MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)

AUGUST 3, 2023
MEETING SUMMARY

CONTENTS

THURSDAY: AUGUST 3, 2023

WELCOME AND INTRODUCTIONS

Call to Order/Roll Call

Dr. Grace Lee (ACIP Chair) called to order and presided over the August 3, 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 1:55 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-2023-0063. 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. Detailed instructions for submissions of names for potential candidates to serve as ACIP members are available on the ACIP website. The deadline for applications for ACIP membership has been extended to September 1, 2023 for the 4-year term beginning in July 2024.

By way of introduction to the topic of the day's meeting, Dr. Wharton briefly reviewed 2 different processes for immunization, passive and active. Passive immunization involves the transfer of preformed antibody produced externally to provide protection to the recipient. Diphtheria antitoxin is still manufactured in horses, but most products for passive immunization come from human immune globulins. Some antibody products are made in cell culture systems. These

antibodies can provide excellent protection, but that protection wanes over time because the antibodies that are given only last so long. Transfer of maternal antibody across the placenta that provides protection in early infancy is another example of passive immunization. In contrast, active immunization that occurs with traditional vaccines comes from the response of the recipient's own immune system. Immunological memory provides prolonged protection than occurs with passive immunization and can be lifelong.

Advances in biotechnology offer the opportunity to prevent infectious diseases with long-acting monoclonal antibodies (mAbs)[1] beyond what can be provided by traditional vaccines. When used for passive immunization, these products can provide a level of protection similar to what is observed with traditional vaccines, but for a limited period of time. They can be especially valuable when full protection is needed without delay and when a traditional vaccine is not available. For some indications, the protection provided by a long-acting monoclonal might be "long enough" to provide protection during the risk period with a single dose for the duration of a respiratory disease season, for a critical part of a pregnancy, or for the duration of travel.

CDC will prioritize for ACIP consideration of those long-acting mAbs for prevention of infectious diseases that are: 1) expected to address conditions that result in a significant burden of disease to the public's health; 2) are not expected, based on the characteristics of the product itself, to present significant implementation issues for immunization providers (e.g., mode of administration, storage and handling, and frequency of administration); and 3) are expected to be priced at a level allowing for incorporation into immunization programs. She returned the floor to Dr. Lee who called upon Dr. John Farley to provide an overview from the Food and Drug Administration (FDA).

John Farley, MD, MPH (Director, CDER/FDA) provided a few opening remarks on behalf of the FDA. He reported that the FDA approved Biologics License Application (BLA)-761328 on July 17, 2023 that licensed nirsevimab-alip injection with the trade name Beyfortus™. The indication was based on the data from adequate and well-controlled trials contained within the BLA and reads as follows:

> BEYFORTUS is a respiratory syncytial virus (RSV) F protein-directed fusion inhibitor indicated for the prevention of RSV lower respiratory tract disease in:
>
> - Neonates and infants born during or entering their first RSV season.
> - Children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season.

The safety and efficacy of nirsevimab were supported by 3 clinical trials, Trials 03, 04, and 05. The primary measure of efficacy was the incidence of medically-attended RSV lower respiratory tract infection (MA-RSV LRTI). It was evaluated during the 150 days after nirsevimab administration. MA-RSV LRTI, the endpoint, included all healthcare provider (HCP) visits (e.g., physician office, urgent care, emergency room visits) and hospitalizations for LRTD disease with worsening clinical severity and a positive RSV test. Trial 03 included 1,453 preterm infants born at ≥29 weeks of gestational age up to <35 weeks of gestation who were born during or entering their first RSV season. Of the preterm infants enrolled in the trial, 969 were randomized to a single dose of nirsevimab and 484 were randomized to placebo. Nirsevimab reduced the risk of MA-RSV LRTI by approximately 70% relative to placebo. The primary analysis group in Trial 04

[1] https://www.who.int/images/default-source/departments/immunization-ivb/pdvac/who-monoclonal-antibodies.jpg?sfvrsn=f0870999_3

included 1,490 term and late preterm infants born at ≥35 weeks gestational age of whom 994 were randomized to a single dose of nirsevimab and 496 were randomized to placebo. Nirsevimab reduced the risk of MA-RSV LRTI by approximately 75% relative to placebo in that trial. Trial 05 was randomized, double-blind placebo-controlled multi-center trial in infants at high risk for severe RSV disease. The trial enrolled 925 preterm infants as well as infants with chronic lung disease (CLD) of prematurity or congenital heart disease (CHD). These patients were randomized 2:1 to receive nirsevimab or palivizumab by intramuscular (IM) injection. The efficacy of nirsevimab for prevention of MA-RSV LRTI in these high-risk patients during RSV seasons 1 and 2 was extrapolated from efficacy in Trials 03 and 04, with demonstration of comparable serum nirsevimab exposures between the high-risk population in Trial 05 and the Trials 03 and 04 populations.

FDA imposed 2 post-marketing requirements. One focused on monitoring the prevalence of RSV variants, including the frequency of known nirsevimab resistance-associated substitutions and the second requirement to phenotypically assess certain RSV-A and RSV-B substitutions. The sponsor has agreed to a number of post-marketing commitments. These include conducting the Harmony Study Extension that will evaluate antibody-dependent enhancement of RSV disease, and conducting an observational US-based long-term study of infants eligible to receive nirsevimab in their first year of life to assess the impact of RSV disease through Day 511 post-dosing. The FDA has determined that a pharmacovigilance strategy is necessary to support coordinated monitoring and assessment of safety information from data sources across both FDA and CDC. ACIP recommendations will be factored into the final pharmacovigilance strategy as appropriate. The full details of this strategy will be finalized in a separate document within 90 days of marketing approval, and this pharmacovigilance strategy may be modified as safety information accumulates during the post-marketing period. Dr. Farley noted that FDA Review Team members joined the meeting and were available to answer questions.

MATERNAL/PEDIATRIC RESPIRATORY SYNCYTIAL VIRUS (RSV) VACCINES

Session Introduction

Sarah S. Long, MD (Chair, Maternal/Pediatric RSV WG) reminded everyone that previous Maternal/Pediatric RSV WG presentations to the ACIP focused on nirsevimab, the long-acting monoclonal antibody against RSV; the epidemiology and burden of RSV in infants; the virology and immunology of RSV; the safety and efficacy of nirsevimab; the cost effectiveness analysis from a CDC model and a comparison with a manufacturer model; the Evidence to Recommendation (EtR) Framework findings for nirsevimab; and clinical considerations for nirsevimab.

Dr. Long indicated that the sole focus of the presentations for this session would be on nirsevimab because on June 8, 2023, the FDA Antimicrobial Drug Advisory Committee (AMDAC) evaluated and voted on 2 questions:

1. Is the overall benefit-risk assessment favorable for the use of nirsevimab for the prevention of RSV lower respiratory disease in neonates and infants born during or entering their first RSV season?

2. Is the overall benefit-risk assessment favorable for the use of nirsevimab for the prevention of RSV lower respiratory tract disease in children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season?

The AMDAC voted 21-0 in favor of the first question and 19-2 in favor of the second question. Many committee members recognized the need for guideline groups such as the American Academy of Pediatrics (AAP) and ACIP to provide additional recommendations on the use of nirsevimab. As Dr. Farley noted earlier, the FDA approved nirsevimab on July 17, 2023 for the prevention of RSV LRTD in neonates and infants born during or entering their first RSV season and in children who remain vulnerable to severe RSV disease through their second RSV season.

The agenda for this ACIP session included updated EtR Framework findings for nirsevimab, nirsevimab implementation considerations, clinical considerations for nirsevimab, Maternal/Pediatric RSV WG considerations and proposed recommendations and voting language, and a Vaccines for Children (VFC) Resolution. Dr. Long concluded with the following proposed ACIP voting language so that members could be thinking about it throughout the presentations:

- ❑ Infants aged <8 months born during or entering their first RSV season are recommended to receive one dose of nirsevimab (50 mg for infants <5 kg and 100 mg for infants ≥5 kg)

- ❑ Children aged 8–19 months who are at increased risk of severe RSV disease and entering their second RSV season are recommended to receive one dose of nirsevimab (200 mg)

Evidence to Recommendations (EtR) Framework: Nirsevimab Updates

Jefferson Jones, MD, MPH, FAAP, CDR, USPHS (CDC/NCIRD Co-lead, Maternal/Pediatric RSV WG) reiterated that the following 2 policy questions were considered by the Maternal/ Pediatric WG regarding nirsevimab:

1. Should one dose of nirsevimab be recommended for infants aged <8 months born during or entering their first RSV season (50 mg for infants <5 kg and 100 mg for infants ≥5 kg)?

2. Should one dose of nirsevimab be recommended for children aged 8–19 months who are at increased risk of severe RSV disease and entering their second RSV season (200 mg)?

The rationale for inclusion of these age groups was that given an average RSV season of 4–5 months, infants aged 8 months and children aged 20 months would be experiencing their second and third RSV seasons, respectively.

As mentioned earlier, nirsevimab is a form of passive immunization against RSV. While it may be referred to as “immunization” during the presentations and discussion, it is passive immunization. Nirsevimab does not provide active immunity. Active immunity results from infection or vaccination, which triggers an immune response. Passive immunity is when a person receives antibodies from an external source. Examples include antibodies transferred from mother to baby through the placenta or breastmilk or direct administration of antibodies, such as intravenous immunoglobulin (IVIG) therapy or monoclonal antibodies such as nirsevimab.[2]

[2] https://www.cdc.gov/vaccines/vac-gen/immunity-types.htm

In terms of the PICO components for Policy Question #1 in this EtR analysis, the population included infants aged <8 months born during or entering their first RSV season. The intervention was nirsevimab (1 injection prior to the start of RSV season or at birth if born during the season, 50 mg if <5 kg or 100 mg if ≥5 kg). The comparison was no nirsevimab prophylaxis. The outcomes included MA-RSV-associated LRTI, RSV-associated LRTI with hospitalization, RSV-associated LRTI with intensive care unit (ICU) admission, RSV-associated death, all-cause medically attended LRTI, all-cause LRTI-associated hospitalization, and serious adverse events (SAEs). In terms of the EtR domains (e.g., Public Health Problem, Benefits and Harms, Values, Acceptability, Feasibility, Resource Use, and Equity), the domains of Benefits and Harms, Feasibility, and Resource Use included updates from what was presented during the February 2023 ACIP meeting.

To review the first domain of the Public Health Problem, data from the National Respiratory and Enteric Virus Surveillance System (NREVSS)[3], the primary source for monitoring RSV seasonality in the US, showed that there was very limited RSV circulation until late Spring 2021 that was followed by a peak in activity in late Summer 2021. Transmission continued throughout the fall into December 2021. The most recent RSV season showed increasing RSV activity starting in late Summer 2022, with a peak in RSV transmission in October–November 2022. To summarize that, the 2022–2023 season began later than the 2021–2022 season but earlier than pre-pandemic seasons. This suggests an incremental reversion to pre-pandemic seasonality with winter peaks and highlights the uncertainty in when the next RSV season will start.

