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Center for Biologics Evaluation and Research (CBER)

Office of Vaccines Research and Review (OVRR)

190th Meeting of the Vaccines and Related Biological Products Advisory Committee

Zoom Video Conference

(Session I)

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Rebecca J. Garten Kondor, PhD	Interim Director, WHO Global Influenza Surveillance and Response (GISRS), Collaborating Center for Surveillance, Epidemiology and Control of Influenza, Influenza Division, Research Microbiologist, Genomic Analysis, Team Lead, Virology, Surveillance and Diagnosis Branch Influenza Division, NCIRD, Centers for Disease Control and Prevention	Atlanta, GA

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Ronald Rabin, MD (Presenter)	Chief, Laboratory of Immunobiochemistry (LIB), DBPAP, OVRR CBER, FDA	
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Designated Federal Officers

LCDR Cicely C. Reese, PharmD	Designated Federal Officer, VRBPAC, CBER, FDA	
CDR Valerie Marshall, MPH	Designated Federal Officer, VRBPAC, Alternate DFO, CBER, FDA	

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Opening Remarks: Call to Order and Welcome

Dr. El Sahly: Good morning, everyone, and welcome to the 190th meeting of the Vaccine and Related Biological Products Advisory Committee Meeting. During Topic I of this meeting, we'll be discussing and making recommendations on the selection of strains for influenza virus vaccine for the 2026 Southern Hemisphere influenza season. I'd like to welcome the members, the participants, and the public viewing the meeting. I would like also to remind my colleagues on the Committee that during the Q&A portions of the meeting to use the raise-your-hand function, so I know that you have a question. And then I will call up on your name, you will go live on camera and then take it from there. Next, I would like to introduce Ms. Cicely Reese, who is the Designated Federal Officer for the meeting today. Ms. Reese.

Administrative Announcements

LCDR Reese: Thank you, Dr. El Sahly. My name is Cicely Reese and it's my honor to serve as the Designated Federal Officer for today's 190th meeting of the Vaccines and Related Biological Products Advisory Committee.

On behalf of the U.S. Food and Drug Administration, the Center for Biologics Evaluation and Research, and the Committee, I'm pleased to welcome everyone to today's virtual meeting. I would like to extend my sincere appreciation to all those who made today's meeting possible, beginning with our Center leadership, Dr. Vinayak Prasad, Center Director, his deputies and the dedicated staff who provide ongoing guidance and support. I would also like to thank the Office of Vaccines Research and Review, led by Dr. David Kaslow, and his deputy for their continued leadership and countless hours their teams have devoted to preparing for today's meeting. My gratitude also goes to our phenomenal ethics and integrity team and the disclosure team, on

detail, to the Office of Shared Services, whose vigilance and readiness to act on short notice are truly commendable. And of course, a very special thanks to our virtual conference center and audiovisual team, who are often the last to receive materials, but the first to arrive each morning ensuring every technical aspect runs seamlessly. To each and every one of you, thank you for your professionalism, dedication, and teamwork. FDA extends its sincere appreciation to the members for their continued dedication and support of this Committee. We ask a great deal of them, stepping away from their demanding roles to contribute their expertise here. Their service helps the FDA fulfill its mission and we are truly grateful for their time, insight, and commitment. And last but certainly not least, we extend our sincere appreciation to our Chairperson, Dr. Hana El Sahly, for her strong leadership and steadfast commitment to this Committee. Chairing an FDA Advisory Committee is not an everyday responsibility and it requires exceptional dedication, preparation, and judgment. We truly are grateful to Dr. El Sahly's continued guidance, professionalism, and service to the Agency, the Committee, and the public we serve.

I will now read information regarding the press and media. For press and media questions, please direct press and media questions for today's meeting to the HHS Press Room at hhs.gov-- Thank you. HHS.gov/press-room/index.html or 202-690-6343. The transcriptionists for today's meeting are Ms. Virginia Diaz and Ms. Myra Angulo. Okay. Next slide, please.

We'll begin today's meeting by taking a formal roll call for the members. When I call your name, please turn on your camera, unmute yourself and introduce yourself by stating your first and last name, organization, expertise or role. And when finished, you may turn your camera off, so we may proceed to the next person. Please, see the displayed slide in which we will begin with the Chairperson, Dr. Hana El Sahly.

Roll Call and Introduction of the Committee

Dr. El Sahly: Good morning. My name is Hana El Sahly. I'm a Professor of Molecular Virology and Microbiology at Baylor College of Medicine. My research focuses on clinical vaccine development.

LCDR Reese: Thank you, Dr. El Sahly. Dr. Bernstein.

Dr. Bernstein: Good morning. My name is Henry Bernstein and I'm a Professor of Pediatrics at the Zucker School of Medicine at Hofstra/Northwell in New York and a Pediatrician at Cohen Children's Medical Center. I'm a general pediatrician with expertise in vaccination and vaccine policy. Good morning.

LCDR Reese: Thank you, Dr. Bernstein. Dr. Durbin.

Dr. Durbin: Yes. My name's Dr. Anna Durbin. I'm a Professor of International Health at the Johns Hopkins Bloomberg School of Public Health. I'm an Adult Infectious Diseases Physician. My research specializes in vaccine development and evaluation. Thank you.

LCDR Reese: Thank you, Dr. Durbin. And we have our Non-Voting Alternate Industry Representative, Dr. Kollmar.

Dr. Kollmar: Hi, good morning. I'm Jim Kollmar, a Pediatrician by training and Scientific Associate Vice President, Global Regulatory Affairs and Clinical Safety, Vaccine Infectious Disease at Merck & Co.

LCDR Reese: Thank you, Dr. Kollmar. Captain Meyer.

CAPT Meyer: Good morning. My name is Sarah Meyer. I'm a Medical Officer at the Centers for Disease Control and Prevention. I'm also a pediatrician and my specialty is in vaccines.

LCDR Reese: Thank you, Captain Meyer. Dr. Monto.

Dr. Monto: I'm Arnold Monto. I'm at the University of Michigan School of Public Health in Ann Arbor and I am a Respiratory Infectious Disease Epidemiologist with interest in vaccines and antivirals. Thank you.

LCDR Reese: Thank you, Dr. Monto. Dr. Omer.

Dr. Omer: Hi, I am Saad Omer. I'm the Dean of the Peter O'Donnell Jr. School of Public Health at UT Southwestern in Dallas. My work focuses on interventional and observational studies of vaccines and infectious diseases.

LCDR Reese: Thank you, Dr. Omer. Dr. Perlman.

Dr. Perlman: Hi, I am Stanley Perlman. I'm a Pediatric Infectious Disease Specialist. My research interest is in Coronaviruses. I work at the University of Iowa.

LCDR Reese: Thank you, Dr. Perlman. Dr. Portnoy.

Dr. Portnoy: Good morning. I'm Dr. Jay Portnoy. I'm a Professor of Pediatrics at the University of Missouri School of Medicine, and I'm an Allergist Immunologist at Children's Mercy Hospital in Kansas City, Missouri.

LCDR Reese: Thank you, Dr. Portnoy. Dr. Rubin.

Dr. Rubin: I am Eric Rubin. I'm at Harvard and the Brigham and Women's Hospital and the New England Journal of Medicine. I'm an Infectious Disease Physician and my lab studies tuberculosis.

LCDR Reese: Thank you, Dr. Rubin. I will now read the Conflict of Interest Statement for Topic I.

Conflict of Interest Statement

LCDR Reese: The FDA's convening today's meeting of the Vaccines and Related Biological Products Advisory Committee, also known as VRBPAC, under the Federal Advisory Committee Act, FACA, of 1972. The VRBPAC will meet in open session to discuss and make recommendations on the strain selection for the influenza virus vaccines for the 2026 Southern Hemisphere influenza season.

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 conflict of interest laws. We have screened the members for potential conflicts of interest related to today's meeting agenda, both their own interest and that of-- Both their own interests and those that are imputed to them, including those of their spouses, minor children, and employers. Based on today's agenda-- Based on the agenda for today's meeting and all financial interests reported by 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.

Dr. Archana Chatterjee has been recused from the meeting based on today's agenda and her financial interests analyzed by FDA. James Kollmar of Merck & Co. is participating in the meeting as Non-Voting Industry Representative acting on behalf of regulated industry. Consistent with Commissioner Makary's April 17th, 2025 statement,

FDA is only including the Industry Representatives in Advisory Committee Meetings where required by statute. FDA is required to include an Industry Representative in today's meeting under 21 U.S.C 355 (n)(3)(c). 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 industry and not any particular association, company, product, or ingredient, and bring general industry perspective to the Committee. Under FDA regulations, although a Non-Voting Member serves in a representative capacity, the Non-Voting Member shall exercise restraint in performing such functions and may not engage in unseemly advocacy-- Unseemly advocacy or attempt to exert undue influence over the other members of the Committee. Dr. Jay Portnoy is serving as the Consumer Representative for this Committee. Consumer Representatives are appointed Special Government Employees and are screened and cleared prior to participating in the meeting. They are Voting Members of the Committee.

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 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 and not their personal views. The following speaker and guest speakers have been screened and cleared to participate in today's meeting: Dr. Rebecca Kondor and Dr. Thomas Platts-Mills.

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 speaker and guest speakers have not reported any such relevant interests. 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 firm, 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. Thank you.

Dr. El Sahly, I now turn the meeting back over to you to commence the Open Public Hearing for Session I.

Open Public Hearing

Dr. El Sahly: Thank you, Cicely. Next on the agenda is the Open Public Hearing Session. I will read the announcement.

Welcome to the Open Public Hearing Session. Please note that 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 sponsor, its product, and if known, its direct competitors. For example, if this-- This financial information may include the sponsor's payment of expenses in connection with your participation in 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. My understanding is that there are no-- No one registered for the Open Public Hearing Session. Is that correct, Cicely?

LCDR Reese: That is correct.

Dr. El Sahly: Okay. So, that concludes the session of the Open Public Hearing.

