

UNITED STATES OF AMERICA
 DEPARTMENT OF HEALTH AND HUMAN SERVICES
 FOOD AND DRUG ADMINISTRATION

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CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

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149TH MEETING OF THE VACCINES AND RELATED BIOLOGICAL PRODUCTS
 ADVISORY COMMITTEE

+ + +

October 4, 2017
 1:00 p.m.

FDA White Oak Campus
 Building 31, Great Room 1503
 10903 New Hampshire Avenue
 Silver Spring, MD 20993

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|---|-------------------------|
| MARK SAWYER, M.D. | Acting Chair |
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| HOLLY JANES, Ph.D. | Voting Member |
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| SARAH LONG, M.D. | Voting Member |
| PAMELA McINNES, D.D.S., M.Sc. (Dent) | Voting Member |
| PATRICK MOORE, M.D. | Voting Member |
| ARNOLD MONTO, M.D. | Voting Member |
| MELINDA WHARTON, M.D., M.P.H. | Voting Member |
| SHELDON V. TOUBMAN, J.D. | Consumer Representative |
| DAVID GREENBERG, M.D. | Industry Representative |

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M E E T I N G

(1:00 p.m.)

1
2
3 CAPT HUNTER-THOMAS: Thank you all for joining us.
4 Dr. Edwards is en route, and she will be joining us shortly if
5 she's not on the line already.

6 So instead of her starting the meeting as a chair,
7 Dr. Mark Sawyer has agreed to be her backup until Dr. Edwards
8 can join us.

9 Dr. Sawyer, you have the floor.

10 DR. SAWYER: Thank you, Serina.

11 Welcome, everybody. Good morning and good afternoon to
12 those joining us all by webcast. I'd like to welcome you to
13 the 149th meeting of the Vaccines and Related Biological
14 Products Advisory Committee.

15 Today's topic is the discussion on the strain selection
16 for the 2018 Southern Hemisphere influenza season. The
17 Committee members are participating in this meeting via
18 teleconference, and hopefully, everybody has succeeded in
19 logging in. And we're awaiting Dr. Edwards, who will join us
20 as soon as she is able.

21 With that, I would like to turn it back over to Ms. Hunter
22 Thomas to do a roll call and have the Committee members
23 introduce themselves.

24 CAPT HUNTER-THOMAS: Thank you, Dr. Sawyer.

25 So we're going to start with a quick check-in to see if

1 Dr. Edwards has joined us yet.

2 Dr. Edwards?

3 (No response.)

4 CAPT HUNTER-THOMAS: And when I do call your name, if you
5 are present, Committee members, after you confirm your
6 presence, please state your organization after you confirm your
7 name.

8 So moving on to Dr. Holly Janes?

9 DR. JANES: Good morning. This is Holly Janes. I'm at
10 the Fred Hutchinson Cancer Research Center.

11 CAPT HUNTER-THOMAS: Thank you.

12 Dr. El Sahly? Dr. El Sahly?

13 (No response.)

14 CAPT HUNTER-THOMAS: Okay. Dr. Long?

15 DR. LONG: Sarah Long here at St. Christopher's Hospital
16 for Children in Philadelphia.

17 CAPT HUNTER-THOMAS: Thank you.

18 Dr. McInnes?

19 DR. McINNES: This is Pamela McInnes, Deputy Director,
20 NCATS, at the NIH.

21 CAPT HUNTER-THOMAS: Thank you.

22 Dr. Moore?

23 DR. MOORE: This is Pat Moore. I'm at the University of
24 Pittsburgh Cancer Institute.

25 CAPT HUNTER-THOMAS: Thank you.

1 Dr. Monto?

2 DR. MONTO: I'm here, Arnold Monto, University of
3 Michigan.

4 CAPT HUNTER-THOMAS: Thank you.

5 And, Dr. Sawyer, would you like to state your
6 organization?

7 DR. SAWYER: Yes. So this is Mark Sawyer. I am a
8 pediatric infectious disease specialist at the University of
9 California, San Diego.

10 CAPT HUNTER-THOMAS: Thank you.

11 Mr. Toubman?

12 MR. TOUBMAN: Sheldon Toubman. I'm an attorney with New
13 Haven Legal Assistance Association in New Haven, Connecticut.

14 CAPT HUNTER-THOMAS: Thank you.

15 And Dr. Wharton?

16 DR. WHARTON: Melinda Wharton. I'm Acting Director of the
17 National Vaccine Program Office.

18 CAPT HUNTER-THOMAS: And also Dr. Levy, please?

19 DR. LEVY: Hi, this is Dr. Ofer Levy. I'm the Director of
20 the Precision Vaccines Program at Boston Children's Hospital
21 and Harvard Medical School.

22 CAPT HUNTER-THOMAS: Thank you.

23 I'd like to circle back and see if Dr. El Sahly has joined
24 us yet?

25 (No response.)

1 CAPT HUNTER-THOMAS: And also check in on Dr. Edwards?

2 (No response.)

3 CAPT HUNTER-THOMAS: Okay. Thank you. We'll --

4 DR. GREENBERG: And Serina, sorry, this is David
5 Greenberg. Can I introduce myself?

6 CAPT HUNTER-THOMAS: Oh, I'm sorry, Dr. Greenberg, yes,
7 please, by all means.

8 DR. GREENBERG: Great. Thanks. David Greenberg serving
9 as the Industry Representative and with Sanofi Pasteur. Thank
10 you.

11 CAPT HUNTER-THOMAS: Thank you, Dr. Greenberg.

12 Okay. We'll now move on to the housekeeping and followed
13 by the Conflict of Interest Statement.

14 Welcome, everyone, again to the 149th -- oh, sorry.
15 Excuse me. I also need to do introductions to the most
16 important people here, the OVRP.

17 DR. GRUBER: Hi, this is Marion Gruber, Director, Office
18 of Vaccines Research and Review, CBER.

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

21 CAPT HUNTER-THOMAS: And also Jackie Katz, please?

22 DR. KATZ: Hi, this is Jackie Katz from the Influenza
23 Division at CDC; also, the WHO Collaborating Center for
24 Influenza.

25 CAPT HUNTER-THOMAS: Okay. Thank you. Okay. Thank you.

1 On behalf of FDA, the Center for Biologics Evaluation and
2 Research, and VRBPAC, we would like to welcome everyone to this
3 meeting.

