

# MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)

SEPTEMBER 22, 2023  
MEETING SUMMARY

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## WELCOME AND INTRODUCTIONS

### Call to Order/Roll Call

**Dr. Grace Lee (ACIP Chair)** called to order and presided over the September 22, 2023 Advisory Committee on Immunization Practices (ACIP) meeting. Dr. Lee conducted a roll call, which established that a quorum was present. A list of Members, *Ex Officios*, and Liaison Representatives is included in the appendixes at the end of this summary document. No conflicts of interest (COIs) were identified.

### Announcements

**Dr. Melinda Wharton (ACIP Executive Secretary, CDC)** noted that copies of the slides for the meeting were available on the ACIP website and were made available through a ShareLink™ file for ACIP Voting, *Ex Officios*, and Liaisons Members. The ACIP is, at its heart, a public body. Engagement with the public and transparency in all of its processes are vital to the committee's work. She indicated that there would be 1 oral public comment session during this meeting, which was scheduled for 2:30 PM Eastern Time (ET). To create a fair and more efficient process, individuals interested in making an oral comment were asked to submit a request online in advance of the meeting. Priority is given to these advance requests. If more people make requests than can be accommodated, a blind lottery is conducted to determine who the speakers will be. Speakers selected in the lottery for this meeting were notified in advance of the meeting. Members of the public also may submit written comments via <https://www.regulations.gov> using Docket Number ID CDC-2023-0076. Information on the written public comment process, including information on how to make a comment, can be found on the ACIP website.

As noted in the ACIP Policies and Procedures manual, ACIP members agree to forgo participation in certain activities related to vaccines during their tenure on the committee. For certain other interests that potentially enhance a member's expertise while serving on the committee, CDC may issue limited COI waivers. Members who conduct vaccine clinical trials or serve on data safety monitoring boards (DSMBs) may present to the committee on matters related to those vaccines, but those members are prohibited from participating in committee votes on issues related to those vaccines. Regarding other vaccines of the concerned company, a member may participate in discussions with the provision that he/she abstains on all votes related to that company. ACIP members state any COIs at the beginning of each meeting. Applications and nominations are being accepted for candidates to fill upcoming vacancies on the committee.

## MATERNAL/PEDIATRIC RESPIRATORY SYNCYTIAL VIRUS (RSV) VACCINES

### Session Introduction

**Sarah S. Long, MD (Chair, Maternal/Pediatric RSV WG)** reminded everyone that each year in the United States (US) children less than 5 years of age, RSV is associated 100 to 300 deaths,<sup>1</sup> 50,000 to 80,000 hospitalizations,<sup>2</sup> approximately 500,000 emergency department (ED) visits,<sup>3</sup> and about 1.5 million outpatient visits.<sup>3</sup> RSV is the leading cause of hospitalization in US infants.<sup>4</sup> Most (68%) infants are infected in the first year of life and nearly all (97%) have been infected by 2 years of age.<sup>5</sup> Approximately 2% to 3% of young infants will be hospitalized for RSV.<sup>6</sup> RSV is the most common cause of lower respiratory tract infection (LRTI) in infants. The highest RSV hospitalization rates occur in the first months of life and risk declines with increasing age in early childhood.<sup>7</sup> About 79% of children hospitalized with RSV under 2 years of age had no underlying medical conditions,<sup>8</sup> which is very important to keep in mind.

Topics of previous WG presentations to the ACIP regarding RSV prefusion F protein (RSVpreF) vaccine have included epidemiology and burden of RSV in infants; virology and immunology of RSV; safety and efficacy of RSVpreF; cost-effectiveness analysis for RSVpreF (CDC model); cost-effectiveness analysis for RSVpreF (comparison with the manufacturer model); Evidence to Recommendations (EtR) framework for RSVpreF; and clinical considerations for RSVpreF.

On August 21, 2023, the Food and Drug Administration (FDA) approved Pfizer's RSVpreF vaccine for use in pregnant people for the prevention of lower risk for RSV lower respiratory tract disease (LRTD) and severe LRTD in infants born and from birth to 6 months of age.<sup>9</sup> The vaccine is approved as a single-dose to begin at 32–36 weeks of gestation. In Phase 2b and Phase 3 trials, vaccination was given during 24–36 weeks gestation. A numerical imbalance in preterm births was observed in RSVpreF vaccine compared to placebo recipients in 2 clinical studies. Available data are insufficient to establish or exclude a causal relationship between preterm birth and RSVpreF. Additionally, a numerical imbalance in hypertensive disorders of pregnancy was observed in RSVpreF vaccine compared to placebo recipients. Starting dosing at 32 weeks gestation can reduce the potential risk of and complications from preterm birth until additional safety data are available. This avoids the risk of extremely preterm births, where there is substantive morbidity and mortality, and very preterm births. Similar vaccine efficacy (VE) in 32–36 weeks gestation compared to the overall study population. FDA has required the manufacturer to conduct post-marketing studies to assess preterm birth and hypertensive disorders of pregnancy, including pre-eclampsia.

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<sup>1</sup> Thompson et al, JAMA, 2003; and Hansen et al, JAMA Network Open, 2022

<sup>2</sup> Hall et al, NEJM, 2009; and McLaughlin et al, J Infect Dis, 2022

<sup>3</sup> Hall et al, NEJM, 2009

<sup>4</sup> Suh et al. JID 2022

<sup>5</sup> Glezen et al, Arch Dis Child, 1986

<sup>6</sup> Hall et al, Pediatrics, 2013; Langley & Anderson, PIDJ, 2011; and CDC NVSN data

<sup>7</sup> Hall et al, NEJM, 2009; and CDC NVSN data

<sup>8</sup> Hall et al, NEJM, 2009

<sup>9</sup> <https://www.fda.gov/news-events/press-announcements/fda-approves-first-vaccine-pregnant-individuals-prevent-rsv-infants>; <https://www.fda.gov/media/171482/download?attachment>; and <https://www.fda.gov/media/171492/download?attachment>

RSVpreF vaccine is one of two available preventive products for RSV in infants. On August 3, 2023, ACIP recommended nirsevimab for RSV prevention in infants. Infants aged <8 months born during or entering their first RSV season are recommended to receive 1 dose of nirsevimab (50 mg for infants <5 kg and 100 mg for infants ≥5 kg). Children 8–19 months of age who are at increased risk of severe RSV disease and entering their second RSV season are recommended to receive 1 dose of nirsevimab (200 mg).

Both nirsevimab and maternal RSV vaccine provide passive immunity.<sup>10</sup> A person develops active immunity from infection or vaccination, which triggers an immune response. Immunologic memory provides prolonged protection that may be lifelong. Passive immunity is the transfer of preformed antibody produced externally to provide protection to the recipient, such as from mother to baby through transplacental or breastmilk transfer; or through direct administration of antibodies, such as intravenous immunoglobulin (IVIG) therapy or monoclonal antibodies. Passive immunity provides temporary protection that wanes with time.

This meeting included presentations on the following:

- RSVpreF Vaccine Safety Surveillance in Pregnancy from The Vaccine Safety Datalink (VSD)
- Maternal RSV Vaccine Safety Monitoring in the Vaccine Adverse Event Reporting System (VAERS) and v-safe<sup>sm</sup>
- An Economic Analysis of RSVpreF Maternal Vaccination
- Economics of Preventing RSV Disease among US Infants by Maternal Vaccination Prior to Birth
- EtR Framework Updates: Pfizer Maternal RSVpreF Vaccine
- Updated Clinical Considerations for Use of Both Nirsevimab and Pfizer RSVpreF Vaccine
- Implementation Considerations for Maternal RSV Vaccine
- Vaccines for Childrens Resolution

In closing, Dr. Long presented the Policy Question under consideration:

“Should Pfizer RSVpreF vaccine be recommended for pregnant people to be given during 32 through 36 weeks gestation to prevent RSV lower respiratory tract infection in infants?”

### **RSVpreF Vaccine Safety Surveillance in Pregnancy from the VSD**

**Malini DeSilva, MD, MPH (HealthPartners Institute)** reminded everyone that the VSD is a collaborative project between CDC’s Immunization Safety Office (ISO) and integrated health care organizations in the US. The VSD monitors the safety of vaccines used in the US through real-world data of rare and serious events following vaccination. The project includes data on approximately 15.5 million individuals across all sites annually, with approximately 115,000 annual live births. Data are organized using a common data model with standardized coding systems. There are 13 VSD sites across the country that provide clinical, methodological, and data expertise, 11 of which provide data for the project.

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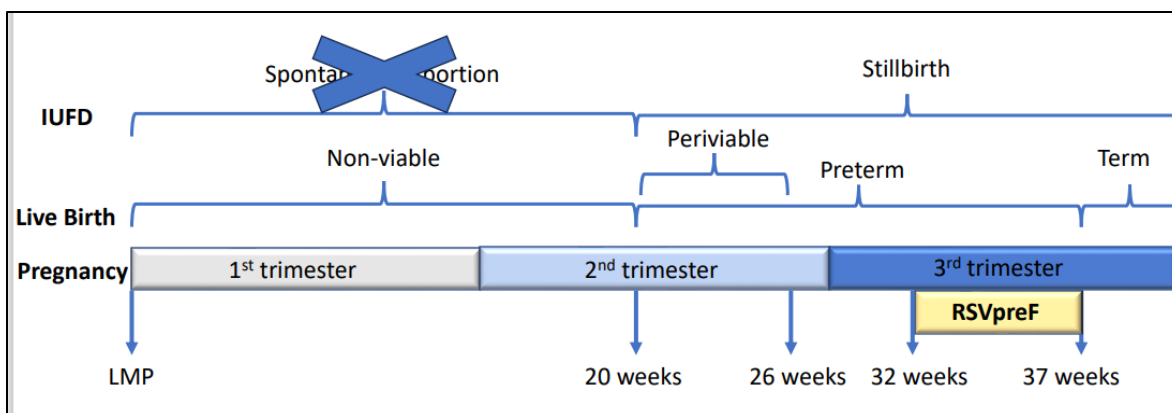
<sup>10</sup> <https://www.cdc.gov/vaccines/vac-gen/immunity-types.htm>

The VSD's data structure is based on a distributed data model in which each VSD site creates standardized data files used in multi-site studies. Each VSD site defines a cohort for inclusion based on enrollment in the site's health plan and/or care received at the VSD site. Once a cohort has been defined, files for vaccine administrations, medical diagnoses, and procedures from inpatient, outpatient, and ED visits and birth and death files are created. The dynamic pregnancy episode files uses validated algorithms for identifying ongoing and completed pregnancies. This file is updated weekly. Information in this file includes the pregnancy start date, or last menstrual period (LMP), gestational age of the pregnancy, and pregnancy outcomes when available. A mom baby linkage file allows for evaluation of infant outcomes following prenatal vaccinations. Ancillary drug or laboratory files are available on an ad hoc basis for specific studies. Automated data files are supplemented with chart reviews as needed.

The VSD has been evaluating the safety of vaccines administered during pregnancy for more than 10 years. The RSVpreF vaccine manufactured by Pfizer has been shown to be effective against severe RSV-associated LRTIs in infants. RSVpreF clinical trial data on safety in pregnant persons identified injection site pain as the most common reactogenicity event and identified an imbalance in preterm births in the vaccinated group. Most preterm births are late preterm, meaning they occurred at 34 to less than 37 weeks gestation, and most occurred more than 30 days after receipt of the RSVpreF vaccine. Preterm birth imbalance was most prominent in a single country. Of note, GSK also was working on an RSVpreF prenatal vaccine, but the clinical trials halted due to an imbalance in preterm birth in the vaccinated population. The etiology for preterm birth associated with RSV prenatal vaccine is unknown.

The goal of prenatal RSV vaccine surveillance is to evaluate the safety of RSVpreF vaccine administered during pregnancy in the VSD's large real-world population. Challenges are that as vaccine uptake is unknown, which makes it difficult to provide any power estimates. Additionally, there may be healthy vaccinee bias, meaning that healthier individuals or those with lower risk pregnancies may be the first to be vaccinated. This is considered in the analyses and when interpreting results. There is uncertainty regarding recommendations for RSVpreF use in administration of this vaccine, which may impact who receives the vaccine. If persons at higher risk for preterm delivery are recommended to receive RSVpreF early in the vaccination window, more preterm births may be identified the vaccinated group. Alternatively, these individuals may be counseled to not receive the vaccine and wait to have their infant receive nirsevimab. The timing of administration during pregnancy overlaps with Tdap recommendations and vaccine administrations are also likely to overlap with influenza and COVID-19 vaccines.

To review the pregnancy outcomes and expected timing for the RSVpreF vaccine during pregnancy, pregnancies are considered "non-viable" prior to 20 weeks gestation, "perivable" from and from 20 through 26 weeks (e.g., meaning there is a reasonable chance of extra uterine survival), "preterm" if the pregnancy ends in a live birth before 37 weeks gestation, and "term" if the pregnancy ends in a live birth at gestational age 37 weeks or thereafter. Intrauterine fetal demise outcomes (IFDOs) include spontaneous abortions that can occur up to 20 weeks gestational age, or a stillbirth that occurs at 20 weeks gestation or later. The yellow box in the following diagram shows the time period during pregnancy when the RSVpreF vaccine has been approved for use. When considering pregnancy outcomes and the RSVpreF vaccine, only outcomes that are possible will be included. Spontaneous abortion is not a possible outcome because of the timing of vaccine and pregnancy:



The primary approach for prenatal RSVpreF surveillance will be through bimonthly surveillance. Validated algorithms will be applied to electronic health data in the VSD population to identify pregnant persons 16–49 years of age at  $\geq 20$  weeks gestation. Excluded pregnancies include those that end in therapeutic abortion, multiple gestation pregnancies, and those with insufficient information to determine the start date of the pregnancy. The exposure being evaluated is RSVpreF vaccination at or after 28 weeks gestation. This is to account for any inaccuracies in gestational age estimation. Pregnant persons vaccinated with RSVpreF are matched to pregnant persons unvaccinated 1:1 based on VSD site and gestational age at vaccination. Propensity scores were created to account for confounding using readily available variables (e.g., pregnant person’s age, pregnancy start date, race, ethnicity, and medical comorbidities).

Adverse outcomes evaluated include acute outcomes and pregnancy-related and birth outcomes. These outcomes were chosen based on biologic plausibility and data from clinical trials, as well as being used in prior vaccine safety studies. To identify these outcomes, an algorithm will be used that was developed for other VSD safety surveillance work, which has been modified for a pregnant population. The algorithm uses diagnoses associated with outpatient, ED, and hospital encounters. Chart confirmation will be used for selected outcomes. The pregnancy-related and birth outcomes that will be evaluated include preeclampsia or eclampsia based on International Classification of Diseases (ICD)-10 codes, preterm birth based on the gestational age at birth, and stillbirth identified from ICD-10 codes with chart-reviewed confirmation.

The next 2 tables show the acute outcomes that will be monitored following vaccination, the risk window for which each outcome will be evaluated, and the VSD background rate per 10,000. These background rates are based on data from COVID-19 studies using the rate in the unvaccinated group. In the first table, the risk window for anaphylaxis is limited to the day of and first day following vaccination and will be studied only in the vaccinated group. The next 3 outcomes (fever, malaise/fatigue, and skin and soft tissue or local allergic reactions) are limited to 7 days following vaccination. All other outcomes listed alphabetically will be evaluated during the 1–21 days and 1–42 days following vaccination. The second table is a continuation of the first.

Outcome	Risk window(s) (days)	VSD Background rate/10,000*
Anaphylaxis	0–1	n/a
Fever	1–7	3.3
Malaise / fatigue	1–7	11.4
Skin and soft tissue or local allergic reactions	1–7	7.0
Acute disseminated encephalomyelitis	1–21, 1–42	0
Acute myocardial infarction	1–21, 1–42	0.3
Appendicitis	1–21, 1–42	0.6
Bell's Palsy	1–21, 1–42	0.8
Cerebral venous sinus thrombosis (CVST)	1–21, 1–42	0.1
Disseminated intravascular coagulation (DIC)	1–21, 1–42	0.3
Guillain-Barré syndrome	1–21, 1–42	0
Immune thrombocytopenic purpura (ITP)	1–21, 1–42	7.6
Lymphadenopathy / lymphadenitis	1–21, 1–42	4.6

\*Identified from unvaccinated pregnant persons, COVID-19 medically attended acute outcomes 1–7 or 1–21 day evaluation

Outcome	Risk window (d)	Background rate/10,000*
Myocarditis / pericarditis	1–21, 1–42	0
Pulmonary embolism (PE)	1–21, 1–42	0.1
Seizure	1–21, 1–42	0.8
Stevens-Johnson syndrome or toxic epidermal necrolysis	1–21, 1–42	n/a
Stroke, hemorrhagic	1–21, 1–42	0.4
Stroke, ischemic	1–21, 1–42	0.4
Thrombosis with thrombocytopenia syndrome (TTS)	1–21, 1–42	n/a
Thrombotic thrombocytopenic purpura (TTP)	1–21, 1–42	n/a
Transverse myelitis	1–21, 1–42	n/a
Trigeminal neuralgia and related disorders	1–21, 1–42	0.1
Venous thromboembolism (VTE)	1–21, 1–42	0.4

\*Identified from unvaccinated pregnant persons, COVID-19 medically attended acute outcomes 1- 21 day evaluation

The next table shows the pregnancy-related and birth outcomes that will be evaluated, the outcome is listed in the left column, followed by the risk window during which each outcome will be evaluated, and the number and percentage of vaccinated clinical trial participants who experienced the outcome from the Phase 3 RSVpreF clinical trial. The outcomes that will be evaluated are preeclampsia and eclampsia, preterm birth, and stillbirth at 1–21 days and 1–42 days.

Outcome	Risk window	Pfizer phase 3 RSVpreF trial, n (%) <sup>‡</sup>
Preeclampsia and eclampsia	1-21, 1-42	68/3682 (1.8) <sup>‡</sup>
Preterm birth (<37 w)	Up to 37 weeks	126/2494 (5.1) <sup>Δ</sup>
Stillbirth	1-21, 1-42	10/3682 (0.3) <sup>‡</sup>

<sup>‡</sup> RSVpreF Phase 3 clinical trial: Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants | NEJM  
<sup>Δ</sup>Preterm birth rate in high-income countries (Slide 23 Evidence to Recommendations Framework: (cdc.gov))

The risk window for preterm birth will vary based on the age of vaccination and will end up to 37 weeks gestation, given that births after 37 weeks gestation are considered term. The percentages shown for the RSVpreF Phase 3 trial are based on all study participants for preeclampsia and eclampsia and stillbirth. For preterm birth, the rate was used from high-income countries since this seemed most applicable to the VSD population.

For the analysis, risk ratios will be determined with corresponding 95% confidence intervals using Poisson distribution with robust variance using a generalized estimating equation (GEE). Censoring within risk windows will be applied when an individual is no longer at risk for the event, due to pregnancy outcomes that occur, or if an unvaccinated match is vaccinated. Adjustments will be included for known confounders. If a preterm birth signal is detected, further exploration into the etiology will be performed. A sensitivity analysis will be performed using alternative matching strategies. Because the RSVpreF vaccine is recommended for use during the same time period when Tdap is recommended, an assessment will be done to explore whether it is possible to evaluate coadministration of Tdap and RSVpreF.

In terms of an example timeline for the planned bimonthly surveillance, if vaccination started in October 2023, the plan would be to capture 2 months of vaccinations followed by a 42-day follow-up period and a 2-month data lag before pulling any data. The first data pull would be in March 2024. Bimonthly surveillance would continue every 2 months.

### **Maternal RSV Vaccine Safety Monitoring in VAERS and v-safe<sup>sm</sup>**

**Pedro L. Moro, MD, MPH (CDC/NCEZID)** described maternal RSV vaccine safety monitoring in VAERS and v-safe<sup>sm</sup>. As a reminder, VAERS is a national passive surveillance system that is the frontline surveillance system that monitors all licensed vaccines in the US. Created in 1990, VAERS is co-managed by the CDC and FDA. A couple of the important strengths of VAERS are that it can rapidly detect safety signals and it can detect rare adverse events (AEs). However, one of its important limitations is that it is not designed to assess causality. VAERS is a hypothesis-generating system that can identify potential vaccine safety concerns that can be studied in more robust systems.

In terms of some of the approaches that can be used to analyze various data in pregnancy reports, VAERS has been used for more than a decade as part of vaccine safety surveillance for vaccines used in pregnancy (e.g., influenza, Tdap, COVID-19). One type of analysis that can be performed using VAERS data is a descriptive analysis, which includes clinical review of individual reports, aggregate descriptions of automated data (e.g., counts of reported AEs).<sup>11</sup> Another is calculation of reporting rates for pregnancy outcomes if doses of RSV vaccine administered in pregnancy or vaccination coverage data are available. Regarding the statistical analyses that may be done, historical approaches have included data mining to assess for disproportionate reporting. This is under discussion for RSV vaccines.

The search for RSV pregnancy reports involves a number of strategies. One strategy is to search Medical Dictionary for Regulatory Activities (MedDRA) codes for the specific terms: exposure during pregnancy, drug exposure during pregnancy, maternal exposure during pregnancy. Another approach is to search for an affirmative answer to Question 8 that asks the patient whether they were pregnant at the time of vaccination. In addition, a string search can be done of text fields (e.g., symptoms, pre-existing illness, medical history) for the term “preg.” Medical records will be requested for all pregnancy reports, including serious and non-serious. Clinicians will review these reports to confirm that they are pregnancy reports and to categorize the main AE of interest.

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<sup>11</sup> Reported adverse events are coded using Medical Dictionary for Regulatory Activities terms (<https://www.meddra.org/>)



VAERS will conduct surveillance of adverse events of special interest (AESIs) after RSV vaccination. Primary AESIs have been selected for historical, theoretical, or observed safety concerns (i.e., in clinical trials). VAERS will obtain medical records for all reports (serious<sup>12</sup> and non-serious). CDC will review records and abstract clinically important information. AESIs may be added to or removed from the list as appropriate. Secondary AESIs will be monitored via periodic (e.g., weekly) automated data tables, but the information will not be abstracted. If a secondary AESI is identified that is being reported frequently under suspicion of a safety concern, that may be added to the primary AESI list. The current listing of primary and secondary AESIs that will be monitored in VAERS for all RSV vaccines, including for reports among pregnant persons, are as follows:

<u>Primary AESIs</u>	<u>Secondary AESIs</u>
<p><b>Outcomes of general interest</b></p> <ul style="list-style-type: none"> <li>• Death</li> </ul> <p><b>Neurologic/neuroinflammatory conditions</b></p> <ul style="list-style-type: none"> <li>• Guillain-Barre Syndrome (GBS), including Miller Fisher variant</li> <li>• Acute disseminated encephalomyelitis (ADEM)</li> <li>• Transverse myelitis (TM)</li> <li>• Chronic inflammatory demyelinating polyneuropathy (CIDP)</li> </ul> <p><b>Allergic reactions</b></p> <ul style="list-style-type: none"> <li>• Anaphylaxis</li> </ul> <p><b>Cardiac conditions</b></p> <ul style="list-style-type: none"> <li>• Atrial fibrillation</li> <li>• Other supraventricular tachycardias (SVT)</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Neurologic/neuroinflammatory conditions</b> <ul style="list-style-type: none"> <li>• Optic neuritis</li> <li>• Multiple sclerosis</li> <li>• Bell's palsy</li> <li>• Encephalitis/Encephalomyelitis</li> <li>• Meningitis/Meningoencephalitis</li> <li>• Myelitis</li> </ul> </li> <li>▪ <b>Other conditions</b> <ul style="list-style-type: none"> <li>• Vaccination errors</li> <li>• AEs following simultaneous administration with COVID-19, inactivated influenza, or other adult vaccines</li> </ul> </li> </ul>

Pregnancy-specific outcomes to be monitored in VAERS and abstracted after maternal RSV vaccine include:

- Premature/preterm birth
- Stillbirth
- Spontaneous abortion
- Gestational diabetes
- Preeclampsia/eclampsia/gestational hypertension
- Birth defects
- Maternal and infant deaths
- Other selected adverse infant outcomes/AEs

Development of a new version of v-safe<sup>sm</sup> began in Summer 2023. This system leverages the existing CDC IT infrastructure and includes e-mail and text messaging options. The first use will be for RSV vaccines received by persons ≥60 years of age in the Fall. Use for maternal RSV vaccines is planned for later in the Fall. The v-safe<sup>sm</sup> objectives are to: 1) characterize local and systemic reactogenicity during days 0–7 zero to seven after vaccination; 2) characterize health impacts during a 6-week post-vaccination follow-up period; and 3) identify participants who report medically-attended events after vaccination and encourage completion of a VAERS report.