Introduction to VRBPAC Meeting Topics

Dr. El Sahly: Next, we will turn to Dr. David Kaslow. Dr. David Kaslow is the Director of the Office of Vaccines Research and Review at CBER, FDA. Dr. Kaslow will give the introduction to the VRBPAC meeting today. Dr. Kaslow.

Dr. Kaslow: Thank you, Dr. El Sahly. So, good morning and welcome to the 190th meeting of VRBPAC. The Office of Vaccines Research and Review is particularly thankful to the FDA staff and to you, VRBPAC members, for the opportunity to hold this meeting in the context of a lapse in appropriations. Today's meeting addresses the timely need to consider updates to the 2026 Southern Hemisphere seasonal influenza vaccine formula and modernization of certain aspects of the chemistry, manufacturing and control, or CMC, of allergenic products. Next slide, please.

For Topic I, we propose a single voting question-- I'm sorry. That is-- Sorry, yes. Thank you. Okay, so we asked VRBPAC to consider two topics today. Topic I focuses on the selection for the 2026 Southern Hemisphere seasonal influenza vaccines and Topic II comprises a proposed comprehensive modernization strategy for allergenic extract standardization that is really meant to fill a 25-year technology gap in our current regulation of these products. Next slide, please.

So, for Topic I, Dr. Jerry Weir will provide an overview of seasonal influenza vaccine strain selection process for the Southern Hemisphere influenza season, and Dr. Rebecca Kondor will present the global seasonal influenza virus surveillance and characterization that really underpin the recommended strain selections for the 2026 Southern Hemisphere influenza season. The Committee will then be asked to discuss those findings and recommendations, and that discussion will be followed by a vote on the specific strain recommendations for trivalent formulations which are shown on the next slide.

So, for Topic I, we propose a single voting question this time for the composition of egg-based only trivalent 2026 Southern Hemisphere influenza vaccines, noting that the recommendation is to update the two influenza A subtypes but not the influenza B type, compared with last year's Southern Hemisphere formula. Next slide, please. Topic II addresses our proposal to modernize our Allergenic Standardization Program based on the extraordinary advancements in science and technology over the last 25 years, particularly in allergenic protein characterization and associated analytical technologies. Next slide, please.

As described in detail in the briefing document, we propose four initiatives. The first two initiatives focus on those allergenic products that have a major specific allergen in the extract. Proposed initiative one focuses on updating major allergen potency standardization for cat dander and pelt extracts, as well as short ragweed pollen extracts, while proposed initiative two focuses on expanding that major allergen extract standardization approach to food allergens and additional environmental allergens. The last two initiatives are focused on allergenics composed of complex extracts with multiple major allergens. Proposed initiative three focuses on characterizing complex extracts using modern liquid chromatography and tandem mass spec technologies, and

proposed initiative four uses that LC/MS/MS technology to optimize the source material for house dust mite extracts. Next slide, please.

So, when proposing Topic II, we were asked by some why this allergenic topic is being discussed at a VRBPAC meeting. And as many of you know, there was a parallel Advisory Committee referred to as APAC that served for 40 years as the place to take allergenic product discussions. Given the frequency of APAC meetings, the last of which occurred almost four years ago, it was decided in the most recent rechartering of VRBPAC that the scope of VRBPAC would be expanded to incorporate allergenic products. So, to support today's allergen standardization discussion, we have four Temporary Voting Members joining today's meeting. These Temporary Voting Members bring specialized expertise in allergy, immunology, and allergen extract development and their participation ensures the necessary scientific expertise is brought to bear on Topic II today. So, let me take this opportunity to thank our four Topic II Temporary Voting Members for joining VRBPAC for Topic II today. Next slide.

So, the agenda for Topic II. So, after our VRBPAC Chair calls the meeting to order after a 30-minute lunch break, we will have two presentations by FDA. The first by Dr. Ron Rabin, who will encompass the first two proposed initiatives on updating major allergen potency standardization, replacing the mid-20th century radial immunodiffusion technology with 21st century ELISA and aptamer-based enzymatic assays. The second presentation by Dr. Ron Rabin and Brad Strader will cover the other two proposed initiatives that focus on the use of liquid chromatography tandem mass spec to measure potencies in complex extracts with multiple major allergens and its application to optimizing the source material for house dust mite extracts. We will then turn to two external speakers. The first by Dr. Thomas Platts-Mills, who will present on approaches to allergens standardization related to dust mites, followed by Ms. Trenna

Repp, who will provide an industry perspective. We will then ask the Committee to discuss Topic II recommendations and then vote on the four questions shown on the next slide.

Again, the first two voting questions focus on those allergenic products that have a major specific allergen in the extract, with question one focused on moving away from that mid-20th century technology for mass concentration measurements of cat hair and pelt and short ragweed pollen extracts. Question two expands on that template for mass concentrations of major allergens to include food and environmental major allergens, while voting questions three and four focus on the last two proposed initiatives directed at those allergenic products that are complex extracts with multiple major allergens and the use of that liquid chromatography coupled with tandem mass spec. Next slide, please.

So that concludes the introduction to today's convening of VRBPAC. Let me thank you for your attention and I will turn the meeting back to you, Chair Dr. El Sahly.

Dr. El Sahly: Yeah. Thank you, Dr. Kaslow. I'd like to invite the Committee members should they have a question to use the raised-hand function. If they have any questions. Okay.

Dr. Kaslow: That was clear.

Dr. El Sahly: There are no questions. Thank you, Dr. Kaslow.

Dr. Kaslow: Okay, thank you. Thanks again.

Introduction to Seasonal Influenza Vaccine Strain Selection Southern Hemisphere 2026

Dr. El Sahly: Next on the agenda is Dr. Weir. Dr. Jerry Weir is the Director at the Division of Viral Products, Office of Vaccine Research and Review, CBER, FDA. Dr.

Weir will give the introduction to seasonal influenza vaccine strain selection Southern Hemisphere 2026. Dr. Weir.

Dr. Weir: Thank you and good morning. As Dr. El Sahly said, I'm going to give an introduction. It's going to be brief, just a little bit of background before we get into the topic. Can I go to the next slide?

Okay, so what's the purpose of today's VRBPAC Committee discussion? It is to make recommendations for the strains of influenza A H1N1 and H3N2 and influenza B viruses to be included in the 2026 Southern Hemisphere formula of influenza vaccines licensed in the United States. We meet about this time every year in October to do this for the following Southern Hemisphere. And the reason is because since 2016 there are two U.S. vaccine manufacturers who have been approved to produce Southern Hemisphere formulations of their influenza vaccines. These are Sanofi Fluzone and Seqirus Afluria, the trade names. Notably both of these vaccines are produced in eggs and that's why we will focus in our discussion and voting question only on the egg formula for these vaccines.

Now, the strain recommendation-- As I said, we do this every year. The strain recommendation and supplement approval for Southern Hemisphere formulations follow the Northern Hemisphere process, which we do in the spring every year, and it uses multiple types and sources of data, including recent influenza virus surveillance and epidemiology data, genetic and antigenic characteristics of recent virus isolates, the serological responses to current vaccines, and of course the availability of candidate vaccine strains and reagents. In the next two slides I'm going to give you just a little bit of background of where we've been recently. Next slide.

Okay, so in March-- In fact, on March 13th of this year, we made a recommendation for the Northern Hemisphere vaccine formulation. This is of course the vaccine that is now on the market and out for use in the Northern Hemisphere and in the U.S. But in March, the FDA recommended only trivalent formulations for the 2025-26 influenza virus vaccines in the U.S., and the following strain compositions were recommended. For the influenza A H1N1, an A/Victoria/4897/2022 (H1N1)pdm09-like virus was recommended for egg-based vaccines. An A/Wisconsin/67/2022 (H1N1)pdm09-like virus was recommended for cell- or recombinant-based vaccines. For the influenza A H3N2 component, an A/Croatia/10136RV/2023 (H3N2)-like virus was recommended for egg-based vaccines, and an A/District of Columbia/27/2023 (H3N2)-like virus was recommended for cell- or recombinant-based vaccines. For the influenza B component of the vaccines, a B/Austria/1359417/2021-like virus, which is from the B/Victoria lineage was recommended, and this recommendation has actually not changed in a couple of years now. Okay, so if you go to the next slide, you see what's happened more recently.

This is the most recent global recommendations for the Southern Hemisphere influenza vaccines for 2026. In other words, next summer-- Our summer, next Southern Hemisphere winter. There was a WHO recommendation made at the end of September, 9/26/2025. At this meeting, both CDC and FDA participated. And the upshot of that meeting was that they recommended that trivalent egg-based vaccines for use in the Southern Hemisphere contain an A/Missouri/11/2025 (H1N1)pdm09-like virus, an A/Singapore/GP20238/2024 (H3N2)-like virus, and again a B/Austria/1359417/2021 (B/Victoria lineage)-like virus. And as I said, since the only two licensed U.S. manufacturers for Southern Hemisphere formulations are egg-based, that is what we

will start our discussion on and vote. And as Dr. Kaslow already said, the question will reflect this recommendation. Next slide.

So, the Committee will discuss and then this will be the voting question. Again, it's the same composition I read in the last one, but we will be asking the Committee for the composition of egg-based trivalent 2026 Southern Hemisphere formulations of influenza vaccines. Does the Committee recommend the following? An A/Missouri/11/2025 (H1N1)pdm09-like virus, an A/Singapore/GP20238/2024 (H3N2)-like virus, and a B/Austria/1359417/2021 (B/Victoria lineage)-like virus. So that's the introduction. You'll hear much more detail from Dr. Kondor about where we got-- How everyone got to this point. But I'm happy to take any questions if any are needed. Over.