4 Today's session has one topic that is open to the public
5 in its entirety. The meeting topic is described in the *Federal*
6 *Register* notice that was published on September 11th, 2017.

7 The press media representative for today's meeting is
8 Ms. Lyndsay Meyer, and the transcriptionist for this meeting
9 today is Mr. Mike McCann.

10 I would like to remind everyone to please check your
11 pagers and your cell phones and make sure that they are either
12 turned off or in silent mode.

13 Committee members, when you're making a comment, being
14 that you are not in the room, please first state your name and
15 speak up so that your comments are accurately recorded for the
16 transcription record.

17 And I will now proceed to the Conflict of Interest
18 Statement.

19 The Food and Drug Administration is convening today,
20 October 4, 2017, for the 149th meeting of the Vaccines and
21 Related Biological Products Advisory Committee under the
22 authority of the Federal Advisory Committee Act of 1972.

23 At this meeting, in the open session, the Committee will
24 discuss and make recommendations on the safety and
25 effectiveness of the selection of strains to be included in an

1 influenza virus vaccine for the 2018 Southern Hemisphere
2 influenza season.

3 The following information on the status of this Advisory
4 Committee's compliance with federal ethics and conflicts of
5 interest laws, including but not limited to 18 U.S. Code 208,
6 is being provided to participants at this meeting and to the
7 public. This Conflict of Interest Statement will be available
8 for public viewing at the registration table.

9 With the exception of the Industry Representative, all
10 participants of the Committee are special government employees
11 or regular federal government employees from other agencies and
12 are subject to the federal conflict of interest laws and
13 regulations.

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

23 FDA has determined that all members of this Advisory
24 Committee are in compliance with federal ethics and conflict of
25 interest laws. Under 18 U.S. Code 208, Congress has authorized

1 FDA to grant waivers to special government employees and
2 federal government employees who have financial conflicts when
3 it is determined that the Agency's need for a particular
4 individual's service outweighs his or her potential financial
5 conflict of interest.

6 However, based on today's agenda and all financial
7 interests reported by members and consultants, no conflict of
8 interest waivers were issued under 18 U.S. Code 208.

9 Dr. David Greenberg is currently serving as the Industry
10 Representative to this Committee. Dr. Greenberg is employed by
11 Sanofi Pasteur U.S. Industry representatives act on behalf of
12 all related industry and bring general industry perspective to
13 the Committee. Industry representatives are not special
14 government employees and do not vote and do not participate in
15 the closed sessions.

16 Mr. Sheldon Toubman is serving as the Consumer
17 Representative for this meeting. Consumer representatives are
18 special government employees and therefore are screened for
19 their financial conflict of interest and screened prior to
20 their participation.

21 Dr. Jacqueline Katz is employed by the Center for Disease
22 Control and Prevention, National Center for Immunization and
23 Respiratory Diseases. She is an expert in influenza virus
24 disease and influenza virus vaccines and internationally known
25 for these achievements. Dr. Katz is a regular government

1 employee and is the speaker for this meeting and has been
2 screened for conflicts of interest. She has been cleared to
3 make a presentation at this meeting.

4 At this meeting, there may be regulated industry speakers
5 and other outside organization speakers making presentations.
6 These speakers may have financial interests associated with
7 their employer and with other regulated firms. The FDA asks,
8 in the interest of fairness, that they address any current or
9 previous financial involvement with any firm whose product they
10 may wish to comment upon. These individuals were not screened
11 by the FDA for conflict of interest.

12 FDA encourages all other participants to advise the
13 Committee of any financial relationships that you may have with
14 any firms, its products, and if known, its direct competitors.

15 We would like to remind members, consultants, and
16 participants that if the discussions involve any other products
17 or firms not already on the agenda for which an FDA participant
18 has a personal or imputed financial interest, the participants
19 need to exclude themselves from such involvement, and their
20 exclusion will be noted for the record.

21 This concludes my reading of the Conflict of Interest
22 Statement for the public record, and at this time, I would like
23 to hand the meeting back over to Dr. Sawyer.

24 DR. SAWYER: Thank you very much, Ms. Hunter-Thomas.

25 So, again, I would like to announce the topic of today's

1 meeting, which is the strain selection for the 2018 Southern
2 Hemisphere influenza season. And our first speaker to
3 introduce today's topic is Dr. Jerry Weir, Division of Viral
4 Products, Office of Vaccine Research and Review at CBER FDA.

5 Dr. Weir?

6 DR. WEIR: Thank you, everyone.

7 I'm going to give just a brief introduction and some
8 background to describe why we're here today and then present
9 the questions that we will be asked to vote on at the end of
10 the presentation.

11 So if you follow the slides that I have put together, the
12 slide number 2 describes the purpose of today's VRBPAC
13 committee discussion. We're here to make recommendations for
14 the strains of influenza A (H1N1 and H3N2) and B viruses to be
15 included in the 2018 Southern Hemisphere formulation of
16 influenza vaccines licensed in the United States.

17 The next slide. So as a little bit of background for
18 today's committee discussion, the World Health Organization
19 makes recommendations for the virus strains to be included in
20 an influenza vaccine. They do this two times a year, one for
21 the Northern Hemisphere, which is recommendations are made in
22 February or March each year for the following winter season;
23 and then the second recommendation is usually made in September
24 for the next year's Southern Hemisphere influenza season.

25 Even though the WHO gets together and makes these

1 recommendations, it's up to each national regulatory authority
2 to approve the composition and formulation of the vaccines in
3 each country. For us, that's VRBPAC provides this
4 recommendation for U.S. licensed manufacturers in February --
5 and this occurs in February and March for all of the influenza
6 vaccines that are used in the Northern Hemisphere influenza
7 season.

8 The FDA's CBER approves license supplements for U.S.
9 manufacturers to incorporate these updated strain
10 recommendations. And this updating of the license usually
11 occurs in June to July, before the start of the Northern
12 Hemisphere season.

13 Back in 2016, there was a U.S. vaccine manufacturer that
14 was approved to produce a Southern Hemisphere formulation for
15 their influenza vaccine, so it is our view that the strain
16 recommendations and supplement approval for the Southern
17 Hemisphere formulation should follow the Northern Hemisphere
18 process. So our meeting today is, in a sense, somewhat of an
19 abbreviated version of the longer, more involved VRBPAC strain
20 selection meeting that we do in February or March for the
21 Northern Hemisphere.