In terms of epidemiology, RSV is the most common cause of hospitalization in US infants. The highest RSV hospitalization rates are in the first months of life. The risk declines by month with increasing age in infancy and early childhood. While prematurity and other chronic diseases increase the risk of RSV-associated hospitalization, most hospitalizations are in healthy term infants. The WG felt that RSV-associated disease in infants born during or entering their first RSV season is of public health importance.

Regarding the Benefits and Harms domain, there have been no updates to the GRADE (Grading of Recommendation Assessment, Development and Evaluation) assessment of the evidence presented in February 2023. However, some additional data were received from pooled estimates combining Phase 2b and Phase 3 clinical trials estimate comparing the nirsevimab arm to the placebo arm in addition to concerns in terms of the certainty of assessment. The estimated efficacy was 79% for MA-RSV LRTI, 80.6% for hospitalization, and 90% for ICU admission. No RSV-associated deaths were recorded, though this outcome could not be evaluated. The estimated efficacy against all-cause medically attended LRTI was 34.8% and against all-cause LRTI hospitalization was 44.9%. The risk ratio comparing SAEs in infants receiving nirsevimab versus receiving placebo was 0.73.

In summary of GRADE for nirsevimab, there is high certainty that Nirsevimab is effective in preventing medically attended RSV and RSV hospitalization. In addition to preventing all-cause medically attended LRTI and LRTI hospitalization, there is moderate certainty that nirsevimab is effective in protecting against RSV LRTI with ICU admission and that SAEs are not more common in infants receiving nirsevimab compared with placebo. Additional safety data were provided during the AMDAC meeting on nirsevimab[4]. The most commonly reported adverse reactions (ARs) were injection site reactions (0.3%) and rash (0.9%). The FDA noted an

[3] https://www.cdc.gov/mmwr/volumes/72/wr/mm7214a1.htm
[4] https://www.fda.gov/advisory-committees/advisory-committee-calendar/june-8-2023-meeting-antimicrobial-drugs-advisory-committee-meeting-announcement-06082023

imbalance in deaths between nirsevimab and the control arms but determined that the deaths were unlikely to be related to nirsevimab.

The sponsor shared data from the ongoing Phase 3b study known as HARMONIE.[5] The HARMONIE study enrolled 8,058 infants. The age at enrollment was: 49% <3 months, 24% 3-5 months, and 28% ≥6 months. Of the infants, 85% were born at term and 50% were born during the RSV season. This study is being conducted in France, the United Kingdom (UK), and Germany. While these results are from August 8, 2022–February 28, 2023, the study is ongoing. The participants were randomized to nirsevimab or no injection, meaning the control group was not given a placebo injection. The primary endpoint was RSV hospitalization, which was a LRTI hospitalization with a positive RSV test. RSV tests were ordered by clinicians for patients with LRTI per the standard of care as opposed to systematically on all patients with LRTI hospitalizations. Participants will be followed for at least 12 months after randomization. At the end of the RSV season, the preliminary efficacy results were released, which were presented during this session. These results were with a median post-randomization follow-up time of 2.5 months. HARMONIE preliminary results reported an efficacy against RSV hospitalization of 83%, 76% against severe disease (e.g., oxygen saturation below 90% and oxygen given), and 58% against all-cause hospitalization with LRTI during the RSV season. For safety, Grade 1 AEs were reported to be slightly higher in the nirsevimab arm (29%) versus the no intervention arm (25%). The rates of Grade 2 and Grade 3 AEs were similar between the nirsevimab and control arms. It is important to note that these results have not been peer-reviewed or published in the scientific literature.

To summarize the Benefits and Harms domain, the overall GADE grade evidence rating was moderate. The results were downgraded based on imprecision for protection against ICU admissions because of few recorded events and imprecision of SAEs because rare events are unlikely to be detected. The WG felt that the desirable anticipated effects of nirsevimab were moderate to large, that the undesirable anticipated effects of nirsevimab were minimal to small, and that the desirable effects outweighed the undesirable effects and favored nirsevimab over no intervention.

The next domain is Values, for which no updates were available. In a survey of people currently pregnant or pregnant within the last 12 months conducted by the CDC, the University of Iowa, and the Rand Corporation on RSV immunizations, only 33% of respondents thought their baby "definitely" or "probably would" get an RSV infection within 1 year after being born. Despite being unsure or perceiving RSV risk to be low, respondents were worried that their baby would need to be hospitalized if they got sick with RSV (mean response 4 of 5, with 5 being most worried). Of the respondents, 70% said they "definitely" or "probably would" get an RSV antibody injection for their baby if safe and effective. The WG determined that the target population probably feels that the desirable effects are large relative to undesirable effects. The WG varied in whether they felt there was important uncertainty about, or variability in, how much people value the main outcomes.

[5] Study not peer-reviewed and information provided directly by sponsor; https://www.clinicaltrials.gov/study/NCT05437510

The next domain is Acceptability with key stakeholders, for which no updates were available. In a survey of US pediatric providers, over 85% agreed that parents need more information about RSV, that immunization could help prevent RSV, and that immunization policy should ensure all children get access.[6] The American Academy of Pediatrics (AAP) and the National Foundation for Infectious (NFID) Disease Roundtable have stated the need for safe and effective RSV prevention products.[7] The WG felt that passive immunization with nirsevimab was or probably was acceptable to key stakeholders.

Feasibility domain considerations were reviewed in the next presentation by Dr. Georgina Peacock, but the WG felt that nirsevimab probably will be feasible to implement.

The Resource Use domain, the primary source of data was a cost-effectiveness analysis performed by the University of Michigan. Since the cost-effectiveness analysis was presented to ACIP in February 2023, the company provided an updated cost estimate of the product. The list price was estimated to be $495 and the cost for the VFC program was estimated to be $395. Assuming nirsevimab is administered as 50% under the VFC and 50% under private insurance, the average price was $445. This price was not final at the time of this session per the WG's understanding. Mortality assumptions were modified to include individuals at increased risk of severe disease and savings from not using palivizumab to those recommended to receive it were incorporated. Other inputs were unchanged from the previous model presented during the February 23, 2023 ACIP meeting. The number needed to immunize with nirsevimab to prevent 1 health outcome was 17 for an outpatient visit, 18 for an ED visit, 128 for inpatient, 581 for ICU admission, 24 per inpatient day, and 194 per ICU day. The cost per health event averted was $2,662 per outpatient visit, $7,473 per ED visit, $19,909 per inpatient admission, $90,494 per ICU admission, $3,687 per inpatient day, and $30,165 per ICU day. The updated base case results of the cost-effectiveness analysis was $102,811 per quality adjusted life year saved. The WG felt that nirsevimab is or probably is a reasonable and efficient use of resources. A full presentation for this updated cost-effectiveness analysis was included in the extra slides.

The primary update to the Equity domain was that that if ACIP recommends use of nirsevimab, ACIP also would vote on a VFC Resolution for nirsevimab. To summarize equity, national studies of death certificates found higher rates among non-Hispanic Black children compared with non-Hispanic White infants and children 1–4 years of age.[8] 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.[9] RSV hospitalization rates were 4 to 10 times higher among Alaska Native and American Indian (AI/AN) children <24 months of age than the rate in the general population.[10] Studies of RSV hospitalization by race and ethnicity have differing results.[11] The WG felt that nirsevimab would increase health equity.

[6] https://admin.allianceforpatientaccess.org/wp-content/uploads/2023/01/AfPA-and-NCfIH_The-Indirect-Impact-of-RSV_Survey-Report_Jan-2023.pdf
[7] AAP COID BGC Pediatrics 2014 Aug;134(2):415-20; and https://www.nfid.org/wp-content/uploads/2022/04/NFID-RSV-Call-to-Action.pdf
[8] Hansen J Infect Dis 2022 Aug 15;226(Suppl 2):S255-S266
[9] Unpublished data from RSV-NET, CDC
[10] Atwell Pediatrics 2023, e2022060435
[11] Hall Pediatrics 2013 Aug;132(2):e341-8; Hall NEJM 2009;360(6):588–598; Iwane Pediatrics 2004 Jun;113(6):1758-64, findings differed by age group; and Rha Pediatrics 2020 Jul;146(1):e20193611, findings differed by age group

Displayed in this table are the WG's judgments of the EtR Framework analysis for the first RSV season indication:

EtR Domain	Question(s)	Work Group Judgments
Public Health Problem	▪ Is RSV-associated disease among infants <8 months of age entering their first RSV season and infants born during the RSV season of public health importance?	Yes
Benefits and Harms	▪ How substantial are the desirable anticipated effects? ▪ How substantial are the undesirable anticipated effects? ▪ Do the desirable effects outweigh the undesirable effects?	Moderate to large Minimal to small Yes
Values	▪ Does the target population feel the desirable effects are large relative to the undesirable effects? ▪ Is there important variability in how patients value the outcome?	Yes/probably yes No consensus
Acceptability	▪ Is nirsevimab acceptable to key stakeholders?	Yes/probably yes
Feasibility	▪ Is the intervention feasible to implement?	Probably yes
Resource Use	▪ Is the intervention a reasonable and efficient allocation of resources?	Yes/probably yes
Equity	▪ What would be in the impact of the intervention on health equity?	Probably increased

The WG felt that the desirable consequences clearly outweigh the undesirable consequences in most settings, with a minority opinion that the desirable consequences probably outweigh the undesirable consequences. The WG recommended the intervention for all infants in their first RSV season.

To review the EtR analysis for the second RSV indication, the population is children aged 8–19 months who are at increased risk of severe RSV disease and who are entering their second RSV season. The intervention was nirsevimab (200 mg [2 x 100 mg] injection near start of second RSV season) and the comparison was no nirsevimab prophylaxis. The outcomes were the same as those used for the first indication. Domains with updates unique to the second season included the Public Health Problem and Resource Use.

For the Public Health Problem, the WG previously presented that they felt the risk groups to receive nirsevimab for the second RSV season could be based on the AAP recommendation for palivizumab for a child's second RSV season.[12] The WG assumed nirsevimab to be cost-saving compared with palivizumab. The proposed recommendation to receive nirsevimab when entering their second RSV season would include the following groups:

- ❑ Children with CLD of prematurity if they require medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) during the 6-month period before the start of the second RSV season
- ❑ Children with severe immunocompromise
- ❑ Children with cystic fibrosis if 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

[12] American Academy of Pediatrics. Committee on Infectious Diseases [Respiratory Syncitial Virus.] In: Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, eds. Red Book : 2021 Report of the Committee on Infectious Diseases. Itasca, IL: American Academy of Pediatrics, 2021

To evaluate the evidence if other risk groups should be considered for a recommendation, CDC conducted 2 analyses, a systematic review of the literature and an analysis of the MarketScan national claims database. The systematic review included any studies that compared RSV hospitalization rates among children with risk factors to a healthy control among children 6–24 months of age. Among 3,825 abstracts reviewed, 6 studies were identified. CLD, CHD, and neuromuscular disease (NMD) were analyzed in these studies. These studies indicated an increased risk of hospitalization for these risk factors. No studies evaluating other risk factors were identified.

