's endorsement of the recommendation and inclusion of it on the immunization schedule that sets the stage for market shaping decisions. With regard to GRADE and EtR as used by the ACIP for decision-making, all participants indicated that the frameworks were helpful for the structure they provided and applicable for future products. Both tools were perceived to be generally effective facilitators in ACIP's decision-making process, providing transparency in how work groups and members assess evidence to inform votes for recommendations.

Still, many participants, including former ACIP voting members, executive secretaries and chairs, indicated the tools were imperfect and required modifications and caveating for many current products. Specific critiques suggest that sometimes the questions developed to drive the review process, often referenced as the policy question or PICO (population, intervention, comparator, outcome), were not well-suited to the framework as laid out, or that the type of data available for review would be considered of lesser quality or reviewed as suboptimal as a result of these assessment tools. All participants recognized the expectation that these frameworks provide the structure and parameters for ACIP to do its work transparently and would likely be used for the foreseeable future, without any recommendations for a superior alternative.

Shifting from how the ACIP makes decisions to the real-world impact of its recommendations, viewpoints varied with regard to the ACIP's intention and interest in shaping the market. Specifically, interviewees had differing opinions as to whether the downstream market influence of an ACIP recommendation directly informs its decision-making. Few participants felt the Committee denies or ignores that its recommendations carry such impact, with one participant noting that the ACIP "*does not appear to want to play or be a market maker. Whoever is making that decision, ACIP or CDC…it's not something they like doing*." Regardless, most participants agreed the ACIP is inherently a

market shaper and as the Committee makes any kind of recommendation for or against the use of an immunization, that decision directly influences the market, including supply, demand, and pricing. ACIP's recommendation can determine the size of the population eligible to receive it; the strength of the recommendation can impact individual behaviors in seeking it out and getting vaccinated; and the addition of the product to the VFC contract means that CDC will directly negotiate a public price for purchasing the product for use within the program.

Further, most participants commented on the ACIP's use of preferential and shared clinical decision-making (SCDM) recommendations, and the issues introduced with the implementation of either type of recommendation. Most participants noted that there is a lack of unanimity regarding the appropriate use and application of either type of recommendation. Commentary from these individuals suggest that while opinions may vary among individual ACIP members, most did not like considering preferential recommendations: voting members likely fear the risk of driving other producers out of the market, relying on a single source for supply, and introducing equity issues among individuals who perceive they may not have access to the preferred immunization. While few participants acknowledged certain products that are significantly superior, in terms of efficacy, durability, and safety, could have a "chance" at a preferential recommendation, historical failures and "embarrassment" have led to a difficult threshold that must be met before the ACIP considers preference among products. In these events, ACIP often relies on extensive real-world observational data collected over multiple years, used to characterize vaccine effectiveness, as opposed to vaccine efficacy which is often assed via clinical trials.

Participants were equally divided on the need and success of SCDM recommendation. Several participants felt strongly that ACIP's decision to continue making SCDM recommendations is a "cop out, that is ineffective for providers and patients." All participants acknowledged how SCDM recommendations are particularly terrible for providers: physicians and pharmacists are left counseling individuals on why they should or should not consider vaccination, and may not be appropriately equipped with tailored education material or adequately compensated for that time. Specifically, in ACIP's decision-making for a SCDM recommendation, one participant noted

"Everyone always says they don't want a SCDM recommendation going into discussions, and somehow, they still end up landing there from time to time. With these recommendations, the message to primary care providers is essentially that we didn't have enough evidence to make a strong recommendation one way or the other, so it's on you as a provider to take all this data and talk about it with your patient. That's a really a tough message. When in reality, the reason ACIP ends up making that recommendation is because they don't think it's a good use of healthcare resources, yet they want the vaccine to be available for people that want it. That's really what it comes down to, because they know that if they recommend against it or stay silent, then it has the potential to kill a product."

As such, though some participants voiced urgency to "eliminate SCDM from the lexicon," others recognize that the recommendation type is not entirely unattractive, allowing for a discussion instead of default vaccination, with the same cost-sharing coverage of a routine recommendation.

Most notably, in reviewing the totality of ACIP's decision-making, no participants suggested this statutory authority and influence be removed. Rather, participants noted the primary issue with ACIP's market shaping is that the ACIP rarely, if ever, acknowledges the role market impact has in informing deliberations and recommendations. Citing the need for transparency, one former voting member criticized,

"What is a bit of a black box is the market engineering that goes on behind the scenes with CDC and the manufacturers. Sometimes it seems to protect a market for a company, or to protect supply. Not that that shouldn't happen; it's just that it needs to be more transparent. If the ACIP wants to say, "we need to protect the marketplace, and we need two manufacturers and that's our priority" -- Say that. But don't come up with an excuse that's not really plausible, based on your stated criteria, as to why you're ignoring all of this evidence, when your decision isn't really science-based but supply-based. That's not unreasonable. But be transparent...It is disingenuous to say you don't want to shape the market, and then make decisions that seem to violate your own framework and pretend certain data don't exist."

Several participants felt this market-driven vs. evidence-based action is particularly apparent in the adult pneumococcal vaccine space, which currently encompasses five vaccines of varying efficacy and serotype coverage, including 23-valent polysaccharide vaccine (PPSV23), first approved for use in 1983.[30] Unlike in other countries, which may adopt a "winner-takes-all' tender market structure to limit choice, the ACIP has acknowledged the importance of maintaining vaccine options; as noted in the quoted comment above, a few participants indicated the need to disclose this as driver in decision-making as opposed to allowing less-efficacious products to maintain equivalent recommendations to those products deemed significantly superior.

As noted, embedded within the theme of ACIP as a decision-maker and market-shaper is its role in the VFC program and ACA coverage. Most participants commented on how ACIP recommendations ultimately equate to access as a result of the linkage between the ACIP recommendations and coverage policies. One participant noted that ACIP's decision to review any immunization is immediately an "*access issue. If a product is reviewed and approved, it becomes a lot easier to get uptake and to get payment."* Multiple participants acknowledged that these recommendations hold significant weight in terms of *"whether somebody's going to pay for your vaccine or not.*" This is supported by significant research which has demonstrated that removing cost as a barrier to vaccination increases access and impacts vaccination behaviors, often improving vaccine coverage rates.[31,32] Still, factors other than cost can impact uptake and differences observed across groups, including the ACIP's interpretation of evidence and clinical guidance development for providers.

Ultimately all participants noted that in the history of ACIP action, functions resulting from policies associated with government purchase or elimination of cost-sharing led to a fundamental change for ACIIP, essentially granting it the ability to make decisions about vaccine coverage. As statutory responsibility empowered the Committee to make legally binding recommendations with insurance coverage implications, most participants acknowledged a significant shift in member considerations and reflections. One participant suggested this responsibility may have also led to changes in how voting members reviewed products.

"It's interesting to understand whether that changed their decisions, that particular change, which of course started with the VFC requirement, but then got blown out with the ACA and also now, subsequent with other changes to the law to improve vaccine coverage - At some level, it makes their decisions more relevant in the real world: it's covered or not, based on what the members all say. That changed how ACIP paid attention, if at all, to think about this stuff.

The Role of Cost-Effectiveness

VFC inclusion and ACA coverage equally influence manufacturer actions and insurer/payor behavior. The relationship between manufacturers and the ACIP was embedded within virtually all participants' insights. Most participants made thematic comments that aligned one particular quote:

"The reason any manufacturer wants the ACIP recommendation is not the ACIP recommendation itself. It's the coverage. An ACIP recommendation is much more helpful for them than AAP recommendations, which didn't guarantee VFC coverage. There's an economic incentive. If a manufacturer wants that VFC/ACA coverage guaranteed, it can probably afford to take a bet that it could win that via ACIP review."

Given this relationship, many participants noted their beliefs that these policy-driven responsibilities ultimately encourage commercial interests for manufacturers, as opposed to public health ones.

"What the ACIP has done is wonderful, in terms of providing first dollar coverage for preventive care. But on the other hand, with the way the ACIP's charter works, and its interaction with the ACA, it seems like it's given the manufacturer basically a blank check. By law, those products have to be covered, and so they can set the price based on what they think is going to make them the most money, not based on what's best for the U.S. public."

Put simply, ACIP recommendations have huge financial implications, for both public and private insurers, and manufacturers alike. However, the shared mission to benefit the public's health can coexist with the industry's prerogative to be profitable. While

manufacturers have leveraged opportunities to scrutinize how ACIP's recommendations and actions may negatively impact access, equity, and revenues[33–35], as much as participants agreed that this responsibility shouldn't be revoked from the ACIP, they also agreed that manufacturers have no interest in losing the VFC entitlement or the ACA coverage implications of a recommendation to ensure broad vaccine access. And as a result, the commercial interest of vaccine manufacturers does not prevent the ACIP from acting in the public's interest, to recommend vaccines that will be covered without cost-sharing.

Still, several participants suggested a perception of diverging goals between the ACIP and manufacturers, as opposed to complimentary ones, and opinions differed based on participant background. Individuals representing federal agencies or who had served as former voting members indicated a variety of evidence-based reasons leading to ACIP's scrutiny of manufacturer behavior and potential withholding or limiting of recommendations. Individuals representing the interests of or working for vaccine manufacturers suggested ACIP decision-making compromised the public health standard in order to not outright deny coverage. The paradox of these opinions was most often related to ACIP's role in reviewing health economics to inform recommendation development.

Uniquely, cost and price are often used interchangeably but hold significant differences, specifically with regard to ACIP's application of health economics. Manufacturer-proposed pricing is among the most important inputs in cost-effectiveness models, which the ACIP uses to inform its recommendation development. The actual cost of the vaccines differs significantly based on the pricing supply chain (wholesale acquisition cost (WAC), Estimated Acquisition Cost (EAC), Average Actual Cost (AAC)). ACIP's pricing considerations in decision-making have been a known complexity in its evaluation process. Though authorizing language qualifies the consideration of economic analyses to support deliberations on vaccine use, there is no mention of immunization pricing in the ACIP's charter; the Committee does not have a formal role as an arbiter of immunization pricing, Still, almost all interview participants commented on how the ACIP increasingly has pushed to know the price of a product prior to recommendation development. As mentioned, understanding product pricing

directly informs modeling used to characterize how cost-effective a product may or may not be. This has led to a narrative that the ACIP could more positively view and broadly recommend any product for use, if the price were low enough. Considering the federal entitlement established with VFC vaccines and the cost-coverage supplemented by the ACA, recognizing the financial impact of immunization, both in terms of direct costs of vaccination and value of prevention, is significant. However, many participants indicated this should not be a primary driver of recommendation development.

