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DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

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CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

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VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE

MEETING #144

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October 13, 2016
1:00 p.m.

FDA White Oak Campus
Building 31, Conference Room B&C
10903 New Hampshire Avenue
Silver Spring, MD 20993

KATHRYN EDWARDS, M.D.	Chair
HANA EL SAHLY, M.D.	Voting Member
BRUCE GELLIN, M.D., M.P.H.	Voting Member
HOLLY JANES, Ph.D.	Voting Member
KAREN KOTLOFF, M.D.	Voting Member
SARAH LONG, M.D.	Voting Member
RUTH LYNFIELD, M.D.	Voting Member
PAMELA McINNES, D.D.S., M.Sc.	Voting Member
ARNOLD MONTO, M.D.	Voting Member
PATRICK MOORE, M.D.	Voting Member
MARK SAWYER, M.D.	Voting Member
MELINDA WHARTON, M.D., M.P.H.	Voting Member
JACK BENNINK, Ph.D.	Temporary Voting Member
VICKY PEBSWORTH, Ph.D., RN	Consumer Representative
LEONARD FRIEDLAND, M.D.	Acting Industry Representative
SUJATA VIJH, Ph.D.	Designated Federal Officer

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MEETING

(1:08 p.m.)

DR. EDWARDS: All right. So I'd like to call this meeting to order. This is the strain selection for the 2017 Southern Hemisphere influenza season.

Sujata, would you like to read the Conflict of Interest Statement?

DR. VIJH: I think we should go down the introductions, Dr. Edwards? If you could handle the members on the phone, and I will ask the FDA staff seated in the room. Just for the record, we need to know who's on the phone.

DR. EDWARDS: Okay. Very happy to. This is Kathy Edwards. I'm from Nashville, Tennessee.

Hana, are you on the phone?

DR. EL SAHLY: Yes, I am on the phone.

DR. EDWARDS: Wonderful. And could you just give a sentence about what you do and where you're from, please?

DR. EL SAHLY: Yes. Hana El Sahly, Associate Professor, Molecular Virology and Microbiology, Baylor College of Medicine in Houston, Texas. Adult infectious diseases trained. I practice clinical infectious diseases, and the bulk of my time is spent in vaccine development research.

DR. EDWARDS: Thank you, Hana.

Lenny Friedland?

(No response.)

DR. EDWARDS: Bruce Gellin?

DR. GELLIN: Kathy, thanks, I'm on. Bruce Gellin. I'm the Director of the National Vaccine Program Office in the Office of the Assistant Secretary for Health at HHS.

DR. EDWARDS: Thank you.

Holly Janes?

DR. FRIEDLAND: Dr. Edwards?

DR. EDWARDS: Yes?

DR. FRIEDLAND: Hi, this is Leonard Friedland. I think I was on mute. Thank you for introducing me, the alternate Industry Representative. Thank you.

DR. EDWARDS: Wonderful. Thank you so much, Lenny.

Do you want to just say a sentence about you?

DR. FRIEDLAND: Yes. I'm a pediatrician and pediatric emergency medicine physician, and I've been involved with vaccine research now for over a decade.

DR. EDWARDS: Thank you.

Holly Janes?

DR. JANES: Yes. Thank you. I am an Associate Member at the Fred Hutchinson Cancer Research Center, and I am a biostatistician. I work in HIV vaccine evaluation as well as some other infectious diseases, and I also have a background in biomarker evaluation. Thank you.

DR. EDWARDS: Okay. Thank you. Karen Kotloff?

DR. KOTLOFF: Yes. I'm a Professor of Pediatrics at the University of Maryland in the Division of Pediatric Infectious Disease. I've been doing vaccine research for most of my career.

DR. EDWARDS: Thank you, Karen.

Sarah Long?

DR. VIJH: She won't be able to speak because she hasn't been able to log into the WebEx. Unfortunately, she can't participate in the discussion then.

DR. EDWARDS: Ruth Lynfield?

(No response.)

DR. EDWARDS: Pam McInnes?

DR. McINNES: Hi, this is Pamela McInnes. I'm at the National Center for Advancing Translational Sciences at the NIH.

DR. EDWARDS: Thank you, Pam.

Arnold Monto?

DR. MONTO: Hi, I'm Professor of Epidemiology at the University of Michigan School of Public Health, and currently we're involved in influenza vaccine effectiveness status.

DR. EDWARDS: Thank you, Arnold.

Patrick Moore?

DR. MOORE: Hi, I'm Pat Moore. I'm at the University of Pittsburgh in the Cancer Virology Program. I work on tumor virology.

DR. EDWARDS: Thank you, Patrick.

Mark Sawyer?

DR. VIJH: He won't be able to be heard because he has not been able to access WebEx at his end.

DR. EDWARDS: Okay. Moving to Wharton, Melinda?

DR. WHARTON: Hi, I'm an adult infectious disease physician, and I'm Director of the Immunization Services Division at the Centers for Disease Control and Prevention.

DR. EDWARDS: Thank you, Melinda.

Jack Bennink?

DR. BENNINK: I'm a viral immunologist at the National Institutes of Health in NIAID.

DR. EDWARDS: Thank you, Jack.

Vicky? Vicky Pebsworth?

DR. PEBSWORTH: Yes. I am the Director of Research and Patient Safety at the National Vaccine Information Center. I am serving as the Consumer Representative. Thank you.

DR. EDWARDS: Thank you.

Sujata, do you want to announce the people that are on the call participating from the FDA?

DR. VIJH: Sure. And I think we just missed Dr. Jackie Katz, but we know she's on the phone. We know that, yeah. It's the second page, yeah.

DR. EDWARDS: I was going to introduce her when she talks, so we --

DR. VIJH: Sure, yeah.

DR. EDWARDS: Thank you.

DR. VIJH: So in the room at the table, we have seated Dr. Jerry Weir and Dr. Marion Gruber.

Could you please just introduce yourselves?

DR. GRUBER: Yeah. Hi, my name is Marion Gruber. I'm the Director of the Office of Vaccines at CBER, FDA.

DR. WEIR: And I'm Jerry Weir, the Director of the Division of Viral Products at CBER.

DR. VIJH: Great.

Dr. Katz [sic], can I take over now just for the administrative remarks?

DR. EDWARDS: Great.

DR. VIJH: Sure. Thank you.

Hello, everyone. I'm Sujata Vijh, the Designated Federal Officer for today's

Vaccines and Related Biological Products Advisory Committee Meeting.

Ms. Rosanna Harvey is the Committee Management Specialist for VRBPAC. Ms. Denise Royster and Ms. Joanne Lipkind are assisting us today with the meeting.

On behalf of the FDA, the Center for Biologics Evaluation and Research and VRBPAC, we would like to welcome you all to the 144th meeting.

Today's session is one topic that is open to the public in its entirety. The meeting topic is described in the *Federal Register* notice of July 27th, 2016. Members, as you know, are participating via teleconference. The public is attending in person or watching via live webcast. We therefore just request your patience and support while we work through the challenges of this kind of format of an Advisory Committee meeting.

The FDA CBER press media contact is Ms. Lyndsay Meyer.

Lyndsay, are you in the audience today? Lyndsay, could you please stand up if you're in the audience so that the members of the press can reach out to you?

Mr. Tom Bowman is the transcriptionist seated at the table.

So I'd just like to make a general comment. Please press the microphones to talk, and switch them off when you've finished speaking for members in the room -- for the staff in the room. Of course, on the phone, by now you already realize that the red button has to be unmuted for you to be able to be heard in the room. Please speak clearly and loudly into the microphone so that the transcriptionist, members, public, and those listening via webcast can hear the discussion.

The Open Public Hearing, if there are any members of the public that would like to make a comment during the Open Public Hearing, please sign in, and your name and affiliation on the form outside, and as well, you would be coming in to this center of the aisle microphone to make your comments. So please do write your

name outside.

I will now read the Conflict of Interest Statement for the public record.

The Food and Drug Administration is convening today, October 13th, 2016, for a meeting of the Vaccines and Related Biological Products Advisory Committee under the authority of the Federal Advisory Committee Act of 1972. With the exception of the Industry Representative, all participants of the Committee are special government employees or regular federal employees from other agencies and are subject to the federal conflict of interest laws and regulations. The following information on the status of this Advisory Committee's compliance with federal ethics and conflict of interest laws, including but not limited to 18 U.S. Code Section 208, are being provided to participants at this meeting and to the public.

The FDA has determined that all members of this Advisory Committee are in compliance with federal ethics and conflict of interest laws. Under 18 U.S. Code Section 208, Congress has authorized FDA to grant waivers to special government employees and regular government employees who have financial conflicts when it is determined that the Agency's need for a particular individual's services outweighs his or her potential financial conflict of interest.

Related to the discussions at this meeting, members and consultants of this Committee have been screened for potential financial conflicts of interest of their own as well as those imputed to them, including those of their spouses or minor children and, for the purposes of 18 U.S. Code Section 208, their employers. These interests may include investments; consulting; expert witness testimony; contracts/grants/CRADAs; teaching/speaking/writing; patents and royalties; and primary employment.

For the topic today, the Committee will discuss and make recommendations

on the selection of strains to be included in an influenza virus vaccine for the 2017 Southern Hemisphere influenza season.

Based on the agenda and all financial interests reported by members and consultants, no conflict of interest waivers were issued under 18 U.S. Code Section 208.

Dr. Leonard Friedland will serve as the acting Industry Representative. Dr. Friedland is employed by GlaxoSmithKline. Industry representatives act on behalf of all related industry. Industry representatives are not special government employees and do not vote.

There may be regulated industry speakers and other outside organization speakers making presentations. These speakers may have financial interests associated with their employer or with other regulated firms. The FDA asks in the interest of fairness that they address any current or previous financial involvement with any firm whose product they may wish to comment upon. These individuals are not screened by the FDA for conflicts of interest.

This Conflict of Interest Statement will be available for review at the registration table.

We would also like to remind members, consultants, and participants that if the discussions involve any other products or firms not already on the agenda for which an FDA participant has a personal or imputed financial interest, the participants need to exclude themselves from such involvement, and the exclusion will be noted for the record. FDA encourages all participants to advise the Committee of any financial relationships that you may have with any firms, its products, and if known, its direct competitors.