22 If you go to the next slide, you see the type of data and
23 types of analysis that will be presented. And this will all be
24 presented by Dr. Jacqueline Katz from the CDC and in a sense is
25 a summary of what went on a week ago at the WHO strain

1 selection meeting. She will present data on the epidemiology
2 of circulating strains. She'll include surveillance data from
3 the U.S. as well as from the rest of the world. As I said,
4 this is summarized from the meeting last week.

5 She'll also present data about the antigenic relationships
6 among contemporary viruses and candidate vaccine viruses. Some
7 of the data that most of you are familiar with will be things
8 like hemagglutination inhibition tests and virus neutralization
9 tests using post-infection ferret serum; also some HI and virus
10 neutralization tests using panels of sera from humans who have
11 received the most recent inactivated influenza vaccines; and
12 she'll probably also include some antigenic cartography, as
13 well as phylogenetic analysis of the HA and neuraminidase
14 genes.

15 The next slide describes the previous recommendations for
16 the Southern Hemisphere. This was done about a year ago, and
17 the WHO recommendation was made on September 29th, 2016. And
18 at that point, the WHO recommended that Southern Hemisphere
19 vaccines contain an A/Michigan/45/2015 (H1N1)pdm09-like virus.
20 They recommended an A/Hong Kong/4801/2014 (H3N2)-like virus.
21 And they recommended a B/Brisbane/60/2008-like virus, which was
22 from the B/Victoria lineage. These were for trivalent
23 influenza vaccines.

24 And then, further, the WHO recommended that any
25 quadrivalent vaccines that were manufactured that would contain

1 two influenza B viruses would contain the three viruses/strains
2 that I just mentioned plus a B/Phuket/3073/2013-like virus from
3 the other B/Yamagata lineage virus.

4 We had a VRBPAC meeting shortly after the WHO strain
5 selection, and the Committee recommended that any U.S.
6 manufacturers of Southern Hemisphere formulations adopt the
7 same strains that I just listed.

8 The next slide. Just to recap what we did at VRBPAC and
9 recommending for the Northern Hemisphere strains back this past
10 February and March -- actually, it was March this year -- there
11 was a WHO recommendation made on March 2nd, 2017, for the
12 upcoming influenza season in the Northern Hemisphere. And at
13 this time, the WHO recommended the following viruses for
14 trivalent influenza vaccines:

15 An A/Michigan/45/2015 (H1N1)pdm09-like virus. This for
16 the Northern Hemisphere was a change from the previous 2016-17
17 Northern Hemisphere season, but as you note, it was the same as
18 the 2017 Southern Hemisphere recommendation that I just
19 mentioned in the previous slide.

20 The Committee also recommended an A/Hong Kong/4801/2014
21 (H3N2) virus -- this was no change from the previous Northern
22 Hemisphere season -- and a B/Brisbane/60/2008-like virus from
23 the B/Victoria lineage, and this was also no change from the
24 previous 2016-17 Northern Hemisphere.

25 The Committee also recommended that any quadrivalent

1 vaccines containing two influenza B viruses contain those three
2 strains, those three viruses, as well as a B/Phuket/3073/2013-
3 like virus from the B/Yamagata lineage.

4 The U.S. VRBPAC recommendation was made in March,
5 March 9th, 2017.

6 The next slide shows a summary of the WHO recommendations
7 for the Southern Hemisphere that were just made about a week
8 ago. This was made on September 27th, 2017. And at this time,
9 the WHO recommended that trivalent vaccines for use in the
10 2017 -- I think that's supposed to be '18 -- Southern
11 Hemisphere influenza season contain the following:

12 An A/Michigan/45/2015 (H1N1)pdm-like virus; an
13 A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus; a
14 B/Phuket/3073/2013-like virus from the B/Yamagata lineage; and
15 then they recommended that any quadrivalent vaccines containing
16 the two B viruses contain those three viruses and a
17 B/Brisbane/60/2008-like virus.

18 The next slide. So the committee discussion today, as I
19 said, will be which influenza strains should be recommended for
20 the antigenic composition of the 2018 Southern Hemisphere
21 formulation of any influenza virus vaccines that are being
22 produced by U.S. licensed manufacturers.

23 The next slide shows the voting questions. What we tried
24 to do, I hope, is make this fairly simple and a slightly
25 simpler process than we use for the Northern Hemisphere, where

1 we vote on all four strains. In this one, since these vaccines
2 are not really for the U.S. -- they're for the Southern
3 Hemisphere but made by a U.S. manufacturer -- we thought we
4 would try to make it simple and have two voting questions.

5 One is for the composition of a trivalent vaccine and in a
6 sense asks you whether you recommend using the three strains
7 recommended by WHO. And that would be Question 1: For the
8 composition of the trivalent 2018 Southern Hemisphere
9 formulation, does the Committee recommend . . . and then these
10 would be the three strains: A/Michigan/45, A/Singapore,
11 B/Phuket.

12 And then a second voting question that would say: For any
13 quadrivalent Southern Hemisphere formulations, does the
14 Committee recommend including the fourth strain, which in this
15 case would be the WHO-recommended B/Brisbane/60/2008-like
16 virus.

17 So that's the quick introduction. I'll turn it back over
18 to the Chair if that's okay.

19 DR. SAWYER: Yes. Thanks very much, Dr. Weir.

20 Let me just ask if any of the Committee members have any
21 questions about the background material that Dr. Weir has
22 provided?

23 MR. TOUBMAN: I do have a question. This is Sheldon
24 Toubman. May I ask it?

25 DR. SAWYER: Yes, please. Go ahead.

1 MR. TOUBMAN: So in terms of jurisdictionally, this is
2 recommendations for the Southern Hemisphere. The Food and Drug
3 Administration is part of the United States government. So is
4 the jurisdiction over this based upon the fact that there are
5 some territories that are in the Southern Hemisphere or
6 Americans in the Southern Hemisphere? Or is it just based on
7 the fact that the manufacturers are licensed in the United
8 States, and so it doesn't matter where they're selling or where
9 they're using their product?