This sentiment was recently reaffirmed at an October 2024 ACIP meeting, as deliberations on a new recommendation for use of pneumococcal vaccines in adults between the ages of 50-59, returned once more to the topic of price.[36] In discussing what most informed his decision-making, one member noted that the price difference between two products that were comparable but not identical was significant, and this differential was enough to drive him to not recommend use for one of the products within the age group. Counterpoints from other voting members indicated that they had different priorities, and different evaluations of domains within the EtR, which outweighed pricing to drive their voting behavior. While both products ultimately received the same recommendation, this is not the first instance where scrutiny of what is deemed to be a high-cost vaccine has had the potential to negatively influence an ACIP recommendation. Most frequently, when no recommendation is made for the use of a product, or the recommendation made is for a narrow population, multiple factors are cited as drivers, including the fact that the price of the vaccine is not assessed to be commensurate with the incidence, burden, or safety concerns of the disease and vaccine.[28]

As such, the frequency of cost, cost-effectiveness, and pricing-related commentary among participants indicates these issues remain unresolved. Commentary from several participants aligned thematically; this group believed companies are aware of how to set prices based on what they perceive ACIP will view positively, and simply choose not to. Collectively, this portion of participants, which included former manufacturer and industry representatives, indicated that manufacturers recognize what price ACIP would expect to ensure a favorable review, but are unlikely to price accordingly, often citing the value of the immunization, the cost of goods, or the need to recoup innovation investment. Counter to the previous “blank check” outlook, many of

these participants suggested they believe the ACIP is reaching a vaccine cost apex. Under a hypothetical scenario, all participants were asked to consider whether they believed ACIP would choose to not recommend an otherwise safe and efficacious product, without other implementation concerns beyond an extremely high cost; many individuals indicated that the Committee could be approaching that point. Citing recently reviewed and recommended RSV products, which ranged from ~$300-$500, one participant suggested "*particularly given what's happened in the last year, there's just a limit to what the ACIP will approve. And if a company decides to test that, they may not like what happens."* Still, the remaining portion of participants indicated they didn't know or didn't think the ACIP would withhold access to an unquestionably safe and effective product due solely to pricing since cost is most often not borne by the patient.

In detailing additional thoughts on vaccine cost and the dynamics of price-setting between manufacturers and the ACIP, participants considered the future need for cost-effectiveness modeling, given its impact on recommendations, competition, and tension between the ACIP and manufacturers. These issues have lingered for some time without resolution: similar concerns were raised in a publication by former CDC staff instrumental to creating ACIP's review framework, suggesting that, "policymaking challenges [needing] to be addressed by ACIP in the future include clarification of the role and impact, if any, of cost effectiveness in making vaccine recommendations."[34]

In exploring opinions for possible solutions, two participants acknowledged

> *"The answer is not to de-incentivize preventive interventions because we think they should be cheap. There's a balance we have to strike. And that's why I feel compelled [the ACIP should] have those conversations, in part because the ACIP is responsible for the VFC program, an entitlement program. At the same time, I think it's important for [ACIP] to be fiscally responsible and to make sure that it's using funds wisely, because there could be another 10 products that come through and at the end of the day resources are not unlimited."*

> *"We've seen the prices of vaccines go way, way up. And the manufacturers will give you all the reasons for why that is, with how much and how expensive it is to run the clinical trials, and they have to recoup their costs. But on the other hand, these are some of the most profitable corporations in the world."*

Still, given the difficulties associated with cost-effectiveness, no participants suggested application of a threshold or a range of cost-effectiveness to ease review of these analyses by ACIP. Several advised against it, indicating it would provide little to no value. Most participants confirmed no explicit threshold was used by members or referenced by the Committee, and reiterated how voting members often differ in their subjective views of cost and cost-effectiveness to inform their decision-making, given the unique and variable burden of disease among different populations. Former voting members noted the sensitivities associated with cost-effectiveness review, with one citing

> *"Threshold discussions are especially painful in the cost-effectiveness realm. I think a lot of members plead, "just tell me what it has to be," and I think the manufacturers also are begging, "just tell me what it has to be too." It's ridiculous. There are so many things we do in medicine that are so much less cost-effective than vaccines. Vaccines are actually the example of the most cost-effective thing we do. And so why should we hold ourselves to some ridiculous standard that doesn't compare to the rest of medicine?*

Certainly, several participants and presumably some current voting members see the public interest in ACIP's recommendations and the first-dollar coverage associated within them, but are significantly more impacted by the ever-growing issue of price controls of healthcare costs and the business of pharmaceutical manufacturing.

Still, manufacturers do often bear the costs associated with vaccine development, including but not limited to the research and technological innovation, cost of goods, and necessary trial design for regulatory approval.[37–39] The time, effort, and resources required to bring an immunization to market was well-understood and acknowledged among several participants, given the $200-$500 million investment over potentially 5–18 years.[38] Several participants also iterated that often these efforts occur at-risk, without any guarantee or understanding of what an ACIP recommendation could look like. As noted by one former voting member, *"manufacturers are the only ones who have the expertise and resources to make vaccines. You don't actually want the government to make a vaccine because it's hard. That's what the hardest part is - manufacturing."* A few additional participants acknowledged the role of manufacturers in vaccine development and recommended that the solution rests in stronger, proactive communication. One work

group member noted that manufacturers should consider more honest messaging around cost considerations, explaining that

> *Manufacturers just need to recoup investment so that they can continue to innovate. If ACIP caps the price to something that is good for review, you'll get this vaccine cheaply. But manufacturers are competing against drugs and other investments, and it won't work. We've had a golden era of immunization because high-priced vaccines spurred companies to invest in better HPV, pneumococcal vaccines, influenza vaccines. If the price was the lowest common denominator, you wouldn't have any of these vaccines here, unless you believe that government can develop vaccines, which I don't. The manufacturers play a key role in developing and manufacturing."*

Given the investment, immunization manufacturers seek and depend on the broadest and simplest recommendations. However, many participants articulated the additional benefits and downstream effects that are associated with any ACIP recommendation. As noted by one participant, "*the vaccine industry not only gets population recommendations, but they also get a whole army of public health professionals to promote their products. As such, [the ACIP has] an obligation to serve the public's interest when it comes to pricing and cost effectiveness."* Comprehensively, the varying yet frequent insights and commentary on ACIP's review of cost and cost-effectiveness, indicate this continues to be a charged thematic area.

External/Environmental Factors on ACIP

Given the critical position of the ACIP and the impact its decision-making has on manufacturers and other organizations, participants considered how external and environmental factors may impact the ACIP. As noted, though the ACIP is an independent advisory committee to the CDC Director and HHS Secretary, whose adoption triggers federal policy, several participants opined on whether the agencies have played a role in steering or dictating ACIP actions. Similar allegations have been made by the general public, which has suggested that ACIP's recommendations are politically motivated, given the politics of immunization, especially in a post-COVID world.[40] Ultimately all participants agreed that politics are inherently embedded within the topic of vaccination, and the Committee must interface with the political elements in vaccine policy-making

without being partisan. Under these circumstances, most participants indicated that the majority of ACIP's decisions were objective, and evidence-based, and it is the ACIP chair and ACIP Executive Secretary's responsibility to maintain such efforts.

> *"The ACIP is not a budget committee or a congressional committee. It's a scientific evidence review committee, and we are keen to preserve the authority that ACIP has and not to abuse it by making the group become a political group. We tried to. That is partly what [the Chair's role] was, or the NCIRD director's role: to just orient people when they got a little askew."*

Still, given the Committee is empowered via federal statue, the ACIP is inherently a part of the political process. Accordingly, several participants suggested that any organization that creates and potentially defers to an advisory committee expects to have some input in what the committee considers. Given the statutory role of the ACIP, and its reliance on CDC-collected surveillance and epidemiological data for decision-making, many participants believed CDC to have similar expectations. However, most participants were quick to articulate that providing input differs from influencing action. When asked, excluding the three individuals who held roles as government staff, all participants suggested some CDC interference or limitations on ACIP discussions, considerations, and votes. Participants shared various examples when they believed CDC leadership had made decisions that restricted or disregarded ACIP responsibilities. The most commonly cited examples related to COVID-19 vaccination, specifically suggestive statements from CDC Directors, the Biden Administration and HHS leadership, about vaccination before votes or recommendations occurred. Participants suggested that public rhetoric from CDC leadership and senior White House officials equated to "telling ACIP members how to vote."

Additional examples referenced Hepatitis, RSV, and meningococcal vaccine recommendations. Several participants shared instances where voting members and work groups requested to consider certain policy scenarios, including reshaping the policy question, changing the strength of the recommendation, the range of ages for the recommendation, or disentangling an entire vaccine schedule to rebuild a simpler, more easily implementable option. A few participants discussed instances where additional

information or topics raised by work group members for public presentation at ACIP were denied, leaving members unaware of critical information or considerations. Further, a few participants suggested these requests for more significant schedule changes were often "shut down" by the CDC. Counter to ACIP's efforts and intentions, such decisions can introduce access issues.

> *"When the CDC lead refused to let the work group do as it had suggested, by objecting very strongly, in my view and in the view of some other members of the work group, it delayed updating and making more assertive vaccine recommendations for 15 years. We were interested in advancing vaccination 15 years ago and the CDC would have nothing of it. They brought it up publicly in one meeting, but in a very controlled fashion; they called on some members who spoke against it and just shut it down."*

Besides leadership, such as the CDC Director or the National Center for Immunization and Respiratory Diseases (NCIRD) Director, ACIP members engage with CDC staff in two manners. There are work group leads, who serve in leadership roles for work groups – coordinating meetings and materials; and outlining steps for evidence review and recommendation timelines. There are also individuals who serve as subject matter experts for disease areas, health economics, data and surveillance, or immunization implementation. With regard to the latter group of CDC staff, most participants spoke highly and positively of their assistance. They acknowledged how much work CDC staff do to provide research and data to address member questions, participating in deliberations to support ideation on the positives and negatives of potential recommendations. However, many participants acknowledged great inconsistency in the management of work groups by CDC work group leads. Specifically, one participant noted how differences in work group engagement and productivity can be "personality-driven" and may be significantly more difficult for newer individuals and newer work groups, where the relationships between manufacturers, ACIP and CDC are not well-established.

Most importantly, all participants voiced concern about how any interference in ACIP decision-making impacts public understanding and vaccine confidence. Many participants indicated these issues could be resolved by better communication between

ACIP, CDC, and the public. As the CDC director endorses ACIP recommendation, he or she has the remit to alter what becomes federal policy. Participants noted that articulating any alterations or modifications to ACIP recommendations, and the evidentiary basis for that decision, could alleviate fallout amongst the public and among immunization experts. As one former work group member noted,

> *"I think there are a lot of reasons to trust the process for someone that has a front seat: I see what happened, I see in general how FDA works. I very much see how ACIP works. So, I have a great deal of trust in ultimately what comes out of those processes. But for the general public, you have to build that trust."*

As a committee operating publicly, transparently, and independently of the CDC, many participants urged for greater clarity in roles and responsibility, particularly to mitigate perceptions of undue influence. Combatting broader vaccine hesitancy, both among the public and among stakeholders who are well-versed in immunization, and efforts to increase vaccine confidence, when possible, was a critical and frequent theme among all participants. It is important to note, however, that a perfectly-formed and efficiently-operating ACIP would not singlehandedly provide the assurance needed to increase trust and confidence in vaccines and vaccination-related decision-making. The ACIP is not independently responsible for decreasing vaccine confidence, and reforms to the Committee will not exclusive remedy population-wide concerns. Still, given the role ACIP recommendations can play in public perception of vaccination, it is important to prudently identify where reforms may significantly combat misinformation and disinformation that can be associated with a hesitancy, and potentially, distrust.

Defining and Designating Vaccines

Participants noted that mitigating hesitation around immunization is not just critical for currently available products, but even more so for future products. Looking ahead and considering how to maintain the ACIP's role for the future, many participants indicated the most imminent and pressing issue before the Committee was increasing understanding of which products would and could be reviewed, and when decisions were made to not review products, who made an appropriate evidence-based justification.

Future immunizations, including those that intend to address illnesses or infections not previously considered vaccine-preventable, or those leveraging novel technologies, were a common theme. All participants indicated the ACIP remains the best-fitting, currently standing committee to review future vaccines and immunizations, even if they include characteristics. Still, even as the most appropriate group to develop recommendations on a large suite of immunizations, understanding how those decisions are made, and which determination criteria are used was a priority for several participants.