This concludes my reading of the Conflict of Interest Statement.

I'd now like to hand over the meeting to Dr. Edwards.

DR. EDWARDS: Thank you so much.

DR. SAWYER: Kathy, this is Mark Sawyer. I just wanted to let you know I think I finally connected.

DR. VIJH: Wonderful, yeah.

DR. EDWARDS: Wonderful.

And just add a sentence or two -- Mark, we all know you, but just to remind everyone where you're from and what you do?

DR. SAWYER: I'm a pediatric infectious disease physician at University of California, San Diego.

DR. EDWARDS: Thank you so much, Mark.

So we're pleased today to be able to discuss the strain selection for the 2017 Southern Hemisphere influenza season. The first speaker will be Dr. Jerry Weir, Director of the Division of Viral Products, the Office of Vaccines Research and Review at CBER.

Jerry?

DR. VIJH: Dr. Edwards, I know that Dr. Ruth Lynfield has also joined in.

Dr. Ruth Lynfield?

DR. EDWARDS: Great. Ruth, would you like to just hum a few bars about what you do, please?

DR. VIJH: Let me just see. One minute.

Dr. Lynfield?

DR. EDWARDS: She's a pediatrician and the head of the Health Department in Minnesota. So, wonderful, Ruth, welcome.

DR. LYNFIELD: Thank you.

DR. VIJH: Go ahead.

DR. EDWARDS: All right. Dr. Weir? The slides are all on the invitation, so you can all follow along.

DR. WEIR: Thank you. I'm Jerry Weir. I'm going to give a quick introduction to today's VRBPAC topic. And what I'm going to try to do is basically explain why we're here and how this differs from some of our usual strain selection meetings.

So I hope everybody has the slides in front of them. They're on the screen in the room here. The second slide simply states the purpose of the meeting today is to make recommendations for the strains of influenza A (H1N1, H3N2) and the B viruses to be included in the 2017 Southern Hemisphere formulation of influenza vaccines licensed in the United States.

The next slide shows a little background of what I hope to explain why we're doing this and why it's different from our previous meetings. So as probably everyone on this Committee knows, the World Health Organization makes recommendations for the virus strains to be included in influenza vaccines twice a year. There's a recommendation for the Northern Hemisphere, which is made in February or March of each year, and there is also a second strain recommendation meeting that occurs that takes place in September. This is for the Southern Hemisphere. So even though the World Health Organization makes these recommendations, it's important to remember that it's actually national regulatory authorities that approve the composition and formulation of vaccines in each country.

So, for example, for us in the Northern Hemisphere in the U.S., after the World Health Organization recommendations were made in February or March of any year, we convene our VRBPAC to make recommendations for U.S.-licensed

vaccines. Our VRBPAC usually occurs within a week or so after the WHO recommendation and takes place in February or March, and this is the recommendation that we use for vaccines that will be made by U.S. manufacturers for the upcoming Northern Hemisphere influenza season. So this is what we do every year. Those of you on the Committee are familiar with this. We've been doing this. This is just our standard procedure.

After the recommendations are made during February/March from the Advisory Committee, it's the FDA and CBER that approve license supplements for each U.S. manufacturer to incorporate the updated strain recommendations, and those usually occur in June, or the actual approval of a supplement occurs in June or July.

But what's changed and the reason we're having this meeting is because recently, earlier in 2016, a U.S. manufacturer was approved to produce a Southern Hemisphere formulation of their influenza vaccine. We felt that we should follow the same procedure for this U.S.-licensed product for the Southern Hemisphere. And there was also the added consideration that we wanted to make sure that all of the package inserts for influenza vaccines were harmonized, were the same in that in those package inserts, there's a reference to the strains that are being used, being approved by U.S. Public Health Service. So that's the reason we're here is because of this particular license approval for a manufacturer to include a Southern Hemisphere formulation.

What we will do during the VRBPAC today is similar to what we typically do in the Northern Hemisphere recommendation in February or March. We'll look at the data. We'll see what's been done previously. And the Committee will be asked to approve or make a recommendation for this particular formulation.

The next slide shows the types of data and the types of analyses that would be presented. We're actually doing a somewhat abbreviated presentation because of the nature of what we're here to discuss, only the Southern Hemisphere recommendation. And so it will be a CDC presentation that presents the epidemiology of circulating strains. This will essentially be a summary of the most recent WHO Southern Hemisphere strain selection consultation, but you'll hear data from around the U.S. and around the world.

And you will hear analyses that include hemagglutination inhibition and virus neutralization tests using post-infection ferret sera, HI and virus neutralization tests using panels of sera from humans receiving recent inactivated influenza vaccines, some antigenic cartography, as well as phylogenetic analyses of HA and NA genes.

Again, this is very similar type of data that we see in the -- that we use in the Northern Hemisphere recommendations. It will be just somewhat of an abbreviated version of that.

The next three slides summarize the most recent recommendations from the WHO, starting with a year ago in September of 2015 when the recommendations were made for the Southern Hemisphere influenza vaccines for this past summer, the Southern Hemisphere winter.

This recommendation was made at the WHO on September 24th, and the recommendations for the trivalent vaccine to be used this past year in the Southern Hemisphere winter were an A/California/7/2009 (H1N1)pdm09-like virus, an A/Hong Kong/4801/2014 (H3N2)-like virus, and a B/Brisbane/60/2008-like virus of the B/Victoria lineage. The WHO further recommended that any quadrivalent vaccines contain those three strains plus a B/Phuket/3073/2013-like virus from the B/Yamagata lineage.

So this is what happened about a year ago. The most recent Northern Hemisphere recommendation was made by the WHO -- this is the next slide -- was made by the WHO in February, February 25th, 2016. And during that meeting at the WHO, there was a recommendation for the following viruses to be used in the trivalent formulation: an A/California/7/2009 (H1N1)pdm-like virus, which was no change from previous recommendations; an A/Hong Kong/4801/2014 (H3N2)-like virus -- this was a change from the previous Northern Hemisphere recommendation, but you'll note it was the same as what had been recommended in the Southern Hemisphere recommendation the previous September; and then the B components were sort of swapped last year in that the B/Brisbane/60/2008 was recommended in trivalents, which this strain was previously recommended for quadrivalents. And the WHO recommended that quadrivalent vaccines contain the above three plus a B/Phuket/3073/2013-like virus.

These were the recommendations from the WHO. Our VRBPAC met on March 4th and made the same recommendations for the U.S.-licensed vaccines.

Now, most recently, in late September, September 29th, 2016 -- this is on the next slide -- the WHO met to make the recommendations for the upcoming Southern Hemisphere influenza vaccines in 2017. And you can see on this slide what was decided just a couple of weeks ago. And that was the WHO recommended one change from the previous recommendation, and that was that the H1N1 now be an A/Michigan/45/2015 (H1N1)pdm09-like virus. The A/Hong Kong/4801 and the B/Brisbane were similar to what was previously recommended both for the Northern Hemisphere and a year ago for the Southern Hemisphere. And quadrivalents were recommended to contain those three viruses plus a B/Phuket/3073-like virus from the Yamagata lineage.

So this is a quick summary of what's been happening over the last few WHO and VRBPAC meetings. You'll see on the next slide a simple statement of what the Committee is here to discuss today, and that's which influenza strain should be recommended for the antigenic composition of the 2017 Southern Hemisphere formulation of influenza virus vaccine produced by licensed U.S. manufacturers?

The last slide shows the voting questions, and we've tried to simplify this from our usual Northern Hemisphere strain selection and only have two questions, one for a recommendation for the three viruses that should be in the trivalent and then a second question about which second B strain should be included in a quadrivalent vaccine.

So that's all I was going to say, and I think Jackie Katz will do the real data presentation.

DR. EDWARDS: Thank you, Jerry.

Are there any questions for Jerry?

(No response.)

DR. EDWARDS: If not, we also want to acknowledge that Dr. Long has signed on.

Sarah, can you just give us a sentence or two about yourself?

DR. LONG: I'm in Philadelphia, and I'm able to hear you all, but I'm not able to see any slides, but I'm keeping up anyhow because I have them elsewhere.

I'm an infectious disease doctor at St. Christopher's Hospital in Philadelphia and long history and interest in vaccine and vaccine policy.

DR. EDWARDS: Thank you, Sarah.

The next speaker will be Jackie Katz. She really needs no introduction, but I will introduce her. She's a Deputy Director of the Influenza Division. She's also the

Director of the WHO Collaborating Center for Surveillance, Epidemiology, and Control of Influenza at the National Center for Immunization and Respiratory Diseases at the CDC.

Jackie?

DR. KATZ: Thank you, Kathy. Can everybody hear me?

DR. EDWARDS: Yes, very well.

DR. VIJH: Dr. Katz, just one second. I heard that maybe members cannot see any slides on the WebEx. Is that true?

DR. KATZ: Yeah, I can't see anything either.

UNIDENTIFIED SPEAKER: Yes.

DR. VIJH: Yeah, because you -- then you won't be able to advance -- I mean, you won't be able to view on the monitor. Give us a few seconds. If you could just give me one second?

DR. KATZ: Sure.

(Pause.)

DR. VIJH: Because you have a 60-minute presentation, so we just want to make sure that you can -- you're comfortable and all the members can also see.

DR. KATZ: Okay. I put the slides in front of me. Oh, here they are. Great.

DR. VIJH: Yeah, excellent.

DR. KATZ: Okay. Can everybody see that now?

UNIDENTIFIED SPEAKER: Yes.

DR. KATZ: Fabulous. Okay. I believe I'm going to have to get somebody in the room to advance the slides; is that right, Sujata?

DR. VIJH: Yes. As you say next slide, then Joanne Lipkind is going to be advancing the slides.

DR. KATZ: Okay. And can people see my pointer that is moving around right now?

(No response.)

DR. KATZ: I guess maybe not, okay.

So the first thing I want to point out is that the slide numbers are at the bottom left-hand side, so if we lose track, I'll be periodically referring to the slide number.

But I'll start on slide number 2. And so as Jerry said, the data I'll be presenting today is based on year-round surveillance of the Global Influenza Surveillance and Response Network, also known as GISRS, comprised of six WHO-collaborating centers, 143 national influenza centers, a number of essential regulatory laboratories, and H5 reference labs. And so the data I'm presenting is the data that was reviewed and summarized and used as the basis for our recommendations that were made a couple of weeks ago in Geneva.