Introduction to Seasonal Influenza Vaccine Strain Selection Southern Hemisphere 2026 - Q&A

Dr. El Sahly: Thank you, Dr. Weir. Please, use the raised-hand function if you have a question to Dr. Weir. Well, I have more of a clarifying question or more of a curiosity, really. You indicated that for the Southern Hemisphere we'll be looking at the egg-based vaccines for production because two manufacturers in the U.S. are suppliers to the Southern Hemisphere. I don't see that recombinant vaccine is on the-- You know, is being distributed to the Southern Hemisphere, although the manufacturer, Sanofi, is the supplier there. And we are seeing now data, whether it's from the randomized trial last year in the 50- to 64-year-old and some data in older individuals that it may be a bit more efficacious. Is it a regulatory issue that it's-

Dr. Weir: -No.-

Dr. El Sahly: -not going through the Southern Hemisphere or--?

Dr. Weir: No. No, it is not a regulatory issue. I mean, we only deal with the companies that come in and ask to license a Southern Hemisphere formula. Others could do it. It's just their choice. And then we evaluate the data, make sure that they're capable of doing it, and make sure that we take the steps so that one doesn't confuse Southern Hemisphere formulation to Northern Hemisphere's. So, no. This is really on-- The manufacturers decide what they want to do as far as U.S. licensure. What they want to pursue.

Dr. El Sahly: Got it. Thank you. I do not see any raised hand in the chat.

Dr. Weir: I think Dr. Portnoy has his hand up on my screen.

Dr. El Sahly: Okay, let me see. Why am I not seeing-- Oh, here we are. Yes, I'm sorry. I was on the wrong-- Yes, Dr. Portnoy. Sorry for that.

Dr. Portnoy: Yeah, good morning, you all. Last year there were actually a quadrivalent vaccine also with the B/Yamagata, and I remember the Committee discussed removing that because the Yamagata vaccine was extinct. I was just wondering, how did that discussion go and what led to the conclusion that we should no longer develop a quadrivalent vaccine?

Dr. Weir: Well, you probably remember, since you were part of some of these. This Committee discussed for a period of a couple of years and recommended that the U.S. not include a fourth component, which was B/Yamagata, and that's what we've been doing for the U.S. now for at least two years. Dr. Kondor can tell you what went on at the discussion at the WHO, but I did notice that they no longer recommended that fourth strain there, either. So, I think that it's finally just gradually made the point that it just really doesn't exist any longer and manufacturers everywhere have started taking it out, not just in the U.S., but she can elaborate on that one when she speaks.

Dr. Portnoy: They finally concluded that it really is extinct.

Dr. Weir: Well, it hasn't been detected now for-- I think we're up to four years or so. But yes, it's been a while now.

Dr. Portnoy: Yeah. That's pretty good. Okay, thank you.

Dr. El Sahly: No other questions? Thank you so much, Dr. Weir.

Dr. Weir: Thank you.

CDC: Global Seasonal Influenza Virus Surveillance and Characterization

Dr. El Sahly: I'd like to introduce now Dr. Rebecca Kondor. Dr. Rebecca Kondor is the Interim Director, WHO Collaborating Center for Surveillance, Epidemiology and Control of Influenza, Lead, Genomic Analysis Team, Virology Surveillance and Diagnosis Branch (VSDB), Influenza Division, National Center for Immunizations and Respiratory Diseases at the CDC. Dr. Kondor will give a discussion of the global seasonal influenza virus surveillance and characterization. Dr. Kondor.

Dr. Kondor: Good morning. Thank you very much for that nice introduction, and thank you to the FDA for inviting me to present on this topic to the VRBPAC Committee. As the Chairperson said, I'll be discussing the global influenza surveillance and characterization that was deliberated to come up with the 2026 Southern Hemisphere vaccine recommendation for the vaccine virus. And so, we'll go to the next slide.

So, the global recommendations occurred in September, as Dr. Weir mentioned, and this was held in Sapporo, Japan, posted by the Japan Institute for Health Security and chaired by Dr. Hideki Hasegawa at the National Institute of Infectious Diseases. And in that recommendation for the 2026 Southern Hemisphere influenza season, the

trivalent egg-based vaccines included recommendations for an A/Missouri/11/2025 (H1N1)pdm09-like virus, an A/Singapore/GP20238/2024 (H3N2)-like virus, and a B/Austria/1359417/2021 (B/Victoria lineage)-like virus. And as mentioned, recommendations for-- The global recommendations also included trivalent recommendations for cell-, recombinant- or nucleic acid-based vaccines. And those include an A/Missouri/11/2025-like-- (H1N1)pdm09-like, an A/Sydney/1359/2024 for H3N2, and continues to have B/Austria/1359417/2021 for the B/Victoria lineage.

Now, as mentioned, there were updates for the H1 and the H3 component compared to the 2025 Southern Hemisphere and the current 2025-2026 Northern Hemisphere vaccine viruses. And we'll-- I'll be able just to give a highlight of the information that was presented that led to these recommendations. So, bear with me that I won't have time to present all of the data. Next slide, please.

So, for more detailed information, I've listed links to the publications from the vaccine composition meeting as well as additional information. And what I won't be able to talk about was the-- Presented and discussed during the consultation, was the summary and antigenic characteristics of zoonotic influenza A viruses and development of candidate vaccine viruses for pandemic preparedness. Now, there was a lot of the data presented and, however, no new development of candidate vaccine viruses was recommended, and as that the current viruses in development or candidate vaccine viruses in development seemed appropriate for the information available. Also included are links to the available candidate vaccine viruses and reagents for both the seasonal and the zoonotic influenza virus vaccines. Okay. Next slide, please.

This shows a global circulation of influenza viruses detected through the Global Influenza Surveillance and Response System since 2022, including both Northern

Hemisphere and Southern Hemisphere activities. And the colors represent the influenza A in the shades of teal, and then subtyped into either (H1N1)pdm09 in the lighter teal and H3N2 in the darker teal. And then also detections of influenza B viruses in a dark orange and a brighter orange for B/Victoria and a light orange for B/Yamagata. What you'll see is the absence of a light orange B/Yamagata lineage, because through the GISRS network we have not detected influenza B/Yamagata-lineage wild-type viruses in circulation after March of 2020. So, looking at the 2025 to 2026 seasons that we'll be discussing here, we can see that the square in red highlights the data available in this reporting period since February 1st, 2025 through the end of August, 2025.

In GISRS, we can see a predominance of influenza A detected during this time period in both the Northern and Southern Hemisphere. However, when we look at the type and subtype, we saw predominance of influenza (H1N1)pdm09, but co-circulation in some regions of H3N2. And I'll get into a little bit more details where there might have been some regional differences. In terms of influenza B/Victoria, we can see co-circulation during the Northern Hemisphere and small numbers of co-circulation during the Southern Hemisphere season. Next slide, please.

This map shows the influenza activity and the global distribution of type and subtype, and I will get into more details of the specific detection of type and subtype in each section. And then, again, encompasses the information from February 1st, 2025 through the end of August, 2025. Here we can see influenza percent positivity in the field in yellow, and we can see that many areas globally saw influenza activity. And then looking at the pie charts, you can see a distribution of influenza A subtypes and B detections during this time period. We'll kind of focus on the Southern Hemisphere countries and regions. And we'll first start off with South America. And in South America you can see influenza positivity mainly in the southern part. And this, again,

was dominated by influenza A (H1N1)pdm09. And looking at parts of Africa, in West and East Africa, it was predominantly (H1N1)pdm09. However, in the southern part of Africa, you can see an H3N2-predominant epidemic. In parts of Asia, we had a mixture of influenza A and B co-circulating. And when looking at the influenza A, in some parts of Asia a H3N2 was more likely predominating. However, in other parts, (H1N1)pdm09 was predominantly detected. In Oceania, especially in Australia, the influenza season was predominated by influenza A (H1N1)pdm09, with very small levels of H3N2, but co-circulation in some areas of influenza B/Victoria. Okay. Next slide, please.

Now I'll give a brief update on the virus characterization of H1N1s leading to the update in the vaccine recommendation. Next slide, please. This map shows the influenza H1N1 detection levels globally since February, and highlighting what I previously showed that in South America it was predominantly an (H1N1)pdm09 activity. In parts of Africa, especially West Africa and parts of East Africa, H1N1 predominated. And then also in parts of East Asia, especially in China, H1N1 in this time period predominated, and as well as parts of Oceania, especially in Australia and New Zealand. Next slide, please.

This is a large phylogenetic tree of the (H1N1)pdm09 hemagglutinin gene, and looks at data encompassing years-- The end of 2023 through the end of August of 2025. And what we can show on the large phylogenetic tree on the left is the genetic diversity, and on the right [it] shows the location of the virus sequence and color coded with the map on the left. So, those from North America will be in dark blue, South America in teal, Africa in orange, Europe in green, Russia in maroon, Middle East in purple, and East and Southeast Asia in red, and Oceania in pink. And this is the same color that I'll be using in the other types and subtypes. And this can show us our regional differences

in the viruses that were detected each season, and trends in changing of the viral clade dynamics and geographic locations.

So, when we look at the phylogenetic tree for H1N1s-- Since the end of 2023, viruses have belonged to our 5a.2a clade in the hemagglutinin. And for the last couple of seasons, the virus recommended for the vaccine has belonged to the 5a.2a1 subclade, and that is the A/Wisconsin/67/2022-like or the A/Victoria/4897/2022-like vaccine virus. And what we've seen since those recommendations is co-circulation of hemagglutinins that belong to either a 5a.2a subclade. Those include those at the bottom of the tree, labeled in the newer updated subclade nomenclature of either C.1.8 or C.1.9. Or viruses belonging to the 5a.2a1 clade, and its subclades labeled in D, and that's D-- D1 through 5. So, what we can see at the very change in the 24 to 25 season is that we had co-circulation of both 5a.2a and 5a.2a1 globally, but we had regional differences in that-- Outside of the Americas it was predominantly 5a.2a viruses that circulated. However, since the beginning of 2025, you can see the number of tick marks under the 5a.2a C.1.9.3 subclade have disappeared. And instead, the viruses circulating since February 2025 have been predominantly from the 5a.2a1 D.3, or now more commonly called the D.3.1 subclade. So, we've seen a replacement of viruses from the 5a.2a with the 5a.2a1 D.3.1 subclade. Next slide, please.

