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Opening Remarks: Call to Order and Welcome

00:10:14 Dr. Monto: Good morning. I'm Arnold Monto of the University of Michigan, and it is my pleasure and honor to welcome you all to the 191st meeting of the Vaccines and Related Biological Products Advisory Committee of the Center for Biologics Evaluation and Research. At this meeting, the topic for open discussion will be the Committee will meet in open session to discuss and choose and make recommendations on the strained composition of influenza virus vaccines for use in the United States during the 2026-2027 influenza season. And I'd like to initially remind the participants that when they speak, not only should they raise their hands, but they should then turn on their audio and video so they can be both seen and heard. Now, I will read initially a portion of the Sunshine Act statement that applies to this sort of a meeting.

00:11:51 For topics such as those being discussed at this meeting, there are often a variety of opinions, some of which are quite strongly held. Our goal is that the meeting will be a fair and open forum for discussion of these issues, and that individuals can express their views without interruption. Thus, as a general reminder, individuals would be allowed to speak into the record only if recognized by the chairperson. This pretty much doesn't apply to virtual meetings. We look forward to a productive meeting. In the spirit of the Federal Advisory Committee Act and the government in the Sunshine Act, we ask that the Advisory Committee members take care that their conversations about the topic at hand take place in the open forum of the meeting. We are aware that members have the interest in speaking with FDA or other individuals during the meeting. However, FDA will refrain from

discussing the details of the meeting with the media until its conclusion, and that applies to the members. Also, the Committee is reminded to please refrain from discussing the meeting at any other time.

00:13:27 Over to Cicely Reese, who is the Designated Federal Officer, who will handle the roll call and various housekeeping issues. Cicely.

Administrative Announcements

00:13:42 Dr. Reese: Thank you, Dr. Monto. And good morning, everyone. My name is Cicely Reese, and it is my privilege to serve as a Designated Federal Officer for today's meeting of the Vaccines and Related Biological Products Advisory Committee. On behalf of the Food and Drug Administration, the Center for Biologics Evaluation and Research and the Committee, I am pleased to welcome everyone to today's virtual session. I would first like to extend my appreciation to our center leadership for their continued support of our Advisory Committee process. I would like to recognize Dr. Vinay Prasad and his Center Director and Deputy Center Director, Dr. Katherine Szarama, as well as the broader leadership team for their guidance and oversight. Their commitment to scientific integrity and public health underpins the important work of this Committee.

00:14:32 I would also like to recognize the Office of Vaccines Research and Review, and that would include several members of the team. Dr. David Kaslow, who is the Director of the Office of Vaccines Research and Review, Dr. Jerry Weir, who is the Director of the Division of Viral Products. Dr. Sudhakar Agnihothram, who is the Associate Director of Office Regulatory Initiatives in OVRR. Dr. Zhiping Ye, who is the Chief and Principal

Investigator, Laboratory of Pediatric and Respiratory Viral Diseases at DVP. And Dr. Manju Joshi, who is a lead biologist with the Office of Compliance and Biologics Quality at the OVRR as well. I would also like to thank them for their scientific rigor reflected in this meeting. It is the result of sustained dedication and collaboration across teams.

00:15:33 In addition, I would like to extend special thanks to our colleagues across the Office of Operations and related offices whose partnerships make these meetings possible. This includes the disclosure and ethics teams, our web posting teams, and our virtual conference center and audiovisual staff. These teams work behind the scenes to ensure compliance, transparency, accessibility, and seamless technical execution. Without their coordination and responsiveness, the Advisory Committee process will not function as effectively as it does.

00:16:07 FDA also extends its sincere appreciation to the members of this Committee. We recognize that each member brings significant professional responsibilities outside of this forum, and we are grateful for their willingness to dedicate time and expertise to support FDA's mission. Their independent scientific insight and thoughtful deliberation are essential to the integrity of the advisory process. And finally, I would like to express our sincere appreciation to today's chairperson, acting chairperson for this meeting, Dr. Arnold Monto, for his leadership across the years. Chairing an FDA Advisory Committee requires careful preparation, steady judgment, and the ability to guide complex scientific discussion in a fair and balanced manner. We are grateful to Dr. Monto for his continued support to the Committee and to the public health mission we serve. To everyone who

contributed to the meeting forward, thank you for your professionalism and collaboration. Next slide, please.

00:17:12 For any press inquiries, please direct press or media inquiries for today's meeting to hhs.gov/press-room/index.html or dial 202-690-6343. The transcriptionists for today are Ms. Virginia Diaz and Ms. Mayra Angulo. We will be-- Next slide, please. Thank you.

00:17:44 We will begin today's meeting by taking a formal roll call for the Committee members. When I call your name, please turn on your camera, unmute, and introduce yourself by stating your first and last name, organization, your expertise or role. And when finished, you may turn off your camera so we may proceed to the next person. And please, see the slide displayed where we will begin with Dr. Arnold Monto, who is the acting chairperson, and we'll start with him, and then we'll go back up to the members.

Roll Call and Introduction of Committee

00:18:16 Dr. Monto: Good morning again. I'm Arnold Monto. I am the Francis Professor Emeritus at the University of Michigan School of Public Health, where I have been for a long time now, and I have studied over this time particularly influenza, but other respiratory infections and how they can be controlled and prevented.

00:18:45 Dr. Reese: Thank you, Dr. Monto. Dr. Durbin.

00:18:59 Dr. Durbin: Thank you. I was having difficulty unmuting. I'm Dr. Anna Durbin. I'm a Professor of International Health and the Director of the Center for Immunization Research at the Johns Hopkins Bloomberg School

of Public Health. I've been at Hopkins since 1999. I'm an internal medicine infectious diseases trained physician who specializes in vaccine trials, particularly against emerging infectious diseases, and also am very involved in the development of human challenge models. I do early phase vaccine clinical trials and efficacy studies. Thank you.

00:19:33 Dr. Reese: Thank you, Dr. Durbin. Dr. Gans.

00:19:37 Dr. Gans: Hi, I'm Dr. Hayley Gans, Pediatric Infectious Diseases at Stanford University. My areas of research focus are on immunology host pathogen interface, including vaccination in both normal and immunocompromised hosts, and also response to vaccines in the immunocompromised. Thank you.

00:20:03 Dr. Reese: Thank you, Dr. Gans. Dr. James Kollmar. Dr. James Kollmar. You may be on mute. Okay. We'll come back to Dr. Kollmar. He may be having some technical issues. Oh, here we are. We'll go on to Dr. Meyer. Thank you.

00:20:37 CAPT Meyer: Good morning. My name is Dr. Sarah Meyer. I'm a pediatrician, and I currently serve as the Acting Deputy Director for Science Implementation in the Immunization Services Division at CDC. And my areas of focus are pediatrics and vaccines.

00:20:51 Dr. Reese: Thank you, Dr. Captain Meyer. We will now hear from Dr. Berger.

00:21:01 Dr. Berger: Hi. I'm Adam Berger. I'm a geneticist with additional training in immunology. Currently, I am the Director of Clinical and Healthcare Research Policy for the National Institutes of Health. Thank you.

00:21:12 Dr. Reese: Thank you, Dr. Berger. We'll hear from Dr. El Sahly.

00:21:22 Dr. El Sahly: Good morning. My name is Hana El Sahly. I am an Adult Infectious Diseases Physician at Baylor College of Medicine, and my research focuses on clinical vaccine development.

00:21:35 Dr. Reese: Thank you, Dr. El Sahly. We'll hear from Dr. Perlman.

00:21:38 Dr. Perlman: Hi, I'm Stanley Perlman from the University of Iowa, Department of Microbiology Immunology. I'm a pediatric infectious diseases specialist and also an expert in coronaviruses.

00:21:50 Dr. Reese: Thank you, Dr. Perlman. Dr. Portnoy.

00:21:56 Dr. Portnoy: Good morning. I'm Dr. Jay Portnoy. I'm a Professor of Pediatrics at the University of Missouri, Kansas City School of Medicine. I'm also in the section of Allergy and Immunology at Children's Mercy Hospital in Kansas City, Missouri.

00:22:12 Dr. Reese: Thank you, Dr. Portnoy. We'll hear from Dr. Rubin.

00:22:19 Dr. Rubin: Hi, I'm Eric Rubin. I'm a Bacterial Geneticist and Infectious Disease Physician at Harvard, the Brigham Women's Hospital in the New England Journal of Medicine.

00:22:31 Dr. Reese: Thank you, Dr. Rubin. And we'll circle back to see if we have Dr. Kollmar. If not, we'll catch him during the break and have him introduced after the break, and we'll have him introduce himself. So, at this point, we'll have next slide, please.

Conflict of Interest Statement

00:22:55 I will now read the Conflict of Interest Statement for the meeting. The FDA is convening today's meeting of the Vaccines and Related Biological Products Advisory Committee or VRBPAC under the Federal Advisory Committee Act, FACA, of 1972. The VRBPAC will meet in open session to discuss and make recommendations on the strained composition of influenza virus vaccines for the United States during the 2026-2027 influenza season.

00:23:23 With the exception of the Industry Representative, the members of the Committee are either special or regular government employees and are subject to federal conflict of interest laws and regulations. Accordingly, FDA has reviewed the financial interests of the Committee members for compliance with federal ethics and conflicts of interest laws. We have screened the members for potential financial conflicts of interest related to today's meeting agenda, both their own interests and those that are imputed to them, including those of their spouses, minor children, and employers. Based on the agenda for today's meeting and all financial interests reported by the Committee members, FDA has determined that all members of this Committee are in compliance with federal ethics and conflict of interest laws. And as a result, no conflict of interest waivers under 18 U.S.C. § 208 have been issued in connection with this meeting.

00:24:18 Dr. Archana Chatterjee self-recused from this meeting. James Kollmar of Merck & Company is participating in this meeting as a Non-Voting Industry Representative acting on behalf of regulated industry. Consistent with Commissioner McCarry's April 17th, 2025 statement, FDA's only including

industry representatives in Advisory Committee meetings were required by statute.FDA is required to include an industry representative in today's meeting under 21 U.S.C. § 355N3C. Industry representatives are not appointed as special government employees, nor are they regular government employees. Industry representatives serve as non-voting members of the Committee. Non-voting industry representatives represent all regulated industries and not any association, company, product, or ingredient, and bring general industry perspective to the Committee. Under FDA regulations, although a non-voting member serves as in a representative capacity, the non-voting members shall exercise restraint in performing such functions and may not engage in unseemly advocacy or attempt to exert undue influence over the other members of the Committee. Dr. Jay Portnoy is serving as the acting Consumer Representative for the Committee. He is a special government employee.

00:25:43 There are speakers and guest speakers at today's meeting who will give a presentation to the Committee, answer questions from the Committee and hand the meeting back over to the chair. They will not participate in the Committee deliberations, render advice to FDA or vote. The speakers and guest speakers participating in this meeting are presenting the views of their professional societies, not their personal views. The following speakers as regular government employees have been screened and are clear to participate in today's meeting. Dr. Lisa Grohskopf and Dr. Rebecca Kondor. The following guest speaker, Mr. William Bill Gruner, has declared no financial interest and has been cleared to participate in the meeting. In the interest of transparency, FDA asks that speakers and guest speakers disclose

any personal financial involvement with a firm, product, or other entity affected by the Committee's discussions to allow the audience and the Committee to objectively evaluate their presentation. Today's speakers and guest speakers have not reported any such relevant interest. Dr. Beverly Taylor is the invited industry presenter who is participating at the request of FDA to provide a general overview of the U.S. vaccine manufacturers. Dr. Taylor is not a voting or non-voting member of the Advisory Committee and will not participate in Committee deliberations, discussions, or voting. Consistent with the Federal Advisory Committee Act and FDA Advisory Committee procedures, invited speakers who provide informational presentations and do not serve as Committee members are not subject to the same financial conflict of interest screening requirements applicable to special government employees appointed to the Committee.

00:27:32 The presenter's role is limited to providing factual and contextual information to assist the Committee's understanding of the subject matter. Accordingly, no conflict of interest determination under 18 U.S.C § 208 was required for this presenter. The presenter will not participate in Committee deliberations or recommendations. FDA asks that all other participants, including the Open Public Hearing speakers, advise the Committee of any financial relationships that they have with any affected firms, its products, and if known, its direct competitors. We would like to remind the members that if the discussions involve any products or firms not already on the agenda for which an FDA participant has a personal or imputed financial interest, the participant needs to inform the DFO and exclude themselves from the discussion, and their exclusion will be noted for the record.

00:28:30 Dr. Monto, I'll now turn the meeting back over to you to commence the Open Public Hearing.

Open Public Hearing

00:28:44 Dr. Monto: We will now begin the Open Public Hearing session. Both the FDA and the public believe in a transparent process for information gathering and decision making. To ensure such transparency at the Open Public Hearing session of the Advisory Committee meeting, FDA believes that it is important to understand the context of an individual's presentation. For this reason, FDA encourages you, the Open Public Hearing speaker, at the beginning of your written or oral statement to advise the Committee of any financial relationship that you may have with the applicant, its product, and if known, its direct competitors. For example, this financial information may include the applicant's payment for your travel, lodging, or other expenses in connection with your participation at this meeting. Likewise, FDA encourages you at the beginning of your statement to advise the Committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

00:30:18 The FDA and this Committee place great importance in the Open Public Hearing's process. The insights and comments provided can help the Agency and the Committee in their consideration of the issues before them. That said, in many instances and for many topics, there will be a variety of opinions. One of our goals for today is for the Open Public Hearing to be conducted in a fair and open way where every participant is listened to carefully and treated with dignity, courtesy, and respect.

00:31:06 Over to you, Cicely, to run the Open Public Hearing.

00:31:10 Dr. Reese: Thank you, Dr. Monto. We will now begin with Open Public Hearing speaker number one. Please unmute and introduce yourself. Thank you.

00:31:29 Ms. Peschin: Good morning. Are you able to hear me?

00:31:32 Dr. Reese: Yes.

00:31:32 Ms. Peschin: Terrific. Thank you. Good morning. My name is Sue Peschin and I serve as the President and CEO of the Alliance for Aging Research. Thank you so much for holding today's meeting and for the opportunity to provide our comments. The advisory committees, including VRBPAC, play a critical role in strengthening public confidence that the FDA's regulatory decisions are informed by rigorous analysis and diverse expert perspectives. So, we thank Commissioner McCarry for his leadership, and we encourage the Agency to continue leveraging these venues to support transparent scientific dialogue moving forward.

00:32:09 Influenza remains a significant cause of severe illness, hospitalization and death, and older adults, children younger than two, and individuals with underlying health conditions are at highest risk. In recent years, between 70% to 85% of seasonal flu-related deaths and 50% to 70% of hospitalizations were among older adults. And at least 90 children have died from seasonal flu this season, and about 85% of those were not fully vaccinated according to the American Academy of Pediatrics. The vaccines for influenza authorized and improved by the FDA have undergone rigorous evaluation and their benefit-risk profile across all approved age groups is

not in dispute. We're also really pleased to see industry pursue and adopt innovations, including newer technologies, with the goals to help develop more precise protection and improve strain matching over time.

00:33:07 But we have a couple of requests for you today. First, we urge VRBPAC and the FDA to provide manufacturers with a timely strain recommendation for the 2026-27 season, and that appears to be the goal today, so thank you very much. Manufacturers begin producing vaccine components as early as February to ensure timely shipping ahead of the fall season. Delays can cause reduced availability and reduced vaccination rates at a time when protection is needed the most. Second, we ask VRBPAC and the FDA to reaffirm that currently approved or authorized influenza vaccines or annual strain updates to those vaccines should not be subjected to new requirements for randomized clinical trials using inert placebos. The WHO has been consistently clear that withholding an effective existing vaccine from trial participants poses an unacceptable, unethical risk.

00:34:00 We certainly support continued follow-up on implementation and monitoring for safety, but if revisions to the FDA's clinical framework for current or future flu vaccines move forward, we ask that they be developed transparently with appropriate opportunity for stakeholder engagement and public comment, and sufficient implementation time to avoid access disruptions. And additionally, to date, the FDA has approved or authorized flu vaccines that provide different options for patients and providers depending on an individual's age, health status, and preferences. And we ask for you to continue that. CDC and ACIP preferentially recommend the use of higher dose or adjuvanted flu vaccines for people aged 65 and older.

We're thankful for that. And the VRBPAC and FDA play an important role in setting the stage for those recommendations.

00:34:52 Influenza poses a year-round risk in long-term care settings. We need to make sure that there's vaccine availability and coverage policies that reflect that reality. That's not your role, but everything that you do sets the stage for what happens after. Thank you so much for your service.

00:35:10 Dr. Reese: Thank you, Ms. Peschin. And we'll have Open Public Hearing speaker number two.

00:35:22 Mr. Tredente: Hi, good morning. My name is David Tredente. I have no conflicts and no relevant financial relationships. I have a few points today that I believe are integral to the advancement of influenza vaccines, and I hope that the VRBPAC can help to implement some of these changes within its operating scope.

00:35:38 Number one, following the extinction of B/Yamagata and the subsequent shift to trivalent vaccines, manufacturers should be encouraged to explore the possibility of returning to quadrivalent flu vaccines by adding an additional H3N2 strain. Since H3N2 typically presents as the most complicated strain to select for, this change could make the process much easier. It has been noted that manufacturers would likely only need to complete relatively simple serology testing to achieve a new quadrivalent license, so there's no good reason to not look into the possibility.

00:36:13 Number two, we need to continue supporting next generation adjuvants like Novavax's saponin-based Matrix-M. Adjuvants like Matrix-M offer a real opportunity to turn flu vaccines into products that can reliably protect

people on an individual level, instead of only aiming to protect infrastructure by lowering severe disease burden on a population level, which is what we get with our current vaccines. This is especially important in a post- 2020 reality where continued cumulative COVID-19 infections make people more vulnerable to other viral infections, increasing their frequency and severity. They also create more favorable immune responses and cover a larger antigenic range of viral variants, which would also facilitate strain selection.

00:36:57 Number three, I believe the indication of both Sanofi's Flublok and Novavax's Nuvaxovid should be expanded to include pediatric populations down to six months of age. The entire body of evidence that we have paints the picture that both of these vaccines are best in class for their respective viral targets with a very tolerable safety profile, and children under the age of nine do not have access to either product. In general, it should be viewed as unacceptable to not prioritize giving our most vulnerable the best protection possible.

00:37:28 Finally, I just want to make a point that CBER should consider convening the VRBPAC in a manner that reflects the reality of COVID-19 being a year-round virus as opposed to a seasonal one. VRBPAC could be more flexible by only convening if and whenever the need to update this strain arises. And if no update is deemed required, then the current vaccine formulations could just remain on the market so there are no gaps in availability. If that is not achievable, at the least, VRBPAC should convene earlier in the season for COVID-19 strain selection, so updated vaccines can be released before children return to school in the fall and before the annual

summer wave of COVID-19 transmission occurs. Okay. Thank you for your time.

00:38:12 Dr. Reese: Thank you, Mr. Tredente. We'll now hear from Open Public Hearing speaker number three.

00:38:22 Mr. Ford: Hello. There we go. Next slide. While this meeting is about influenza, it's impossible to plan for the future without discussing the elephant in the room. Pathogens have more opportunities for serial passage than at any time in our lives. Next slide. The 25-26 flu season is proof of a reduction in population level of immunity demonstrated by new dominant variants emerging faster than we can produce vaccines. In the shadow of the COVID pandemic, suppressed immune systems are now common. Pathogens will have more hosts and dominant variants will emerge more quickly. Changes need to be made to our strategy before it's too late. Vaccine manufacturers have made promises either we need mRNA production to step up, creating more versions each year, or we need protein-based vaccines that protect against more strains and more variants. In addition, the bar for protection is simply too low, which reduces production and in turn reduces uptake. Next slide.

00:39:24 The WHO's cartography says it all. Next slide. With this much antigenic drift, any choice is only giving the opportunity for more advanced mutations in a different clade leading to ineffective vaccines. Next slide. Looking at the history of influenza vaccines, the standard dose response was set almost 50 years ago, and it's okay to expect more from vaccine manufacturers today. Next slide. While at the same time, all the variables around the flu are

changing. The season is starting earlier. The virus is hitting harder and uptake is going down in our most vulnerable populations. Next slide.

00:40:01 We have to meet those changes before it's too late. Higher response ACIP-preferred comparators should be the new standard of production. Until then, the standard dose should be better understood as a minimum response. This is only the tip of the iceberg when it comes to matters of needing to make our vaccines more effective. The more immune suppression the public suffers, the less effective vaccines will become. While at the same time, meetings simply do not happen frequently enough to take advantage of the ability to update to meet new variants. Next slide. Instead of doubling down on products with limited reach, we should support next-generation saponin-based adjuvants like Matrix-M. There are multiple advantages that have been demonstrated. Next slide. Also, as a side note, when introducing combo vaccines, which are coming, standalone vaccines should not be automatically deprioritized. Next slide.

00:40:51 VRBPAC should meet for strain selection more often. The WHO meets twice a year, the FDA and CDC should do the same. Right now, I am also asking the VRBPAC Committee to schedule an earlier meeting to select COVID variants for the 26-27 season, early enough that updated vaccines can be ready for the start of the school year because COVID is a year-round virus that peaks outside of the normal respiratory virus season. Roughly 70% of infections start with children in the household. Next slide. It is in this Committee's best interest to push for a higher standard. I hope this will include demand for increased vaccine responses and the development of products that meet an expectation higher than simply a non-inferior

guideline. Making better vaccines is the best way to increase uptake. Thank you, everyone.

00:41:35 Dr. Reese: Thank you, Mr. Ford. Back to you, Dr. Monto, to close out the Open Public Hearing.