As you can see there from the slide, we have the nine advisors from the collaborating centers and ERLs. They're the voting members and the ones that make the actual recommendations, as well as 22 other observers that provided scientific input.

Next slide, please?

So slide number 3 shows the overall global availability of viruses to the Global Influenza Surveillance and Response System. You can see in green all of the countries that shared viruses during this period from February to September. And this is the period of virus circulation I'll be focusing on. So you can see we've got a very good representation globally.

Next slide, please?

So this is the surveillance information from the WHO FluNet. This shows what happened at the tail-end of the Northern Hemisphere season. So as you will recall when I talked to you in February, we were actually experiencing in the U.S. quite a low season, but the season peaked quite late, in mid-March, and that was true for many parts of the world. This is the numbers of specimens that were positive for influenza by subtype in the Northern Hemisphere, and you can see the peak there is several months into the beginning of 2016. And the viruses in pale blue, pdm09 viruses clearly were dominating early in the season, and then later in the season, influenza B viruses also took an upswing and predominated late in the season.

Next slide, please?

For the Southern Hemisphere, you can see also that the (H1N1)pdm09 viruses predominated in most regions of the Southern Hemisphere, but there was also a later H3. And you can see that towards the later weeks, for weeks 30 through 36 or so there. You can see that dark blue reflecting the H3N2 viruses. And this is the Southern Hemisphere in some regions of the world, particularly in Australia and New Zealand. They're having quite a late season and quite a lot of H3N2 activity.

So next slide, please?

So this breaks down the type, subtype, and lineage of virus that was detected through FluNet. And you can see, it was roughly 50/50 overall with influenza A versus influenza B. And among the influenza A viruses, (H1N1)pdm09 viruses predominated, whereas with the influenza B virus, although there's still a lot of non-lineage-determined viruses, the B/Victoria lineage predominated overall.

Next slide, please?

And then next slide, please?

So I'm focusing now -- the next several slides will be the characterization of

(H1N1)pdm09 viruses. And you can see from this slide that there was quite a bit of regional to widespread outbreak activity in the Americas, Europe, and Asia, and some activity also in the Southern Hemisphere.

Next slide, please?

So the next slide, which is the number of H1N1 viruses actually detected by the WHO GISRS system, shown in red is the numbers for the current 2016, and you can see that that peak is quite larger above compared with previous years, particularly the 2013 season, shown in green, which was another H1N1 season. So quite a lot -- and 2014 -- so quite a lot of H1N1 activity in this past year.

Next slide, please?

So this describes some of the genetic groups that I will be speaking about. This data is a summary of all of the sequence information for the hemagglutinin genes that are present in our GISAID sequence database, and this is data from viruses collected since February to the present time.

So as you may recall from the February meeting, in recent years, 6B viruses have predominated, and they are shown in blue. But in around August or September of last year, there was an upswing of a new genetic subgroup referred to as 6B.1, and this is shown in orange. There was also another genetic subgroup identified, 6B.2, shown in green. And you can see what's happened in the last 6 months is that the 6B.1 viruses have really predominated and taken over from 6B viruses. There are still a few pockets left in Africa and South America, but even the more contemporary viruses from South America are really 6B.1 viruses. There's still some 6B.2 detected in most parts of the world, and it's seen most frequently in China.

Next slide, please?

So this is a compressed phylogenetic tree. It actually represents all of the

sequences, and clearly, you can't see them because there's so many. But this is data that is provided by the University of Cambridge collaborators. And the ladder to the far right of the slide shows the viruses circulating in the last 18 months. Each little bar, colored bar, is a virus. And the viruses are color-coded by the regions of the world, which you can see either in text there in the legend or also shown as the little map at the bottom of the slide.

And so if you just focus on, say, the last 6 months, which is February to August, you can see that huge preponderance of 6B.1 viruses. And at the very bottom of that ladder, you can see a very intense dark blue set of sequences, and they represent the large H1N1 season we had in North America, and particularly in the U.S. At the top, you can see the viruses that are still circulating, but not as frequently, in the 6B.2 genetic group.

Next slide, please?

So this is actually a much, much smaller phylogenetic tree. It's greatly simplified, and only a few representative viruses are shown. But again, if you look at the pie chart on the bottom left of the slide, you can see the very large segment that is orange, or the 6B.1 viruses, which are accounting for about 98% of the viruses since February. You can see these viruses in the top half of the phylogenetic tree. These viruses have signature changes in the hemagglutinin at residues 84, 216, and notably at 162. And this change confers an additional glycosylation site.

So just to give you some reference, the California/07 vaccine virus is at the very bottom of the tree in red. And the new vaccine candidate that the WHO recommended is at the base of the 6B.1. It's Michigan/45/2015-like virus, also shown in red.

So within 6B.1, there's not a lot of genetic diversity at the moment, but -- and

then there's also in the bottom half, you can see the 6B.2 viruses, and although these are being sporadically detected in different parts of the world, they're not nearly as frequent in number, and they have signature changes in the HA1 at 152 and 173, and they also have a couple changes in HA2.

Next slide, please?

So this is just to show you some of the accumulation of amino acid substitutions that have occurred in the evolution of H1N1 viruses. Shown on the left is the three-dimensional structure of the California/7/2009 vaccine virus, and you can see the different antigenic sites for H1, which are shown in either light blue, dark blue, or green.

On the right-hand side is the Michigan/45/2015 (6B.1) reference virus. And so you can see that prior to the emergence of 6C.1, the 6B viruses had acquired changes at 185, which is in antigenic site Sb, and also a change at 203, which is in antigenic site Ca, and also the 163Q change. In addition, the 6B.1 viruses, as I noted in the previous slide, have acquired this 162 change, which is right next to 163 in antigenic site Sa.

So next slide, please?

So this is a phylogenetic tree of the neuraminidase genes, and you can see that the viruses fall into -- are categorized into the same 6B.1 and 6B.2 genetic groups. And there's really not a lot of diversity within the 6B.1 viruses. In Michigan/45, it's sort of right there towards the lower part of the 6B.1 viruses.

Next slide, please?

So this is the first antigenic table I'll be showing you. And just to remind you, so what we do here is we take a panel of reference viruses, and these are the reference antigens on the top left-hand side of the table. There are ten of them. We

raise ferret antisera by infecting the ferret, and then we collect this post-infection antisera. And so the top half of the panel is our reference for our standard. And each of the titers in red reflect the homologous titer -- the virus with its particular ferret antisera.

Then, the test antigen, the antigens in 11 through 30, are the circulating viruses separated by the regions from which they've been obtained. So we have in this slide viruses from the U.S., South America, Europe, and regions of Africa and Asia. And if you look at the highlighted titers in yellow, these are the titers against the California/07 reference viruses, so the vaccine virus either propagated in eggs or in MDCK cells.

And so we look at these titers, and we compare the titers of circulating viruses to these homologous titers in red. And if you do so, you'll see that all of these titers of the circulating viruses are mostly within twofold, and in one case within fourfold, of the homologous titers to California/7 itself. And so this indicates that we're not seeing antigenic change with the ferret reference antisera. And this is also true if we raise ferret antisera to more contemporary 6B.1 and 6B.2 viruses, which are the titers that you'll see in the rest of the tree. We don't see any difference between 6B.1 and 6B.2 viruses themselves using ferret reference antisera.

So if you'll go to the next slide?

So this is again antigenic cartography data from the University of Cambridge. And this really just visualizes all of the HI data that the different collaborating centers have produced. And in yellow, you can see the viruses since 2016, and beneath these are the viruses in blue from previous years. And again, this is data based on the HI using ferret reference antisera, and you can see that, very clearly, all these viruses cluster tightly around the California/7/2009 reference vaccine virus.

Next slide, please?

Uh-oh. If you'll just bear with me a minute, my screen has just died.

Okay. So several months ago, we got our final data from the CDC U.S. VE network. And some of you will be familiar with this network that provides annual estimates of vaccine effectiveness. And the final data that was obtained was broken down by age group, because overall, the VE for H1pdm09 virus for 2015 and '16 were a little lower than we had seen previously.

And it was determined that this low, overall lower response was being driven by a particularly low VE in a certain age group that represented adults that were in the sort of 30 to late 50 age group. And this was an age group that Scott Hensley and colleagues, previously of the Wistar Institute, had been studying serologically and had found that some individuals in this age group, although they were making responses to the California/7 vaccine virus, were not responding well to the more contemporary viruses of the H1pdm09 group.

And so because of this VE and because of the work Scott had done, we went back and looked at human sera to see whether we could see any antigenic differences. And we chose to use the sera that was available to us, which is sets of -- panels of sera from adults that had been vaccinated in the prior five seasons, where California/7/2009 had been the (H1N1)pdm09 vaccine virus.

So what we did with this sera, which is both pre and post, and the pre is shown in blue, the post is shown in orange, and you can see that we have responses here to not only (H1N1)pdm09 viruses but also ten former seasonal H1 viruses. And in looking at this response to the earlier seasonal viruses, we could discriminate adults born over the period from the early '60s to about 1985 that had experienced the USSR/77-like virus when it reemerged in the late '70s.

And you can see there's a group of individuals that make the response to earlier seasonal viruses. And the top left panel, there's -- this individual represents a profile that we saw in a number of individuals, where they made response to the California/7 vaccine upon immunization, didn't make any response to subsequent 6B and 6B.1 viruses that we tested. However, others in this same birth cohort did, and this is shown in the lower left panel, where individuals got vaccinated, they made a boosting response to old seasonal viruses but also to all of the viruses we tested against, including 6B.1.

And then in this age group of adults, we also found that there was a group that likely had been primed with Taiwan/86-like virus. And these individuals all showed good reactivity to the California/7 vaccine virus and then to subsequent H1pdm09 viruses.

So this suggested to us that there were indeed some individuals -- although in our limited panels we only saw this in a minority of individuals. Nevertheless, we took these sera from both individuals that had been USSR/77 primed, both the ones that could respond to other H1N1 viruses and those that did not, and we made pools of those viruses and tested them further.

So if you'll look in the next slide?