10 DR. WEIR: I think your interpretation of it is correct.
11 A couple of years ago, as I said, we were approached by one
12 manufacturer that said that they would like to produce a
13 Southern Hemisphere formulation, and they would like to add
14 that to their license. So if they add it to their license,
15 then we would like to follow the same sort of procedure of
16 getting your VRBPAC input on what they produce even though it
17 is not going to be marketed in the United States.

18 MR. TOUBMAN: Thank you.

19 CAPT HUNTER-THOMAS: Are there any other questions
20 before -- thank you, Dr. Weir. Are there any other questions
21 before we move on?

22 DR. MOORE: Yes. This is Patrick Moore. I was just
23 curious about that last comment. So the Southern Hemisphere
24 vaccine cannot be purchased in the United States at all
25 currently?

1 DR. WEIR: This is Jerry Weir again. That is my
2 understanding. You would actually probably have to directly
3 ask the manufacturer how they intend to distribute it, but my
4 understanding is they mainly make this for use somewhere else.
5 And just for -- and maybe this won't clarify it. It's not
6 really a traveler's vaccine either. It is just a license
7 formulation of their vaccine.

8 DR. MOORE: The reason why I'm asking that is we'll see in
9 the next presentation that the antigen change may be important
10 for Northern Hemisphere as well, and I'm just wondering whether
11 this vaccine has the potential to be available for the
12 Northern -- or for the United States.

13 DR. WEIR: Again, I think the manufacturer would probably
14 have to tell you that, should that situation happen. I
15 actually don't know.

16 CAPT HUNTER-THOMAS: Okay. Thank you.

17 Dr. Sawyer, would you like to introduce our next speaker?

18 DR. SAWYER: Yes. Thanks very much, Dr. Weir, for your
19 background.

20 And now for the details of the WHO deliberation and the
21 background for the strains that have been selected, I'd like to
22 re-introduce Dr. Jacqueline Katz from the Centers for Disease
23 Control, who's already been formally introduced. So I will
24 just turn it over to Dr. Katz.

25 DR. KATZ: Okay. Thank you, Dr. Sawyer.

1 Good morning and good afternoon to everybody. I'll be
2 presenting a summary of the wealth of data that was deliberated
3 on last week in Melbourne, Australia, for the 2017 Southern
4 Hemisphere Influenza Vaccine Virus Composition meeting.

5 If you'll turn to the next slide, just some details about
6 the WHO system. This is known as the Global Influenza
7 Surveillance and Response System, or GISRS. This system, which
8 includes 6 WHO collaborating centers, about 143 national
9 influenza centers from 113 countries, 4 essentially regulatory
10 laboratories, and multiple H5 reference laboratories, performs
11 year-round surveillance for influenza viruses, both seasonal
12 and novel influenza viruses that emerge from animals.

13 At the meeting held September 25th to the 27th, last week,
14 the chair was Dr. Takato Odagiri from the WHO collaborating
15 center in Japan. I helped Dr. Odagiri co-chair this meeting.
16 And in total, the nine voting advisors are the directors of the
17 six collaborating centers and three central regulatory
18 laboratories. In addition, there were 24 observers from
19 multiple national influenza centers, H5 reference laboratories,
20 others from the WHO collaborating centers, and ERLs, our
21 academic partners, such as the University of Cambridge, and our
22 veterinary sector partners from OFFLU.

23 Next slide, please. So this slide shows the different
24 countries, areas, and territories that shared viruses with the
25 WHO collaborating centers during this period, from February to

1 August 2017. And you can see that most regions of the world
2 were represented.

3 Next slide, please. This slide gives us the global
4 circulation of influenza viruses for both the Northern
5 Hemisphere season starting around weeks 43, 44 there, shown
6 along the x-axis. And you can see that large peak, first peak,
7 which is the Northern Hemisphere season. Most of the viruses
8 were influenza A viruses, shown in various shades of blue.

9 And for the Northern Hemisphere season, you can see the
10 very dark blue is not subtyped. The slightly lighter, teal
11 blue color is H3N2 viruses. And then the pale blue, which is
12 really barely visible along the x-axis there, are (H1N1)pdm09
13 viruses.

14 So you can see for the Northern Hemisphere season, H3N2
15 viruses predominated. B viruses are shown in various shades of
16 orange. And so you can see that there -- as we see in many
17 seasons, there was a light peak of B viruses in the Northern
18 Hemisphere.

19 Moving towards the right-hand side of this graph, you can
20 see a more modest rise in the number of specimens reported
21 to -- received by WHO labs. And for the Southern Hemisphere
22 season, so you can see, again, the majority is H3N2, with much
23 smaller amounts of influenza B and influenza A(H1N1).

24 Next slide, please. And this just shows proportionally
25 the percentage of viruses by subtypes reported to WHO, most of

1 them influenza A, and the largest proportion being H3N2, and
2 more equal proportions of the influenza B viruses although,
3 here, there's a large proportion where the lineage, the
4 Victoria or B/Yamagata, is not determined. And about 10% of
5 the viruses were influenza A(H1N1)pdm09. So I'll start with a
6 more detailed description of the (H1N1)pdm09 viruses.

7 Next slide. And then next slide again. So, overall, the
8 circulation for (H1N1)pdm09 viruses was at a lower level
9 globally, taking second place to H3N2 viruses for the tail-end
10 of the Northern Hemisphere season and for the majority of the
11 Southern Hemisphere season. But you can see a few regions,
12 particularly Mexico and regions in the Indian subcontinent in
13 particular, that had quite a robust H1N1 season. And the H1N1
14 virus is, in fact, predominated in their season, in countries
15 like India, Bangladesh, Nepal, and the Maldives, for example.

16 Next slide, please. This is the number of (H1N1)pdm09
17 viruses detected by GISRS. And you can see, compared with the
18 black line, which is the 2016 season, which was a high H1N1
19 season, 2017 is quite modest overall. And that's shown by the
20 red solid line.

21 Next slide, please. So this is what we're now referring
22 to as a mega-tree. This is all of the genetic data available,
23 hemagglutinative (H1N1)pdm09 viruses made available to the
24 GISAID EpiFlu database, which is used by the collaborating
25 centers to compare the genetic sequence data of influenza

1 viruses prior to vaccine consultation meetings. This is
2 developed by our colleagues at the University of Cambridge.

3 And the main point is you can see towards the right-hand
4 side of the slide, they're separated out by month starting from
5 January 2016 going up to August 2017. Each little colored bar
6 represents a sequence of a virus isolated and color coded by
7 the region in which it was isolated.