<sup>12</sup> Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly or birth defect

## **An Economic Analysis of RSVpreF Maternal Vaccination**

**David W. Hutton, PhD, MS (University of Michigan)** provided some updates since his June 2023 presentation to the ACIP to report the findings of an additional vaccine efficacy scenario, additional timing scenarios for which the vaccine might be administered in specific months of the year, a gestation scenario from 32–36 weeks, and an updated cost per vaccine dose scenario. The initial efficacy scenario has not changed,<sup>13</sup> with sigmoid downward sloping efficacy during the 6 months, using the average efficacy during these periods based on average 6 months efficacy. Hospitalization efficacy was based on hospitalization efficacy from the trial and efficacy against outpatient visits was based on efficacy and medically-attended LRTIs. A scenario also was evaluated with flat efficacy during those 6 months, and then back down to 0 efficacy after that. In both of the last 2 scenarios, 0 efficacy was assumed after 6 months. The new scenario is more optimistic, with slightly higher efficacy in the first 6 months. The efficacy against hospitalization in this scenario was based on efficacy against severe-medically attended RSV LRTI observed in the trial, which was slightly than the efficacy used in the base-case. In this optimistic scenario, it was assumed that there is declining efficacy for months 6–9.

In the initial base-case, RSVpreF given year-round was evaluated. The new scenarios assessed cost-effectiveness if RSVpreF is given during specific months of the year and if RSVpreF is administered in specific ranges of months throughout the year: April-February, May-February, June-February, August-January, September-January, and September-December. Another change was a scenario in which the mother was vaccinated from the beginning of week 32 through the end of week 36 of the pregnancy, which is a narrower range than was used in the trial but is what the FDA has settled on. In the new scenario, it was assumed that the vaccine must be given within 2 weeks before birth for the vaccine to confer protection. It was assumed that for a baby born within 2 weeks of administration, there would be no efficacy of the vaccine. If it is assumed that for 100 pregnant persons, 50 intend to vaccinate, 48 actually get vaccinated because 2 might give birth before that, and 3 of the 48 would be vaccinated within 2 weeks of delivery—that would result in 45 being vaccinated in time (e.g., within 2 weeks before delivery).

In June, Dr. Hutton presented numbers based on 1000 births. During this session, he presented the results based on the entire US birth cohort per year assuming 50% uptake of the RSVpreF vaccine across the first RSV season. Another major update for this scenario is a cost of \$295 per dose. That is an increase from the \$200 per dose estimate used in June, which is a significant increase in the price per dose. In terms of the results, the number needed to vaccinate (NNV) to avoid an outpatient visit (40), an ED visit (115), an inpatient stay (242), an ICU admission (1100), an inpatient day (45), or an intensive care unit (ICU) day (367) was very similar to what was shown in June. It was about 4% higher because of the later timing of vaccination in weeks 32–36 due to slightly more people being vaccinated within 2 weeks of birth. But basically, this is very similar to what was reported in June.

In the updated scenario, the total cost were higher due to evaluating a larger cohort of 3.66 million births, assuming 50% intended uptake in RSVpreF group. The intervention cost is higher relatively-speaking because the vaccine price per dose increased by just under 50% from the previous scenario. The cost per event averted also was higher than shown in June because the price per dose is a little bit less than 50% higher than what was assumed in June. For example, the cost to avert an inpatient stay would be about \$68,000 per inpatient stay averted. The

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<sup>13</sup> Kampmann et al 2023

incremental cost-effectiveness ratio (ICER) in the updated scenario is now about \$400,000 per quality-adjusted life year (QALY) gained. This is driven primarily by the increased cost of the vaccine dose compared to the cost used in June.

Looking at sensitivity analyses showing how various changes in the assumptions will change the ICER, the rankings of which parameters are most important are similar to those seen in June. Prematurity potentially can increase the ICER dramatically, though hopefully that is less likely with later administration of RSVpreF. The QALY impacts of RSV also are likely to have large impact on the ICER. The vaccine price is an important driver of cost-effectiveness. The cost of inpatient care also can have a large impact on the cost-effectiveness of vaccination. VE also can have a large impact on cost-effectiveness. One of the scenarios was varying how VE was modeled. When flat efficacy was assumed, the ICER was about \$365,000 per QALY gained. The updated scenario used a more optimistic higher and longer efficacy. The ICER under this scenario was about \$286,000 per QALY gained.

In a sensitivity analysis varying efficacy, hospitalization cost, and mortality the base cost was \$11,000 per hospitalization. Varying the hospitalization cost from the base cost to higher costs, the cost-effectiveness ratio would decrease as hospitalization costs increase. With a more optimistic VE (e.g., higher and longer efficacy) the cost-benefit ratio would decrease as well. With more deadly RSV, there would be a 1% risk of dying in the hospital instead of 0.1%. The cost per vaccine dose also can have a major impact on cost-effectiveness. With a base-case price of \$295 per dose, the cost per QALY is close to \$400,000. If the vaccine cost per dose was lower, the ICER would decrease as well.

Everything just shown was assuming the vaccine is given year-round. Now looking by month and by specific ranges of months to determine the cost-effectiveness ratio if RSVpreF is given in a particular month of the year, it is important to remember that RSV is seasonal and there are many infections in the wintertime. If RSVpreF is given right before wintertime so that it has 6 months of efficacy during that peak, the cost of that administration would decrease dramatically. For instance, if RSVpreF is given during any month between February–July, the cost-benefit ratio would be over \$500,000 per QALY. If given during October–November, the cost-effectiveness ratio would range from approximately \$111,000 to \$115,000 per QALY. The cost of administration could be dramatically lower if RSVpreF is given right before the peak of the RSV season. Looking at ranges of months and recalling that the base-case was about \$400,000 per QALY if given year-round, if it was given during the range of September–December, the ICER would be approximately \$141,000 per QALY.

To summarize, the limitations of this updated analysis are similar to the ones reported in June. The model structure does not include risk groups or dynamic transmission. Given that this is a new vaccine, the impact of the vaccine on transmission and indirect effects is unknown. Inputs also are still uncertain with respect to RSVpreF costs, QALYs lost, impact URTIs, and prematurity. All of these scenarios assumed that no infants will be receiving nirsevimab. RSVpreF may improve RSV outcomes, but it also will increase costs. RSVpreF has the potential to be cost-effective, but the results are sensitive to a wide variety of assumptions, including rate of prematurity; cost per dose (~\$65,000–\$68,000/QALY); hospitalization costs (cost-saving–\$440,000/QALY); efficacy (~\$280,000–\$680,000/QALY); QALYs lost (~\$100,000–\$800,000/QALY); and month of administration (~\$110,000–Millions/QALY).

Looking now at the economics of the combined use of Pfizer maternal RSVpreF vaccine and nirsevimab, ACIP recommended the use of nirsevimab On August 3, 2023. This raises the following questions about how to think about combinations of RSVpreF and nirsevimab:

- ❑ If it is known that RSVpreF has been administered to the pregnant person in time, how cost-effective is it also to provide nirsevimab to the infant?
- ❑ If it is known that the infant definitely will receive nirsevimab, how cost-effective is it to provide RSVpreF to the pregnant person?

In terms of updates since the June ACIP meeting, the assumption was made in the updated analysis that RSVpreF would be administered in weeks 32–36. Because of this, the assumption also was made that the infant is full-term and there would be no need for palivizumab for any newborns considered in this analysis. The updated analysis also considered some higher risk populations and assumed that they were not premature. In addition, the new timing of RSVpreF administration was considered. There is no evidence of efficacy with the combined use of these products. Therefore, the assumption was made that efficacy would be equal to the highest of nirsevimab or RSVpreF, which is higher. That is, efficacy would not be higher than from the most effective product and there would be no combined synergistic efficacy. That is the same assumption that was made in June.

Assuming administration of nirsevimab at birth to the infant of someone who received RSVpreF, nirsevimab would provide additional efficacy on top of what RSVpreF would provide. If the baby was born in August, they would have some RSVpreF efficacy. If nirsevimab was given on top of that in October, there would be an increase in efficacy. As a reminder, peak infections are typically in the December–February timeframe, and additional efficacy would be desired during that peak timeframe.

To highlight the incremental benefit of adding nirsevimab on top of RSVpreF for infants of persons vaccinated with RSVpreF during pregnancy at least 2 weeks prior to delivery, there would be a higher risk or increased multiplier on the risk of hospitalization. There would be no change in outpatient incidence, ED incidence, costs per outcome, or QALY per outcome. Looking at the incremental benefit of adding nirsevimab on top of RSVpreF by month and risk if nirsevimab is given at birth during October–March compared to a baby born in April–September who would not be given nirsevimab at birth but would receive it at the start of the RSV season in October or November, the incremental cost-effectiveness of adding nirsevimab looks better if given to babies born in April, May, June, July, August, and September. If given at the beginning of the season in October and November, the cost-effectiveness ratios would be much lower. The ICERs are much higher for infants who are at 3-, 6-, and 10-times higher risk of hospitalization. That is, it is much more valuable to give them nirsevimab on top of RSVpreF.

Particularly for babies born in the summer, giving nirsevimab at the beginning of the season would result in an ICER \$150,000 per QALY gained and lower. For potentially higher risk individuals born during the season, the ICERs for nirsevimab given at birth might look good for higher risk populations. Assuming that nirsevimab is given to all infants born year-round to vaccinated mothers, the NNV to avoid an inpatient visit for an average risk child would be over 200 infants to avoid 1 inpatient visit. Adding nirsevimab to all infants born year-round to vaccinated mothers would be quite expensive for people at average risk at \$400,000 per QALY. Providing nirsevimab to infants at 6 times the risk born to vaccinated mothers would be about \$40,000 per QALY gained and might be cost-effective.

In a scenario of giving nirsevimab in October–November to babies born in April–September, rather than at birth, born to mothers who received RSVpreF at least 2 weeks prior to delivery, the NNV was similar but slightly lower than if giving nirsevimab year-round. It would be more cost-effective to provide nirsevimab to infants born since April–September at the beginning of the RSV season at about \$300,000 per QALY for infants at the lowest risk and about \$200,000 per QALY for infants at 3-, 6-, and 10-times higher risk. In a scenario of adding nirsevimab during the season for infants born October–March to mothers who received RSVpreF at least 2 weeks prior to delivery, the NNV would be higher because they already would have a lot of RSVpreF protection during that time period. The ICER would be \$600,000 per QALY if given to average risk babies. That is, it would be less cost-effective to give these babies nirsevimab on top of their RSVpreF protection.

Regarding the incremental benefit of adding nirsevimab on top of a baby’s RSVpreF protection, there is some additional benefit beyond RSVpreF protection. The ICERs are high, but could be lower for higher-risk populations, particularly born if they are born off-peak. In terms of the incremental benefit of adding RSVpreF on top of nirsevimab if it is known the infant will be receiving nirsevimab, the ICERs are very high. Similar to what was seen previously, this scenario would be over \$10 million per QALY for many months of the year. The best month of the year would be April, although the ICER still would be \$2.4 million per QALY gained if nirsevimab was given to babies whose mothers received RSVpreF at least 2 weeks prior to delivery. The incremental benefit of adding RSVpreF on top of nirsevimab would be very marginal beyond nirsevimab protection and the ICERs would be extremely high.

In summary of scenarios involving combinations of RSVpreF on top of nirsevimab, a limitation is that there are no efficacy data on these combined products. Therefore, these scenarios are all based on assumptions about what the efficacy might be. Nirsevimab may add additional protection on top of RSVpreF, particularly for high-risk infants. Adding RSVpreF on top of Nirsevimab would add marginal effectiveness at a very high cost in the general population.

### **Economics of Preventing RSV Disease among US Infants by Maternal Vaccination Prior to Birth**

**Ismael R. Ortega-Sanchez, PhD (CDC/NCIRD)** summarized the key elements and findings of 2 economic studies, the Pfizer Model and the University of Michigan-CDC (UM-CDC) Model, focused on the economics of preventing RSV disease among US infants by maternal vaccination prior to birth. In the last 8 to 9 months, the 2 models were updated several times. In this summary, Dr. Ortega-Sanchez focused only on the vaccine so there was no discussion about the last component of Dr. Hutton’s presentation regarding nirsevimab. For full disclosure, Dr. Ortega-Sanchez indicated that he has been part of the team conducting the CDC model.

The starting point of the 2 economic models was the policy question regarding potential recommendations for the use of RSV vaccine in pregnant mothers, “Should Pfizer RSVpreF vaccine be recommended for pregnant mothers to be given during 32 through 36 weeks gestation to prevent RSV lower respiratory tract infection in infants?” To consider the economics of the policy question is to consider simultaneously the health benefits and costs of vaccination, namely, “Is vaccinating pregnant mothers prior to birth to protect infants against RSV’s cost-effective?” To address this question, the 2 models used the same comparator, unvaccinated mothers and the standard of care (SoC) for infants. They focused on analyzing the cost-effectiveness of vaccinating pregnant mothers 32–36 weeks of gestation  $\geq 2$  or more weeks prior to the birth with RSVpreF vaccine compared to no vaccine.

The policy question has important implications for 2 groups of elements. The comparison of the 2 economic models focuses on the appropriateness of the modeling approach selected; the inputs for RSV disease burden, RSVpreF, VE, and costs; and how the strength and influence of the assumptions on the outcomes. The 2 models followed similar designs. Both used a static analytical decision-making approach, relied on sensitivity analyses and probabilistic simulation, modeled a hypothetical cohort of all pregnant mothers in the US year-round, selected a timeframe of the first year after birth, accounted for loss of income associated with temporary productivity loss and the loss of premature RSV-associated infant mortality. Once the modeling study was set, the 2 models were fed by different types of input data, including clinical, epidemiological, economic, QALY, vaccine characteristics, health care resource utilization (HCRU) and cost, and indirect costs. Across models, the source and specific values and assumptions of these parameters have some overlaps, but there were marked differences as well. The boxes below list the standard outcomes estimated and reported by the 2 models:

	<i>Pfizer</i>	<i>UM-CDC</i>
Prevention of:		
• RSV LRTI ED/OC visits	✓	✓
• RSV LRTI hospitalizations	✓	✓
• RSV-associated deaths	✓	✓
QALYs saved	✓	✓
<b>\$/QALY saved</b>	✓	✓
Number needed to vaccinate (NNV) to avert an:		
• RSV LRTI hospitalization	✓	✓
• RSV-associated death	✓	✓

Dr. Ortega-Sanchez emphasized that once the models are built this way, it is necessary to work in reverse in order to go first with the outcomes and then analyze what happens with the inputs.

The base case estimate for vaccinating pregnant mothers in the vaccination window of 32–36 weeks gestational age year-round would be approximately \$400,000 per QALY gained when vaccine costs are \$295 per dose. Additionally, the CDC model reports cost per specific type of health outcome prevented and the NNV to prevent hospitalization, ED visits, outpatient visits, and deaths associated with RSV LRTI. the base case estimate for maternal vaccination in the vaccination window of 32–36 weeks gestational age year-round would be approximately \$85,000 per QALY gained when vaccine cost is \$295 per dose. The Pfizer cost per QALY is supported with its probabilistic sensitivity analysis (PSA) when simultaneously providing the input and variables in the model. Most of the simulations included in the base case were somewhat costly, but with gains in QALY. Approximately 65% of the simulations in the Pfizer model had a cost-effectiveness ratio that was less than \$100,000 per QALY. Even though both models assumed the same vaccine cost per dose, vaccination window of 32–36 weeks of gestational age, and year-round vaccination administration, the CDC results costs per QALY were still much higher than those of Pfizer. Specifically, the CDC estimates of the cost per QALY and the cost per hospitalization of births were about 5 times higher than those of Pfizer and about 10 times higher for the cost per death prevented. The CDC model reported a 65%

higher NNV to prevent hospitalization and 300% higher in the number needed to prevent an RSV-associated death. The first takeaway for the committee is that both models agree that maternal vaccination will be relatively costly, but it also will prevent LRTI and hospitalization and will save QALYs among infants and caregivers.

To understand these persistent discrepancies in the UM-CDC model and the Pfizer model, an effort was made to identify the sources of these differences. The CDC model's 1-way sensitivity analysis ranked the most influential input variables. The probability of prematurity ranks first, followed by RSV QALYs lost, disease-specific inpatient cost, and VE against hospitalization. In a similar fashion, Pfizer also reported one-way sensitivity analyses. The most influential variables were VE, followed by medical costs for hospitalization, vaccine duration of protection when truncated at 6 months, and the case fatality rate among hospitalized infants with RSV LRTI. Except for RSV hospitalization risk and seasonality and vaccine-associated AEs, the other elements identified in the Pfizer and UM-CDC models included, which were explored further:

- Vaccine efficacy
- Duration of protection and waning
- RSV Case fatality rate
- Medical cost of RSV hospitalization, ED and Outpatient care
- QALYs lost by patients and caregivers

First, 2 elements that did not explain these differences were the risk of hospitalization and RSV seasonality as input data used in both models were practically the same. Specifically, the risk of RSV hospitalization data used in both models was based on laboratory-confirmed RSV-associated hospitalization by age in months from the New Vaccine Surveillance Network (NVSN). This includes only RSV cases that manifests as LRTI. Therefore, unlike the uncertainty in RSV hospitalization that was a question for discussion for older adults, it is not what could explain the difference in outcomes in infants. Likewise, RSV seasonality was based on data from the National Respiratory and Enteric Virus Surveillance System (NREVSS). The 2 main explanatory factors turn out to be VE and case definition. Although both models use the same source for VE,<sup>14</sup> which reports the data from the Phase 3 clinical trials from Pfizer, each model picked different data points from this source mainly because none of the Pfizer Phase 2 endpoint definitions overlap ideally with a case definition used by the US burden data. For hospitalizations, the CDC model used average VE over months 0–6 reported by RSV LRTI hospitalization, with an average value of 56.8%. The Pfizer model used VE for severe RSV-positive MA-LTRI as a proxy for VE against RSV-LRTI requiring hospitalization, and efficacy against RSV-positive MA-LRTI was used as a proxy for VE against RSV-LRTI treated in the ED. VE for late preterm infants was assumed to be 83.3% of corresponding values for full-term infants.

This also will help to understand the duration of protection. Although assessing the difference about the initial VE is important, it is more about the assumption of performance over time. In the Pfizer model, the linear assumption was based on 4 data endpoints reported from Phase 3 data until 180 days after vaccination, or the equivalent of 6 months, followed by the assumed impact from the 6<sup>th</sup> to the 9<sup>th</sup> month. That is discriminated by a full-term versus late-term. The CDC model used a 6-month efficacy against hospitalization or MA RSV-associated RTI. The duration of protection reached 0 at 6 months. They noted a higher level of uncertainty of the

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<sup>14</sup> Kampmann et al New England Journal of Medicine. 2023 Apr

waning assumption beyond available Phase 2 data. The CDC model tried to minimize this uncertainty impact on its outcomes. Therefore, there was no effectiveness after the 6<sup>th</sup> month.

Although the base-case case fatality rates for hospitalization were basically the same in both models, the distinction is that Pfizer inputs used a higher case fatality rate for late preterms using mortality rates for all pre-terms. Therefore, the same rate included for extremely early, early, and late preterms were used as the dominator for the case fatality rate for all preterms. Regarding medical costs, the input values using the Pfizer model were 2 times higher for hospitalization to about 4 times higher for ED and outpatient visits than the ranges used by the CDC model to reach the average cost value using. While the source of the CDC model is a publicly available meta-analysis review of many publications. The source of the Pfizer model is reported as data on file and not yet available for examination. The committee members should bear in mind that the higher the input values, the lower the ICER would be, or the equivalent, the more cost-effective the vaccination program would be.

Cost-effective analysis programs should include not only the cost of vaccines or vaccine administration, but also the risk of vaccine-associated AEs and associated costs. Using data reported from the Pfizer Phase 3 trial, both models included the rate of injection site reactions and associated costs, including the cost of outpatient visits. The difference was when dealing with hypothetical serious adverse events (SAEs) or when considering the incremental risk of prematurity. The potential increased risk of AEs considered in the CDC model, when modeled in the base case or as a potential scenario could influence the ICERs and significantly increase the cost of the intervention.

In terms of the QALY impact of RSV outcomes in both patients and caregivers, the point estimates scores used in both models were the same for the caregivers. The difference was in the patient scores, which were somewhat higher in the CDC model. The second difference was that the CDC model also relied on ranges from each of these scores, which allowed for the analysis and sensitivity analysis of the impact of them. Unlike CDC, the Pfizer model considered only the point estimate for the base case without viability, and as a consequence quality loss was not identified as an influential variable in the Pfizer model.

Up to this point, the comparisons focused on the inputs used in the models. The idea at this point was to determine how sizeable differences in cost per QALY could be explained from outcomes estimated using different input values and assumptions. One way to cross-validate the models is to see if one model could imitate the other by selecting some input values and assumptions. Looking at the cost per QALY for selected scenarios using a CDC model focusing on combining Scenarios A (cost of RSV-LRTI hospitalization: \$20,000 or \$50,000) and B (UM-CDC model with same VE duration of protection as Pfizer) that included price, medical costs, and assumptions of duration of protection, the specific impact on the cost per QALY drops to \$234,000 per QALY. That is still 2 times higher than the cost per QALY reported by Pfizer. Two other important scenarios reported were Scenario E with a potential increase in the risk of prematurity in 1% or 2% points, which could range from about \$900,000 if it is only 1% point increase in the risk of prematurity to more than \$1.3 million per QALY if it is a 2% point increase in the risk of prematurity. Scenario F deals with the timing of vaccination. CDC is the only model that presented timing of vaccination. Vaccinating mothers with births in September–January would provide a cost per QALY of less than \$200,000 as opposed to February–July, which will be in the millions per QALY.



By the same token, Pfizer attempted to replicate the CDC outcomes by sequentially using CDC inputs and assumptions. For Scenario A, the cost per QALY estimate with selected CDC inputs and the cost per QALY value were close to what was reported by CDC at approximately 85%. Scenario A was \$343,000 per QALY in the Pfizer model, which was very close to the \$400,000 per QALY reported by CDC. When Pfizer used its own model with some of the selected CDC inputs and returned most of its own inputs and assumptions piece-by-piece and cumulatively, Pfizer returned to his initial VE. It returned to the duration of protection and medical costs that Pfizer used and to approximately \$83,000 per QALY, which is basically the same one that was reported by them in the base case scenario. Since they were able to replicate some of the analyses, it seems that the inputs and the assumptions that are being used in the models are crucial.