So this, again, is now a typical HI assay using a panel of our ferret reference antisera against different -- against the California/7 viruses as well as against different 6B and 6B.1 and 2 viruses. And you can see that if you look at the far -- so, first of all, if you look at the body where we have post-infection ferret antisera, you can see that, as I showed you on the previous HI table, none of these ferret sera discriminate any of these viruses, whereas if we take the pools of the human sera, and these are shown in A through F, panels A through E -- or pools A through E, in

general, show a greater than or equal to eightfold reduction in titers to contemporary 6B.1 and 6B.2 viruses, shown in the pale green and the dark green. There's also reduced responses to the 6B virus. And the pool on the far left, pool F, represents the pool from the individuals that did not discriminate the more contemporary 6B, 6B.1, and 6B.2 viruses. And you can see that generally in their titers.

So next slide, please?

So the previous table I showed you was a fairly nontraditional approach to looking for antigenic difference with the H1N1 viruses. As Jerry said in his introduction, we also generally look at panels of pediatric, adult, and older adult populations that have been vaccinated with the current used vaccine and look at their ability to respond to different contemporary viruses.

And so this is an example of this with the pediatric population. So these are very young children, less than 3 years of age, that are receiving their first influenza vaccine, and they received the Northern Hemisphere 2015 and '16 QIV, which contains California/7. We're comparing in this figure with a reference virus propagated in MDCK cells. And we do this because most of our circulating viruses that we are testing with are all grown in MDCK cells. And this avoids the differences we might see if we compare with egg-propagated viruses, which as you can see in this slide typically give much higher titers.

So if we use the California/7 MDCK as our comparator and it is set at -- the geometric main titer is set at 100%, you can see that the two 6B.1 viruses, Michigan/45 and Panama/318595, as well as a 6B.2 virus, Iowa/53, are really showing borderline significant reductions. And we have used a 50% reduction as the significant threshold for significant reduction compared with the response to the vaccine virus. And so you can see the 6B.1 viruses are right below that, and the 6B.2

is just on the borderline.

Next slide, please?

And so this is similar data from the Australian collaborating center to use the same pediatric sera and test it against another two 6B.1 viruses that were circulating in the Southern Hemisphere, one from Singapore and one from Victoria, Australia. And you can see a similar profile, that they're seeing substantially reduced responses to the 6B.1 viruses in this pediatric population.

Next slide, please?

So, in summary, our view of the data for (H1N1)pdm09 viruses determines that the 6B.1 viruses were predominating globally, although the 6B.2 viruses were still being seen, and this was most frequently detected in China. But still, 6B.1 results are predominating in that region.

Because we had seen vaccine effectiveness, a reduction in vaccine effectiveness in a subset of adults in the 2015-16 season, we thought we needed to explore this further because using our ferret antisera and the traditional HI test, we were not able to antigenically distinguish between recent circulating viruses and the vaccine virus.

However, when we used pools of adult human serum, we were able to discriminate that the 6B.1 and 6B.2 viruses were poorly inhibited by these pools which were obtained from some individuals. And when we looked at the pediatric population, we also so that their responses, although they had robust responses to California/7/2009 vaccine virus, they had reduced titers to some 6B.1 and 6B.2 viruses. We didn't see this consistently for older adults and adults, and that's, I believe, because the response is a lot more heterogeneous with increasing age.

So I'm going to move on to H3N2 viruses. Next slide, please?

And so you can see in this map of the world, you can see that there were

sporadic to regional outbreaks of H3N2 viruses in February in many parts of the world. And I'll just highlight the dark red in Australia, which is indicative of their widespread H3N2 activity in recent months.

Next slide, please?

So the 2016 H3N2 virus numbers detected by GISRS is shown in red. So you can see, compared to other seasons, this has been quite a modest H3N2 season.

Next slide, please?

And as always, H3N2 viruses are providing an interesting and varying profile in terms of their characterization. So this, again, is pie charts representing the distribution of the different genetic groups of the hemagglutinin of the H3 since February. You'll remember that the 3C.2a viruses were predominating in most regions of the world back when I spoke with you in February. And this is still true. You can see in Africa, Asia, Europe, Oceania, and Central and South America, this is true.

There's some pockets of the 3C.3a viruses, shown in purple, but what was quite unexpected was that, in North America -- and this is really being driven by the sequence data from the U.S. -- that we actually had, since February, more 3C.3a viruses than 3C.2a viruses circulating in the U.S. But over the whole season, 3C.2a did still predominate in our Northern Hemisphere season. And at the present time, we're seeing small outbreaks of H3N2, which are both 3C.2a or 3C.3a. In the sort of lead-up to our season, we've seen some summer small outbreaks where -- so both viruses are still clearly circulating.

Next slide, please?

So, again, this is another mega phylogenetic tree. If you'll just look at the shading in blue, that's the data since February. And you can see that, at the top, the

3C.3a viruses, and these are shown mostly in dark blue because that's where they're predominating, there has been a small number of 3C.3a viruses in New Zealand in recent months and a handful seen in Australia and other parts of the world. But the predominance in Australia and other Southern Hemisphere regions is 3C.2a.

If you'll look at the lower part of the tree, you can also see there's another area boxed in, in green. And this represents a group of 3C.2a viruses that have acquired additional mutations. And this group is particularly noteworthy because it's expanding in size. And since February, about 42% of all 3C.2a viruses have been in this genetic subgroup. And so it was decided at the recent meeting that we would give this a new name. And so we're referring to these now as 3C.2a1.

Next slide, please?

Okay. I don't see the slide advancing. Oh, there it is. Thank you.

So this, again, is a smaller tree, and highlighted at the top, you can see this genetic subgroup, the 3C.2a1. So these are viruses that have acquired in their HA changes at 171, 406, and 484. And some viruses also have a change at 121K. And then you'll see other viruses in the lower part of the tree. And at the bottom of the 3C.2a -- and I'm afraid they're not color-coded in red -- but you'll see the Hong Kong/4801 virus is going to be the current vaccine viruses.

I should point out that the color-coding for the strain name is based on the month of isolation. So the viruses in orange and pink are the most recent viruses from June and July. And so you can see that there are 3C.2a viruses being isolated from the U.S. and other parts of the world, as well as if you look at the bottom part of the tree, the 3C.3a viruses.

And there's one group here I want to point out in particular, and this is a group that we found in New York and Missouri, some summer outbreaks or late-

summer outbreaks of 3C.3a viruses. And these particular viruses belong to a genetic group that have changes, a number of changes, including at residue 144, which confers the glycosylation site, and 193. And these are at the head of the molecule. And I'll come back to these viruses in my next slides.

If you look at the pie chart overall, you can see that the -- so this is for all genetic group sequences isolated globally since February. And you can see about three-quarters of still 3C.2a viruses and a little more than one-quarter of the 3C.3a viruses. And this is driven heavily from the sequencing that we do at the U.S. CDC, where we're sequencing all viruses that come to us. So this may actually be a slight overrepresentation of 3C.3a because we sequence everything.

Next slide, please?

So this is the phylogenetic tree of the neuraminidase genes. Again, you'll see the same genetic subgroups, the 3C.3a and 3C.2a viruses. And at the base of the tree are the viruses that represent -- in this tree, we have Michigan/15, which is our Hong Kong/4801-like reference virus. So not too much more to note there.

Next slide, please?

So before I talk about the antigenic properties of the H3N2 viruses, I just want to remind you that these viruses remain extremely challenging, particularly the 3C.2a viruses, because although they grow in tissue culture, they don't hemagglutinate with blood cells, and particularly in HI tests, where we have another problem, which is in the propagation step of growing these viruses, some of the viruses acquire changes in the neuraminidase which allow them to bind more actively to red blood cells. And so they can interfere with the HI assay.

And to avoid this interference, we add the anti-neuraminidase inhibitor, oseltamivir. And when we do that, there are many viruses that we just can't titer

anymore, and we just don't -- are unable to do antigenic characterization using the HI. And therefore, we're using other assays like virus neutralization assays. These are also referred to as the focus reduction assay or a plaque reduction assay. They're essentially very similar assays that detect the ability of the antibodies to inhibit neutralization. And these are particularly being used for the 3C.2a to confirm or characterize these viruses. Fortunately, the 3C.3a viruses have better properties and can be more readily characterized by the HI assay.

Next slide, please?

So this is another HI table from CDC. And again, it's set up in the same way as for the H1N1, so I won't go through that again. We've got our reference viruses at the top and our reference ferret antisera across the top, and the test antigens from 14 to 32 representing a lot of viruses from the U.S. and Asia and South America, I believe. And highlighted in yellow you can see these are two viruses that our -- our Hong Kong/4801-like reference viruses.

So in looking for antigenic similarity or difference, we're comparing the homologous titer, in this case, particularly, the Michigan/15 antisera, which has a homologous titer 320. And when looking at the titers that the ferret antisera has with the different circulating viruses -- and you can see that the majority of viruses, the genetic groups are shown on the far right of the table -- most of them are 3C.2a viruses. And these are well inhibited by the reference ferret antisera to the Hong Kong/4801-like viruses.

However, boxed in red, there's a set of 3C.3a viruses, and these are viruses from Missouri and New York that I highlighted in the phylogenetic tree that have a number of mutations, and they are conferring reduced activity with ferret antisera raised to the Hong Kong/4801-like viruses, although they are still well -- they're

reacting well with antisera to other 3C.3a viruses. And while this isn't true for all 3C.3a viruses, we do see a higher frequency of 3C.3a viruses that are low reactors in our HI test compared to the 3C.2a viruses for antisera raised to Hong Kong/4801-like viruses.

Next slide, please?

So thank you. The next slide, slide 32, shows again -- visually shows the HI data for all of the collaborating centers, with the green dots representing the 3C.3a viruses, the red dots representing the 3C.2a viruses, and the blue dots representing the older 3C.3 genetic group from which these subgroups derived.

And so you can see this is a very similar pattern to what we saw back in February, just with more dots, that 3C.3a and 2a viruses are overlapping, but they can be distinguishable in some cases. And in our hands this season at CDC, because we've had both 3C.3a and 2a viruses, we see proportionally that most groups are still well inhibited by the Hong Kong/4801 virus, but a greater proportion of 3C.3a viruses are low reactors. But overall, we're still seeing -- maybe I'll just go to the next slide.