8 So the main point to make here is that the (H1N1)pdm09
9 viruses circulating globally still belong to the 6B clade, and
10 the 6B1 subclade of viruses is still predominating globally,
11 with little if any 6B2 viruses reported in this particular
12 period and just a very small number of older 6B viruses being
13 reported from -- a couple from the U.S. and some from Africa.

14 Next slide, please. So this is a slightly larger tree,
15 although the sequences that are shown here are not
16 proportionally representative of all of the viruses. But you
17 can see just the main trends here. And so the main thing I
18 want to point out, close to the base of the 6B1 portion shown
19 in bold in red is the Michigan/45 virus, which is the vaccine
20 virus that was used in the Southern Hemisphere this season;
21 it's also in the 2017-18 Northern Hemisphere vaccine.

22 And so most of the viruses -- and these are color coded by
23 the months in which they were isolated, so quite a number from
24 May, June, and July at the top of the tree. You can see that
25 there's not a very large amount of genetic diversity happening

1 at the moment among the 6B1 viruses, with the exception of the
2 group at the top of the tree, which according to modelers is
3 the most rapidly growing group of viruses. And these viruses
4 contain substitutions at 74R and 295V within the hemagglutinin
5 protein. And some of these viruses are now also having another
6 substitution of S164T. So these are the viruses to keep our
7 eye on moving forward.

8 Next slide, please. However, when we look antigenically
9 using ferret reference sera made against a panel of different
10 influenza viruses -- and they're shown along the top horizontal
11 bar there across the top of this hemagglutination inhibition
12 table, which I believe this is from the London collaborating
13 center, and then the viruses shown on the right-hand side in
14 red, the corresponding homologous reference viruses against
15 which the sera has been raised. And then below that in black
16 are the test viruses.

17 So these are the circulating viruses that have been grown
18 in cell culture and are being evaluated for how similar or
19 different they are from the vaccine virus Michigan/45/2015. So
20 if you'll turn your attention to the column highlighted in
21 yellow, that shows antisera raised to the vaccine virus
22 Michigan/45, with a homologous titer of 1280, shown in red.

23 And then if you look at the test viruses down the lower
24 part of the column, you can see that the titers there all fall
25 roughly almost within twofold -- most within twofold and all

1 within fourfold of that homologous titer 1280. And that tells
2 us that antigenically, the circulating viruses using this
3 ferret reference antisera are similar to the Michigan/45
4 vaccine virus.

5 There's a number of other antisera here, too, some other
6 6B1 viruses. And generally, they're all showing the same
7 thing. So using ferret reference antisera, we're not seeing a
8 signal for antigenic change.

9 Next slide, please. So if we take all of the HI data from
10 the five different collaborating centers that produced this
11 data, you can see that in this table we see that all of the
12 collaborating centers show 93% or greater relatedness of
13 circulating viruses to the Michigan/45. And in total, so 95%
14 of almost 2,000 viruses tested are showing antigenic similarity
15 with the Michigan/45 vaccine virus, and only approximately 5%
16 of the viruses are showing -- are yielding, reacting with
17 antisera, giving titers that indicate that they are reacting
18 poorly.

19 Next slide, please. And so this is shown visually through
20 antigenic cartography, again, provided by our University of
21 Cambridge partners. And here you can see the older vaccine
22 virus, California/7, the new vaccine virus, Michigan/45 in red,
23 and then color coded in blue are the older viruses and in
24 yellow the more recent viruses circulating in late 2016 and
25 2017. And you can see that they're still forming a tight

1 cluster around the Michigan/45 vaccine virus.

2 Next slide, please. So we also test circulating viruses
3 for how well they are inhibited by antisera, or serum, I should
4 say, from individuals that have been vaccinated with the recent
5 vaccines. And here, we have panels from two Southern
6 Hemisphere regions. The yellow is panels from adults and older
7 adults in Australia. And this actually -- sorry -- this data
8 just shows the adult population, but the results with older
9 adults were similar. And then in Peru, we also had a Southern
10 Hemisphere region where we had a small panel of sera from
11 healthcare workers, also younger adults.

12 And so we've tested these sera against a number of
13 contemporary 6B1 viruses represented by the virus Maldives/446
14 and South Auckland/2, both egg- and cell-propagated viruses.
15 And in this figure, we're comparing the response that was seen
16 against the reference virus, Michigan/45, grown in cells as
17 representing the vaccine virus. If that post-vaccination GMT,
18 geometric mean titer, of the response to Michigan/45 is set at
19 100%, then we've compared the proportionate response against
20 all the other viruses.

21 And so you can see that we're not seeing any reductions.
22 We consider that red bar set at 50%. If we find geometric mean
23 titers that are below that 50%, that indicates that there is a
24 significant difference against the circulating virus compared
25 with the reference vaccine virus.

1 And as you can see, in this case, for both of the panels,
2 either from Australia or Peru, the contemporary 6B1 viruses did
3 not show -- in fact, they showed geometric mean titers that
4 were similar to the Michigan/45 cell-grown virus. And this
5 data from CDC, and we also performed a similar analysis against
6 the egg-propagated Michigan/45 and saw similar results.

7 Next slide, please. So, in summary, from February to
8 September 2017, global circulation of (H1N1)pdm09 viruses was
9 generally low. The vast majority of viruses belonged to the 6B
10 clade. And within that clade, the vast majority of viruses
11 belonged to the subclade 6B1.

12 The majority of recent viruses were antigenically
13 indistinguishable from the current vaccine virus,
14 Michigan/45/2015, using post-infection ferret antisera and HI
15 testing. And then sera obtained from humans that had been
16 vaccinated with the Southern Hemisphere components were all
17 antigenically similar, giving similar geometric mean titers to
18 that seen with either egg- or cell-propagated Michigan/45
19 viruses.

20 So I'll move now onto the H3N2 viruses. And as you'll
21 appreciate in a moment, this is a far more complex picture for
22 the H3N2s than what we're seeing with the H1N1s.

23 Next slide, please. So as I've already mentioned, the
24 H3N2 viruses predominated globally both in the Northern
25 Hemisphere season as well as in the Southern Hemisphere

1 seasons. And you can see quite widespread activity in many
2 parts of the world.