00:41:42 Dr. Monto: Now we're going into the meeting itself. And first, we will get an introduction from Dr. Jerry Weir, the Director of the Division of Viral Products, Office of Vaccine Research and Review, FDA. Dr. Weir.

Introduction

00:42:05 Dr. Weir: Thank you, Dr. Monto. And welcome everyone to our annual VRBPAC strain selection meeting. As Dr. Monto said, I'm going to provide just a very brief introduction to today's meeting, and we can go to the next slide.

00:42:22 Okay. So, the purpose of today's VRBPAC is, as you already know, to discuss and make recommendations on the virus strain composition for influenza virus vaccines for use in the United States during the upcoming 2026-27 influenza season. The reason we do this is because influenza virus hemagglutinin and neuraminidase glycoproteins undergo continuous antigenic drift. And it's been known for many decades that vaccine effectiveness is greatly reduced when there is a poor match between the vaccine antigens and the HA and the NA of circulating virus. And that's why we get together to discuss this so that the influenza vaccine antigen composition can be updated to better match circulating virus strains. Strain composition recommendation, the process is complex, and it takes into consideration multiple types of data, including recent virus surveillance and

epidemiology data, genetic and antigenic characteristics of recent virus isolates, serological responses, and vaccine effectiveness estimates to current vaccines, and the availability of candidate vaccine virus and reagents. And you will hear today data on all these different types of data.

00:43:38 Ultimately, it's the responsibility of each national regulatory authority to approve the composition and formulation of influenza vaccines for use in that country. In the United States, that responsibility rests with the Center for Biologics in the FDA. And the Center for Biologics in the FDA has chosen to use its Advisory Committee as part of this process in an open, transparent fashion. The next two slides will show the most recent recommendations that we've made for the use of influence for the composition of influenza vaccines. Next slide.

00:44:13 Okay. About a year ago, FDA recommended only trivalent formulations for the season that we're in now, 2025-26. The VRBPAC played a key role in transitioning from quadrivalent to trivalent formulations with the demise of the B/Yamagata strain. And a year ago, we recommended compositions for egg-based vaccines and cell- and recombinant-based vaccines, as we usually do. I'm probably not going to read all of these, but we have a H1N1 strain recommendation for X vaccines as well as for a different one for cell- and recombinant-based vaccines. We made recommendations for the H3N2 component for both egg-based vaccines and cell- and recombinant vaccines, and we made a recommendation for influenza B, which was a B/Austria strain for the B/Victoria lineage, which had been in the vaccine for several years. More recently-- Next slide.

00:45:11 We met with the VRBPAC just this past October to make recommendations for Southern Hemisphere formulations. And the reason we do that is because we have a couple of U.S. licensed manufacturers who produce licensed vaccines. For the Southern Hemisphere, we follow the same process as we do for the Northern Hemisphere or for the U.S., which is what we're doing today. In October, we recommended an A/Missouri pdm09-like virus and A/Singapore (H3N2)-like virus, and again, the B/Austria (B/Victoria lineage)-like virus.

00:45:44 So, today's agenda is shown on the next slide, the next to the last slide. This will be the layout of the agenda today. As I said, you're going to hear a lot of data from our CDC colleagues. You will hear U.S. influenza virus surveillance and global influenza virus surveillance and characterization. You'll get a report from the DoD on the influenza virus surveillance and mid-season vaccine effectiveness, followed by reports on the most recent candidate vaccine strains and potency reagents that are available. And finally, you'll hear comments from manufacturers' representatives about the process as well as their plans for the coming year. Through all of this, we'll hear the data, but you'll hear the recommendations, the global recommendations for next year's 2026-27 composition, and that will be the starting point of our discussion and voting questions at the end of the day.

00:46:38 The voting questions are shown on the next slide, the last slide. You'll see them again later, but basically we break this down for simplicity purposes into two voting questions, one for egg-based vaccines and the second one for cell- and recombinant-based vaccines. And so, the two questions will be the following. "Does the Committee recommend a 2026-27 formulation for

egg-based influenza virus vaccines in the U.S. that contain the following virus strains: An A/Missouri/11/2025 (H1N1)pdm09-like virus, an A/Darwin 1454/2025 (H3N2)-like virus, and a B/Tokyo/EIS13-175/2025 (B/Victoria lineage)-like virus? The second question will be, "Does the Committee recommend a 2026-27 formulation for cell- and recombinant-based influenza vaccines in the U.S. that contain the following virus strains: An A/Missouri/11/2025 (H1N1)pdm09-like virus, an A/Darwin/1415/2024 (H3N2)-like virus, and a B/Pennsylvania/14/2025 (B/Victoria lineage) virus?" That's the introduction. I'm happy to answer questions or turn it back to you, Dr. Monto. Thank you.

00:48:03 Dr. Monto: Thank you, Dr. Weir. We have a few minutes for questions either about the history or about the process of our meeting today. Raise your hands and then turn on your cameras. Dr. Rubin.

00:48:42 Dr. Rubin: Thanks so much, Dr. Weir. I did want to ask a question relative to the public presentations. What happened to the ability to manufacture quadrivalent vaccines? By switching to a trivalent vaccine, did we lose the ability to quickly make another quadrivalent vaccine?

00:49:04 Dr. Weir: No. Well, first of all, let me clarify. Are you talking about the ability to make a quadrivalent vaccine containing that second B strain or some other--

00:49:12 Dr. Rubin: No, not the second B strain. For any quadrivalent. Obviously, we don't want a Yamagata anymore.

00:49:18 Dr. Weir: Yes, that's true, and nothing's changed there. My understanding is most manufacturers retain the capacity to manufacture up to four strains. I

doubt that there's been a quick change there. The switch to something that's more complicated, a quadrivalent formulation with a completely different composition, requires quite a bit more, several more steps though. One, there has to be a need, there has to be a recommendation for that, and each manufacturer would have to present and come up with data to show that that particular composition is justified and supported by data. Just like when we went from a trivalent vaccine a decade or more ago to a quadrivalent containing two Bs, each manufacturer had to update their license with data to support that new composition. So, it would require quite a bit more work along with a recommendation and a clinical medical need for that new composition.

00:50:17 Dr. Rubin: Thank you.

00:50:22 Dr. Monto: And if I could interject, Dr. Weir, where would that recommendation come from?

00:50:29 Dr. Weir: Well, okay, I can only give you the one example of how we got there with the quadrivalent vaccines containing two Bs. There became a sort of global consensus that that sort of composition was needed, and there were discussions at the WHO globally, and there were discussions in this Advisory Committee about the need for that quadrivalent vaccine for at least a couple of years before it happened. So, I think the consensus has to be developed first that there's a need for that. At least that's how it happened with the development of the quadrivalent containing two Bs.

00:51:03 Dr. Monto: And it would not require our prior identification of another (H3N2) strain for this experimental work.

00:51:15 Dr. Weir: Well, okay. So, two things. Besides the need for this, yes, manufacturers-- Each manufacturer would have to have the data for their license to show that your example that you just gave, that the inclusion of two H3s could be supported by data. There was no interference that you got the expected response. So, they would each have to generate that sort of data to update their license.

U.S. Influenza Surveillance and Preliminary Vaccine Effectiveness Estimates, 2025-26 Season

00:51:42 Dr. Monto: Thank you very much. No more hands are raised that I can see. So, we go next to hear from Lisa Grohskopf, who is at the Epidemiology and Prevention Branch Influenza Division at CDC, who will speak on U.S. influenza surveillance and preliminary vaccine effectiveness estimates from the past season. Dr. Grohskopf.

00:52:15 Dr. Grohskopf: Hi, good morning. Can you hear me?

00:52:18 Dr. Monto: Yes, we can.

00:52:19 Dr. Grohskopf: Excellent. Thank you so much, Dr. Monto, and thanks everybody for the opportunity to be here today. Good morning. I'm going to be presenting for you an overview of 2025-26 season U.S. influenza surveillance to date, and also a summary of the preliminary United States seasonal influenza vaccine effective estimates for this season. Just want to note at the start, the data presented today represent currently available information and are subject to change as more data become available over the coming weeks. Next slide.

00:52:52 So, we're going to start first with the U.S. surveillance summary describing influenza activity thus far for this season. The information that follows comes from the most recent CDC FluView report, which is available at the link shown. Fluview is updated every week on Fridays. This report contains data as of surveillance week eight. That's the week ending February 28th, 2026, and this is the report that came out last Friday. The next update will be tomorrow, March 13th. Next slide.

00:53:24 So, we're going to start with virologic surveillance, and that'll be these first two slides with some charts to go over. These first two slides cover virologic surveillance and summarize influenza testing information reported to CDC by clinical and public health laboratories on a weekly basis.

00:53:42 This first slide of the two covers the results for influenza tests performed and reported weekly to CDC by a nationwide network of clinical laboratories. The data from clinical laboratories includes the percentage of specimens tested that are positive for influenza, which is used to monitor whether influenza activity is increasing or decreasing from week to week. Among the positive tests, these data also report the relative proportion of influenza A versus influenza B viruses. The X-axis here is surveillance week, and you'll see that in most of the slides going forward. The right side Y-axis is the scale for the percent of influenza tests that are positive, and that's shown in the body of the graph by the black line for all results. And then there are two different colors. We have yellow for the flu A viruses and green for the flu B viruses. The left side Y-axis is the scale for the number of positive specimens, and those are represented proportionally in the chart by the colored bars, yellow for flu A, green for flu B.

00:54:45 Overall, the percent of tests positive has decreased since peaking in late December, but remains elevated at 15.8%. Among the positive tests, if you look at the colored bars, you can see that over time since the peak, we've had a relative increase in the proportion of influenza B viruses while the proportion of influenza A has decreased. Next slide, please.

00:55:08 So, this second chart summarizes results that are obtained from the public health laboratories. The data from public health laboratories is generally subtyped and typed for lineage for the A and B viruses respectively. So, the data from the public health laboratories are used to monitor the proportion of circulating influenza viruses that belong to each influenza type and lineage-- Type, subtype and lineage. As in the last slide, we have surveillance week on the X-axis. The number of positive specimens is on the Y-axis and is represented in the chart by the variously colored bars.

00:55:44 Overall, for the season, influenza A(H3N2) viruses, which are denoted by the red, have predominated with substantially lesser proportions of (H1N1)pdm09, which are shown in orange. Of note, among 1,532 H3N2 viruses genetically characterized since September 28th, 2025, over 90% were identified as subclade K, which is also known as subclade J.2.4.1. H3N2 subclade K was initially identified by CDC in August 2025. These viruses have changes in the hemagglutinin gene and have been characterized as antigenically drifted in comparison to the virus selected to represent A(H3N2) as a component of the U.S. 2025-26 seasonal influenza vaccines. Subclade K viruses have been observed internationally, not just in the United States, and will be mentioned a bit further in Dr. Kondor's presentation. Just switching briefly to influenza B, these are denoted by the

green portions of the bars. All lineage-tested viruses that are wild type have been B/Victoria. We have no naturally occurring B/Yamagata viruses detected since March 2020. Next slide.

00:57:05 So, we're going to switch gears a little bit and move on to discuss outpatient-attended influenza-like illness surveillance. Influenza-like illness or ILI is not laboratory-confirmed influenza. It's a symptomatically defined diagnosis defined as respiratory illness, including fever plus cough or sore throat. Therefore, illnesses collected here can be caused by other viruses such as SARS-CoV-2, RSV, or an assortment of other circulating respiratory viruses. However, ILI activity often temporarily mirrors influenza specific surveillance data. For example, the influenza positive testing percentages reported a couple of slides back that summarized virologic surveillance from the clinical laboratories, as well as other indicators of a laboratory-confirmed influenza activity. So, the percent of outpatient illnesses that were for ILI thusly sort of provide a surrogate index for following trends in outpatient medically-attended influenza through the season. The percent of outpatient visits that were for ILI is also one of the indices used by CDC along with estimated influenza associated hospitalizations and deaths to characterize the severity of an influenza season.

00:58:18 This slide summarizes the percent of outpatient medical visits that were for ILI as reported weekly to CDC by approximately 3,000 outpatient facilities reporting to ILINet. The current 2025-26 season is the red line with the superimposed circles, and the five previous seasons are also shown. Similarly to the percent of influenza tests that were positive that was reported in the earlier slide for neurologic surveillance, the percent of

outpatient visits that were for ILI peaked in late December and have declined since. However, this proportion is still above the national baseline of 3.1%. The national baseline, which is that dotted line that goes horizontally across the graph, is calculated based on the mean percentage of patient visits for ILI during non-influenza weeks for the most recent three influenza seasons. Next slide.

00:59:14 Okay, so the next two slides summarize laboratory confirmed influenza-associated hospitalization rates from FluSurv-NET. This system includes counties from 14 U.S. states and represents about 10% of the U.S. population. We're going to see two slides with these data. They're the same data just shown a little differently to illustrate different points.

00:59:36 The first slide shows influenza-associated hospitalization rates per 100,000 population for each week. So, you're going to see again, we have surveillance week on the X-axis, and as we move from week to week, what you're seeing in the lines is the rate for that week. We have, again, in red, the 25-26, the current influenza season, and the five previous seasons also shown, one that is excluded is 2020-21, which was, as I'm pretty sure everybody remembers, the first full season that coincided with the early COVID-19 pandemic during which we saw historically low levels of influenza circulation. For the current 2025-26 season, hospitalization rates peaked in late December, at overall across age groups at 13.3 per 100,000 population. This peak is close in magnitude to that scene last season, which was 24-25 shown in blue, but it occurred a bit earlier in the season. Also, you can see it's a narrower sharper peak covering less time than last season. Next slide.

01:00:42 So, here we have data that is basically presented instead of from week-to-week estimates cumulatively. So, it's the same rate data from FluSurv-NET, but this time shown as cumulative rates. We're still looking at rates over the course of time, but this time they're additive over time, so the rate goes up from week to week to week. As of March 6th, the estimated cumulative hospitalization rate across all ages was 76 per 100,000, which is the third highest observed since the 2010-11 season. By age group, the highest cumulative rate thus far is among adults 65 and older at 251.3 per 100,000. This is an age group that is typically, in most seasons, the one that has the highest hospitalization rates. Cumulative rates for pediatric cases overall were the second highest since 2010-11, at 43.4 per 100,000. Among children, the rates were highest among the very youngest under one year at 125.5 for 100,000, followed by those aged one to four years at 67.7 per 100,000. Next slide, please.

01:01:48 So, our last two surveillance charts are mortality data. There are two of them. This slide is from the National Center for Health Statistics, or NCHS, Mortality Surveillance System. NCHS collects death certificate data for all deaths occurring in the United States. The data shown here are those deaths, which are classified based on ICD-10 multiple cause-of-death codes as having been associated with influenza. So, that's specifically including ICD-10 codes J09 to J11. These data are aggregated by week of death occurrence. As in previous slides, the surveillance week is on the X-axis. The percent of deaths reported to be due to influenza is on the left Y-axis and is represented in the chart by the red line. The number of deaths reported to be due to influenza is on the right Y-axis and is represented in the chart in orange.

Based on surveillance data available on March 6, 2026 and representing deaths that occurred during the week ending February 28th, 2026, 0.7% of these week eight deaths were due to influenza. This percentage decreased as compared with week seven. Next slide.

01:03:09 The last surveillance figure we'll go over. This summarizes laboratory confirmed influenza-associated pediatric deaths. Influenza-associated pediatric mortality became nationally not notifiable in 2004. For surveillance purposes, an influenza-associated pediatric death is defined as a death in a person under 18 years of age, resulting from a clinically compatible illness that was confirmed to be influenza by an appropriate laboratory diagnostic test with no period of complete recovery between illness and death. Demographic and clinical information is collected on each case and reported to CDC. As of February 28th, 2026, 90 influenza-associated pediatric deaths have been reported for this season. Among children in this group who were eligible for influenza vaccination and with known vaccination status as of now, approximately 85% of reported pediatric deaths this season have occurred in children who were not fully vaccinated against influenza. Next slide.

01:04:20 So, before we move on to VE, just to summarize surveillance, as of February 28th, 2026, seasonal influenza activity remains elevated nationally. In recent weeks, we've seen a shift such that influenza A activity has decreased and influenza B activity is increasing nationally. Influenza A(H3N2) viruses predominated overall, with over 90% of those belonging to subclade K among those tested, which again is a subclade characterized as antigenically drifted from the influenza A(H3N2) represented in the

current season vaccine. The cumulative influenza-associated hospitalization rate estimated by FluSurv-NET is the third highest since 2010-11. Specifically for those children under 18 years, it's the second highest since that season.

01:05:12 Overall season severity based on estimated ILI outpatient visits and influenza associated hospitalizations and deaths is currently characterized as moderate across all age groups. Considering children and adults separately, it's characterized as moderate severity among adults 18 through 64 and 65 years and older; and high severity among children zero through 17 years. 90 influenza-associated pediatric deaths have been reported thus far this season and among those children, approximately 85% of those eligible for vaccination were not fully vaccinated against influenza. Next slide, please.

01:05:49 So, next we're going to move on to a summary of preliminary 25-26 U.S. influenza vaccine effectiveness estimates coming from three CDC influenza vaccine effectiveness networks. These estimates are coming out in publication today in the Morbidity and Mortality Weekly Report. Next slide. Just a little background about the three networks. These data come from three VE networks at CDC, which evaluate vaccine effectiveness against laboratory-confirmed influenza for children, adolescents, and adults in both inpatient and outpatient settings. The three networks are the New Vaccine Surveillance Network or NVSN, which includes children and adolescents, six months through 17 years, who present for outpatient visits, emergency department or urgent care visits, and hospitalizations.

01:06:40 Second, we have the U.S. Flu Vaccine Effectiveness Network or US Flu VE, which includes children and adolescents through six months through 17

years and adults, 18 years and older, who present for outpatient visits, emergency department visits, and urgent care. And the Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network, or VISION. This includes children and adolescents, six months through 17 years, and adults 18 years and older on presenting for emergency department and urgent care visits, and hospitalization. Next slide.

01:07:16 This map summarizes the geographic distribution of sites participating in these three networks. Taken together, they include patients from 16 U.S. states. Next slide. To summarize, some of the elements of the methods from these three networks. All enrollees are patients presenting for outpatient or inpatient care who have symptoms of acute respiratory illness. Dates of enrollment for the information I'll be presenting today are for fall 2025 through early 2026. The design for all three networks is a test negative design comparing influenza vaccination odds among case patients with influenza confirmed by molecular assay versus control patients testing negative for influenza and SARS-CoV-2. Vaccination status is reported as receipt of any 2025-26 seasonal influenza vaccine, according to medical records, immunization registries, claims data, and/or self-report. Next slide.

01:08:21 For these analyses, vaccine effectiveness or VE is calculated as one minus the adjusted odds ratio times 100 and expressed as a percentage. Adjustments are made for geographic region, age, and calendar time of illness. VISION also adjusts for sex and race and ethnicity. US Flu VE also adjusts for days between illness onset and enrollment, self-reported general health status, and sex. VE estimates are calculated for influenza A subtypes A(H1N1)pdm09 and A(H3N2) when possible. This is not always possible

due largely to numbers when we substratify data into various substrata. Also, subtype is not available in the VISION network. VE is not estimated for some age groups and settings in types/subtypes when the sample size is small or confidence intervals are wide. Next slide, please.

01:09:21 So, we're going to summarize the VE results in the next few tables and some charts. We're going to split these out by pediatric versus adult age groups, and we'll start with pediatric patients VE for any influenza that is all flu, influenza A and B collectively. Vaccine effectiveness estimates ranged for pediatric patients across all flu, A and B, from 14% to 48% across the networks. These estimates were statistically significant in the outpatient and inpatient components of NVSN at 41% and 48% respectively, and in the outpatient component of VISION at 38%. Next slide.

01:10:04 The next couple of slides summarize information stratified where possible by type and subtype. Looking at influenza A overall, VE estimates ranged from 10% to 38% among outpatients in all three networks, and 42% to 48% among inpatients in NVSN and VISION with the NVSN estimates being statistically significant. Next slide.

01:10:29 For influenza A(H3N2) specifically, estimated outpatient VE was 35% and statistically significant in NVSN and was 2% and not statistically significant in the US Flu VE network. Estimated inpatient VE was 38% in NVSN and was statistically significant. Next slide. And the last slide in the pediatric series is on pediatric VE against influenza B. For influenza B, only outpatient VE could be estimated. Estimated VE ranged from 20% to 71% across the networks and was statistically significant at 71% in NVSN and 45% in VISION. Next slide.

01:11:21 So, now we're going to switch gears to present the results for adults. The first slide is all adults 18 years and older VE against any influenza. So again, all flu, A and B, not subtype or type specific. Vaccine effectiveness estimates for this group ranged from 22% to 34% across the networks with all three estimates being statistically significant. And you'll note here that we no longer have the NVSN estimates because that network does not include adults. Next slide. Sorry, it only includes children.

01:11:56 We have adult VE next against influenza A. For influenza A, estimated outpatient VE for adults was 21% in the US Flu VE network and 34% in VISION, the latter of which was statistically significant. Estimated inpatient VE was 30% in VISION and was statistically significant. Next slide. For adult VE against influenza A(H3N2), only outpatient VE in the US Flu VE network could be estimated and it was 11% and not statistically significant. Next slide. For influenza B, only outpatient VE could be estimated. We have an estimated outpatient VE of 22% in the US Flu VE network that was not statistically significant. It was 63% in VISION, which was statistically significant. Next slide.