Next slide, please?

Okay. So this is a summary of, first of all, HI data from the four different collaborating centers that are doing HI. And we're looking at, again, low ability of the viruses to react with antisera raised to cell-propagated Hong Kong/4801 because that gives us the true measure of whether there's antigenic drift in the circulating viruses. And you can see, by and large, that all of the centers have findings that a very high proportion, over 90%, are antigenically like Hong Kong/4801 viruses.

However, when we look with antisera raised to egg-propagated Hong Kong/4801, we see a reduced number of viruses that are well-covered by these

antisera. And this is to do with the properties of the viruses grown in eggs. And you can see that for two of the centers, the CNIC and the CRICK, the majority of viruses are antigenically like Hong Kong/4801. For the other two centers, the proportion is somewhat reduced.

And so some of this is also dependent on the particular antisera that is used or has been developed at each of the centers. And that's why it's important to look at this big picture overall. So we still see overall a majority of the viruses are well inhibited by the antisera to egg-propagated Hong Kong, although it's substantially less than what we see with the cell-propagated viruses.

Next slide, please?

So this is an example of the neutralization focus reduction assay. This was a test done at the Australian collaborating center. It's set up the same way that the HI is. And shown boxed in red are the ferret antisera raised to the reference Hong Kong/4801 viruses, the 3C.2a viruses. And shown in yellow is the reference cell-propagated Hong Kong/4801. And you can see that, again, there's some 3C.2a and a few, just a few 3C.3a viruses here, and the majority of these viruses are well inhibited with the antisera raised to Hong Kong/4801 grown in cells.

And I want to draw your attention to the viruses that I've highlighted in pink, the 3C.2a viruses in the second column there. All of these viruses belong to that new genetic subgroup 3C.2a1 and have this additional set of mutations. So when we look at these viruses, we don't see that they are antigenically distinguishable from the other 3C.2a viruses.

Okay. Next slide, please?

So this is, again, a summary now of -- this is data from CDC and data achieved from the neutralization assay. And it's comparing the reactivity of the viruses that we

tested with antisera raised either to the 3C.2a reference virus, the Hong Kong/4801-like viruses, or the 3C.3a viruses, the Switzerland/2013 virus.

And we're using sera from viruses that are grown either in cells or in eggs. And you can see the top panel that in this test, in this series of tests, we found that 86% of the viruses tested were well inhibited by Hong Kong/4801-like antisera. And they were also well inhibited, 95%, by the Switzerland antisera if the viruses were grown in cells.

If we look at the antisera from viruses propagated in eggs, we can see that quite a large proportion of viruses are not well inhibited by antisera raised to the egg-propagated Switzerland, about 92%, whereas a lower proportion of viruses are low-reactive to the antisera from Hong Kong/4801. And I'll come back to this in my conclusion.

Next slide?

So this is also another demonstration of a neutralization assay. And here we're now looking at panels of pre- and post-inspection sera either from adults or older adults. And these were sera from individuals that, in Australia, had received the 2016 Southern Hemisphere vaccine. And so this vaccine contains the Hong Kong/4801 vaccine components. And we're comparing the responses to quite a number of circulating viruses shown along the *x*-axis.

The arrow indicates the homologous response to the Hong Kong/4801 virus grown in cells. And you can see that our 50% threshold there is shown in a red dotted line. And you can see that the reactivity to all of the viruses, both 3C.2a and 3C.3a viruses, are all well above that threshold, suggesting that we're not seeing any decrease in the reactivity of vaccinated individuals in this panel -- in these panels with the currently circulating viruses.

Next slide, please?

So to conclude for the H3N2 viruses, we've seen the activity, while there was some moderate activity in Europe, Asia, and the Americas, there's been more recent activity in Oceania, including in Australia and New Zealand. The viruses collected since February are predominantly 3C.2a viruses in most regions of the world. But we did see 3C.3a predominate in the U.S. and, so far, in New Zealand from samples that we -- that the Australian collaborating center had characterized.

Ferret antisera raised against our cell-propagated 3C.3a reference viruses inhibited a majority of the viruses either by the HI or by the neutralization test. And this included a new subgroup of genetic subgroup, the 3C.2a1 viruses. We did see somewhat reduced inhibition against some 3C.3a viruses, but again, these were in a minority of cases.

Ferret antisera raised against the egg-propagated 2a viruses generally neutralized the circulating viruses better than antisera raised to egg-propagated Switzerland, the 3C.3a reference virus. And this was the pattern that we saw back in February, so this still holds.

If we look at an example of our human serology data, we find that using the microneutralization assay, that we did not see significant reductions in HI titers to contemporary cell-propagated -- or to contemporary viruses relative to the cell-propagated Hong Kong/4801 vaccine virus.

Next slide, please?

If you bear with me again, I've just lost my screen.

Okay. Thank you. So we're on to influenza B viruses. And as you saw from my earlier slides, there was actually quite a bit of B activity globally this year. And this is shown in the distribution of widespread outbreaks in parts of North America and

Europe and Asia and regional activity in South America and Oceania.

Next slide, please?

So, overall, this is just showing you the distribution of the two influenza B lineages, B/Victoria and B/Yamagata, over the last several seasons. You can see in green the B/Victoria lineage and in blue the B/Yamagata lineage. So, overall, you can see that the B/Victoria lineage predominated in the 2016 season.

Next slide, please?

And this is, again, the pie chart. So you can see this broken down a little better now by region. So the Victoria genetic subgroups are the V1As, and this is by far the most predominant group. I think for all of the collaborating centers, they found only one V1B virus, so we don't really need to consider those. So you can see the Victoria lineage V1A viruses in orange are really predominating Europe, Asia, Africa, and also in Central/South America,

Again, in North America, we saw about a 50/50 split with the B/Yamagata lineage, and the Y3 B/Yamagata lineage is what's predominating globally right now amongst the Yamagata, and so this is the lineage that was saw in North America. It's also pretty much 50/50 in Oceania with available data, but you'll see that the numbers are very small there.

Next slide, please?

So, again, this just shows you relative to past seasons that we've had quite a large number of influenza B viruses detected by the WHO system this year.

Next slide?

So I'll speak first about the B/Victoria.

Next slide, please? Sorry. And the next one? Thank you.

So this is a phylogenetic tree of the B/Victoria HA gene. Shown in yellow, a

virus has actually been circulating since February. They were essentially all V1As, so really nothing too remarkable here other than the global distribution.

Next slide, please?

And this is a simplified genetic tree. Again, you'll see right at the bottom of the tree is the B/Brisbane/60/2008. That's the vaccine virus. Amongst the V1A viruses that have acquired the changes at 129, 146, and 117, that's their signature changes. But after that, there's just pretty little diversity in the V1A genes right now. And you can see that their global distribution amongst the B/Victorian lineages is almost -- it's virtually 100%.

Next slide, please?

And similarly, in the neuraminidase genes, there's not a lot of genetic diversity in the V1A lineage. At the bottom of the tree, I'll point out -- and you'll see this with the B/Yamagata viruses later on -- there's a group of B/Yamagata viruses that are reassortant and have actually acquired the Victorian neuraminidase, and they are represented at the bottom half of the tree. And still we've seen this for a number of years, low-level isolation, but they still seem to be out there and pretty much circulating globally but at a very low level.

Next slide, please?

So, again, a hemagglutination inhibition test. And you can see the two columns of titers to the left of the table highlighted in yellow. These are looking at the responses to antisera raised to the Brisbane/60 reference viruses. And we can see that all of the viruses in this table are really well inhibited by antisera raised to the cell-propagated Brisbane/60 reference virus. We do see a larger number of -- and it looks there's it's actually even an eightfold reduction with one virus there against antisera raised to egg-propagated Brisbane. But in general, they're still well

inhibited; circulating viruses are well inhibited by antisera raised to either egg- or cell-propagated B/Brisbane.

Next slide, please?

So this is again an antigenic cartography, far more modest numbers of viruses tested. But you can again see that the 2016 viruses, shown in yellow, are really clustered around the B/Brisbane/60/2008, which is the cell-propagated reference virus.

Next slide, please?

So this is a summary of the data from the collaborating centers, and not all centers had antisera raised to both egg- and cell-propagated. But you can see that the overall -- if we look at antisera raised to cell-propagated Brisbane, that 99% of the viruses are antigenically like the Brisbane/60. And it's a slightly lower proportion of viruses when reacted with the antisera raised to egg-propagated Brisbane. If they're down to 86%, this is mostly driven by one collaborating center that has ferret antisera to their egg-propagated B/Brisbane that does not react well. But they're the only group that saw that.

Next slide?

And so this is again using human serology. This is a panel of adults and older adults that received either the 2015-16 Northern Hemisphere vaccine or the 2016 Southern Hemisphere quadrivalents. So these are quadrivalent vaccines. They had B/Brisbane as the primary component.

And you can see, similar to other figures I've shown like this, that when we compare to the B/Brisbane cell-propagated, which is shown by the arrow, we can see that viruses overall, B/Victoria viruses, didn't show significant reductions, although there were a few viruses and particularly reference viruses, the B/Florida viruses,

that did show differences. We don't really know why this is, but the B/Florida egg, we know that it's got a unique substitution, which would make it look different from other egg-propagated viruses. But there's no clear substitution in the B/Florida cell-propagated that we can speak to that would confer this reduction. But overall, for all the viruses tested, we didn't see this as the general pattern.

Next slide, please? And next slide?

So moving on to the B/Yamagata, again, this is a very homogeneous group of viruses at the present time. Shown in yellow are the viruses circulating over the last 6 to 8 months. They're predominantly all Y3. If you squint and look really hard, you can see that there's a very small number of Y2 lineage viruses that are still out there, but essentially, the genetic subgroup Y3 is predominating worldwide.

Next slide, please?

And this is just another phylogenetic tree, with just representative viruses. You can see here that the pie chart on the left, the dark blue represents the Y3. The section in the paler blue actually represents the reassortant viruses that had the Victoria lineage in neuraminidase. And these are shown towards the bottom of the tree in the Y3 group. And just below that group, you can see shown in red the Phuket/3073/2013. And this is the B/Yamagata component of quadrivalent vaccines at the present time.