3 Next slide, please. The circulation of viruses in 2017
4 shown in the red bar, these are the number of viruses detected
5 by GISRS. You can see a peak for the Northern Hemisphere in
6 the early weeks of 2017 and another bump around week 27 through
7 30, which is the Southern Hemisphere. And this is noteworthy
8 because rarely do we see a real bump in the number of viruses
9 for the Southern Hemisphere. The surveillance there is less.
10 But this smaller peak does reflect the robust season that is
11 currently winding down, particularly in places like Australia.

12 Next slide, please. So this is just a global snapshot of
13 the different clades and subclades circulating at the moment.
14 H3N2s genetically are getting increasingly more complex, as you
15 will see in a moment. But just to focus your attention, the
16 viruses we've talked about for the Northern Hemisphere season,
17 so the older viruses started out in the 3C.3 group. That's
18 shown in red. And as you can see, we see virtually none of
19 those anymore. I think there was one isolated in Asia, but you
20 can hardly pick it up in this pie chart.

21 We also had the 3C.3a viruses, shown in purple. You'll
22 remember several seasons ago, we had the Switzerland/2013
23 vaccine virus. That was a 3C.3a virus. And except for North
24 America, where we did still see a small number of these
25 viruses, they also appear to be dying out and very small

1 numbers detected in other regions.

2 So the viruses that are still predominating are the 3C.2a
3 clade, shown in the dark orange, and within this clade is the
4 subclade 3C.2a1. And so you can see the varying proportions of
5 these two groups in different parts of the world. Asia and
6 Oceania had approximately equal circulation of 3C.2a and 2a1,
7 whereas Africa saw more 3C.2a, and Europe, North America, and
8 Central/South America had a predominance of 3C.2a1.

9 Next slide, please. So this just really highlights the
10 complexity of what we're seeing at the moment. So we have
11 within each of the 3C.2a and 2a1 clades that I've been telling
12 you about, we've further subdivided into additional genetic
13 subgroups. And so the 3C.2a1 viruses at the top of this tree
14 and highlighted in the red boxes at the right-hand side of the
15 screen, you can see that there are at least five different
16 genetic groups.

17 We've called out five genetic groups that we're tracking
18 because we see these having increased in size over the last --
19 within the last year. But there's different dynamics occurring
20 within each genetic group, and each genetic subgroup is maybe
21 circulating differentially throughout the world. And I'll show
22 you that information in a moment.

23 But so you can see, we have the group referred to -- so
24 the 3C.2a1s are really the base. Sequence change is about
25 halfway down the tree. You can see a box that says N171K,

1 I406V. These are the signature changes that occurred as the
2 3C.2a1 viruses emerged.

3 In addition, and I know it's hard for you to see this on
4 the tree, most circulating viruses at the moment also have a
5 substitution at 121. And that is defining the majority of the
6 3C.2a1 viruses. In addition, there is additional subgroups.
7 And I won't call out of all of these different genetic
8 subgroups, but signature changes are highlighted in the boxes.

9 Similarly, if you look at the bottom half of the tree for
10 the 3C.2a viruses, there are at least three genetic groups.
11 One is represented by this at the bottom, N31S, D53N. There's
12 also a number of additional amino acid changes which are too
13 numerous to talk about in one go.

14 But you'll see that there's quite a bit -- if you look at
15 the colored bars, there's quite a bit of pink there, and that
16 represents recently circulating viruses from Oceania. So this
17 subgroup predominated in Oceania amongst the 3C.2a viruses but
18 haven't really been seen anywhere else in the world. And it is
19 believed by modelers to not be likely to become more
20 predominant globally.

21 Then there's the 144K, 121K group and then another group
22 referred to as 131K and 142K. At the very bottom of the tree,
23 there's the 3C.3a group. And as I mentioned earlier, these are
24 really not predominating anywhere in the world right now.

25 So next slide. So just to highlight the complexity of

1 these genetic subgroups, this is representing now just taking a
2 snapshot of the 3C.2a viruses. So this is 3C.2as that do not
3 include the 3C.2a1 viruses. And you can see the three
4 different genetic subgroups that I called out in the previous
5 figure, and they're color coded.

6 And you can see that there's really different proportions
7 of these viruses circulating in different parts of the world,
8 with North America and Asia and Central/South American having
9 the 131K, 142K viruses predominating. But in Oceania, as I
10 mentioned, the 31S group is predominated. And elsewhere, the
11 121K, 144K has predominated, particularly in Europe and with
12 small numbers also in Africa.

13 If we turn to the next slide, you can see this gets even
14 more complex, with more colors for the 3C.2a1 viruses. And
15 this is CDC's breakout of the different genetic subgroups. So
16 we've actually broken it down into more than was just included
17 in the previous phylogenetic tree. But you can see again that
18 a lot of the viruses shown in the pale pink that are
19 circulating globally belong to the 92R, 121K, 311Q subgroup,
20 with varying proportions.

21 For example, in Europe, they saw a different genetic
22 subgroup shown there in the sort of greenish color, and that
23 was the 121K, 13K group. And elsewhere, another group, there's
24 also the 3C.2a1 consensus group, which is all viruses that are
25 the initial progenitors of this clade. So a very mixed and

1 diverse and geographically distinct picture for circulation of
2 these different genetic subgroups.

3 Next slide, please. So this is some summary data I'll
4 show you, first of all, and then I'll show you some actual
5 examples of our HI and virus neutralization data. But this is
6 a summary of all the antigenic characterization, first of all,
7 in this first set of tables, looking at how well the
8 circulating viruses are related to the existing vaccine virus
9 represented by the reference cell-propagated virus, Hong
10 Kong/4801-like virus.

11 And you can see -- I don't think we need to go through all
12 the numbers, but the top part of the table shows the results
13 using the hemagglutination inhibition assay. And you can see
14 there that the vast majority of over 1300 viruses tested are
15 antigenically similar to the Hong Kong/4801-like reference
16 virus propagated in cells. And if we do test viruses using a
17 virus neutralization test, the same is true.

18 As a reminder, we're using this addition test, the virus
19 neutralization test, because many of the viruses have -- H3N2
20 viruses circulating globally at the moment have properties
21 whereby it's very difficult or not possible to test them using
22 the hemagglutination inhibition assay. So we have to move to a
23 different type of assay to evaluate them antigenically. And,
24 therefore, we have additional data with the virus
25 neutralization test, far fewer numbers of viruses tested, but

1 again, a reasonable number when we combine all of the data from
2 the different collaborating centers.