01:12:59 So, this will be on our last table and our last set of results. This time it's for the subset of adults aged 65 years and older. Again, we're starting with VE against any influenza, all types and subtypes, A and B. The estimated VE against any flu, A and B, in these adults ranged from 40 to 41% across-- Sorry, 30% to 41% across three networks. All estimates were statistically significant. Next slide. Looking to the extent that we can for type information, for flu A viruses among adults 65 years and older, estimated outpatient VE was 30% in the US Flu VE network and not statistically

significant. The VE estimate was 40% in VISION and was statistically significant. Estimated VE was for the inpatient's 31% in VISION and was statistically significant. Numbers were insufficient to permit influenza A subtype and influenza B specific estimates for this age group of adults. Next slide.

01:14:11 So, in summary, vaccination with a 25-26 influenza vaccine reduced the risk for medically-attended influenza outpatient visits and hospitalizations among children, adolescents, and adults across 16 U.S. states. Vaccination was effective against influenza A and B viruses and showed protection against A(H3N2) in children and adolescents. Vaccine effectiveness was lower than in recent previous influenza seasons. Next slide.

01:14:38 So, this is my last slide and closing. I just want to express appreciation for the CDC, really the entire division because everybody does work that contributes to these data. In particular, I want to express appreciation for the CDC Influenza Division Surveillance and Influenza Prevention and Control teams, as well as all of the collaborators and contributors to these networks. Thank you very much for your attention.

U.S. Influenza Surveillance and Preliminary Vaccine Effectiveness Estimates, 2025-26 Season – Q&A

01:15:01 Dr. Monto: And thank you, Dr. Grohskopf. A lot of work presented from a lot of different people. I'm sure there are going to be questions and comments from the group. Please raise your hands and then turn on your-- Okay, Dr. El Sahly.

01:15:22 Dr. El Sahly: Thank you, Arnold, and thank you, Lisa, for this very thorough presentation. I just wanted to ask a question that pertains to vaccine coverage. In the most recent VRBPAC or the one that preceded it, we guessed that the B and H3N2 potential mismatch may happen, but I wanted to also gauge the issue of vaccine coverage. Have there been any changes in the vaccine coverage to partially explain the slightly lower VE compared to previous year? Or do you think it's mostly attributable to the mismatch in antigen versus vaccine?

01:16:12 Dr. Grohskopf: Thanks, Dr. El Sahly. Really good question. I don't think we know exactly. One thing that we need to consider is that these results are still preliminary. We're dealing with results that were accumulated up through the early part of this year. The VE teams are going to be continuing to look at results as we get through to the fall, and typically the more final estimates are presented in the fall. We do know that there's geographic variability among the different sites as far as proportions of things, for example, H3N2 versus H1N1 and subclade K. We also do know that in recent seasons, there have been consecutive drops starting the first season after the pandemic in vaccine coverage, pretty much across populations. Because the various networks that we have to assess VE annually don't focus on all flu, they focus on medically-attended flu. It is conceivable that some drops could be in some respect due to drops in coverage. We also know though that we do have the issue of subclade K this season, so I think that's something that we're all going to be thinking about as we go forward and refine VE estimates.

01:17:31 Dr. El Sahly: Okay. Thank you. And do you think that home-based testing explains also some of what we are seeing in terms of the wide confidence interval, or you don't think it's a big component in the epi findings?

01:17:49 Dr. Grohskopf: I don't know that we know that for certain at this point. I think it's possible that if people do test at home and their symptoms aren't especially severe, they might not present for care, which could conceivably reflect numbers. One thing that I'm sure you could notice in the graphs is that we do have some VE estimates for which the confidence intervals are wider and for which there's a higher degree of uncertainty, and the different populations in which that occurs can fluctuate from year to year. As home-based testing becomes more and more commonly done, it'll be interesting to see how things evolve going forward.

01:18:22 Dr. El Sahly: Okay. Thank you.

01:18:23 Dr. Grohskopf: Thank you.

01:18:25 Dr. Monto: Dr. Gans.

01:18:28 Dr. Gans: Hello, and thank you for that presentation. I really enjoyed hearing it. And I had some questions about the differences in the vaccine efficacy between the different groups that are looking at it. I was curious, you may have said this at the beginning and I missed it. What do you account for the differences in the vaccine efficacy between those assessments? Because they varied quite a bit, and I'm just wondering what you think is behind it. That's my first question I'd want to--

01:19:05 Dr. Grohskopf: Okay. Thanks, Dr. Gans. One thing that has generally held from year to year is that in the different networks and in the different sites within the different networks, the underlying distribution of the population ages can be different. And also we do know that we tend to present, at least on a high level, our virologic surveillance data on a national level, but we also know that there are different subpopulations in different geographic areas of the country where we will see different proportions of H3 as opposed to H1, or different proportions of B as opposed to A. And more likely than not, these have some effect on what we see in terms of differences. Sometimes as we move forward with the season and move towards more final estimates, things start to look a bit more cohesive. And again, these are interim preliminary estimates, so we'll see what those are like going forward.

01:20:00 Dr. Gans: Yeah, I think that relates to my second question about not only getting more granular about that data. I know you did some subtypes, but you did present some of that, and so that might actually be helpful. But I also wondered about we have 16 sites. We've actually had, I think, about a stable number of contributors. I'm wondering about how we expand that and think about really getting broader data in that regard, because I think that would be more representative. I think this data doesn't support-- At least for what we see in pediatrics, and you did mention that the children that we see hospitalized are largely unvaccinated, or as you say, not fully vaccinated. And I'm not sure that that sort of data is actually really represented in the vaccine efficacy numbers that people hear. So, I'm just wondering how we can capture some of that better.

01:21:11 Dr. Grohskopf: That is a really important point and a good question. We know historically, for example, some age groups are relatively less represented, for example, in the networks that we have. The US Flu VE Network has always included all adults 65 and older, but in some seasons, there aren't, for example, enough data to be able to get even an uncertain estimate of VE depending on the numbers that we're seeing. And then of course, as we substratify by age groups, and then by type and subtype, the numbers just get thinner, which is why sometimes we just can't present estimates.

01:21:51 And moreover, another point is that numbers, if they're small, also make it difficult to, for example, calculate something that many people are interested in, which are vaccine type-specific VE estimates, you know, cell versus egg or high-dose versus recombinant. There's some seasons where that's been possible to do, but not always. Ideally, in an ideal world, we would have more data, and I think that's always something that's a good thing to have. But in terms of how exactly to achieve that at this moment, I think we need to wait and see what happens with that. Thank you.

01:22:39 Dr. Monto: Dr. Grohskopf, I am going to try to speculate a little bit about some of the differences we're seeing this year. Most years, the difference between the various networks is not as large as it is this year. And is it possible that because the US Flu VE network is more likely to see milder medically attended illness than the other networks, that we're seeing something with influenza—again, speculation—mid-season estimates that we really are hard-- It's difficult to see ordinarily. And that is that the vaccine's preventing more severe disease, better than milder disease. We

always say that it's happening, but it's been very difficult to demonstrate. What is your opinion, off the-- On the record, I guess, about this speculation?

01:23:56 Dr. Grohskopf: Thanks, Dr. Monto. I mean, I think-- I don't think I have an answer, to be honest, but I think that the point you raised is a very good one. For all of these networks, again, we're not measuring VE per se against infection. All of these networks focus on individuals, include individuals who presented for care. And we have two networks that include hospitalization, US Flu VE focusing on outpatient. We may be missing some folks—that's entirely possible—who simply don't present for care. And--

01:24:33 Dr. Monto: But among those that present for care, the Flu VE Network, anybody who comes into a clinic, that meets the case definition.

01:24:47 Dr. Grohskopf: Correct. I don't have a ready explanation for why the--

01:24:54 Dr. Monto: And it's mid-season, besides, so things may change.

01:24:56 Dr. Grohskopf: It's mid-season besides-- Yeah, things change. I mean, there are a number of things that happen over the course of time. We actually are still in the flu season and we're at the time these results were closed, so we will have more information as it goes forward. There's also more verification of vaccination status as we go through time. And again, we do know that there are some baseline differences in the demographics as far as age across the various networks. Whether these things explain at all, I can't say, but it's something we continue to examine.

01:25:29 Dr. Monto: Yeah. It's worth thinking about. Dr. Berger.

01:25:33 Dr. Berger: Hi. Thanks, Dr. Dr. Grohskopf. I hope this is a pretty simple question. You had mentioned that subclade K represents 90% of the A cases that have been detected so far. I just want to know, has that been static from the beginning or was that a rise that led to 90% overall?

01:25:52 Dr. Grohskopf: I'm not sure. I can check on that and get back to you, but in recent-- Since about the start of the calendar year, yes, I believe that's been pretty stable. I can also-- Dr. Kondor, my laboratory colleague, might also be able to comment on that.

01:26:08 Dr. Berger: Thanks.

01:26:13 Dr. Monto: Anyone else want to make comments? Usually it's an issue of managing the many hands raised, but today we don't have as many hands to be raised, so it's a different situation. Seeing none and seeing that we're early, why don't we have our break and be very generous about it and let's do it for 20 minutes instead of for 10. So it really is a break.

01:26:54 Dr. Grohskopf: Thanks very much.

Global Influenza Virus Surveillance and Characterization

01:49:32 Dr. Monto: Welcome back to the 191st meeting of the VRBPAC. Before we go on to the next presentation, I would like to ask Dr. Kollmar, who didn't have a chance to introduce himself at the start of the meeting, to do so right now. Dr. Kollmar.

01:49:58 Dr. Kollmar: Hi, my name's James Kollmar. I am the Alternative Industry Representative. I currently work at Merck & Co as an Associate Vice President in Global Regulatory Safety. Thank you.

01:50:14 Dr. Monto: Thank you. Now, we go back to our regular agenda. We now will be hearing from Rebecca Kondor, Interim Director of the WHO Global Influenza Surveillance and Response, Collaborating Center for Surveillance of Epidemiology and Control of Influenza at CDC. Dr. Kondor.

01:50:52 Dr. Kondor: Hello, Dr. Monto. It's wonderful to be here today and present. Okay. I'm going to go ahead and get started and give a Global Influenza Surveillance and Characterization update for influenza viruses today for the VRBPAC. Okay. Next slide, please.

01:51:11 Quick overview of the influenza viruses which cause seasonal epidemics. We have co-circulation each season of human influenza viruses. We have one group of the alpha influenza viruses, which are subtyped into H3N2 and H1N1. For the beta influenza viruses, while we used to have two co-circulating lineages, since March 2020 we have only had the B/Victoria lineage cause epidemics. And so again, we've had a lot of discussions with this group on the transition for vaccine recommendations from quadrivalent to trivalent.

01:51:52 Now, influenza viruses that have major antigens in the surface, and that includes the hemagglutinin responsible for virus attachment. A lot of the antibodies that are produced post-infection or vaccination are targeting the hemagglutinin molecule. We also have the neuraminidase. Its protein's functions are important for exit from the infected cell, and both antibodies and antiviral drugs inhibit this protein. And just to remember, when we talk about influenza, we're talking about a negative sense RNA genome with eight gene segments for these alpha and beta viruses. Next slide, please.

01:52:35 Influenza vaccine composition recommendations are done for both platforms and specific timelines. The WHO convenes technical consultations to recommend viruses for each component of mental ones of vaccines, so the H1N1, the H3N2, and the B/Victoria lineage. And recommendations are split into egg-based vaccines and cell culture-, recombinant protein- or nucleic acid-based vaccines to encompass the currently licensed vaccine manufacturing processes and those in clinical development or under licensure at the moment. Now, it's important to talk about why there may be a prototype different name between those for egg-based or cell-based, and that's due to the vaccine platforms having different requirements and optimal growth, but both of the candidates for the particular platform represent the most suitable candidate for the new subclade of interest. And then as we are here today, FDA convenes the VRBPAC to recommend the viruses for U.S. vaccine manufacturing.

01:53:48 Timing of influenza vaccine recommendations. I've shown in the graph at the bottom the Northern Hemisphere timing. While the typical Northern Hemisphere season can last anywhere from October through May, the vaccine recommendation for the next season is made usually in February. And the reason that the timing of why we're making the vaccine recommendation for the following season while we're still within the current season is due to the time it takes for production, regulatory approval, and distribution of the manufactured vaccines. In September, the WHO will convene a technical consultation for the Southern Hemisphere vaccine recommendation for their following hemisphere. Okay. Next slide, please.

01:54:38 And as mentioned by Dr. Weir during the vaccine composition meeting, there are a lot of information that's presented and used in the decision process for the recommendations. Now, the overall goal are to identify influenza antigens that will elicit immunity against diverse or diverging viruses that will likely co-circulate in the future. And ideally, we're trying to select an antigen that would confer a breadth of immunity across multiple subclades of viruses to reduce risks. And so I won't go into detail, but I hope to highlight with the slide here the different types of data that are presented and discussed during the recommendation, going from surveillance, genomic and antigenic characterization, and a lot of integration of data, not only from each collaborating center, but also with collaborators and modelers.

01:55:39 And we also look at the human serology component. This is looked at not only post-vaccination with the current 25-26 Northern Hemisphere vaccines, but also looking at data from post-exposure studies. Interim vaccine effectiveness through the GIVE collaboration is presented as well as updates to previous seasons. And lastly, one of the most critical parts of the vaccine selection process is having available candidate vaccine viruses for the new subclades of interest. And so a lot of discussion and a lot of work with the global influenza surveillance and response systems is to create and have available characterized candidate vaccine viruses at the time of VCM. Next slide, please.

01:56:29 So as mentioned previously, here are the global influenza surveillance and response systems, influenza vaccine recommendations for the 2026-2027 Northern Hemisphere influenza season. I've color coded changes from

previous vaccine recommendations. As you'll notice, in orange, we have the H1N1 component. This is the A/Missouri/11-like for both egg-based and cell-based. And this particular virus was recommended for the 2026 Southern Hemisphere, but it is different from the currently used 2025-2026 Northern Hemisphere vaccine. And then both the H3N2 and the B/Victoria components recommendations have been updated. For H3N2, the vaccine component recommendation is an HA subclade K, and that's Darwin/1454/2025-like for egg-based, or Darwin/1415/2025-like for cell-based. For the B/Victoria lineage, we've selected a recommendation for the HA subclade C.3.1. For egg-based, this is the B/Tokyo/EIS13-175/2025-like; and for cell recombinant- or nucleic acid-based vaccines, the B/Victoria C.3.1 recommended virus is B/Pennsylvania/14/2025-like. Next slide, please.

01:58:09 So the vaccine recommendation is published on the WHO website, and in addition to that, there are listed candidate vaccine viruses for the different platforms, and the status of that will be updated as information becomes available. I also want to highlight that during the vaccine composition meetings, we also look at zoonotic influenza or pre-pandemic viruses to understand whether or not new candidate vaccine virus development for emerging zoonotic viruses is needed, and that information is also available on the WHO website. Next slide, please.

01:58:48 Now I'm going to give an overview of the global detection through the global influenza surveillance and response systems of influenza viruses. And I've boxed here the reporting period that the rest of my presentation will focus on, and that's September 2025 till the end of January 2026.

Although however, this shows the two preceding Northern Hemisphere seasons, and we can see with the change in colors from the blue-green to orange co-circulation of both influenza A and influenza B, but the subtype of influenza A has changed depending on the season. The previous 2024-2025 Northern Hemisphere season was predominated by an influenza A(H1N1)pdm09, and lower proportions of H3N2 and B/Victoria. However, as we shift to look at the data since September, we can see the predominance of the influenza A(H3N2) with lower circulation of H1N1 and more recent-- Increases in influenza B in the more recent weeks. Next slide, please.

02:00:05 This will give an overview now of differences by geographic region for the types and subtypes and influenza activity. Again, the same reporting period, September 2025 through January 2026. Of note, we can see the Northern Hemisphere countries and regions had that high predominance of H3N2, but there was some variability in the amount of co-circulation of H1N1 detected or influenza B. In parts of the Southern Hemisphere, we continued to have influenza activity a little bit outside of their typical patterns. In some regions, this was due to H3N2. In others, this was also due to influenza B. And we'll get into maps for each individual type and subtype later on as well. Next slide, please.

02:01:00 Okay. Now I'll focus on the data presented for the (H1N1)pdm09 virus vaccine. Next slide, please. This starts and looks at the amount of H1N1 detected through GISRS. In red, we can see the calendar year 2025 and we can go from week 1 through 52. And we can see that, as mentioned before, the 24-25 Northern Hemisphere season was H1N1 predominant. You can see with a high number of detections in red, and those detections decreased

over time. However, you can see the effect of the Southern Hemisphere, which was also initially H1N1 predominant in weeks 18 through 27. Overall, starting in week 40, we can see an increase, but small numbers of H1N1. And as we look back to weeks 1 through 6 for 2026, we can see small detections of H1N1 overall. Next slide, please.

02:02:04 Now, this map shows the increased detections of (H1N1)pdm09. We can see that parts of central and tropical South America, as well as parts of Central Africa and Europe and South Africa and Oceania during this time period had a larger proportion of viruses as H1N1 detected through their surveillance systems. But overall, co-circulation globally. Next slide.

02:02:36 I'm going to first give an overview of the phylogenetic hemagglutinin. And the nomenclature that we have adopted is the Next clade/subclade nomenclature, where before we used to talk in broad terms of clades, I'm now going to be a little bit more specific in talking about specific HA subclades. Now, H1N1 was previously split into the 5a.2a and the 5a.2a.1 clades, but now we want to focus on the subclades. As presented in October, what we saw in the 24-25 Northern Hemisphere season was the shift from co-circulation of 5a.2a and 5a.2.a.1 subclades into a predominance of a 5a.2a.1 D.3.1 subclade. And this particular HA has continued to dominate the detections of H1N1 and of course continue to evolve as influenza viruses do. We've actually split out a particular subclade from D.3.1 into D.3.1.1 to look to see how this subclade has circulated in different global patterns.

02:03:52 The tick marks on the right of the tree show not only the month of collection, but the location of the sequence data. And we can see for the D.3.1 global circulation, seeing colors across all of the global space. And for the D.3.1.1, we can see a lot of detections in Europe and also recently in North America. And so I'll go into more fine detail of the overall clade and subclade proportions in the next slides. Next slide, please.

02:04:32 Okay. So on the left, we have the global view of all available H1N1 sequence data. This is looking at a year time point, so all the way back to February 2025 till the end of January when the data was available. And this again reemphasizes the sweep and increase of viruses from the D.3.1 or the D.3.1.1 subclade over time and during this reporting period. So those in orange represent the former co-circulating C.1.9 and C.1.9.3 viruses, which have been displaced greatly by the D.3.1 and the D.3.1.1. On the right, I'm showing the U.S. influenza season, and then we kind of look at this at week 40. So this starts at the end of September, and this is the data presented during the vaccine composition meeting for the United States, and it will backfill and change as data becomes available. And we can see that the U.S. data is very similar to the global data and that we had co-circulation of the D.3.1 and the D.3.1.1 subclade during this reporting period. Next slide, please.

02:05:57 We also look at trends in different geographic regions to see whether there could be some circulating subclades that are different than the global trends. However, overall, we are seeing very similar trends in the regions that are seeing that predominant D.3.1 and co-circulation and increase in detection of the D.3.1.1s. Okay. Next slide, please.

02:06:27 And this map, again, we break it down even further at a country level to see there were some parts of the world, specifically we'll call out West Africa, that still had detections of the C.1.9 and the C.1.9.3 as also a part of Madagascar as well. So we are seeing trends at the country level, which are a little bit different than we see at the regional or global levels. But another way that we look at the data to understand the circulation of the different subclades and the trends that we see over time. Next slide, please.

02:07:07 This slide gives an overview of the antigenic information presented by the collaborating centers during the vaccine composition meeting. Again, narrowing down the viruses by their collection date, specifically looking at viruses collected since September 1st, 2025. And you can see that there were a number of influenza viruses tested across each lab. And overall, we're going to target the data for the ferret antisera raised to the 2026 Southern Hemisphere vaccine candidate, A/Missouri/11/2025. And the reason that we're doing this particular analysis is because we'd like to see whether or not the vaccine recommendation for the Southern Hemisphere is an appropriate recommendation to keep for the Northern Hemisphere. Data from the ferrets in an HI assay against sera raised against either the cell-grown Missouri or the egg-grown Missouri show good recognition of the circulating viruses. And again, most of these are the D.3.1 and the D.3.1.1 viruses, but we'll look into more detail in the next slide.

02:08:23 This map, this figure, actually shows the genotype to phenotype integration that CDC presents in our report, showing the phylogenetics of the viruses on the left—and this is again as the hemagglutinin—and we can break in half the tree into the D.3.1s in dark purple and the D.3.1.1s in lighter purple. And

specifically, we're asking the question: are we seeing any ferret antisera recognition differences between the D.3.1s and the D.3.1.1s? And in this analysis, you can see across the phylogenetic space of the hemagglutinin, we are seeing good recognition with the ferret antisera to the Missouri/11 against both the D.3.1 and the D.3.1.1 viruses. And then we also had a subset of the 5a.2a tested, and these were also well-recognized. So we saw very few viruses with additional substitutions that were not well-recognized by these particular ferret antisera. Next slide, please.

02:09:30 This data shows the same antigenic information I showed previously in a table form, but instead uses antigenic cartography by our collaborators at the University of Cambridge. Cartography helps put into space the viruses that are tested to ask whether or not viruses with different changes in the HA are recognized and are closely related to each other using that ferret antisera in our hemagglutinin inhibition assays. And so the main question that we were asking of these analyses is: where are D.3.1 and D.3.1.1 viruses localized in the antigenic cartography? These again are in dark purple for D.3.1 and lighter purple for D.3.1.1. And as you can see on maps created from either data from the Francis Crick Institute on the left or CDC Atlanta on the right, both D.3.1 and D.3.1.1 co-localized in the same antigenic space. I've also included serum circles showing the reference viruses ferret antisera to the Missouri/11/2025-cell on the left and the Missouri/11/2025-egg on the right. And we can see that that ferret antisera recognizes the vast majority of the D.3.1s and the D.3.1.1s in circulation, and also recognizes as well the other co-circulating viruses. On CDC's map in particular, you can see in a bright pink there are some viruses that are outside that serum circle. These are

particular viruses with changes at positions 130 that we were seeing in very small numbers, but one that we are continuing to monitor for. Okay. Next slide, please.