So, genetically, again, these viruses are not changing much at the present time. There's subgroup of viruses. If you look at the top of the tree, there's a group that has a change at 212, and we see that elsewhere in the tree.

Next slide, please?

And again, the neuraminidase showing the Phuket vaccine virus. And although there's small clusters of viruses that had substitutions, none of these are really

expanding or, as you'll see in a moment, have antigenic significance.

Next slide, please?

Okay. So this is an HI, representative HI of the Yamagata lineage viruses. And highlighted in yellow are the two vaccine virus reference viruses, the egg- and cell-propagated Phuket/3073. You can see that all of the test viruses and many of these are from the U.S., South America, and Bangladesh, Afghanistan. We can see that all of the viruses are well inhibited by antisera raised to cell-propagated B/Phuket. And in this test, also, they're all well inhibited by antisera raised to egg-propagated B/Phuket.

Next slide, please?

And this is just a graphic representation of that data, but it's all the data from the collaborating centers. And you can see that the 2016 viruses in yellow were all clustering around the B/Phuket/3073 vaccine virus.

Next slide?

And this is a summary of all of the HI data from the different collaborating centers. Again, not all of the centers had serum run -- sera raised to cell-propagated Phuket. But if we look at the right-hand part of the table, you can see where antisera to cell-propagated Phuket was used. We're essentially getting 100% of the viruses are similar to B/Phuket by HI.

And this is also true if we look at antisera raised to egg-propagated B/Phuket. In total, over 1,000 viruses tested, and 94% of them show antigenic similarity. And again, the one outlier is one of the collaborating centers, VIDRL, from Australia, that has antisera to egg-propagated Phuket that is showing more low reactors, but this was not seen by the other centers.

Next slide?

So, finally, this is again human serology. This is two pieces of data. The top panel is from the China CDC. The bottom panel is from the Australian CDC. And again, this is looking at sera from adults vaccinated with the 2015-16 Northern Hemisphere or the 2016 Southern Hemisphere quadrivalent and compared with the response to cell-propagated B/Phuket/3073.

And you can see that there's one or two viruses there. There's a cell- and egg-grown Sichuan virus. This is a virus from China that reacted poorly. This virus does have a mutation in -- I believe it's in amino acid residue 212, which is one I pointed out. But we don't think that there's anything significant about these viruses because other viruses in this group react just fine.

For the Australian response below, you can see again that they have two contemporary B/Yamagata viruses, and they're responding very well to their reference virus. So we're not seeing any reduction in the ability of post-vaccination human sera in adults to respond to circulating viruses.

Next slide?

So, in summary, the B/Victorian lineage viruses predominated in many countries but circulated in approximately equal proportions in some countries, including the U.S. The B/Victorian lineage viruses, the vast majority of them were V1A. And the recently circulating viruses were well inhibited by ferret antisera raised against cell-propagated Brisbane. And also, I didn't point it out in the tables, the Texas, which is also a candidate vaccine virus.

The human HI antibody mean titers against some representative B/Victoria lineage virus was reduced compared to HI titers to the cell-propagated vaccine virus Brisbane/60, that this -- when we looked at all the data together, this cumulative response was not significantly reduced.

And with the B/Yamagata lineages viruses, again, the vast majority still belong to the Y3 clade. The recently circulating viruses are well inhibited by ferret antisera raised against the cell-propagated B/Phuket viruses. And the human HI antibody titers against some representative B/Yamagata lineage viruses were reduced compared to cell-propagated vaccine virus B/Phuket. But again, when we looked across the board at all the viruses tested together, we didn't see a significant reduction.

Next slide?

So, finally, considering all of these data, this led us to recommend the following viruses be used for the trivalent influenza vaccine in the 2017 Southern Hemisphere season: A/Michigan/45/2015-like (H1N1)pdm09 virus; an A/Hong Kong/4801/2014-like virus, H3N2 virus; and a B/Brisbane/60/2008-like virus. For the quadrivalent vaccine containing two B components, the above viruses plus the B/Phuket/3073/2013-like virus.

Next slide?

So that ends my presentation, and I'd just like to acknowledge all of the year-round work of all the collaborating centers, the national influenza centers that really detect the viruses and provide them to us, as well as our University of Cambridge partners, our essential regulatory partners. And in the U.S., we have many public health partners, including the USAFSAM and NHRC. And also, just many, many people at CDC.

Thank you. I'll take questions.

DR. EDWARDS: Thank you, Jackie. That was wonderful.

I think one possibility might be those individuals that have questions, if they could push their raised hand, then I could call on them, and then we wouldn't have

each other interrupting anyone.

So are there any questions?

(No response.)

DR. EDWARDS: Perhaps I could start with a question then. Do you have concerns about the recent H3N2 isolates from New York and Missouri, that they may eventually be poorly matched?

DR. KATZ: Yes. I mean, they are not well matched. We've seen earlier in the season a handful of viruses of a different genetic group within 3C.3a viruses that also had -- were not well inhibited by Hong Kong/4801. These viruses haven't seemed to spread, and at this point, we've seen multiple different genetic clusters within the 3C.3a viruses. So, certainly, if for some reason one of these genetic subgroups that are reacting poorly with Hong Kong/4801-like viruses, if they were to predominate, yeah, then we may have a reduced match.

But at this point, really, I mean, we also -- I didn't include any of the data, but we also spoke with predictive modelers. They now are also including the data into the vaccine consultation meetings. And for both -- there's two main groups, and both of those conclude, based on the available genetic data and the antigenic data in some cases, that the 3C.2a viruses are going to continue to predominate. And I think everybody is perplexed by why we saw 3C.3a viruses towards the end of our season.

So, again, flu is always surprising, and we really can't say at this time. But I think since 2a's have predominated globally, I can't predict, but it's likely that we will see a lot of 2a viruses still this season. So we may have a mixture. That may be what happens. I don't know.

DR. EDWARDS: Are there any other clarifying questions?

DR. MONTO: This is Arnold.

DR. EDWARDS: Go ahead, Arnold.

DR. MONTO: Jackie, as you know, we've been working with Scott Hensley on the issue of the K166Q mutation in the H1N1 virus. And we just had a paper accepted for *JID* on that subject. And what are the characteristics of the A/Michigan virus in terms of that mutation?

DR. KATZ: So it's typical of 6B viruses. So I think Scott is -- there's a slightly different numbering, but it's the 163Q is what it is. So I refer to it as 163. It's the same substitution that Scott refers to as 166.

DR. MONTO: Okay. Is it H1 numbering and H3 numbering? Is that what's going on here or --

DR. KATZ: I think that might be, yeah. Yes. I'm not sure, but there is -- all of the collaborating centers use a numbering system for H1 that is 163. It's the same residue, though.

DR. MONTO: Okay. Thank you.

DR. KATZ: Okay.

DR. EDWARDS: I cannot see the hands that are risen. So even though I suggested it, I can't read it. So --

DR. VIJH: I can --

DR. EDWARDS: Sujata, would you please just announce those who have questions and raised their hands? Thank you.

DR. VIJH: Yeah. Dr. Jack Bennink -- I think that was -- I don't know who that was. And then Dr. Mark Sawyer has his hand up. And just these two.

DR. EDWARDS: Wonderful.

Jack, do you want to start?

DR. BENNINK: Yeah. This is Jack Bennink. What I wanted to ask you about,

Jackie, is the table that's on page 19 in the slides or on the other thing. And I think it's, I don't know, page 7 in the CDC thing. But you know, when you look at the California and Michigan on this, in column C, or E -- excuse me -- in column E, it's supposed to be -- is that a single person's serum versus the pooled serums in F?

DR. KATZ: So columns A, B, C, and D and F are pooled sera. Column E is a single sera.

DR. BENNINK: Yeah, when you look at that, okay, do you -- was it looked at in a lot of other ways, where there were a lot of single sera looked at, you know, in terms of that, because it's so low with the Michigan compared to the other? Is the Michigan really high there because there were some really super -- you know, a few really good responders and a lot of people that don't respond very well, or what do you really take of that data when you compare those two sets in terms of making the choice for Michigan?

DR. KATZ: Okay. So we can't say that a majority of people have this profile, so what we did is we looked at 300 pairs of pre- and post-vaccination adult sera from individuals who'd received the last five seasons' Northern Hemisphere vaccine. And amongst those, as I pointed out in the earlier slide, a subset of individuals -- and it's a minority of individuals that have -- are in a certain age group that have been primed with USSR, they failed to recognize -- so their individual sera does not recognize the 6B.1 and 6B.2 viruses. But there is a substantial amount of other individuals where the response is just fine.

So this was an opportunity for us to use human sera to say -- all we're saying is we can see a difference if we use some human sera. But the problem is we can't really relate that back at all directly to the reduced vaccine effectiveness in this age group. It's a hypothesis. We're looking at two different, very different sets of data. So all I'm

showing in this slide is that if we take pools of sera or an individual serum from these individuals, we can now discriminate where ferret antisera is not able to do so.

Did that answer your question?

DR. BENNINK: Yeah. It does sort of, but you know, just looking at a single individual here that, you know, responds much more poorly to Michigan than the California, you know --

DR. KATZ: Right. But these other --

DR. BENNINK: -- look very good.

DR. KATZ: Sorry? The other pools don't look good. So A, B, C, D don't -- they are all reduced to 6B.1 and 6B.2. The panel F looks fine.

DR. BENNINK: Right.

DR. KATZ: And we do see that in a lot of individuals. So we really don't understand what proportion of the population really has this reduced recognition of 6B.1 and 6B.2 viruses following vaccination with California/7. This is just a snapshot to say we can see it; we don't know how predominant it is really.

DR. BENNINK: Yeah. And while I'm on -- another question about the H3N2 is, in terms of the Switzerland, when the Switzerland is grown in eggs versus the Hong Kong grown in eggs, are there -- do you know the specific amino acid, some specific amino acid changes that are made in Switzerland versus Hong Kong?

DR. KATZ: Yes. I don't have it at the tip of my fingers right now, but I can get that for you. There are clearly changes for any egg-grown virus. And I'm just blanking on what the particular ones are with Switzerland versus Hong Kong. Certainly changes --

DR. BENNINK: Yeah --

DR. KATZ: Sorry.