In terms of limitations, the factors not considered may result in overestimating the ICER, underestimating the cost-effectiveness of maternal vaccination, by both models. In the base case, both models assumed no protection against upper respiratory tract infection (URTI), no benefits of vaccination for vaccinated pregnant mothers, and no out-of-pocket costs accrued by caregivers during an infant RSV illness. Neither model included RSV-related costs incurred after discharge from RSV-associated hospitalization or ED department visits, such as productivity losses incurred by caregivers after discharge. Both models assumed no indirect effects of vaccination (e.g., no protection against RSV transmission among unvaccinated people).

In conclusion, differences in key inputs among the Pfizer and CDC models explain differences in the results. Among the key differences are initial VE and assumptions about protection waning, medical cost data, QALYs associated with RSV LRTI outcomes for patients and caregivers, and vaccine-related AEs. In addition, the CDC model identified 2 important factors that could drive the results and make the difference—hypothetically severe vaccine-associated AEs and timing of vaccination for RSV when it targeted to specific periods in the RSV season. In terms of the base case in both models, maternal vaccination would significantly reduce RSV disease burden and disease costs in infants. Data from clinical trials used in both models support the reduction in RSV disease and associated costs. However, the economic value of vaccinating pregnant people to protect infants could increase costs. Reasonable vaccine price and duration of protection, combined with careful design of seasonal interventions, will determine the cost-effectiveness value of routine vaccination of pregnant people during the 32–36 weeks of gestational age.

### **EtR Framework Updates: Pfizer Maternal RSVpreF Vaccine**

**Katherine E. Fleming-Dutra, MD (CDC/NCIRD)** presented EtR Framework updates for the Pfizer Maternal RSVpreF vaccine. She reminded everyone that the policy question before the ACIP was, “Should Pfizer RSVpreF vaccine be recommended for pregnant people to be given during 32 through 36 weeks gestation to prevent RSV lower respiratory tract infection in infants?” Notably, the dosing window represented a change from the policy question discussed during the June ACIP meeting. The reason for this change was because On August 21, 2023,<sup>15</sup> FDA approved the Pfizer RSVpreF vaccine for use in pregnant people as a single dose to be given at 32 through 36 weeks gestation. In the Phase 2b and 3 trials, vaccination was given during 24 through 36 weeks gestation. The change was made to avoid the risk of extremely preterm births where there is substantive morbidity and mortality and very preterm birth. FDA considered that the benefit of vaccine efficacy when the Pfizer RSVpreF vaccine is administered

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<sup>15</sup> <https://www.fda.gov/news-events/press-announcements/fda-approves-first-vaccine-pregnant-individuals-prevent-rsv-infants>; and <https://www.fda.gov/media/168185/download>

between 32 and 36 weeks outweighed the risk of vaccination, including the potential risk of preterm birth and hypertensive disorders of pregnancy. Throughout the presentation, these were denoted as the approved dosing interval (32–36 weeks gestation) and the trial dosing interval (24–36 weeks gestation). In terms of the PICO question, the intervention was updated to reflect the approved dosing interval at 32–36 weeks gestation. Otherwise, the population, comparison, and outcomes remained the same.

In terms of the Public Health Problem domain, RSV infection is the leading cause of hospitalization in US infants. Most (68%) infants are infected in the first year of life and nearly all (97%) by age 2.<sup>16</sup> Approximately 2% to 3% of young infants will be hospitalized for RSV.<sup>17</sup> RSV is a common cause of LRTI in infants. The highest RSV hospitalization rates occur in the first months of life, all young infants are at risk, and risk declines with increasing age in early childhood.<sup>18</sup> Approximately 79% of children hospitalized with RSV who are less than 2 years of age had no underlying medical conditions.<sup>19</sup> The WG agree unanimously that RSV among infants is of public health importance.

Moving to the Benefits and Harms domain, the WG had data for all 11 outcomes for the Grading of Recommendation Assessment, Development and Evaluation (GRADE) for this analysis. Data were available from 2 trials, Pfizer’s Phase 3 trial and an earlier Phase 2b trial in pregnant people. In terms of how these data were used for GRADE and the benefits and harms domain overall, there were data from both trials on the dosing interval and from the FDA approved dosing interval. The number of maternal participants by vaccine and placebo arms in the Phase 2b and Phase 3 are shown in this table:

Trial phase	Dosing interval	Number of Participants*	Decision regarding use in GRADE
Phase 2b trial <sup>1</sup>	Trial dosing interval (24–36 weeks gestation)	Vaccine (received phase 3 dose and formulation): 115 Placebo: 117	Yes. Data for GRADE were limited to participants who received placebo or phase 3 vaccine formulation and only included for safety outcomes. Study was not designed to assess efficacy.
Phase 2b trial <sup>1</sup>	Approved dosing interval (32–36 weeks gestation)	Vaccine (received phase 3 dose and formulation): 45 Placebo: 44	No. Safety data are further limited by small sample size. Presented as supplemental data.
Phase 3 trial published analyses <sup>2,3</sup>	Trial dosing interval (24–36 weeks gestation)	Efficacy set / Safety set Vaccine: 3495 / 3682 Placebo: 3480 / 3675	Yes. Trial was designed and powered using a 24–36 weeks dosing interval.
Phase 3 trial, post-hoc analysis <sup>1</sup>	Approved dosing interval (32–36 weeks gestation)	Efficacy set / Safety set Vaccine: 1572 / 1653 Placebo: 1539 / 1632	No. Trial was not powered for this interval for efficacy, and safety data would be limited in power to detect harms. Presented as supplemental data.

\*For phase 2b trial and phase 3 trial safety set, number of maternal participants are listed. For phase 3 trial efficacy set, number of infants participants are listed.

<sup>1</sup> Data provided by Pfizer

<sup>2</sup> Kampmann et al. Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants - PubMed (nih.gov)

<sup>3</sup> Vaccines and Related Biological Products Advisory Committee May 18, 2023 Meeting Briefing Document- FDA

In both phases, less than half of the maternal participants receive the intervention in the approved dosing interval, meaning that the power to assess safety and efficacy was reduced. Therefore, for GRADE, the outcomes as assessed in the full trial population with the trial dosing interval of 24–36 weeks were used consistent with the trial design. The post-hoc analysis using data from the approved interval was used as supplemental data. To summarize the effect, estimates, and concerns in uncertainty of the assessment for the benefits for this vaccine assessed at 0–180 days of life, VE against medically attended RSV-associated LRTI in infants was 51%, and efficacy against hospitalization for RSV-associated LRTI in infants was 56.8%.

<sup>16</sup> Suh et al. JID 2022

<sup>17</sup> Hall et al, Pediatrics, 2013; Langley & Anderson, PIDJ, 2011; and CDC NVSN data

<sup>18</sup> Hall et al, Pediatrics, 2013; and CDC NVSN data

<sup>19</sup> Hall et al, Pediatrics, 2013

Additional data received since June included the important outcomes of ICU admission for RSV hospitalization in infants with an efficacy of 42.9%, and mechanical ventilation with an efficacy of 100%. Both estimates had very wide confidence intervals, and thus the certainty assessments were downgraded due to very serious concerns for imprecision. Additionally, there are now data for all-cause hospitalization for LRTI with an efficacy of 28.9%, with a confidence interval that crossed the null. Therefore, the certainty assessment was downgraded for serious concern for imprecision.

Regarding the certainty of assessments for harms, changes from June included the downgrading of 3 outcomes (e.g., SAEs in pregnant people, SAEs in infants, and preterm birth) for serious concerns about indirectness due to the difference in the trial dosing interval compared to the approved dosing interval. This was done because 55% of the Phase 3 trial population and 62% of the Phase 2b trial populations did not receive vaccine doses during the approved dosing interval. There is likely less opportunity for SAEs during pregnancy to occur, including preterm birth, when dosing starts at 32 weeks gestation as compared to 24 weeks gestation. In particular, the risk of preterm birth likely would be lower with dosing starting at 32 weeks than with a dosing window that starts at 24 weeks gestation.

Overall, the summary of GRADE showed that the Pfizer RSV maternal vaccine is effective in preventing medically attended RSV-associated LRTI in infants with high certainty in the evidence. This vaccine may be effective in preventing hospitalization for RSV-associated LRTI in infants, with moderate certainty. The vaccine may be effective in preventing ICU admission for RSV hospitalization in infants, with low certainty. The vaccine may be effective in preventing mechanical ventilation for RSV hospitalization in infants, with low certainty. The vaccine is not effective in preventing all-cause medically attended LRTI in infants, with moderate certainty. The vaccine may be effective in preventing all-cause hospitalization for LRTI in infants, with moderate certainty. SAEs in pregnant people were balanced between the vaccine and placebo groups, with low certainty. Reactogenicity in pregnant people was balanced between vaccine and placebo groups, with moderate certainty. SAEs in infants were balanced between the vaccine and placebo groups, with low certainty. Preterm births were unbalanced between the vaccine and placebo groups, with very low certainty in the evidence. This resulted in an overall evidence type of “Very Low.” In GRADE, the overall evidence type is driven by the lowest quality of evidence for critical outcomes, and here was driven by the evidence rating for the critical harm of preterm birth being very low.

Comparing the effect estimates for benefits for each of the GRADE outcomes from the full Phase 3 trial using the pre-specified trial dosing interval (24–36 weeks gestation) and the efficacy estimates for the same outcomes from the Phase 3 trial limited to participants who received doses during the approved dosing interval (32–36 weeks gestation), the point estimates were relatively similar for each of the outcomes. The confidence intervals were much wider when limited to the approved dosing interval, which is to be expected given the smaller number of participants who received vaccination in the approved dosing interval.

The Phase 3 efficacy against severe medically attended RSV-associated LRTI was a co-primary trial endpoint but was not included in GRADE. The reason for this is that this outcome was not included by the WG as an *a priori* critical or important outcome for vaccine policy decisions. However, the WG felt that this was important to present as part of the supplemental data in the EtR Framework. Shown here side-by-side are the Pfizer definitions of severe medically-attended RSV LRTI on the left and medically attended RSV LRTI on the right, which was included by the WG as a critical outcome for GRADE. The differences in these two definitions are highlighted in blue:

Pfizer Trial Definition	WG Definition
<p>Severe medically-attended RSV-associated LRTI* required at least 1 of the following signs/ symptoms:</p> <ul style="list-style-type: none"> <li>- Fast breathing (respiratory rate <math>\geq 70</math> (&lt;2 month of age [60 days]) or <math>\geq 60</math> (<math>\geq 2</math> to 12 months of age) breaths per minute</li> <li>- SpO2 measured in room air <b>&lt;93%</b></li> <li>- <b>High-flow nasal cannula or mechanical Ventilation</b></li> <li>- <b>ICU admission for &gt;4 hours</b></li> <li>- <b>Unresponsive/unconscious</b></li> </ul>	<p>Medically-attended RSV-associated LRTI* required at least 1 of the following signs/symptoms:</p> <ul style="list-style-type: none"> <li>- Fast breathing: respiratory rate <math>\geq 60</math> (&lt;2 months of age [60 days]) or <math>\geq 50</math> (<math>\geq 2</math> to 12 months of age) breaths per minute</li> <li>- SpO2 measured in room air <b>&lt;95%</b></li> <li>- <b>Chest wall indrawing</b></li> </ul>

\*Medically attended visit includes inpatient and outpatient encounters. Additionally, definition also required RT-PCR or nucleic acid amplification (NAAT) test positive for RSV. Blue text denotes differences between the two definitions. SpO2= Peripheral capillary oxygen saturation  
1. Kampmann et al. Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants - PubMed (nih.gov)  
2. Vaccines and Related Biological Products Advisory Committee May 18, 2023 Meeting Briefing Document- FDA

In terms of VE against severe medically-attended RSV LRTI in the trial dosing interval and the approved interval, at 0–180 days after birth efficacy was 69.4% in the full interval and 76.5% in the approved interval. It is important to note that not all of the 81 infants who met the severe RSV definition within 0–180 days after birth were hospitalized, nor did all infants who were hospitalized for RSV meet the severe definition. Comparison for estimates from the full Phase 3 trial dosing interval to the approved dosing interval, the point estimates for relative risk were similar but the confidence intervals were wider. Specifically for preterm birth, the relative risk in the vaccinated group compared to the placebo group using the full trial dosing interval was 1.20 with a 95% confidence interval of 0.99 to 1.46. The relative risk with the approved dosing interval was 1.15 (0.82, 1.61) with a wider confidence interval consistent with decreased power to detect this outcome. The confidence intervals were overlapping between the 2 estimates.

As a reminder, the WG chose preterm birth as a critical outcome because a trial for a similar GSK maternal RSV vaccine,<sup>20</sup> also a stabilized prefusion F-protein vaccine, was halted due to an imbalance of preterm births, with higher numbers in the vaccine compared to the placebo group. In that trial, there also was an imbalance in neonatal deaths, which was determined to be a consequence of the preterm birth imbalance. The imbalance in preterm births was seen in low- and middle-income countries (RR: 1.57, 95% CI: 1.17, 2.10), but not high-income countries (RR: 1.04, 95% CI: 0.68, 1.58). The imbalance was observed from April–December 2021, but not consistently after December 2021. The reason for the imbalance in preterm births in the trial remains unclear.

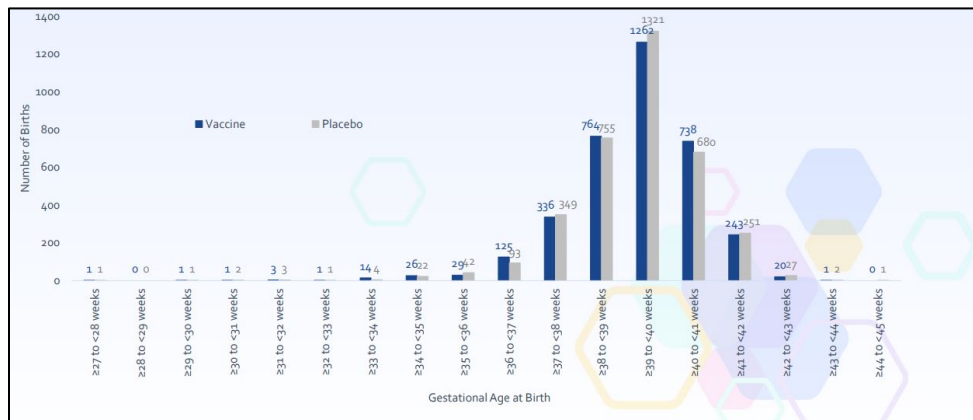
To describe the Pfizer RSVpreF vaccine Phase 3 trial data comparing the trial versus the approved dosing interval in more detail, in the full trial with the trial dosing interval, 5.7% of births were preterm in the vaccinated group compared to 4.7% in the placebo group. When dosing is limited to the approved interval, 4.2% of births in the vaccine arm compared to 3.7% in the placebo arm were preterm, showing that the rate of preterm birth decreased as there was less opportunity to be born preterm. Also, the imbalance between the vaccine and placebo groups narrowed with the approved dosing interval. In terms of low birth weight ( $\leq 2500$  grams) and neonatal jaundice, low birthweight and neonatal jaundice were both more common in the full trial population in the vaccinated group compared to placebo group. However, the confidence intervals between those 2 groups overlapped and the differences were not significant. When limited to the approved dosing interval, 4.1% of infants in the vaccine arm had low birth weight compared to 3.4% in the placebo group. Neonatal jaundice was slightly less

<sup>20</sup> <https://www.fda.gov/media/165621/download>

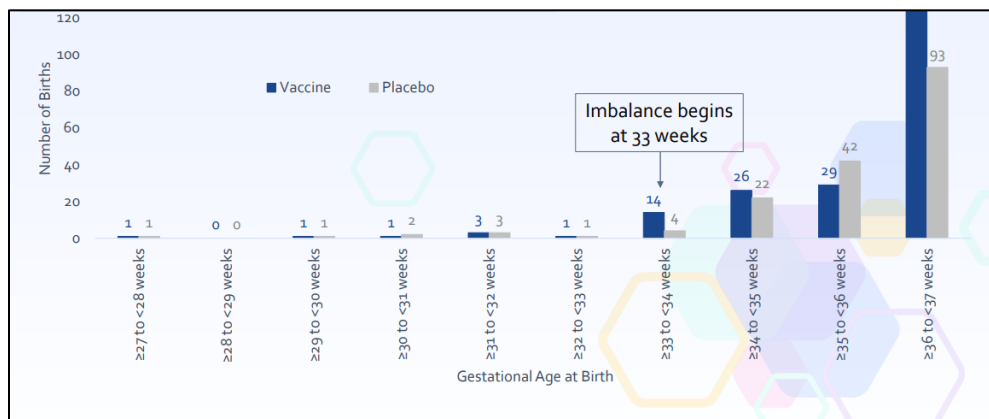
common among the vaccinated group compared to the placebo, but the confidence intervals overlapped.

During the June ACIP meeting, ACIP members requested additional data regarding the Pfizer maternal RSV vaccine, including the rate of preterm birth by calendar month of birth, birth by week of gestational age, percent of births that were preterm by country, and adverse pregnancy outcomes. Enrollment in the Pfizer Phase 3 trial started in June 2020. The earliest births in the trial were inevitably preterm, so the rate was high in both the vaccine and placebo groups. For Pfizer, the imbalance was more prominent during August–December 2021 and then again in April–May of 2022.<sup>21</sup> As a reminder, the GSK imbalance was present in April–December 2021. Looking at preterm birth rates by calendar time in the approved dosing interval, preterm birth was less common overall and the temporal patterns were less clear.

Additionally, ACIP requested a histogram on the number of births by week of gestational age from the full Phase 3 trial with the trial dosing interval (24–36 weeks gestation), shown here with the vaccine arm in blue and the placebo arm in gray:

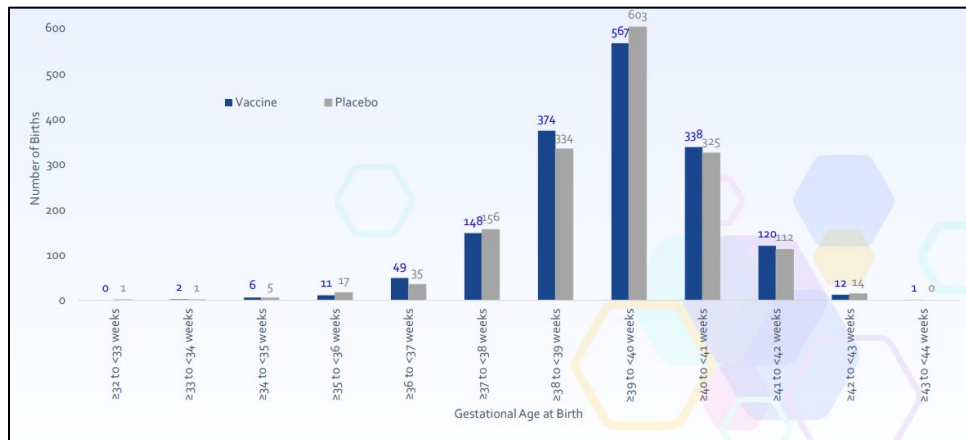


The next histogram shows preterm births only (<math>< 37</math> weeks gestation), which illustrates that the imbalance in preterm birth begins at 33 weeks gestation:



<sup>21</sup> Data source: Pfizer response to ACIP, unpublished data, July 2023

Looking at a histogram of births by gestational age limited to participants who received doses during the approved interval (32–36 weeks gestation), the imbalance is less prominent and is only clearly present at 36 weeks:



The ACIP also requested the percent of preterm births by country in the Phase 3 trial. Importantly, the US data was the single largest country contributing to the trial and accounted for just under half of all trial participants. In the full trial dosing interval of 24–36 weeks in the US, 5.7% of births in the vaccine arm were pre-term compared to 5.3% in the placebo arm. However, in the approved dosing interval in the US, the direction of this imbalance reversed with 4% of births in the vaccine arm being preterm compared to 4.4% in the placebo arm.

The ACIP also requested data on adverse pregnancy outcomes. Looking at select pregnancy-related SAEs occurring at any time after vaccination up to 6 months after delivery for the full Phase 3 trial population,<sup>22</sup> maternal SAEs occurred in 16.2% of the vaccine arm compared to 15.2% of the placebo arm, with overlapping confidence intervals. FDA is requiring post-marketing studies to assess hypertensive disorders of pregnancy, including pre-eclampsia. In the full trial population, pre-eclampsia occurred in 1.8% of the vaccine recipients versus 1.4% of the placebo recipients. Gestational hypertension occurred in 1.1% of vaccine recipients and 1% of placebo recipients. Hypertension occurred in 0.4% of vaccine recipients and 0.2% of placebo recipients.

Another consideration of interest is inflammatory neurologic events.<sup>23</sup> The Pfizer maternal RSV vaccine is the same formulation and dose approved for use in adults  $\geq 60$  years of age. Within the trials for this product, a potential safety signal of inflammatory neurologic events was identified among adults  $\geq 60$  years of age. A total of 3 cases of interest were recorded among 20,255 investigational vaccine recipients  $\geq 60$  years of age and no cases were observed among placebo recipients. The details of these cases were discussed during the June ACIP meeting during the session on RSV vaccines in older adults. As a reminder, these cases included 1 case of Guillain-Barré Syndrome (GBS), 1 case of Miller Fisher syndrome (MFS; a GBS variant), and 1 case of undifferentiated motor-sensory axonal polyneuropathy with worsening of pre-existing

<sup>22</sup> Table 3 ABRYSV0 package insert Package Insert-ABRYSV0 (STN 125768) (fda.gov); Includes all SAEs from vaccination to 6 months post-delivery (up to approximately 10 months, depending on the gestational age at the time of vaccination). In the phase 3 RCT, eclampsia occurred in 5 participants (3 in the RSVpreF group and 2 in the placebo group) and HELLP syndrome occurred in 5 participants (2 in the RSVpreF group and 3 in the placebo group).

<sup>23</sup> Melgar et al. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023 | MMWR (cdc.gov)

symptoms. No GBS or other demyelinating events were reported in the Phase 2 or 3 trials among pregnant people.<sup>24</sup> The background rate GBS syndrome in pregnant people is much lower than that among older adults.<sup>25</sup> In the VSD during 2004–2015, there were 2 cases of GBS in pregnant people with an incidence rate of 2.8 per million person years.<sup>26</sup>

In summary of the Benefits and Harms domain, the WG felt that this is an efficacious vaccine that can prevent RSV LRTI in young infants. However, there was no consensus among the WG regarding the clinical importance of the preterm birth imbalance observed in the clinical trials. WG members found several points concerning preterm birth. Although not statistically significant, an imbalance in preterm births was seen in the full trial population. The trial was powered for efficacy outcomes and was not designed or powered to detect a 20% increase in preterm birth. There may have been less precise dating of gestational age in some sites and countries in the trial, but there is no reason that this should bias towards a preterm birth imbalance among vaccinated compared to placebo recipients. The pre-term birth signal in the GSK maternal RSV vaccine trial, which also is a stabilized prefusion F-protein vaccine, added to the WG's concern.