02:11:24 So, this represents data presented by CDC as part of the human serology data, where we're looking at human post-vaccination sera from the United States across different age groups and different vaccine platforms. In this case, we're looking at individuals that were vaccinated with the 2025-2026 Northern Hemisphere vaccine components. And this was the A/Wisconsin/67/2022-like for the cell-based and the A/Victoria/4897/2022-like for the egg-based vaccines. And what we're looking at in this analysis is asking the question about post-vaccination geometric mean titers against the vaccine, whether or not the geometric mean titers against these emerging subclades show inferior or non-inferior titered ratios. So what we can look at is whether or not we see virus-- The data colored in blue or in orange. If the data is in blue, that means that the ratio between the geometric mean titers of the vaccine and the emerging group show that there are very similar titers post-vaccination with the current vaccine. And that's true for the data that was presented from CDC, although there was some variation in some labs presented from the other collaborating centers. But in general, data from the CDC shows that post-vaccination showed robust antibody titers to the current vaccine, and those antibodies well-recognized, both the D.3.1, the D.3.1.1, and the C.1.9 reference virus tested. Now, of note, in order to do this type of analysis, we have to preselect the responders in our study to those that respond well to the vaccine. So these are preselected already to look at good responders to the vaccine. Okay. Next slide, please.

02:13:35 Now, another part of the reports coming in from our collaborating centers is to perform genetic or phenotypic analysis for antiviral susceptibility, specifically focusing on neuraminidase inhibitors or endonuclease inhibitors. And looking at the H1N1 viruses, over 1,161 viruses were examined, and 15 viruses showed evidence of reduced susceptibility to neuraminidase inhibitors. Now we looked at the molecular basis for some of those reduced susceptibility and found seven had a position change at position 275 in the neuraminidase, and another eight had two mutations at positions 223 and 247 in the neuraminidase. It also should be noted that the particular change at 247 alone does not confer any change in susceptibility to neuraminidase inhibitors, but we are seeing that as in a lot of viruses that are currently circulating. So that change is a popular change in more recent viruses. Now, for endonuclease inhibitors, we looked at the PA gene in both genetic analysis and phenotypic analysis, and no H1N1 viruses showed evidence of reduced susceptibility. Okay. Next slide, please.

02:15:06 So, now I'll just give a summary of the (H1N1)pdm09 data presented that led to the vaccine selection. So for phylogenetics, (H1N1)pdm09 viruses circulated globally, but did not predominate in any region. The vast majority of the HA genes were characterized belonging to the D.3.1 or the D.3.1.1 subclades. Next slide, please.

02:15:38 Our antigenic characterizations showed in hemagglutinin inhibition assays, post-infection ferret antisera showed good recognition of both the D.3.1 and the D.3.1.1 HA subclades, and that was true with post-infection ferret antisera raised to the current vaccine virus, as well as the proposed Southern Hemisphere, Missouri/11-like vaccine virus. Next slide, please.

02:16:06 Our human serology studies. Again, we're looking at 2025-2026 responders against a small subset of representative viruses from clades C.1.9.3 and the D.1.3 and the D.3.1.1-- D.3.1 and D.3.1.1. Little tongue twister there. When compared to the cell responses for the Wisconsin/67, post-vaccination geometric mean titers were significantly reduced for a few circulating viruses from D.3.1 and D.3.1.1. Together, the data supported recommending the A/Missouri/11/2025 (H1N1)pdm09-like (D.3.1) viruses as the (H1N1)pdm09 vaccine antigens for the 2026-2027 Northern Hemisphere. Okay. Now I'm going to transition on the next slide into the H3N2 data. Next slide, please.

02:17:10 So again, we're looking at detections of H3N2 viruses by the Global Influenza Surveillance and Response Network. We'll again look at 2025 in red, starting with week one, and seeing a small number of detections during the beginning of 2025, and an increase in detections starting around week 36 and peaking at around week 50 and 51. And we're starting to see in 2026, starting back at week one in green, a decrease of those detections overall. So, a large number of H3N2 viruses predominating the viruses detected through GISRS during this time period. Next slide, please.

02:18:00 So if you remember back to the H1N1, we had not as many countries filled in red. So this is a good example of when we see an H3N2 predominant season in the Northern Hemisphere, we have high detections of H3N2 across all of the countries in the Northern Hemisphere. We're also continuing to detect H3N2 activity in parts of temperate South America and tropical South America during this time as well.

02:18:30 So, as noted during Dr. Grohskopf's talk for the H3N2 season in the United States and our influenza season overall, the timing of that season was pretty typical, beginning to really see an increase in detection of influenza viruses above our baseline in November. However, in several countries in North America, of note, Japan and the UK, they saw an earlier beginning of their influenza season responsibly due to the H3N2 virus that we'll talk about in the next couple of slides. So, there were different timing differences for the Northern Hemisphere activity, and there were also out of seasonality detections of H3N2 in parts of temperate Southern Hemisphere. Okay. Next slide, please.

02:19:29 So again, looking at the phylogeography, looking at a very large number of sequence data that is available from the GISRS collaborating network, we can see since 2024 to 2026, a change in the viruses going from J.2 and its many, many subclades, into the predominance of the J.2.4 subclade K viruses. So, what's important to look at here is: what did we have in the previous Northern Hemisphere season? So, looking at the line between 24 and 25, we can see lots of tick marks in blue and green and red representing multiple co-circulating subclades of J.2.1, J.2.3, J.2.5, and J.2.2, as well as J.2.4. So we had very complicated circulations of H3N2s during last season's Northern Hemisphere season. While there was no one predominant subclade, we had a lot of regional differences in which subclade predominated.

02:20:48 If we look at what happened over 2025, we had some of these subclades really reduce in their detection, namely the J.2.1s and the J.2.5s, and instead we had the continuing detection of J.2.3.viruses. I will name out mostly

Central and South America as well as parts of North America detected these viruses during their Southern Hemisphere season, and then continuing detections of the J.2.2 in parts of Asia, and then the J.2.4 being seen initially in parts of Asia, and then spreading globally once it emerged as the subclade K. And we can see for 2026, we have the majority of viruses that have sequenced data available belonging to the subclade K, but still some co-circulation of the J.2.3, and in smaller circulation, the J.2.2. Now, next slide, we'll look more at both the global, the U.S., and then the regional outlook. Next slide, please.

02:21:58 So, the global view should repeat similar patterns to what I just mentioned before, in that we had at the beginning of 2025 a co-circulation of multiple J.2 subclades, and over time, a change in which one was predominating. But really after June of 2025, we can see the increase of the subclade K and the predominance of subclade K since then, but continuously co-circulation of the J.2.4s, the J.2.3s, and the J.2.2s. So for the U.S. view, again, we're looking just at our season. This is looking at the end of September until now. Since the end of September, the majority of viruses have been subclade K, but we did have initial co-circulation previous to September of the J.2, the J.2.3, the J.2.2, and the J.2.4. And you can see that there were low levels of detections of J.2.4 and J.2.3 since October. Next slide, please.

02:23:13 Okay.This is repeating the increase in detection of subclade K in all regions, but highlighting South America being a little bit different in that the higher proportion of J.2.3 is detected during their Southern Hemisphere season, as well as as seeing J.2.4 and subclade K more equally in current weeks. So, this is kind of a good overview of how there could be regional differences in

the subclades which circulate and predominate. However, in this case, all regions now are subclade K predominant. Next slide, please.

02:23:54 This is, again, looking at country-level data where we can see where there were some countries that when they had influenza H3N2, they were only J.2.3 in South America, or you had that co-circulation of the subclade K or the J.2.4. There are some countries in Africa that have not yet detected subclade K, but are still detecting J.2.4s, and then you can see some of the different proportions in parts of Asia as well. And then also in Africa, there are some countries that are still detecting J.2.2 viruses during this reporting period. So, H2N2s keep us on our toes, and this is the one way where we want to always be looking retrospectively of what has been successful, but also mindful that there may be still country and regional differences than what we see at the global level. Next slide, please.

02:24:54 So, this data looks at our antigenic analysis for H3N2 using HI assays. In this case, we're looking at ferret antisera raised to the 2025-26 vaccine viruses. That would be a J.2. So for cell-based, that was A/District of Columbia/27/2023-like; or for the egg-based, A/Croatia/10136RV/2023-like. Now, if we look at the proportion of HI assays that showed greater than eightfold reduction, we can see that in some collaborating centers, including the CDC, this was quite high for the reporting period of September till now. And average is greater than 50 in all. However, there were some differences depending on the collaborating center, and this can be due to the viruses that they received and tested during this time period. However, overall, we can see a reduction of H3N2s that were well recognized with either the District of Columbia ferret antisera, or ferret antisera raised to the egg Croatia.

02:26:07 At the bottom, we can look at data that's done through neutralization-based assays. At CDC, we use the HINT. In this, we see a similar pattern to the HI assays where we see greater reductions in recognition of viruses that were circulating during this time period. And that was true for either ferret antisera raised to the cell District of Columbia or the egg Croatia. Okay. Next slide, please.

02:26:37 So, as we did with the H1N1, we wanted to look at the vaccine recommendation for the 2026 Southern Hemisphere season to see whether the reactivity pattern of this particular vaccine virus-- How that looked with the more recently circulating viruses since September. For the 2026 Southern Hemisphere, we have a J.2.4 vaccine virus represented for the cell by A/Sydney/1359/2024-like viruses; and for the egg, A/Singapore/GP20238/2024-like viruses. Again, we can see a difference in results based on the collaborating center, where some collaborating centers saw fairly good recognition for the majority. There were some collaborating centers that showed higher levels of reductions, and that's true for both the ferret antisera raised to the cell and the egg by hemagglutin inhibition. When we look at our virus neutralization data, we can see a fairly good recognition of the majority of viruses by the ferret antisera raised to the Sydney cell, but poor recognition in neutralization-based assays with ferret antisera raised to the Singapore egg. Next slide, please.

02:28:01 So, with this piece of information, as I mentioned, we're looking at the current Northern Hemisphere vaccine, and then we're also asking for the most previously updated J.2.4 vaccine viruses. Will these still be appropriate? And now that we've had more information and more viruses

circulating that could have different genetic and antigenic properties than we had seen back in September. Now, if we look overall at our ferret antisera raised to the District of Columbia, the J.2 vaccine reference viruses, we see the pattern that viruses that have been split into the J.2.3, the J.2.4, and the subclade K, HA subclades, showed poor-- Were poorly recognized with ferret antisera raised to the J.2.

02:28:55 This pattern we presented in October to VRBPAC, and looking at where the substitutions that define these particular subclades are located on the hemagglutinin, many of these include changes in antigenic sites B and A and near the receptor binding pocket, and also include mutations which could affect glycosylation motifs. This is especially true when looking at the J.2.4 and the subclade K viruses, which have a couple of different positions which have potential changes in glycosylation patterns. We're also seeing the subclade K changes in antigenic site D as well at position 173.

02:29:42 So, now that we have these molecules in your mind, we can take a look at our ferret antisera to Sydney/3549, the J.2.4. Our data looking at an HI and HINT assays with ferret antisera raised to J.2.4 showed poor recognition of the J.2.3 viruses. This is again because of the different changes that they have between each other in the antigenic sites A and B. When we looked at the data for ferret antisera raised against Sydney to the viruses from subclade K with those additional mutations, shown on the right in red, there have, in most part, good recognition of many of the subclade K, but we are seeing more recent J.2.4s have about half of the mutations that we see in subclade Ks. And when we look at data with the ferret antisera raised to Sydney/3549, we're starting to see reductions against these particular J.2.4s

as well as the subclade Ks. And our ferret antisera raised to reference viruses for subclade K, such as A/Darwin/1415/2025, better recognized the subclade K viruses as well as the more recently evolved J.2.4 viruses. And we can see some of these patterns on the next integrated phylogenetic and genetic tree on the next slide.

02:31:14 So here, again, we're looking at the hemagglutinin, and we're looking at the phylogenetic tree splitting up with the subclades. In brown, subclade K; in bright blue, J.2.4s; in yellow, J.2.3s; and then in darker blue and lighter blue, the J.2s and the J.2.2s. The reactivity pattern for our ferret antisera to DC/27 in both HI and neutralization-based assays showed only good recognition of viruses expressing HAs from either J.2 or J.2.2 subclades, but poor recognition of the J.2.3s, J.2.4s, and the subclade Ks. Improved recognition of J.2.4s and subclade Ks were seen with our ferret antisera raised to the J.2.4 reference virus. However, we were seeing some viruses in both the K and more recent J.2.4s with greater than eightfold reduction. We're also seeing poor recognition of the J.2.3s with ferret antisera to the J.2.4 reference virus, as well as reduced recognition backwards to the J.2s and the J.2.2s. Next slide, please. Please.

02:32:40 So, this is an HI assay from the WHO collaborating center in Australia showing how the ferret antisera raised to the current vaccine as well as the 2026 Southern Hemisphere recommended vaccine viruses compared to ferret antisera to the subclade K, cell, and egg reference viruses. And this hopefully repeats the pattern that I mentioned, that looking at more recent J.2.4s and the subclade K viruses, we see better recognition with ferret antisera raised to the subclade K viruses than we do to the current vaccine or

the proposed 2026 J.2.4 vaccine. And then on the next slide, we'll look at more antigenic cartography, again, highlighting a couple of things.

02:33:33 First, when we look at data on the left, we're looking at our neutralization-based assay from the CDC, and on the right, HI assay from the collaborating center in Tokyo. Now, we've color coded the different HA subclades and particular changes that they have. And I want to highlight that in red, we have the J.2 viruses, and these were the viruses that circulated previously; but in the other colors, we're seeing the evolution of different subclades of J.2, in particular in aqua, these are J.2 viruses with 135K, which predominated in the U.S. last season; and in light blue, viruses of the J.2.4 subclade. And then you can see in a bright green the subclade K viruses. And in addition to bright green, you'll see a lighter blue. These are those recent J.2.4 viruses that have some of the mutations also seen in subclade K, clustering closely with the subclade K viruses, and distinct from the J.2.4 viruses represented by the Sydney/1359 reference virus. Now, at the very bottom of the map, we can see orange viruses, which represent the J.2.5s that previously circulated. And then in darker green and brown, viruses representing the J.2.3, including ones with additional substitutions at position 154.

02:35:08 As noted in October, what's very good to see on this cartography is a directionality in the antigenic characteristics of the two predominant clades, the J.2.4 and subclade Ks versus the J.2.3 viruses. They are antigenically distinct from the District of Columbia, but they're also antigenically distinct from each other, making it very difficult to select a vaccine antigen which would recognize both equally well. Now, we can also see, again, the

evolution from the J.2.4s into the subclade K viruses, seeing in some hands with the neutralization assay, a more clear reduction and change in the location of subclade Ks and more recent J.2.4s, and with some HI data that's not as clear. So, when we look at this information we're able to see a couple of patterns, most notably that looking at Sydney itself, it is distinguishable from the current subclade K viruses, and viruses in subclade K and more recently in the J.2.4s are well recognized, showing that serum circle on the left and the right to the subclade K reference viruses, Darwin/1415 for the cell, and Darwin/1454 for the egg. However, we can recognize that the ferret antisera does not recognize the J.2.3 virus as well. Next slide, please.

02:36:47 So again, we're presenting the CDC data for the U.S. vaccine human serology studies across different platforms, mainly cell-based and recombinant, as well as high-dose egg in the elderly. The 25-26 H3 component was District of Columbia/27/2023-like. We can look at the first column, and that is looking at post-vaccination titers of the good responders. And what we can see is pretty high titers across the board from different age groups and vaccine platforms to the current DC/27 vaccine. When we go and look at the representative viruses for the emerging groups, the J.2.3, the J.2.4, the subclade K and the J.2.5, we can see distinct patterns of statistically inferior responses to the J.2.3 and the subclade K viruses across nearly all of the age groups and platforms that is shown here in this figure.

02:38:00 But we are seeing that the actual post-vaccination titers were still quite robust, but the ratio between what was the titer for the vaccine versus the titer of the emerging virus that we're testing was significantly different. We're also showing in the pediatric age groups, so these are individuals that

have never been vaccinated before, so they're getting their first two doses of the influenza vaccine. They also showed reductions against the J.2.4s. Now, other collaborating centers performing human serology, either with the same panel of sera or with different panels showed similar reductions to the J.2.3 and the subclade K in most panels and in most labs that tested. Next slide, please.

02:38:55 So, another summary of our antiviral susceptibility data. We had data for over 4,000 H3N2 viruses, and two viruses showed evidence of reduced susceptibility, and both had a substitution in the neuraminidase at position 119. For endonuclease inhibitors, again, over 4,000 viruses examined, and there were more viruses here that had genetic markers that could have potential reduced susceptibility to endonuclease inhibitor baloxavir marboxil, and that included changes of positions 38 or at position 199 of the PA. Next slide, please.

02:39:41 So, in summary of the phylogenetics, we can see that the J.2 subclades, while they are the predominant overall, we have a lot of diverse subclades that we're concurrently following. And over this time period, we're really seeing that subclade K, which was actually evolved from the J.2.4s and has its official designation as a J.2.4.1 being predominant during this time period. Subclade K viruses have changes of positions 2, 144, 158, 160, 173, 328, and 378. And of note, the changes at positions 144 and 135 that it shares with J.2.4 lead to a change in glycosylation. So, when we have a look at what viruses circulated during this reporting period, we can detect subclade K in all regions and predominating in many of the countries. But of note, to remind ourselves that we still have circulation of other J.2

subclades, notably the J.2 or J.2.3 in South America or the J.2.2 or J.2.4 in Africa and Asia. Next slide, please.

02:41:05 So, our antigenic characterization. I'll first kind of go over a repeat of the current vaccine for the Northern Hemisphere. That's our district of Columbia or Croatia reference viruses of the J.2. They poorly recognize the majority of viruses that circulated, and then that's more specifically viruses from the J.2.3, J.2.4, or subclade K. When we look at ferret antisera to our reference viruses for J.2.3, these viruses, ferret antisera, only recognized their own J.2.3 subclade viruses well and had poor recognition of other subclades. Now, looking at the data for the Singapore and Sydney-like viruses representing the 2026 influenza Southern Hemisphere vaccines, this is where we saw for the most part good recognition of many of the J.2.4 viruses and subclade K, but we did start seeing reductions with accumulative mutations in the J.2.4 and many of the subclade Ks. And we found that subclade K viruses and those J.2.4s with those mutations, specifically calling out mutations at positions 79, 144, 158, 160, and 328, J.2.4 viruses with these particular substitutions showed better recognition by post-infection ferret antisera raised against our subclade K reference viruses of cell-grown Darwin/1415 and egg grown-Darwin /454. Next slide, please.

02:42:43 Our human serology studies. Again, we're using the individuals vaccinated with the J.2 Northern Hemisphere vaccines and against our emerging subclades of the J.2s, J.2.3, J.2.2, J.2.4, J.2.5, and subclade K. We saw in many of the recent panels against many of the viruses reduced post-vaccination titers. And so this in general was the data that supported recommending a cell-propagated Darwin/1415/2025 subclade K-like virus

and an egg-propagated Darwin/1454 subclade K-like virus as the H3N2 vaccine antigens for the 2026-2027 Northern Hemisphere. Next slide, please.

02:43:36 Influenza B viruses. Okay. Well, we'll just be talking about B/Victoria, because as mentioned again, no detections of B/Yamagata viruses after March 2020. Next slide. Overall detections of influenza B viruses, if we look back at 2025, we had the majority of detections happen in weeks 6 through 11 of 2025, and then you can see a sharp decrease in detections over time, and then an increase in detections after week 40. And then as you can see, going back to week one and in green, that increase in detections that are currently happening. And this is happening mainly in North America and parts of East Asia. But as the season is not yet over with, we'll have additional data for the rest of the Northern Hemisphere in a couple of weeks. Okay. Next slide, please.

02:44:35 Where we can see influenza activity from September to January. You don't see a lot of countries greater than 20% positive, but there were pockets in central and the tropical part of South America, as well as temperate South America that had significant B activity detection during this time period, as well as parts of Africa and South Asia. Next slide, please.

02:45:03 Now, talking more about the genetics and characterization of B/Victoria viruses. Next slide. So, for the B/Victoria HA phylogenetics, we can look at data since 2024, and we really, really want to highlight two main groups of viruses. The first are all of these viruses have a progenitor of the V1A.3a.2 HA, meaning that compared to what circulated years ago, these viruses have

a three amino acid deletion in the hemagglutinin. When we look at the HA, we can split them into C subclades, and this were initially broken up in the mid 2020s, or early 2020s, into C.1 through C.5. In more recent years, the majority of viruses that circulated have been one of the C.5 subclades. As you can see, C.5.1, 5.6 and 5.7 are noted on the tree, near the bottom of the tree. And you can see from 2024 to 2026, different colors representing global co-circulation of these viruses. There also wasn't a predominance of any of these C.5 subclades, and said there was regional differences in which subclade predominated.