Given the limited evidence available in the systematic review, CDC conducted an analysis of the MarketScan national claims database for select risk factors for severe RSV disease during the second RSV season using data from 2015–2021. Using International Classification of Diseases (ICD)-9 and ICD-10 codes, children were identified with and without selected conditions (e.g., CLD, CHD, Down syndrome, NMD, pulmonary malformations, immunodeficiency, cystic fibrosis) and children who were hospitalized with RSV. The rates of RSV hospitalization among children with a chronic condition were compared to children without any of these chronic conditions. Increased rates of hospitalization were seen for all conditions. It is important to note that a primary limitation in this study is that RSV testing may be more common for children with risk conditions, inflating RSV-specific hospitalization rates.

Several prior studies have documented increased incidence of RSV hospitalizations among AI/AN children.[13] One study found that rates of RSV hospitalization in AI/AN children were 4 to 10 times the average rates of US children overall aged 12–23 months as determined from the New Vaccine Surveillance Network (NVSN).[14] These studies have been conducted in specific populations and may not be broadly representative of the risk in all AI/AN children. Findings of these studies do not separate environmental, sociocultural, or other factors that may increase severe disease risk. And some AI/AN communities are also in remote areas that can make transportation of children with severe RSV to an appropriate health care setting more challenging.[15]

To summarize the Public Health Problem domain, the WG group felt that evidence for RSV burden among children 8–19 months entering their second RSV season with specific risk conditions is limited. The WG felt that nirsevimab should be recommended to the same groups the AAP recommends for palivizumab for the second RSV season. The WG also felt that nirsevimab should be recommended to AN/AI children entering their second RSV season. In addition, the WG felt that RSV disease among children who are at high risk of severe disease[16] in their second RSV season was of public health importance.

[13] Atwell 2023 Pediatrics 2023 Jul 14;e2022060435; Karron et al. J Infect Dis 1999; Holman et al. Pediatrics 2004; Lowther et al. J Ped Infect Dis 2000

[14] Atwell 2023 Pediatrics 2023 Jul 14;e2022060435

[15] American Academy of Pediatrics. Committee on Infectious Diseases [Respiratory Syncytial Virus.] In: Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, eds. Red Book: 2021 Report of the Committee on Infectious Diseases. Itasca, IL: American Academy of Pediatrics, 2021.

[16] For groups recommended to receive palivizumab in their second RSV season by the American Academy of Pediatrics and American Indian and Alaska Native children

Moving to the Benefits and Harms domain, a pharmacokinetic trial[17] was conducted that randomized children at risk of severe RSV disease to palivizumab or nirsevimab. In the second RSV season, 220 participants received nirsevimab and 42 received palivizumab. Among those who received nirsevimab, 2 pharmacokinetic endpoints have been reported. The Day 150 nirsevimab concentrations compared with the Phase 3 Prevention of Medically Attended Lower Respiratory Tract Infection Due to Respiratory Syncytial Virus in Healthy Late Preterm and Term Infants (MELODY) efficacy trial among late preterm and term infants that showed efficacy. The proportion of participants who had an area under the curve (AUC) nirsevimab concentration above a target based on the efficacy trial data in term and preterm infants of 12.8 mg day/ml.

Among recipients of nirsevimab, Day 150 concentrations were higher in the high-risk infants who received 200 mg in the second RSV season (Trial 05) that infants who received 50 mg (if <5kg) or 100 mg (if >5kg) in Phase 3 MELODY trial (Trial 04). For the other pharmacokinetic endpoint among recipients of nirsevimab in the second RSV season, most had an AUC nirsevimab concentration above the target threshold. Among infants with CLD and CHD, 97.7% and 100% respectively had concentrations above that target threshold. For safety, no AEs were judged to be related to nirsevimab or palivizumab in the second RSV season follow-up period.[18]

In summary of GRADE for the second RSV season, nirsevimab may be effective in preventing MA-RSV LRTI, but with low certainty. The prevalence of SAEs was not significantly different in the intervention group or control group, but the certainty of evidence was very low. No data were available for other outcomes. Overall, the evidence rating was very low certainty (Type 4). This was downgraded on indirectness because of the use of pharmacokinetic data as a surrogate for efficacy, the population did not include children who match the proposed indication outside of CLD and CHD, the study was small in size, and no placebo group was included for a comparison. For groups recommended to receive palivizumab in their second RSV season by the AAP and AI/AN children, the WG felt that the desirable anticipated effects were moderate, the undesirable anticipated effects were minimal, and the desirable effects outweighed the undesirable effects and favored nirsevimab over no intervention.

No additional data were available for the domains of Values or Acceptability specific to high-risk populations in their second RSV season. The WG determined that for groups recommended to receive palivizumab in their second RSV season by the AAP and AI/AN children, the target population probably feels that the desirable effects are large relative to undesirable effects. The WG also felt that there probably was not important uncertainty or variability in how much people valued the main outcomes. The WG felt that prevention with nirsevimab was, or probably was, acceptable to the key stakeholders. For feasibility, an additional visit to a provider might be needed for administration of nirsevimab prior to the beginning of the second RSV season. The WG felt that nirsevimab was probably feasible to implement among children 8─19 months of age at increased risk of severe RSV disease entering their second RSV season for groups recommended to receive palivizumab in their second RSV season by the AAP and AI/AN children.

[17] Domachowske J, Madhi SA, Simões EAF, Atanasova V, Cabañas F, Furuno K, et al. Safety of nirsevimab for RSV in infants with heart or lung disease or prematurity. New England Journal of Medicine. 2023;386(9): 892–894. doi:10.1056/NEJMc2112186

[18] Source: FDA briefing document for Antimicrobial Drugs Advisory Committee June 8, 2023 meeting

For the Resource Use domain, the inputs were updated similar to the cost-effectiveness analysis for the first RSV season indication. As presented in February 2023, theoretical groups of children with increased risk were created with 2, 4, 6, and 10 times higher risk than the general population 8–19 months as of October for beginning of RSV season. Compared with February, 2 scenarios were created to account for the uncertainty in mortality in this group. As previously presented, the incidence of RSV-associated hospitalization and incidence per hospitalization were increased. For the other scenario, the incidence of RSV-associated hospitalization was increased. However, the mortality per hospitalization was not changed because of lack of evidence. No increases were made to the incidence of outpatient and ED visits, healthcare costs, or quality adjusted life years (QALY) lost with RSV disease for these increased risk groups due to lack of data.[19] The cost was updated to $890 for nirsevimab per child based on 2 times the $445 per dose assumed in the first season analysis to account for the 200 mg injections needed. Baseline mortality estimates were modified to include high-risk individuals and other inputs were unchanged similar to the first season model. This table displays the updated results:

	Incremental Cost-Effectiveness Ratio ($ / quality adjusted life year)	
Increased Risk category	RSV Hospitalization incidence increased	RSV hospitalization incidence and mortality per hospitalization increased
1x (base)	$1,557,544	$1,557,544
2x	$1,147,756	$836,270
4x	$726,983	$280,740
6x	$512,337	$118,912
10x	$294,775	$25,328

The WG felt that nirsevimab use among children 8–19 months of age entering their second RSV season who are at increased risk of severe disease is probably a reasonable and efficient allocation of resources. Like all domains, this assumes increased risk of severe disease refers to groups recommended to receive palivizumab in their second RSV season by the AAP and also including AI/AN children.

For the Equity domain, no updated information is available. As previously presented, equity issues differ by chronic condition among infants and young children. AI/AN children have reported higher hospitalization incidence rates than the general population during their second RSV season. Non-Hispanic Black and Hispanic populations have higher reported rates of preterm birth than non-Hispanic White populations. The WG felt that nirsevimab use probably would increase health equity.

[19] Same assumption as previous model presented at February 23, 2023 ACIP meeting

Displayed in this table are the WG's judgments of the EtR Framework analysis for children at high risk entering their second RSV season:

EtR Domain	Question(s)	Work Group Judgments
Public Health Problem	▪ Is RSV disease among children 8–19 months who are at increased risk of severe disease of public health importance?	Yes
Benefits and Harms	▪ How substantial are the desirable anticipated effects? ▪ How substantial are the undesirable anticipated effects? ▪ Do the desirable effects outweigh the undesirable effects?	Moderate Minimal Favors nirsevimab
Values	▪ Does the target population feel the desirable effects are large relative to the undesirable effects? ▪ Is there important variability in how patients value the outcome?	Probably yes Probably no
Acceptability	▪ Is nirsevimab acceptable to key stakeholders?	Yes / Probably yes
Feasibility	▪ Is the intervention feasible to implement?	Probably yes
Resource Use	▪ Is the intervention a reasonable and efficient allocation of resources?	$890: Probably yes
Equity	▪ What would be in the impact of the intervention on health equity?	Probably increased

After reviewing the totality of the data presented during this session and acknowledging uncertainties around the aspects of the data, the WG felt that the desirable consequences probably outweigh the undesirable consequences in most settings, with a minority opinion that desirable consequences clearly outweigh the undesirable consequences. The WG proposed to ACIP to recommend the intervention for groups recommended to receive palivizumab in their second RSV season by the AAP and for AI/AN children.

Nirsevimab Implementation Considerations

Georgina Peacock, MD, MPH, FAAP (CDC/NCIRD) briefly reviewed some of the many implementation considerations related to nirsevimab, such as the definition of "vaccine," cost, storage and handling, hospital dosing, outpatient dosing, coding and Immunization Information Systems (IISs), timing of vaccination, second year vaccinations, vaccine administration, safety reporting, and vaccine confidence and demand. There are some mitigation strategies and CDC is exploring others internally and with its partners in the field.

One issue that has arisen is the definition of "vaccine." There is no statutory definition of "vaccine" in the statute for the VFC program (section 1928 of the Social Security Act).[20] There also is no statutory definition of "vaccine" in the Affordable Care Act (ACA) (section 2713 of PHS Act),[21] or its implementing regulations, which has a provision that mandates coverage of vaccine recommendations included on CDC''s immunization schedules. Therefore, CDC has determined that nirsevimab is eligible for inclusion in the Childhood Immunization Schedule and the VFC. It is important to note that some states do have different definitions of "vaccine" in their state statutes, which may affect the state purchase of vaccine in universal purchase states. However, it does not affect the use of federally purchased vaccine in states.