WG members also found several aspects of the data to be reassuring regarding the preterm birth imbalance. When using the full trial dosing interval, most preterm births (60%) were more than 30 days after vaccination. There is no known biologic mechanism for vaccines to cause preterm birth, particularly more than 30 days after vaccination. When assessed among those vaccinated during the approved dosing interval of 32–36 weeks, data on preterm birth were reassuring to the WG. Specifically, the imbalance in preterm birth was still present but lessened. Most infants born preterm in the vaccine group were born at 36 weeks. In the US, which was the single largest contributing country in the trial, the imbalance in preterm births reversed from the trial dosing interval (trial dosing interval: 5.7% in vaccine vs. 5.3% in placebo recipients; approved dosing interval: 4.0% in vaccine vs. 4.4% in placebo recipients). Overall, the majority of the WG members felt that the approved dosing interval of 32–36 weeks gestation could reduce the potential risk of preterm birth and the potential for complications from preterm birth, both by preventing preterm birth and because babies born late preterm are less likely to have complications from preterm birth. This was their major safety concern.

When asked how substantial the desirable anticipated effects are of the Pfizer maternal RSV vaccine for the critical and important outcomes, the WG was split between “Large” and “Moderate,” with a narrow majority choosing “Large.” When asked how substantial the undesirable effects are of the Pfizer maternal RSV RSVpreF vaccine for the critical and important outcomes, the WG responded that they were “Small.” When asked about the balance of desirable and undesirable effects, the WG determined that the balance favored the intervention of the Pfizer maternal RSVpreF vaccine.

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<sup>24</sup> <https://www.fda.gov/media/168185/download>

<sup>25</sup> Myers TR, McCarthy NL, Panagiotakopoulos L, Omer SB. Estimation of the Incidence of Guillain-Barré Syndrome During Pregnancy in the United States. *Open Forum Infect Dis.* 2019 Mar 15;6(3):ofz071. doi: 10.1093/ofid/ofz071; and Sejvar JJ, Baughman AL, Wise M, Morgan O. Population Incidence of Guillain-Barré Syndrome: A Systematic Review and Meta-Analysis. *Neuroepidemiology* 2011;36:123–133

<sup>26</sup> Myers TR, McCarthy NL, Panagiotakopoulos L, Omer SB. Estimation of the Incidence of Guillain-Barré Syndrome During Pregnancy in the United States. *Open Forum Infect Dis.* 2019 Mar 15;6(3):ofz071. doi: 10.1093/ofid/ofz071

Moving to the Values domain, the results of a values survey of pregnant and recently pregnant people conducted during December 2022–January 2023 conducted by the University of Iowa, RAND, and the CDC were presented during the June ACIP meeting. Among the respondents, 68% had knowledge of RSV prior to taking the survey and 61% of respondents said they “definitely” or “probably” would get an RSV vaccine while pregnant. Among those who did not respond that they “definitely” would get an RSV vaccine while pregnant, safety concerns, lack of RSV knowledge, and concerns about vaccination causing or intensifying RSV infection were the top reasons for not wanting an RSV vaccine during pregnancy.<sup>27</sup> It also is important to look at the uptake of other vaccines in pregnancy. In the US, coverage for recommended vaccines among pregnant people decreased during the pandemic and varies by race and ethnicity.<sup>28</sup> TDAP vaccination coverage was 53.5% in the 2020–2021 season and 45.8% in the 2021–2022 season. Rates of TDAP coverage were higher in White, non-Hispanic women than among Black, non-Hispanic women during the 2020–2021 and 2021–2022 seasons.

When asked whether the WG felt that pregnant people feel the desirable effects are large relative to the undesirable effects, the answered “probably yes.” When asked if there is important uncertainty about, or variability in, how much pregnant people value the main outcomes, the WG was evenly split between “probably important uncertainty or variability” and “probably not important uncertainty or variability.”

There were limited data to inform the Acceptability domain and no updates since the June ACIP meeting. A study in England<sup>29</sup> assessed support of an RSV vaccine among maternity health care professionals (HCP), specifically obstetricians and midwives. If the vaccine was routinely recommended, 47% of responders said they “definitely” would recommend the vaccine, 34% “likely” would support a routinely recommended RSV vaccine, 14% were “not sure,” 4% said “unlikely,” and 0.5% said “very unlikely.” When asked if RSV prevention with the Pfizer maternal RSV vaccine was acceptable to key stakeholders, the majority of the WG answered “yes” and a minority answered “probably yes.”

In terms of the Feasibility domain, the storage and handling requirements, the vaccine is supplied as single 0.5 mL dose or as a 5-pack or 10-pack of single-dose kits. Reconstitution is required, with a single dose vial of lyophilized powder and reconstitution supplies included in the kits. The product should be refrigerated (2°–8°C) in the original container and protected from light. After reconstitution, the product should be administered within 4 hours and otherwise discarded.<sup>30</sup> Additionally, most pregnant patients receive Tdap vaccine in an obstetrician’s or midwife’s office. Therefore, it is likely that pregnant patients also most often would receive RSV vaccine at their prenatal care provider’s office.<sup>31</sup>

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<sup>27</sup> CDC and University of Iowa/RAND survey, unpublished

<sup>28</sup> Flu, Tdap, and COVID-19 Vaccination Coverage Among Pregnant Women – United States, April 2022 | FluVaxView | Seasonal Influenza (Flu) | CDC; <https://www.cdc.gov/flu/fluview/pregnant-women-apr2022.htm>

<sup>29</sup> Wilcox CR, Calvert A, Metz J, et al. Attitudes of Pregnant Women and Healthcare Professionals Toward Clinical Trials and Routine Implementation of Antenatal Vaccination Against Respiratory Syncytial Virus: A Multicenter Questionnaire Study. *The Pediatric Infectious Disease Journal*. 2019 Sept;38(9):944-951. DOI: 10.1097/INF.0000000000002384.

<sup>30</sup> [Package Insert - ABRYSVO \(STN 125769/26\) \(fda.gov\)](https://www.fda.gov/oc/ohrt/ABRYSVO-STN-125769-26)

<sup>31</sup> <https://www.cdc.gov/flu/fluview/pregnant-women-apr2022.htm>



Another important consideration for feasibility is simultaneous administration of RSV vaccine with other vaccines in pregnant people. Pregnant people potentially may be eligible to receive RSV, Tdap, COVID-19, and influenza vaccines during the same visit. There are limited data regarding simultaneous administration, but there was a Pfizer study<sup>32</sup> in healthy non-pregnant women 18–49 years of age on simultaneous administration of Tdap and Pfizer RSV vaccine that found decreased immune response to pertussis components, meaning that the non-inferiority criteria were not met. However, given the lack of correlates of protection for pertussis, it is unclear how this might impact protection against pertussis from maternal Tdap when simultaneously administered with RSV vaccine. Tdap is recommended every pregnancy, preferably during the early part of gestational weeks 27–36,<sup>33</sup> which means that Tdap preferably would be given before 32 weeks and RSV vaccine would be given at or after 32 weeks. However, in MarketScan data from 2018–2021,<sup>34</sup> about half of captured Tdap doses were given before 32 weeks gestation.

Another important consideration is that RSV vaccine is 1 of 2 available preventive products for RSV in infants. Either RSV vaccination during pregnancy or nirsevimab administration for the infant after birth can be used to prevent RSV disease in infants. The WG felt strongly that both products are not needed for most infants. The pregnant person and their prenatal care provider will need to make the decision during pregnancy regarding which RSV prevention product to use. Many prenatal care providers may not have time to discuss options for RSV prevention with their patients. In addition, prenatal care providers may not feel equipped to discuss nirsevimab since this product will be given to the infant after birth.

Regarding the timing of RSV vaccine dosing during the calendar year, RSV vaccine dosing could be implemented for pregnant people as a seasonal campaign or year-round. The WG unanimously supported the use of a seasonal dosing strategy for maternal RSV vaccine because this would maximize cost-effectiveness, maximize the benefits for infants, and target RSV vaccine dosing to infants who will be in the first months of life during the RSV season. Importantly, nirsevimab is available for infants who are born out of season for whom maternal vaccine protection would have waned by RSV season. The WG supported seasonal dosing beginning in September and going through January in most of the continental US based on typical pre-pandemic seasonality. This aligns with implementation of influenza vaccine and would simplify implementation for prenatal care providers. The WG felt that jurisdictions in which RSV seasonality differs from most of the continental US should have flexibility regarding start and stop of administration of RSV vaccine in pregnant people. These jurisdictions include Alaska and jurisdictions with tropical climates (e.g., parts of Florida, Puerto Rico, US Virgin Islands, Hawaii, Guam, and US-affiliated Pacific Islands).

When asked whether the Pfizer maternal RSV vaccine is feasible to implement, the majority of the WG answered “yes” and a substantial minority answered “probably yes.”

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<sup>32</sup> Peterson et al. Safety and Immunogenicity of a Respiratory Syncytial Virus Prefusion F Vaccine When Coadministered With a Tetanus, Diphtheria, and Acellular Pertussis Vaccine. *The Journal of Infectious Diseases*. 2022 June 15; 225(12): 2077–2086. doi: 10.1093/infdis/jiab505

<sup>33</sup> CDC, <https://www.cdc.gov/vaccines/vpd/dtap-tdap-td/hcp/recommendations.html>

<sup>34</sup> MarketScan data, 2018-2021

Regarding the Resource Use Domain, the ACIP heard presentations earlier from Drs. Hutton and Ortega-Sanchez on economic analyses. Dr. Hutton showed scenarios for cost-effectiveness by months of RSV vaccine dosing during the calendar year. The base case was about \$400,000 per QALY. If the months of dosing were limited to target dosing to pregnant people whose infants would be in the first months of life during the RSV season, the ICER decreased and the cost-effectiveness improved. Importantly, the ICER would be \$167,000 per QALY if dosing is provided during the September–January timeframe. The WG interpretation was that while RSV vaccine may improve outcomes, it also would increase costs. The base case model showed an ICER of about \$400,000 per QALY and assumed year-round dosing of this vaccine and typical RSV seasonality in most of the continental US. The WG felt that this vaccine would not be cost-effective under the base case conditions. However, cost-effectiveness would be improved by using a seasonal dosing strategy during September–January in most of the continental US. Thus, the WG unanimously supported the use of a seasonal dosing strategy.

When asked whether Pfizer maternal vaccine use would be a reasonable and efficient allocation of resources, a substantial majority of the WG answered “probably yes” and a substantial minority answered “yes.” It is important to note that the WG responses were based on seasonal dosing for RSV vaccine specifically during September–January in most of the continental US.

Data for the final domain of Equity have been presented before. National studies of death certificates found higher rates of RSV-associated deaths among non-Hispanic Black children compared with non-Hispanic White infants in children 1–4 years of age.<sup>35</sup> ICU admission rates for RSV among non-Hispanic Black infants <6 months of age were 1.2 to 1.6 times higher than among non-Hispanic White infants.<sup>36</sup> In one study, RSV hospitalization rates were 4 to 10 times higher among Alaska Native and American Indian (AI/AN) children <24 months than the rate in the general population.<sup>37</sup> However, it is important to note that the study was limited to specific populations and might not be broadly representative of risk in all AI/AN children.

Regarding Medicaid coverage for pregnant people and vaccines during pregnancy, by federal law, all states provide Medicaid coverage for pregnancy-related services to pregnant women with income levels up to 138% of the federal poverty level.<sup>38</sup> In 2021, 41% of mothers had Medicaid at the time of birth,<sup>39</sup> making Medicaid the largest payer for maternity care in the US. If recommended, ACIP would vote on a Vaccines for Children (VFC) resolution for the vaccine for pregnant people <19 years of age. Beginning on October 1, 2023, when the Inflation Reduction Act of 2022 (IRA) provisions become effective, state Medicaid agencies will be required to recover vaccines and their administration without cost-sharing for nearly all adult beneficiaries covered under traditional Medicaid, if the CDC recommendations apply. Regarding other insurance coverage, meaning commercial insurance for vaccines during pregnancy under the Affordable Care Act (ACA) and its implementing regulations, ACIP recommendations that have been adopted by CDC and are listed on CDC’s Immunization Schedules generally are required to be covered by group health plans and health insurance issuers without any cost-sharing requirements.

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<sup>35</sup> Hansen et al. The Use of Death Certificate Data to Characterize Mortality Associated With Respiratory Syncytial Virus, Unspecified Bronchiolitis, and Influenza in the United States, 1999–2018 *J Infect Dis*. 2022 Aug 15;226(Supplement 2): S255–S266.

<sup>36</sup> Unpublished data from RSV-NET, CDC.

<sup>37</sup> Atwell et al. RSV Among American Indian and Alaska Native Children: 2019 to 2020 *Pediatrics*. 2023 Aug 1;152(2):e2022060435

<sup>38</sup> <https://www.kff.org/womens-health-policy/issue-brief/medicaid-coverage-for-women/>

<sup>39</sup> <https://www.medicaid.gov/sites/default/files/2023-04/beneficiary-profile-2023.pdf>

When asked what the impact of the Pfizer maternal RSV vaccine on health equity would be, the WG's answers ranged and there was no clear majority. The most common answer among the WG was "probably increased," the second most common was "probably no impact," and the third most common was "increased."

In summary, regarding the use of the Pfizer maternal RSV vaccine to prevent RSV in infants, the WG judged this is an important public health problem, the desirable anticipated effects are large, the undesirable anticipated effects are small, the balance of desirable and undesirable effects favor the intervention, and that the target population probably feels the desirable effects are large relative to the undesirable effects. Half of the WG chose that there is probably important uncertainty or variability in how patients value the outcome, and half chose there is probably not important uncertainty or variability. The WG judged that the intervention is acceptable to key stakeholders, is feasible to implement, and is probably a reasonable and efficient allocation of resources with seasonal dosing. The WG had varied answers as to whether the intervention would increase health equity, ranging from probably no impact to increased health equity. The majority of the WG felt that the desirable consequences probably outweigh the undesirable consequences in most settings, and a substantial minority felt that the desirable consequences clearly outweigh the undesirable consequences in most settings. The majority opinion was in favor of recommending the Pfizer maternal RSV vaccine, and there was a minority opinion to recommend the intervention based on shared clinical decision-making.

To summarize the WG's considerations overall, for benefits and harms, the majority of the WG was supportive of the intervention with the Pfizer maternal RSV vaccine for pregnant people with the approved dosing interval of 32–36 weeks gestation. They found the data on preterm births, when assessed among those vaccinated during the approved interval, to be reassuring. They felt the approved dosing interval of 32–36 weeks gestation would reduce the potential risk of preterm birth and the potential for complications from preterm birth, which was their major safety concern. All WG members endorsed the importance of post-introduction vaccine safety monitoring. The WG unanimously supported the use of a seasonal dosing strategy, which would maximize benefits and cost-effectiveness. The WG supported that RSV vaccine dosing should occur during September–January in most of the continental US and felt that jurisdictions in which RSV seasonality differs from most of the continental US should have flexibility regarding start and stop of administration of RSV vaccine in pregnant people.

The WG also considered the implications of RSV vaccine being 1 of 2 available preventive products for RSV in infants. The WG expressed that pregnant people should have options for RSV prevention, given that nirsevimab may not be readily available in all settings. In addition, pregnant people and their providers may have preferences regarding these 2 products. The WG also stated that pregnant people should be made aware that they either could receive RSV vaccine during pregnancy or that nirsevimab could be given to the infant, but that most infants would not need both. The WG expressed that pregnant people should be informed regarding the risks and benefits of both products before making a decision.

The WG had extensive discussions regarding a full recommendation versus a shared clinical decision-making recommendation. Most WG members support a full recommendation. They felt the approved dosing interval would reduce the potential risk of, and complications from, preterm birth. They stressed the importance of clear vaccine recommendations and noted that providers who will help pregnant people decide which product to receive generally have less familiarity with the data than ACIP does. They expressed that shared clinical decision-making recommendations can be confusing, hard to implement for providers, can lead to lower vaccine confidence and uptake of vaccine, and potentially could influence support for the vaccine in

lower- and middle-income countries where nirsevimab may not be available. A minority of WG members supported a recommendation with shared clinical decision-making. They noted that without shared clinical decision-making, a full recommendation could result in some providers recommending RSV vaccine during pregnancy without discussing with pregnant patients that nirsevimab is an option. They cited the potential risk for preterm birth and neuroinflammatory events and cited that the same vaccine is recommended under shared clinical decision-making for adults  $\geq 60$  years and older. It is important to note that ACIP generally makes shared clinical decision-making recommendations when individuals may benefit from vaccination, but broad vaccination of people in that group is unlikely to have population-level impacts. As discussed during the June ACIP meeting, the WG noted that currently there are no data available on the efficacy of the first lifetime dose during subsequent pregnancies, or the safety of additional doses given in subsequent pregnancies. The WG felt that it was too early to decide whether additional doses should be given in subsequent pregnancies due to the lack of data, that additional data are needed to inform whether additional doses in subsequent pregnancies would be indicated, and that recommendations can be updated in the future.

With all of this in mind, the proposed voting language put forward for a potential vote during this meeting was as follows:

“Maternal RSV vaccine is recommended for pregnant people during 32 through 36 weeks gestation, using seasonal administration, to prevent RSV lower respiratory tract infection in infants.”

### **Updated Clinical Considerations for Use of Both Nirsevimab and Pfizer RSVpreF Vaccine**

**Jefferson Jones MD, MPH, FAAP, CDR USPHS (CDC/NCIRD)** discussed the updated clinical considerations for the use of maternal RSVpreF vaccine and nirsevimab. Beginning with the proposed clinical considerations for use of the maternal RSV vaccine, as Dr. Fleming-Dutra reviewed, the WG discussion points that shaped these considerations included that as proposed, the maternal RSV vaccine would be recommended for pregnant people during 32–36 weeks gestation with seasonal administration or during September–January in most of the continental US in jurisdictions with seasonality that differs from most of the continental states, including Alaska and jurisdictions with tropical climates (e.g., parts of Florida, Hawaii, Puerto Rico, Guam, US Virgin Islands, and the US-affiliated Pacific Islands). In those jurisdictions, providers would follow state, local, or territorial guidance on the timing of administration. The maternal RSVpreF vaccine may be administered simultaneously with other eligible vaccinations.<sup>40</sup>

Before reviewing the clinical considerations for use of both the maternal RSV vaccine and nirsevimab, Dr. Jones summarized the considerations of the WG. He first discussed 2 groups of infants born to vaccinated mothers who were previously considered for nirsevimab during the June ACIP meeting, preterm infants and infants born outside of the RSV season. As proposed regarding infants born prematurely, the maternal RSV vaccine recommendation is for administration beginning at 32 weeks gestation. From the time of maternal vaccination, 14 or more days are likely needed for development and transplacental transfer of maternal antibodies to protect the infant and nirsevimab is recommended for infants born within 14 days of vaccination. The earliest an infant can be born and have maternal vaccine-induced protection is

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<sup>40</sup> <https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html>

34 weeks gestation. This means that all infants born at <34 weeks gestation will be recommended to receive nirsevimab.<sup>41</sup>

Regarding infants born outside of the RSV season, protection from maternal vaccination may begin to wane after 3 or more months. For example, this has been seen with the influenza and COVID-19 vaccines.<sup>42</sup> WG members initially were concerned that some infants born outside of the RSV season and born to vaccinated mothers may benefit from nirsevimab in order to boost protection when entering the RSV season. However, because maternal RSV vaccine administration is now proposed to be recommended during September–January, most infants of vaccinated mothers will be born during the RSV season during October–March. Mothers of infants born outside of the RSV season during April–September will not have been vaccinated, and nirsevimab will be recommended for these infants.

Other WG considerations regarding the use of both maternal RSV vaccine and nirsevimab included that there are 2 products available to protect infants from RSV LRTI. For infants born to vaccinated mothers, the addition of nirsevimab may provide incremental protection, but there are no efficacy data on the use of nirsevimab in infants born to vaccinated mothers, so this is unknown. There also are no safety data on the use of nirsevimab in infants born to vaccinated mothers, but nirsevimab trials included infants with maternal infection-induced antibodies and the risk is likely minimal. The WG felt that for most infants, administering both products is not needed and would not be a reasonable and efficient allocation of resources based on the cost-effectiveness analysis presented earlier in the day. Of note, documentation of maternal vaccination status may not be available to the infant's HCP.

Most WG members felt that pregnant people should be aware that both maternal vaccination and nirsevimab are options when deciding whether to be vaccinated. However, HCP of pregnant people may not have the time or feel equipped to discuss nirsevimab when counseling. The WG felt that in rare situations, flexibility is needed for providers to be able to administer nirsevimab when it is clinically warranted for infants born to vaccinated mothers. Examples include conditions in pregnant people resulting in an inadequate immune response to vaccine or decrease in transplacental antibody transfer.<sup>43</sup> Also, infants who have undergone cardiopulmonary bypass leading to a loss of maternal antibodies<sup>44</sup> and infants with sufficiently increased risk for severe disease to warrant nirsevimab because of the potential increased benefit.

The following are the proposed clinical considerations for the use of the maternal RSV vaccine and nirsevimab:

- Either maternal vaccination or use of nirsevimab in the infant is recommended to prevent RSV LRTI, but administration of both products is not needed for most infants.
- Health care providers of pregnant people should provide information on both products and consider patient preferences when determining whether to vaccinate the pregnant patient or to not vaccinate and rely on administration of nirsevimab to the infant after birth.

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<sup>41</sup> <https://www.cdc.gov/vaccines/pregnancy/vacc-during-after.html>

<sup>42</sup> Kampmann NEJM 2023; Nunes F1000Res 2018;and Zerbo Nat Commun 2023.

<sup>43</sup> Palmerira Clin Dev Immunol 2012

<sup>44</sup> Feltes J Pediatr 2003

It is important to note that both products are safe and effective in preventing RSV LRTIs in infants. The following displays potential information that could be shared with patients on the relative risks and benefits of a maternal RSV vaccine and nirsevimab:

Maternal RSV vaccine	Nirsevimab
<p><b>Benefits</b></p> <ul style="list-style-type: none"> <li>• Provides protection immediately after birth</li> <li>• May be more resistant to virus mutation</li> <li>• Avoids injection of infant</li> </ul> <p><b>Risks</b></p> <ul style="list-style-type: none"> <li>• Protection reduced if fewer antibodies produced or are transferred from mother to baby (e.g., mother immunocompromised or infant born soon after vaccination)</li> <li>• Potential risk of preterm birth</li> </ul>	<p><b>Benefits</b></p> <ul style="list-style-type: none"> <li>• Studies of antibody levels suggest that protection might wane more slowly</li> <li>• Can provide antibodies directly if infant receives less antibodies from mother</li> <li>• No risk of adverse pregnancy outcomes</li> </ul> <p><b>Risks</b></p> <ul style="list-style-type: none"> <li>• Potentially limited availability during 2023-2024 RSV season</li> </ul>

Relative benefits of maternal vaccination include that a maternal vaccine provides protection immediately after birth, when infants are at the highest risk for severe RSV disease. A maternal vaccine may be more resistant to virus mutation compared with monoclonal antibodies, although RSV does not mutate rapidly. While both products require an injection, use of a maternal vaccine avoids injection of the infant. Relative risks of maternal RSV vaccination include that maternal vaccine-induced protection is reduced if fewer vaccine-induced antibodies are produced or are transferred from the mother to the baby (e.g., mother immunocompromised or the infant is born soon after vaccination). There is a potential risk of preterm birth, but administration at 32–36 weeks reduces this risk.