We can look at this in another geographic view, looking at the diversity plot over time by geographic region. And again, splitting up the hemagglutinin of the viruses sequenced by the different clade and subclade nomenclature I just mentioned. And what you can see for all regions where there's sequence data available for this time period, we can see the emergence and the eventual overtake of viruses from the 5a.2a1 D.3.1 subclade. Okay. Next slide, please.

Another visualization shows that change in viral clade dynamics by location, where the Americas on the left continued to have co-circulation of both 5a.2a and 5a.2a1, whereas globally, in the eastern part of the globe, 5a.2a viruses predominated. And that was before January 2025. And then the next slide, again, repeating in places with detections of influenza (H1N1)pdm09 since February the predominance of this 5a.2a1 D.3.1 subclade. Okay. Next slide, please.

This summarizes the antigenic analysis of (H1N1)pdm09 viruses in hemagglutinin inhibition assays. And in these assays, we use a naïve ferret post-infection model, and these ferrets are infected with the egg- or cell-grown vaccine reference viruses. And this is for the 2025 Southern Hemisphere vaccine viruses. And as mentioned previously, the cell-based was the A/Wisconsin/67/2022-like from 5a.2a1, and the egg-based was A/Victoria/4897/2022-like. Now, looking across the GISRS collaborating centers, we can see that the vast majority of sera in this assay to the vaccine viruses recognized the viruses tested quite well. Again, using that post-infection ferret antisera in a naïve ferret antisera model. This tells us that there are antibodies to the vaccine that will recognize the circulating viruses well. Next slide, please.

This shows an integrated genotype and phenotype analysis created by CDC showing the results of our ferret antisera HI against the circulating diversity. And so, we can see in the phylogenetic tree-- In this case, we have the 5a.2a1 viruses at the top section of the tree, and you can see the D.3.1 in the purple bar representing a good majority of the viruses tested and sequenced during this time period. And at the bottom you can see viruses from the 5a.2a subclade represented by mainly the C.1.9.3 subclade. When we look at the results of our ferret antisera, we can see good recognition of all viruses with this ferret antisera. And the very small number had particular substitutions

that we've seen previously in the ferret model to show reductions. So, mainly inside SA or SB. Okay, let's go to the next slide, please.

What I wanted to show is an additional analysis that's run in our hemagglutinin inhibition. Previously, we just reported against the vaccine viruses, but in our analysis, we include reference viruses that represent the other circulating viruses clades. In this case, viruses from C.1.9, C.1.9.3, and then additional 5a.2a1 viruses from the D.3.1 subclade represented here in the HI assay with ferret antisera arrays to the cell-grown A/Missouri/11/2025, in addition to the vaccine viruses previously mentioned. And the trend in many of the collaborating centers has been that, although the ferret antisera arrays to the vaccine viruses recognized many of the circulating viruses from both 5a.2a and 5a.2a1 subclades well, we're starting to see antigenic drift with our reference viruses from the 5a.2a subclades against the D.3.1 viruses. Also in the ferret model, we're also seeing good recognition of both 5a.2a and 5a.2a1 viruses when the ferret antisera is raised against the D.3.1 reference virus.

Now, another way that we can look at our antigenic information is looking at antigenic cartography. I'm actually going to go to the next slide and probably advance one more. And now we'll have some labels. In this slide, we're looking at results across multiple HI assays performed here at CDC against the H1N1 viruses and the circles represent the test viruses and they're colored by which hemagglutinin subclade they belong to. We can see in a light teal there is our viruses from the 5a.2a C.1.9, and they cluster quite well together and are very similar to the virus representing the vaccine candidate Victoria/4897 and Wisconsin/67. Those are kind of right in the middle on top of those teal viruses. Viruses from 5a.2a1, either the D or the D.3.1 subclade, are shown in purple and a darker, brighter teal. These, you can see, are above the 5a.2a C.1.9 viruses. And so, what we're seeing is not right on top of each other. Again, showing an

antigenic drift between the 5a.2a subclades and the 5a.2a1 viruses which circulated. And this is also showing how well our ferret antisera to Missouri/11, the D.3.1 reference virus, recognizes-- And you can see that in the serum circle, any viruses that are recognized within eightfold of the homologous titer of Missouri/11 are within that serum circle. And we just have a few viruses outside of that serum circle and many of those have that additional substitution I mentioned in the position 155. Again, very small numbers of those and not consistently circulating. Okay. Next slide, please.

So, another layer that we look at in our serologic analysis of antigenic results for H1N1s is looking at human post-vaccination sera. In this case, we have different panels of Southern Hemisphere vaccine viruses. We have three panels from Australia, which include cell-based, egg-based, and for the elderly, an egg-adjuvanted vaccine. And then from Peru and South Africa we have an egg-based trivalent vaccine. When we look at these studies, the majority of our panels are selected from-- Sera that's tested is selected from individuals who have an appropriate immune response post-vaccination, so have that fourfold rise in titer and a titer greater than 40, meeting the correlator protection. So, we're really assessing individuals that respond very well to the vaccine, whether or not the antibodies post-vaccination recognize the circulating diversity that we have across the H1N1 virus. And in this assay, while we do see good recognition of many of the different viruses, we are seeing reductions across some of the genetic diversity in the 5a.2a1 and the 5a.2a viruses that circulated. Next slide, please.

Another thing that we looked at is vaccine effectiveness, and this is trying to understand whether or not there's a difference in vaccine effectiveness against the different viruses that co-circulated from the 5a.2a and the 5a.2a1 subclades. And we can look at the different colors. Those in blue recommend the estimated vaccine effectiveness for individuals against the D.3 subclades and then that in red against the

5a.2a C.1.9 subclades. In some estimates in different regions, we can see pretty similar vaccine effectiveness estimates. However, in other panels, especially those shown at the top, from Australia and Europe, we can see that there's been a little bit of a trend to lower vaccine effectiveness against the D.3 subclades. And we also looked at, and had an ability to look at, individuals from our vaccine network that were breakthrough infections or those that were not vaccinated and looking to see which viruses they were infected with.

In this case, we had an opportunity to look at individuals that were infected with the D.3.1 viruses and we're looking at their acute and convalescent sera. And in this assay, we were able to see that the majority of individuals had very low sera and antibodies recognizing either the vaccine viruses or the D.3.1 virus that they were eventually infected with in their acute sera. However, individuals in their convalescent sera had strong, robust immune responses to the virus that they were infected with, the D.3.1. And this convalescent sera well recognized the test viruses that we included in the assay from both the 5a.2a and the 5a.2a1 emerging viruses. So, individuals that were infected with the D.3.1 virus showed good recognition of our circulating diversity. Next slide, please.

So, another summary that we do during this time is looking at antiviral susceptibility. The two classes that we looked at are neuraminidase inhibitors and endonuclease inhibitors. Nearly 4,000 H1N1 viruses were examined and 96 showed evidence of reduced susceptibility to neuraminidase inhibitors. Many of these had an H275Y NA substitution, two had a Q136K, and you can see the remaining six had a mixture of different substitutions. In endonuclease inhibitors, we did not see very many that had substitutions. However, there were three that had an E199G substitution in the polymerase PA gene and one had an I38T substitution. Next slide, please.

So, in summary, an important noted for H1N1s is that they circulated globally and predominated in most regions. We also saw that while initially in previous seasons we saw this co-circulation of subclades from 5a.2a and 5a.2a1, during this time period, viruses from subclade D.3.1 have largely displaced all of the 5a.2a viruses in circulation. Next slide, please.

For antigenic characterization, while post-infection ferret antisera to our representative vaccine viruses recognized 5a.2a and 5a.2a1, ferret antisera from 5a.2a1, the D.3.1 reference virus, also recognized recently circulating viruses from the 5a.2a and 5a.2a1 clades. We are starting to see a different recognition for post-infection ferret antisera raised against the subclades of C.1.9.3 and C.1.9. Next slide.

Our human serology studies using-- Conducted from the Southern Hemisphere 2025, showed that in vaccinated human serum panels by HI assay against the recent viruses from the C.1.9, C.1.9.3, and the 5a.2a1 subclades D.3 and D.3.1-- We did see some significant reduction in circulating viruses across the genetic diversity that I just mentioned. The data supported recommending an update to the H1N1 to the A/Missouri/11/2025 (H1N1)pdm09-like (D.3.1) virus as a vaccine antigen for the 2026 Southern Hemisphere. And again, most of this is showing that viral clade dynamics and recommending that A/Missouri is a more appropriate vaccine antigen for the future diversity that we expect to come out of the D.3.1 viruses. Next slide, please.

Now we'll shift on to the H3N2 virus characterization summaries. Next slide. H3N2 activity from February till the end of August-- You can see, in this case we still had detections in the Northern Hemisphere earlier in this time period, parts of South America saw co-circulation, although H1N1 predominant. And then in Africa, I already mentioned the differences in influenza A detected with parts of the southern part of

Africa having predominant H3N2 viruses. And then also can see a continued co-circulation and in parts of South Asia and South and Southeast Asia detections and co-circulation of H3N2. Next slide, please.

So, the phylogenetic diversity of the H3N2 hemagglutinin gene, again, showing the same timeframe, so the end of 2023 until the end of August of 2025, all of the viruses that circulated-- Nearly all belong to our clade 2a.3a1 that we've seen for the last couple of years, and we've again subdivided them into new subclades. In this case, we can look at J.1 and J.2. The vast majority of viruses that circulated since February belong to the J.2 subclades. And we did see some significant emerging subclades within this group. Specifically, we'll call out J.2.1, J.2.2, J.2.3, J.2.4, and J.2.5. And again, we can see the collection region by the color of the tick mark. And we can see during this time period co-circulation of many of these emerging groups. But we are seeing some regional differences in the new subclades that are emerging. And I'll show that better on the next slide, please.