Participants were interviewed in the months following the ACIP's pediatric RSV mAb (nirsevimab) recommendation and VFC adoption. This product prompted many stakeholders, including those interviewed, to consider the defining features of an immunization versus a vaccine for the purposes of the ACIP review, prompting calls for pre-defined criteria. While one participant noted that the CDC *"has worked on things to make it clear what the parameters for relevant immunizing agents are,"* to date, no public guidance has been developed and determination criteria have only been briefly reviewed at one public ACIP meeting.[41,42]

With regards to decision-making related to the RSV mAb, all participants had limited ability to pinpoint which individual made the ultimate decision that the product would be reviewed by the ACIP. Many participants were also unable to articulate on what scientific basis the decision was made to treat the mAb like a more traditional vaccine, though several highlighted product characteristics that were shared with pre-existing and concurrently reviewed pediatric vaccines (i.e., maternal RSV immunization). Participants were evenly split as to whether they believed this specific recommendation decision would establish a precedent for all future mAbs and immunizations. In terms of designation efforts, several participants were aware of targeted advocacy and engagement from mAb manufacturers and immunization stakeholders, who worked together with partner groups to encourage a more favorable stance and optimal review position by the ACIP. One participant noted that some manufacturers started the efforts *"years ago, basically creating a lobby voice to push CDC and encourage ACIP to review."*

Given the long lead time needed to increase awareness of future products, their unique clinical features, and their ability to address unmet needs, understanding perceptions of ACIP's role with these products is significant. With regard to specific

nomenclature and definitions, most participants indicated that they believed ACIP has the remit to review both product types, as some acknowledged its title as

the Advisory Committee on Immunization Practices, and not the Advisory Committee on Vaccines. Other participants articulated that,

- *"My understanding is that there's nothing in the legal language of either ACIP's charter or the VFC program that specifically defines a vaccine as an active immunization, and so passive immunization can count."*

- *"I don't know when they started looking at passive protection or immunoglobulins, but that's certainly not new. That's part of their role and I think that's a continuation of something that's been true for some lengthy period of time."*

- *"I don't think there's a need to obsess about if there is there a difference between the two."*

Participants also acknowledged the evolution in-progress for which products were perceived to be reviewable by the ACIP. Former voting members and liaisons noted use of a more "traditional" definition and application of a vaccine during their tenures. Given the evolution, many participants vocalized the importance of gaining clarity around this definition from the CDC and the ACIP, highlighted the importance for developers, providers and other stakeholders to understand "the rules of the road."

For criteria or referent product characteristics that could be reviewed by the ACIP in the future, one participant supported development of a specific architecture:

"In the context of thinking about products that are preventive products for infectious diseases, and provide vaccine-like protection, what is meant by vaccine-like is that it: addresses a population health issue, and can be administered like a vaccine. So, it's not something you give every three months, it's not something that has to be given by intravenous infusion. It's not something that is so expensive that a normal immunization partner could never stock the product under any circumstances…So some of the things in that immunization space may be fabulous products with a lot of benefit for individual patients, but they're not population health products. There's just no way they could be used like we use a vaccine."

Among other participants, downstream management and vaccine price were commonly cited as critical defining features, followed by the demonstration of an impact on population versus individual health. As noted, while cost has been heavily debated by the ACIP, many participants commented that high prices for immunizations serve as a functional barrier for providers:

> *"For example, a $10,000 mAb, given every other year with super complicated cold-chain requirements, and things that are very difficult -- that product's not going to be considered by ACIP. Because if ACIP does consider it, and it's pediatric, it needs to go into VFC. And if a product goes into VFC, VFC providers are required to carry it. If you have something that's very expensive, or very complicated, it's a burden on VFC providers required to carry it and becomes very difficult."*

This was a clear concern among several participants in their forecasting of challenges for future, more costly products. Clearly, defining future products remains a complicated and unresolved issue for the ACIP, which most participants indicated negatively impacts vaccine providers and partners. While the ACIP takes issue with rising vaccine prices, in an environment where healthcare costs in general are increasing, higher price vaccines introduce challenges for providers, even when recommended and covered, due to their bulk purchasing for stocking in advance of retrospective product and administration reimbursement. Still, one former CDC employee indicated the lack of explicit guidance to define and designate future vaccines may be intentional: "*to be clear, the absence of a definition does provide some flexibility, so I am not advocating for this issue to be resolved."*

Beyond ACIP's review of the products, understanding the defining features of these products have important downstream implications. While not a common concern among participants, one complicating factor among novel immunizations includes the management of a vaccines vs. immunizations post-launch, particularly for the purposes of safety monitoring. Both the FDA and CDC share governmental responsibility of monitoring and analyzing safety concerns for vaccines. Though safety was not a common talking point among participants, safety plays a significant role in historic and mounting vaccine hesitancy. Currently, most vaccines recommended by the ACIP and the CDC and

routinely given to children or pregnant women are also accounted for via the National Vaccine Injury Compensation Program (VICP), which provides compensation to people found to be injured by certain vaccines.[43] Some currently recommended products, like COVID-19 vaccines and mAbs, are not included within VICP, and one participant noted that this presents both an interesting legal question and an issue needing consideration prior to market launch of future products. Specifically, *"if it's covered as a vaccine for purposes of ACIP, is it also a vaccine for purposes of vaccine injury? Because that starts to become a valuable suite of benefits."*

Looking ahead, understanding both the defining features and the relevant decision-makers of products to be reviewed by the ACIP was a common appeal amongst most participants. While several participants were not eager to make binding predictions for any class of immunizations, such as mAbs, they did feel precedent set by the RSV mAb suggested similar products could follow an ACIP review pathway. Even with the recent shifts, participants noted precedent for one type of novel immunization, such as a mAb, did not equate to precedent nor guaranteed review for other immunization types, such as more therapeutic vaccines. For immunizations that feature no prophylactic or preventive characteristics, intended purely for "individual patient care," most participants felt these products were not appropriate for ACIP review and recommendation. As for products that contain both preventive and therapeutic properties, while all participants were interested in seeing the products come to market with broad coverage and access, various features drove whether or not they thought they would be reviewed by the ACIP. As advised by one participant,

> *"I've learned with ACIP not to draw such fine lines and distinctions. I use the charter to guide decision-making around what should be included or not. But things evolve, there's new innovations, there's new technologies, we can't always predict from 30-40 years ago how we should define prevention activity. So I think about it in terms of public health impact, and in terms of preventability."*

ACIP In the Future

While considerations for the ACIP's sustainability and future evolution were interwoven in preceding themes, all participants deliberated on other adjustments the

ACIP could make to maintain its critical role in vaccine policymaking in the future. While praising the amount of information shared publicly via its website and ACIP meetings, participants suggested even more benefit from development and publication of member standard operating procedures and onboarding material. Similar to FDA's publication of various guidance for industry detailing the agency's considerations for data use in decision-making[44], ACIP and CDC could share material that details considerations and criteria ACIP members are assessing in their evaluation. While "User Guides" and supporting material have been shared by CDC documenting the steps and expectations for GRADE, EtR, and health economics analysis, these materials serve to provide instruction without evaluation criteria. Several participants suggested more prescriptive materials be developed and circulated, for member use and external reference, related to how decisions for which products to be reviewed are made, how manufacturers should engage in such early deliberations, and how decisions such as preferential or SCDM recommendations may be achieved. Additionally, participants noted the benefit of public policy landscape and environmental presentations, detailing the broader implications of recommendations on vaccine coverage, pricing, reimbursement, and access. While many members are practicing clinicians or research and well-versed in various specialties of vaccine science, establishing baseline knowledge of the vaccine access pathways resulting from ACIP recommendations, or the complexities of aligning immunization information systems (IIS) and clinical decision support for immunization (CDSi) with more complex recommendations, may better inform ACIP member recommendation development and understanding of feasibility and implementation. Though it is not within ACIP's charge to be responsible for the downstream events, understanding its role in influencing these milestones and events via recommendation development can serve to ensure a comprehensive and holistic understanding of vaccine access and administration.

Most practically, several participants noted that questions of quality improvement, procedural reform and committee development could be taken under review by a reactivated "General - Best Practices" work group.[45] Historically serving in a permanent and not task-oriented role, the Best Practices work group facilitated the evaluation and review of procedures and frameworks that would be adopted by the Committee to establish its best practices. The work group was charged with review of assessment tools,

such as GRADE and EtR, in an effort to bring greater systematization to ACIP's work. The group has since been disbanded, and participants noted reactivating the work group could serve to initiate the dialogue needed to address some of the thematic concerns detailed in interviews.

Virtually all participants spoke of the need for a continuous and concerted communication effort to repair post-pandemic perceptions of the ACIP and its responsibilities. When discussing issues in each of the other five thematic areas, all participants indicated the effectiveness of increasing communications around ACIP-related decisions. Notably, one participant commented that,

> *"The thing that occurs to me: in the process after a meeting, there are at least a dozen organizations, my own included, that feel the need to create their own communication, whether it's a webinar or some other summary of what just happened. I've never been to a meeting before where suddenly there were 18 summaries of what just took place. I think that right there is a signal that there's clearly a communication issue."*

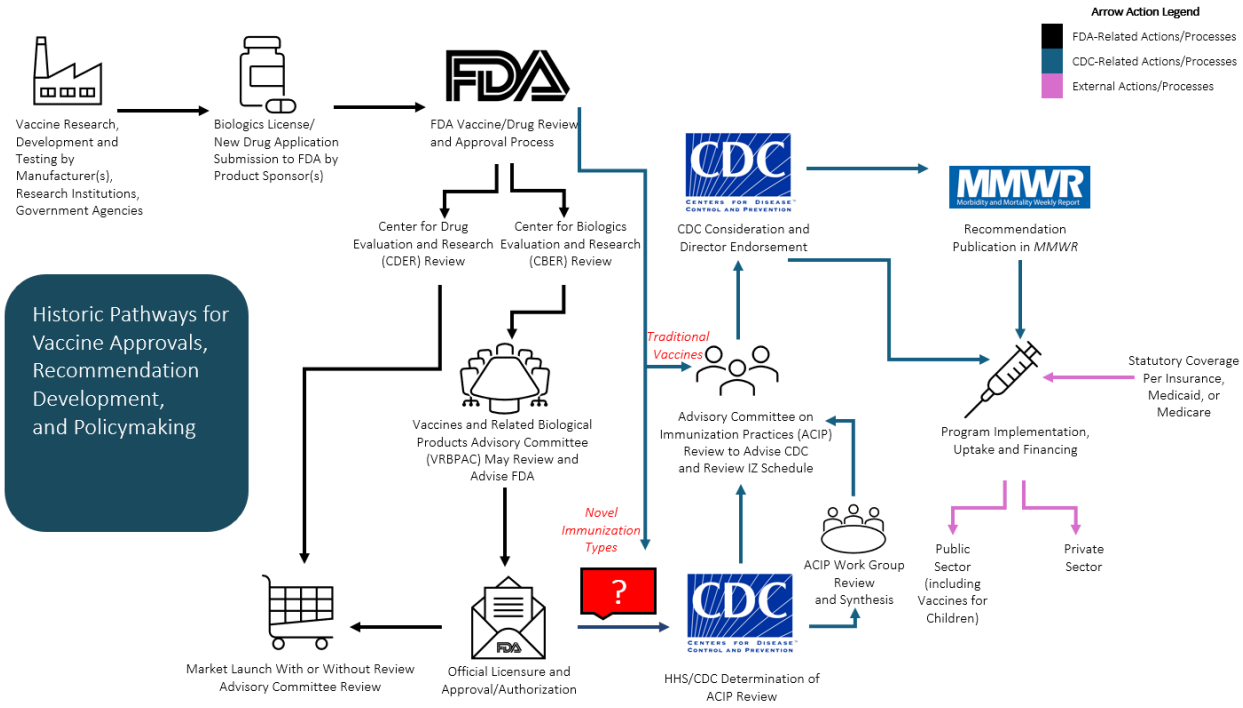
In its role as a federal advisory committee, ACIP must improve clear and transparent communication of the evidence used to drive recommendations, the reasoning behind related decisions and what other data or research informed actions taken by the Committee. While other regulatory bodies and committees exist that assess value and evidence as a product comes to market, most participants commonly cited the weight an ACIP recommendation carries among primary care providers, including pediatricians, and pharmacists, and urged increased communication, transparency and swift action in reviewing and recommending immunizations.