[20] https://www.ssa.gov/OP_Home/ssact/title19/1928.htm
[21] https://www.federalregister.gov/documents/2015/07/14/2015-17076/coverage-of-certain-preventive-services-under-the-affordable-care-act

Nirsevimab is a costly product. If nirsevimab is recommended by ACIP, it will be covered by insurance and included in the VFC program. It is important to make sure that there is equitable access to nirsevimab. The cost of nirsevimab is a potential implementation barrier, particularly for outpatient settings or ambulatory practices. In the provider agreement for VFC providers, there is a provision that if a practice has both public and private payers, they must carry stock. Recognizing that this may be challenging for some practices, CDC is working through some potential short-term solutions that could be implemented during the ramp-up of inclusion of nirsevimab in the VFC program.

This product is similar to other routine vaccines for children in terms of storage, handling, and administration. Nirsevimab is administered as an intramuscular (IM) injection using a single-dose pre-filled syringe and can be administered simultaneously with other childhood vaccines. Dosing is weight-based (50 mg if <5 kg; 100 mg if ≥5 kg; 200 mg (2x100 mg) for high-risk children entering second RSV season). Storage and handling are similar to other routine vaccines. Nirsevimab is stored in a refrigerator at 2-8^0 C and may be kept at room temperature (20-25^0 C) for up to 8 hours.

There have been some questions about scope of practice issues. Different jurisdictions or states may have different scope of practice statutes related to who can administer injectable therapeutics versus vaccines. CDC conducted a scan of different state statutes or laws to determine who is allowed to administer therapeutics. It appears that in most states, medical assistants who frequently do administer vaccines also will be able to deliver injection drugs. While there is some variability, this does not appear to be major issue related to scope of practice.

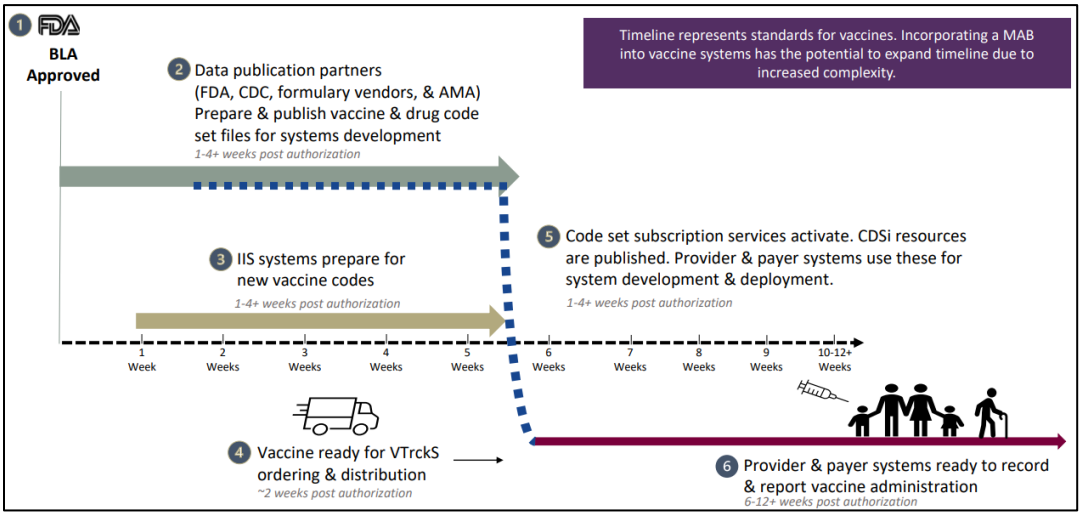
There have been conversations about where doses will be given and the age of the infant. Approximately 10% of birthing hospitals participate in the VFC program. There has been a suggestion that if nirsevimab were to be given in the hospital, this would be similar to what is done with hepatitis B vaccine. Hepatitis B vaccine is bundled into a payment model for newborn care. It is important to note that hepatitis B vaccine costs approximately $13 to $16 a dose.[22] If nirsevimab were to be included in a bundled payment model, it may take time for that to be put into practice. Regardless of where the dose is given, it is critical to ensure that documentation of nirsevimab administration and all parties involved are sent to the primary care provider (PCP). There are some potential challenges with nirsevimab being entered into IISs since it is a therapeutic versus a vaccine. Comprehensive maternal-neonatal records will become even more critical if maternal RSV vaccine is licensed and recommended and will adds to the need for communication between maternal records, hospital records, and ambulatory settings or primary care offices. Regarding outpatient administration, communication from the birthing hospital is extremely important related to this product. CDC also recognizes that an initial investment by pediatricians who are unsure on the demand for this product may create some challenges. Historically, there has been a lag in insurance payments for new products.

Because of the uniqueness of this product, there is a need to consider different coding requirements. The initial meeting and American Medical Association (AMA) decision pertaining to Current Procedural Terminology (CPT) codes classified nirsevimab as a drug or a therapeutic. That means that currently, it is associated with an administration code that does not include a counseling component and is not eligible for a standalone counseling component. CDC understands that there are efforts underway potentially to propose a unique code for this

[22] https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html

product that would include counseling and storage and handling components. Again, there may be potential challenges in recording the doses in IISs.

This graphic depicts the complexity of the steps involved in paring systems for administering a newly authorized vaccine across the US, which illustrates that there are numerous processes and partners involved and that it takes time:



To further detail IISs and vaccine forecasting considerations, coding of nirsevimab as a therapeutic instead of a vaccine could create challenges with internal provider ordering, provision of a vaccine record, and interoperability and data exchange with electronic health records (EHRs) and IISs. In addition, there are some forecasting issues related to Clinical Decision Support (CDS) systems for immunizations. The dosage is determined by weight, but CDS systems do not have access to patient weight. This could create challenges with forecasting doses. Second season recommendations also may be challenging. In addition, CDS systems are unable to take into account maternal vaccination history for forecasting of infant nirsevimab immunization.

Special considerations also add complexity. Timing of vaccination is based on RSV season. Tropical climates may have different or unpredictable seasonality when compared with most of the continental US (CONUS). There also is variability in different localities. For example, seasonality in Alaska is less predictable and of longer duration. For those who are going to receive a second dose, high-risk populations must be defined and palivizumab recommendations must be clarified in the setting of nirsevimab availability.

Reporting of AEs is more complicated for nirsevimab than other immunizations being classified as a therapeutic versus a vaccine. If nirsevimab is administered alone, suspected AEs are reported to MedWatch. If nirsevimab is administered simultaneously with any vaccine, suspected AEs are reported to the Vaccine Adverse Event Reporting System (VAERS) and additional reporting to MedWatch will not be needed.

In terms of introduction of nirsevimab in the context of coming out of a pandemic during which there have been many conversations about vaccine confidence and demand, it is not clear whether physicians and the public will accept this new product and/or what the demand would be. In addition, this is occurring at the same time as commercialization of COVID-19 vaccine and seasonal influenza vaccine administration. Vaccine hesitancy and the need for counseling

are anticipated regarding all vaccines and products. In addition, there have been efforts to weaken school immunization requirements and expand vaccine exemptions at the state level. This also feeds into vaccine confidence and demand issues.

In conclusion, this summarizes just some of the potential issues with implementation of nirsevimab. The risks during this season's rollout include timing of availability of doses, provider hesitancy, and uptake. The recommendations will be complex with regard to hospital versus outpatient administration and seasonality and timing. Lessons learned with respect to hepatitis A and B should be considered. In addition, there may be unintended consequences. Therefore, it is important that all partners involved in this are thinking through potential implementation issues moving forward to ensure that the product has good uptake and infants are protected.

Discussion Points

Dr. Poehling requested that the FDA or the vaccine manufacturer share the list price and bounds in the most recent iteration. Because there is availability of the product in 2 formulations (e.g., 50 mg and 100 mg) she asked for confirmation that they both would be priced the same in order to ensure that infants can receive the appropriate dosing without an additional cost concern. Another potential concern that Dr. Peacock raised regarding the CPT code defining nirsevimab as a drug or therapeutic. While the ACA covers vaccines, there are a lot of private insurance plans that have high deductibles. This raised a concern about whether large co-pays could be anticipated for many families.

Dr. Ritchey responded that Sanofi Vaccines is committed to making Beyfortus™ successful and cost-effective for all infants entering their first RSV season. Consistent with the analysis shared by ACIP and the WG, assuming an all-infant recommendation and inclusion in the VFC program to ensure access for those infants, Sanofi Vaccines' pricing will be cost-effective with a commercial list price of $495 and a lower VFC price of $395 to reflect that volume that is purchased through the program. The 50 mg and 100 mg formulations would be $495, which means that 2 doses given for 200 mg would be $990.

In terms of private insurance and the potential for high co-pays, Dr. Peacock reached out to billing experts and reported that nirsevimab would be covered under the ACA as an immunization with no co-pay if it is recommended by the ACIP.

Dr. Talbot asked whether the AMA would reconsider its classification of nirsevimab as a drug and therapeutic. When the term "drug and therapeutic" is used, patients are going to think that this is a treatment for RSV rather than a prevention. This will make educating families much more difficult.

As a member of the WG, Ms. Stinchfield (NAPNAP) thanked Dr. Peacock for outlining the significant implementation challenges discussed with the WG. Coming from the private sector hospital and clinic settings, she encouraged all of her colleagues across the US to use Dr. Peacock's very detailed presentation as a template for the work that needs to be done and starting now with the patient education, staff education, storage and handling, electronic medical records (EMRs), et cetera. The numerous considerations for implementation should not be barriers. They are just going to take some work beginning immediately.

Dr. Hopkins (NFID) emphasized that addressing potential issues around collaboration and communication would be critical to do as soon as possible with regard to this product and for RSV prevention in infants in general.

Regarding the cost-effectiveness results for children 8–19 months of age, Dr. Cieslak (CSTE) said he was surprised to see that the WG thought the costs were reasonable. He asked Dr. Jones to explain the risk category for the base case scenario and the rationale for apparently upping that 10-fold in the sensitivity analysis.

Dr. Jones indicated that the baseline risk was based on those who would be entering their second RSV season in October who would be 8–19 months of age per NVSN rates for the general population. Because the analysis was considering those at increased risk and there was a lack of data on what the hospitalization rate would be for these increased risks, theoretical risk groups were created to estimate what the rates may be. This was the reason the WG did not expand beyond those who already were recommended to receive palivizumab. Instead using palivizumab as a 5-dose monthly monoclonal antibody product for those who are recommended to receive palivizumab, switching them to nirsevimab would be assumed to be a cost-saving in that scenario. That is the scenario the WG interpreted as being a reasonable allocation of resources.