Okay, so, this is looking at the geographic regions, looking more at the J.2 subclades which circulated. And we can see one trend in nearly all of the regions, and that is the bright teal of J.2.4 emerging and in many other regions increasing in proportions during the end of this reporting period. In North America, our H3N2s predominated at the beginning of our season. However, after February it was mainly (H1N1)pdm09 predominant, but we can see emergence and co-circulation of many J.2 subclades, including J.2.3 and J.2.4 in more recent months. In South America, a little bit different trend in that not a lot of J.2 viruses have been detected, and instead it's been co-circulation of both J.2 and J.2.3 viruses. Next slide, please.

So, this is again showing the change in clade dynamics from September to January, showing a lot of J.2 in this dark blue, and just small amounts of lighter J.2.2, and that bright teal of J.2.4 seen mainly in parts of South Asia. And then if we switch to our February till now-- The next slide, please. Here's where we can see the expansion of countries that have detected viruses in the J.2.4. You can see parts of North America, Europe, Africa, and more parts of South and Southeast Asia, and parts of Oceania. And then in that orange J.2.3, you can see detections in North America, South America, and just a few other regions. So, we are seeing co-circulation of viruses in different, genetically diverse subclades, and as we'll talk about whether or not these particular subclades have antigenic differences, we can see interesting clade dynamics in the expansion of J.2.4 in nearly all regions. Next slide.

When we look at our antigenic analysis from this time period-- Again, we're using our post-infection naïve ferret antisera in HI assays in this result. And again, the infections were either with the District of Columbia/27/2023-like cell-grown virus or the Croatia/10136RV/2023-like egg-grown virus. And we can see in these trends small proportions of viruses in the HI, around 7%, with ferret antisera arrays to the DC cell-based, and larger proportions of reductions when we compare that to the homologous titer of the egg-based vaccines, over 41%, showing greater than eightfold reduction in titer.

We look at these same sets of viruses in another assay looking at virus neutralization on the next slide. And we can see a similar proportion of reductions in the viruses tested, around 7% for DC/27, and for the egg-based we can see 24% reduction. So, in the majority of the viruses that circulated, we saw good recognition with our ferret antisera. However, we are starting to see antigenic drift. And if we go to the next slide, again, this integrated genotype and phenotype analysis is asking, well, "Are there

molecular determinants for this antigenic drift? Are there specific substitutions in the hemagglutinin molecule that we can identify with the reductions seen in our post-infection ferret antisera?" For this, you'll see that we have a lot of different subclades marked by the different colors in the bar. We can see for J.2 viruses, the majority of viruses with our ferret antisera raised to DC/27, either in the HI or the virus neutralization assay, show good recognition of the J.2 viruses.

We also saw good recognition of the J.2.2 viruses, and these viruses were the predominant HA subclade, which circulated in parts of South Africa that I mentioned had a pretty strong H3N2 epidemic this season. The subclades where we saw more significant reductions include the subclades of J.2.3, J.2.4, and J.2.5. These subclades were emerging during the beginning of the year, and as I've shown previously, we can see some clade dynamics in terms of how they are increasing in their detections in different regions. In the next slide, I'll try to explain some of the changes which could be responsible for this antigenic drift detection with our ferret antisera.

So, if we look at a hemagglutinin monomer and look at where the substitutions are in these new emerging subclades, our District of Columbia/27 is a J.2. And if we look at changes in the J.2.3 and the J.2.5 viruses, here we can see they share changes at positions 158, which is at the very top of the molecule, and a major antigenic binding site. J.2.3 viruses also share an additional change at position 189. So, these viruses have similar changes, but a little bit different. But sharing that 158K substitution. If we now look at the J.2.4 viruses, these viruses share a change at position 135 and in the 135-- This is in antigenic site A and near the receptor binding pocket. And this change at 135 actually leads to a loss of a glycosylation site in this particular part of the molecule. And what I also show here is that K189R substitution, which is in antigenic site B, we can see that that is also present in these J.2.4 viruses. So, we see two different antigenic

binding sites showing mutations compared to the DC/27 in the J.2.4 viruses. And more recently, within the J.2.4, there's always emergence of evolution, but a particular note-- We've seen additional substitutions, actually quite high number of substitutions, that are also within important antibody binding sites. These include substitutions I've labeled here, the J.2.4+7. So, in addition to the 135K substitution and the 189 and in the base of the J.2.4 viruses, these viruses in particular have additional substitutions at both 158 and 160 in site B, and an additional substitution at position 144, which could add back a putative glycosylation site. And then also a substitution shown at position 173 in addition to other changes not in antigenic binding sites. So, quite a significant number of mutations in these particular viruses. And again, really leading edge in terms of detecting them in more recent collection dates. So, this is explaining some of the changes on the surface of the hemagglutinin in these emerging groups where we've seen reductions in our DC/27 ferret antisera model. So, again, positions 158, 158 in conjunction with 189, positions 135 in conjunction with 189, or these further evolved with additional substitutions at 158, 160, and 144. So, next slide, please.

When we look at our antigenic cartography of where the placement of these viruses are in our antigenic cartography space, what is interesting to note is that these different subclades of J.2.4 and J.2.5 and J.2.3 are not antigenically related. They're actually quite antigenically distinct from each other. This is a common problem with H3N2 viruses, where we have co-circulation of antigenically distinct subclades. And so, a common problem that needs to always be addressed. In this case, we can see viruses from the J.2.3 and the J.2.5 subclade in green and orange co-localized together in the bottom right of the antigenic maps or in the right on the one from Melbourne. We can see viruses from the J.2.4 in light blue or those with additional substitutions in a very light aqua right above them. So again, we're seeing antigenically distinct subclades and

we're seeing even further antigenic drift in viruses from that recently emerging J.2.4 subclade. Next slide, please.

When trying to find an optimal vaccine antigen that would recognize all of the genetic diversity that we've observed emerging and with the data on clade dynamics, it's been extremely difficult to find a single virus that would recognize all of the diversity well. And although the virus-- The information that we have from ferret antisera and vaccine effectiveness to the DC/27 and the Croatia-like do a fairly good job of recognizing the J.2 viruses, we are starting to see those significant reductions in the J.2.3, the 2.5, and the J.2.4 viruses. And because of the differences that these viruses have between each other, they don't recognize each other at all. So, the J.2.4 is distinct from the J.2.3, and making ferret antisera to reference viruses from these particular subclades shows that we don't have good recognition-- Cross-recognition. When we are looking at an appropriate vaccine viruses to the emerging and likely to predominate J.2.4 viruses, we see good recognition using ferret antisera raised to the reference viruses for the Sydney/1359 in the cell-based or the Singapore/GP/20238/2024 egg-based virus shown in the circle around the north on the right antigenic cartography there. And that includes viruses with those additional substitutions I mentioned at positions 158, 160, and 173, and 144 in the J.2.4 viruses. Next slide, please.

So, this gives an overview of the human post-vaccination serum analysis from the panels I mentioned in the H1N1. And here we are seeing reductions in our post-vaccination human sera panels to many of the J.2 further evolved subclades that I mentioned in terms of J.2.1, J.2.2, J.2.3, J.2.4, and some in the J.2.5. And so, we are seeing significant reductions to many of those important emerging subclades. Next slide, please.

Summary for the antiviral susceptibility for H3N2. Of the 1,716 H3N2 viruses examined, no viruses showed genetic or phenotypic evidence of reduced inhibition to neuraminidase inhibitors. Similarly, no viruses showed reduced susceptibility to endonuclease inhibitors as well. Next slide.

To recap the always-difficult-to-give short summary on the dynamics of the hemagglutinin diversity, we can see that although all of the viruses belong to this 2a.3a1 subclade, we have further diversification and noted that the J.2 was predominant. But there are emerging viruses in the J.2.1 to J.2.5, and the substitutions in these emerging viruses are showing antigenic drift not only from the current vaccine virus but also between each other quite significantly. And then, importantly to note that the J.2 viruses are continuing to circulate in many geographic regions, and of note, that emerging and recently expanding group within that. And not to forget the J.2 viruses which were detected in higher proportions in South America. So, still a complex situation of the viruses for the H3N2 diversity. Next slide.

So, antigenic characterizations; and in summary, although the ferret antisera model recognized from the DC/27 or the Croatia/10136RV, while they recognize most viruses well, viruses in the emerging subclades, particularly J.2.3, J.2.4, and J.2.5, were recognized poorly. When trying to find a vaccine virus which could recognize all diversity, that was not possible. But we did see trends that if some of the substitutions were shared, for example, between the J.2.3 and the J.2.5, they share an N158K. We did see cross-recognition with that ferret antisera. However, poor recognition of viruses with the J.2.4. And then, when looking at the J.2.4, we saw good recognition with our reference viruses, Sydney/1359 and Singapore/GP/20238, to the J.2.4s, including those with those notable amino acid substitutions that have recently emerged. However, recognition of other viruses from the J.2 subclades poorly. Next slide.

Our human serology studies-- Again, we looked at a lot of viruses across that J.2 diversity and when compared to titers against the cell-propagated District of Columbia/27/2023-like vaccine reference viruses, post-vaccination HI GMTs or virus neutralization GMTs against many of the recent viruses, particularly of note the J.2.2, 2.3, 2.4 and 2.5 subclades, were significantly reduced. So, this in part is the data that supported recommending a cell-propagated Sydney/1359/2024-like, a J.2.4 virus or cell-based, and an egg-propagated Singapore/GP/20238/2024-like as the H3N2 vaccine antigens for the 2026 Southern Hemisphere. Next slide, please.