IV. Considerations and Recommendations

Extended discussions with 16 participants helped to better characterize the vaccine approval and review process, in an attempt to anticipate the future review of vaccines and novel immunizations. As a result of the challenges and experiences detailed by interview participants, discussions served to highlight areas where targeted reform efforts could simplify ACIP's process, help improve relationships between the ACIP and manufacturers, increase perceptions of objectivity, and minimize concerns regarding

politization of the science. Participants aided in clarifying the order of operations and matrix of relationships that take place for a vaccine to be reviewed, approved, recommended, and brought to market (Figure 1). While those familiar with launching a vaccine understand the process and parties responsible, historically, this information has not been well-documented. Characterizing similarities between vaccines and immunizations, which have historically been reviewed as drugs, is critical as similar innovative products seek review by vaccine advisory groups, like the ACIP, and come to market.

Figure 1. Traditional Relationships and Pathways for Vaccine Approval



Recommendations: Decision-Making Authority and Transparency

While participants clarified many critical steps of the vaccine approval and policymaking process, certain unknowns remain. Leveraging the insight from participants and drawing from the themes previously summarized, 14 primary recommendations are identified. While the more granular and targeted recommendations allow for easier identification of tactical action and remediation, essentially all of the recommendations are rooted in general concerns related to ACIP's decision-making authority and

transparent operation. Importantly, these recommendations are simply options that should be considered, based upon literature review and expert insights. Proper monitoring and evaluation, and more important implementation science methodology should be conducted in order to determine which options are best to implement. An additional, third-party evaluation may serve to identify other, novel recommendations that should be prioritized for the effective reform of the ACIP and its standing. Further, these recommendations below, and others proposed by any formal external evaluation of the ACIP, need to be considered in the context for the new administration in 2024. Regardless, it remains critically important to review the top-level recommendations informed by all discussions related to the current research.

Most critically, all participants were unable to provide firm details on the primary decisionmaker for whether a vaccine or immunization comes before the ACIP (Figure 1, Red Box). While this most frequently was in reference to whether the recently-reviewed RSV mAb immunization would ACIP-reviewed and included within VFC like other pediatric vaccines, it also applied to historic products (e.g., immune globulins). Among the general recommendations, it is clear there is benefit in HHS or CDC clarity to external stakeholders regarding the individual(s) or the chain-of-command responsible for decision-making. Given the number of immunizations currently moving through research and development pipelines, it would be advantageous to understand who may be making this decision, what agency/entity they sit within, and by which policies or criteria they are likely to make decisions. Given the political structure and hierarchy for decision-making in public health agencies, such as HHS, CMS and CDC, the public-serving nature of the ACIP and the fundamental principle for transparency, understanding how this decision is made and by whom is key for productive collaboration. As significant investment is required to successfully bring safe and effective products to market, the power to make policymaking decisions for products that could benefit from statutory preventive service coverage should be communicated transparently.

As critical as it is to understand who holds decision-making power, it is equally important to understand the determination criteria against which these products will be assessed. While many participants referenced the shared characteristics between immunizations and vaccines (clear public health need, implementation and administration

by similar providers, large scale population impact), many reiterated these points were not articulated by CDC or ACIP in their final decision to review the product. Based on participant perspectives, it is clear that a public discussion and development of referenceable materials outlining the statutory policy or public health-based determinations for ACIP-eligible products is necessary. Simply, understanding what will and won't fall under the purview of the ACIP, well in advance of product development and launch, will bring greater clarity and support manufacturers in investments and decision-making. As an exemplar, the United States Preventive Servies Task Force (USPSTF) has clearly defined criteria for topics that are within the scope of the Task Force.[46] This criteria is used to assess the topical relevance of possible preventive services, in advance of a vote on the potential nomination for inclusion in the Task Force's portfolio.[46] In addition to the clear definition of criteria for relevant topics within USPSTF's remit, the Task Force prioritizes communication of this process, and incorporates public commentary and feedback into each step of its recommendation development. This approach allows for significantly greater feedback than ACIP's processes. Given the ACIP and USPSTF are governed by similar statutes and equally committed to transparent recommendation development, CDC and ACIP should collaborate to develop product selection and review criteria for relevant products, allowing clear understanding of suitability in advance of formal review of the products by work groups. Though the USPSTF faces its own unique challenges, including longer timelines for review, these steps, and their public record, help to increase clarity around the Task Force's role and actions while making the group beholden to its outlined methodology. Based on participant scrutiny, it is clear the ACIP could benefit from similar measures.

Ultimately, (1) direct identification of the primary decision-maker, (2) definition of determination criteria, and (3) clearer communication of both of those elements, via unified and transparent messaging, from HHS, CDC, and ACIP, could serve to mitigate many current issues and countless future concerns. While actionable recommendations to reform ACIP's acute communication, transparency and decision-making issue are important, discussions with research participants revealed the need for a greater shift in the frame of mind by key individuals, including those on the ACIP, about the

Committee's role in policymaking. The true crux of ACIP's power is that the law, both via statute, administrative law, and agency action, already gives ACIP the authority to determine whether a preventive drug approved for the market will become a covered service, which inherently dictates the survival and success of the product. The lack of knowledge about the individuals in decision-making power is concerning and may be reflective of an overarching lack of knowledge, or worse, concern in the execution of ACIP's authority to provide first-dollar coverage and remove cost-sharing for significant public interest

These concerns were interwoven throughout all participant interviews, making it clear that recommendations for their improvement must be underscored in order to safeguard the role and evolution of the ACIP and eventually support a potential shift in mindset. As such, recommendations for 14 strategic actions were characterized to ensure reform related to all three elements could be addressed, with tailored granularity (Table 2).

These recommendations are meant to be practical, targeted and beneficial to the Committee's standing with the vaccine community, reinforcing its public health commitment as explicitly written in the ACIP charter. Informed by participant feedback and knowledge of it structure and operations from a prior analyses of the legal framework of ACIP's authority and governance[24], the recommendations captured in the table below were developed to help extend the tenure of the ACIP, ensuring its maturation and evolution of the Committee for long-term success. These recommendations may also serve to re-establish the necessary guardrails that the Committee is neither influenceable nor inoperative. It's important to note that the reforms outlined below are not the sole responsibility of the ACIP. Each reform recommendation is tied to a prior discussion theme, and presented with relevant context from participant discussion. Further, recommendations include the responsible individual(s)/agency(ies), an assessment of feasibility/implementability, and overall prioritization. An additional matrix was developed to assess feasibility/Implementability against the impact of adoption for each recommendation. Of note, not all recommendations could or should be adopted at once. Categorizing by the thematic areas from the entirety of discussions, the ACIP and CDC may focus on certain categories or various recommendations across categories in an

effort to foster stakeholder-informed improvements. In an effort to comprehensively address the viewpoints of the participating individuals and their various positions, recommendations may serve to benefit both ACIP and immunization manufacturers. Given concerns raised related to the ACIP's longevity and its role as a "rubber stamp committee" going through the motions, incorporating some of this collected feedback may help to bolster the Committee's public standing, particularly as political sentiment towards vaccines and immunizations shift.

Table 2. Policy and Procedural Recommendation for ACIP Sustainability

Coding Theme	Recommendation(s) for Reform	Responsibility Party/Entity	Implementability/Feasibility	Impact
ACIP as an Organization Now	**Expansion in membership:** Increase the number of voting members to support active work groups and increase member bandwidth	**HHS, CDC:** The ACIP Executive Secretary is responsible for reviewing candidates prior to confirmation by CDC and HHS. HHS Secretary has the ability to confirm and/or remove members.	**Moderate Implementability:** Membership increases may require an ACIP charter update (not due until 2026) and respective approval from Steering Committee, including senior federal agency leaders.	**High:** Given the pipeline of pending products, with increasing and differing complexity, more members are needed as soon as possible to support bandwidth constraints and minimize delays in reviews.
	Diversification of membership background and expertise: Expand and solicit expert backgrounds, shifting from historical pediatric-focus backgrounds to include those with different specialties/expertise (e.g., maternal, gerontology) and also understanding of vaccine development	**HHS, CDC:** The ACIP Executive Secretary is responsible for reviewing candidates prior to confirmation by CDC and HHS. HHS Secretary has the ability to confirm and/or remove members.	**Easy Implementability:** Relevant expertise, as listed within ACIP's charter, is already expansive and flexible, primarily considerations include current member terms (4 years). Other expert types may be conflicted out from participation, which signals for increased efforts to identify non-biased candidates or refine conflict of interest stipulations.	**High:** Given the expanding nature of vaccine indications and the growing adult-focused platform, more members are needed as soon as possible to better inform age- and population-appropriate recommendations.

Coding Theme	Recommendation(s) for Reform	Responsibility Party/Entity	Implementability/Feasibility	Impact
	(e.g., vaccinology and product development)			
	More annual meetings, held in-person: Increasing the number of meetings and returning to an in-person format will allow for increased, more current information sharing, and support detailed recommendation development timeline issues.	**HHS, CDC:** The ACIP Executive Secretary is responsible for the Committee's overall management. HHS Secretary has the ability to sign off on and/or revise the charter.	**Easy Implementability:** A change or increase in meeting frequency/cadence may or may not necessitate ACIP charter adjustment and may be allowed under ad hoc capabilities. Members will need to consider growing commitment. More meetings and the return to in-person may increase in estimated annual operating costs and/or staff time.	**High:** A return to in-person meetings could be adopted by the next ACIP meeting and would greatly improve stakeholder perceptions of ACIP's transparency and commitment to collaboration. Additional meetings have historically been permitted and accommodated without issue.
Decision-Making	**Clear identification/ delineation in decision-making authority for products:** The final arbiter of ACIP-eligible products, particularly novel non-traditional immunizations,	**HHS:** As the final arbiters ACIP recommendations and coverage of the US immunization schedule, HHS can clearly designate and clarify who/what divisions within the	**Easy Implementability:** Increased clarity could be gained from some document or memo that details how the decisions are made, and what the chain of command is. A reference that clearly examines decision-making around the RSV mAb, as a	**Medium:** Many manufacturer pipelines have relevant unique immunizations that could benefit from clarity sooner rather than later, though none launching in advance of ACIP's