3 And then, again, overall, by this test you can see -- the
4 similar result is what we see with the HI in that 86% of the
5 viruses were well inhibited by antisera raised to the cell-
6 propagated Hong Kong reference virus. And these data indicate
7 to us that, antigenically, we're not seeing a difference with
8 the currently circulating 3C.2a or 2a1 viruses relative to the
9 reference Hong Kong/4801-like viruses.

10 Next slide, please. However, we see a slightly different
11 picture when we now compare the circulating viruses to
12 reference viruses that are propagated in eggs. And these are
13 more representative of the viruses that are used for egg-based
14 vaccine production.

15 Again, the top part of the panel is shown by HI. Overall,
16 you can see that the proportion of viruses that are well
17 inhibited by antisera raised to the egg-propagated Hong
18 Kong/4801-like virus is generally quite a bit lower than what
19 we saw in the previous table. And overall, 51% of viruses
20 tested were similar. And roughly 50% of viruses were
21 antigenically different from or poorly inhibited by antisera
22 raised to egg-propagated Hong Kong/4801-like virus.

23 And this difference is exacerbated even more in the virus
24 neutralization tests. This is in part due to issues we have
25 with the titers to the egg-propagated viruses in virus

1 neutralization tests tend to be very high. So the fold
2 differences with circulating viruses that are all grown in
3 cells appears to be even greater.

4 So in this table you can see when we measure by the virus
5 neutralization test, only about 35% of the viruses tested were
6 well inhibited by the antisera raised to Hong Kong/4801-like
7 egg-propagated viruses. So, taken together, these data tell us
8 that, antigenically, the viruses have not moved on, but there
9 is a difference when we compare the circulating viruses with
10 the reference viruses that represent the egg-propagated viruses
11 that are used in the vaccine.

12 And this is data -- the next table -- the next slide,
13 please. Okay. So this is, again, a more complex table, an
14 example of HI data, a table shown at CDC. And I'll just
15 highlight a couple of things. As I showed you with the H1N1
16 data, the ferret antisera are shown across the top horizontally
17 of the table, and the test viruses, the reference viruses and
18 then the test viruses, are shown down the vertical line.

19 If you just look at the far right hand, you'll see the
20 viruses are also categorized by the HA group, the 3C.2a, 2a1,
21 or 3C.3a that they belong to, and then broken down even
22 further, the signature changes that represent the different
23 genetic subgroups that we've been keeping an eye on.

24 But the bottom line of this table is if you look at the
25 highlighted numbers in yellow and focus on the fifth column in,

1 and this is antisera raised to our Hong Kong/4801-like
2 reference virus, Michigan/15, it has a homologous -- the
3 antisera raised to Michigan/15 has a homologous titer of 320.
4 And if you cast your eye down the column, you can see there are
5 a few what we call low reactors, viruses that react with the
6 sera and titers that are eightfold or greater lower than the
7 homologous titer.

8 And in this table, a number of these viruses are the 3C.3a
9 viruses. And we're seeing, particularly with the CDC data
10 because we had the opportunity to test more 3C.3a viruses, that
11 quite a number of these viruses are antigenically distinct from
12 the vaccine reference viruses. But the majority of 3C.2a and
13 2a1 viruses, even those belonging to these different genetic
14 subgroups, are antigenically similar to the Hong Kong/4801
15 cell-propagated reference virus, Michigan/15.

16 Next slide, please. This is shown again. This is again
17 CDC data. This is now a focus reduction. It's a virus
18 neutralization assay. And if you'll look at the highlighted
19 columns again, this table is set up in the same way as the HI
20 table. And again, our reference antisera to the cell-
21 propagated Hong Kong/4801-like virus, Michigan/15, has a
22 homologous titer of 2560.

23 And if you look down the column, most of the circulating
24 viruses tested -- and these are viruses from -- a couple from
25 the U.S. but also from South America and Africa and Europe.

1 And you can see that the majority of these viruses, with one
2 exception down the bottom there, which is a 3C.3a virus, but
3 all the other 3C.2a1 and 2a viruses are reacting at titers that
4 are within fourfold of the homologous titer 2560, indicating
5 that these were antigenically similar to the Hong Kong 4801
6 reference virus.

7 However, if we look at the very first column there, it's
8 not highlighted. It says A/Hong Kong/4801. This is antisera
9 raised to the egg-propagated Hong Kong/4801 reference virus.
10 It has a very high homologous titer of 1280. And you can see
11 the majority of circulating viruses are giving -- reacting at
12 titers that are indicating that they are poorly inhibited by
13 this reference antiserum.

14 And just one more. So next slide, please. So I've
15 included this slide. This is another virus neutralization
16 data. This is by the Melbourne collaborating center. And just
17 to show you some data with the reference virus
18 Singapore/INFIMH-16-0019. It's highlighted there in the red
19 bar. And you can see the homologous titer of this antisera is
20 1280. And if you look down the list of test viruses here,
21 again broken out by their different genetic subgroups and their
22 clade or subclade, you can see that antisera raised to this new
23 3C.2a1 virus actually does a very good job at inhibiting the
24 circulating viruses tested.

25 So next slide, please. So this is a summary of data from

1 the Melbourne collaborating center. And if you look down the
2 column that says "Antisera against," there's a number of cell
3 and egg pairs. That means these are viruses that have been
4 isolated from the same original clinical material either in
5 cells or eggs. So we have a true pair to compare.

6 In some cases, we don't have a pair; we just have an
7 egg-propagated virus or a cell-propagated virus. But there's
8 at least six different egg-propagated viruses here that were
9 compared with the Hong Kong/4801 egg-propagated virus. And
10 this is just a subset of the egg isolates that were produced
11 amongst the different collaborating centers. There's at least
12 another five or six that have been evaluated in the same way.

13 And the bottom line is what we're looking for is a virus
14 whose reference antisera inhibits the circulating viruses at a
15 higher proportion than what we're seeing with antisera raised
16 to the Hong Kong/4801 egg-propagated virus. And you can see,
17 if you look at the horizontal rows here highlighted in yellow,
18 the second one gives the proportion of viruses that were poorly
19 inhibited. So that's the last column that says greater than or
20 equal to eightfold. If you'll look down that column and look
21 against the Hong Kong/4801 egg antisera, you'll see that 39% of
22 the viruses were poorly inhibited by this antisera.