Now we'll transition into the influenza B viruses. Next slide. So, influenza B activity-- We'll see that this is since February, and so, parts of Northern Hemisphere saw higher detections of influenza B viruses during this period in Europe and parts of Asia, and also parts of West and South Asia. However, the majority of countries reporting in the Southern Hemisphere saw low levels of influenza B activity and much higher levels of influenza A. Next slide, please. Influenza B/Yamagata. Next slide, please. As I mentioned earlier, there have been no confirmed detections of circulating B/Yamagata/16/88-like lineage viruses since March 2020. It continues to be recommended that the B/Yamagata lineage antigen should be excluded from influenza vaccines because it's no longer warranted. And at this point the WHO Committee is no longer going to have updated recommendations for the B/Yamagata lineage component. So, all evidence that we have in our Global Influenza Surveillance and Response Systems have not detected influenza B/Yamagata lineages now for over five years. Next slide, please.

So, now we'll talk more about the characteristics of the B/Victoria lineage viruses which circulated. Next slide. So, the phylogenetic tree of the HA for the B/Victoria lineage viruses since the end of 2023 shows the majority of viruses belong to

this B/Victoria 3a.2 subclade. I remember-- This is a three-amino acid deletion compared to viruses which previously circulated, and the B/Austria/1359417 has been the recommended B/Victoria lineage vaccine antigen since the Southern Hemisphere 2022. When we, again, break up the hemagglutinin into new subclades, in this case C.1 through C.5, we can see over this time period co-circulation and different regional detections of different subclades of the C.1 through C.5. And we're going to note in particular the C.5 has been split out into C.5.6, 5.1 through 5.7, but more recently looking at co-circulation of C.5.1, 5.6 and 5.7, and a new emerging group in the C.5.6.1s. So, the vast majority of viruses which were sequenced during this time period belong to one of these C.5 subclades, which I just mentioned. We want to note, at the very top you can see a C.3 subclade, and it's to C.3.1 and C.3.2 subclades, and you can see some dark blue detections. And these are detections of this particular subclade during the end of the Northern Hemisphere season in North America. And we'll talk more about the particular viruses later there. Next slide, please.

Now looking at, again, by a geographic region, there really isn't a very good summary except that the C.5.1, 5.6, 5.6.1 and C.5.7 co-circulated in all regions in different proportions. Where we did see a little bit difference is in North America with that emergence of the C.3.1 after 2025 and some increase in its circulation during this time period. So, that's the notable difference for the B/Victoria viruses. Next slide, please. Here we can see the detections and variability by region of which of the C.5 subclade predominated. Again, seeing regions where C.5.1 predominated. Other regions were C.5.6 or its 5.6.1 subclade, and then also the co-circulation of the C.5.7. Next slide, please.

Looking at the antigenic characterization results by the collaborating centers, here's where we can see that there were differences by collaborating center, and this will

mainly be dependent on which viruses they had to test. We can see that overall there was good recognition in HI assays by either the cell- or egg-grown B/Austria/1359417-like vaccine reference viruses. However, you can see in the CDC data a higher proportion of viruses with greater than eightfold reduction to the homologous titer of our vaccine viruses. Next slide, please.

So, the genetic determinants of why we're seeing a higher proportion in the CDC data-- And here we can see that the phylogenetic tree and on the right showing the breakout of which of the C.5 subclades or at the very bottom, the C.3 subclades, C.3.1 and C.3.2 which circulated, and our test results at CDC-- We can see good recognition of C.5.1, 5.7, and C.5.6 and its subclades, with our ferret antisera to B/Austria, but very poor recognition in viruses from the C.3.1 and the C.3.2 subclades. Now, looking at the hemagglutinin of these particular subclades, they independently had the same mutation at position 197 from aspartic acid to asparagine, and this adds a glycosylation site-- Putative glycosylation site on the hemagglutinin. And we've seen over the time for B/Victoria viruses and B viruses in general the addition and subtraction of putative glycosylation sites associated with antigenic drift. So, in this case we can see an antigenic drift detection with viruses with that additional glycosylation site added. And we saw more C.3.1 than C.3.2. Next slide, please.

When we're looking at antigenic cartography, the subclades of the C.5 I've mentioned co-localized together and are well recognized by ferret antisera to the B/Austria. We can actually go to the next slide to see that serum circles. Where we're seeing outliers-- Again, are viruses with that C.3.1 or C.3.2 with that glycosylation change. These are shown in the darker blue outside of the serum circles here. Next slide, please. Our post-vaccination sera is very similar to the data that we have with post-infection ferret antisera, and that significant reductions we're not seeing against viruses

from the C.5 subclades. Instead, significant reductions were seen against viruses from the C.3.1 subclade, with that glycosylation change. However, this particular subclade, again, had very limited geographic detections and the majority of viruses that are currently circulating belong to these C.5 subclades. Next slide.

For antiviral susceptibility, over 1,500 B/Victoria viruses were analyzed and five showed evidence of reduced or highly reduced inhibition by neuraminidase inhibitors. When looking at endonuclease inhibitors, no viruses showed evidence of reduced susceptibility to baloxavir. Next slide.

So, in summary, we have that co-circulation of genetic diversity of the clade 3a.2 viruses, predominantly seeing viruses from C.5.1, 5.6 and C.5.7, and then that lower proportion of circulating and that regional detection of the C.3.1 and the C.3.2 viruses, with the notable antigenic drift being able to detect it not only with our ferret antisera but significant reductions seeing in post-vaccination human sera profiles. Next slide, please. So, again, titers were significantly reduced, related only to the C.3.1 viruses in our human serology assays. And this, in total, is the data that supported maintaining the B/Austria/1359417/2021-like viruses as the B/Victoria lineage of vaccine antigens for the 2026 Southern Hemisphere season.

So, this concludes my presentation and I'm happy to turn it over to the Chair and be able to answer any additional questions. Thank you.

CDC: Global Seasonal Influenza Virus Surveillance and Characterization - Q&A

DR. El Sahly: Thank you, Dr. Kondor and team, for this large body of data and the presentation. Please raise your hand if you have a question, and I see the first question from Dr. Durbin. Dr. Durbin.

Dr. Durbin: Great, thank you so much. That was a wonderful presentation. This may be a little bit theoretical, but given we used to have quadrivalent influenza vaccines, has there been any thought, given the divergence in the H3N2, to recommend two different strains for H3N2? Because that genetic map was really between the J.2.3, J.2.5, and J.2.4 was quite significant and I'm a little bit concerned about a mismatch. Thank you.

Dr. Kondor: Yeah. Dr. Durbin, thank you. That has been an active area of discussions for vaccine development. Currently-- The currently licensed influenza vaccines do not allow for more than one H3N2 antigen, but I know that there's been some preclinical studies to see the feasibility of more than one H3N2 antigen in newer licensed vaccines. Thank you. But I agree that's an important area of research that needs to be done.

Dr. El Sahly: I have a follow-up question on the H3N2 story, which is-- It seems that the District of Columbia strain had better cross-reactivity with the-- Than the Croatia strain. These are both in our Northern Hemisphere vaccine this year, and the difference was both in human sera and in ferret sera. And at times, you know, depending on what you showed, it's significant. So, any explanation or projection here regarding what are we going to see in terms of effectiveness?

Dr. Kondor: I can't answer--

Dr. El Sahly: [Indiscernible - 01:32:04] 2017-2018, when we lost that glycosylation site and we ended up with differences between egg-based versus non-egg-based vaccines.

Dr. Kondor: Right. I think you are pointing out that the difference between the DC and the Croatia are which platform the virus is propagated in. And DC is a cell-based, whereas the Croatia virus was grown in eggs and has additional mutations that allow the virus to grow in eggs. This is a common thread for influenza viruses grown in these two

different platforms in that mainly viruses grown in eggs need to acquire mutations in and around the receptor binding pocket to be able to grow in eggs. And often this leads to antigenic differences between when we raise ferret antisera to the egg-grown viruses and test them against the virus-- Circulating viruses which we grow in cells. So, egg adaptations occur in order to allow the viruses to be manufactured in eggs. However, there always is the potential for an antigenic drift difference between viruses grown in eggs versus those that circulate.

Dr. El Sahly: Yeah, I agree. However, the difference is really significant this time, at least-- In a couple of the slides you've shown that the recognition between these two strains, the one selected for the cell versus the one selected for the egg, seems to be significant this time. I mean, it's probably more of an issue for the Northern Hemisphere than the Southern Hemisphere, which is what we're discussing here. But anyway. Doctor--

Dr. Kondor: And let me just clarify a little bit on that. When I show the human serology data, we use different reference anchors for the GMTs. So, on the top section of the human serology section, we used the cell-based virus as our control for getting our effect for the egg-based or the cell-based vaccine. And so, we're seeing similar individuals that get an egg- versus a cell-based vaccine show good titers-- Or the egg-based show reductions just to the significant subclades that I mentioned. When we use the egg-grown virus in our assays, it tends to have a really high homologous titer and in that case shows differences in recognition in the cell-based viruses used in the assay.

Dr. El Sahly: Thank you. Dr. Perlman.

Dr. Perlman: Yeah, so, I have a question-- A couple of questions. One is are you getting the same number of samples virus isolates for analysis as you have in the past or

has it been any sort of fall off, like we've seen with SARS-CoV-2? And the second thing is-- Something we've discussed in the past is whether just looking at antibodies is really sufficient, whether we should be looking at cellular immunity too to see if that has any effect, and this might relate to differences in clinical disease that occur as this virus mutates. I don't know if there's new data on that as well.

Dr. Kondor: Thank you, Dr. Perlman. Your second point, I'll answer first in terms of, yes, it's an active area of interest to understand the role of the cell-mediated immunity in disease for influenza, although I don't have any data to present for this particular question. For the first question, in terms of samples that we've received. You know, the U.S. has a robust national surveillance program for influenza. And so, we have a good amount of viruses coming in from our U.S. partners as part of the Global Influenza Surveillance and Response System, and we also at CDC receive international specimens, and there have been some changes in the numbers of specimens that we've received since February. However, we're working to-- With our colleagues to improve that. There's good recognition and availability of viruses to test throughout the network, so you'll see changes in the numbers by different collaborating centers on which viruses they test, but overall, there was a robust number of viruses tested during this time period.