Coding Theme	Recommendation(s) for Reform	Responsibility Party/Entity	Implementability/Feasibility	Impact
	should be identified and referenceable.	agency play a role in deciding whether a product is eligible to be reviewed by ACIP.	case-study, would be simple to develop.	February 2025 meeting.
	Development and dissemination of referenceable determination criteria: Defining which criteria or characteristics are used for decision-making is critical for transparency and costly strategic planning for vaccine and immunization stakeholders.	**CDC, CDC-Based ACIP support staff, Input from Healthcare FACAs:** Delegated authority by HHS, CDC likely houses the experts to support development and refinement of determination criteria, in addition to the communication and education of stakeholders. The ACIP Executive Secretary is responsible for compliance with FACA law. FACAs, like USPSTF, can provide models and insights.	**Difficult Implementability:** CDC and ACIP may see benefits in flexibility of not having an explicit list of criteria. Implementability requires a comprehensive understanding of the pipeline and developmental market to appropriately consider eligible/ineligible product features. A reference that clearly examines decision-making criteria and determining characteristics of the RSV mAb, as a case-study, would be simple to develop.	**High:** Many manufacturer pipelines have relevant unique immunizations that could benefit from clarity sooner rather than later, though none launching in advance of ACIP's February 2025 meeting.
	Introduction of public dialogue and	**CDC:**	**Medium Implementability:**	**High:**

Coding Theme	Recommendation(s) for Reform	Responsibility Party/Entity	Implementability/Feasibility	Impact
	stakeholder input on PICO and policy question development: The policy question development process (or characterization of the PICO question) should shift from work groups to public meeting discussions, allowing for input from non-voting member stakeholders.	A new approach as ushered in by CDC and HHS staff, involving ACIP members and attendees, would help to clarify expectations between manufacturers and the Committee.	Policy questions and PICOs are increasingly shared in advance, but deliberations related to their development occur privately, a decision made by the CDC. Of note, issues may arise related to premature consideration of proprietary information, so discussions must be sensitive to pending evidence and to membership during WG review process vs. at time of actual vote (i.e., lag in time between product in development to launch).	Manufacturers have recently been increasingly surprised by ACIP's decisions to develop policy questions that do not mirror indications (in terms of target populations, dosing, schedule/timing). Addressing these divergences by including stakeholders within the deliberation and question development process would increase collaboration/buy-in and align more closely to other FAC procedure (e.g., USPSTF).
	Development of quantitative domain-based assessments with scoring:	**CDC, ACIP Best Practices Work Group:** This will require WG reactivation and	**Difficult Implementability:** Development of a new tool or rubric, to be embedded within an existing and qualified framework will require	**Medium:** This is likely to be a lengthy process and will require individuals within

Coding Theme	Recommendation(s) for Reform	Responsibility Party/Entity	Implementability/Feasibility	Impact
	Though the review frameworks leveraged by the ACIP have provided structure, they still incorporate some subjective consideration. A scoring system or rubric to support evidence assessment, by domain would increase clarity.	support from CDC to develop, validate, and implement a novel tool or system to support more systematic, objective assessments of frameworks evidence for quantitative evaluation. This could include a review of frameworks used by other NITAGs.	significant resources (time, expertise, etc.). This would also benefit from the re-establishment of WG, which could impact individual bandwidth and require increased resource use/support from CDC.	CDC and ACIP to have bandwidth to research novel approaches for quantitative assessment of data, across all EtR framework domains. While it will boost rigor, reproducibility, and general clarity around decision-making, it is a long-term goal.
The Role of Cost-Effectiveness	**Public discussion and deliberation on the need for a cost-effectiveness threshold:** There currently are no standard thresholds used for the assessment of cost-effectiveness for all vaccines. Clarification of the formally appropriate range of incremental	**HHS, CDC, ACIP:** Decision-making on the role of cost or economics in policy-making is at the discretion of federal entities, likely by in-agency subject matter experts (disease and economic). Accepted ranges, with modest deltas, should be determined by non-industry experts to	**Difficult Implementability:** Developing a cost-effectiveness threshold range that is relevant/applicable to all vaccines and still prudent of public health needs, is difficult. Anticipating the decision-making that follows cost-effectiveness assessments stemming from developed thresholds requires consideration. At a minimum, CDC should allow for public dialogue around the general	**High:** Given the constant challenges associated with understanding how ACIP made cost-effectiveness analysis models and decisions, this should be prioritized. Again, at a minimum, allowing for an ACIP meeting to serve as a forum for general discussion would be beneficial.

Coding Theme	Recommendation(s) for Reform	Responsibility Party/Entity	Implementability/Feasibility	Impact
	cost-effectiveness ratios is critical.	understanding cost-effective vs. cost-saving vs. cost-infective products.	topic of cost-effectiveness at ACIP.	
	Education of members on cost vs. price vs. cost-effectiveness: Historic comments from ACIP voting members suggest individuals may not understand the intricacies of vaccine cost vs. price for individuals vs. systems. Public education or the development of public materials detailing the application of these terms/inputs will help to establish a shared baseline of knowledge.	**CDC-Based ACIP support staff:** Likely driven by the ACIP Executive Secretary and executed by CDC support staff, an internal evaluation or listening sessions to understand how members perceive cost, cost-effectiveness, and resource use review can support the material development for educational purposes.	**Easy Implementability:** This recommendation requires little, in terms of statute amendments or even revisions to ACIP procedural materials. It will simply rely on the organization and understanding of voting members' perceptions of cost vs. cost-effectiveness and a tailored approach to homogenize internal knowledge.	**Low:** While this reform may not decisively change the decision-making process, acknowledgement in the baseline level of membership knowledge on these items, and their implications in terms of recommendation development, and more so coverage and access, would be an easy way to address stakeholder concerns.

Coding Theme	Recommendation(s) for Reform	Responsibility Party/Entity	Implementability/Feasibility	Impact
External/Environmental Factors on ACIP	**Operation without influence by federal agencies or entities:** Perceptions of ACIP's independence and objectivity can significantly impact immunization behaviors. To assuage concerns of undue influence by political agencies (CDC, FDA, HHS) increased communication and sharper actions are needed to clarify the ACIP's role vs. the government's responsibility, authority, and expectation.	**CDC, External Groups (i.e., US. Government Accountability Office (GAO)):** It is the role and responsibility of the ACIP Executive Secretary to ensure ACIP operates in compliance with FACA law. This should include the appropriate level of guarding the independent and evidence-based pillars of the Committee. An external group, such as GAO, could also review and make statements and/or recommendations.	**Difficult Implementability:** The general political and environmental sentiment towards vaccines, and more broadly, towards delegated executive functions, can significantly shift the adoption of this recommendation. Understanding what clearly and confidently assures the public that ACIP's recommendations are evidence-based and not influenced by other factors will require significant qualitative research.	**Low:** The general political and environmental sentiment towards vaccines, and more broadly, towards delegated executive functions, can significantly shift the prioritization of this recommendation. Given other reforms to support ACIP's standing within the public, this recommendation could reasonably be deferred.
Defining and Designating Vaccines	**Emphasized designation as an immunization review committee:**	**HHS:** As the final arbiter and authorizer of ACIP's recommended immunization	**Medium Implementability:** Again, the general political and environmental sentiment towards vaccines, and more broadly, towards delegated	**Low:** Again, the general political and environmental sentiment towards

Coding Theme	Recommendation(s) for Reform	Responsibility Party/Entity	Implementability/Feasibility	Impact
	To avert any further confusion, both internal and external to the ACIP, HHS could firmly clarify that the ACIP plays a significantly role in recommendation development for vaccines and immunizations used as tools in the prevention of communicable diseases. This includes novel immunizations (antibodies, immune globulins).	schedule, HHS has the remit to explicate on what products fall under the authority of the ACIP and this includes defining their relevant characteristics. Designation like this, even as a proclamation, at the federal level will help to ensure consistent understanding of ACIP's authority and role.	executive functions, can significantly shift the adoption of this recommendation. However, an HHS-authorized affirmation and emphasis on the role of the ACIP for novel immunizations will prevent future confusion as to why certain products are or are not reviewed.	vaccines, and more broadly, towards delegated executive functions, can significantly shift the prioritization of this recommendation. However, this recommendation can be adopted with a simple memo or letter from HHS secretary, acknowledging the evolving space of vaccines and immunizations.
	Formal development of determination criteria for future immunization review: Both participants and members seek clarity on which products are or can be reviewed by	**CDC, HHS:** Given the deep bench of public health, vaccine, and laboratory experts within the CDC, the agency is best poised to support the development (and	**Medium Implementability:** Developing definitions for which products can or cannot be reviewed by the ACIP removes the flexibility the Committee currently has for making such determinations. Creating a framework to qualify future immunizations	**High:** Given the recent review and recommendation development for the RSV mAb, vaccine stakeholders and immunization manufacturers seek

Coding Theme	Recommendation(s) for Reform	Responsibility Party/Entity	Implementability/Feasibility	Impact
	the ACIP. The formal development and dissemination of characteristics assessed to be the defining features of vaccines and immunizations reviewed by the ACIP is critical.	refinement) of vaccine-specific and immunization-specific criteria applicable for ACIP. HHS will likely need to provide final authorization.	as ACIP-eligible or not will require significant understanding of the shifting science in vaccines and immunizations.	clarity in understand which products could be reviewed by the ACIP, as that significant impacts and informs clinical trials efforts.
ACIP In the Future	**Increased Material Development and Publication:** As recommended via prior themes (see above), CDC and ACIP can increase access to more of the documentation and materials used to inform decision-making (e.g., earlier publication of WG slides, new member onboarding materials).	**CDC:** The development, generation, and publication of ACIP materials are the responsibility of CDC support staff. Increased development, or if already available, publication of internal procedural materials will support efforts for transparency. Further, given the expectation for punctual manufacturer	**Medium Implementability:** It is possible there are readily available references ACIP has access to that guide its understanding of recommendation development (e.g., onboarding/training materials, primers on key vaccine topics); These materials and others developed for ACIP meetings (CDC-led session presentations) should be made available publicly, in advance of meetings.	**High:** Voting members carry different levels of understanding vaccine implementation, coverage, and policy; prioritizing establishment of a standardized, baseline level of basics is ensures evidence is unlikely to be misinterpreted. Further, timely information is a key pillar of transparency.

Coding Theme	Recommendation(s) for Reform	Responsibility Party/Entity	Implementability/Feasibility	Impact
		provision of data/presentations, CDC should meet similar expectations.		
	Re-establishment of Evidence-Based Practices Work group: The work group previously was effective in selecting the GRADE and EtR frameworks to drive decision-making and should be reactivated to consider what actions or structures may be needed to support future vaccine and immunization review.	**CDC-Based ACIP support staff, ACIP Steering Committee:** Given significant interest and/or support from ACIP members, the ACIP Executive Secretary is responsible for deciding when a WG should be created, deactivated, or reactivated.	**Easy Implementability:** A new WG may be associated with a potential increase in estimated annual operating costs and/or staff time. ACIP WGs must include two or more ACIP voting members, one of whom serves as Chair and CDC staff members. Otherwise, WGs are frequently activated and terms of reference for their overarching objectives can be easily developed and refine	**High:** Prioritizing the development of a non-vaccine specific work group, focused on maintaining the best practices of the ACIP is critical. It allows for continuous monitoring and evaluation of structure, processes, and allows for from introspection/ reflection on what modifications can be may for quality improvement and sustainability.