Dr. Loehr asked Dr. Jones to clarify if Slide 55 was saying that some people have a higher risk but there are no data. He asked for clarification about whether there were any data on the children who received palivizumab to give them a sense of how much more likely they are to be in the hospital than the average 12-month-old or 18-month-old. He agreed that switching to nirsevimab would be very expensive if the increased risk is not significant.

Dr. Jones responded that the lack of data on the increased incidence rate of hospitalization or other health outcomes for those at increased risk is most concerning. Based on the lack of data in a review of the evidence, the AAP recommends palivizumab only in the second season for a fairly select group. The WG reviewed that paper and did the systematic review, and found a very limited set of data that showed an increased risk of 2, 4, and 4 times the risk. The MarketScan analysis showed higher prevalence ratios of hospitalization, but the WG had considerable concern about whether those represent the truth or if those are inflated due to RSV testing of high-risk populations versus the general population. Given the lack of data, the WG did not have confidence in what the rates would be.

Dr. Loehr agreed that if nirsevimab is on the immunization schedule, it will get covered without co-pay under the ACA. However, he reiterated something he has brought up many times. This will take time. He just had to research this for a presentation and confirmed that insurance companies have 1 year after approval and until the following plan year. If ACIP approved a product in February 2023, insurance plans would have until February of 2024 to cover it without cost. If the ACIP approved nirsevimab during this meeting, it could be 18 months before it would be covered. There are insurance companies that would begin covering it immediately upon approval of the ACIP's recommendation by the CDC director. He encouraged insurance colleagues to simply adopt that policy because it is in the best interest of patients and communities.

Dr. Lee invited Dr. Grubb from America's Health Insurance Plans (AHIP) to comment on this, recognizing that there is heterogeneity by health plan.

From a state health department point of view, Ms. Bahta highlighted that bundling as has been done with hepatitis B may be a challenge going forward with only 10% of hospitals enrolled in the VFC program. It would be a major onboarding project to get state programs enrolled in the

VFC program. There also would be major challenges in practically implementing screening for eligibility.

Dr. Daley expressed appreciation for the additional thought and care the WG put into including AI/AN populations in terms of second season dosage. Given the data that were presented on 4 to 10 times the hospitalization rate during the second season, the argument is compelling. However, he wondered about the aspects of acceptability and feasibility whether there are any data to speak to the ability to implement that as a strategy.

Dr. Jones indicated that while they do not have any specific data points, they have been in discussions with colleagues from the Indian Health Service (IHS) and CDC's Office of Tribal Affairs and Strategic Alliances (OTASA) that works with the agency's tribal partners and are continuing to receive feedback. These clinical considerations are being proposed and a VFC vote was planned during this meeting, but there are always opportunities to receive more feedback.

Dr. Clark (IHS) reported that the IHS is in the process of evaluating the logistical implications of this recommendation for the IHS system of care, including federal, tribal, and urban programs. This is a high priority given the increased risk to the IHS's patient population.

Dr. Poehling emphasized that as Dr. Peacock mentioned in her presentation, careful thought must be given to the potential for an RSV vaccine recommendation for pregnant persons. This would be the first time that a vaccine given to a pregnant person would make a modification necessary in the vaccines that person's child receives. This has major implications for IISs and in terms of avoiding record scatter and duplication of efforts.

Dr. Lee pointed out that this is a new era with regard to thinking about prevention more broadly. In terms of innovation, this is an important step forward for prevention activities. However, implementation does take time and there are a lot of complexities with regard to this type of product. This is one of the first products the ACIP is considering in this way. Everyone must work together to consider how to set up implementation in systems across various settings. While this is going to be difficult in the short-term, this product will open up many more opportunities and will have major benefits in the long-term. Recognizing that the numbers would be small, she asked whether there are any data on immunocompromised populations to understand whether at 150 days, the level of immunity is durable.

Dr. Jones indicated that the company had a small safety trial in an immunocompromised population and called upon Sanofi Vaccines to comment further.

Dr. Christian Felter, Sanofi, reported that the immunocompromised study is ongoing. While there are no additional data at this point, the pharmacokinetics of nirsevimab is consistent across populations. Significant differences have not been observed in any populations. It is known that the duration of protection lasts at least 50 days and there are signals that it may last longer than that.

Ms. Rebecca Coyle (AIRA) pointed out that Dr. Peaccock did a fabulous job of outlining many of the challenges for IISs. About 80% of the data come from EHRs and pharmacy systems, which is a very heterogeneous group of systems. She cautioned that there will be challenges with EHRs in terms of how quickly EHRs can adopt this and enter it into their systems to be able to send it to an IIS.

Proposed Clinical Consideration Updates for Nirsevimab

Jefferson Jones, MD, MPH, FAAP, CDR, USPHS (CDC/NCIRD Co-lead, Maternal/Pediatric RSV WG) reviewed proposed clinical consideration updates for nirsevimab. For the timing of nirsevimab, providers should target administration in the first week of life for infants born shortly before the start of the RSV season for infants <8 months of age and shortly before the start of the RSV season for children 8–19 months of age who are at increased risk of severe RSV disease. While the optimal timing for nirsevimab administration is shortly before the season, it may be given at any time during the RSV season for age-eligible infants and children who have not yet received a dose. Based on pre-pandemic patterns, this means nirsevimab could be administered in most of the continental US from October through the end of March.

Because the timing of the onset, peak, and decline of RSV activity may vary by jurisdiction, providers can adjust administration schedules based on local epidemiology. For infants born shortly before or during the RSV season, nirsevimab should be administered within 1 week of birth. Administration can be during the birth hospitalization or in the outpatient setting. Infants with prolonged birth hospitalizations due to prematurity or other causes should receive nirsevimab shortly before or promptly after discharge. Tropical climates may have seasonality that differs from most of the continental US or that is unpredictable. This may include Southern Florida, Hawaii, Guam, Puerto Rico, the US Virgin Islands (USVI), and the US-affiliated Pacific Islands. In Alaska, RSV seasonality is less predictable, and the duration of RSV seasons is often longer than the national average. Providers in these jurisdictions should consult state, local, or territorial guidance on the timing of nirsevimab administration.

In accordance with CDC's general best practices for immunizations, simultaneous administration of nirsevimab with age-appropriate vaccines is recommended. In clinical trials, when nirsevimab was given concomitantly with routine childhood vaccines, the safety and reactogenicity profile of the co-administered regimen was similar to the childhood vaccines given alone.[23] When co-administered, nirsevimab is not expected to interfere with the immune response to other childhood immunizations.[24]

Children 8–19 months of age are recommended to receive nirsevimab when entering their second RSV season because of increased risk of severe disease. This includes children with CLD 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 with 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; and AI/AN children.

Nirsevimab is recommended for infants <8 months of age born during or entering their first RSV season, including those recommended to received palivizumab by the AAP.[25] Nirsevimab is recommended for children 8–19 months of age with increased risk of severe RSV disease and entering their second RSV season, including those recommended to receive palivizumab by

[23] https://www.accessdata.fda.gov/spl/data/2f08fa60-f674-432d-801b-1f9514bd9b39/2f08fa60-f674-432d-801b-1f9514bd9b39.xml
[24] Espocito Front Immunol. 2021 Aug 11;12:708939
[25] American Academy of Pediatrics. Committee on Infectious Diseases [Respiratory Syncytial Virus.] In: Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, eds. Red Book: 2021 Report of the Committee on Infectious Diseases. Itasca, IL: American Academy of Pediatrics, 2021.

AAP. Per the FDA label, children who have received nirsevimab should not receive palivizumab for the same RSV season.[26]

In terms of precautions and contraindications, providers administering nirsevimab should follow ACIP's general practice guidelines for immunization. Nirsevimab should not be administered to persons with a history of severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a product component. As mentioned in an earlier presentation, AEs after administration of nirsevimab without co-administration with any vaccine can be reported to MedWatch online at www.fda.gov/medwatch or by phone at 1-800-FDA-1088. AEs or suspected AEs events following co-administration of nirsevimab with any vaccine should be reported to the VAERS and additional reporting of the same AE to MedWatch is not needed.

WG Considerations / Proposed Recommendations

Jefferson Jones, MD, MPH, FAAP, CDR, USPHS (CDC/NCIRD Co-lead, Maternal/Pediatric RSV WG) summarized WG considerations and presented the proposed recommendations. In terms of safety monitoring for nirsevimab, FDA will monitor safety reports submitted by patients, providers, and the manufacturer to the FDA Adverse Event Reporting System (FAERS) and VAERS. FDA will monitor other data sources, including the scientific literature, the applicant's periodic safety reports, ongoing clinical studies, and potential other sources (e.g., medical billing and EHRs). CDC will monitor reports submitted to VAERS that involve simultaneous administration of nirsevimab with childhood vaccines and also will monitor the safety of nirsevimab in the Vaccine Safety Datalink (VSD). CDC will leverage existing vaccine effectiveness platforms. The NVSN is an active surveillance system for acute respiratory infection (ARI) at 7 pediatric medical centers that can assess effectiveness against outpatient and ED visits and hospitalizations. This platform can capture nirsevimab receipt through parent interviews, medical record reviews at the primary care provider and birth hospital, and through state IISs. Virtual SARS-CoV-2, Influenza, or other Respiratory Viruses Network (VISION) is a multi-site EHR-based network that can assess effectiveness against ED and urgent care visits, hospitalization, and critical illness. Nirsevimab effectiveness analyses will be limited to integrated healthcare system sites that will have more complete capture of nirsevimab receipt through IIS linkage and claims data. CDC will monitor nirsevimab effectiveness throughout the season, but end-of-season estimates likely will be the most accurate. The power to estimate effectiveness depends on nirsevimab uptake and RSV incidence.

RSV genomic surveillance also will be important. Mutations resulting in nirsevimab resistance have been rarely reported.[27] Sanofi and AstraZeneca are sponsoring INFORM-RSV, a global genomic surveillance study in children less than 5 years, to monitor evolution of RSV strains, F-protein antigenic sites, and their relationships with clinical features of RSV disease.[28] CDC is planning genomic surveillance of pediatric and adult RSV specimens, including whole genomic surveillance. This surveillance will monitor for changes in the F-protein that might result in nirsevimab resistance.