DR. BENNINK: Yeah. There seems to be some critical ones, you know, between -- that are made in Switzerland, not in Hong Kong, that are really reducing significantly the egg-grown Switzerland more than the Hong Kong one.

DR. KATZ: Right. And I mean, it's very -- I don't think it's that straightforward. It also depends on the properties of the egg-grown viruses and how they react with antisera, because sometimes in the assay, particularly in the focus reduction assays, the neutralization assays, we'll see antisera that has very high homologous titers. And that is one contributing factor to seeing a lot of reduction. And we know that doesn't really represent antigenic change; it's a feature of the egg-grown viruses and how immunogenic perhaps they are in ferrets.

DR. BENNINK: Thank you.

DR. KATZ: So it's -- okay.

DR. EDWARDS: Mark Sawyer, do you have a question?

DR. SAWYER: Yes. Thank you for that great presentation and trying to make it clear to those of us who don't work in influenza on a daily basis. And I apologize if my question has been addressed in the details of that data. But I do recall at our last meeting in March a comment that the B/Victoria Brisbane strain had had a long and notable surface, but there were some indications that it was beginning to not be as effective. I didn't hear any of that today. Am I not recalling right, or is there -- I guess really my question is there any suggestion that the B/Brisbane needs to be modified in the near future, if not right at this moment?

DR. KATZ: Yeah, no, that's a great question. And that probably certainly was suggested in February. And the basis of that was that in our antisera raised to egg-propagated Brisbane, we saw an increasing number of fourfold reductions. And we thought that that at the time was a trend that we would then start to see a lot of low

reactors. But, in fact, that really hasn't happened. And the antigenic profile as well as the genetic profile has remained quite stable. Nevertheless, we know that the Brisbane has -- components have been around for a long time, and so all of the collaborating centers are working on looking -- on deriving new, potentially new vaccine components. But at this time, with the data we had, we really felt there was no strong evidence to make a change.

DR. SAWYER: Okay. Thank you.

DR. EDWARDS: Patrick Moore?

DR. MOORE: Jackie, that was masterful. That was great. But can we go to slide number 5? And I have a couple of questions to ask you about that.

DR. KATZ: Okay. Hello, are you there?

DR. MOORE: Jackie?

DR. KATZ: Yeah, I'm here. I'm just trying to pull up slide number 5. Okay. Sorry. If you can just ask your question, I'll find slide number 5.

DR. MOORE: Sure. In slide number 5, it's just surveillance data.

DR. KATZ: Okay.

DR. MOORE: And you show that there's an increase in H3 infections from week 26 through 36, which are concerning to me because if there is a strain emerging that isn't covered by the vaccine, then, of course we'd want to know about that for the Northern Hemisphere early as well.

DR. KATZ: Um-hum.

DR. MOORE: Now, as I understand it, the Hong Kong/4801 has been in use throughout the world for at least a year and a half. And so are these failures of the vaccine, do we know, or also if I understood your presentation correctly, there was both 3C.2 in Australia, but you said there was 3C.3, which is similar to the strain

that's circulating in the U.S., in New Zealand. And I'm just wondering are they being covered adequately by the Hong Kong/4801, or is that just a matter of poor vaccine coverage, or what are your thoughts on that? And should we take a closer look at that poor coverage?

DR. KATZ: Right. So couple of things there. So slide 5 just demonstrates viruses reported to the WHO system. That doesn't say anything about whether individuals were vaccinated or not, and we could assume since most parts of the world don't have very high vaccine coverage, probably these are -- many cases are from non-vaccinated individuals.

The late-season rise in H3 that we saw on that slide is probably due to the Southern Hemisphere season. Yes, in Australia, they had predominantly 3C.2a, which is what the Hong Kong/4801 vaccine virus is. But in New Zealand, surprisingly, they had a few 3C.3a viruses. These were the genetic groups that were slightly different to what we saw in the U.S. We did see generally that genetic group; they had an additional mutation that really didn't change them any way that we could see.

I think you're right. We need to keep an eye on this. So we have limited data at this time about how the vaccine effectiveness of the 2016 H3N2 component is. So they're just finishing up their season, and while there are vaccine effectiveness studies that go on in Australia and that I'm not sure about in New Zealand this year, the numbers of people that they enrolled and the overall vaccine coverage is quite low. So it's difficult to get very good estimates, so I think the final data will be developed in the next month or so as their season ends, and we'll have more of an idea of how well the Hong Kong/4803 did. But the most robust data will come from Australia, and they predominately had 3C.2a.

DR. EDWARDS: Dr. Gellin?

DR. GELLIN: Thanks, Kathy.

Jackie, thanks a lot. That's quite a magnum piece of work.

My question is about this vaccine effectiveness by year of birth. I guess that's a new analysis or I haven't -- I missed it previously. My question, though, is since we're talking about a vaccine for the Southern Hemisphere, and I think if I understood this right, the work was done on people in the Northern Hemisphere, do you know what the applicability is for people who live in the Southern Hemisphere?

DR. KATZ: You're talking about the H1N1?

DR. GELLIN: That's right. That's right --

DR. KATZ: Yeah, as I said, their season's estimates are quite limited at this time. I mean, they did have the same California/7 component. The current Southern Hemisphere and our Northern Hemisphere vaccine still had California/7 in them. So in that respect, they're comparable. And so we believe that -- and we've looked at both panels of sera from individuals vaccinated in Australia versus those vaccinated in the U.S. And in general, we see the same sort of reactivity patterns. But by and large, if we just take 20 paired sera from adults, we don't really -- you know, it's only a few individuals where we can discern this difference in a few, this priming difference.

DR. GELLIN: Thank you.

DR. KATZ: Okay.

DR. EDWARDS: Any other questions of Jackie?

DR. BENNINK: Yes. I want to ask another question in terms of this. Jackie, do you know the numbers from different countries of people that get vaccinated in the Southern Hemisphere, you know, to sort of have a rough idea? And have those

countries -- like if the majority lives in Australia and New Zealand, let's say --

DR. KATZ: Right. So it's very low coverage. I want to say it's somewhere between 10 and 20%. I don't, again, have the figures. I'd say it's no more than 20%, and I think it's probably less than that for Australia. And I'm not sure. It's probably comparable or less for New Zealand. They really just have recommendations for high-risk groups' vaccination, and some states also vaccinate children because they have a statewide program for it. So we're talking a very different level of coverage to what we see in the U.S., which is sort of approaching 50% coverage of the population. And so that's one reason that it's far more difficult to get accurate vaccine effectiveness estimates.

DR. BENNINK: So in looking at this, though, you know, have those countries voted yet on the WHO recommendations, and have they chosen that they're going to follow those recommendations, the ones that use the vaccine the most? Do you know?

DR. KATZ: So I don't know about the individual countries and what each individual regulatory authority will do, but my assumption is, as this happened in the past, is they usually go along with the WHO recommendations for Southern Hemisphere.

DR. BENNINK: Okay.

DR. KATZ: But I don't know when the Australian group will actually do that.

DR. BENNINK: I'll come back to that in a second, but will this also affect, for example, U.S. military that is in the Southern Hemisphere?

DR. KATZ: If they use the 2017 Southern Hemisphere vaccine composition, it could, yeah. I think most military personnel, or at least the ones where studies are done here, I mean, in the U.S. before deployment, they would receive Northern

Hemisphere vaccines, I'm guessing --

DR. BENNINK: I guess part of the issue that, you know, is a little bit of a thing here is that if -- not that I'm thinking that this is the way it is or anything else, but if you -- if the Committee made decisions that were different from a country in the Southern Hemisphere, and this company is trying to make things that are related to the U.S. approval versus approval in a country that's going to be using it or where they're going to be trying to use it, it sort of makes things difficult.

DR. KATZ: Right.

DR. BENNINK: And maybe Jerry has something to say about that as well.

DR. KATZ: So maybe I could just make the point because I think your concern is about the evidence for the recommendation to move to Michigan/45. So, really, the collective data, we understood for several years that these viruses were changing genetically. And it's become apparent in the last year or so that the ferret antisera, although it can discriminate antigenic changes, it's perhaps focused more on looking -- on eliciting antibody to a different immunodominant site in the ferret. And so our concern was that some of the substitutions that had accumulated and that we were certainly seeing in 6B.1 viruses were not being recognized by ferret antisera.

So the recommendation was made not to protect a very small group of individuals. It was made because we felt that there was now sufficient evidence to move on and select another candidate. But also, with the thinking that with this new virus, that it wouldn't hurt, you know, it wouldn't lessen the protection for the general population. So it might benefit a few, but it certainly wasn't going to affect -- make a difference and would be equally as good as California/7 probably for the majority of the population --

DR. EDWARDS: Thank you.

DR. BENNINK: Yeah, I think, yeah, I'm probably not quite as worried as you may think, although I ask the questions because I think it is an important question and things like that. But it's really a little bit more of the -- what this last question was is a little more of a conundrum in terms of, you know, if we -- the concern is if we told a company, okay, you have to make something different than what is here, or even if we went along with the WHO recommendations and then one of the major, you know, countries that is giving the most vaccines in the Southern Hemisphere, okay, makes a recommendation that is against what the WHO is, or something like this, then you sort of start putting, you know --

DR. KATZ: Right.

DR. BENNINK: -- the companies that, you know --

DR. KATZ: Yeah.

DR. BENNINK: -- where they can't sell their vaccine.

DR. KATZ: Well, maybe Jerry can clarify, I mean, why this is the VRBPAC decision this time. But also, I mean, historically, the Southern Hemisphere countries and manufacturers have really gone along with the WHO recommendations.

DR. BENNINK: And that's a good thing, I think, yes.

DR. EDWARDS: Are there any additional questions?

DR. VIJH: I think Dr. Jerry Weir would like to say something.

DR. EDWARDS: Okay.

DR. WEIR: I'm not sure what I can add except that, yes, I mean, in a sense, if you look on the -- I didn't say this earlier, but if you look on the FDA website, you'll see that the only company we're really referring to is Sanofi Pasteur that updated their license to make this vaccine. And the fact is we don't actually know what their plans are for how they will distribute it and use it and whether the market is really

other countries or not. So I think I'm just going to have to defer in that sense of not knowing what their plans are.

Marion may want to elaborate more?