Of note, all the recommendations for ACIP reform (Table 2) are associated with modifications to administrative agency action and internal procedure and are not effectuated by amendments to existing ACIP-related statutes. Most recommendations suggest revisions to CDC-developed and HHS-approved ACIP governance materials (i.e., charter, framework user guides). The recommendations neither seek to revoke nor restrict the role of the ACIP, and also do not arbitrarily expand powers and remit beyond what have been delegated by statute. Current provisions which presume the ACIP's existence and responsibility have mostly been written in a manner that allows for the flexibility needed by the Committee to complete its current functions in addition to adoption of some of the recommendations. And while this level of autonomy has granted CDC and HHS, together with the ACIP, to establish the necessary procedures for functioning, it is these same processes that require reconsideration and continuous quality improvement, particularly given the increasing number of innovative immunizations. Further, in an assessment of the entities or individuals responsible for implementing possible reforms, it is clear that many of these actions fall not on ACIP itself, but on HHS, CDC and the federal staff supporting the Committee. It is these same agencies and individuals who have the ability to evaluate and potentially improve the functions of the ACIP. However, given the number of recommendations developed, it is critical to understand how to best prioritize them for an effective and productive impact.

Table 3. Reform Recommendation Prioritization and Implementation Matrix

		Impact		
		Low	**Medium**	**High**
Implementability	**Easy**	• Education of members on cost vs. price vs. cost-effectiveness	• Clear identification/ delineation in decision-making authority for products	• Diversification of membership background and expertise • More annual meetings, held in-person • Re-establishment of Evidence-Based Practices Work Group
	Medium	• Emphasized designation as an immunization review committee		• Expansion in membership • Introduction of public dialogue and stakeholder input on PICO and policy question development • Formal development of determination criteria for future immunization review • Increased Material Development and Publication
	Difficult	• Operation without influence by federal agencies or entities	• Development of quantitative domain-based assessments with scoring	• Development and dissemination of referenceable determination criteria • Public discussion and deliberation on the need for a cost-effectiveness threshold

Reorganizing recommended actions by their implementability and assessed impact (Table 3), it is easier to identify which recommendations for reform could and should be prioritized for adoption. Focusing on recommendations that were assessed to be more feasible and easily implementable, there are certainly some suggestions that could be "quick wins" with big impact (Diversification of membership background and expertise; More annual meetings, held in-person; Re-establishment of Evidence-Based Practices Work Group). Inversely, some recommendations, such as those perceived to have lower impact and implementability could be deprioritized and considered for more long-term evaluation (Operation without influence by federal agencies or entities). Recommendations which are of high impact but difficult to implement (Development and dissemination of referenceable determination criteria; Public discussion and deliberation on the need for a cost-effectiveness threshold) require significant consideration in any assessment for ACIP reform, in order to better forecast the "return on investment" to taking on such an effort. Suggestions to publicly deliberate on and establish criteria that may later be used to determine whether a product should or should not be reviewed by the ACIP and whether or not it should or should not receive a recommendation for use based on health economics modeling requires significant foresight or the ability to acknowledge that over time, the criteria will need to be reassessed to evolve. To conclude that certain interventions or disease-preventing products do not fall within ACIP's remit, and that others do not warrant recommendation due to the potential for uncontrolled costs is counter to the very fundamental interest of the ACIP itself. Vaccines and immunizations alike have significant public health impact, and the ability to grant access to these very crucial interventions via insurance coverage is a primary part of ACIP's charge. In order to strengthen ACIP's process, it is important that significant consideration is given to the recommendations developed, coupled with introspective monitoring and evaluation for quality improvement. The outcomes associated with the recommendations, either when adopted in combination or even singularly, could help to reinforce the public perception of the Committee among stakeholders, including manufacturers, vaccine providers and advocates, and the informed and interested public.

Any efforts taken to contemporize the ACIP will ultimately depend on the external political landscape and the overarching sentiment towards vaccines and immunization.

Recent events have made this focus on the ACIP even more timely. Given recently regulatory policies in front of the Supreme Court and the outcome of the 2024 election, there is an increased focus on healthcare spending, mandated coverage of preventive services, and vaccination specifically. Many of the questions raised recently include assessments of the power of the HHS Secretary and other executive powers on a federal advisory committee like the ACIP. Findings from this analysis have underscored not only how multiple statutes presume the existence of the ACIP, but also how experts recognize the continued need for the ACIP and it's critical role in disease prevention and control. Given the shift in policy, science, and values since its establishment, the ACIP has been central in developing evidence-based recommendations for product use; in order to continue doing so in sustainable way, public health authorities should consider how adopting some of these recommendations may appease and improve the future of vaccination, particularly in a climate that may increasingly become vaccine-averse. Independent of political and public sentiment, emerging infections and pandemics are ever-looming and the ACIP plays a pivotal role in assessing the safety, efficacy, and implementation considerations of interventions to prevent significant public health burden. Even with the recognition of the ACIP's significant, it remains important to encourage evolution for the Committee, to properly carve out its role and responsibility with US healthcare policy to ensure its legitimacy with broad support.

V. Limitations

While it appears to be among the few relevant assessments focused on critiquing the role of the ACIP[47], and the first of its kind to focus on primary research to inform ACIP evolution, this research and the interpretation of findings as it is not without limitations. Most notably, standing voting members, and individuals actively engaged in current work group discussions could not be recruited for participation due to existing involvement in recommendations and product review. Had they been able to participate in discussions, these individuals have the most real-time knowledge of how recent deliberations of novel immunizations have unfolded, how decisions with regard to these and other products have been made, and the individuals most responsible for making those decisions. Further, as previously noted, given participants' backgrounds and various histories

serving directly on or collaborating with the ACIP, the nature of the participant sample conveniently skewed in favor of interviewing people directly involved in ACIP's processes. The final interview sample may maintain a general more positive outlook on the ACIP and insights on what may or may not drive public perceptions in decision-making is speculative at best. That does not negate its emergence and characterization as a key theme nor substantively limit the findings but is worth noting. Similar, author experiences, including previous work with the CDC, the ACIP, and recently with vaccine manufacturers, may have informed and influenced data analysis, increasing the risk of bias in the findings and recommendations. Future research, possibly led by the ACIP or the CDC, should seek sample from both active and former ACIP membership, in an effort to support continuous quality improvement and better understand where confusion or discordance among voting members remains high. Such an effort may better support the development of tailored, and ideally public, member onboarding material, to ensure standardized baseline understanding of roles and responsibilities.

As the ACIP and its work groups are often in the process of reviewing procedures, there is a possibility some of these recommendations and calls for actions have previously been considered by those charged with running the ACIP. As materials describing similar efforts have not been made public, and as specific work group considerations are kept private due to their proprietary nature, it is difficult to discern if and why recommendations such as these have not been implemented to date. As ACIP's internal procedural matters are not published and transparent in the same way as its meetings and proceedings, there may be evidence-based reasons reforms have not been previously adopted. However, given the ACIP's commitment to transparency, an open dialogue related to these items may be valuable.

Further, given how embedded participants are in immunization policy and vaccination within the US, which can be is a rapidly evolving landscape, information and access to ACIP action or decision-making, may have changed over the course of the 3.5 months of interview, which may have influenced participants' responses. To combat this challenge, interview questions were adapted to remain broad and allow for the breadth of experiences of participants from the initial interviews (November) to the later interviews (February); at the same time, interview questions were also tailored to account for

potential increased familiarity with certain subject matter areas. A more robust analysis in the future may instead employ more rigorous quantitative survey or implementation science strategies, for increased standardization and robustness, as opposed to the semi-structured approach used for this research.

VI. Conclusion

Given it's 60-year trajectory and expansive impact on immunization policy and vaccination within the US, the ACIP warrants a formal evaluation of its role, and the need for a fresh look at the functions and processes currently employed to ensure they are fit-for-purpose going forward. As such, in-depth interviews conducted with individuals familiar with immunizations and the recommendation development process served to reiterate the importance of vaccines as a vital tool for disease prevention, and the significant role of the ACIP in granting access to such products. Consensus among participants reaffirmed that the ACIP remains the most suitable and knowledgeable group of experts to critically review such products and develop recommendations that establish statutory coverage requirements. Despite the evolution in the type of vaccines available within the US market, and the innovative technologies moving through biopharmaceutical pipelines, participants indicated that the ACIP's structure and processes were generally well-adapted to support review of the future immunizations. However, the critical need to communicate decision-making, including criteria for decision-making related to eligibility or applicability of certain products for ACIP review, was a common theme among interviewees. The impact and importance of understanding the role of cost-effectiveness and price in recommendation development ran through commentary consistently, as most participants felt that the manufacturer-based pricing of many current and forthcoming immunizations would hamper the ACIP's ability to make broad recommendations for use. Moreover, as more vaccine approvals are forthcoming, there is an opportunity to utilize lessons learned to optimize the relationship between the public, providers, manufacturers, the ACIP, and the CDC. The data from this qualitative analysis provides a comprehensive overview of how various players within the space, including those who have formerly served on the ACIP as work group and voting members, perceive the Committee can sustain its roles and responsibilities in an

environment with growing vaccine hesitancy and coverage/uptake concerns. Detailed, tactical recommendations for reform, if adopted, can serve to improve relationships between manufacturers and the ACIP with some "easy wins," which is critical to support the continued investment, research and development into lifesaving and disease-preventing vaccines. The future success of the ACIP will depend on its capacity to lean on its fundamental duty to operate transparently and its ability to receive and disseminate detailed and consistent information related to decision-making for recommendation development to appropriately influence healthcare behaviors among key stakeholders and promote innovation, acceptance, and confidence of future immunizations.

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Appendix 1. GWU IRB Outcome Letter

THE GEORGE WASHINGTON UNIVERSITY

WASHINGTON, DC

Date: October 30, 2023
To: Heinrich, Janet, PhD
From: The George Washington University Committee on Human Research, Institutional Review Board (IRB), FWA00005945
Subject: **IRB# NCR235215** , "*An Assessment of the Advisory Committee on Immunization Practices (ACIP): Evaluating the Evolving Form and Agility with Future Vaccine Products*"

Exempt Determination Date: 10/30/2023

The request for an exemption determination for the above-referenced study has been completed. The study was determined to be research that is **exempt** from IRB review under DHHS regulatory **category 2** The project as described in the application may proceed without further oversight by the OHR.

The exemption determination applies only to the project described in your IRB Application. Any changes that may alter in any way the risks to participants, type of information to be accessed, addition of new populations, or change in PI may not be instituted without submission of a Modification within the iRIS system and further review by the OHR prior to implementation of the changes. Please note, it is the responsibility of the GW research team to ensure all approved research personnel have up-to-date CITI training at all times in order to conduct human subjects/participants research.

For Exempt studies involving collaboration with external institutions/sites: Research studies that are registered as exempt are not eligible for institutional reliance agreements. Please reach out to any collaborating site(s) that will be engaged in human subjects research activities on this study to discuss next steps according to their reviewing Institutional Review Board's policies and procedures. If you have questions, please contact the GW Office of Human Research.

Questions or concerns regarding the exemption determination made for the study should be directed to the GW Office of Human Research at ohrirb@gwu.edu or (202) 994-2715.