The relative benefits of nirsevimab include studies of antibody levels suggesting that protection from nirsevimab might wane more slowly. Administration of nirsevimab can provide antibodies directly if an infant receives less antibodies from the mother. Since nirsevimab is provided after birth, there are no risk of adverse pregnancy outcomes. Relative risks of nirsevimab include that there may be potential limited availability of nirsevimab during the 2023–2024 RSV season. In the setting of a maternal vaccine, nirsevimab would be recommended for infants <8 months of age born during or entering their first RSV season if the mother did not receive the RSV vaccine or it is unknown if the mother received an RSV vaccine or mother was vaccinated, but the infant was born <14 days after vaccination. Nirsevimab is not needed for most infants born ≥14 days after maternal vaccination.

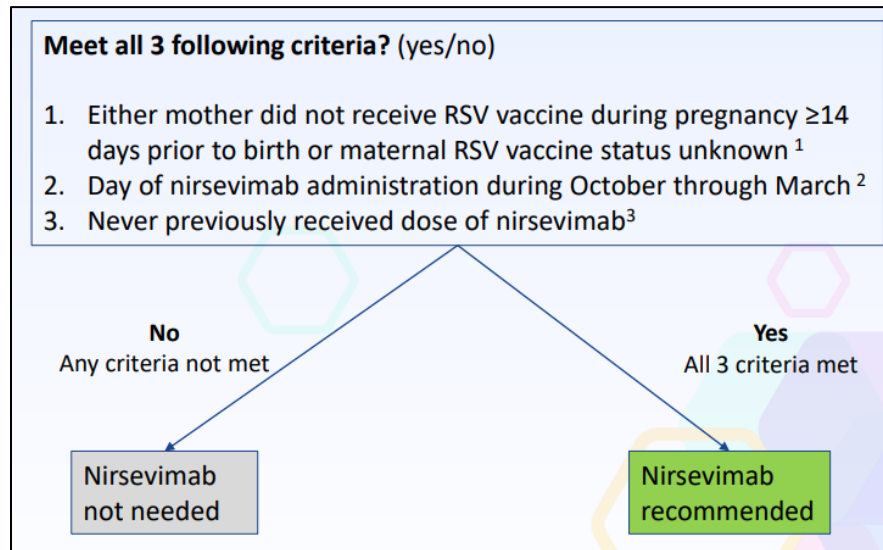
Nirsevimab can be considered in circumstances when the mother has received RSV vaccine ≥14 days prior to birth. Nirsevimab can be considered in rare circumstances, per the clinical judgment of the HCP, the potential incremental benefit of administration is warranted. One example is infants born to pregnant people who may not mount an adequate immune response to vaccination (e.g., people with immunocompromising conditions) or have conditions associated with reduced transplacental antibody transfer (e.g., people living with HIV infection).<sup>45</sup> Other examples include infants who have gone undergone cardiopulmonary bypass, leading to a loss of maternal antibodies<sup>46</sup> or infants with substantial increased risk for

<sup>45</sup> Palmerira Clin Dev Immunol 2012

<sup>46</sup> Feltes J Pediatr 2003

severe RSV disease (e.g., hemodynamically significant congenital heart disease or ICU admission requiring oxygen at discharge). Recommendations for nirsevimab can be summarized in the following algorithm.

*Nirsevimab is recommended to all infants aged <8 months on the day of administration who meet all 3 of the following criteria:*



Details on timing, including special situations and flexibility, are described in the footnotes:

<sup>1</sup>For most infants age <8 months whose mother received RSV vaccine 14 or more days prior to birth, nirsevimab is not needed. Nirsevimab can be considered in rare circumstances when, per the clinical judgment of the healthcare provider, the potential incremental benefit of administration is warranted. These situations include infants born to pregnant people who may not mount an adequate immune response to vaccination (e.g., people with immunocompromising conditions) or have conditions associated with reduced transplacental antibody transfer (e.g., people living with HIV infection), infants who have undergone cardiopulmonary bypass leading to loss of maternal antibodies, and infants with substantial increased risk for severe RSV disease (e.g., hemodynamically significant congenital heart disease, intensive care admission and requiring oxygen at discharge).

<sup>2</sup>While the timing of the onset and duration of RSV season may vary, nirsevimab may be administered October through the end of March in the majority of the continental United States. Providers may adjust timing of administration based on guidance from public health authorities (e.g., CDC, health departments) or regional medical centers. Although optimal timing of administration is just before the start of the RSV season, nirsevimab may also be administered during the RSV season to infants and children who are age-eligible. Infants born shortly before or during RSV season should receive nirsevimab within one week of birth. Nirsevimab administration can occur during the birth hospitalization or in the outpatient setting. Infants with prolonged birth hospitalizations related to prematurity or other causes should receive nirsevimab shortly before or promptly after hospital discharge.

These were previously presented during the August ACIP meeting under nirsevimab and described in the published nirsevimab recommendation in the *Morbidity and Mortality Weekly Report (MMWR)*.

## **Implementation Considerations for Maternal RSV Vaccine**

**Georgina Peacock, MD, MPH (CDC/NCIRD)** presented maternal RSV vaccine implementation Considerations, including the following:

- Vaccine storage, handling, and administration
- Cost of vaccine
- Insurance coverage
- Supply and availability
- Complexity of immunization schedule
- Vaccine demand and coverage in pregnant people
- Obstetric and pediatric provider roles in vaccination decisions
- Immunization information systems
- Communication challenges

For Pfizer RSV vaccine storage, handling, and administration, the overall clinical implementation is similar to other vaccines. It is stored at 2° to 8° C and administered as a single dose through an intramuscular (IM) route. Additional steps are required for dilution, including reconstitution of the lyophilized antigen component with the sterile water diluent component.<sup>47</sup> The proposed recommendations to ACIP allow for simultaneous administration with other recommended vaccines, and there is some consideration that increasing the number of vaccines could lead to limited storage space.

There has been a lot of conversation already about cost of the vaccine at \$295 a dose for the Pfizer RSV compared to Tdap that is approximately \$46 to \$52.<sup>48</sup> This cost is lower than the infant nirsevimab cost of \$495 for the private sector cost. Reimbursement and cost recovery challenges already have been identified by providers and practices as implementation barriers for maternal immunization. Among providers, financial concerns are a leading barrier to maternal immunization.<sup>49</sup>

Related to insurance coverage, most pregnant people are covered by some form of private payer or Medicaid. About 52% of pregnant people have private insurance, 41% have Medicaid, and about 4% are likely uninsured and are considered “self-pay.”<sup>50</sup> If recommended, ACIP would vote on a VFC resolution for maternal RSV vaccine in people aged <19 years. For people ≥19 years of age, there would be limited availability through the 317 program in jurisdictions. In terms of insurance coverage for infant nirsevimab, the ACIP already recommended nirsevimab as a routine immunization. Therefore, it will be covered under the ACA without cost-sharing by the patient starting in the effective plan year.<sup>51</sup> Anecdotally, plans are starting to let people know that they will start covering nirsevimab when it becomes available in the coming weeks. Nirsevimab is included in the VFC program for eligible children, so about 50% of children in the US will be able to access nirsevimab at no cost.

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<sup>47</sup> <https://www.fda.gov/media/168889/download?attachment>

<sup>48</sup> Current CDC Vaccine Price List | CDC

<sup>49</sup> <https://www.sciencedirect.com/science/article/abs/pii/S0749379717306396#0010>

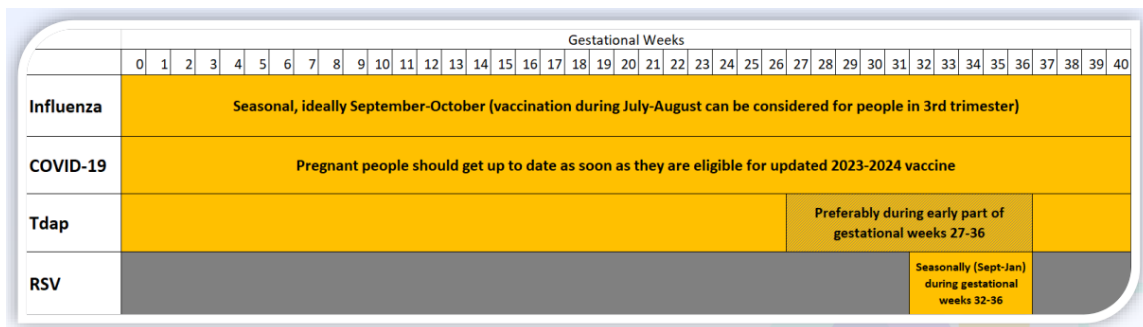
<sup>50</sup> <https://www.cdc.gov/nchs/products/databriefs/db468.htm>

<sup>51</sup> <https://www.law.cornell.edu/uscode/text/42/300gg-13>



With regard to supply and availability of maternal RSV vaccine and nirsevimab during the 2023–2024 RSV season, there are no anticipated supply/demand mismatches. Because the Pfizer maternal RSV vaccine is the same product in use for adults ≥60 years of age, availability is expected shortly after ACIP recommendations. Nirsevimab likely will be available in late September or early October. There were some conversations during the last ACIP meeting about delivery in birthing hospitals versus outpatient settings. Efforts are underway to increase the number of birthing hospitals that will administer nirsevimab, particularly under the VFC program.

It is important to point out the increasing complexity of the maternal immunization schedule as illustrated in this figure:



The maternal immunization schedule is increasingly complex in terms of different timing of vaccines based on the season and/or gestational age, with seasonal timing varying in some locations. In addition, there is a limited window for RSV vaccine administration. The willingness of pregnant people to accept multiple vaccines in pregnancy also is unclear. In a survey of pregnant people, approximately 12% said they would accept no vaccines and about 49% said they would accept 1 or 2 vaccines.<sup>52</sup> Uptake of vaccines among pregnant people has declined and disparities persist.<sup>53</sup>

Important decisions will need to be made regarding whether to administer maternal RSV vaccine or infant nirsevimab. Studies continue to demonstrate that HCPs are pregnant people’s most trusted source of information on vaccines, and that provider recommendation is a strong predictor of vaccination.<sup>54</sup> However, one survey showed that two-thirds of obstetricians did not feel comfortable providing information about routine childhood immunizations or that that was their role.<sup>55</sup> In terms of pediatric provider roles in immunization decisions, recommendations for nirsevimab that are contingent upon knowledge of maternal vaccination status could be challenging if the pediatric provider does not receive the maternal record. Verbal reports of vaccines received during pregnancy may not be reliable.<sup>56</sup> Therefore, pediatric providers may need to make decisions on nirsevimab administration without having complete information on maternal vaccination status.

<sup>52</sup> CDC and University of Iowa/RAND survey, unpublished

<sup>53</sup> <https://www.cdc.gov/flu/fluview/pregnant-women-apr2022.htm>

<sup>54</sup> Lutz C, et al. Understanding barriers and predictors of maternal immunization: Identifying gaps through an exploratory literature review. *Vaccine* 36 (2018): 7445-7455

<sup>55</sup> <https://link.springer.com/article/10.1007/s10995-011-0936-0>

<sup>56</sup> <https://www.cdc.gov/mmwr/volumes/66/wr/mm6641a3.htm>

Moreover, state Immunization Information Systems (IISs) vary in what they capture related to adult immunization. Pregnancy status is not identified in IIS, though potentially RSV vaccine administrations in adult women <age 60 years of age could be used as a proxy for RSV vaccine administration. There is not a way currently to link maternal and infant immunization records in IISs, so it is not possible through these systems at this point to use that to forecast whether infant nirsevimab immunization is needed. In some state policies, there is not an ability for pediatric providers to review adult records or records of individuals who are not their patients.

As always in immunization implementation, there are some communication challenges. This includes use of terms like “vaccine” for the maternal product versus “immunization” for the infant product. Conveying potential risks and benefits of each approach and helping the pregnant person make an informed decision, including the potential but undetermined risk of preterm birth with maternal immunization, is going to take time for providers. Discussing financial implications with a patient in a setting of uncertainty related to coverage in the first year of implementation may be challenging.

A lot of work is being done at CDC to address communication activities. There has been formative research and message testing, including with focus groups and in-depth interviews to help inform the ultimate communication activities that will be done for the public. There have been surveys of parents of young children and also pregnant and recently pregnant people. With that information, patient and provider education materials are being developed. There also are some partnerships with HCP organizations and organizations that serve pregnant people. There also is an intention to utilize social media across all of CDC’s platforms.

### **Vaccines for Childrens Resolution**

**Jeanne Santoli, MD, MPH (CDC/NCIRD)** indicated that the purpose of this resolution was to: 1) add an RSV vaccine for pregnant people aged <19 years to the program; and 2) update the language regarding the recommended vaccine schedule for nirsevimab to take into account RSV vaccine for use during pregnancy. The eligible groups include pregnant people aged <19 years. The recommended vaccination schedule and intervals included the language that was reviewed during this session:

- ❑ During 32 through 36 weeks gestation, with seasonal administration. This would be during September through January in most of the continental United States. In jurisdictions with seasonality that differs from most of the continental United States (e.g., those with tropical climates, Alaska), providers should follow state, local, or territorial guidance on timing of administration.
- ❑ Either RSV vaccination during pregnancy at 32 through 36 weeks gestation or nirsevimab administration for infants age <8 months shortly before or during the RSV seasons is recommended to prevent RSV lower respiratory tract infection, but both products are not indicated for most infants.

### **Recommended Dosage**

Refer to product package inserts.

### **Contraindications and Precautions**

Contraindications can be found in the package inserts available at:

<https://www.fda.gov/media/168889/download?attachment>

For the nirsevimab component, the only change was that now there are 2 components to the eligible groups:

- Infants aged <8 months born during or entering their first RSV season
- Children aged 8-19 months as noted in Table 1 who are at increased risk of severe RSV disease and entering their second RSV season

No changes were made to the Table 1:

**Table 1. Children at increased risk of severe RSV disease**

Children with chronic lung disease of prematurity who required medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) any time during the 6-month period before the start of the second RSV season
Children with severe immunocompromise
Children with cystic fibrosis who have manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest imaging that persist when stable) or weight-for-length <10th percentile
American Indian and Alaska Native children

Language was added to Table 2 for the first season stating, “whose mother’s receipt of RSV vaccine is unknown or who was born within 14 days of maternal vaccination” and the rest of the resolution is the way it appeared in August 2023:

**Table 2. Immunization Schedule**

RSV Season	Schedule	Timing
First RSV Season	One dose of nirsevimab for infants aged <8 months born during or entering their first RSV season whose mother did not receive RSV vaccine, whose mother’s receipt of RSV vaccine is unknown, or who was born within 14 days of maternal vaccination.	Administer from beginning shortly before the start of the RSV season until the end of the season
Second RSV Season	One dose of nirsevimab for children aged 8–19 months who are at increased risk of severe RSV disease and entering their second RSV season (see Table 1)	

This recommended vaccination schedule and intervals language also has been added and there is some language in each component of the resolution that refers to the other components:

“For most infants aged <8 months born during or entering their first RSV season whose mother received an RSV vaccine 14 or more days prior to birth, nirsevimab is not needed. Nirsevimab can be considered in rare circumstances when, per the clinical judgment of the healthcare provider, the potential incremental benefit of administration is warranted.”

The recommended dosage, contraindications and precautions, and standard documents statement about ACIP recommendations or notices within 6 months remained unchanged:

### **Recommended Dosage**

Refer to product package inserts.

### **Contraindications and Precautions**

Contraindications and Precautions can be found in the package inserts available at:

<https://www.accessdata.fda.gov/spl/data/2f08fa60-f674-432d-801b-1f9514bd9b39/2f08fa60-f674-432d-801b-1f9514bd9b39.xml>

[If an ACIP recommendation or notice regarding RSV prevention is published within 6 months following this resolution, the relevant language above (except in the eligible groups sections) will be replaced with the language in the recommendation and incorporated by reference to the publication URL].

### **Pfizer Statement**

**Luis Jodar, MD (Chief Medical Officer, Vaccines & Antivirals, Pfizer)** thanked the ACIP for the opportunity to speak. Pfizer is excited about the recent FDA approval of the maternal indication for RSV vaccine, ABRYSVO™. Last Fall, the US experienced a triple epidemic of RSV, influenza, and COVID-19 infections, making national headlines. With the threat of another triple epidemic, having multiple options for RSV prevention for infants will be more important than ever. As shown in the data on efficacy in the randomized controlled trials (RCTs), the maternal RSV vaccine provides infants with a high degree of protection against RSV immediately from birth when infants are at highest risk for severe disease and maintains this protection for at least 180 days. This is even more important when considering equity. Medicaid recipients miss or cancel a substantial proportion of their well-child visits in the first 6 months of life, with only 25% attending all recommended well-child visits. In contrast, more than 90% of Medicaid mothers attend at least 1 visit prior to delivery. With an estimated 41% of pregnant individuals on Medicaid, maternal immunization provides a secure, stable, and equitable approach to RSV prevention for newborns.

Regarding the concern raised about an imbalance in pre-term births, the totality of the data supports a favorable benefit-risk profile for maternal vaccination as supported by the external Data Monitoring Committee (DMC), the FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC), and FDA licensure. The US indication of 32–36 weeks is reassuring about the potential risk of preterm birth. Pfizer has committed to 4 post-licensure pharmacovigilance studies. The safety surveillance systems in place through Pfizer's post-marketing commitments, along with the CDC and FDA systems presented during this meeting, are sensitive, timely, powerful, and can detect any safety signals should any arise. Pfizer wants to assure the committee that a robust supply of vaccine is already available to providers and is ready to be implemented through existing vaccine programs. The RSV season is already starting and, for the first time, there potentially could be 2 important routinely recommended options for RSV prevention for infants. Pregnant persons now will be able to have an informed discussion with their obstetricians and other maternal health providers, as they do for all routinely recommended maternal vaccines, and make an informed decision on which option is best for them and their baby. Dr. Jodar emphasized that the RSV vaccine would be a lower cost option and overall could result in a lower budget impact for the US healthcare system. Pfizer thanked ACIP and the WG for their careful deliberations and dedication to preventing infectious diseases.

## **Liaison Organization Statements**

**Brenna Hughes, MD, MSc, FACOG (ACOG)** thanked the leadership of ACIP and the WG on behalf of the American College of Obstetricians and Gynecologists (ACOG) for their collaboration on this topic and for inviting ACOG to share its position and expert opinions regarding the maternal RSV vaccine. It is critical that the OB-GYN voice be considered particularly as implementation considerations are discussed. ACOG remains unequivocally supportive of a full recommendation for maternal RSV vaccine for pregnant individuals. This RSV vaccine is efficacious and could decrease the risk of severe disease in many infants. While nirsevimab is clearly highly efficacious, it may not be available or may not be preferred by a parent or health care facility as the primary intervention. Therefore, ACOG believes it is critical to ensure that pregnant individuals can access this RSV vaccine to give their newborns protection after birth. As a practicing obstetrician and member of the RSV Vaccine WG, Dr. Hughes has reviewed these data extensively, along with the other experts on the WG, and has discussed these data with ACOG experts and leadership. They have evaluated all of the available data regarding the risk of premature delivery, and currently consider this outcome to be a theoretical risk, with the benefits of vaccination outweighing the hypothetical risk of AEs. Therefore, ACOG feels that this vaccine should be recommended. Finally, ACOG continues to encourage the collection of additional data to inform future policy considerations, and looks forward to collaborating with the CDC and other organizations to ensure optimal implementation of strategies to decrease the burden of RSV disease in infants.

**Carol Hayes, CNM, MN, MPH, FACNM (ACNM)** provided comments on behalf of the American College of Nurse Midwives (ACNM), the largest professional association representing certified nurse midwives and certified midwives in the US. ACNM sets the standard for excellence in midwifery education and practice in the US and strengthens the capacity of midwives in developing countries. ACNM members are primary care and sexual and reproductive health providers for people throughout their lifespans, with a special emphasis on pregnancy, childbirth, gynecological, and reproductive health. ACNM has participated actively in the ACIP and the CDC Task Force on Maternal Immunizations and regularly updates and encourages members to recommend the 3 standard maternal immunizations throughout a shared decision-making model. The midwifery model of care puts women and pregnant people at the center of care and encourages members to share scientific evidence on choice surrounding immunizations so that pregnant families can make the best decisions for themselves. After reviewing the evidence on the safety and efficacy of the maternal vaccine, as well as the incidence of RSV cases in newborns and infants, ACNM strongly recommends that ACIP support the availability of this vaccine to all pregnant people from 32–36 weeks of gestation. ACNM believes that pregnant individuals should be informed of the benefits and the risks of maternal RSV vaccine, and the vaccine should be available to those who choose it without any barrier to access, such as cost, referral, or approval by a third party. Given the rise and the prevalence of RSV cases among newborns, ACNM believes that pregnant people should be able to access a vaccine that is proven to prevent LRTD and severe LRTD caused by RSV in infants from birth to 6 months of age.

## **ACIP Discussion Points, Observations, Suggestions for RSV Vaccine**

### *Following Presentations by Dr. DeSilva and Dr. More*

- ACIP expressed gratitude to Drs. DeSilva and More for sharing the proactive plans to monitor RSV vaccines.
- In terms of an inquiry about how pregnancies with multiple gestations (e.g., twins, triplets, et cetera) would be monitored since they have a risk for being preterm, Dr. DeSilva indicated that multiple gestations will be excluded from the initial planned evaluation. However, a more comprehensive end-of-season evaluation is being planned and consideration will be given to how to account for multiple gestation births.
- In response to a request about a status update on how the v-safe<sup>sm</sup> monitoring of RSV vaccines received by persons  $\geq 60$  years of age is going, Dr. Anne Hause from the v-safe<sup>sm</sup> program indicated that the new version of v-safe<sup>sm</sup> is still in the final stages of development, with a launch planned in Fall 2023 for RSV vaccines among older adults and anticipated for maternal RSV later in Fall 2023. Dr. Shimabukuro added that while they have received a small number of reports for the older adult population, no unusual or unexpected patterns have been seen at this point.
- Regarding whether any “back of the envelope” calculations have been done yet using different assumptions for uptake to understand what would be expected in terms of accrual of pregnancies in the VSD, Dr. DeSilva indicated that there is uncertainty about vaccine uptake, and they are awaiting recommendations for use, but it is anticipated that they will be well-powered to detect significant differences in preterm birth within 6 months of vaccine eligibility. Additionally, there are plans to perform some preterm and stillbirth surveillance that will be separate from this plan by monthly surveillance that would only be descriptive, but it would be limited to the vaccinated population and can be performed somewhat more quickly. These results lack a control population, so this would not be statistical comparisons.
- In terms of whether there would be monitoring of infant pertussis infection in the first 2 months of age given the lower pertussis antibodies with simultaneous vaccination with an RSVpreF vaccine and Tdap for which the clinical significance is unknown, Dr. DeSilva indicated that the VSD focuses on safety and not necessarily effectiveness of vaccines. There are other groups within the agency who have plans in place to study post-licensure effectiveness of maternal RSV vaccine.
- Regarding whether there is a systematic way to capture illnesses other than RSV or concomitant illnesses that occur during pregnancy that could increase risk of outcomes of interest, Dr. DeSilva replied that they will be capturing medically-attended events. If an illness rises to the level of seeking medical attention, there could be some information about concomitant infection with RSV or other infections that are not RSV. This would be dependent on how the provider codes what they are seeing. Consideration can be given to how some additional covariates potentially could be included, such as diagnosed respiratory illnesses—especially if testing is involved.
- Regarding a comment that it would be beneficial to capture respiratory illnesses other than or concomitant with RSV and coadministration of vaccines among pregnant people, Dr. Moro indicated that VAERS will capture other vaccines received at the time of vaccination with RSV.
- A lesson learned from COVID-19 vaccines is that when vaccines were received in public settings (e.g., pharmacy, grocery store), people often were not informed about v-safe<sup>sm</sup> and no paperwork was provided. It would be beneficial for the v-safe<sup>sm</sup> team to implement a campaign with the chain pharmacies, grocery stores, the American College of Obstetricians and Gynecologists (ACOG), and the American College of Nurse-

Midwives (ACNM) to promote v-safe<sup>sm</sup>. It is an incredibly valuable tool for monitoring side effects.