For the indication for infants <8 months of age born during or entering the RSV season, the WG found that nirsevimab is safe and effective in reducing the risk of RSV disease, including hospitalization due to RSV. The WG shared the concerns as outlined in the presentation by Dr. Peacock on implementation considerations. The WG felt that the use of nirsevimab would be a reasonable and efficient allocation of resources, but many WG members prefer a lower cost per

[26] https://www.accessdata.fda.gov/spl/data/2f08fa60-f674-432d-801b-1f9514bd9b39/2f08fa60-f674-432d-801b-1f9514bd9b39.xml
[27] Ahani et al. Nat Comm 2023 14:4347; and Wilkins et al. Lancet Infect Dis 2023; 23: 856–66
[28] Tabor 2020 Dec 17;59(1):e01828-20

dose. The WG felt that there were limited efficacy and safety data for the indication for children 8─19 months of who had increased risk of severe RSV disease and were entering their second RSV season. Additionally, there were limited data on the burden of severe disease in the second RSV season for children with chronic conditions. Therefore, the WG supported the recommendation of nirsevimab being given to children 8─19 months of age entering their second RSV season for those who are recommended for palivizumab by the AAP in their second RSV season and for AI/AN children as described in clinical considerations. The following is the proposed ACIP voting language:

- ❑ Infants aged <8 months born during or entering their first RSV season are recommended to receive one dose of nirsevimab (50 mg for infants <5 kg and 100 mg for infants ≥5 kg)

- ❑ Children aged 8–19 months who are at increased risk of severe RSV disease and entering their second RSV season are recommended to receive one dose of nirsevimab (200 mg)

Discussion Points

Referring to Slide 5, Dr. Loehr requested clarification that nirsevimab will not interfere with measles, mumps, and rubella (MMR) and varicella vaccines. In general, there are considerations for immunoglobulins and live vaccines. In addition, he asked for clarification about when to start nirsevimab.

Dr. Jones replied that the WG had a presentation and discussion on this. The data are fairly limited on nirsevimab being co-administered with vaccines and immunogenicity. Per discussions with expert input from CDC immunologists, the risk appears to be low. Per the FDA label and CDC's general best practices for immunization, the WG felt it appropriate to recommend co-administration of nirsevimab for age-appropriate vaccines.

Dr. Natalie Thornburg emphasized that there are not a lot of data on co-administration of monoclonal antibody prophylaxis with childhood immunization, given that they are not yet widely used. There are some data for infants who have received palivizumab, with no indication that they interfere with vaccine responses. Most of the data that are available for co-administration of vaccines or inhibition of vaccines deal with live-attenuated vaccines. Obviously, this product is not a vaccine. It is a passive immunization product for which the mechanisms of inhibitions are not relevant.

In terms of when to start nirsevimab, Dr. Jones reiterated that the trials showed an efficacy of 150 days and that there were some data suggesting that efficacy may last longer than 150 days. It is important to try to time administration between October through March, which is shortly before the RSV season.

Dr. Poehling requested input from FDA or Dr. Shimabukuro about how they would collaborate with the FAERS and VAERS systems in terms of ensuring that everything is captured and there is a complete picture.

Dr. Shimabukuro responded that first and foremost, CDC works closely with FDA to monitor vaccine safety. For nirsevimab, CDC has worked closely with the Center for Drug Evaluation and Research (CDER), the Center for Biologics and Research (CBER), and NCIRD to develop a comprehensive monitoring approach. As mentioned, the home for possible AEs involving

nirsevimab will be the FDA's FAERS system. Reports involving nirsevimab and other vaccines will be sent to VAERS. There is a process for addressing mis-routed reports.

Dr. Poehling stressed that the cost per dose was weighing heavily on her. While she understood that these have been expensive studies and the company's process needs to compensate for that work, she remained concerned about equity. Hospitals will have 1 week to administer this and there will be a cost differential for a baby born in July versus one born in October. Therefore, it seemed prudent to have private practices administer it versus the hospital. Also exacerbating this issue is the rural-urban differential in that locations in rural America would not have access to this.

Dr. Sanchez emphasized that if nothing else was learned from COVID-19, it was that no one knows when the RSV seasons will start this year. Continued monitoring of local epidemiology will help to understand when the optimal time will be to start administering nirsevimab. In terms of implementation issues, this is a new medication that will be given to every infant <8 months of age. However, the benefit will be huge. The main issue for him is whether they will be able to get a supply for the coming season. Those who have been administering palivizumab really want nirsevimab. While there will be issues of implementation, he does not think they will be insurmountable.

Dr. Talbot expressed concern about nirsevimab being referred to interchangeably as a drug and therapeutic even though ACIP is treating it as a vaccine. For the purpose of monitoring, considerable effort needs to be made to term this one way to prevent some of the complications that will occur.

Dr. Daley noted that he had received some detailed questions from colleagues, such as whether it would be considered an administration error if a child who is 8.5 months old and is not in a high-risk group presents in December during a bad RSV season and receives nirsevimab. He also stressed the importance of communication to providers about what to say when parents ask whether nirsevimab is a vaccine. He feels like those conversations are going to come up thousands of times, and it would help providers to be able to answer this question in a transparent, honest, and succinct way.

Dr. Jones indicated that the current recommendation is that nirsevimab is recommended for children less than 8 months of age. Having high-risk conditions is an exception. Children 8–19 months who are at increased risk of severe RSV disease and entering their second RSV season are recommended to receive one 200 mg dose of nirsevimab. CDC is working on education and other materials to help providers and webinars and updated websites are planned for the near future.

Based on the available evidence, Ms. McNally requested more information about whether there is any reason to believe that there would be harm to an infant if there was maternal vaccination and nirsevimab was given to the infant. In addition, she asked whether a Vaccine Information Statement (VIS) sheet would be provided to parents of infants receiving nirsevimab and what the adjudication mechanism would be for claims of potential injury from nirsevimab.

Dr. Jones noted that questions referring to maternal vaccine are generally deferred pending FDA licensure of a maternal vaccine. Maternal antibody from infection is certainly present in infants, and nirsevimab was likely given to infants born to mothers who were infected recently or during pregnancy. The consensus is that there is not thought to be any risk from that.

Dr. Peacock indicated that there would be something similar to VIS sheets. Because nirsevimab is not a vaccine, the sheet will be called something else but will look similar.

Dr. Grimes from the Health Resources and Services Administration (HRSA) indicated that for vaccines, the criteria for coverage is typically for routinely administered vaccines and adjudication is through the national Vaccine Injury Compensation Program (VICP). That is when a vaccine has been recommended by CDC for routine administration to children or pregnant women, subject to an excise tax by federal law, and added to the Vaccine Injury Table by the Secretary of HHS. The Vaccine Act that governs the VICP does not define "vaccine." Of those 3 criteria are met, there is potential route for coverage within the VICP. The VICP and VFC programs are separate. Inclusion in the VFC would not trigger inclusion in the VICP or vice versa.

Dr. Lee praised the work that CDC is doing with AHIP, but expressed concern about the financing of prevention. While nirsevimab is a fantastic product that has not been available previously and that has many benefits in terms of the durability of protection compared to other antibody products that have been used previously for high-risk children, there are challenges in the ambulatory setting. Pediatricians, family practice doctors, and birthing hospitals essentially have been asked to pay upfront for the cost of products, including vaccines, and then hope for adequate reimbursement. Pediatricians and family practitioners in small practices will be bearing the brunt the upfront cost and potentially losing money to be able to deliver these preventive interventions. In terms of thinking about more innovative strategies for prevention, she put out a general plea for reconsideration of where the risk will occur. The high cost is a burden and disincentive for getting people to do the right thing. Dr. Lee emphasized the critical importance of aligning incentives and securing the ability to ensure adequate reimbursement, even at-cost reimbursement.

Dr. Grubb (AHIP) stressed that while activities would depend upon what the ACIP recommends, compliance issues would be very similar to compliance issues for any other vaccine. She noted that other members of AHIP had joined the meeting, and they would take the input back to AHIP. This is going to involve a multi-layered response because there are many questions with regard to issues, such as coding. AHIP looks forward to working with CDC and ACIP on these issues.

Dr. Kotton stressed that because nirsevimab is passive immunization, there could be issues entering administration into the immunization record and other places. For instance, it was difficult to get Evusheld into the immunization records in Epic.

Dr. Jones replied that CDC is aware of this issue and continues to work with national and internal partners to address it.

Dr. Poehling said that while she liked the voting language that was presented and recognized that it was time-limited, ACIP was in a difficult position because FDA was currently reviewing a maternal vaccine. The way she interpreted the language was that if the maternal vaccine is subsequently approved, both nirsevimab and the maternal vaccine would be given. She stressed that she was not ready to make that decision during this meeting and requested input on the WG's thoughts about how they thought the ACIP should address this. For example, would ACIP have to meet again to vote on maternal vaccine.

Dr. Jones reiterated that the WG would revisit the recommendation at such time that a maternal vaccine is licensed by FDA.

Dr. Lee confirmed that the ACIP would have to convene again to vote on a maternal RSV vaccine and discuss any implications related to the use of nirsevimab at that time.

Dr. Fryhofer (AMA) said that speaking as a practicing physician, she applauded the WG's recommendation to include giving a dose of nirsevimab to AI/AN children in their second RSV season. Based on the presentations, the rate of RSV hospitalization for these children is 4 to 10 times that of the general population. It also is known that the maternal mortality rates for their mothers are over twice as high as rates for white women. ACIP and practicing physicians often hear about VAERS, but are not as familiar with FAERS. She was relieved to hear that CDC and FDA work so closely together to make sure that any reported concerns will be made available to the appropriate agency. In terms of CPT coding, she attended a meeting earlier in the year as AMA Board Chair of the AMA CPT Advisory Committee. The nuances discussed throughout the day in the ACIP meeting between vaccines and passive immunizations like nirsevimab have been anticipated and the issues are already being discussed. And as pointed out in Dr. Peacock's presentation, the issue about it not being eligible for standalone counseling is an important one that she will share with the AMA Advisory Committee.

Dr. Whitley-Williams (NMA) applauded the WG and presenters for their careful considerations and deliberations. She noted that she just returned from the national meeting of the National Medical Association (NMA), which is comprised predominantly of African-American physicians. The presentations during that meeting included a talk on RSV vaccines and another on nirsevimab, which were well-received. In attendance were pediatricians, physicians, academicians, and inner city and rural providers. Concerns were raised about how nirsevimab would be recorded and that registries may not be available in the rural areas. She urged that any communications emphasize the importance of the first of nirsevimab being given in the hospital prior to discharge, particularly in rural areas where nirsevimab may not be included as part of the armamentarium of medications. Also important is clear communication that this is a biologic not a vaccine.

Dr. Loehr said he was looking forward to 2 years from now when this was all in the past. This is a spectacular advancement that is going to help families and offices and keep children out of the hospital that will be covered by insurance 2 years from now and all implementation activities will be in place. While there will be growing pains, he emphasized that they should not lose sight of how important this advancement is. With regard to the vote language in front of the ACIP, he favored the first proposal completely. He was wrestling with the second proposal, given that it would be a very expensive proposal recommendation with a lot of extrapolations. However, he thought it would promote equity. While he had not decided yet how he would vote, he wanted to express his hesitation about the second proposal.