Appendix 2. Research Informed Consent Form

Informed Consent for Participation in a Research Study

Title of Research Study: ***An Assessment of the Advisory Committee on Immunization Practices (ACIP): Evaluating the Evolving Form and Agility with Future Vaccine Products***

Investigator: ***Elif Alyanak, MPH – Milken Institute School of Public Health, The George Washington University***

KEY INFORMATION:

You are invited to take part in a research study about the Advisory Committee on Immunization Practices (ACIP). You are being asked if you want to take part in this study because the research team believes your previous work/research/experience makes you knowledgeable on the topic. As you may be familiar, the ACIP develops recommendations on the use of vaccines within the US, and which serve as insurance coverage standards and impact access to vaccines. In recent years, scientific developments have led to changes in the vaccine landscape, and this research study aims to characterize current immunization policies and their applicability to new vaccines and vaccine-like products. Your participation in this research will support understanding of existing vaccine decision-making and policy setting processes, particularly for novel vaccine technologies. Your insights will be used to support the development of recommendations for future changes or policy modifications. This interview is for academic, doctoral research and will not be used for any purpose beyond the investigator's dissertation. Findings will be shared in aggregate, so your responses will be pooled together with feedback from the other participants and will be identified. This interview is expected to take no longer than 60 minutes, and is completely voluntary. You

may decide to not answer any question or withdraw from participating at any point. Please feel free to ask the researcher questions during the consent process and use the contact information on this form to ask questions later.

WHAT IS THE PURPOSE, PROCEDURES, AND DURATION OF THIS STUDY?

By doing this study, we hope to learn your opinions and feedback on the US vaccine review process, including the ACIP's role, authority, and agility. We also hope to learn whether the committee, in its existing form, has the authority to continue similar decision-making for vaccine-like products or needs to be delegated additional remit to develop recommendations for future products, such as monoclonal antibodies and/or therapeutic vaccines. Upon receipt of your consent, your participation in this research by virtual interview will last roughly 60 minutes.

WHAT ARE THE REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

Taking part in this research will not help you directly, however the benefit to society will be a better and extremely timely understanding of the Advisory Committee on Immunization Practices (ACIP) and the vaccine recommendation development process within the US. Your participation can help to provide clarity on how vaccine policies are made, in an effort to increase public trust and understanding in a critical public health process.

WHAT ARE THE REASONS YOU MIGHT NOT CHOOSE TO VOLUNTEER FOR THIS STUDY?

The study has minimal risks, however, by participating in the interview, you may feel some emotional stress/discomfort answering the research questions. You are free to skip any questions or stop taking the survey at any point. Additionally, though extra measures will be taken to ensure privacy and confidentiality, there is a small chance someone not on the research team could find out that you took part in the study or somehow connect your name with the information collected.

DO YOU HAVE TO TAKE PART IN THIS STUDY?

You do not have to take part in this research. It is your choice whether or not you want to take part. You can agree to take part and later change your mind. If you choose not to take part or choose to stop taking part at any time, there will be no penalty to you or loss of benefits to which you are otherwise entitled.

WHAT IF YOU HAVE QUESTIONS OR CONCERNS?

The person in charge of this study is Elif Alyanak. The person providing additional executive oversight to this research is Janet Heinrich. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study Elif's contact information is: ealyanak@gwu.edu. Additional, Jan's contact information is jheinrich@email.gwu.edu.

This research is being overseen by an Institutional Review Board ("IRB"). You may talk to them at 202-994-2715 or via email at ohrirb@gwu.edu if 1) you have questions, concerns, or complaints that are not being answered by the research team or if you wish to talk to someone independent of the research team or 2) you have questions about your rights as a research subject.

Detailed Consent Form:

WHY AM I BEING INVITED TO TAKE PART IN A RESEARCH STUDY?

We invite you to take part in a research study because the research team believes your previous work/research/experience make you very knowledgeable on the topics and questions above. Your familiarity with the content provides you with the knowledge and perspective to provide insights on how the Advisory Committee on Immunization Practices (ACIP) actually functions and how vaccine recommendations and policies are developed and implemented within the US.

WHO CAN I TALK TO IF I HAVE QUESTIONS?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at by email at ealyanak@gwu.edu or jheinrich@email.gwu.edu.

This research is being overseen by an Institutional Review Board ("IRB"). You may talk to them at 202-994-2715 or via email at ohrirb@gwu.edu if:
You have questions, concerns, or complaints that are not being answered by the research team or if you wish to talk to someone independent of the research team.
You have questions about your rights as a research subject.

WHY IS THIS RESEARCH BEING DONE?

Recently, novel immunizations and new vaccine technologies/platforms have increased in development pipelines and come to market. Some of these products are considered to be vaccine-like, and function similar to traditional vaccines, preventing illness and disease. Others appear to be vaccines, but may have both preventive and therapeutic properties (i.e., can be given to individuals already exposed to or infected with specific illnesses to provide therapy). The ACIP is the decision-making body for vaccines and develops immunization policy for the US. These recommendations are then used to set the insurance coverage standard for the majority of individuals within the nation, which allows people to access vaccines at no cost to them. Given the public health impact vaccines have in preventing disease and the critical coverage benefit of ACIP recommendations, this research aims to understand if the committee can and should be making recommendations on the use of these novel products. Most recently, in August 2023, one such product, a long-acting preventive monoclonal antibody, was approved for use by the FDA and subsequently was recommended for use by the ACIP and added to the national immunization program known as the Vaccines for Children (VFC) program. This research aims to assess external insights on that process and to collect feedback related to the review of future products.
The research team will leverage findings and feedback from interview participants to develop policy and program recommendations which may alleviate any challenges characterized and to increase accessibility to important disease-preventing tools.

HOW LONG WILL I BE IN THE STUDY?

We expect that you will be in this research study, participating as an interviewee, for roughly 60 minutes.

HOW MANY PEOPLE WILL TAKE PART IN THIS RESEARCH STUDY?

We expect 20 people will take part in the entire study.

WHAT HAPPENS IF I AGREE TO BE IN THIS RESEARCH?

Upon consenting and agreeing to be in this research, the lead investigator (Elif Alyanak) will reach out to coordinate an interview date and time that works for your availability. You will receive one (1) email to schedule the interview, and one (1) email which includes the link and platform (Microsoft Teams) through which the interview will be conducted. Instructions on how to access and join the interview will also be included in that email.

One (1) day prior to the interview, the interviewer will send one (1) reminder email and offer the opportunity to ask any additional questions you may have.

At the beginning of the interview, the interviewer will reconfirm you willingness and consent to participate in the research and will ask for your permission to record the interview (audio and video). These recordings will strictly be used for data collection purposes (transcript, coding, review for accuracy). These recordings will not be used for any purpose beyond data collections – they will not be used for any presentations or publications and will not be reviewed by individuals outside of the research team.

The interview will take roughly 60 minutes. It will be conducted virtually, and will involve you as a participant with one (1) interviewer.

There is no expected follow-up for this research – upon interview completion the interviewer will thank you for participation and re-confirm contact information for any questions you may have.

The full research analysis is expected to be completed by April 2024.

WHAT HAPPENS IF I AGREE TO BE IN RESEARCH, BUT LATER CHANGE MY MIND?

You may refuse to participate or you may discontinue your participation at any time without penalty or loss of benefits to which you would otherwise be entitled. If you decide to leave the research, please contact the research team before March 2024, so that

they can remove your findings from the research and analysis. Upon termination, all research records will be destroyed and will not be further maintained.

IS THERE ANY WAY BEING IN THIS STUDY COULD BE BAD FOR ME?

The risks and discomforts associated with participation in this study are not expected to be greater than those ordinarily encountered in daily life or during the performance or routine physical or psychological examinations or tests.

However, by participating in the interview, you may feel some emotional stress/discomfort answering the research questions. You are free to skip any questions or stop taking the survey at any point. Additionally, though extra measures will be taken to ensure privacy and confidentiality, there is a small chance someone not on the research team could find out that you took part in the study or somehow connect your name with the information collected.

However, the following steps are being taken to reduce this risk:

Responses will be pooled together with other respondents/participants, and only critical individual, de-identified quotes will be used for emphasis

Data will also be saved and stored using coding, with a Master Coding Link document stored in a separate, secure location

Data will also be encrypted and password-protected for storage and security purposes.

Information will only be shared with research team, when necessary, using a encrypted and secure file transfer program

The Master Code Link fill be destroyed 1 year following research/dissertation submission, and all other research records will be maintained for three (3) years before also being destroyed.

The records of this study will be kept private. In any published articles or presentations, participant's brief and high-level backgrounds will be used to describe subject content knowledge (current professional positions will not be shared).

Your records for the study may be reviewed by departments of the University responsible for overseeing research safety and compliance.

WHAT HAPPENS IF I BELIEVE I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

You should promptly notify the research team in the event of any injury as a result of being in the study.

If you believe that you have been injured from taking part in this study, you should seek medical treatment from GWU Hospital and/or the GWU MFA or through your physician or treatment center of choice. Care for such injuries will be billed in the ordinary manner to you or your insurance company.

You will not receive any financial payments from GWU, GWU Hospital and/or the GWU MFA for any injuries or illnesses. You do not waive any liability rights for personal injury by signing this form.

WILL BEING IN THIS STUDY HELP ME IN ANY WAY?

You will not receive any benefits from participating in this research.

Taking part in this research will not help you directly, however the benefit to society will be a better and extremely timely understanding of the Advisory Committee on Immunization Practices (ACIP) and the vaccine recommendation development process within the US. Your participation can help to provide clarity on how vaccine policies are made, in an effort to increase public trust and understanding in a critical public health process.

WHAT HAPPENS TO MY INFORMATION COLLECTED FOR THE RESEARCH?

To the extent allowed by law, we limit your personal information to people who have to review it. We cannot promise complete secrecy. The IRB and other representatives of this organization may inspect and copy your information.

ARE THERE ANY COSTS FOR PARTICIPATING IN THIS RESEARCH?

There are no anticipated costs associated with your participation in this research.

WILL I BE PAID FOR MY PARTICIPATION IN THIS RESEARCH?

You will not be paid for your participation in this research.

WHAT ELSE DO I NEED TO KNOW?

It is anticipated that this research will be completed by December 2024. If manuscripts are accepted for journal publication, you will be informed upon acceptance.

Signature and Consent Authorization

By signing below, you agree that the above information has been explained to you and you have had the opportunity to ask questions. You understand that you may ask questions about any aspect of this research during the course of the study and in the future. Your signature documents your permission to take part in this research.

_____

Printed name of subject

_____

_____

Signature of subject Date

Appendix 3. Comprehensive Interview Discussion Guide/Pre-read Material

Introduction

As part of my (Elif Alyanak) doctoral dissertation, I am conducting research to better understand how the Advisory Committee on Immunization Practices (ACIP) derives its powers and authority to operate as a federal advisory committee which develops recommendations on vaccine use. As a result of provisions included in the Affordable Care Act (ACA) and the Inflation Reduction Act (IRA), these recommendations have mandatory insurance coverage and cost-sharing implications. I'm interested in characterizing many details related to the ACIP, including its form and function, and how it has evolved its approach and receptivity to novel preventive products in recent years. This includes vaccines with new technologies, long-acting passive immunizations like preventive monoclonal antibodies (mAbs), and vaccines that can have both preventive and therapeutic indications. Additionally, I'm interested in understanding how the evolution of vaccine product pipelines may be shaping and shifting the vaccine policy landscape. With many pending novel products, it is important to understand how, HHS, CDC and ACIP's roles may have been informed by and responded to these scientific advances over recent years and how they may continue adjust over time. As such, many questions in this interview will focus on both traditional vaccines and active immunizations, as well as novel non-traditional or vaccine-like products, including monoclonal antibodies (mAbs) for prevention, nosocomial vaccines, and therapeutic vaccines.