02:46:34 Now, if we look at the hemagglutinin, what they did have in common is a particular substitution at position 197 from D to E that were characteristics of the C.5s. Up at the top of the phylogenetic tree, we can see the C.3 subclade and the C.3.1 subclade. Pretty small numbers in 2024, but starting between the change in 2024 to 2025, we can see tick marks in a dark blue from North America. And then over the middle of 2025, I can see this in parts of Asia and also South America. And more recently, again, continuing detections in South America, North America, and parts of Asia. C.3 viruses in the hemagglutinin share three changes in the HA at positions 128, 154, and 208. And C.3.1s actually revert one of those positions at position 208 back to an S, and have a change at position 197, so from aspartic acid to an asparagine, which adds a potential glucosylation site. If we look at more recent C.3s that have been circulating in the last couple of months in parts of East Asia, they have additional changes in the HA at positions 255, 267, and also share that same mutation at position 197 to an asparagine, adding in the potential glycosylation. So the C. 3.1s that are circulating in the Americas

have the same glycosylation pattern as the C.3s circulating in parts of East Asia. And I'll show more data later on to show that these viruses are anagenically similar to each other with ferret antisera. Next slide, please.

02:48:36 So, looking at global views over time, again, since February, we have that co-circulation of many C.5 subclades, and then the expansion of C.3.1s at the beginning through May of 2025, but then the retraction, and then the increase in proportion of its detections since October. And then in light green, you can see the increase in detections of these C.3 viruses. Specifically, these ones have that additional glycosylation change in position 197, which wasn't seen in previous C.3s. If we look at the U.S. data on the right, again, I'm looking at the end of September until now, we also had that co-circulation over the summer of the C.5 subclades, but when influenza activity began in October, we were seeing an increase in the proportion of the C.3.1s, and that proportion and dominance of C.3.1s has continued throughout the season, including in the more recent weeks—as Dr. Grohskopf mentioned—where we're seeing a predominance of influenza B in our clinical lab data. We are seeing low levels of C.3, as well as still co-circulation in a lower level of the C.5 subclades. Next slide.

02:49:57 This, again, shows regional differences where we are really only seeing at the moment major changes of C.3.1 in North America, detection of it co-circulating in South America. The other regions really haven't had a lot of viruses from the C.3.1s yet. Instead, again, they're still seeing levels of viruses from the C.5 subclades, apart from East Asia, which again, saw that increase of C.3 that coincided with the increase of the influenza B activity in those regions. So, in terms of parts of the world that are having current

influenza B-led epidemics, North America and parts of East Asia, these are being predominated by the C.3.1 or the C.3 lineages. Next slide, please.

02:50:53 Another map, again, showing country-level differences, which makes things difficult to pick a single subclade, but you can see here the trends that I just mentioned about North America and East Asia. Next slide.

02:51:11 Okay. Antigenic results. Our five collaborating centers get data globally. However, some regions-- Some collaborating centers have a different catchment area than the other, and so, this can lead, again, to differences in the reactivity patterns of our ferret antisera, depending on which viruses we have to test. So, you'll notice that viruses from our collaborating center in China, the Francis Crick Institute in the UK, and VIDRL in Australia show good recognition of the influenza B viruses with a ferret antisera to the B/Austria vaccine, which has been the recommended vaccine virus for Northern Hemisphere since the 2022-2023 season. However, higher proportions of viruses show greater than eightfold reduction in our collaborating centers from Japan as well as the CDC. Again, reflecting the higher proportion of the C.3.1 and the C.3 viruses in these particular collaborating centers.

02:52:15 When we look at our ferret antisera raised to B/Austria, we can see a mixed result. We have some data from some of the collaborating centers showing good recognition. We see a mixed recognition in CDC and Japan's data, again, showing reductions coinciding with the C.3s and the C.3.1s. And then, the Francis Crick Institute, their ferret antisera to the B/Austria shows poor recognition, and potentially due to egg adaptations and which egg

adaptations, the virus that they created ferret antisera to. It looks like our ferret antisera does not have additional substitutions compared to the cell, where the ferret antisera in the UK collaborating center has a change of position 141. And again, that ferret antisera has continued to show poor recognition of the cell-ground viruses in the HI assay. Next slide, please.

02:53:18 So, our integrated genetic and antigenic information, the phylogenetic tree on the right, and the different locations of the viruses are colored. We can see, again, the C.5 subclades—5.1, 5.7, 5.6, and 5.6.1—had global distribution and were well recognized showing less than and equal to twofold reductions with our ferret antisera to B/Austria. But when you look at the C.3 and the C.3.1s at the bottom of the tree, again, located in North America, South America, and parts of East Asia, we're seeing poor recognition with our ferret antisera to B/Austria, showing, again, evidence of antigenic drift in the C.3 and the C.3.1 viruses that, again, have that particular substitution that changes the glycosylation pattern. Next slide, please.

02:54:18 So, looking at our hemagglutinin inhibition tests in the different collaborating centers-- This is going to repeat the pattern I just showed you, where our ferret antisera raised to the cell Austria showed poor recognition, so, higher reduction in ferret antisera compared to the homologous titer for B/Austria against viruses from the C.3s and the C.3.1s. Again, we have a global distribution from East Asia, the Americas, for the C.3 and the C.3.1s. And when we look at the C.5 subclades, they're well recognized with that ferret antisera. And that's true for ferret antisera raised to the other C.5 subclade reference viruses, showing poor recognition of the C.3 and C.3.1s,

but better recognition of the other C.5s. When we raise ferret antisera to our representative virus B/Pennsylvania/14 from C.3.1, we see a good recognition across the C.3 and the C.3.1s, and pretty fair recognition of the other circulating C.5 subclades, but a similar pattern than that particular virus is not well recognized with the ferret antisera raised to the current vaccine or the reference viruses.

02:55:35 Okay. Now, if we look at data from the collaborating center in Japan-- This is comparing ferret antisera for the egg Austria vaccine virus to a potential reference virus for the egg Tokyo/EIS13-175/2025, which represents the C.3.1.

02:55:55 Here again, the ferret antisera to B/Austria shows poor recognition, so, equal or greater to eightfold reductions against the circulating cell-grown viruses of C.3 and C.3.1. When we look at the ferret antisera for the-- Against C.3.1 egg-grown Tokyo, this particular egg-grown virus has a mutation that occurred during growth in eggs that actually changes position 199, which is the third position of the glycosylation site that was gained in the C.3.1 viruses and more recently in the C.3 viruses. So, there is not a putative glycosylation site at position 197 in the egg-grown Tokyo.

02:56:46 Now, ferret antisera to this does show reductions against the C.3 in the C.3.1s, and actually shows good recognition of the C.5, but highlights an issue of viruses growing in eggs, especially for influenza B, where there may be egg adaptations required in order to successfully isolate and grow in eggs. And unfortunately, in this case, it changes the glycosylation pattern, which does also affect antigenicity in our HI assays. Next slide, please.

02:57:24 So, if we look at our antigenic cartography showing CDC data on the left and the data from the collaborating center in Japan on the right, we can see that the serum circle for our reference virus, for Pennsylvania/14 from C.3.1, well recognizes the C.3 and the C.3.1 viruses that are circulating, and also has good recognition of the other C.5 subclades. But we're seeing a little bit change in the position of the serum circle for the Tokyo-based ferret antisera that's raised to the Tokyo egg, where there will be some C.3 and C.3.1s outside of that serum circle showing reductions, again, due to the egg adaptations in the B/Tokyo egg. Next slide, please.

02:58:18 In our human serology data—this is presenting CDCs data—again, we're looking at post-vaccination with the 25-26, which is the B/Austria-like B virus. And again, these are good responders to the vaccine. We're looking at pediatric populations, the very young, the 3- to 8-year-olds, and then the adults against either the cell or recombinant, and then our elderly greater than 65 who received the high-dose egg-based vaccines. And this-- The good responders showed robust antibody response to B/Austria, but significant reductions in GMT titers relative to B/Austria against the reference virus Pennsylvania/14 to the C.3.1s. And that was seen again, all of these age groups showed the similar patterns of reductions. However, we didn't see similar reductions in the C.5 subclades of viruses tested. And similar patterns were also seen against the egg-grown Austria as well. Next slide, please.

02:59:28 So, for our antiviral susceptibility-- Over 500 influenza B/Victoria viruses were analyzed, and only two showed evidence of reduced or highly reduced susceptibility. In particular, they had substitutions at position 464 of the

neuraminidase. And when looking at the PA gene, there were no viruses that had either genetic or phenotypic evidence of reduced susceptibility to baloxavir marboxil. Next slide, please.

02:59:59 So, in summary, we have some complicated co-circulation of different HA subclades for B/Victoria. We're going to focus and make it a little bit more simple. We have the C.5 viruses; they all share that D197E and have continued to co-circulate over the last couple of years at various proportions in different regions, with none of the C.5s ever really becoming predominant. We had that lower initial circulation of C.3 viruses that share that 128, the 154, and the 208. And more recently, the C.3.1 subclade that had that additional glycosylation change of position 197 and the reversion at 208, which we saw in the previous U.S. season, and again, dominating the U.S. season as well as being detected in parts of the Americas, both North and South America.

03:00:57 And in more recent viruses collected that are causing epidemics in East Asia are part of the C.3 subclade that have evolved since the initial subclade emerged to include not only the same glycosylation change—an addition at position 197 as seen in the C.3.1s—but additional substitutions at position 255 and 267. Next slide, please.

03:01:27 So, our antigenic characterization for B/Victoria viruses can be seen as, if the ferret antisera is raised to the B/Austria, it has good recognition of the C.5 subclades, but poor recognition of the C.3 and the C.3.1 viruses. When we look at our C.3.1 reference antisera to the cell-grown B/Pennsylvania/14, we see good recognition of the C.3, C.3.1, and other of the C.5 subclades as

well. When we look at all available egg isolates for potential vaccine use for subclade C.3 and C.3.1, they all have different mutations upon adaption that led to the removal of the potential N-glycosylation site at position 197. And those mutations could either be at position 197 or 199. In particular, the egg isolate where I showed ferret antisera, the Tokyo/EIS13-175, has a substitution at position 199.

03:02:33 When we look at post-infection ferret antisera against this particular egg-grown virus, we are seeing some reductions in recognition of the C.3 and the C.3.1, telling us that ferret antisera is able to recognize glycosylation pattern differences or changes at positions 199 between the cell-grown virus and the egg-grown virus used for the ferret antisera production. Okay. Next slide, please.

03:03:02 Our human serology studies, again, looked at representative viruses from the C.3, 3.1, C.5 subclades with post-vaccination sera of individuals who received the B/Austria-like vaccine viruses. In these results, geometric mean titers were significantly reduced for recently circulating viruses against the C.3, 3.1, and then that was shown again over different age groups as well. So, this data supported recommending a cell-propagated B/Pennsylvania/14/2025-like from C.3.1 virus and an egg-propagated B/Tokyo/EIS13-175/2025-like from C.3.1 as the B/Victoria vaccine antigens for the 2026-2027 Northern Hemisphere. Next slide, please.

03:03:58 So, just a huge acknowledgement to the Global Influenza Surveillance and Response Systems, including the National Influenza Centers, the collaborating centers, reference labs, and our collaborators at University of

Cambridge and modelers at NextStrain and Previr that all presented data during the vaccine composition meeting technical aspect. And then in the United States, the CDC Influenza Division and FDA CBER for their analysis that went into these vaccine selections, as well as our U.S. public health laboratories that help make our U.S. surveillance so strong. And just want to thank you everybody, and I'll turn it back over to Dr. Monto.

Global Influenza Virus Surveillance and Characterization - Q&A

03:04:37 Dr. Monto: Thank you, Dr. Kondor. A very clear presentation of a lot of data this year. I don't recall a season recently where not only are all three types and subtypes being replaced, but also two of them replaced from what was in the Southern Hemisphere vaccine that was just chosen six months ago. Am I correct?

03:05:14 Dr. Kondor: Yes, it's not-- It has happened before, but it has been a couple of years. But I think it also highlights the ability to have candidate vaccine viruses available to make the change when the data recommends it.

03:05:28 Dr. Monto: Correct. I'm just thinking about the manufacturing and things of that sort. Dr. Gans.

03:05:40 Dr. Gans: Thank you so much. Thank you for that amazing presentation. I very much enjoyed the clarity, as Dr. Monto had described. My question really is about if you think about the optimal way in which we could think about the data that you presented and then think about how we could protect people against, sort of, influenza. It seemed to me-- My read is that we do pretty well, even currently, even with the changes Dr. Monto had suggested in some of the different ones for H1N1 and B-- B's a little bit different, but

it's really the H3N2s that we continue to struggle with. And I think this conversation started last year when we were thinking about removing the fourth strain, so, going from quadrivalent to trivalent and taking the B out. People had already recognized some of the issues around the H3N2s and wanting to think about would an optimal vaccine actually include two different antigens within that group.

03:06:57 And I wondered, as you've spent a lot of time with this data, does that seem like a scientifically sound approach to really covering those different ones? Since, particularly that group, it's just hard to predict and seems to actually have some variation that could be really more optimally covered with two different antigens.

03:07:25 Dr. Kondor: Thank you, Dr. Gans. Yes, I agree that the H3s are always an extra special challenge for not only surveillance, but also for the selection of an optimal vaccine antigen. There have-- And I encourage additional work to be done on whether or not multiple hemagglutinins for the same subtype could have improved vaccine effectiveness. So, we have yet to have a licensed vaccine with two H3 antigens, but I do hope that that clinical work continues to see whether or not that does have improved effectiveness.

03:08:01 There are also potentially other strategies to have improved effectiveness that I know is active preclinical work being done, so that in the future we have additional influenza vaccines that could potentially have more breadth of protection across the genetic and antigenic diversity of the circulating viruses.

03:08:23 Dr. Gans: Right. So, I guess that's a really good way of thinking about how we need to kind of prepare; it's to think about novel ways of dealing with this, but also think about having people look at the efficacy of a quadrivalent that would include two H3N2s. So, I think that would be a good recommendation.

03:08:50 Dr. Monto: I agree totally with the-- As I think most of you have recognized with the idea of trying to see whether we could include two type H3 and two viruses in the vaccine as a quicker way to improve the vaccine than some of the long-term strategies, which will probably do a better job. But, Dr. Kondor, this year was even a bigger challenge because I don't think the K subclade really showed itself very early and sort of snuck up on us. Am I correct?

03:09:39 Dr. Kondor: Yes. In fact, I'll give a little bit of my own experience with subclade K. In terms of CDC's analysis, it really wasn't until sequence data was available from both the National Surveillance in the United States and our Respiratory Surveillance, as well as our Travelers Genomic Surveillance, where we first detected viruses that had the mutations that eventually became subclade K. And this was in the very beginning of August. And so, these small numbers of very interesting viruses [Indiscernible – 03:10:12] obviously highlighted to our subject matter experts that they needed additional testing, and we quickly were able to get antigenic characterization to show potential antigenic drift, and then put into full gear by the end of August our candidate vaccine virus development for the egg and the cell platforms. And also, you know-- So, this is the end of August, beginning of September. We're halfway into the vaccine

composition meeting reports. And again, it's very helpful to make a vaccine update when you have candidate vaccine viruses.

03:10:49 And although both our center and the center in Melbourne immediately started working on vaccine candidates, by the September VCM, we did not have a subclade K virus available. And that's why we knew that it was starting to have early epidemics in the Northern hemisphere by the VCM in September, and that's why it was part of the decision-driving factors for why a J.2.4 was recommended because there were available vaccines to that virus, which again is the progenitor for the subclade K, but doesn't have all of those additional substitutions in the site A and B that I mentioned.

03:11:27 Dr. Monto: Thank you. We know it's a tricky virus. Dr. El Sahly.

03:11:37 Dr. El Sahly: Thank you, Arnold, and thank you, Rebecca, for this wonderful presentation. I have a couple of questions. One pertains to the H3N2, to stay on that. The cartography shows two sort of-- Where we are right now with the vaccine we got, and then two antigenic destinations, one being K and one being J.2.3, right?. K, we just discussed, is the one that predominated in the U.S. and other locations, but what do we know epidemiologically about the J.2.3? Has it circulated here before? Are we exposed to it by virtue of infection, et cetera? Because I don't think we were vaccinated against it. And it could be, I guess, one of the destinations where we are heading based on what you showed us.

03:12:50 Dr. Kondor: Yes. Thank you, Dr. El Sahly. I will say that with J.2.3 and J.2.4, we had active discussions in February of last year when they were first being emerging and identifying in the Global Influenza Surveillance

and Response System because of their completely different sets of substitutions in the antigenic site A and B, and the ability that our ferret antisera to the J.2s didn't recognize either very well. So, we did have quite a conundrum of seeing two co-circulating but antigenically distinct subclades. And this is going back to the difficulty in prediction for H3N2—of which one will circulate where—where we only really have good retrospective information. And at that time in February, I guess we had some really early detections of J.2.3 in parts of Europe.

03:13:49 However, over the course of the summer, we really didn't see it circulate globally. Instead, it was more centralized to Central and South America, while the rest of the Southern Hemisphere saw it either for their H3N2s, a J.2.2 or a J.2.4.

03:14:09 So, during the Southern Hemisphere season of 2025, again, we had different co-circulating viruses. Actually, if you look at the regional differences, we had J.2.3 in South America, J.2.2 in South Africa, and J.2.4 in the small numbers of data coming out of Oceania or in Australia. So, not only did we have regional differences, but we had these antigenic differences as well.

03:14:36 So, for the United States, if we look over our summer period-- Our U.S. public health labs do year-round surveillance. So, we're able to have information for very low levels of circulation of influenza, but we're still getting information of what viruses are responsible for any influenza detections in the United States. And that's where we had a lot of turnover from one subclade to the other, including the J.2.4 and the J.2.3 over the summer.

03:15:07 And then as we got into the beginning of our influenza season, that's where we already had that detection and increase of subclade K quite quickly globally and in the United States, but some states had a higher proportion of other viruses circulating, particularly the J.2.3s or the J.2.4s. And so, if we looked at state by state, we could have potentially significantly differences in the populations. However, as the season progressed, the vast majority became subclade K.

03:15:43 But what we do with surveillance is, as I mentioned, you know, we're trying to get the most information on the predominant one, but we're still trying to understand those that are in lower circulation and what-- How are they changing. What new mutations are they acquiring and could they potentially be a future replacement for the current predominating viruses. So, for J.2.3, we're continuing to make new candidate vaccine viruses for this group, as well as other offshoots of the J.2.4s that we've detected that have potential some antigenic changes. So, our work for developing candidate vaccine viruses isn't only going after subclade K, but continuing to have potential options for the other diversity that we detect through our surveillance.

03:16:31 Dr. El Sahly: Okay, thank you. Now-

03:16:32 Dr. Monto: -Thank you.-

03:16:32 Dr. El Sahly: -the other question for-- If I'm-- Do you want me to ask later, Arnold?

03:16:37 Dr. Monto: Why don't you ask later? We have a few--

03:16:39 Dr. El Sahly: Okay.

03:16:40 Dr. Monto: A few other hands at the moment. Dr. Perlman.

03:16:46 Dr. Perlman: Yeah, so, relating actually to the last answer, is the CDC using or thinking about using AI at all to start predicting some of the changes that might come up? Because it seemed like if that worked, that would be a wonderful way to supplement what you're doing now.

03:17:03 Dr. Kondor: Yeah. So, part of the work that we collaborate with in the GISRS system for the vaccine composition does use predictive modeling. That's with collaborators at Previr and NextStrain. And so, in both of the last several years, they've been producing models predicting which viruses would likely predominate in the next three to six months, and also what are the available candidate vaccine viruses and which are predicted to have the most efficacy for the currently circulating viruses. So, we have been using evolutionary models to try to track and predict which viruses will likely to circulate in the future. But I agree that there is a wealth of opportunity for different types of predictive models for not only vaccine selection, but for preparedness of future epidemics.

03:17:57 Dr. Perlman: And have those predictions worked since you've had them for a while? Were they able to predict what was going to happen?

03:18:03 Dr. Kondor: Yeah, sometimes. Sometimes they are right on, and other times the virus is very tricky and outmaneuvers us all.

03:18:12 Dr. Perlman: Okay, thanks.

03:18:15 Dr. Monto: Not surprising at this point. Dr. Meyer.

03:18:19 CAPT Meyer: Thank you. Thank you, Dr. Kondor. And also to Dr. Grohskopf for these excellent presentations from CDC. I wanted to talk a little bit about influenza B for a second. So, I appreciate just how much work goes into this, and there are so many different data sources to triangulate, to kind of come up with the strain suggestion. And for me, watching the influenza A-- Those progressed, and I completely saw how we got to where we did. For B, I was looking a little bit more at the phylogeography and the extended diversity plots and was just struck by-- And you kind of alluded to it. But just really struck how the subclade C.3.1, sorry, C.3.1, you know, it was mostly North America with some extension to East Asia, but it didn't-- At least unless I missed it, it didn't seem to have much more global expansion, whereas the C.5 subclades continued to circulate in a lot of other regions.

03:19:24 So, I know we're tasked with thinking about strain selection for the U.S. So, the C.3.1 strain kind of fits with where our needs are. But I'm just kind of curious, on the global scale, was there a lot of discussion about this? Was it a clear-cut decision based on--? Was there predicted-- Was there continued predicted expansion of C.3.1 or predicted regression of the other? Or how was that thought through on the global scale?