*Following Presentation by Dr. Hutton and Dr. Ortega-Sanchez*

- It is clear that the cost of the vaccine is a very important determinant in terms of cost-effectiveness, but RSV is a prevalent and costly disease. With that in mind, Pfizer was given the opportunity to speak to whether \$295 was going to be the or if there would be any decrease in cost.
- Donna Altenpohl, Pfizer, confirmed that the original price was \$295 per dose for both the maternal and older adult indications and that the Pfizer vaccine is the same product and formulation for both indications. The product has one National Drug Code (NDC) and one Current Procedural Terminology (CPT) code for reimbursement, which Pfizer took into consideration. Pfizer's pricing strategy is guided by the value that their innovation brings to patients and society, with the goal of achieving the broadest possible access for patients. Based on the results of the Pfizer cost-effectiveness analysis, they priced their vaccine to be both cost-effective and reflect the value that it will bring to helping prevent RSV for older adults and infants. As they shared with the ACIP WG, the RSV maternal vaccine will be a lower cost option and could result in a lower budget impact to the US healthcare system.
- The expense of this vaccine is very disappointing, particularly in the context of making a recommendation for all pregnant people to receive the vaccine. It would be beneficial for the ACIP to know the cost of this vaccine to countries outside of the US to understand whether it is overpriced in the US or if the price is standardized throughout the world.
- Donna Altenpohl, Pfizer, indicated that they have a tiered pricing strategy outside the US that allows the price to be contingent upon the affordability of each individual country. As they are beginning to launch the RSV maternal vaccine, the pricing will be decided at that point. Given that Pfizer has not confirmed all of its pricing, it would be inappropriate to try to comment or speculate on that at this point beyond saying that they have not finalized the price depending on whether there is separate pricing for the older adult indication and the maternal vaccination. The global pricing strategy is tiered based on the affordability of each and every country, with the goal of making sure there is affordable access for all eligible patients.
- Slides 6 and 7 in Dr. Hutton's presentation show the difference in waning between 1, 6, and 9 months. Since maternal antibodies fade away by 6 months, it was not clear which of the 2 slides was a more realistic representation of efficacy and whether there would still be antibodies between 6 and 9 months or a dramatic decrease at 6 months. There are maternal antibody data for other illnesses.
- Dr. Hutton replied that during their conversations, they thought 6 months was a conservative assumption and that there are a lot of data to suggest that antibodies would be gone after that. Because that is not known for certain, they had a couple of different scenarios.
- Referring to Slide 15 in his presentation, Dr. Ortega-Sanchez added that the 2 assumptions about duration of protection were shown side-by-side. The pink shaded area in each model denotes a higher level of uncertainty of the waning assumption beyond available Phase 3 data. There are no data that that support whatever the vaccine efficacy to say that there will be some protection. The CDC model assumed a more conservative assumption to minimize the uncertainty about whatever vaccine protection will be received after 6 months.

- To the point about other maternal antibody data, Dr. Fleming Dutra confirmed that there are data from other vaccines (e.g., Tdap, influenza, and COVID vaccines) that indicate that post-maternal effectiveness of these other vaccines usually has waned by 6 months.
- It is important to understand that while maternal antibodies can persist in the infant as late as 18 months, the protective level of antibody is the issue. With other vaccines, the antibody level is significantly reduced after 3 to 6 months. Although some antibodies can be detected, the levels probably are too low to be considered efficacious for whatever disease one is trying to prevent.
- Dr. Jessica Atwell, Pfizer, provided more context regarding the data that inform antibody persistence in infants beyond 6 months. In addition to the data from Pfizer's Phase 3 clinical trial, they also have data from their Phase 2b study that measured antibody persistence in infants out to 6 months and compared those levels between infants born to vaccinated individuals and unvaccinated individuals. They were significantly higher among infants born to vaccinated individuals compared to infants born to women who received placebo in the Phase 2b trial. They used the half-life of antibody decay from those data to then extend the potential antibody persistence beyond the 6-month time point. That modeling, which was shared with the WG, showed persistence even beyond 9 months out to 12 months. Because there is no correlative of protection for RSV, it is difficult to make direct assumptions about how those antibody levels may translate, but certainly Pfizer has data to support persistence in infants beyond 6 months, which were critical for informing the assumption about persistence of antibodies and potential benefit. If a pregnant person received RSVpreF 3 weeks before delivery, the practitioner would have to weigh the question of what the additional value would be of adding nirsevimab on top of that. If it is known the infant will definitely receive nirsevimab, it would be reasonable to consider the value of adding RSVpreF on top of that.
- Regarding an inquiry about whether, with the information about the monoclonal antibody and the vaccine on top of that having some benefit but at a very costly rate, there ever would be a scenario in which monoclonal antibody could not be given to infants and there would have to be reliance on mother's immunization, there is no known contraindication to giving both. Dr. Hutton said it would be a reasonable intuitive assumption that there would be some added incremental benefit. Dr. Long added that it was very perceptive for ACIP members to be asking these questions, and that later presentations would later "thread the needed" pertaining to what circumstances would allow a physician to give nirsevimab after a pregnant person has been properly immunized.
- Hearing that the cost per QALY for RSVpreF is about \$400,000 at a dose of \$295 per dose and recalling that during the August 3, 2023 ACIP meeting the cost per QALY for nirsevimab was \$100,000 at a cost of \$495 per dose, the difference was unclear.
- Dr. Hutton responded that there is a lot going on. The major element in the simulation modeling of nirsevimab is that efficacy is slightly better at the beginning, so slightly higher efficacy is one difference. Another difference is that nirsevimab can be given at the peak of the RSV season. An infant born in April, May, June, or July would be given nirsevimab to have peak efficacy during the season. Those are a couple of the factors that affect the differences in the cost-effectiveness of nirsevimab versus what was shown regarding RSVpreF during this session. The cost-effectiveness of RSVpreF looks much better when it is given right before the peak of the RSV season when it will confer the highest levels of efficacy.
- Regarding an observation that there did not seem to be a comparison of the cost of either the pregnant person receiving maternal vaccine or the baby receiving nirsevimab, Dr. Long indicated that there are no head-to-head comparisons because these are



standalone products that have been assessed. The recommendation for a possible vote during this meeting pertained on to the vaccine product. However, that did not preclude the possibility of occasional unusual situations in which a vaccine would be given before delivery followed by nirsevimab after delivery. Dr. Jones added that the base case scenario of giving the vaccine alone is the cost-effectiveness when not giving nirsevimab on top of it. Essentially, it was being presented as if either RSVpreF or nirsevimab was given.

- In terms of an inquiry about projected uptake rates, Dr. Hutton responded that the UM-CDC model assumed 50% uptake. A nice round number like 50% typically suggests that it is an assumption. There are limited data about uptake at this point beyond the surveys that have asked people about their intent, which suggests that 50% might be a reasonable assumption. Given the anticipated implementation challenges, Dr. Long thought 50% uptake would be optimistic for the vaccine this year.
- In an ideal world, it seemed that the precision public health approach of considering seasonality would be the best-case scenario. However, there are issues of the complexity of implementation in terms of such tight timing, the cost and burden on teams who are trying to deliver the vaccine in a precise manner, and so forth—even if that precision might lead to a better investment in health overall.
- ACIP members continued to struggle with the cost of RSVpreF vaccine. While they acknowledged and understand that the studies were expensive and Pfizer needs to recoup their costs, \$295 per dose is a hard cost to swallow. It is known that the higher the price of a vaccine, the higher the disparities.

*Following Presentations by Dr. Fleming-Dutra, Dr. Jones, Dr. Peacock*

- To set the stage for this discussion session, Dr. Long made a few comments on the underpinnings of the WG considerations and recommendations for ACIP's consideration. The WG was very concerned about the imbalance in prematurity, especially in the shadow of the GSK vaccine that was not pursued. The WG likely would not have come to consensus on a non-suffixed recommendation for 24–36 weeks. “Non-suffixed” meaning with shared clinical decision-making. The data on vaccination at 32–36 weeks gestation, coupled with the information that the prematurity that occurred in the trials was an average of 4 plus weeks after immunization was not associated with reactogenicity at the time of immunization, made the WG more sanguine with 32–36 weeks gestation. They thanked the FDA for making that restriction and not having the WG have to do that as a first potential restriction. The second restriction of the seasonal administration, although this is not terribly popular, goes with the influenza season. That also, for most of WG, was based on a safety consideration. Given the potential risk of prematurity, year-round administration may not benefit the infants born in April–September. That was the reason for that restriction. Regarding cost in terms of the base case, she did not think the WG would have come to consensus for a recommendation. It was only the seasonal use that, while it may be somewhat off-putting to some, that was the only way in which this could get down to a QALY that was acceptable in their minds or similar to other vaccine or preventions that allowed the WG the ability to present a non-suffixed recommendation to the ACIP. In addition, there are no head-to-head trials of these products or of safety. The WG thought that there would be mitigation of the potential risk of prematurity, et cetera. In terms of how ACIP considers the WG's very restricted suggestions for the use of nirsevimab after the receipt of appropriately timed vaccine, that the ACIP takes into consideration that these are both “antibody paint” and that the “antibody paint” will wear off. They do not change the epidemiology of RSV disease and the goal is not to prevent RSV infections in every individual. This can only reduce the

morbid consequences of RSV by a certain degree. Pediatricians and others already have already expressed concerned about the cut-points for nirsevimab and the vaccine. The cut-points are based on data. Because this is not a vaccine that will change the epidemiology, prevent herd, provide long-term protection, the cost must be acceptable as possible because these are extraordinarily and probably unreasonably priced products. The WG would say, “Bring on the competition to bring the costs down in the US.”

- Dr. Talbot said she thought this might be the most complicated vaccine recommendation for young adults that ACIP has had in a long time. She is worried about the complication of the time period. While influenza and COVID vaccines are given during that season, they are given to everybody regardless of where they are in their pregnancy. She also is concerned that in the adult world if someone gets the same vaccine twice, the same vaccine may be paid for twice. That is, if a mother has gotten the RSV vaccine but is confused because she received 4 vaccines, 2 vaccines, or 3 vaccines and the pediatrician is left in a position to give the child the antibody, someone is going to have to pay because that is double-dipping since ACIP would be recommending one or the other. She wondered what the benefit would be of this vaccine if every child would be given antibody.
- Dr. Long emphasized that it is always good to have 2 products. It is not known what manufacturing will be like in the future or if after the first year of use, one or the other would make them more hesitant to use one or the other.
- Dr. Poehling said that in speaking to parents who have recently given birth, some would prefer to take a vaccine rather than have their child get a shot. She also has had cases recently, including one in which the father of the child had a significant bleeding disorder, who did not want the child to have any sticks for any reasons because it would be unknown at that point whether the child was going to have a bleeding disorder. There will be multiple cases like that. There is a lot of complexity. Clearly documenting the information so that everybody knows what has and has not been received is going to be extraordinarily important. It also builds upon what has been said repeatedly during previous meetings that having an immunization registry for all is desperately needed. She recalled that Dr. Peacock’s presentation showed that 52% of persons who are pregnant have private insurance, 41% have Medicaid, and 4% are self-pay. She thought they needed to dive deeper into this. The ACA states that private insurance has to cover the vaccine, but that is not immediately. She wondered whether there are any data on how many private insurances are paying for the RSV vaccine for adults  $\geq 60$  years of age.
- Dr. Grubb (AHIP) said that while she did not have those data readily available, she would try to obtain the information for the ACIP.
- Dr. Poehling emphasized the importance of the people listening to understand that there is a delay before insurance companies actually pay for the vaccine. In addition, it was her understanding the 317 funds recently have been decreased, which could impact individuals 18–19 years of age who do not fall under Medicaid or the VFC program.
- Dr. Peacock confirmed that while the 317 funds have not decreased, there is limited availability of funds since there are more vaccines that potentially could be paid for uninsured adults through this program. For context, 317 program funds are allocated to all immunization awardees so that they can purchase some vaccine. Typically, this program is used for uninsured adults, sometimes fills in gaps related to children, and also is used for outbreak funds.

- Ms. Hance (CMS) confirmed that Medicaid will cover the vaccine for adults who have Medicaid who are covered under a CDC ACIP recommendation. That coverage is separate from the 317 program.
- Dr. Sanchez said he favored a shared clinical decision-making recommendation because there are 2 options that need to be discussed with the pregnant individual. The first would be by her obstetrician who will need to discuss vaccination at 32–36 weeks gestation, but also will need to discuss that the other option is nirsevimab. Pediatricians who will be taking care of the infants would have to tell the mother the baby cannot get nirsevimab if she chose to receive the RSVpreF vaccine. Regardless of whether those discussions are easy or hard, they must be had. With that in mind, he asked whether there would be an option to vote on shared clinical decision-making.
- Dr. Lee requested that the team display the proposed vote language. She said that in her opinion, every recommendation should be a shared decision similar to all medical care that clinicians provide. To her, the distinction about the recommendation was not about whether the process occurred. It was more about a universal recommendation versus more of a selective recommendation. Even a full recommendation would not mean that this discussion should not happen. In fact, this discussion should occur with every pregnant person to make sure that they are aware of the options. She did not think that a shared clinical decision-making recommendation would change that. She noted that while there always is an opportunity to amend proposed voting language, she would like to focus on the displayed proposed language from the WG to make sure everyone had an opportunity to comment.
- Ms. Bahta agreed that the feasibility of having 2 products that would be given at 2 different times to 2 different audiences would be challenging. Colleagues in her own health department are struggling with how to implement nirsevimab and how to reconcile that if the RSVpreF vaccine also is recommended. She also cautioned that because RSVpreF is being implemented among older adults and the vaccine is very costly, there could be competition over a limited supply and/or limited availability if maternal vaccine is recommended. Given that there were 2 wonderful options, it was extremely difficult not to be supportive of the recommendation as proposed. While she supported it and agreed that every vaccine provided to patients should be explained, she wanted to highlight her concern about the feasibility of implementation.
- Dr. Loehr strongly supported the seasonal nature of the recommendation. He noted that one insurance company that typically has been slow to implement recommendations is covering nirsevimab effective immediately, and he expressed gratitude to all of the insurance companies that are doing likewise in order to get it administered within this season. He asked whether the WG considered adding a sentence stating that this recommendation is for pregnant persons not intending for their infants to receive nirsevimab, or if there was a reason not to include such language. For instance, if he knows an infant will receive nirsevimab, he would not recommend maternal RSV vaccine.
- Dr. Poehling noted that one insurance in North Carolina has agreed to pay for nirsevimab in the outpatient setting. They are still awaiting word on the inpatient setting. She continues to remain concerned about the cost and who is going to cover it.
- Dr. Long responded that including that language might be a tacit implication that ACIP might not prefer this vaccine. At this point this year, not knowing more than what they do about efficacy and safety, they probably would not want to do this. She agreed with others that while it did not rise to the level of a policy decision, this absolutely should be a shared decision between a doctor and patient. That is best addressed in the clinical considerations. If anyone was wondering why in the world a decision ever would be

made to withhold nirsevimab or give the vaccine on top of the plan for nirsevimab, they occur at different times in the pregnancy and there may be compelling reasons. For example, if it was identified in utero that a baby had significant congenital heart disease and no safety issues had been identified, she would want to save that person for nirsevimab and not risk any potential AEs by giving the vaccine during pregnancy. While she favored the spirit of Dr. Loehr's suggestion, she did not favor including it in the language per se.

- Dr. Sanchez suggested that there could be another angle. For example, a fetus diagnosed with severe congenital heart disease or other malformation may stay in the neonatal intensive care unit (NICU) for an extended period of time. While every effort is made to prevent RSV infection in the NICU, it does occur. If nirsevimab is not going to be given until discharge, this could be a compelling reason to vaccinate the pregnant person to ensure that the baby benefits from maternal antibody at least through the time of discharge. In any case, they have recommended that nirsevimab be given irrespective of whether the mother was vaccinated. He thought that should be kept as a clinical consideration.
- Dr. Long expressed gratitude to Dr. Sanchez for raising this issue and stressed that he has been instrumental in helping the WG understand all aspects, especially of perinatology. However, she did not think monoclonal antibody or anything else should be given in the NICU to protect infants in the nursery. Infection control should do that. If infection control fails, then monoclonal antibody can be given. She also thought protection from maternal antibody could be long gone before an infant with severe congenital heart disease was discharged from the NICU.
- Dr. Sanchez clarified that he was not suggesting giving nirsevimab to infants in the NICU until the time of discharge and agreed that infection prevention and control is preferable. However, some infections do occur. His thinking was that if a term baby had maternal antibodies, at least for the first several weeks before they have their surgery or bypass, that it might also be beneficial, and the risk should be low because of infection prevention practices.
- Dr. Kotton expressed her support for the proposed recommendation language as presented. She thought it was easy to understand and that it is imperative for the public to clearly understand what the ACIP is recommending. Shared clinical decision-making has been very confusing, so she would not support that.
- Regarding the shared clinical decision-making comments, Dr. Hughes (ACOG) emphasized that obstetricians are highly experienced with and routinely perform counseling for all patients who receive vaccines, and this would be no different. She agreed with Dr. Long's assertion that for this reason, the recommendation did not rise to the level of shared decision-making policy and she would support the full recommendation on behalf of ACOG.
- Dr. Talbot pointed out that it seemed this recommendation was telling their obstetric colleagues that all pregnant persons should receive the RSVpreF vaccine between 32–36 weeks and unless the fetus has a condition, and the infant then could not get monoclonal antibody if the pregnant person was vaccinated. If a pregnant person was 32–36 weeks near the end of the RSV season, it was not clear what this would mean for the infant in terms of qualifying for monoclonal antibody.
- Dr. Jones clarified that there was voting language and the clinical considerations. The WG discussed all of this at length and there were some differing opinions among the WG members. The majority felt that the voting language proposed for the vaccine would be appropriate. The voting language for the vaccine was to convey that either product is recommended and administration of both is not needed. The decision of which option to

choose should occur at the time when deciding whether to vaccinate the pregnant person.

- Dr. Long added that if the pregnant person chooses the vaccine, then the practitioner would indicate that at birth, the baby would not need nirsevimab except in rare instances. It is true that the mother has a choice, but it is merely a choice like choosing different colored shoes with different heights of heels. Some will choose to protect their infant by vaccinating themselves, and others will choose for their baby to have nirsevimab. Given the anticipation that this season will be messy in terms of who receives what and who pays for what, whether there are risks, and what the effectiveness of these products will be, the WG wanted to offer the best possible accommodations.
- Dr. Jones confirmed that all of the details that should occur in discussions with patients would be covered in the clinical considerations and emphasized in the suite of educational materials, the *MMWR*, the Vaccine Information Statement (VIS), et cetera. This includes specification of the rare situations in which there are insufficient antibodies either because they were not produced after vaccination in a pregnant person or there is decreased transplacental transfer. For those who will have potential waning of antibodies and waning protection by the time RSV season peaks, because the recommendation would be from September–January and infants would be born to those mothers during the RSV season.
- With regard to the vote, Dr. Lee said she believes this is a good vaccine product with a favorable benefit-risk balance, particularly with the efforts to mitigate potential risks. This is an excellent option to protect infants from hospitalization. If there was not a monoclonal antibody available such as nirsevimab, she thought the cost-effectiveness conversation might have been slightly different. In terms of the struggle with cost-effectiveness, which always is an important domain, the decision is sensitive to this domain. The intervention itself and maternal vaccine development in general are incredibly important investments with regard to future directions with the US vaccination programs as a country. She wanted to recognize that cost-effectiveness is about the value of the vaccine and the value of the investment. The proposed vote the WG asked the ACIP to consider in terms of seasonal dosing of RSV vaccine seemed extremely helpful to ensure that they are making the investment as worthwhile as possible. The cost-effectiveness ratio is still high-ish, recognizing that they do not have an explicit threshold by any means. This will be one of the more expensive interventions the ACIP has recommended, so she wanted to call out that seasonal dosing is a way to at least get into a more reasonable range. Recalling an earlier conversation, she said she thought the ACIP's role is only to comment on the value of this vaccine in the US. As they learned during COVID, having products available such as these RSV vaccines or passive immunization become more available to low- and middle-income countries that might not otherwise have access is something they need to consider. She encouraged their manufacturing sector colleagues to consider how such innovative products can be made available in countries at an affordable price, recognizing that each country is different, but also recognizing that there is a greater responsibility from a public health perspective.
- Dr. Sanchez said he thought one of the problems was that it was impossible to consider this vaccine in isolation, because the fact is, there is another product. Unfortunately, there is not a head-to-head trial comparison of the 2 products with respect to either efficacy or effectiveness. Discussions must be had with the pregnant person because there are options, and each medical decision should be shared decision-making. There should be a lot of education about both products.

- Dr. Loehr said he wanted to go on record that he believes an infant receiving nirsevimab is better based on the evidence that it has better efficacy. It also is more cost-effective. Therefore, he did not want it to be an equal representation. He recognized that they were not going to make a preferential statement and that a lot more data would accumulate over the next couple of years to determine in the long-run which is better. He doubted they ever would have head-to-head information. If he was presenting this to a pregnant person, he would recommend giving nirsevimab to their child if that is what they wanted. If not, then the vaccine would be another option. This is just a small nuance.
- Dr. Sanchez emphasized that to him, the signal for prematurity was a major concern for him and the WG. The FDA did help with this issue by approving vaccine administration at 32–36 weeks gestation. Nevertheless, mothers should be made aware that this needs to be monitored and there will be post-licensure and post-recommendation surveillance.
- Dr. Bell emphasized that one complication is going to be that the pregnant person is likely going to be seeing a different doctor during pregnancy than the doctor who will be taking care of their child. Tools must be made available quickly to physicians, which is something the partners and professional organizations can help to facilitate. It is difficult to make a choice without all of the tools.
- Dr. Talbot emphasized that her feeling was that this would be incredibly complicated. There is a great option that can be given to children, which will protect more children and that is more cost-effective. The vaccine seems like an incredibly complicated, way out of the atmosphere expensive option that would not result in much benefit and would increase confusion in terms of whether the pregnant person received vaccine or received it and then delivered too early. She did not believe this would improve care and would make providing care more difficult. If they simply say the child should receive the monoclonal, the recommendation would be a very simple and cost-effective mechanism. With an adult immunization registry in every state, using this mechanism may put children at risk and/or leave the parent stuck with a \$500 bill because only one method would be paid for.
- Dr. Poehling emphasized that as a newborn provider, she evaluates the charts of the moms and babies. It may not be easy, but it is definitely doable.
- Dr. Hughes (ACOG) emphasized that it is absolutely routine for obstetricians to collaborate with their pediatric colleagues to review maternal charts. It is done every day regarding testing like hepatitis B testing. Those results are always communicated. While ACOG recognizes that there are some complexities to ensuring that the charts are complete related to receipt of vaccine, it is quite doable. Also acknowledging the fact that this is fairly complex, ACOG and its colleagues at the Society for Maternal Fetal Medicine, plan to partner with other entities like AAP, AAFP, and ACNM to ensure that there is a solid implementation strategy to assure that these challenges are met.
- Dr. Poehling made a motion to approve the language as presented, which Dr. Loehr seconded.