This interview will take between 45 to 60 minutes and your explicit responses will be blinded and summarized. Your identity will not be disclosed and no comments or quotes will be directly attributed to you. With your permission, if there are certain individual responses made that are particularly impactful and significant to the research question, I may report that/those quotes. However, they will not be attributed to you. With your permission, I will record the interview, both audio and video, to aid in transcription for internal analysis. However, the recordings will be used solely for the purposes of recordkeeping – they will not be used for any presentations of future research. You may choose to discontinue and withdraw from the research at any time.

Acronym Reference	
ACIP	Advisory Committee on Immunization Practices
CBER	Center for Biologics Evaluation and Research
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research
FDA	Food and Drug Administration
HHS	Department of Health and Human Services
mAb	Monoclonal Antibody
VFC	Vaccines for Children
VRBPAC	Vaccines and Related Biological Products Advisory Committee

Background

The vaccine landscape is changing with novel vaccine platforms coming to market and other innovative approaches to preventing infection under development. As such, there is limited consensus on the defining characteristics and parameters of future products, which may influence how these products are reviewed, approved, and recommended. Unlike traditional vaccines, which activate the immune system to prevent a future infection if exposed, some novel approaches are using the immune system in different ways to prevent or treat disease. To begin, it would be beneficial to detail the novel types of products, which include mAbs, nosocomial vaccines, and therapeutic vaccines, to provide context for how they're defined for the purpose of this research.

Product Type	***Definition***	***Source***
Monoclonal antibody (mAb)	Laboratory-made proteins that mimic the immune system's ability to fight off harmful pathogens such as viruses. • mAbs may be used preventively when passively infused for pre-exposure prophylaxis. • mAbs may be used as treatment when administered following disease exposure or acquisition	FDA, JAMA
Nosocomial Vaccine	Vaccines used to prevent infections acquired as a patient while receiving healthcare in a hospital or other facility which were not present at the time of admission	WHO
Therapeutic Vaccine	Vaccines administered to persons who have already manifested signs and symptoms of infection by the targeted organism.	WHO

Questions

Section I: Current Vaccine Policy Environment and ACIP Recommendation Development

The ACIP plays a critical role in access to and use of immunizations within the US. The following questions aim to solicit your opinions on the current immunization regulation and vaccine policy environment, as constructed by FDA, CDC and ACIP. All information, including both macro details of agency scope and authority as well as more micro details, related to standard operating procedures and inner workings, are relevant.

1. To your knowledge, who ultimately deems what is and is not a vaccine?
    a. Is it determined by the modality (e.g., oral vs. intramuscularly vs. intravenously)?
    b. Is it determined by the indication of the product (e.g., preventive, therapeutic, both)?
    c. Is it determined by the manufacturer or a federal agency?
2. To your knowledge and experience, what are the implications for an immunization product that is reviewed by FDA's CBER vs. CDER?
    a. Do you think that has a role on whether it is a vaccine that could be reviewed by the ACIP?
3. To your knowledge and experience, what is the relationship between the Vaccines and Related Biological Products Advisory Committee (VRBPAC) and the ACIP?
    a. Would you say their work is duplicative or complimentary?
    b. Do you believe their data/evidence needs differ significantly? Should their evidence needs differ more?
4. Are all vaccine products reviewed by VRBPAC?
    a. Should all vaccine products be reviewed by VRBPAC?
    b. Should VRBPAC review of a product influence whether or not the ACIP should review a product?
5. Can you describe how a product is generally selected for review by the ACIP?
    a. Is that decision made by the ACIP? The CDC? HHS?

6. How familiar are you with the frameworks the ACIP uses to support their evidence appraisal and decision-making (e.g., the GRADE approach and the Evidence to Recommendation (EtR) framework)
    a. To your knowledge and experience, how closely does ACIP follow its own stated and documented procedures?
    b. Do you believe any steps and measures the ACIP takes to complete review of a product and develop a recommendation for its use are superfluous?
    c. Do you believe the scrutiny the ACIP provides to different study methodologies (e.g., randomized control trials vs observation, real world data trials) is warranted and continues to be justifiable?
7. Generally speaking, do you believe the ACIP is an efficient committee that conducts its business within reasonable timeframes?
8. Do you believe the ACIP is in need of any modifications or transformations to adapt its authority to operate within more agility and efficiency?
    a. Do you the ACIP needs to operate with more transparency? What do you think that could look like?
9. Do you believe the ACIP is in need of any modifications or transformations to adapt its authority to new/future product review?
10. Stepping back, when you consider the variety of products that have gone through regulatory approval, do you think historically there have been major changes in the way industry and biopharmaceutical manufacturers interact with regulatory authorities?
    a. Particularly regarding sharing data?
    b. Particularly for novel products or technologies?
11. Similarly when you consider the variety of products that have gone through advisory committee review, do you think historically there have been major changes in the way industry and biopharmaceutical manufacturers interact with these entities?
    a. Particularly regarding sharing data?
    b. Particularly for novel products or technologies?

Section II: Recent Regulatory and Policy Evolution and Reform

As the environment of immunization changes, it's important to understand and forecast how entities traditionally involved in the creation of immunization programs and vaccine recommendations may adapt to or address new products. These next questions pertain to mAbs, nosocomial vaccines and therapeutic vaccines.

Many manufacturers are now in the process of developing a mAb as a novel strategy to provide immediate immunity against an acute respiratory viral infection. Unlike currently available preventative products, this product may not require seasonal updates and will provide effective and significant protection without delay. Most recently a mAb for use in the prevention of respiratory syncytial virus (RSV) in infants was licensed by the FDA, reviewed by the ACIP, and included in the Vaccines for Children Program (VFC).

1. To begin, besides the product mentioned, are there any products on the market that you consider to be mAbs for prevention? Any pipeline products?
2. Based on your knowledge of current possible pathways, describe the optimal pathway for regulatory bodies and recommending authorities to approach mAbs for prevention. Does this approach differ from that for traditional vaccine products?
    a. Probe: *[If expert provided an example of existing mAb for prevention product above*] Is this the pathway that X product took?

Shifting slightly, there has also been an increase in innovation with more vaccine-like products in development stages for a nosocomial vaccine. This product aims to provide protection against a highly contagious bacteria that may often be harmless, but as an opportunistic pathogen, can cause infections among certain high-risk individuals. Infections are most frequent among individuals with certain chronic conditions or among those with frequent healthcare setting exposure or hospital stays.

3. Are there any products on the market that you consider to be nosocomial vaccines? Any pipeline products?

4. Based on your knowledge of current possible pathways, describe the optimal pathway for regulatory bodies and recommending authorities to approach nosocomial vaccines. Does this approach differ from that for traditional vaccine products?
    a. Probe: *[If expert provided an example of existing nosocomial vaccine product above]* Is this the pathway that X product took?

The final product of interest could be categorized as a therapeutic vaccine. This vaccine aims to provide treatment or prevent disease exacerbation rather than prevent onset. It will be given to individuals who have been diagnosed with the illness, including but not limited to infectious diseases, chronic conditions, and cancers. While the primary indication is to provide treatment, some may have additional benefits, such as providing protection against transmission (e.g., for use with sexually transmitted diseases).

5. Are there any products on the market that you consider to be therapeutic vaccines? Any pipeline products?
    a. Probe: If a product can both treat an existent case and prevent the transmission of additional cases, in your experience, could it still be treated like a conventional vaccine?
6. Based on your knowledge of current possible pathways, describe the most optimal pathway for regulatory bodies and recommending authorities to approach therapeutic vaccine products. Does this approach differ from that of traditional vaccine products?
    a. Probe: *[If expert provided an example of existing therapeutic vaccine product above]* Is this the pathway that X product took?

More broadly:

7. To your knowledge, have regulatory authorities and recommending bodies discussed how to regulate and/or recommend vaccine-like products (including all the types of mAbs, nosocomial, and therapeutic vaccines)?
    a. Do these conversations include discussions of remit over non-traditional vaccines?

b. Are there deliberations related to data and endpoints needed for decision-making?

Section III: Future Receptivity to Evolution and Reform

To date, mAbs for prevention have received FDA approval. Examples include Evushield (COVID-19 pre-exposure prophylaxis), Synagis, and Beyfortus (prevention of RSV). Though Synagis was not initially reviewed by ACIP, Beyfortus was reviewed by ACIP, recommended for use, and included within the VFC program.

1. As more mAbs come to market, will the role of mAb recommendation continue to fall to the ACIP?
2. Do you envision that there will need to be novel work groups formed specifically for mAb review? Or will they fall within the existing disease-specific work groups?
3. If not ACIP, what group or committee would make recommendations or guidance on the use of these products?

To date, no nosocomial vaccines have been approved by the FDA.

1. Given the FDA's hypothetical approval for use of a nosocomial vaccine, what do you envision as ACIP's role in their respective review and recommendation prior to market entry?
2. Previous conversations among ACIP regarding StaphVax (nosocomial staph vaccines) indicated product manufacturers were also working together with other technical advisory committees to develop guidelines and recommendations for use – would it make more sense for another group to also be developing recommendations for the use of nosocomial vaccines? Why or why not?

To date, therapeutic vaccines have received FDA approval but have not been reviewed and recommended by the ACIP, as they have been viewed as primarily pharmaceutical products (e.g., Provenge, a cellular immunotherapy indicated for prostate cancers).

1. Do you envision ACIP's role evolving to include reviewing and recommending therapeutic vaccines or vaccine-like targeted immunotherapies?
    a. If so, do you suspect there would need to be formal changes made to committee procedural and governance documents to lead to that change? What would that look like?
    b. If not ACIP, what group or committee would make recommendations or guidance on the use of these products?

More broadly:

1. **Are the necessary regulatory authorities and policies/relationships in place and clear to support approvals for mAbs? Nosocomial vaccines? Therapeutic vaccines?**
2. **What vaccine recommendation frameworks and policies are you familiar with that have been utilized in the development of recommendations for use?**
    a. **Probe: Can you provide some examples of existing frameworks that have been used?**
    b. **Are the necessary policy authorities and relationships in place and clear to support approvals for mAbs? Nosocomial vaccines? Therapeutic vaccines?**

Section IV: Evidence Generation and Evidentiary Review Methods Necessary to Address Future Product Needs

1. For future products, what criteria do you believe need to be met for ACIP to review such interventions?
2. Keeping ACIP's GRADE and EtR frameworks in mind, do you believe those frameworks need to evolve to appropriately capture necessary data for novel vaccine products?
    a. What may need to change specifically in those evidence assessment frameworks?
    b. How do the unique needs for personalized vaccines, (e.g., cost effectiveness, health equity, benefits and harms) factor in?

    c. How might the different randomized control trial characteristics for therapeutic vaccines (e.g., case reports, small clinical trials that are not generalizable) factor into GRADE considerations?
3. What role do national decision makers' and public and health workers' perceptions around new vaccines play?
    a. What do you believe are the barriers/challenges that prevent them from reviewing vaccine-like products?
4. What evidence generation requirements are necessary to address future product needs?
    a. How will regulators prioritize outcomes? For example, how will they determine the primary outcome of interest for products like therapeutic vaccines, where an individual already has the illness?
        i. How would "effectiveness" or prevention be measured?
        ii. Will correlates of protection, surrogate or proxy outcomes, or "contiguous efficacy" be considered?
        iii. What level of population health benefit could be considered to drive a product to be subject to ACIP review?
        iv. What role does ACIP play in reviewing that population health benefit vs. the price/cost-effectiveness of the product?
        v. How would regulators approach cases when there is no defined incidence or carriage of disease?