03:19:54 Dr. Kondor: Thank you, CAPT Meyer. Yeah. Yes, there was active discussion on this recommendation being for the Northern Hemisphere and understanding that the influenza activity for influenza B in the Northern Hemisphere hasn't been similar. In fact, it's only been North America and more recently East Asia that has started to see that increase in predominance of influenza B. Parts of Europe have had very little influenza B activity. So,

although I'm showing proportions of the sequence data, that's not necessarily scaled to the actual number of detections, and that's why I hoped I was able to say that, in terms of epidemics that were influenza B forward, they really have been responsible from the C.3.1 and the C.3 in East Asia. So, that taking in together, the use of B/Austria as a vaccine for several years now and understanding that not only is there a lack of immunity post-vaccination to the C.3.1s with the B-Austria—but that's true across all age groups, meaning that there's likely low levels of population immunity to the C.3 and the C.3.1s—were the major determinants in this decision.

03:21:10 CAPT Meyer: Thank you. That's really helpful.

03:21:15 Dr. Monto: Dr. Berger.

03:21:18 Dr. Berger: Thanks, Dr. Gallahar [sp?] That was a great presentation. I just want to thank you for going through everything so clearly, and you and Dr. Grohskopf laying out everything that we're looking at in terms of the data in such a good way. I also wanted to ask about the B strain and mostly just because of the differences you showed in recognition for the C.3 and C.3.1 subclades, between what you're recommending for egg versus cell culture. And what I'm wondering about is, do you plan on collecting data that differentiates between those two vaccines being provided so we can get a better sense of vaccine efficacy from that potential difference?

03:21:58 Dr. Kondor: Thank you, Dr. Berger. I don't know about being able to have a dataset for vaccine efficacy for the different B platforms of vaccines. However, I will have data in the next year when looking at post-vaccination antibody titers in individuals from the United States receiving either a cell-

based, a recombinant-based, or an egg-based vaccine, where we can start to answer some of those questions in terms of the types of antibody responses post-vaccination the different platforms will have. But this information that I showed with our human serology isn't powered to show immunogenicity or effectiveness. It's instead specifically asking about breadth of immunity post-vaccination, but will be something that we'll be taking a strong look at.

03:22:50 Dr. Berger: Thank you. And that's why I'm asking if there's a plan to collect this data so we can actually see if there's an impact on efficacy later, not looking at it from here. Thank you.

03:23:01 Dr. Kondor: And I will plug in the final estimates for the U.S. vaccine networks where there is data available. We will be looking at the HA clade and subclade level information and seeing whether that could be responsible for some of the changes in the vaccine effectiveness seen in our U.S. vaccine networks. We did see a lot of C.3.1 in our U.S. vaccine network so far. So, another question that we hope to be able to pose with the data and see whether we're able to get a significant answer out of it. Thank you.

03:23:40 Dr. Monto: Dr. El Sahly, do you want to finish your questions?

03:23:46 Dr. El Sahly: Sure. I had a question pertaining to the neuraminidase drift. Are we seeing comparable drifts in the neuraminidase, especially with the H3N2, which is the most vexing of the problems?

03:24:06 Dr. Kondor: Yes. And I realized after I submitted my presentation-- I only got an hour, so I couldn't show all of the data that was presented, but we did not have presented during this VCM antigenic information specifically on changes in the neuraminidase. However, we had a lot of data

looking at the phylogenetic clades and subclades of the neuraminidases. They get broken out just like the HAs are into NA subclades based on particular substitutions and their expansion. And we do a lot of work to look at the co-evolution of viruses with particular HA changes and which neuraminidase and not only the clade or subclade or specific amino acid changes that those viruses possess.

03:24:56 So, we're looking at this more on a predictive antigenic than we are on actual looking at antigenic drifted characterization data. For all of our vaccine virus selections, we also are not only taking into account which HA they represent, but whether or not the neuraminidase that the vaccine viruses possess are the same across platforms and represent the majority of viruses from that particular HA subclade. So, that's kind of the data for neuraminidase that I didn't present, but was part of the vaccine selection process.

03:25:34 Dr. El Sahly: I mean, as we discuss periodically in this Panel, moving ahead with novel ways to improve VE, and it seems that the big elephant in the room seems to always be the neuraminidase, but-- In addition to the other proposed improvements. But thank you for that.

03:26:01 Dr. Monto: Thank you. Just one further comment before we break for lunch. Dr. Kondor, it's getting to be very confusing when we see the old designations that are just basically geographic, and now we have all this cladal information. Has any thought been given to expanding the designation of the viruses so we can tell what clade is represented?

03:26:35 Dr. Kondor: So, we've just published a paper discussing the nomenclature that I presented today in influenza and other respiratory virus that explains the rationale for trying to do a more agnostic naming convention beyond geography, and instead focus on how often we create new clades and subclades and when we go to an alias. So, explaining where we go from a J.2.4.1 to a subclade K, because we're able to track smaller clades with more precision by doing that rather than trying to do larger clades. So, this is kind of part of the needs of doing predictive modeling for clade frequencies. We need to be able to have appropriate breakdowns of different subclades in order to see these maybe very small dynamic changes in the viruses that are circulating. So, there isn't a plan to include location as part of the subclade nomenclature.

03:27:44 Dr. Monto: Good, because location really doesn't tell us a whole lot anymore. Okay. It's time to break for lunch and we are going to have, as designated, 30 minutes. So, since it's 20 after now, we will return in 30 minutes Eastern, or everywhere. 30 minutes. So, we break for lunch, returning in 30 minutes.

Department of War Influenza Surveillance and Mid-Season Vaccine Effectiveness

00:06:27 Dr. Monto: Welcome back to our meeting on strain selection for the 2006-2007 [sic] year. It's my pleasure next to recognize that the military has been doing studies on influenza surveillance and vaccine effectiveness over many years. And next, Bill Gruber-- Bill Gruner, who is the Program Manager and Molecular Biologist at the U.S. Air Force School of Aerospace

Medicine at Wright-Patterson Air Force Base. He will talk to us about surveillance and effectiveness. Over to you.

00:07:34 Mr. Gruner: Okay. Thank you, Dr. Monto. Hello and good afternoon, everyone. As you said, my name is Bill Gruner and I'm going to be presenting the Department of War's U.S. and International Influenza Surveillance Activities for the 2025-26 season. Next slide, please.

00:07:51 So, I want to start by reiterating that I have no conflicts of interest and to report that the views presented here are only of the authors. Next slide.

00:08:01 So first, I'll give a brief overview of the DoW surveillance efforts. I'll then present mid-year vaccine effectiveness estimates for two distinct populations. One estimating VE against influenza-like illness in DoW healthcare system beneficiaries. And a second study, a VE study of our active component service members. I'll then go into the phylogenetic diversity and antigenic characterization for the viruses that we've further characterized in the DoD surveillance population. Next slide, please.

00:08:35 Influenza surveillance in the DoW is a large part of several public health initiatives with programs extending to over 400 locations in 30 countries. We monitor U.S. military personnel and their healthcare dependence, as well as fostering public health relationships with foreign entities and local nationals. We closely monitor our active component personnel for respiratory diseases like influenza through numerous testing and characterization methods such as rapid tests, PCR, culture, sequencing, and serology. And in turn, we utilize these health encounters for the collection of

surveillance data, reporting of said data, and sharing with national and global partners. Next slide, please.

00:09:16 The many aspects of the DoW Influenza Surveillance Network are facilitated by the Defense Health Agency's Global Health-- Global Emergency Infection Surveillance Branch, represented by Commander Gallaway as Head of the Respiratory Focus Area. Surveillance efforts represent all six geographic combatant commands, so the global footprint is substantial. And of note, one thing that distinguishes the DoW population from the general population is that service members typically have a higher vaccination rate. Next slide, please.

00:09:48 Influenza RT-PCR data are collected locally and submitted monthly through DHA channels. On this slide, the number of specimens positive for each circulating subtype per epi week are graphed on the X-axis and the percent positivity is represented by the black line. The data on the top are from our partners in Ghana while the data on the bottom represent the aggregated influence activity in this region from the WHO GISRS's efforts. We'd like to show this slide to illustrate that these DoD efforts can provide a significant contribution to regional testing efforts. Next slide, please.

00:10:22 So, alternatively, our surveillance systems can provide key insights into where to direct characterization efforts when patterns may deviate from the global trends. For example, this slide comparing GEIS and WHO data from Asia shows an observed spike of (H1N1)pdm09 in the fall of 2024 and then a higher relative circulation of influenza B throughout early 2025 in the

GEIS data, which is not explicitly observed in the GISRS data. Next slide, please.

00:10:52 So, now I'll transition to our first vaccine effectiveness study, which represents the mid-season VE estimates for DoW healthcare beneficiaries. This will be excluding our active component service members. Next slide, please.

00:11:07 This beneficiary investigation utilizes the DoW Global Respiratory Pathogen Surveillance Program, which leverages an infrastructure of greater than a hundred sentinel sites, heavily concentrated in the United States and Germany. The program requests a systematic sampling of 6 to 10 ILI encounters weekly from each installation for subsequent lab testing and questionnaire submissions. This study is a test-negative case-control design. Cases include laboratory-confirmed influenza by PCR and/or viral culture and our subset to peak season activity that occurred between November 9th and February 21st. The ILI case definitions are described here and they come from questionnaires and patient records as well. Next slide, please.

00:11:53 Our models here adjusted for age, month of illness, and region as needed for 12 different analyses shown below. Analyses were conducted for all dependents, adults, or children for all influenza categories, except for adults and children with (H1N1)pdm09, and then adults with influenza B, just due to low numbers of those groups there that we can perform analysis. Next slide, please.

00:12:19 In all, we had 312 cases and 692 controls with 31% and 69% vaccination rates in these groups respectively. To be considered vaccinated, an

individual needed to present with symptoms 14 days or more after receiving the 2025-26 Northern Hemisphere influenza vaccine. In the figures on the right, you can see the breakdown of the influenza subtypes included in this study from the United States and from the OCONUS or outside of the United States locations in the top right and in total on the bottom. Next slide, please.

00:12:53 This is a quick overview of the study participant demographics illustrating the slight majority were female. Most tended to be under the age of 18, and most of our samples were collected from December through February, with the highest number collected in January. Next slide, please.

00:13:13 So, here are the percent VE calculations and their confidence intervals from this study, with statistically significant results in red. Adjusted VE ranged from 18% to 75% across the various categories. VE was moderate to high for A(H3N2) and significant in all of the dependent groups for H3, with 75% VE for adults being the highest. VE was also high and significant for influenza B with all dependents at 63%, and higher generally for adults in all the categories where available. Results were not significant for any of the A(H1N1)pdm09 or for children in the overall influenza A, any subtype, or the influenza B categories. Next slide, please.

00:13:59 So, this slide just shows a force plot of the same adjusted VE calculations for easier visualization and comparative results of the confidence intervals between the different groups. Next slide, please.

00:14:13 So, we'll now transition to VE estimates against medically attended ambulatory influenza infections among active component U.S. service

members. Next slide. This study was also a test-negative case-control design for outpatients. This was done using active component personnel from across all military services, including recruits, and included those stationed in the continental United States, as well as those stationed in foreign locations, from December 1st through February 11th. As in the beneficiary studies, influenza cases were confirmed by PCR or culture, but in this study, rapid test positives were used to define cases as well, while controls did not include negative rapid tests. Models in this study were adjusted for age, sex, prior vaccination in the previous five years, and month of diagnosis. Next slide.

00:15:07 So, here you can see the age distribution of cases and controls in this study. The large numbers were from the 18- to 24-year-age group, which is interesting because in previous active component VE studies, the largest age typically is in the 30- to 39-year-old range. Next slide.

00:15:27 Most of the vaccine types included in the study were IIV, most of the subjects were vaccinated previously within five years, and most of the cases were influenza A. Over 700 cases of A(H3N2) and influenza B were used. However, only 51 A(H1N1)pdm09 cases were available for this study. Next slide.

00:15:49 Here we show the VE estimates against both influenza A and B, as well as the A subtypes (H1N1)pdm09 and H3N2. Once again, statistically significant estimates are in red, showing moderate adjusted VE for H3N2, and moderate to low protection for the all influenza and influenza A, all

subtype groups. There's also a force plot here for easier visualization. Next slide, please.

00:16:17 So, now I'll transition to our genetic and antigenic analysis, starting with the global distribution of the sequences that we analyzed, followed by a separate analysis, each for each subtype; A(H1N1)pdm09, A(H3N2), and B/Victoria. Next slide, please.

00:16:36 This figure illustrates the footprint where our influenza genetic data are originated from this season, with 1,300 viruses that were collected and analyzed and sequenced from September 2025 to February 2026. The majority of influenza viruses characterized were H3N2, with approximately 10% each of (H1N1)pdm09 and B/Victoria. And similar to other surveillance systems, we did not see any B/Yamagata viruses in circulation. Some regions such as Europe, West Africa, and a few HHS regions of the United States had a higher relative circulation of H1N1 than others, while South Korea, East Africa, and other HHS regions in the United States had a higher relative circulation of B/Victoria. And as a note, that I noted from Dr. Kondor's presentation and from the WHO, we did seem to have a higher amount of flu B in our United States data than some of the other surveillance systems. Next slide, please.

00:17:35 So, now on the phylogenetic analysis for A(H1N1)pdm09, this is the hemagglutinin, with time being represented along the X-axis, so the more recent collections are further to the right of the tree. The 2025-26 Northern Hemisphere vaccine strain selections are shown in red, and the 2026-27 WHO Northern Hemisphere vaccine strain recommendation is shown in

orange. The bars immediately to the right of the tree show results for the HINT assay that was previously discussed by Dr. Kondor. The plot shows DoW circulating virus neutralization by ferret antisera derived from the 2025-26 and 2026-27 WHO vaccine-like strains. So, here the high reactors are shown in orange and the low reactors are shown at greater than a fourfold difference to either the (H1N1)pdm09 vaccine strain in red. Subclades in the trees are indicated by color in the legend or by the solid black vertical lines to the far right of the tree.

00:18:34 And so, you can see the subclade D.3.1 represented in the dark blue and D.3.1.1, which is nested within the D.3.1 at the top of the tree, co-circulated in fairly even proportions during the season. However, we did see a slight majority of D.3.1, which contains the strain recommendation A/Missouri/11/2025. We also continued to see low level circulation of the subclade C.1.9 and C.1.9.3.

00:19:00 Of note, no changes to the glycosylation sites occurred for our H1N1, but we did observe one consensus sequence that was identified with the neuraminidase substitution H275Y and another one that had the I223V and S247, which make it for the neuraminidase inhibitor antiviral resistant, although we did not perform minor variant analysis and we did not perform any phenotypic confirmations just yet. Next slide, please.

00:19:31 This slide just shows the same subclade distributions throughout the season, so both in total strain numbers on the left and then represented as a proportion of the total for any one month on the right. So, you can see the replacement of D.3.1 by D.3.1.1 as it occurred by December. And although

it's preliminary with not all February sequence data in yet, we can see that D.3.1 appears to be increasing again recently. Next slide, please.

00:20:00 So, shifting to the antigenic data for (H1N1)pdm09; these results are an antigenic map of neutralizing titers produced with the HINT assay using ferret antisera against MDCK propagated test and reference strains. The colored squares represent antisera while the small colored circles represent circulating strains, and the larger colored circles represent the reference strains. The colors are corresponding to the clades listed in the bottom right in the legend. Each square in the grid represents a twofold difference in titer and the large blue circle represents an eightfold difference from the antisera to the 2026-27 WHO Northern Hemisphere strain recommendation, A/Missouri/11/2025. Although the antisera to A/Wisconsin/67/2022 in the green square and A/Missouri/11/2025 in the blue square fall very close to each other, you can see the slightly higher number of the D.3.1 viruses in blue and the D.3.1.1 viruses in the darker blue fall within an eightfold range to the A/Missouri/11 reference strain antiserum. Next slide, please. Next slide, please. Thank you.

00:21:15 So, this is just a titer table of the HINT data that was used to generate the antigenic cartography on the previous slide. The reference antisera are across the top and then the vaccine, or-- The vaccine CVV and then the test reference viruses are down the left side. So, while both the 2025-26 vaccine strains in orange and the 2026-27 WHO Northern Hemisphere recommendations in green show good protection against the D.3.1 and D.3.1.1 strains, with generally moderate protection against the other

subclades, you can see that Missouri/11 in the green has a slightly higher number of strains that fall within an eightfold threshold. Next slide, please.

00:21:57 But for the H3N2 HA segment, we saw an overwhelming majority of subclade K, which I think will come as no surprise to anyone at this point. That's representing the purple on the tree. And so, similar to other global trends, we continue to see very low level circulation of the other subclades, the J.2, J.2.2, J.2.3, and J.2.4. And then similar to the H1N1 tree, the H3N2 2025-26 vaccine strain, the A/District of Columbia/27/2023, is shown in red and then the 2026-27 WHO Northern Hemisphere strain recommendations, the A/Darwin/1415/2025 and the A/Darwin/1454/2025 are shown in the orange. And again, the bars on the right show the high and low reactors to DC27 and A/Wisconsin/114/2025, which is an A/Darwin/1415/2025-like virus. It's suggesting fewer low reactors to the 2026-27 WHO recommendations.

00:23:01 Most of the circulating strains here shared the loss of a glycosylation site from T135K-- Excuse me. And the gain of a glycosylation site from S144N. We did have several one off changes to glycosylation sites, but they're too hard to fit in the branches here, so they're not shown. We did not observe any consensus sequence substitutions that were indicative of any antiviral resistance, although again, no minor variant analysis or phenotypic testing has been performed. We did have 23 viruses that shared the F79V, S144N, M158D, I160K, and T328A, which were mentioned by Dr. Kondor earlier. Next slide, please.

00:23:51 And so again, this slide just shows the H3N2 clade proportions throughout the season, both as a total number on the left and then as a proportion on the right. And you can see the overall dominance of the subclade K throughout. However, we did have other subclades such as J.2.4 that have still remained even recently. Next slide, please.

00:24:12 And this is the endogenic map for H3N2, as with the H1N1 cartography, the small colored squares, although hard to see in this one, represented the reference antisera. The small colored circles represent circulating viruses and the large colored circles represent the reference viruses. Subclade K viruses are colored red here while the J.2 viruses represented by the 2025-26 vaccine strain selections, A/Croatia/10136/RV, and A/District of Columbia/27/2023 in blue, followed by other colorations for the remaining J.1 and J.2 subvariants.

00:24:48 So here, the large circle represents an eightfold difference from the antisera to the cell, A/Wisconsin/114/2025 which, as a reminder, is the A/Darwin/1415-like strain. And you can see that that circle encompasses most of the subclade K viruses and many of the other subclade viruses pretty well. Okay. Next slide, please.

00:25:10 And then in this titer table for H3N2, you can see that-- Egg A/Michigan/105/2025, and the cell A/Wisconsin/114/2025 in green, which, once again, are Darwin/1454 and Darwin/1415-like viruses respectively, generally have higher titers than the 2025-26 vaccine strain selections in orange, and they have fairly broad coverage across most of the other

subclade viruses, especially compared to anti-serum raised against the J.2.1 through 4. Next slide, please.

00:25:46 So lastly, we have the analysis for B/Victoria, starting with the HA phylogenetic tree here. The majority of the sequences characterized belonged to the subclade C.3.1, while we also did observe moderate circulation of C.3 and C.5.6 and low level circulation of C.5.1, C.5.6.1, and C.5.7. Most of our B/Victoria viruses were collected in the United States. Therefore, this higher proportion of C.3.1 highlights Dr. Kondor's observation of increased C.3.1 in North America.

00:26:16 The 2025-26 vaccine strain, A/Austria/1359417/2021 shown here in red and the cell-propagated 2026-27 WHO Northern Hemisphere vaccine strain recommendation, B/Pennsylvania/15/2025, which is a C.3.1 virus, is shown in orange. In the bars on the right for the high and low reactors, you can see several low reactors to B/Austria, but none to B/Pennsylvania. Nearly all of the C.3 viruses shared the D197N, which has caused the loss of a glycosylation site, and 15 of the viruses had the D197N, S255P, I267B substitution groupings that Dr. Kondor mentioned earlier. And, once again, no consensus sequence substitutions here were indicative of antiviral resistance, although no minor variant analysis or phenotypic analysis had been done yet. Next slide, please.

00:27:15 In this figure, once again, the total and proportional subclade dynamics, this time for B/Victoria, throughout the season you can see the drastic shift of a majority from C.5.6 to C.3.1 that occurred in December, and the continued

persistence of. We do still have some C.5.6 and C.3s existing even recently. Next slide, please. Thank you.

00:27:41 In this figure—the B/Victoria antigenic cartography—you can see a distinct clustering of the subclade C.3.1 viruses away from most of the other subclade references and test strains. The circle represents an eightfold difference from the antisera to A/Pennsylvania/14/2025 there in the middle. Next slide, please.

00:28:03 And this is the titer table of the HINT titers for B/Victoria. You can see the overall higher titers for the B/Pennsylvania/14/2025 in green across most subclades in comparison to the A/Austria strains in the orange, especially with the higher titers, again C.3 and C.3.1, while still providing moderate protection against the C.5 subclades. And I know we did not have the B/Tokyo strain available for characterization. So, it was excluded from most of these, but other than the couple differences mentioned earlier, we can sort of use B/Pennsylvania as a proxy. Next slide, please.

00:28:42 So, in summary, the DoW maintains an extensive respiratory surveillance network. VE for beneficiaries was high for A(H3N2) in all dependents with flu B, and then higher for adults and children generally. VE in the active component service members were moderate for A(H3N2) and low to moderate overall for all of influenza A.

00:29:05 So, we have many partners to thank for their contributions, either the RT-PCR data or sequence data. So, there's certainly a lot of people that are involved in this work and we wouldn't be able to do this without them. So, big thanks to them. Next slide, please.