In terms of the second proposal, Dr. Long pointed out that the groups who are part of the AAP recommendations are already receiving palivizumab, which would be much more expensive than nirsevimab. The only expansion of the group would be to include AI/AN children who are at 6 to 10 times higher risk for severe disease and hospitalization than the general population. The WG thinks that this would be a very small group of children of about 1% of the population of children 8─19 months. These children already are costing a lot of money because of palivizumab and there are not sufficient data to say that the indication for passive protection should be removed for those who are already receiving palivizumab.

Dr. Jones added that the second indication is expected to be cost-saving for children who currently are recommended by AAP to receive palivizumab. Another consideration for the AI/AN Children is that there are many geographic areas where children who get severe RSV require emergency air transport to receive appropriate medical care, which was another consideration of the WG.

Ms. Howell indicated that she was representing the Association of Immunization Managers (AIM), which is a membership association comprised of the 64 federally-funded state, territorial, and city health agencies that administer immunization programs at the local level that administer the VFC locally and oversee the implementation of IISs. As a group, AIM has been anticipating nirsevimab availability for a while and has been looking forward to planning assumptions and collaborating with CDC and others to overcome the challenges regarding implementation. She pointed out that there is a fee cap in the VFC for the administration of vaccines that are included in the VFC, and asked whether the fee cap also would apply to nirsevimab even though it is being classified as a drug and not a vaccine.

Ms. Hance, Centers for Medicare and Medicaid Services (CMS) indicated that because nirsevimab would be administered under the VFC program, the vaccine administration fee ceiling would have to apply. She explained that the ceiling is the amount a state Medicaid agency can reimburse a provider, and that a state Medicaid agency has the flexibility to set the rate up to that ceiling.

Dr. Poehling made a motion to approve the ACIP voting language as presented, which Dr. Sanchez seconded.

Dr. Hopkins (NFID) commented that the National Foundation for Infectious Diseases (NFID) has posted a number of educational materials on RSV and that following the actions of the ACIP on nirsevimab, they will continue to provide educational materials supporting providers, patients, and families going forward.

Dr. Lee asked whether there is a minimum interval for children who might be eligible in their second RSV season, such as a child who is born at the end of season one but who a practitioner wants to protect through season two.

Dr. Jones responded that there is no minimal interval. Based on pre-pandemic seasonality, high-risk infants born at the end of March would be a little over 6 months before the beginning of October when the second RSV season would start.

In terms of equity, Dr. Daley pointed out that there is a risk of making health equity worse or increasing inequity with a new product that has so many challenges. While there appears to be a great opportunity to improve health equity with nirsevimab, it is extremely important to consider those who are coming from a more disadvantaged situation, such as living in a rural area of the country. Regarding implementation, he asked Dr. Peacock to speak to how the ACIP could help with some of the challenges she raised in her presentation and whether there were any other issues the committee should discuss during this public session.

Dr. O'Leary, Pediatric Infectious Diseases Society (PIDS), noted that many of the PIDS concerns were addressed during this session and expressed excitement about the potential to prevent many hospitalizations. PIDS is working internally and with its partners in the federal, state, and local governments to focus on the issue of equity as this product is rolled out. AAP

also is working on potential implementation issues and barriers, including communications and crafting implementation guidance for its partners.

Dr. Peacock expressed appreciation for all of the comments and the recognition that implementation is going to be challenging. It is important to remember that this is a new and very exciting product, and this is going to be a transitionary season. She captured a list of important issues raised related to insurance, coding, equity, et cetera. The VFC is an example of a program that has successfully addressed health equity issues over the last 30 years. It provides access not only to children who are on Medicaid, but also children who are under-insured or uninsured and AI/AN children. All of these considerations are very important, and it will be necessary to work hand-in-hand with vaccine providers, physicians, nurses, health departments, and others who are involved to ensure that as much access as possible is provided during the initial implementation and moving forward. It appears that this season may be different from the last couple of years. As a reminder, hepatitis B began with a different recommendation and eventually became given regularly in hospitals. In the near-term with the rollout, more nirsevimab may be given in the outpatient setting. It is important to take a step back and appreciate that this is an amazing time in terms of RSV.

Vaccines for Children Resolution

Jeannie Santoli, MD, MPH (CDC/NCIRD) explained that the purpose of this resolution was to add the monoclonal antibody preparation nirsevimab for infants to prevent RSV disease to the VFC program. The first eligible group is infants <8 months of age born during or entering their first RSV season. The second eligible group is children 8─19 months of age as noted in Table 1 who are at increased risk of severe RSV disease and entering their second RSV season. Table 1 describes children at increased risk of severe RSV disease and Table 2 explains the recommended immunization schedule and dosage intervals.

For recommended dosage, readers are referred to the product package insert. For contraindications and precautions, readers are referred to the package inserts available at: https://www.accessdata.fda.gov/spl/data/2f08fa60-f674-432d-801b-1f9514bd9b39/2f08fa60-f674-432d-801b-1f9514bd9b39.xml.

The following standard statement regarding updates based on published documents also is included in the resolution:

[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.]

Discussion Points

Referring to Slide 10, Dr. Daley suggested working on the wording of the timing. While he thought they knew what was intended, it could be clearer.

Dr. Kotton's requested further clarification of what was meant by "children with severe immunocompromised" meant and asked whether further definitions would be provided.

Dr. Jones replied that initially, specific examples were included. However, there was concern that if the recommendations were overly prescriptive, it may miss others who would qualify.

Dr. Long added that those caring for immunocompromised patients are the best ones to make these decisions.

Dr. Kotton advocated for clinicians to have some type of guidance, but then leave a more open clause like, “as well as other children deemed to be severely immunocompromised by their care team.” She stressed that clinicians have been clamoring for fairly specific guidance from the CDC regarding immunization recommendations, as it can be hard to fully understand what the recommendations mean. From her perspective, further guidance could be useful. Outstanding guidance was provided by the CDC during the COVID-19 pandemic regarding the definition of who is moderately to severely immunocompromised, which she thought changed the field for the better. She suggested including additional input.

Dr. Lee agreed that it would be extremely beneficial to have at least some “big picture” guidance on that in the Clinical Considerations.

Ms. Goode (APhA) requested clarification on the second vote language about whether someone receiving a dose in the first season before 8 months of age should receive a second dose in the second season.

Dr. Jones clarified the recommendations were independent, with the second pertaining to children at increased risk. The FDA label specifies that those who received palivizumab in their first RSV season can receive nirsevimab in their second RSV season. There are no disqualifications for the second RSV season related to what did or did not happen in the first RSV season.

Dr. Long stressed that this was somewhat confusing, but the WG wanted to be sure not to use the words “second dose” so that the recommendation would not be misinterpreted as 2 doses being needed.

Dr. Poehling made a motion to accept the VFC Resolution as proposed with the clarification in the table as noted during the discussion. Dr. Sanchez seconded the motion.

PUBLIC COMMENTS

Overview

The floor was opened for public comment on August 3, 2023 at 2:00 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-2023-0063. Visit http://www.regulations.gov for access to the docket or to submit comments or read background documents and comments received.

Public Comments

Ms. Susan Hepworth
National Coalition for Infant Health

Thank you so much and thank you for this opportunity to make these comments on behalf of the National Coalition for Infant Health. We are made up of more than 200 professional, clinical, community health, and family support organizations—all with the focus of improving the lives of all infants and their families. I just first want to thank the committee for prioritizing this review of this immunization. I know the committee has undertaken so much over the last few years throughout the public health emergency, so we appreciate your prioritizing this review among what I know are many other competing priorities. We are incredibly pleased and want to thank you for voting in favor of the VFC resolution. This is a huge step toward ensuring equitable access and reducing the burden of RSV. I would like to make one additional comment and that is the coalition's strong support of equitable and timely access to this prevention in hospitals, birthing centers, and provider settings. I know this was something that was included in a recent letter from the American Academy of Pediatrics as well. With strong, clear guidance and recommendations from the CDC for babies to receive this new immunization prior to being discharged from the hospital, all babies will have the opportunity to be immunized and protected before they even leave the hospital setting. I think this measure is what is truly going to ensure equitable access for all infants, and it is also going to ensure a major reduction in the burden of RSV. As has been spoken about in prior meetings, the burden of RSV is multifaceted. It is not just medical, but it is emotional, and it is financial for families as well. With clear guidance, I think we will be able to ensure that we will not have further existing health disparities. I just want to thank you all for what you do to protect and improve the health and safety of our nation's infants and children. Thank you for the opportunity to give these comments.

Laura Burns
Transplant Recipients and Immunocompromised Patient Advocacy Group

My name is Laura Burns and I represent TRAIPAG, Transplant Recipient and Immunocompromised Patient Advocacy Group. Being immunocompromised and vulnerable to disease, we have a deep sense of kinship with the infants so vulnerable to RSV. We urge you to protect these children and to recommend nirsevimab for RSV prevention. It has been approved by the FDA and, with your vote, it will be covered by insurance as required under the ACA. But insurance only covers about 50% of babies, so ACIP members, we intrigue you to resolve that nirsevimab be added to the Vaccines for Children program so that all babies can be protected. Nirsevimab would be the first passive immunization product to be included in the CDC Immunization Schedule, but we think that there is little distinction to be made between active and passive immunization. The key is what prevents disease. Indeed, Congress sees it this way, too. Under 26 USC 4132, the term "vaccine" means "any substance designed to be administered to a human being for the prevention of one or more diseases." Nirsevimab fits that bill. Looking to the future, TRAIPAG anticipates you will be faced with a similar decision greatly affecting our health. Our group represents people of all ages, from people with blood cancers, autoimmune diseases, organ transplants. Since most of us have low or no response to vaccines, in all fairness, we need alternative preventions. A number of monoclonal antibodies, for example, are in development for the prevention of COVID: Invivyd, AstraZeneca SUPERNOVA 3152. Also, antivirals. If one or more of them "passes muster" with the FDA, we hope that ACP will show the same deliberative care for vulnerable adults that you're showing today for infants and that you recommend passive immunizations when they work. This in turn would guarantee that insurance will cover it. Likewise, as there is no vaccines for adults

program yet, the CDC should include whichever preventions work, active or passive, in both the bridge access and the VFC programs. This will ensure equity and that everyone, child or adult, will have affordable access to life-saving immunizations at least through 2024. Thinking back, I want you to know that Evusheld was a godsend for us and for our families and friends who got to be with us. So was REGEN-COV for post-exposure prophylaxis (PEP) before that. Unfortunately, not all of us had access. With commercialization, equitable access is an even larger issue, but one you should tackle. If you will indulge me for just a few seconds, Dr. Lee, we were truly heartened by your comments today earlier about how groundbreaking this step is and how it opens up new avenues for preventing disease in the immunocompromised. While it may be initially complicated, it will be well worth working through those issues. Thank you and thank you all very, very much for all you do. We urge you to vote “yes” on all of these.