#### *Following Dr. Santoli's Presentation*

- For Table 1, it was suggested that the additional language be revised to read, “whose mother did not receive the vaccine, whose mother’s vaccine status is unknown, or who was born within 14 days of maternal vaccine.”
- Dr. Santoli indicated that the language could be updated for clarity.

## **PUBLIC COMMENTS**

### **Overview**

The floor was opened for public comment on September 22, 2023 at 2:30 PM ET. Given that many more individuals registered to make oral public comments than could be accommodated during this meeting, selection was made randomly via a lottery. Dr. Lee provided a gentle reminder that the ACIP appreciates diverse viewpoints that are respectful in nature and issue-focused rather than comments directed at individuals. The comments made during the meeting are included in this document. Members of the public also were invited to submit written public comments to ACIP through the Federal eRulemaking Portal under Docket Number ID CDC-2023-0076. Visit <http://www.regulations.gov> for access to the docket or to submit comments or read background documents and comments received.

### **Public Comments**

#### **Mr. Paul Hennessy Individual**

Hi. I was supposed to comment at the meeting on the 12<sup>th</sup>, but I think only 1 person spoke during public comments. So, I definitely urge you to look into that issue. I know there are a lot of commenters who didn't get to speak. But, yeah, I'm here to talk about the future of vaccine rollouts, not just RSV, but COVID as well. You know, I thank the ACIP for approving those 3 vaccine options last week. But a once-a-year shot does not go far enough, considering protection wanes after about 5 months and there's multiple waves of COVID per year. COVID is not the flu, so a shot schedule like the flu just isn't working. A once-a-year vaccine just isn't enough to protect us from a virus that fuses brain cells, causes blood clots, is linked to diabetes, dementia, and more. Furthermore, COVID and RSV are airborne illnesses, so the vaccine-only approach doesn't properly reduce transmission as much as it can. You know, clean-air tech and masking must be encouraged along with vaccines and even required in places like medical settings. Pediatric approval for the Novavax COVID vaccine is also needed as soon as possible. You know, I definitely appreciate that the RNA has been approved, but children, like adults, deserve the choice. Novavax was shown to wane less quickly than mRNA and offer broad immunity against variants. Successive doses actually enhance protection as well as offer some upper respiratory protection. Children deserve this excellent choice as well. Finally, just going forward, I'd definitely like to urge ACIP to approve vaccines before surges. That includes both COVID and RSV. Moderna's and Pfizer's COVID vaccines were ready, and I believe submitted a number of months ago, but it took until September to get approval. It's so important to approve both COVID and RSV vaccines before the school year so children are protected going to school. Thank you.

#### **Jane Hull, PT, MPH TRAIPAG**

I'm Jane Kaplan Hull I'm speaking on behalf of TRAIPAG, which is a patient advocacy group whose members are transplant recipients and/or are immunocompromised. We strongly urge the committee to recommend the RSV maternal vaccine and to add it to the Vaccines for Children Program so as to immunize the child through the mother. Our TRAIPAG Advocacy Group commends the committee for placing the mAb, nirsevimab, not sure I'm saying that right, on the Vaccines for Children Program and taking the groundbreaking step of recommending

passive immunization, which ensures that it will be covered. We urge the committee to do likewise if and when a monoclonal antibody or antiviral prophylaxis against COVID is authorized by the FDA. This would be especially crucial to the population of immunocompromised people who do not respond to vaccines and will greatly benefit from effective vaccine or prophylactic treatments that can both save lives and improve quality of lives for those affected. We would also hope that the committee in future deliberations recommend the RSV vaccines, not just for the 60 and over, but give access to the RSV vaccines for those who are immunocompromised or high risk and those living or working with vulnerable populations. Thank you for giving me the opportunity to speak.

**Dr. Roselie Bright, ScD**  
**COBID Safe Maryland**

Hi. Good afternoon. I'm Roselie Bright. I have a Doctor of Science in Epidemiology and had a 30-year career as a Federal Medical Product Epidemiologist. For meaningful consideration of public input, the substantive materials for CDC Advisory Committee meetings, the slides, white papers, et cetera, should be available to the public for at least a week before the meetings to allow adequate time for thoughtful, in-depth public review and comment. People who have already signed up for comment should be notified the same day the materials become available. The oral public comment session needs to be expanded to at least an hour and occur before motions and votes. RSV vaccines have been approved by the FDA for older adults and infants a month ago. The one under consideration today was also approved by FDA for pregnant people and infants. I support expanding the use of RSV vaccines and have several points regarding the specific RSV vaccine under consideration and RSV vaccines in general: 1) for non-pregnant adults, the RSV vaccine has been approved for people 60 years old and over. I urge the sponsors to quickly study the usefulness of the [inaudible] all people at high-risk from RSV and all people in professions and situations that often interact with people who are at high risk of RSV, that is, health care workers, patients and visitors, and childcare and school staff and children, etc.; 2) RSV infections have risen significantly year over year during the COVID-19 pandemic. If the rise is due to immune damage from COVID-19, the potential benefit of offering the [inaudible]; 3) Three, RSV circulation is seasonal, typically starting during the fall and peaking in the winter. The peak RSV hospitalization season has been moving to earlier in the calendar year in the specific surveillance areas of the US. Please offer the RSV vaccine in the summer to prevent the surges that have recently been starting in September; 4) because getting the RSV vaccine is recommended for a narrow window of pregnancy, 32 to 36 weeks of gestation, availability for pregnant people needs to be speedy to help as many pregnant people as possible this fall; 5) RSV vaccine efficacy wanes. That's fine for pregnancy and infancy. However, please consider recommending that pregnant people should be revaccinated during each subsequent pregnancy. In addition, older adults should be offered semiannual vaccinations; and 6) RSV is part of the trio of airborne viruses that CDC is already campaigning about. While the COVID-19, influenza, and RSV vaccines reduce the risk and severity of infection, they don't entirely eliminate infections and some people should not take them. I ask CDC and the vaccine sponsors to include other precautions against airborne viruses in your public messages, including N95 or higher quality masks, otherwise known as respirators, and air cleaners with high-efficiency particulate air (HEPA) filters and fresh air ventilation [inaudible] especially if those that vulnerable patients must attend as staff or clients, including health care facilities, schools, and prisons. Thank you for this opportunity to comment.



## VOTES

**Dr. Grace Lee (ACIP Chair)** requested that the language for the votes be displayed for the recommendation and VFC votes.

### **Vote #1 RSV Maternal RSV Vaccine Recommendation**

Maternal RSV vaccine is recommended for pregnant people during 32 through 36 weeks gestation, using seasonal administration, to prevent RSV lower respiratory tract infection in infants.

#### **Motion/Vote #1 Maternal RSV Vaccine**

Dr. Poehling made a motion to approve the proposed Vote #1 recommendation stating, “Maternal RSV vaccine is recommended for pregnant people during 32 through 36 weeks gestation, using seasonal administration, to prevent RSV lower respiratory tract infection in infants.” Dr. Loehr seconded the motion. No COIs were declared. The motion carried with 11 affirmative votes, 1 negative votes, and 0 abstentions. The disposition of the vote was as follows:

**11 Favored:** Bahta, Chen, Daley, Lee, Loehr, Long, McNally, Poehling, Sanchez

**1 Opposed:** Talbot

**0 Abstained:** N/A

### **Vote #2 VFC Resolution Maternal RSV Vaccine**

Approve the Vaccines for Children (VFC) resolution for RSV maternal vaccine.

#### **Motion/Vote #2: VFC Resolution Maternal RSV Vaccine**

Dr. Loehr made a motion to approve the proposed Vote #2 recommendation for the VFC Resolution stating, “Approve the Vaccines for Children (VFC) Resolution for RSV maternal vaccine.” Dr. Poehling seconded the motion. No COIs were declared. The motion carried with 11 affirmative votes, 1 negative votes, and 0 abstentions. The disposition of the vote was as follows:

**11 Favored:** Bahta, Chen, Daley, Kotton, Lee, Loehr, Long, McNally, Poehling, Sanchez

**1 Opposed:** Talbot

**0 Abstained:** N/A

## **Discussion Points: Voting Members**

Dr. Poehling emphasized what an exciting day this was because throughout her career, RSV has been a difficult disease, given that there have been no options beyond supportive care treatment. There were over 1.5 million outpatient visits, over half a billion ED visits, and 58,000 to 80,000 RSV hospitalizations last year, which was a dramatic example. The vast majority, almost 80%, of children less than 2 years of age have no underlying conditions. There is nothing simple about this RSV vaccine or nirsevimab, but they both offer hopes. They have done this before with COVID vaccine. She thinks that if everybody is willing to chip in and do their part, this is feasible and will improve the well-being of many families throughout the nation.

Dr. Bell said she wanted to take advantage of her gray-haired status and reflect for a moment on the issue of complicated recommendations for which implementation is unclear and there are a lot of challenges. To Dr. Lee's point earlier that in looking back over the decades, these types of recommendations have provided opportunities for innovation, availability of options, and improvements over the longer term even if the beginning is extremely bumpy. This is another example that perhaps will lead to improvements in physician education, patient decision-making, communication between the obstetrical and pediatric worlds, and addressing disparities. Even though ACIP members may be feeling at the moment that this is very complicated and will be difficult to implement, in the longer term it will result in new options that will improve children's health.

Dr. Sanchez agreed completely. He thought the discussions throughout the day had been extremely helpful because he certainly has struggled with his decision throughout the time that he has been on the RSV WG. He has fluctuated back and forth, but thought the day's discussions steered him clearly through the amazing work that has been done. There are challenges and complexities, but there are options for mothers and HCPs. Physicians also have personal preferences that are part of the physician-patient discussion. He thought the options were great. Pediatricians, infectious disease specialists, and neonatologists have to prevent serious RSV disease in babies. He thought it was fantastic that they had achieved this vote, as well as the nirsevimab vote. He could not have imagined better options for infants and children, which is what they have been striving for—especially for high-risk babies. He urged more discussions with obstetricians, mothers' healthcare providers, and pediatric family practices. Just like they need to know the mother's syphilis, HIV, and hepatitis B status, they also will need to know whether the mother received the RSV vaccine. Hopefully, this will ultimately improve care and communication with obstetric providers.

Dr. Brooks said he was reflecting back on the days when they thought PCV discussions were complex. Yes, RSV has been very complex. However, they likely are going to have more complex decisions to make moving forward. Dovetailing on what Dr. Sanchez said, one of the things that struck him was that a large number of obstetricians feel uncomfortable with discussing vaccine decisions. Looking at the schedule, there are 4 vaccines that theoretically could be available or needed for a pregnant person (RSV, COVID, influenza, and Tdap) between October through March. That is half of the year—a significant amount of time where there are going to be some really interesting discussions. They need to lean on the American College of Obstetricians and Gynecologists (ACOG) to work with their members to feel more comfortable with these discussions. To him, one of the benefits is a fundamental concept of vaccination, which is that generally speaking, the ideal is for a person to get vaccinated at the earliest opportunity or the concept of immediate protection. The earliest opportunity would be before the mother delivers. People's situations may change. Someone might leave the country,

their insurance status may change, their perspective on protection of a child from RSV may change, et cetera. It is very important to get them vaccinated as soon as possible. Notwithstanding Dr. Loehr's statement that nirsevimab seems to be a more efficacious and cost-effective, it is excellent to have this option of the vaccine for the pregnant person prior to the birth of the child.

Ms. McNally said she struggled with this recommendation for the reason that she does not know what the counseling looks like for the mother who asks her obstetrician if she should get this vaccine and the mother who asks the child's pediatrician what she should do. Because of that, she agreed with Dr. Lee that the stakeholder medical associations could get together and prepare a statement about this issue. She thought that would be immensely helpful for the consumer. She also observed that it seemed like the ACIP had discussed shared clinical decision-making recommendations a lot more lately. That gives her a certain level of discomfort as a consumer because while she believes there is a place for shared clinical decision-making, it makes her nervous that there could be some baseline assumptions about the knowledge that consumers have for risk of disease. She wondered whether there is a way to talk about best practices to revisit the idea of shared clinical decision-making in order to help ACIP arrive at better decisions of the future regarding vaccine recommendations.

Dr. Talbot reiterated how important it is that medical societies work on this process. The pneumococcal vaccines have been complicated for years and had to be written out of the infectious disease boards because they were too complicated. She worries that this has created another very complicated recommendation. What happened with pneumococcus was low immunization rates. She implored every society to talk. There needs to be massive education and it has to be better than what was done for pneumococcus.

Dr. Kotton said that while she appreciated how complicated the decision-making was through all of this, she was excited to see that they were at a time in which there is a shared clinical decision-making recommendation for adults  $\geq 60$  years of age, an RSV vaccine for pregnant people, and monoclonal antibodies for infants. This is a horrible disease for many, especially immunocompromised persons. She is cautiously optimistic that there will be diminished rates of disease in multiple communities that hopefully will result in decreased transmissions to vulnerable populations. This is an exciting time in the medical world, and she is excited to see what things will look like with multiple protective vaccines for many different populations.

Dr. Long said that she was outrageously grateful for the ACIP to think this through again with the WG. She could not add up all of the hours that they have struggled with this. She appreciated everyone's comments and thought this was the right decision to make. They will see, through what may be a very messy year, whether one rises to a preference over the other and hopefully that both will become less expensive.

### **Discussion Points: Liaisons**

Patsy Stinchfield (NAPNAP) commented that during the 20 years she has been participating in the ACIP, this has got to be one of the more complex decisions that has been before this committee. As a member of the RSV WG, she acknowledged the phenomenal work they did. There were intense deliberations during the WG meetings, and the presentations and conversation during the meeting were very good in terms of highlighting the difference of opinion and complexities. Having listened to so many of these conversations over the years, she agreed that this is complex and challenging. However, it was one of those times when they needed to focus on the policy questions before them. Is it safe? Is it effective? Is it feasible?

They did not get to ask whether it is easy, but they know it is not going to be easy? What will happen is that practice will follow ACIP policy, and the committee will re-review, discuss, and measure in the future. The practice barriers are what they need to be working on at this time. The clinician is the linchpin and is the one who is going to be discussing the options available. They will need to be prepared for their own educational needs, attending the Clinician Outreach and Communication Activity (COCA) calls, listening to National Foundation for Infectious Diseases (NFID) webinars, and making sure they are prepared to share this with families. She very much agreed with Dr. Lee's observation about the quality improvements and that they cannot wait until they have all of the technical, financial, and other reimbursements in place when they have a very good product before them. They must make sure that they are communicating with their peers and parents alike, taking the barriers into consideration but not letting the barriers stop them from advancing a very good product.

## ADULT AND PEDIATRIC IMMUNIZATION SCHEDULE ADDENDUM

### Presentation

**Sarah Schillie, MD, MPH, MBA, CAPT USPHS** discussed the addition of an addendum to the immunization schedules. As a reminder, the immunization schedules are published on an annual basis, typically every February.<sup>57</sup> There are two separate schedules, the Child and Adolescent Immunization Schedule that covers birth through 18 years of age and the Adult Immunization Schedule that covers  $\geq 19$  years of age. There are multiple sections in each of these schedules that summarize the approved ACIP policy, including the Cover Page, Tables that contain graphic rows of recommendations, Notes, and an Appendix. The schedules are published in 3 formats: PDF, webpage, and app. The 9 professional organizations listed here partner with CDC to approve the schedules, and some of these professional organizations publish the schedules:

- American College of Physicians ([www.acponline.org](http://www.acponline.org))
- American Academy of Family Physicians ([www.aafp.org](http://www.aafp.org))
- American College of Obstetricians and Gynecologists ([www.acog.org](http://www.acog.org))
- American College of Nurse-Midwives ([www.midwife.org](http://www.midwife.org))
- American Academy of Physician Associates ([www.aapa.org](http://www.aapa.org))
- American Pharmacists Association ([www.pharmacist.com](http://www.pharmacist.com))
- Society for Healthcare Epidemiology of America ([www.shea-online.org](http://www.shea-online.org))
- American Academy of Pediatrics ([www.aap.org](http://www.aap.org))
- National Association of Pediatric Nurse Practitioners ([www.napnap.org](http://www.napnap.org))

Traditionally, the schedules are published in February each year, but the publication process starts in October with the ACIP vote. In November and December, professional organizations approve the schedule. In December and January, the drafts are developed and cleared for the *MMWR* reports and *Annals of Internal Medicine* report for the adult schedule. In February, the schedules are published along with the accompanying *MMWR Notice to Readers* and *Annals of Internal Medicine* report. The timeliness of schedule publication has several important implications. First, some insurers link vaccine reimbursement to the vaccine listed on the immunization schedules. Second, the ability of certain HCP to administer immunizations also is related to the schedule. For example, some states link pharmacists' immunization authority to the schedule. Third, HCP knowledge and practices are related to the immunization

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<sup>57</sup> [www.cdc.gov/vaccines/schedules/index.html](http://www.cdc.gov/vaccines/schedules/index.html)

recommendations. For example, if a HCP is referring to a schedule that is several months old, they may not be aware of the most recent ACIP recommendations.

The ACA addresses immunization coverage and is interpreted by CMS. According to the ACA, insurers must provide coverage for and must not impose cost-sharing restrictions for immunizations that have a routine recommendation and that are listed on the immunization schedules of the CDC. Of note, the ACA does not specify the layout of the immunization schedule. Legally, CDC has discretion regarding the design of the immunization schedules. The entire document constitutes the schedule, not just the graphic bars or the tables.

CDC takes a 3-pronged approach to address schedule timeliness. The immediate strategy consists of the addition of addenda to help bring the schedule up-to-date. The short-term strategy involves publication of the entirety of the schedule shortly after the October ACIP vote. The longer-term strategy is to consider sustainable approaches to ensure the schedules remain dynamic and responsive, and to engage partners in the planning process. Regarding the addition of the addenda to the 2023 immunization schedules, the addenda will contain ACIP recommendations that occurred after the 2023 schedule was published. The plan was to release the 2023 immunization schedules with the addenda the week following this meeting. With this addition, all ACIP recommendations will formally be part of the CDC Immunization Schedules.

To describe the changes related to adding the addenda to the schedules, a red bar will be added to the top of the cover page to refer users to the addendum. A fifth step, also referring users to the addendum, will be added to the steps of to how to use the document. Any new vaccine recommendations will be added to the table on the cover sheet. Here is the addendum for the Adult Immunization Schedule, which consists of 1 page and includes vaccines for which recent recommendations have been made, a synopsis of those recommendations, and the effective date of the recommendation:

<b>Addendum</b> Recommended Adult Immunization Schedule, United States, 2023		
In addition to the recommendations presented in the previous sections of this Immunization Schedule, ACIP has approved the following recommendations by majority vote since October 20, 2022. The following recommendations have been adopted by the CDC Director and are now official. Links are provided if these recommendations have been published in <i>Morbidity and Mortality Weekly Report (MMWR)</i> .		
Vaccines	Recommendations	Effective Date of Recommendation*
COVID-19 (Moderna, Pfizer-BioNTech)	<ul style="list-style-type: none"> <li>All persons ≥6 months of age should receive 2023–2024 (monovalent, XBB containing) COVID-19 vaccines as authorized under EUA or approved by BLA.</li> <li>For detailed information, see: <a href="http://www.cdc.gov/covidschedule">www.cdc.gov/covidschedule</a></li> </ul>	September 12, 2023
Respiratory syncytial virus (RSV)	<ul style="list-style-type: none"> <li>Adults 60 years of age and older may receive a single dose of Respiratory Syncytial Virus (RSV) vaccine, using shared clinical decision-making.</li> <li>For detailed information, see: <a href="http://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm?s_cid=mm7229a4_w">www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm?s_cid=mm7229a4_w</a></li> </ul>	June 27, 2023
Poliovirus (IPV)	<ul style="list-style-type: none"> <li>Adults who are known or suspected to be unvaccinated or incompletely vaccinated against polio should complete a primary vaccination series with inactivated polio vaccine (IPV).</li> <li>Adults who have received a primary series of trivalent oral polio vaccine (tOPV) or IPV in any combination and who are at increased risk of poliovirus exposure may receive another dose of IPV. Available data do not indicate the need for more than a single lifetime booster dose with IPV for adults.</li> </ul>	June 27, 2023
Influenza (IIV4, ccIV4, RIV4, LAIV4)	<ul style="list-style-type: none"> <li>All persons ages ≥6 months with egg allergy should receive influenza vaccine. Any influenza vaccine (egg based or non-egg based) that is otherwise appropriate for the recipient's age and health status can be used.</li> <li>Affirm the updated <i>MMWR</i> Recommendations and Reports, "Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices—United States, 2023–24 Influenza Season" <a href="http://www.cdc.gov/mmwr/volumes/72/rr/rr7202a1.htm">www.cdc.gov/mmwr/volumes/72/rr/rr7202a1.htm</a></li> </ul>	June 27, 2023
<small>*The effective date is the date when the CDC director adopted the recommendation and when the ACIP recommendation became official</small>		

The addendum for the Pediatric Schedule is similar. It also is also 1 page, and is depicted here:

<b>Addendum</b> Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2023		
<small>In addition to the recommendations presented in the previous sections of this Immunization Schedule, ACIP has approved the following recommendations by majority vote since October 20, 2022. The following recommendations have been adopted by the CDC Director and are now official. Links are provided if these recommendations have been published in <i>Morbidity and Mortality Weekly Report (MMWR)</i>.</small>		
Vaccines and Other Immunizing Agents	Recommendation	Effective Date of Recommendation*
COVID-19 (Moderna, Pfizer-BioNTech)	<ul style="list-style-type: none"> <li>All persons ≥6 months of age should receive 2023–2024 (monovalent, XBB containing) COVID-19 vaccines as authorized under EUA or approved by BLA.</li> <li>For detailed information, see: <a href="http://www.cdc.gov/covidschedule">www.cdc.gov/covidschedule</a></li> </ul>	September 12, 2023
Respiratory syncytial virus [RSV-mAb (Nirsevimab)]	<ul style="list-style-type: none"> <li>All infants younger than 8 months and born shortly before or during the RSV season should receive 1 dose of nirsevimab within 1 week of birth either in hospital or outpatient setting</li> <li>Infants younger than age 8 months not born during RSV season and now entering their first RSV season should receive 1 dose of nirsevimab shortly before the start of RSV season</li> <li>Infants aged 8–19 months with chronic lung disease of prematurity requiring medical support (e.g., chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) any time during the 6-month period before start of the second RSV season; severe immunocompromise; cystic fibrosis with weight for length &lt;10th percentile; or with manifestation of severe lung disease (e.g., previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest imaging that persist when stable) should receive 1 dose of nirsevimab shortly before start of second RSV season</li> <li>Infants 8–19 months who are American Indian or Alaska Native should receive 1 dose of nirsevimab before start of second RSV season</li> <li>Infants who are age-eligible and undergoing cardiac surgery with cardiopulmonary bypass should receive 1 additional dose of nirsevimab after surgery</li> <li>For detailed information, see: <a href="http://www.cdc.gov/mmwr/volumes/72/ww/mm7234a4.html">www.cdc.gov/mmwr/volumes/72/ww/mm7234a4.html</a></li> </ul>	August 3, 2023
Poliovirus (IPV)	<ul style="list-style-type: none"> <li>Adolescents age 18 years who are known or suspected to be unvaccinated or incompletely vaccinated against polio should complete a primary vaccination series with inactivated polio vaccine (IPV).</li> <li>Adolescents age 18 years who have received a primary series of trivalent oral polio vaccine (tOPV) or IPV in any combination and who are at increased risk of poliovirus exposure may receive another dose of IPV. Available data do not indicate the need for more than a single lifetime booster dose with IPV for adults.</li> </ul>	June 27, 2023
Influenza (RV4, ccIV4, RV4, LAIV4)	<ul style="list-style-type: none"> <li>All persons ages ≥6 months with egg allergy should receive influenza vaccine. Any influenza vaccine (egg based or non-egg based) that is otherwise appropriate for the recipient's age and health status can be used.</li> <li>Affirm the updated <i>MMWR</i> Recommendations and Reports, "Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices—United States, 2023–24 Influenza Season" <a href="http://www.cdc.gov/mmwr/volumes/72/rr/rr7202a1.htm">www.cdc.gov/mmwr/volumes/72/rr/rr7202a1.htm</a></li> </ul>	June 27, 2023
Pneumococcal (PCV15, PCV20)	<ul style="list-style-type: none"> <li>Use of either pneumococcal conjugate vaccines (PCV) PCV15 or PCV20 is recommended for all children aged 2–23 months according to currently recommended PCV dosing and schedules.</li> <li>For children with an incomplete PCV vaccination status, use of either PCV15 or PCV20 according to currently recommended PCV dosing and schedules is recommended for:               <ul style="list-style-type: none"> <li>Healthy children aged 24–59 months</li> <li>Children with specified health conditions(2) aged 24 through 71 months</li> </ul> </li> <li>For children aged 2–18 years with any risk condition who have received all recommended doses of PCV before age 6 years               <ul style="list-style-type: none"> <li>Using ≥1 dose(s) of PCV20: No additional doses of any pneumococcal vaccine are indicated. This recommendation may be updated as additional data become available.</li> <li>Using PCV13 or PCV15 (no PCV20): A dose of PCV20 or PPSV23 using previously recommended dosing and schedules is recommended.</li> </ul> </li> <li>For children aged 6–18 years with any risk condition who have not received any dose of PCV13, PCV15, or PCV20, a single dose of PCV15 or PCV20 is recommended. When PCV15 is used, it should be followed by a dose of PPSV23 at least 8 weeks later if not previously given.</li> </ul>	June 27, 2023

\*The effective date is the date when the CDC director adopted the recommendation and when the ACIP recommendation became official

In summary, the release of the 2023 Immunization Schedules with the Addenda is anticipated during the week following this meeting. This will formally incorporate all ACIP recommendations into the 2023 CDC Immunization Schedules. There are also plans for short- and long-term sustainable strategies to address schedule timeliness and will ensure partner engagement with this process.