Dr. Perlman: Thank you.

Dr. El Sahly: Dr. Monto.

Dr. Monto: An observation and a question. Usually, when we see the Southern Hemisphere strain selection, we often wish that we had the opportunity to get the H3N2 that's being recommended for the Southern Hemisphere in our current Northern Hemisphere vaccine. And for that, we're going to need new platforms and things like

that, which may be some time in coming. And my other observation, Dr. Durbin already mentioned, and that is we have been saying for a number of years, especially after it was clear we were going from a quadrivalent to a trivalent vaccine, that we should have two H3N2 viruses in the vaccine as long as we could show that there wasn't interference or some other phenomenon taking place. My question, when you started showing neuraminidase, I was hoping you were going to say something about neuraminidase drift, since we do recognize that neuraminidase is a secondary correlate of protection-- Independent correlate of protection. Is anybody really looking at this right now with all the work and all the clade diversity that gets worse and worse every year?

Dr. Kondor: Regarding the neuraminidase, when we do the genetic analysis, we are looking at all genes of influenza viruses and we are looking at the neuraminidase and we are tracking the clade dynamics for neuraminidase substitutions, and we are seeing that with the D.3.1 viruses for H1N1, they did tend to have a lot of reassortment and trying out a lot of diversity of the neuraminidase gene. However, we did not have additional neuraminidase antigenic information during this vaccine consultation meeting. But it is an active area that we're trying to get more consistent antigenic drift for the neuraminidase-- For the vaccine [Indiscernible - 01:38:54]. Thank you.

Dr. Monto: And I'm happy to see that you are tracking antiviral resistance, because if we go into a mismatched year, that's going to be even more important. Thank you.

Dr. El Sahly: Thank you. I have a question pertaining to the B. As you indicated, for two or three years now we've been going with the same strain. So, between infection and vaccination, the population has sort of immunity to that particular lineage or strain I should say. There's a new lineage that's emerging, the C.3.1 and the C.3.2, which is a bit distant from the Austria. The modus operandi as we understand it is trying to understand

what's the background, what we've been vaccinated with and what have we been exposed to, and see what are we not covering and what seems to be on the horizon. Was there a particular rationale why not a strain closer to the C.3 or the C.3.1 was not chosen?

Dr. Kondor: Yeah, and mainly that's due its limited detection outside of the Northern Hemisphere. During other parts of the year, where we had more significant influenza B epidemics, those were predominated by the C.5 subclades. So, it was more the proximity of where it was circulating and not seeing it associated with significant epidemics necessarily.

Dr. El Sahly: Okay. So, it has to do with the distribution, the geographic distribution.

Dr. Kondor: Correct.

Dr. El Sahly: And, I guess, taking a bet that is not going to be the one going to the southern half, which is understandable, but I wanted to point that out. Thank you. Dr. Bernstein.

Dr. Bernstein: Thank you. I may not be interpreting the global surveillance maps correctly, but the B lineage did seem to be more prominent in certain continents and more in the Southern Hemisphere. What drives more of the B lineage prominence over the A viruses?

Dr. Kondor: Yeah, that's a great question. I don't have an answer for you on that exactly. I think it's a mixture of population immunity that's driving an [Indiscernible - 01:41:39] in that region of particular viruses. And so, there's opportunities for different dynamics based on the population immunity structure there.

Dr. Bernstein: Thank you. And I did want to add to what Dr. Durbin and Dr. Monto said about the consideration for two H3N2 strains in future vaccines perhaps. Thank you.

Dr. El Sahly: Thank you. Thank you, Dr. Bernstein. I have a question pertaining to the VE slide. You have shown a slide with VE for the H1N1 from different continents. Do you mind pulling that one up? Maybe-- I just wanted to clarify that I understood it.

Dr. Kondor: My apologies. I don't have control.

Dr. El Sahly: Oh, okay. It's in the H1N1.

Dr. Kondor: Right. So, that slide was--

Dr. El Sahly: Slide 16? May be slide 16? Let's try slide 16. Could be wrong, but-- No, it's the one probably a couple before or couple after. Regardless. In Europe, it seemed that the VE was very different than anywhere else. Was it an issue of the diagnostic or the diagnostics used? Because we saw a few publications in the last month or so, where-- From Europe, where it was based on ICD-10 code to ascertain the VE of flu vaccines versus the NVSN, for example, that you showed on the same slide where it is PCR-confirmed. Do you think the difference in VE had to do with the diagnostics used?

Dr. Kondor: I don't believe it's the diagnostics. It just depends on the study capabilities of whether or not they had sequenced information available from all of their cases. And so, I'd have to go back and look at that particular Europe result and see what kind of information was available for that particular study result.

Dr. El Sahly: Okay. Thank you. To the issue of having more than H3N2 in the vaccine, my colleagues Dr. Monto, Dr. Durbin, and Dr. Bernstein commented on that. I know it gets complicated with the issue of the antigenic interference and antigenic-- Negative antigenic interference based on what's been circulating before and the year of birth,

etcetera, etcetera. But what has been also another low-hanging fruit is the neuraminidase. It's an independent correlate of protection. It is less, at least so far, subject to drifts and shifts, and has been demonstrated again and again in terms of its importance in infection and disease. And in my viewpoint, that is definitely a low-lying fruit where antigenic interference may not be an issue and would potentially improve VE if we have more antigenic space to occupy, I guess, with the Yamagata removal.

Dr. Kondor: All of these are active questions that we are working on with our preclinical vaccine development. For the currently licensed vaccines, again, we are unable to recommend more than one H3N2 antigen. And then as you mentioned with the neuraminidase, whenever we make our vaccine recommendations, we are taking into account information available on the diversity of the neuraminidase. And in most cases, the vaccine viruses also represent an update in the neuraminidase. All of them have not just the HA from the recommended vaccine virus, but also the neuraminidase for that particular virus as well. So, both are updated in the recommendations. However, we don't necessarily have a lot of information on antigenic drift for the neuraminidase during these decisions.

Dr. El Sahly: Thank you. Dr. Perlman.

Dr. Perlman: Yeah, just a follow-up on the question there. So, when you look at vaccine efficacy, do you have the capability to go back and look at the viruses in the people who broke through and had an infection to see if that actually correlates with some of the drift that you're describing?

Dr. Kondor: Yes. In the U.S. VE networks we're able to have sequencing of all of the influenza-positive cases and whether or not they're vaccinated or not. And this is-- I mean, this season we actually did a lot of work to see what particular viruses individuals

were infected with. In particular-- And then, as I mentioned with the H1N1s, also look at acute and convalescent sera of these individuals to understand some of the reasons why we're seeing influenza infection. And again, as has been previously shown in several studies, most individuals have-- When we look at their acute sera, they have very low titers to either the vaccine or the virus that they were infected with. And so, they don't have a correlate of protection necessarily for an influenza infection. And then we can look at-- Even individuals who may have a history of vaccination for that season. So, we are seeing that in some individuals post-vaccination, they don't mount an immune response that we would consider to be protective.

Dr. Perlman: So, do you think that's more important than the drift the fact that they've just mounted a very poor immune response?

Dr. Kondor: I think it's two parts, because not only did they not have enough protective antibodies to the vaccine virus, but they also didn't have enough protective antibodies to that drifted virus as well. So, it's both. Looking at both of those amounts of antibody response shows, you know, lack of protection.

Dr. Perlman: Thank you.

Dr. El Sahly: Dr. Durbin.

Dr. Durbin: Yes, I have more of a comment than a question. And that's just, it's more, I guess, focused or relevant to the Northern Hemisphere viruses. But the recombinant vaccine, I believe is HA-only, which would limit neuraminidase protection, of course, because it isn't contained. And again, just having FDA consider expanding the allowance of a recommendation to two H3N2 viruses might be helpful because, again, just in Northern Hemisphere viruses use of the recombinant vaccine would not include neuraminidase. Thank you.

Dr. El Sahly: Yeah. Any other questions to Dr. Kondor? Use the raised-hand function. Okay. Well, thank you so much, Dr. Kondor. I don't see any additional questions. So, next on the agenda, we get a 10-minute break. It is 10:16 Eastern Time. Let's reconvene at 10:27 Eastern Time.

Committee Discussion, Recommendations, and Voting

Dr. El Sahly: Next on the agenda is the Committee discussion, recommendations, and voting. We have had a very detailed presentation by Dr. Kondor pertaining to the rationale of the selection of the three strains for the Southern Hemisphere flu vaccine, and there were some engaging questions and answers with Dr. Kondor from the Committee, and now we will be discussing this amongst ourselves. I invite the Committee members to use the raised-hand function to voice any comment questions, concerns about the vaccine recommendations. Dr. Rubin.

Dr. Rubin: Perhaps I should have asked this during Dr. Kondor's presentation, but when we did have the discussion about moving from a quadrivalent to a trivalent vaccine, we encouraged that, but I hoped that we would retain the capability to make a quadrivalent vaccine in part to deal with some of the antigenic drift that we discussed before, and I just wonder if we've lost any capacity to do that in the switch.

Dr. El Sahly: That's really a question to Dr. Weir. Dr. Weir?

Dr. Weir: Yes. So, all of the manufacturers who had licensed quadrivalent vaccines, which would contain two influenza B strains, retained those licenses. They're not active. They put them on an inactive list, but yes, they would still be able to-- If a B/Yamagata strain emerged, they would be able to reactivate those licenses. So, they still have that. I would suspect as far as manufacturing capacity, they still would have that ability, too, but I guess we'd have to ask each of them individually. But I think the

answer to your question is yes, we haven't lost anything as far as a quadrivalent vaccine that would contain two B strains.

Dr. Rubin: Thank you.

Dr. El Sahly: Dr. Durbin.