Claire Hannan
Executive Director
Association of Immunization Managers

Good afternoon and thank you for the opportunity to comment on the potential implementation of the RSV monoclonal antibody, nirsevimab. We are excited that this groundbreaking opportunity to protect infants from RSV. I’m Claire Hannan, Executive Director of the Association of Immunization Managers, or AIM. AIM is a membership association whose members direct the immunization programs in the 64 federally-funded state, territorial, and local health agencies. In partnerships with CDC, these jurisdictions administer the Vaccines for Children, or VFC, program and work to assure protection of the population through vaccination. Last week, we polled jurisdictions about their ability to incorporate nirsevimab into their programs, including the Vaccines for Children program, and you’ve discussed this mightily today already. Among respondents, 52% report that their immunization information systems can document nirsevimab, 22% cannot, and 26% report that it is unknown. Reported challenges include lack of funding for the IIS vendor and lack of information on coding. 68% report that their IIS can be used for ordering nirsevimab in the VFC program, 14% that their IIS cannot be used, and 18% report unknown. Additional time and funding were the cited barriers to incorporate into IIS ordering applications. Additional challenges cited in the poll include the lack of participation of birthing hospitals in the VFC program, concern about data exchange between electronic health records and IIS, and lack of adequate time and guidance to prepare. The poll demonstrates that time and funding are needed to incorporate this new product into VFC and other existing programs. However, the jurisdictions have not received guidance or assumptions to prepare for potential recommendation, such as the information needed to incorporate nirsevimab into VFC ordering applications and packaging and storage information. Jurisdictions have not been able to hold discussions with CDC or IIS vendors to address challenges with coding and tracking. What is most concerning to the incorporation of this potentially life-saving product into existing childhood programs is that jurisdictions have suffered an average loss of 20% in funding for their IIS due to rescission of COVID funds. ACIP is holding this special meeting in August in order to vote on this life-saving product in time for the upcoming flu and RSV season. However, jurisdictions responsible for implementation have not been involved in the planning discussions. The lack of federal communication to and coordination with jurisdiction immunization programs continues to impact the ability of immunization program managers to roll out new and important products with maximum impact. They cannot be expected to deploy critical products such as nirsevimab without the information and time needed to execute these programs. We urge our federal partners to find ways to work with jurisdictions and provide planning assumptions earlier in the process and to share critical information as it becomes available. Thank you so much for the opportunity to comment today.

VOTES

Dr. Grace Lee (ACIP Chair) pointed out that while the votes for the recommendations were moved and seconded together, the ACIP would vote on each proposed recommendation and the VFC Resolution separately:

Vote #1 RSV Maternal/Pediatric Recommendations

Infants aged <8 months born during or entering their first RSV season are recommended to receive one dose of nirsevimab (50 mg for infants <5 kg and 100 mg for infants ≥5 kg).

Vote #2 RSV Maternal/Pediatric Recommendations

Children aged 8–19 months who are at increased risk of severe RSV disease and entering their second RSV season are recommended to receive one dose of nirsevimab (200 mg).

Vote #3: VFC Resolution: RSV Maternal/Pediatric

Approve the Vaccines for Children (VFC) Resolution for nirsevimab.

Motion/Vote #1 RSV Maternal/Pediatric

Dr. Poehling made a motion to amend the proposed Vote #1 recommendation stating, “Infants aged <8 months born during or entering their first RSV season are recommended to receive one dose of nirsevimab (50 mg for infants <5 kg and 100 mg for infants ≥5 kg). Dr. Sanchez seconded the motion. No COIs were declared. The motion carried with 10 affirmative votes, 0 negative votes, and 0 abstentions. The disposition of the vote was as follows:

10 Favored: Bahta, Chen, Daley, Lee, Loehr, Long, McNally, Poehling, Sanchez, Talbot
0 Opposed: N/A
0 Abstained: N/A

Motion/Vote #2 RSV Maternal/Pediatric

Dr. Poehling made a motion to amend the proposed Vote #2 recommendation stating, “Children aged 8–19 months who are at increased risk of severe RSV disease and entering their second RSV season are recommended to receive one dose of nirsevimab (200 mg).” Dr. Sanchez seconded the motion. No COIs were declared. The motion carried with 10 affirmative votes, 0 negative votes, and 0 abstentions. The disposition of the vote was as follows:

10 Favored: Bahta, Chen, Daley, Lee, Loehr, Long, McNally, Poehling, Sanchez, Talbot
0 Opposed: N/A
0 Abstained: N/A

Motion/Vote #3: VFC Resolution RSV Maternal/Pediatric

Dr. Poehling made a motion to amend the proposed Vote #3 recommendation for the VFC Resolution stating, "Approve the Vaccines for Children (VFC) Resolution for nirsevimab." Dr. Sanchez seconded the motion. No COIs were declared. The motion carried with 11 affirmative votes, 0 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, Talbot
0 Opposed: N/A
0 Abstained: N/A

Discussion Points

Dr. Talbot expressed her excitement about nirsevimab, which she thinks will be incredible and life-changing. She emphasized that as had been pointed out, there are a lot of logistics to work out.

Dr. Long recognized the remarkable, committed work of the WG who engaged in many discussions about all of the issues raised during this meeting. She felt that the WG thoroughly dealt with what they could based on the available data and their best assumptions for the unknowns. This is a milestone in that it is the first antibody protection against the remarkably high remaining burden of disease in children, so parents should be relieved that they will not have to be concerned about the likelihood that their children could be hospitalized with RSV disease. As with every breakthrough, there is the feeling of responsibility and the burden that this is the first time an antibody will be administered universally. All of the safeguards are in place and there have been no signals of AEs within the small trials that were conducted. The WG also does not believe there is any biologic plausibility that there will be any interference with any immunization or live virus vaccine. The WG was extraordinarily disappointed with the price-setting of the manufacturer and wanted to assure the ACIP and public that should a maternal vaccine be licensed, the WG will address the cost issue of that product as well.

Dr. Sanchez agreed that this is great and exciting news for a product that everyone has been eagerly awaiting. There has been considerable experience with palivizumab, which has to be given monthly and has high costs as well. Practitioners have been waiting to be able to give safe and effective protection to every baby and this is fantastic news. While this is just the first step, it is an extremely important step in the right direction for the major public health problem of RSV.

Dr. Lee echoed all of the comments regarding what an amazing milestone this is, emphasized the importance of continuing to monitor ongoing effectiveness and safety, and pointed out the importance of the ACIP hearing updated presentations in the future to demonstrate that there is follow-up on these specific areas and the impact of implementation on equity. While she recognized that implementation is not necessarily the purview of the ACIP, how nirsevimab use gets implemented and its impact on equity may impact how the ACIP rethinks recommendations in the future. She expressed gratitude to the CDC team, the FDA team, the WG, and everyone else who has done a phenomenal job steering this through and getting this product to market.

Dr. Daley thank CDC colleagues for their work on getting the ACIP to the point at which they could vote on a VFC Resolution for nirsevimab. He suspected that it was not an easy undertaking. He emphasized that the folks within CDC are tremendously devoted to public health and have been doing everything they could to make this happen. He recalled that during the February 2023 ACIP meeting, this looked somewhat more daunting, yet now they had voted on the recommendations and the VFC Resolution. He expressed gratitude to those who saw this as so important to include this in the VFC Program in order to provide the maximum public health benefit for RSV.

Dr. Romero added his thanks to the members of the ACIP and the WG for all of the deliberation and work they all put into this effort. This marked a historic event and he thought they would be able to look back in a short period of time and see what a major impact this vote has had on the health and well-being of children in the US. He said he thought this would mark one of the major accomplishments of the ACIP, for which he congratulated the committee.

CERTIFICATION

Upon reviewing the foregoing version of the August 3, 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

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LEE, Grace M, MD, MPH
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Term: 8/4/2021 – 6/30/2023

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Term: 12/24/2020 – 6/30/2024

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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
ACOG	American College of Obstetricians and Gynecologists
ACP	American College of Physicians
AE	Adverse Event
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
AMDAC	Antimicrobial Drug Advisory Committee
AOA	American Osteopathic Association
APhA	American Pharmacists Association
AR	Adverse Reaction
ARI	Acute Respiratory Illness
ASTHO	Association of State and Territorial Health Officers
AUC	Area Under the Curve
BLA	Biologics License Application
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research
CDS	Clinical Decision Support
CHD	Chronic Heart Disease
CLD	Chronic Lung Disease
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
DoD	Department of Defense
DSMB	Data Safety Monitoring Board
ED	Emergency Department
EHRs	Electronic Health Records
EMR	Electronic Medical Record
ET	Eastern Time
EtR	Evidence to Recommendation
FAERS	FDA Adverse Event Reporting System
FDA	Food and Drug Administration
GRADE	Grading of Recommendation Assessment, Development and Evaluation
HARMONIE	Hospitalized RSV Monoclonal Antibody Prevention
HCP	Healthcare Personnel / Providers
HHS	(Department of) Health and Human Services

HRSA	Health Resources and Services Administration
ICU	Intensive Care Unit
IDSA	Infectious Disease Society of America
IHS	Indian Health Service
IIS	Immunization Information System
IM	Intramuscular
IT	Information Technology
IVIG	Intravenous Immunoglobulin Therapy
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
MELODY	Prevention of Medically Attended Lower Respiratory Tract Infection Due to Respiratory Syncytial Virus in Healthy Late Preterm and Term Infants
mAbs	Monoclonal Antibodies
MMWR	*Morbidity and Mortality Weekly Report*
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
NFID	National Foundation for Infectious Diseases
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NMA	National Medical Association
NMD	Neuromuscular Disease
NVAC	National Vaccine Advisory Committee
NVPO	National Vaccine Program Office
NVSN	New Vaccine Surveillance Network
OIDP	Office of Infectious Disease and HIV/AIDS Policy
OTASA	Office of Tribal Affairs and Strategic Alliances
PCP	Primary Care Provider/Practitioner
PCR	Polymerase Chain Reaction
PEP	Post-Exposure Prophylaxis
PHAC	Public Health Agency Canada
PICO	Population, Intervention, Comparison, Outcomes
PIDS	Pediatric Infectious Disease Society
QALY	Quality-Adjusted Life Year
RCT	Randomized Controlled Trial
SAB	Spontaneous Abortion
SAE	Serious Adverse Event
SAHM	Society for Adolescent Health and Medicine
SHEA	Society for Healthcare Epidemiology of America
SME	Subject Matter Expert
UK	United Kingdom
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
VICP	National Vaccine Injury Compensation Program
VIS	Vaccine Information Statement
VISION	Virtual SARS-CoV-2, Influenza, or Other Respiratory Viruses Network
VSD	Vaccine Safety Datalink
WG	Work Group