## Liaison Statements

**Jason Goldman, MD, FACP (ACP)** provided a statement on behalf of the ACP. The American College of Physicians, with over 160,000 members and the largest single specialty medicine organization representing all internal medicine specialists, greatly appreciates the work of the CDC and the Advisory Committee on Immunization Practices, especially the willingness to work with the vaccine schedule. The ACP understands the challenges of analyzing copious amounts of data to put forth the best evidence-based recommendations. However, there is a need for timely updates to the vaccine schedule so that practicing physicians can have guidance in implementing those guidelines. Obviously, one of those challenges is the delay created between approval by the committee, sign-off by the CDC director, and final publication of the schedule. The ACA allows insurance companies to have up to a year to cover these life-saving vaccines, but many will start that year at final publication and not at approval by the committee. It is imperative that the schedule be updated, approved, and published as quickly as possible to avoid unnecessary delays in implementation. The ACP appreciates the willingness of the CDC to expedite this process. The lack of insurance coverage creates unnecessary barriers to access to care and further exacerbates healthcare disparities as uninsured and underinsured patients will not have access to these vaccines. The ACP also strongly agrees with the need for

a Vaccine for Adults program to address those gaps in coverage so patients can get the vaccines they need. Finally, the ACP would ask the vaccine manufacturers to provide vaccines fairly and equitably without preferential distribution to large systems and non-physician entities so that the physicians can vaccinate patients in their offices in a timely manner. Specifically, the delays in distribution of influenza vaccines this season to many physician offices has created hardships for patients and decreased access to care. Once again, the ACP is supportive of the good work of the committee and looks forward to continued collaboration to advance health equity and access to life-saving vaccines.

**Sean O'Leary, MD, MPH (AAP)** provided a statement on behalf of the AAP. The immunization delivery system is complex, with many interrelated parts that need to work together to ensure that the nation's children can receive timely and equitable access to vaccines. This is particularly true when new vaccines are recommended by the Advisory Committee on Immunization Practices. Once the ACIP makes a recommendation for a new vaccine and the CDC director signs off on the recommendation, this prompts a series of steps that are critical to ensuring smooth and equitable rollout. The publication of official CDC recommendations is an essential step in this process. As an example, consider the PCV20 vaccine, the pneumococcal conjugate vaccine, which was recommended by the ACIP during its June meeting. AAP members have recently reported that some VFC programs are providing only PCV20 and that some vaccine-buying groups are directing people to use this vaccine over other pneumococcal vaccines. However, this is problematic because a lack of formal recommendations in an updated immunization schedule or publication in *MMWR* is leading to payment denials for PCV20, as well as delays in TRICARE coverage for children in military families. Timely updates to the immunization schedule would provide pediatricians with an authoritative source for the latest immunization recommendations, which is invaluable at the point-of-care to maximize every opportunity to vaccinate. The American Academy of Pediatrics strongly supports the efforts of the CDC to update the immunization schedule on an as-needed and timely basis.

**Jean-Venable "Kelly" Goode, PharmD, BCPS, FAPhA, FCCP (APhA)** provided a statement on behalf of the nation's 330,000 pharmacists for the American Pharmacist Association. APhA is pleased to provide supportive comments on the importance of timely updates to the vaccine schedules. APhA, representing the profession of pharmacy, is honored to be one of the organizations granted the opportunity to review and indicate support of the adult vaccine schedule. Over the past 20-plus years, pharmacists and their teams have protected the public from vaccine-preventable diseases by recommending and administering vaccines, most notably of late, administering well over half the COVID-19 vaccines during the pandemic. APhA recommends updating the schedules as recommendations and clinical guidance are approved by ACIP. It is important for policy and patient access to vaccines. An example is the RSV vaccine. ACIP voted on the recommendations in June for the vaccine to be administered as soon as vaccine becomes available and throughout the RSV season. However, currently, it will not be on the vaccine schedule until February. States regulate vaccine administration by pharmacists and pharmacy personnel. Several states require that vaccines must be on the CDC/ACIP recommended schedule for pharmacists or pharmacy personnel administration. The gap means that many thousands of patients will not have access to the RSV vaccine until February if the schedule updates are not accelerated. Given the number of patients who receive their vaccines from a pharmacy team member, especially those in rural and medically underserved areas, it is imperative that the vaccine schedules be updated as new vaccines become available and recommended by CDC ACIP. Therefore, APhA strongly supports timely updates to the vaccine schedule for newly recommended vaccines to facilitate access to vaccination by pharmacists and pharmacy team members, and that payers be strongly informed

that they do not need to wait for publishing of the *MMWR* for the updated schedule to begin coverage for the ACIP recommended vaccines.

**Pamela Rockwell, DO (AAFP)** provided a statement on behalf of the AAFP. Family physicians provide care for people of all ages from birth through end of life, including care for those who are pregnant. AAFP feels strongly that timely updates to the vaccination schedules are extremely important to allow family physicians and other health care professionals determine who is due for vaccination and quickly. Many of the newly updated recommendations are scattered throughout CDC web pages and not easily accessed. As we enter the fall respiratory season, many family physicians have expressed disappointment that updates on several vaccines, including influenza, pneumococcal, RSV, and COVID-19, are not easily accessible on the Harmonized Child, Adolescent, and Adult Vaccination 2023 schedule. It was encouraging to hear from Dr. Schillie about the addendum to be added to the immunization schedules next week. To summarize, AAFP encourages continuous and additional timely updates to the schedules as new vaccine recommendations are added or amended, as these are essential to ensure continued prevention of disease and improve public health through vaccination.

**Robert H. Hopkins, Jr., MD (Medical Director, NFID)** provided an update on behalf of the National Foundation for Infectious Diseases. NFID thanked the ACIP for its ongoing work to ensure the availability of safe and effective vaccines and monoclonal antibodies to help protect the most vulnerable individuals from RSV, and for the addition of the ACIP schedule and plans to continue to update these schedules in the future to avoid some of the challenges with reimbursement and coverage. RSV impacts individuals of all ages, including premature infants and infants younger than 6 months. Each year in the US, RSV is estimated to cause more than 2 million outpatient visits; 58,000 to 80,000 hospitalizations; and 100 to 300 deaths among children under 5 years of age. While immunizing pregnant women will be a tremendous step toward RSV prevention, healthcare professionals will continue to need clear guidance and education to inform their decisions with patients and parents about the use of vaccines in pregnant women and/or nirsevimab in infants. NFID is committed to collaborating with CDC and partners in educating healthcare professionals and the public to help facilitate the effective use of these active and passive tools in RSV prevention. The low uptake among pregnant women of vaccines to prevent influenza and COVID-19 underscores the importance of building confidence in all recommended vaccines. As partners in protecting public health, we must focus on using all available tools to prevent RSV and protect those most at risk. For 50 years, NFID has been dedicated to educating and engaging the public, communities, and healthcare professionals about infectious diseases across the lifespan. NFID commends the tireless efforts of ACIP in guiding US immunization policy and stands ready to support the work of ACIP and CDC, which is instrumental in saving lives and protecting public health.

**Patsy Stinchfield RN, MS, CPNP (NAPNAP)** provided a statement on behalf of NAPNAP, the National Association of Pediatric Nurse Practitioners to add her voice to so many of the other association colleagues to say how important the updated schedule is. It is our tool. It is an outline. It is not all of the details, but it is critical for us to practice. Also, the great work that we have had with our RSV vaccines and products will make that schedule even more important. On behalf of pediatrics, we all know that RSV, in that in the infant age group as well as the older age group, can be a devastating disease. Today is a very, very great day in the prevention of disease in both the young and the old.



**Kayla McFeely, PharmD (NACDS)** made a statement on behalf of the National Association of Chain Drug Stores. The NACDS strongly supports an updated schedule in an expedited fashion. As was presented, this issue is causing real-world vaccine access barriers and delayed vaccine uptake. Today, this is resulting in unnecessary scope of practice barriers in certain states that hinder pharmacists' ability to administer RSV vaccines for older adults and it is impacting health insurers' willingness to cover these vaccines. NACDS encourages CDC and ACIP to help avoid this challenge in the future by updating the immunization schedules effective immediately upon new recommendations in order to mitigate unnecessary access barriers and delays in vaccine uptake. NACDS is very much looking forward to the addenda in the coming week.

**Dr. Zimmerman MD, MPH (APRT)** said he was joining the chorus on behalf of the Association of Prevention, Teaching, and Research in supporting ongoing efforts to update the immunization schedule in a more real-time fashion for two basic reasons. One is to make it easier for practitioners and clinicians to keep up-to-date with the rapid patient changes in vaccine science, and second is for what has been mentioned by so many others—the financial barriers. This is particularly important as he works in a Federally Qualified Health Center (FQHC) where he sees firsthand the issues of disparities, equity, and the financial barriers to preventive services, including vaccinations.

### **Closing Remarks**

Dr. Lee thanked all of the ACIP Liaison Members for engaging so deeply and passionately about the issue, and CDC and Dr. Schilley for leading these discussions. It was clear that there is consensus for a dynamic immunization schedule and for it not to be a barrier to implementation. She emphasized that it had been a tough few years for everyone, including a tough month for their CDC colleagues. As everyone could tell, the same people are presenting week after week and preparing for these meetings. She recognized them for the incredible work that they do on behalf of the committee and on behalf of the public to be able to make sure that there is robust deliberation on all of these decisions that are in front of the ACIP. She expressed appreciation to the CDC for ensuring that these challenging decisions are discussed openly and transparently through the convening of the advisory committee. As challenging as it is to meet so frequently, as a member and soon to be a member of the public, she thinks this is an incredibly important process that continues to be upheld by the CDC—even through the pandemic. Those who are providing the vaccines and counseling patients and the health care workforce on vaccines and immunizations appreciate being able to hear these discussions in order to be able to better reflect the nuances, complexities, and deep understanding and thought that goes into these decisions. These are not simple decisions that the ACIP makes on behalf of the US population, but the decisions have a lot of thought and care put into them by the CDC team, WG members, ACIP members, Liaisons, and *Ex Officio* partners. It is incredible to be able to bring this to the public in such a thoughtful and meaningful way. She thanked everyone for their hard work throughout the day and over the past few years. With no additional business, she officially adjourned the meeting.

## CERTIFICATION

Upon reviewing the foregoing version of the September 22, 2023 ACIP meeting minutes, Dr. Grace Lee, ACIP Chair, certified that to the best of her knowledge, they are accurate and complete. Her original, signed certification is on file with the Management Analysis and Services Office (MASO) of CDC.

## ACIP MEMBERSHIP ROSTER

### CHAIR

LEE, Grace M, MD, MPH  
Associate Chief Medical Officer for Practice Innovation  
Lucile Packard Children's Hospital  
Professor of Pediatrics, Stanford University School of Medicine  
Stanford, CA  
Term: 8/4/2021 – 6/30/2023

### EXECUTIVE SECRETARY

WHARTON, Melinda, MD, MPH  
National Center for Immunization and Respiratory Diseases  
Centers for Disease Control and Prevention  
Atlanta, GA

### MEMBERS

BAHTA, Lynn, RN, MPH, CPH  
Immunization Program Clinical Consultant  
Infectious Disease, Epidemiology, Prevention & Control Division  
Minnesota Department of Health  
Saint Paul, Minnesota  
Term: 7/1/2019 – 6/30/2023

CHEN, Wilbur H, MD, MS, FACP, FIDSA  
Professor of Medicine  
Center for Vaccine Development and Global Health  
University of Maryland School of Medicine  
Baltimore, MD  
Term: 12/23/2020 – 6/30/2024

DALEY, Matthew F, MD  
Senior Investigator  
Institute for Health Research, Kaiser Permanente Colorado  
Associate Professor of Pediatrics  
University of Colorado School of Medicine  
Aurora, CO  
Term: 1/4/2021 – 6/30/2024

KOTTON, Camille Nelson, MD, FIDSA, FAST  
Clinical Director, Transplant and Immunocompromised Host Infectious Diseases  
Infectious Diseases Division, Massachusetts General Hospital  
Associate Professor of Medicine, Harvard Medical School  
Boston, MA  
Term: 12/23/2020 – 6/30/2024

LOEHR, Jamie, MD, FAAFP  
Owner, Cayuga Family Medicine  
Ithaca, New York  
Term: 7/26/2021 – 6/30/2025

LONG, Sarah S, MD  
Professor of Pediatrics  
Drexel University College of Medicine  
Section of Infectious Diseases  
St. Christopher's Hospital for Children  
Philadelphia, Pennsylvania  
Term: 12/24/2020 – 6/30/2024

MCNALLY, Veronica V, JD  
President and CEO Franny  
Strong Foundation  
West Bloomfield, Michigan  
Term: 10/31/2018 – 6/30/2022

POEHLING, Katherine A, MD, MPH  
Professor of Pediatrics and Epidemiology and Prevention  
Director, Pediatric Population Health  
Department of Pediatrics  
Wake Forest School of Medicine  
Winston-Salem, NC  
Term: 7/1/2019 – 6/30/2023

SÁNCHEZ, Pablo J, MD  
Professor of Pediatrics  
The Ohio State University – Nationwide Children's Hospital  
Divisions of Neonatal-Perinatal Medicine and Pediatric Infectious Diseases  
Director, Clinical & Translational Research (Neonatology)  
Center for Perinatal Research  
The Research Institute at Nationwide Children's Hospital Columbus, Ohio  
Term: 7/1/2019 – 6/30/2023

TALBOT, Helen Keipp, MD  
Associate Professor of Medicine  
Vanderbilt University  
Nashville, TN  
Term: 10/29/2018 – 6/30/2022

## **EX OFFICIO MEMBERS**

### **Centers for Medicare and Medicaid Services (CMS)**

HANCE, Mary Beth  
Senior Policy Advisor  
Division of Quality, Evaluations and Health Outcomes  
Children and Adults Health Programs Group  
Center for Medicaid, CHIP and Survey & Certification Centers  
for Medicare and Medicaid Services  
Baltimore, MD

### **Food and Drug Administration (FDA)**

Center for Biologics Evaluation and Research  
Food and Drug Administration  
Silver Spring, MD

### **Health Resources and Services Administration (HRSA)**

GRIMES, Reed, MD, MPH  
CDR, USPHS  
Director, Division of Injury Compensation Programs  
Health Systems Bureau  
Health Resources and Services Administration  
Rockville, MD

### **Indian Health Service (IHS)**

CLARK, Matthew, MD, FAAP, FACP  
Physician  
Chair, IHS National Pharmacy & Therapeutics Committee  
Durango, CO

### **Office of Infectious Disease and HIV/AIDS Policy (OIDP)**

MARSHALL, Valerie, MPH, PMP  
CDR, USPHS  
Deputy Director  
Office of the Assistant Secretary for Health  
Department of Health and Human Services  
Washington, DC

### **National Institutes of Health (NIH)**

BEIGEL, John, MD  
Associate Director for Clinical Research  
Division of Microbiology and Infectious Diseases  
National Institute of Allergy and Infectious Diseases (NIAID)  
Bethesda, MD

## **LIAISON REPRESENTATIVES**

### **American Academy of Family Physicians (AAFP)**

ROCKWELL, Pamela G, DO  
Associate Professor, Department of Family Medicine, University of  
Michigan Medical School  
Medical Director, Dominos Farms Family Medicine  
Ann Arbor, MI

### **American Academy of Pediatrics (AAP)**

O'LEARY, Sean, MD, MPH  
Professor of Pediatrics  
Pediatric Infectious Diseases  
General Academic Pediatrics  
Children's Hospital Colorado  
University of Colorado School of Medicine

### **American Academy of Pediatrics (AAP)**

Red Book Editor  
KIMBERLIN, David, MD  
Professor of Pediatrics  
Division of Pediatric Infectious Diseases  
The University of Alabama at Birmingham School of Medicine  
Birmingham, AL

### **American Academy of Physician Assistants (AAPA)**

LÉGER, Marie-Michèle, MPH, PA-C  
Senior Director, Clinical and Health Affairs  
American Academy of Physician Assistants  
Alexandria, VA

### **American College Health Association (ACHA)**

CHAI, Thevy S., MD  
Director of Medical Services  
Campus Health Services  
University of North Carolina at Chapel Hill Chapel Hill,  
NC

### **American College Health Association (ACHA) (alternate)**

LEE, Sara, MD  
Assistant Vice President of University Health and Counseling Services  
Chief Health Officer  
Case Western Reserve University  
Cleveland, OH

**American College of Nurse Midwives (ACNM)**

HAYES, Carol E., CNM, MN, MPH  
Lead Clinician  
Clinical Quality Compliance and Management  
Planned Parenthood Southeast Atlanta, GA

**American College of Nurse Midwives (ACNM) (alternate)**

MEHARRY, Pamela M., PHD, CNM  
Midwifery Educator, Human Resources for Health  
In partnership with University of Rwanda and University of Illinois, Chicago

**American College of Obstetricians and Gynecologists (ACOG)**

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## ACRONYMS USED IN THIS DOCUMENT

AAFP	American Academy of Family Physicians
AAP	American Academy of Pediatrics
ACA	Affordable Care Act
ACHA	American College Health Association
ACIP	Advisory Committee on Immunization Practices
ACNM	American College of Nurse-Midwives
ACOG	American College of Obstetricians and Gynecologists
ACP	American College of Physicians
AE	Adverse Event
AESI	Adverse Events of Special Interest
AHIP	America's Health Insurance Plans
AI/AN	American Indian/Alaskan Native
AIM	Association of Immunization Managers
AIRA	American Immunization Registry Association
AMA	American Medical Association
APhA	American Pharmacists Association
AR	Adverse Reaction
ARI	Acute Respiratory Illness
ASTHO	Association of State and Territorial Health Officers
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research
CMS	Center for Medicare and Medicaid Services
COI	Conflict of Interest
CONUS	Continental United States
CPT	Current Procedural Terminology
CSTE	Council of State and Territorial Epidemiologists
DFO	Designated Federal Official
DMC	Data Monitoring Committee
DSMB	Data Safety Monitoring Board
EBV	Epstein-Barr Virus
ED	Emergency Department
EHRs	Electronic Health Records
EMR	Electronic Medical Record
ET	Eastern Time
EtR	Evidence to Recommendation
FDA	Food and Drug Administration
FQHC	Federally Qualified Health Center
GBS	Guillain-Barré Syndrome
GEE	generalized estimating equation
GRADE	Grading of Recommendation Assessment, Development and Evaluation
HCP	Healthcare Personnel / Providers
HCRU	Health Care Resource Utilization
HHS	(Department of) Health and Human Services
HRSA	Health Resources and Services Administration
ICD	International Classification of Diseases

ICER	Incremental Cost-Effectiveness Ratio
ICU	Intensive Care Unit
IDSA	Infectious Disease Society of America
IFDO	Intrauterine Fetal Demise Outcomes
IHS	Indian Health Service
IIS	Immunization Information System
IM	Intramuscular
IRA	Inflation Reduction Act of 2022
ISO	Immunization Safety Office
IT	Information Technology
IVIG	Intravenous Immunoglobulin Therapy
LMP	Last Menstrual Period
LRTD	Lower Respiratory Tract Disease
LRTI	Lower Respiratory Tract Illness
MA-RSV LRTI	Medically-Attended RSV Lower Respiratory Tract Infection
MASO	Management Analysis and Services Office
MedDRA	Medical Dictionary for Regulatory Activities
mAbs	Monoclonal Antibodies
<i>MMWR</i>	<i>Morbidity and Mortality Weekly Report</i>
NACCHO	National Association of County and City Health Officials
NACI	National Advisory Committee on Immunization Canada
NAPNAP	National Association of Pediatric Nurse Practitioners
NCEZID	National Center for Emerging and Zoonotic Infectious Diseases
NCIRD	National Center for Immunization and Respiratory Diseases
NDC	National Drug Code
NFID	National Foundation for Infectious Diseases
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NMA	National Medical Association
NNV	Number Needed to Vaccinate
NREVSS	National Respiratory and Enteric Virus Surveillance System
NVSN	New Vaccine Surveillance Network
OIDP	Office of Infectious Disease and HIV/AIDS Policy
PCP	Primary Care Provider/Practitioner
PHAC	Public Health Agency Canada
PICO	Population, Intervention, Comparison, Outcomes
PIDS	Pediatric Infectious Disease Society
PSA	Probabilistic Sensitivity Analysis
QALY	Quality-Adjusted Life Year
RSV	Respiratory Syncytial Virus
RSVpreF	RSV Prefusion F Protein Vaccine
SAE	Serious Adverse Event
SAHM	Society for Adolescent Health and Medicine
SHEA	Society for Healthcare Epidemiology of America
SoC	Standard of Care
URTI	Upper Respiratory Tract Infection
US	United States
USG	United States Government
USVI	US Virgin Islands

VAERS	Vaccine Adverse Event Reporting System
VE	Vaccine Efficacy
VE	Vaccine Effectiveness
VFC	Vaccines For Children
VRBPAC	Vaccines and Related Biological Products Advisory Committee
VSD	Vaccine Safety Datalink
WG	Work Group