Dr. Durbin: Okay. This is the obvious follow-up question. We haven't lost the capability for quadrivalent with two B strains. How arduous is the regulatory process if you wanted a quadrivalent with two H3N2? Or is there any flexibility, for instance, to have a quadrivalent and which for makeup of those viruses, whatever the makeup is, that it's more flexible so that you can be more-- You can respond to different changes more quickly?

Dr. Weir: So, the answer to the question about how arduous is it, I guess would depend on whom you're asking. Manufacturers might have a different view than I do. From a regulatory point of view, yes, there are things that would have to be done. They would have to update their license. To update their license, they have to have data to support that updating. And I think it was Dr. Monto that mentioned about interference. That would be one of the things that will obviously have to be shown. You add two influenza A three strains, do you get the same type of response to both of them? There's a very in-the-weeds technical problem of can you distinguish those two in a potency assay? So, there are technical things that would have to be worked out. Then, of course, there has to be the clinical need to drive that, and who would recommend that. So, I can sit here and tell you it's probably not that hard, but it does require some studies and it does require data to support that sort of updating. I don't think-- Well, we've never had the ability-- Like I said, we've had licenses for a quadrivalent that contained one H1, one H3, and two influenza Bs. That licensure was supported by data, and if one wanted

to change that, they would have to have supporting data to support any recommended change. That helped?

Dr. Durbin: It does. I think we're almost in a catch-22, though, because it's difficult without, I guess, strong guidance-- And I guess this will be driven by epidemiological data in the future to see if we really do need two H3N2s.

Dr. Weir: Well, so, if you think back, we kind of went over this when we did these VRBPACs about taking away one of the strains and we rehashed the history of how we got to quadrivalents. And it also was a slow process where we debated it for years about whether it was needed and it was a kind of question of who wanted to go first.

Dr. Durbin: Yeah.

Dr. Weir: Finally, some manufacturer, and I think this was the live-attenuated, did the study, showed that it could be done, and that push, and then there was a recommendation for a fourth strain if someone made a quadrivalent, and then the other manufacturers sort of fell in line because I guess it became a marketing sort of thing, too. So, yes. Someone has to go first. That's true.

Dr. Durbin: Yeah. Thank you very much.

Dr. Weir: Okay, thanks.

Dr. El Sahly: Any other questions to get the discussion going? Dr. Monto?

Dr. Monto: Just an observation after Jerry's comments. One of the main things that drove the decision to start making the quadrivalent vaccine was capacity; that there was sufficient capacity to produce the vaccine. And it's clear that if they did produce a quadrivalent vaccine and have gone to trivalent vaccines and sales have not increased,

that the capacity is there. So, it's really a decision that the community has to push, because it's been talked about for some time and the necessary serologic studies, which I believe, Dr. Weir, are the only ones that would have to be done, not efficacy studies, need to be made. It seems like something which is not very hard to do compared to many of the other challenges the vaccine manufacturers have had. And the additional effect, even if it's not a diverse year, that we may even see better H3 antibodies in general with a somewhat high dose. Thank you.

Dr. El Sahly: Yeah. I guess, Dr. Monto, that is important-- In addition to the question of antigenic interference, meaning they have to be distant enough, the issue of-- It's really related to having a totally different antigen versus just having a higher content, which results in higher cross-reactivity. But I agree with you that the question can be answered in preclinical and clinical developmental pathways along with the other question of what would neuraminidase inclusion do. Okay. Any other questions? I don't see any raised hands. I guess Dr. Kondor convinced us enough with this very detailed presentation that she had. Cicely, I think I'll turn it over to you now for the questions.

LCDR Reese: Yes, thank you. Thank you, Dr. El Sahly. This is Cicely Reese, DFO. The question before the Committee is a voting question. We can go ahead and display the voting question. Thank you. Voting Members will use the Zoom platform to submit their vote for this 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 question into the record and all clarifying questions are complete, we will announce that voting will begin. A voting window will appear where you can submit your vote. There will be no discussion during the voting. 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. Once all Voting Members have

selected their vote, I will announce that the vote is closed. Please note there will be a momentary pause as we tally the vote results and return Non-Voting Members into the meeting room. Next, the voting results will be displayed on the screen. I will read the voting results from the screen into the record. Thereafter, the Chairperson will go down the list and each Voting Member will state their name and their vote into the record. Voting Members should address their rationale for the vote. Are there any questions about the voting process before we begin? Okay. Dr. El Sahly, would you proceed with reading the question as it's written? Thank you.

Dr. El Sahly: Sure. Voting question for the Committee: "For the composition of egg-based trivalent 2026 Southern Hemisphere formulations of influenza vaccines, does the Committee recommend an A/Missouri/11/2025 (H1N1)pdm09-like virus, an A/Singapore/GP2020-- 20238/2024 (H3N2)-like virus, a B/Austria/1359417/2021 (B/Victoria lineage)-like virus?"

LCDR Reese: Okay, so if there are no further questions, then we will begin voting on question one. Next slide, please.

Voting has closed and is now complete. The voting results will be displayed. Okay. So, we have the voting results, which are nine yeses, which is a unanimous vote. And Dr. El Sahly, if you would like to move on and go around to have people explain their vote into the record. Thank you.

Dr. El Sahly: Yes, absolutely. Thank you all for voting on the question number one. We begin with Dr. Saad Omer. Dr. Omer, you said "Yes." Any comments?

Dr. Omer: Yeah, but, so, nothing significant to add. But based on the data presented, both the genetic and antigenic data presented, I think it's a reasonable case to vote "Yes" for this recommendation.

Dr. El Sahly: Okay. Thank you. Dr. Monto, you voted "Yes."

Dr. Monto: I voted "Yes" and have no additional comments to what I've said before. I think it would be very good to begin to think again about the neuraminidase because we don't even require it in the vaccine. That's quite clear. Thank you.

Dr. El Sahly: Thank you. Dr. Meyer.

CAPT Meyer: Thank you. Yes. I think just to start off, I just want to commend my CDC colleague, Dr. Kondor. I thought that was such a great detailed presentation and every time I see one of these, I'm so impressed with the amount of work and painstaking detailed laboratory data that gets compiled for these, and I think it really speaks to just the value of strong global laboratory networks. So, first, I just wanted to get that stated, that I really appreciated that talk. I think there was a large amount of data presented that I thought does support the proposed recommendations. We did hear about some of the challenges, particularly with the H3N2 lineage, but I do think that there was data presented that did support this recommendation. And then, I do think from a pragmatic standpoint, alignment with the WHO recommendations makes the most sense. Thank you.

Dr. El Sahly: Thank you. Dr. Perlman, you voted "Yes."

Dr. Perlman: Yes, I voted "Yes." I thought the data were compelling for the vaccine composition. I also agree with Dr. Meyer about the great job that the CDC did in the presentation, and I have nothing else to add.

Dr. El Sahly: Thank you. I voted "Yes," and I also-- I'm a little-- Maybe this is not warranted, but I'm a bit anxious about the B strain. Of course, the saving grace is that the B is usually milder and less-- Associated with less mortality than the A. But

probably we may be seeing something evolve there to move us from the Austria, but given the geographic distribution, I agree not to take a chance. And I echo what I just stated earlier, that it is time for manufacturers and the scientific community to start evaluating improving the vaccine by capitalizing on the neuraminidase data we have. And I want to finish by thanking the WHO and the CDC for the data they gathered as presented so elegantly by Dr. Kondor. Dr. Rubin?

Dr. Rubin: I agree with everything that's been said. I noticed that I think I'm off the Committee in January, so this may be my last flu presentation. And I also want to commend the CDC and FDA and WHO staff for doing such a great job with us.

Dr. El Sahly: Thank you. Dr. Durbin.

Dr. Durbin: Thank you. I don't have a lot to add. I also really want to thank the CDC presentation. I thought it was incredibly informative, in depth, easy to understand, and very helpful in making these recommendations. I voted "Yes" based on the depth of the data and the scientific evidence that was presented for this. I would encourage-- I guess I have to encourage a manufacturer to be the first to step forward in looking at two H3N2 strains, but I do hope that that additional research will be done to make the vaccine even better. Thank you.

Dr. El Sahly: Dr. Bernstein. Sorry, Dr. Portnoy. Dr. Portnoy, you've voted "Yes."

Dr. Portnoy: Yeah. Yeah. I turned my monitor on and then I turned it off because I wasn't sure-- But I voted "Yes." The data was very compelling. I'm always amazed at how much information is presented to us, both genetic, epidemiologic and surveillance. It's just impressive. I'm also impressed by how we can respond to changes in the variants of the influenza as they evolve over time and respond by developing new strains and having them available in the vaccines as well. So, I think that I want to

commend the CDC, the FDA, the World Health Organization. I think you do an amazing job and makes me comforted just to know that that surveillance program is still in place given all of the uncertainties in today's political climate. So, thank you very much.

Dr. El Sahly: Thank you. Dr. Bernstein, you also voted "Yes."

Dr. Bernstein: Thank you, Dr. El Sahly. I don't really have anything-- I echo all of my colleagues' comments. Clearly, I must admit Dr. Kondor's presentation was incredibly impressive. I learn something every year going through this. I think science is driving these decisions, which I think is really very important and I really don't have much more to add than what's already been said.

Adjournment

Dr. El Sahly: Okay. Well, thank you all for the discussions and the votes. To summarize the discussion, everyone was thankful for the CDC and WHO body of data as presented so eloquently by Dr. Kondor, and everyone concurred with the selection for these three strains for the Southern Hemisphere flu vaccine. Comments were raised pertaining to improving the flu vaccines by utilizing what we know so far on the neuraminidase role and protection, the potential use of additional H3N2, generating data on the-- Preclinical and clinical, on the utilization of this path to improve the flu vaccines among others. And, yeah, I think that was the summary. I hope I didn't miss any other major questions. And now we adjourn the Topic I. We do have a 30-minute break. Is that correct, Cicely?

LCDR Reese: That is correct. 30 minutes.

Dr. El Sahly: 30 minutes. So, now it is 11:00 am Eastern Time. Let's reconvene at 11:30.