00:29:20 And continuing my summary, most of the A(H1N1)pdm09 sequences were in subclade D.3.1, and although the data weren't shown, the dominant NA subclade was D.1. These strains were more closely related genetically and antigenically to the 2026-27 WHO Northern Hemisphere vaccine strain selection, A/Missouri/11/2025, than they were to the current strain selections, the A/Wisconsin/67 and A/Victoria/4897. Most of our H3N2 strains were subclade K, and though also not shown, most of the NA clades were B.4.2.2.

00:29:57 Circulating H3N2 viruses were more closely related to genetically and antigenically to the 2026-27 WHO Northern Hemisphere vaccine strain recommendation, A/Darwin/1415/2025-like virus, A/Wisconsin/114/2025, and the A/Darwin/1454/2025-like virus, A/Michigan/105/2025, than they were to the current strain selections of A/District of Columbia/27 and A/Croatia/10136/RV.

00:30:27 And finally, most B/Victoria strains were subclade C.3.1. The dominant NA clade was B.7.1, though also not shown. Circulating B/Victoria viruses were more closely related to the 2026-27 WHO Northern Hemisphere vaccine strain. Recommendations B/Pennsylvania/14/2025, and by proxy the B/Tokyo/EIS13-175 strain than they were to the current strain selection of the A/Austria/1359417/2021. Next slide, please.

00:31:00 And so with that, I want to thank you all for the opportunity to be here and present our data to you, and I will now open it up for any questions.

Department of War Influenza Surveillance and Mid-Season Vaccine Effectiveness - Q&A

00:31:09 Dr. Monto: Thank you very much for a clear presentation. Questions? Please, raise your hands. Dr. Gans.

00:31:22 Dr. Gans: Thank you so much, Dr. Gruner, for that. I feel, and maybe I misunderstood a little bit, but in your vaccine efficacy data, you showed really high rates of vaccine efficacy for the H3N2, but you also showed that K was the predominant. So, what is your sort of rationale for that?

00:31:49 Mr. Gruner: Well, there's a couple takeaways here. Yeah, I'd observed that as well. And then-- Our high vaccine effectiveness do kind of go up against a lot of the other national ones that are reported in the GIVE report. But a couple things that are occurring here is, you can have a lot of memory cells in your immune system that can stir up other antibodies to other subclades. And so, we have in the DoD, highly vaccinated population that gets vaccinated every year sequentially. So, I think there's a lot of immune memory that's going on there, as well as the differences between the antigenics and then the vaccine effectiveness is, you know, humans aren't ferrets. So, the ferrets are naive, so you're looking at purely naive differences between the different clades antigenically there. Whereas, once again, with the humans you can have all sorts of other antibodies produced with that.

00:32:54 Dr. Monto: Thank you. Not seeing any other hands raised-- Oh, Dr. El Sahly. Last minute.

00:33:02 Dr. El Sahly: Yeah, just a comment actually to Dr. Gruner and Dr. Gans in that also the UK observed-- I'm not going to say high VE this season against the--

00:33:14 Dr. Monto: I don't think it was that high.

00:33:15 Dr. El Sahly: No, it was comparable. I was going to say comparable. I was expecting it to be low, given the case circulation, but it was comparable. And that's why I was asking if, I don't know, the end didn't drift as much or what happened, but--

00:33:29 Dr. Monto: I don't know if we've seen later-- That was a really preliminary estimate. I don't know what's happened since.

00:33:39 Dr. El Sahly: The one in the UK?

00:33:41 Dr. Monto: In the UK.

00:33:42 Dr. El Sahly: Yeah, I don't think there was an update. It was prelim, like the one we saw here for the United States, and the VE was comparable despite the circulation of the K. That's what I was going to say.

00:33:59 Mr. Gruner: Yeah. And similar to what Dr. Grohskopf had mentioned, this is a mid-season VE analysis, so, still a lot more data to be collected this season, so, things can certainly change by the end of the year.

00:34:12 Dr. Monto: Dr. Gans, do you have your hand up again?

00:34:15 Dr. Gans: I do. Thank you. I was going to let other people have a chance, but no one's coming up. Can you describe a little bit, then, the individuals who actually did get disease in your population of highly vaccinated group?

What stood out to you about them? Why were they prone to--? You know. We all know that there's breakthrough. I'm just trying to get at your, sort of, thought, which I actually think is a good thought that overall we have high levels of memory in our communities, I guess, depending on the community rates of either getting infected previously or being immunized, but trying to understand a little bit more about those. I don't know if they're breakthrough, because I'm presuming they were immunized since they're in your population of highly immunized, but maybe you could talk a little bit about that.

00:35:16 Mr. Gruner: Yeah, I mean, I don't know exactly which ones were vaccinated and which weren't. I do have some information as far as symptomology, because we do collect that in the questionnaires. And in the cases compared to the controls, the significant symptoms that we had were fever, chills, body aches, cough, and fatigue. But yeah, I think in our data, 79% of the beneficiaries were vaccinated, if that-- It does tend to be higher than the general population. I think the general population is about 45% right now. So, it's a little bit higher, but not everybody was vaccinated, so not all of those are technically breakthroughs. But we do generally have a younger population, so they tend to be more healthy with fewer severe complications.

00:36:06 Dr. Gans: Yeah. I just think that when people hear these rates of vaccine efficacy while yours were actually high, we just have to be careful how that is sort of interpreted. These are largely efficacious at least to severe disease, at least in pediatrics, the ones that we see that are hospitalized, again, largely

fall in the under-vaccinated group. So, there is some efficacy which we are not capturing in all of this data that we're presenting.

Candidate Vaccine Strains & Potency Reagents

00:36:45 Dr. Monto: Well, thank you again. And next, we move on to candidate vaccine strains and reagents. Let's now realize the reagents are very important in developing the new vaccines, and we're going to hear from Dr. Manju Joshi, who's the Lead Biologist in the Division of Biological Standards and Quality Control at CBER. Dr. Joshi.

00:37:28 Dr. Joshi: Good afternoon. Thank you, Dr. Manto, for the kind introduction. In my presentation today, I'm going to be talking about the candidate vaccine strains and potency reagents and how we are kind of looking at the upcoming Northern Hemisphere influenza season. Next slide, please. So, I will briefly go-- Rather quickly go over the viruses which were recommended for production of 2026 Southern Hemisphere influenza vaccines, because [Indiscernible - 00:37:50] is a background about what kind of reagents we have in stock. Then, we'll have to talk about the ability of potency reagents for vaccine testing, and what are our thoughts and plans for, once the Committee decides on the new strains, what are plans for 2026-27 Northern Hemisphere influenza reagents, potency testing reagents. Next slide, please.

00:38:28 So, talking of influenza A, the H1N1 type, for Southern Hemisphere seasonal influenza vaccine, the recommendations were, for egg-based vaccines was an A/Missouri/11/2025 (H1N1)pdm09-like virus, and that for the cell culture-based was-- Cell culture-, recombinant, as well as nucleic

acid-based vaccine, the same recommendation was Missouri/11/2025. Data collected and reviewed by the GISRS system support the same vaccine composition for 2026-27 Northern Hemisphere seasonal vaccine. An important component of any vaccine manufacturing would be the candidate vaccine viruses, and as I've indicated here, different CVVs are available for this group of viruses from various sources listed here.

00:39:28 Come to the second component for the trivalent vaccine, the influenza H3N2 component, for Southern Hemisphere seasonal influenza vaccine, for egg-based vaccine an A/Singapore/GP20238/2024 (H3N2)-like virus was recommended. And for-- Sorry, split the slide, please. Next slide, please. I'm sorry about that. I will start. So, I don't have to repeat all the things, but for egg-based was an A/Singapore/GP20238 virus and for cell culture-, recombinant and nucleic acid-based vaccine A/Sydney/1359/2024 (H3H2)-like virus was recommended.

00:40:19 Based on the data collected and reviewed by GISRS, they support a change in the current composition and they have proposed an inclusion of a new H3N2 virus, which is for egg-based vaccine an A/Darwin/1454/2025-like virus and for cell culture-, recombinant- and nucleic acid-based vaccine an A/Darwin/1415/2025-like virus. Again, at present time, as previous speakers have elegantly said, and a lot of work goes into that and various candidate vaccine viruses, the prime requirements for manufacturing are being developed and the list keeps on going and they keep coming. But last, the information when I made these slides are that candidate vaccine viruses for this group are also available from both CDC in the U.S. and from VIDRL in Australia, and I'm sure the list will be going further.

00:41:23 Coming to the third component-- Next slide, please. Coming to the third component, the B component, which is from Victoria lineage, for Southern Hemisphere seasonal influenza vaccine, for egg-based, we have B/Austria/1359417/2021-like virus, and the same virus was recommended for the other platform, which is the cell, recombinant or nucleic acid platforms. Again, with the start of all the surveillance data analysis, a change has been proposed based on the GISRS data, which indicates that for egg-based vaccines, it will be a B/Tokyo/EIS13-175/2025-like virus. And for cell culture-, recombinant and nucleic acid-based vaccines, it will be a B/Pennsylvania/14/2025-like virus. And, right now,-- I mean, candidate viruses are coming up, more would be added to the list pretty soon or have already been done since yesterday, but there are candidate vaccine viruses available. So, we have-- What was there and what we have, the new strains which have been proposed.

00:42:47 Now, based on the current thought and the surveillance, what the data is showing, let's look at what the potency testing reagents are. Next slide. So, since there was a change in H1N1 component for the Southern Hemisphere, we and other regulatory laboratories had prepared the potency testing reagents, and here listed are the reagents we had prepared. I will just point out what CBER had prepared. We had reagents prepared for A/Switzerland/6849/2025 (IVR-278) virus, which was used in vaccine testing. We had prepared reference potency testing, reference antigen and antisera. Other laboratories had also prepared their own reagents, and these were made available to manufacturers. As far as the cell-based vaccines--

For cell-based vaccine testing, the reagents were prepared by TGA in Australia and they were made available. Next slide, please.

00:43:57 At this point, what I can say is: if, based on the strain, this Committee recommends there will be a need for making the new reagents with whatever the changes are proposed, and we, in DBSQC at CBER, will work with manufacturers to prepare and calibrate new reference antigens and antisera that is needed for vaccine potency testing. We'll put all our efforts to make sure that the reagents are available in a timely manner, which will not cause any problems for manufacturers, and we'll be able to successfully use them in the vaccine testing at our end as well. So, I think that's it for me. Thank you. I can take any questions.

00:44:51 Dr. Monto: Thank you. Very succinct and to the point. Questions? Thank you again.

00:45:10 Dr. Joshi: Thank you.

Comments from Manufacturer Representative

00:45:11 Dr. Monto: We now go to the next step. After we have the reagents, we go to manufacturing and we're going to hear from Dr. Beverly Taylor, head of Global Influenza Scientific Affairs at CSL Seqirus. Dr. Taylor.

00:45:36 Dr. Taylor: Thank you, Dr. Monto. Can you hear me okay?

00:45:38 Dr. Monto: We can.

00:45:39 Dr. Taylor: Great, great. I'd like to thank the organizers for, once again, giving us the opportunity to present to the VRBPAC Committee and

provide the industry perspective. My name is Beverly Taylor and I work for CSL Seqirus. However, I'd like to highlight that this presentation has been informed through consultation by the influenza vaccine manufacturers who supply the U.S., and that is AstraZeneca, CSL Seqirus, GSK, and Sanofi. Next slide, please. Okay, this is my disclosure statement. I am an employee of CSL Seqirus, and I own shares in the company. Next slide, please.

00:46:30 These are the key messages that we're going to cover in our presentation today. We really wanted an opportunity to talk about the transition from QIV to TIV in time for the Northern Hemisphere 24-25 season, as we haven't had the opportunity to do that previously. Once we talk about the Northern Hemisphere 25-26 campaign and the successful delivery of vaccines for that campaign, really to focus a little bit on the continued decline of influenza vaccine coverage rates in the U.S.

00:47:09 We also want to give updates on the CBD Nagoya Protocol and other compounding Access and Benefit Sharing obligations as they continue to hinder influenza virus supply, even for those manufacturers located in the U.S. And finally, the importance of global scientific collaboration and sharing of surveillance and virus data for public health decision making. Next slide, please.

00:47:41 I'd like to start off with this slide because there are many, many aspects that go into the influenza vaccine strain selection as we know, and it really is a balancing act in helping to deliver a successful influenza vaccination campaign. So, we start off on the top right. We need robust, comprehensive and timely global surveillance, and what that allows is the strains which are

selected to be as well-matched as possible to the circulating strains of influenza. We also need to be able to produce the vaccine so that we have timely availability of vaccine for the vaccination campaigns for the upcoming influenza season. Dr. Kondor talked about how important it is to have the CVVs ready in time for the season, so that timely supply of CVVs and potency assay reagents is really important. And also, the current timing of the vaccine strain recommendation allows us to manufacture sufficient doses to supply the demand for the upcoming season.

00:49:08 The choice of candidate vaccine viruses is really important for manufacturers, and it's really important for us to have a choice of CVVs for each of the subtypes so that we can choose the CVV which gives us the optimal yield in our manufacturing processes. And that will allow us to supply sufficient vaccine doses to support the recommendations and increase vaccine coverage rates. Next slide, please.

00:49:43 Okay. So I'm just going to talk a little bit about the transition to TIV. We'd like to recognize that it was actually the VRBPAC Committee that really, really pushed for this transition. And the transition, as with all things, was quite complex for us to achieve. There were lots of changes to production procedures, both in production and in testing. There were also product licenses which had to be updated not only for the U.S., but around the rest of the world. And also, many of us have multi-year contracts, so there were many contracts that needed to be changed to accommodate this. But I have to say that the industry worked in close collaboration with CBER. We submitted the regulatory files according to the timelines that were outlined, and we obtained the necessary CBER approval for the TIV distribution to

the agreed timing. And we also would like to recognize that VRBPAC understood that some of the U.S. approved vaccines for ex-U.S. countries did not transition to TIV as quickly, and so they continued to make a recommendation for quadrivalent for those countries.

00:51:25 So, we did, through this collaboration, successfully transition to TIV in the U.S. for the Northern Hemisphere 24-25 influenza season. I'd just like to highlight that the U.S. was the only country to transition in this timeframe, and that was made possible through the agility demonstrated by the regulators and the regulatory system in the U.S. and the strong partnerships across all stakeholders, including manufacturers. I'd also like to highlight that there were no delays to the season's vaccine supply through this transition. Next slide, please.

00:52:12 So, for the Northern Hemisphere 2025-26 season, the WHO recommended a change from the previous Northern Hemisphere to an A/Croatia for the H3N2 egg components of the vaccine and for the cell or recombinant-platform vaccines, a change of the H3 to the A/District of Columbia. This change had already been made for the Southern Hemisphere 25 season. And so, moving from hemisphere to hemisphere, there was no change in the vaccine composition. And then, on the 13th of March last year, the FDA/CBER recommendation was announced and it was aligned with the WHO vaccine recommendation apart from the supply of trivalent formulation was given because there was no B/Yamagarta component. Next slide, please.

00:53:30 Okay. So, this is just reflecting the changes that have happened since the Northern Hemisphere 2025-26, WHO, and FDA/CBER vaccine strain recommendations. We can see that moving from Northern Hemisphere 2025-26 to Southern Hemisphere 2026, there were two changes to the vaccine composition recommendation, both to the H1N1 and the H3N2. The B/Victoria remained the same, and WHO was still making a recommendation for QIV. For the Northern Hemisphere 2026, obviously we just have the WHO recommendation up till today. We saw no further change in the H1N1 from the Southern Hemisphere. However, this is a change from the last Northern Hemisphere, and we saw two further changes to the H3N2 and the B/Victoria itself.

00:54:43 So, Dr. Kondor gave a very comprehensive overview of the surveillance. It was obvious to us that there would be a change to the H3N2 because of the predominance of the K viruses. And we also thought there was a high potential for a change in the B/Vic as well. So, from the Northern Hemisphere to Northern Hemisphere, as Dr. Monto highlighted, there are three changes, but from the Southern Hemisphere to the Northern Hemisphere, there were two changes. Okay. Next slide, please. Oh, I should have highlighted here that for the first time in February this year, WHO did not make a recommendation for B/Yamagarta.

00:55:31 So, where are we with our preparations for the upcoming Northern Hemisphere season? Well, for the H1N1, there was no change recommended. There were CVVs and potency assay reagents already available, so we're in good shape for the H1N1. For H3N2, the strain was updated. We did have CVVs for the K viruses, which were available. We

have been able to do some early characterization work on those viruses, and potency assay reagents are being prepared. For the B/Victoria, the strain was also updated. The egg-based CVVs will not be available until mid-March, but potency assay reagents will be prepared once the suitability of the CVVs are confirmed. Next slide, please.

00:56:39 I just wanted to show this slide again. We have used this slide before, but really I want to highlight a couple of things. In us moving from TIV to QIV, we're still carrying out some production at risk prior to the strain change-- Strain recommendation. We're doing less than we did before when it was QIV, but in order for us to supply the required number of doses, not only for the U.S., but also globally, we have to start some production at risk, so that is still the case. And then the activities which are highlighted with the double-sided red arrows are just indicating steps in our process, which still take the same length of time, whether it's trivalent or quadrivalent vaccine. So, if you look at the top arrow, this is looking at, with a strain change, we still need the production and standardization and calibration of reagents for those new strains.

00:57:51 And with two strain changes, it doesn't matter if that's trivalent or quadrivalent, that production time and calibration time remains the same. The other area that remains the same is everything from the point at which we've made each monovalent separately. So, formulating the final vaccine, the filling and packaging, the regulatory approvals and the distribution all take the same time whether we're supplying a trivalent or a quadrivalent vaccine. So, I just wanted to highlight that because it's not that we've got

25% less in the vaccine, and therefore it takes us 25% less time to make it. It's not that simple. I just wanted to highlight that point. Next slide, please.

00:58:49 So, moving on to the vaccine uptake in the U.S., the disease burden from influenza persists. However, since the COVID-19 pandemic, we've seen the U.S. influenza vaccine uptake and coverage rates decline year on year, and this is despite having plenty of vaccines available. The figures here on the right are obviously taken from CDC. So, we can see that at least based on the CDC estimates, at least 24 million flu illnesses have been estimated, at least 11 million flu medical visits, at least 310,000 flu hospitalizations and at least 20,000 flu deaths estimated using their model. And it's not just a small drop that we've seen, but since the 2019-20 season, we've seen a 23% decrease in the number of vaccines supplied in the U.S. Next slide, please.

01:00:07 And if we look here, we can just see the cumulative doses in millions of doses of influenza vaccines distributed by season. So, the 2019-20 line is sort of a light brown- with light brown dots, and actually the 2021-2022 season almost completely overlaps that line. So, what we saw in 2020-21 was actually an increase in the number of doses distributed and this was during the COVID pandemic when there was a risk of what was referred to as a twindemic overwhelming the health systems. The year after that, the 2021-22 season, we saw the number of vaccines distributed fall to pre-COVID levels. But since that season, year on year, we've seen a decrease in the number of vaccines distributed and we're now supplying approximately 40 million doses less than we were in the 2021-2022 season. Next slide, please.

01:01:34 I wanted to talk a little bit about the access and benefit sharing systems, recognizing that the U.S. is not a signatory to the Convention of Biological Diversity, but these access and benefit sharing systems impact all companies worldwide, including U.S. companies. And there are two access and benefit sharing systems under the Convention for Biological Diversity. One is the CBD Nagoya Protocol, and that covers physical samples. And the other is the CBD multilateral mechanism for sharing the benefits of the use of digital sequence information. So, the Nagoya Protocol, we've been dealing with it for a number of years, and every season we check for any Nagoya obligations for the use of seasonal candidate vaccine viruses. So, we know there are some countries which do not have Nagoya Protocol legislation, but we actually use a lawyer through the International Industry Association, the IFPMA, to check what the current status of Nagoya legislation is in countries, particularly if we're seeing a CVV from that country for the first time.

01:03:06 The supply of influenza viruses is impacted by this. And since 2018, we've now seen over 40 seasonal viruses being delayed, which reduces our choice of which viruses we use. And for the Southern Hemisphere 2026, there was a recommendation for an A/Missouri-like virus. So, the A/Switzerland virus was listed by the WHO as a "-like virus". And we actually didn't experience any delays for this approval because the Swiss system, number one, had been used before, two is very clear and the instructions and the forms you have to fill out are very straightforward. And there's also no negotiation needed because the Swiss authorities do not want any benefits for the use of

the viruses from their country. They just want to track who is using a genetic resource from their country.

01:14:12 It's really difficult keeping up with all the legislation because there are national laws and the status and the laws in each country are not kept up to date. And many of the delays are also experienced due to a lack of resources in some countries. So, it's something that we face every season. We've got a system for dealing with it, but it is a hurdle for us to get over.

01:04:43 In late 2024, this new multilateral mechanism for the use of digital sequence information came in, and companies are expected to contribute either through this system or to comply with the national access and benefit sharing laws, because some of the Nagoya laws actually include DSI, and the contribution rates depend on the company size with business sectors that heavily use DSI, which includes vaccine companies, a suggested rate of 0.1% of total revenue or 1% of total profits, regardless of whether DSI was used for every product. So, this is an indicative rate at the moment, which means it's not finalized, but I just wanted to highlight this because these are some additional hurdles that we have to get over before we know we have legal certainty to move forward with certain CVVs. Next slide, please.

01:05:49 So, on these access and benefit sharing systems, the bottom line is that rapid and unhindered supply of influenza viruses and their sequence information for both seasonal and influenza viruses with pandemic potential is critical if we're going to be able to prepare the vaccines in time. And this global access and benefit sharing landscape is becoming extremely complex. So, as well as the CBD systems that I've just mentioned, the Nagoya Protocol and

this DSI mechanism, we have the WHO Pandemic Agreement being negotiated, and we still have the WHO Pandemic Influenza Preparedness Framework, which impacts all manufacturers. And this does cause delay in virus sharing.