DR. GRUBER: All right. I'm using a different microphone. This is Marion Gruber. I mean, this is an interesting discussion and an interesting thought. And I think, you know, we'll -- I think we would certainly be interested in hearing your recommendations today. But as we're not, you know, licensing this, you know, the strain composition for the upcoming Southern Hemisphere season right away, I think we certainly can take, you know, this discussion a little further in terms of having some exchange with, you know, regulatory agencies in the Southern Hemisphere. So that's something for us to, I think, consider.

DR. EDWARDS: Thank you.

Are there any other comments or any other questions to Dr. Katz?

(No response.)

DR. EDWARDS: Then I would like to ask if there are any individuals who would like to speak in the Open Public Hearing?

(No response.)

DR. VIJH: There are no Open Public Hearing speakers that signed up, Dr. Edwards.

DR. EDWARDS: Wonderful. So then I think it's not necessary for us to read that statement; is that correct?

DR. VIJH: That's right.

DR. EDWARDS: Good. Okay. So I understand that we're going to take a 5-minute break, and then we'll come back and discuss our thoughts about the votes and then vote. So I think 5 minutes we can all return.

DR. VIJH: Yeah, please don't log off. Do nothing. Just leave, you know, leave everything the way it is and just please come back in 5 minutes.

DR. EDWARDS: Thank you.

(Off the record at 3:05 p.m.)

(On the record at 3:11 p.m.)

DR. VIJH: Yes, Dr. Edwards, we can get started. It's open to discussion and then followed by recommendations and voting.

DR. EDWARDS: Good. That sounds wonderful.

So I guess, first of all, I think that it's very important for us to understand the two questions that were posed, that Jerry posed for us. And basically, the questions are two. Number one, to approve the composition of the trivalent 2017, including the A/Michigan (H1N1), the A/Hong Kong (H3N2), and the B/Brisbane B/Victoria lineage. And then the second question will be the addition of the B/Yamagata strain. So these two questions will be voted on separately.

Okay. Are there any questions or comments that people would like to make about these -- about, first of all, the first question? Any comments or questions people would like to share?

(No response.)

DR. EDWARDS: I can't see the raised hands, but if you want to share something, please just go ahead and say what you're thinking.

DR. VIJH: I think it's Dr. Leonard Friedland has his hand up, and Dr. Jack Bennink. I don't know who put their hand up first.

DR. EDWARDS: Okay. Well, let's let Lenny start. Lenny, would you go ahead and ask your question, and then we'll go to Dr. Bennink.

DR. FRIEDLAND: Yes. Thank you. Just a comment. I wanted to thank the

presenters. From the previous, it was not as clear to me as it was from the presentation on the rationale for switching to the A/Michigan strain in the Southern Hemisphere formulation. So thank you very much. It's now very clear to me, and I understand why the recommendation has taken place.

DR. EDWARDS: Jack?

DR. BENNINK: No, I didn't have any further questions, but thank you. I agree with Leonard that Jackie did a terrific job.

DR. EDWARDS: It was a real tour de force, absolutely.

Would people prefer to go around and talk about their impressions or the answers to the questions, or are people ready to vote?

UNIDENTIFIED SPEAKER: I'm ready.

DR. EDWARDS: Okay.

DR. LONG: Ready to vote.

DR. VIJH: I just need a few minutes to set up the voting by the WebEx.

DR. EDWARDS: Okay.

DR. VIJH: Could you please have patience with me just for a couple of minutes?

DR. EDWARDS: Sure.

DR. VIJH: I need to start the poll. So what I'm going to do is --

DR. EDWARDS: We don't want any controversy on the voting procedure.

DR. VIJH: So there are two questions that the Committee has to vote on. And Joanne, are we able to project them on the monitors?

So you're going to be voting for Question 1, which includes A, B, and C for the trivalent vaccine, and Question 2 for the quadrivalent vaccine. So we are using WebEx, which will not be visible to the public. But because simultaneous voting is

required, members will be voting via WebEx. So what I'm going to do is I'm going to post the questions by WebEx. The members can see it basically, and I'm going to give them a few minutes to either vote yes, no, or abstain to the Question 1.

Dr. Edwards could perhaps read the question. In the mean time, I can set it up via the polling.

DR. EDWARDS: Sure.

DR. VIJH: And I'll open the poll for about 2 minutes. Because there are several members that are voting, I just need time to scroll through to see that everybody has voted. Once you see the question, the voting members as well as the temporary voting members, please vote and submit your vote. Only vote yes, no, or abstain. And after I see everybody has voted, I'm going to close the poll and then basically read each individual vote for the record and tally the final vote.

DR. EDWARDS: Okay. So the first question is: For the composition of the trivalent 2017 Southern Hemisphere formulations of influenza vaccine, does the Committee recommend inclusion of an A/Michigan/45/2015 (H1N1)pdm09 virus, inclusion of an A/Hong Kong/4801/2014 (H3N2)-like virus, and inclusion of a B/Brisbane/60/2008-like (B/Victoria lineage) virus?

(Pause.)

DR. VIJH: I'm just posting the question in a few seconds. We're doing this for the first time, so let's see. So the poll is now open for Question No. 1. Please vote yes, no, or abstain.

(Pause.)

DR. VIJH: Okay. So I think everybody has voted because -- let me just check.

DR. EDWARDS: Will you be reading the names and the votes, then?

DR. VIJH: That's correct. I'm just trying to figure it out.

DR. EDWARDS: Okay.

DR. VIJH: Give me one second.

DR. EDWARDS: Sure.

DR. VIJH: So I'm going to close the poll. So I have the table in front of me, and I'm going to read it. And if you think that I made a mistake, please speak up.

So it's Dr. Mark Sawyer, yes. Please give me a few seconds. I just need to keep track of this. Dr. Sarah Long, yes; Dr. Hana Sahly, yes; Dr. Bruce Gellin, yes; Dr. Melinda Wharton, yes; Dr. Jack Bennink, yes; Dr. Katherine Edwards, yes; Dr. Karen Kotloff, yes; Dr. Pamela McInnes, yes; Dr. Arnold Monto, yes; Dr. Vicky Pebsworth, yes; Dr. Holly Janes, yes; Dr. Moore, yes.

So I think I've called everybody's name out except Dr. Lynfield. Dr. Lynfield, yes. So the 14 votes are yes, 0 noes, and 0 abstain. So the Committee votes unanimously for a yes vote for Question 1.

Thank you.

DR. EDWARDS: Thank you.

DR. VIJH: So I didn't realize. Was this visible on the screen? Everybody can see the --

DR. EDWARDS: Yes, it is.

DR. VIJH: Oh, wonderful.

DR. EDWARDS: It works very nicely.

DR. VIJH: That's beautiful, yeah.

So now we can move on to the second question. Dr. Edwards, while you read it, I'll get ready with it.

DR. EDWARDS: Wonderful. So the second question is: For the quadrivalent 2017 Southern Hemisphere formulation of the influenza vaccine, does the Committee

recommend the inclusion of the B/Phuket/3073/2013-like virus of the B/Yamagata lineage as the second influenza B strain in the vaccine?

(Pause.)

DR. VIJH: This one, please, could you just give me a few minutes?

DR. EDWARDS: Sure.

DR. VIJH: I'm just locating the file, and then I'm going to post it and then do the same thing again.

(Pause.)

DR. VIJH: Okay. I basically added the second question. And the poll is open. It says Question 1, but it's actually the second question, quadrivalent formulation.

DR. EDWARDS: Right, yeah.

(Pause.)

DR. VIJH: Okay. Looks like everybody has voted, 14 members. I'm going to close the poll. I'm going to give it a few more minutes. Looks like maybe -- okay. I believe everybody has voted.

Okay, great. Now, this time I can use the monitor. So for the second question, I'm going to read the individual votes. It's come out differently. Dr. Mark Sawyer, yes; Dr. Sarah Long, yes; Dr. Hana El Sahly, yes; Dr. Bruce Gellin, yes; Dr. Patrick Moore, yes; Dr. Melinda Wharton, yes; Dr. Jack Bennink, yes; Dr. Katherine Edwards, yes; Dr. Karen Kotloff, yes; Dr. Pamela McInnes, yes; Dr. Arnold Monto, yes; Dr. Ruth Lynfield, yes; Dr. Vicky Pebsworth, yes; and finally, Dr. Holly Janes, yes.

So it's 14 members who voted yes, a unanimous vote of yes, 0 noes, 0 abstain. So that's the vote for the second question.

That closes the voting. Thank you.

DR. EDWARDS: Thank you. You've done a masterful job of orchestrating this. I think that we have addressed the questions, then. Thank you for participation.

Is there any other thing that we need to do before we close the call?

DR. VIJH: No. Thank you, Dr. Edwards, for chairing the session. You did a fabulous job with this kind of format, and for all the members in the audience and the viewers watching, thank you all for your patience.

DR. GELLIN: Kathy, this is Bruce. Can I just make one comment?

DR. EDWARDS: Please.

DR. GELLIN: So it was quite a process, and I congratulate all who did it. I think getting back to the conversation that Jack Bennink and Jerry Weir had about how this might be -- how vaccines might be used in the Southern Hemisphere, given the number of products already available and the potential for confusion, I think that when the FDA announces or puts these results on this website or whoever else does it, to be clear what this is about and what it's not, but I think it could be -- people could worry that there's some other vaccine they have to go find. We still need to find out what the company's intentions are for its availability for U.S. citizens who might be traveling or for the military. But I think it's important to be clear since this is the first time we've had this kind of conversation about Southern Hemisphere, what we did and what it means.

Thanks.

DR. EDWARDS: Certainly, those are very, very insightful questions and I think certainly should be entered into our discussion as you go forward.

Any other comments?

(No response.)

DR. EDWARDS: Okay. Thank you very much. Everyone have a nice rest of the

day.

DR. VIJH: Thank you all.

DR. EDWARDS: Okay. Bye.

(Whereupon, at 3:27 p.m., the meeting was adjourned.)

CERTIFICATE

This is to certify that the attached proceedings in the matter of:

VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE

MEETING #144

October 13, 2016

Silver Spring, Maryland

were held as herein appears, and that this is the original transcription thereof for the files of the Food and Drug Administration, Center for Biologics Evaluation and Research.

TOM BOWMAN

Transcriptionist