01:06:38 I'll just give one really quick example. The PIP Framework supposedly should enable us to access influenza viruses with pandemic potential without any hindrance. However, depending on the route at which the virus is obtained, if it hasn't come through the WHO GISRS and it's come through one of the animal surveillance routes, it actually falls under the Nagoya Protocol. And we have one case of a virus from Africa, an H5N1 virus, which was recommended as a CVV by WHO in September 2022, and we still do not have access to that virus. So, this is a real issue that we are tackling.

01:07:31 There's some acknowledgement of the need to prevent overlapping requirements between all these systems, which are referred to as "instruments", but it's unclear how this will be achieved in practice. So, what we don't want is delay after delay because we're fulfilling the obligations in each one of these instruments. We do continue to be very active and engaged in discussions and provide this feedback, but just really for your awareness that this is going on in the background, doesn't just impact influenza, obviously, it impacts all viruses. Next slide, please.

01:08:23 So, we know that you understand this, but Dr. Kondor's presentation really well illustrated how rapidly viruses can spread across the world and sometimes the differences that we see in different regions. It's really

essential that we have a comprehensive overview of emerging viruses, including where they originated from and what the transmission patterns are, and are they beginning to predominate or are they not going to win the race as it were?

01:09:06 And just really wanted to reiterate the importance of international cooperation and the exchange of data and biological materials, and how vital that is for vaccine development and distribution in the U.S. and globally. And we really appreciate CDC's continued involvement in the global vaccine composition meetings and feel that this continues to foster this collaboration, which is really, really crucial for both seasonal and pandemic readiness. Next slide, please, which I think might be my last slide.

01:09:48 So, the key takeaways from the presentation are that the industry aligned very well and worked closely with CBER to obtain the necessary approvals for the successful transition from QIV to TIV in time for the U.S. Northern Hemisphere 2024-2025 seasonal vaccine supply. For the Northern Hemisphere 2025, seasonal influenza vaccines contained and updated A/H3N2 subtype, which there was an actual no change from the Southern Hemisphere 25 vaccines, and the WHO recommendation that was just made in late February for the upcoming Northern Hemisphere 26-27 season had two updates to the H3N2 and B/Vic, but the H1N1 had already been updated for the Southern Hemisphere 26 season.

01:10:47 Since the COVID-19 pandemic, U.S. influenza vaccine uptake and vaccine coverage rates have declined year on year. I've just highlighted the concerns of the Nagoya Protocol, the DSI mechanism, the Pandemic Agreement, and

the lack of legal clarity, and the risk of us seeing stacking obligations with these agreements and the impact that that has on the supply of seasonal and pandemic influenza vaccine manufacturing and how rapidly we're able to respond in an emergency.

01:11:25 And the final point, just to reiterate again, that the global scientific collaboration and transparent sharing of samples and data is critical for public health decision-making. Next slide, please. I think it's just-- Thank you so much for your attention and the opportunity to present the manufacturer's perspective. Thank you, Dr. Monto.

Comments from Manufacturer Representative - Q&A

01:11:50 Dr. Monto: Thank you so much. And thank you for bringing up some important elements and complications that we don't generally think about or even discuss here on the VRBPAC, because really things like the Nagoya Protocols have been lurking around for quite some time and have never really been fixed in an adequate way. Questions from the group, please. Yes, Dr. Gans.

01:12:37 Dr. Gans: Thank you so much for that. I agree with Dr. Monto, It's really helpful for us to understand all the perspectives on this. You talked a lot about timing, having enough time using current data. Do you find the timing of this meeting in particular helpful to that timeline? We're always straddling having a meeting at a time when we have enough data, but also enough time to provide any manufacturing issues related to recommendations. Our colleagues in the WHO, of course, met earlier, and I'm just wondering if there would be recommendations around the ideal

perfect timing of meetings if this information that happens today or the discussions that happen today are something that should occur right now. This is ideal or at a different point in time. That's my first question.

01:13:41 My second question is that you've probably heard discussions starting last year about the difficulty in the H3N2, thinking about changing recommendations to think about having two different strains for that, so going to a different quadrivalent, and what are the thoughts around that?

01:14:07 Dr. Taylor: Thank you, Dr. Gans. Regarding the timing of the meeting, we would not want to see the meeting any later. It's really important that we get confirmation of the strains fully acknowledging that we need sufficient data to make that recommendation as well. But for the current vaccine manufacturers, this timing of the meeting, it's important that it doesn't get pushed out any later. In response to the H3N2 question, yes, the H3N2 viruses are problematic. I know there has been discussion. I mean, even when we were talking about-- Even before we took the B/Yamagata out of the vaccine, there was talk about the potential for-- I think Dr. Monto, you referred to it as maintaining the antigenic weight of the vaccine and adding a-

01:15:15 Dr. Monto: -I don't remember, but that was a good idea. And I thought we could do it a lot more seamlessly than we did.

01:15:24 Dr. Taylor: Yeah. Yeah. Well, of course. I mean, first of all, we'd have to go through clinical trials, we'd have to get regulatory approval, and there are also some technical challenges. So, if two H3s are very different, then it might be an obvious decision to have two H3s, but if there's not such a big

difference, do we still put the two H3s in? We may see interference between the two viruses. Certainly testing, the potency testing, poses some technical challenges which have to be overcome. So, we agree it's an interesting idea. Some preliminary work has been done, but there are a number of hurdles for us to get over before we can think about this new quadrivalent.

01:16:30 Dr. Monto: The problem from my mind is that we've been talking about it, but we've seen very little data. And the question then is who takes the lead? And it's something which perhaps we could have further discussions about because it seems as if there's a bit of hesitancy to take the first step. What is your response to that?

01:17:04 Dr. Taylor: I know that some companies have done some preliminary work on this. It's probably too preliminary to report on right now. I would say the cost of clinical trials is not small. And so I think we'd really-- There probably needs to be more discussion around this and what support there would be for a new quadrivalent vaccine. You know, if we could see that this was something that was clearly needed and there was support for it, then that would provide a bit more support for manufacturers to further investigate, I think.

01:17:52 Dr. Monto: Right. And this is not in a vacuum because there are other things that are going on in terms of updating or improving influenza vaccines, especially in terms of-- What we're talking about is greater breadth.

01:18:10 Dr. Taylor: Yeah.

01:18:11 Dr. Monto: And there are other approaches being looked at. Any other questions from the group before I thank Dr. Taylor again for a very instructive presentation? Seeing none, thank you again.

01:18:29 Dr. Taylor: Thank you very much.

Committee Discussion

01:18:31 Dr. Monto: And now we have some time available for a more general discussion among the group. So, let's have first some discussion in general, since we've talked about a lot of different things and then focus on the strains themselves before we lead into the vote. So, general discussion from the members, those who have votes, let's say. Dr. Durbin.

01:19:13 Dr. Durbin: I just wanted to say I thought the presentations today were incredibly informative and really, really helpful to discussion. I don't have a lot-- I don't have any questions regarding what was presented. I think the follow-up questions were informative, and I just want to thank all of the presenters for really a wonderful presentation of data that really, I think, makes our decision-making a lot easier. Thank you.

01:19:44 Dr. Monto: Dr. El Sahly.

01:19:47 Dr. El Sahly: Thank you, Arnold. My question is-- Well, we can ask questions to the presenters in general now, right?

01:19:56 Dr. Monto: Yes.

01:19:57 Dr. El Sahly: Okay. So, it's between a comment and a question, which is vaccine coverage. I brought that up earlier in the day to understand the nuances

of the B data, and then later in the day, the industry representative indicated that they are supplying less and less vaccine to the American market, which means probably less and less uptake of the vaccine. I am wondering if a general overview of vaccine uptake can be incorporated in the deliberations we have here without, of course, veering into the details.

01:20:50 Dr. Monto: But it's my understanding it's not that the vaccine is not available for the U.S. market. It's that there has not been the demand.

01:21:01 Dr. El Sahly: Exactly. Exactly. And-

01:21:02 Dr. Monto: -For the U.S. market. And I'm not sure if this comes under the purview of this Committee, although I'd be very happy to hear from either the FDA or the CDC folks how this might be-- How we might have a role. It's certainly-- Whatever the efficacy, if people aren't getting the vaccine, we're not going to see protection. Doctor-

01:21:40 Dr. El Sahly: -I wasn't looking for a role for this Committee, which is more into the licensing end of the equation, just understanding the epi data in general. That's what I was--

01:21:50 Dr. Monto: Well, Dr. Grohskopf.

01:21:57 Dr. Grohskopf: Hi, thanks for that question. Similarly, I can't really answer the question about the role of the Committee and using it for decision-making, but certainly if it's thought that having some kind of an update about that might be thought helpful in terms of interpreting the VE data, and if that's requested, we can do that. One thing to consider, a couple of things to consider. Those data similarly to the VE data are collected throughout the season. They're not

finalized usually until the fall, and we would have to ask our colleagues in the appropriate division to be able to do that, but that's something we can pursue if the Committee wants it. Also, coverage data tends to come from various surveys, and there might be differences in the sampling, which might not, at least for the CDC data, necessarily coincide with the VE data sites. So, there would be caveats, of course, but it's something that should the Committee want it, we can, of course, pursue being able to do that. It's not data that our division produces. It's a sister division, but that's something we can look into if it's desired. Thank you.

01:23:09 Dr. Monto: I think it might be useful for future deliberations. Clearly, we can't do a whole lot right now. Given it was last year's data that were-- This past season's data that we'd be looking at. Dr. Gans.

01:23:32 Dr. Gans: Thanks so much. I did want to continue on this concept because I do feel that some of the role of this Committee, given that we are presenting data that is widely thought about within the general population, that we should state some of the other efficacies that vaccines have because it does relate to what this Committee does. If there's low uptake in these markets, there's going to be a disincentive for our colleagues within industry to make vaccines. And so, I think it is actually relevant to the work that this Committee does, and in particular in the discussions that we have.

01:24:28 One of the ways in which I think there's been some misconception is when we rely so heavily on vaccine efficacy because we need that for our decision making, but I'm not sure that the general public understands when we use words like low efficacy, not as efficacious and language such as that. So, I do think that

we're using data just to look at what is the concordance between a strain and what should be put into the vaccine, and how immunity to that in particular varies myopically and is associated. I do think we need to have broader discussions about what are not only the sort of value to individuals and the value to society for having vaccines that do prevent, particularly, and I'll talk from the pediatric standpoint, hospitalizations in healthy people who don't otherwise have a reason to go to the hospital.

01:25:26 The other part of that, of course, is a qualitative type of evaluation. And then, if we want to talk about broader impacts of what vaccine versus natural immunity could do, because I think there's also a conception in the public sphere that having natural immunity is better than having vaccine immunity and not understanding some of the other adversity that could come. So, for instance, I mean, I don't know what is compelling to people, but talking about the cardiovascular effects of having these viral illnesses. I do think that there is some responsibility of this Committee to think more broadly about what it is that we are considering in terms of the vaccination.

01:26:14 Having said that, I mean, I think that the data that is in front of us is very compelling for the recommendations that are facing us today. The only additional conversation that I think this Committee needs to have, and we've been having it, but to your point, Dr. Monto, we've been having it and we are not sure what further discussion or pressure needs to be put on having a discussion about how we can actually prepare vaccines in a timely way that can use the data that we are all getting and be able to move more nimbly between the data and a recommendation.

01:27:03 So, we've been talking about an H3N2 that really needs to be expanded, probably to give us better vaccine efficacy if we really want to talk about it from that standpoint. And I think, just like going from a quadrivalent to trivalent, there was some frustration in this group to have to discuss it for years before things happen. So, I would urge our colleagues and maybe it's us as a responsible group to urge more forcefully to have those studies available so that we can be more nimble in what we would like to do.

01:27:43 Dr. Monto: Thank you. And as just a general comment, the SARS-CoV-2 pandemic shifted the attention not only of the public, but of the scientific community away from influenza because the same people very largely that were working on influenza went to work on the prevention of SARS-CoV-2 and development of vaccines.

01:28:33 And this happened just when the approach to a broadly-based influenza vaccine was really moving forward. And really what we have to do is recoup, reexamine where we are, and I'm not sure where that ought to be done because things have changed in many respects since before the pandemic and more recently, but we really need to focus and we need to focus on the broad picture. And we've talked about the two H3N2 strains in the vaccine, but there are a lot of other approaches and they ought to be looked at comprehensively and-- Also, in a way to let the public know how we are looking to make a good vaccine a better vaccine.

01:29:29 After that preaching to the converted, any other comments before we look at any comments about the specific strains in the vaccine? Yes, Dr. Meyer.

01:29:52 CAPT Meyer: Thank you. I was just going to add-- On top of what the other panelists have also said, I just really wanted to thank all of the presenters today. I

thought this was an excellent session, very clear, very comprehensive. I think as it relates to the strains and what we're talking about, I think the entire set of presentations laid out very clearly in a way that leads me to support the proposed recommendations. I didn't see any indication that we should move into a different direction, so that's where I stand on this. Thank you.

01:30:31 Dr. Monto: Okay. Any further comments about the strains? And I'm not going to ask people to explain their votes because generally we are all in agreement with the recommendations that are put in front of us. Any further comments? Seeing none, are we prepared to move to a vote? Are we ready to do that so early in the afternoon?

01:31:22 Dr. El Sahly: Are you asking the Committee members or Cicely?

01:31:25 Dr. Monto: I'm asking both because-

01:31:28 Dr. El Sahly: I can vote early.

01:31:29 Dr. Monto: I think we're ready to vote. I just vote.

01:31:33 Dr. Reese: That's perfectly fine.

01:31:35 Dr. Monto: Okay.

Recommendations and Vote

01:31:37 Dr. Reese: Okay. So, we'll move into the voting portion of the meeting. And the questions before the Committee today, there are two questions. There are both voting questions. The voting members will use the Zoom platform to submit their votes for the meeting. If you're not a voting member, you will be moved to a breakout room while we conduct the vote. After the chairperson

reads the voting questions into the record and all clarifying questions are complete, which we have come to that understanding, we will announce the voting will begin. A voting window will appear where you will submit votes at the same time for one and-- Number one and number two. There will be no discussion during the voting session. You should select the button in the window that corresponds to your vote, “yes,” “no,” or “abstain.” Please note that once you click the submit button, you will not be able to change your vote.

01:32:37 Once all voting members have selected their vote, I will announce the vote as closed. Please note there will be a momentary pause as we tally the vote results and return the non-voting members into the meeting room. Next, the vote results will be displayed on the screen. I will read the vote results from the screen into the record. Thereafter, Dr. Monto will go down the list and ask each voting member to state their name and how they voted. As he mentioned, he will not ask you to provide your justification because he said that would not be needed in this scenario. So, Dr. Monto, if you would, please read the voting questions into the record for the Committee. Thank you.

01:33:24 Dr. Monto: Okay. Does the Committee recommend a 2026-27 formulation for egg-based influenza virus vaccines in the United States that contain the following virus strains: an A/Missouri/11/2025 (H1N1)pdm09-like virus and an A/Darwin/1454/2025 (H3N2)-like virus, and a B/Tokyo/EIS13-175/2025 (B/Victoria lineage)-like virus? And that is the first question. Are we voting now for number two as well?

01:34:15 Dr. Reese: No, we’re going to do the two-

01:34:17 Dr. Monto: -That's what I thought. We're doing them in sequence. So, we vote for one right now.

01:34:25 Dr. Reese: No, we're going to vote for one and two, so you can read both questions.

01:34:28 Dr. Monto: Oh. We're voting for the cell and recombinant as well? Okay.

01:34:30 Dr. Reese: Yes.

01:34:33 Dr. Monto: Does the Committee recommend a 2026-27 formulation for cell- and recombinant-based influenza vaccines in the United States states that contain the following virus strains: an A/Missouri/11/2025 (H1N1)pdm09-like virus and an A/Darwin/1454/2025 (H3N2)-like virus, and a B/Pennsylvania/14/2025 (B/Victoria lineage)?

01:35:08 Dr. Reese: Okay. Thank you, Dr. Monto. The voting will now begin.

[Voting in progress]

01:47:20 Dr. Reese: Thank you, everyone, for your patience. We had some technical difficulties. The voting has now closed and is now complete. The voting results will be displayed. Okay. My 53-year-old eyes can barely see that, but I can tell that we have-- For question one, we have a unanimous vote of seven yeses and zero nos, zero abstains. For question two, we also have seven yeses, zero nos, and zero abstains. Okay. Dr. Monto, if you would like to just go down the line and have everybody state their name for the record and how they voted.

01:48:31 Dr. Monto: Thank you. Okay. It seems a bit superfluous to do it, but I guess we need to do it for the record. Does everybody see the names that are on the left, which started with Dr. El Sahly? So Dr. El Sahly, you go first.

01:49:00 Dr. El Sahly: To give comments?

01:49:02 Dr. Monto: No, this is to announce how you voted. We're doing it differently.

01:49:07 Dr. El Sahly: Oh, I announce-- Okay. Okay. Sorry. I thought you-

01:49:10 Dr. Monto: And you can do it for both. We don't have to go down twice.

01:49:13 Dr. El Sahly: Okay. All right. I voted yes for questions one and questions two.

01:49:19 Dr. Monto: And so did I. I voted yes for-- Dr. Gans.

01:49:26 Dr. Gans: Dr. Hayley Gans, I voted yes for both questions one and two.

01:49:32 Dr. Monto: Dr. Meyer.

01:49:34 CAPT Meyer: Hi, I voted yes for questions one and two as well.

01:49:37 Dr. Monto: Dr. Berger.

01:49:39 Dr. Berger: I also voted yes for both questions one and two.

01:49:43 Dr. Monto: Dr. Durbin.

01:49:45 Dr. Durbin: I voted yes for questions one and two. Thank you.

01:49:48 Dr. Monto: Dr. Pearlman.

01:49:50 Dr. Pearlman: I voted yes for questions one and two.

01:49:53 Dr. Monto: Okay. I guess we're all in it for the record.

01:49:59 Dr. Reese: Okay.

Closing Remarks and Adjournment

01:50:03 Dr. Monto: Now, we have a couple of options and if anybody wants to explain their votes, they can do so now. It is not required. And then, if there are any further comments, this is your time to raise your hand and make a comment. Seeing no hands raised, I'll just say that we've had a very efficient meeting in a very complicated year where we were reminded about how difficult strain selection is, that it's a little bit of science, a little bit of luck in coming up with the right strains for the vaccine, which is why we really need a broader vaccine so that we don't have some of the issues that we've been discussing all day today.

01:51:40 Other than that, I just want to thank everyone who has put this meeting together and more importantly, done a wonderful job gathering the data, doing the analysis, and doing it under sometimes difficult circumstances. So, again, thank you all. And I'd like to turn the meeting over to Dr. Reese, who will be inviting Dr. Kaslow to speak, or anyone else from FDA, from CBER, who would like to add his comments to mine.

01:52:43 Dr. Reese: Okay. Well, I was looking for Dr. Kaslow. I don't see him join, but I'll see if he-

01:52:49 Dr. Monto: -That's what I was wondering when you end early.

01:52:54 Dr. Kaslow: There you go.

01:52:55 Dr. Monto: There he is.

01:52:56 Dr. Reese: There he is.

01:52:57 Dr. Kaslow: Thank you. There I am. Thank you, Chair Monto. So, let me start with a few brief reflections before ending with some thank yous. Today, VRBPAC convened for the 191st time to discuss in an open public session to consider a complex set of evidence that inform the recommendations for the 2026-2027 Formula for U.S.-licensed vaccines. The totality of evidence includes not only domestic data but information from a global surveillance system. Opening the aperture beyond domestic data to ensure a comprehensive view of an ever-evolving pathogen is the best hope for optimally effective seasonal influenza vaccines. As I think you all noted, today's VRBPAC discussion went well beyond the voting questions. It brought into the public discourse emerging issues that warrant consideration and being better prepared for future respiratory seasons. It also highlighted the scientific and technical challenges of always having to chase the rapid evolution of these, and I think you called it tricky viruses. As Dr. Weir pointed out, the way forward starts with defining and getting to a shared understanding of the unmet medical need, and then thoughtfully and comprehensively framing the problems to be solved. Just like your prior discussions in 2023 and 2024 on the transition from quadrivalent to trivalent vaccines and your sage advice last October to keep a close eye on the influenza B/Austria-like virus that hadn't changed for a number of years, your discussion today is yet another call to action for even more effective seasonal influenza vaccine. So, thank you again for another robust evidence-driven discussion to drive improving public health against a very serious and life-threatening pathogen.

01:55:19 I'll end by first thanking the open public hearing speakers, the private citizens and organizations that posted comments to the docket. The office hears you and considers your points in our internal discussions. Let me also thank all of the invited presenters for their outstanding interventions today. You drove a robust public discussion, noting both the strengths and the gaps in the evidence. And the setting for those presentations would not have occurred without a large team here at FDA to host yet another flawless VRBPAC. So, thank you, FDA Advisory Committee staff, our AV staff, and my colleagues in OVRR.

01:55:59 And finally, a sincere thanks to today's VRBPAC members for your courage in the name of public service. Your service is vital for enhancing public trust. And I'll end by saying we look forward to a 192nd convening of VRBPAC. So, with that, I'll turn it back to our DFO. Thank you.

01:56:22 Dr. Reese: Thank you, Dr. Kaslow. And thank you also, Dr. Monto, Committee Members and speakers for your time and contributions. This concludes the 191st meeting of the Vaccines and Related Biological Products Advisory Committee meeting. The meeting is adjourned at 2:39 P.M.

[Recording stopped.]