23 If you look at some of the antisera raised to other egg-
24 propagated viruses, above that, there's a Brisbane/32 egg, 64%
25 were poorly inhibited. If you look further down, there's a

1 Norway/3806. It's just in white. It's 94% of the viruses
2 tested were poorly inhibited. And so on. Another Singapore
3 virus, GP2646, 99% of the viruses tested were poorly inhibited.

4 So this is telling us that these representative egg
5 isolates that are being produced are no better than the Hong
6 Kong/4801, and we're really looking for something that might do
7 better than Hong Kong/4801. And so the only virus that's shown
8 in this table -- and it was really true for other viruses that
9 I haven't shown here, but a number of viruses that were
10 generated either at the London collaborating center or worked
11 up at CDC, and none of these viruses behaved any better than
12 the virus shown in blue here, which is the Singapore INFIMH-16-
13 0019/2016 virus, where although it's a relatively small number
14 of viruses tested to date, because it's a recent reference
15 virus, very few, so only 4%, were poorly inhibited, suggesting
16 that this egg-propagated virus is a better match with the
17 circulating viruses at this time.

18 Next slide, please. So just moving to a bit more of the
19 genetic analysis, this is a simplified phylogenetic tree of the
20 HA gene. And just to show you again, it's like the mega trees
21 we saw before. The 3C.3a viruses that aren't circulating
22 widely are shown at the bottom of the tree there, with
23 Switzerland/2013 being that reference virus and a past vaccine
24 virus.

25 About a third of the way up among the 3C.2a viruses is the

1 Hong Kong/4801/2014, which is the current vaccine virus. And
2 then above that at the base of the 3C.2a1 genetic subgroup is
3 this new Singapore/INFIMH-16-0019 virus. And this virus has
4 the signature changes as I mentioned, the 171K and the 121K,
5 representing most of the 3C.2a1 viruses circulating now. In
6 addition, it's got a substitution at 142G.

7 So next slide, please. So I'm going to move briefly to
8 the neuraminidase. I think this is the first time we have
9 included antigenic data on the neuraminidase, and this is being
10 made available by Maryna Eichelberger and her colleagues at
11 FDA. And they've been able to do some limited antigenic
12 characterization of neuraminidases of recently circulating
13 3C.2a and 2a1 viruses.

14 And the bottom line is that they're finding that the
15 neuraminidase is antigenically distinct from the Hong
16 Kong/4801/2014 virus. And I'll show you why that is
17 genetically in just a moment.

18 But you can read this pretty much the same way you would
19 read an HI, although it's performed by a different assay which
20 measures antibodies' ability to inhibit the neuraminidase
21 activity. It's called an enzyme-linked lectin assay, or ELLA.
22 And it's performed using reassortants that have an irrelevant
23 HA, so we don't get interference from antibodies against the
24 HA.

25 And so, just briefly, ferret antisera was produced against

1 either the Hong Kong/4801/2014 virus or a Switzerland/2013
2 virus. And the main take-home message here is if you look at
3 the homologous titer of the Hong Kong ferret antisera to the
4 Hong Kong/4801/2014 virus at 1280 and then look at the three
5 bottom viruses that are from 2016 and 2017, you can see that
6 there's a greater than -- or eightfold reduction in the titer,
7 suggesting that the neuraminidase of these more contemporary
8 viruses are antigenically different from Hong Kong/4801.

9 And this is also borne out by some limited analysis with
10 adult sera from humans that received recent vaccines containing
11 the Hong Kong/4801-like vaccine component. And again, these
12 three bottom viruses from 2016 and '17 are showing reduced
13 geometric mean titers compared to the titer of 226 against the
14 Hong Kong/4801 virus.

15 Next slide, please. So this is a phylogenetic tree. And
16 again, it's a very dense tree, so I know there's no way you can
17 read the individual names there. But the point to make here is
18 the arrow at the bottom that shows the Hong Kong/4801 vaccine
19 virus is at the base of the tree and actually falls within the
20 3C.3a genetic group whereas the Singapore/INFIMH-16-0019 virus
21 falls within the 3C.2a1 group. So this was something unusual
22 about the Hong Kong/4801 itself, that its neuraminidase was
23 actually more similar to older 3C.3a viruses.

24 Next slide, please. So, finally, for the H3N2s, we also
25 looked at human serology, so this is showing here post-

1 vaccination geometric mean titers measured by the
2 hemagglutination inhibition assay from people vaccinated with
3 either the 2016-17 Northern Hemisphere vaccine or the 2017
4 Southern Hemisphere vaccine. Both of these vaccines contain
5 the Hong Kong/4801-like virus as the recommended H3N2
6 component.

7 And here we're looking at the ability of the virus, of
8 test viruses along the horizontal x-axis there to react with
9 the individual human sera from individuals that received the
10 Hong Kong/4801-like vaccine virus. And we're comparing here to
11 the egg-propagated Hong Kong/4801. So that's set at 100% on
12 the far left-hand side of this figure.

13 And you can see that because most of these are cell-
14 propagated vaccine viruses that are tested, we see a very
15 substantial reduction compared to the reference egg-propagated
16 virus, with everything falling below the 50% mark.

17 Next slide, please. If we look at this comparison where
18 we compare against the cell-propagated Hong Kong/4801, and that
19 is set at 100%, and that's the smallish bars set at 100 there
20 for the cell-propagated viruses, either Hong Kong/4801 or
21 Michigan/15, you can see that, still, there is a number of
22 cell-propagated viruses, for example, Delaware/32,
23 Washington/16, some of the Singapore viruses there, that are
24 showing -- and a Chinese virus that I won't pronounce because
25 I'll butcher it, a couple of Chinese viruses -- where we're

1 seeing overall reduced geometric mean titers compared to the
2 geometric mean titers of the cell-propagated Hong Kong/4801-
3 like viruses.

4 I'll also just call out you can see on the far left there
5 a direct comparison of the Hong Kong -- of the titers we see
6 against the Hong Kong/4801 egg-propagated virus versus the
7 cell-propagated virus. And this is one of our challenges is
8 that the cell-propagated viruses are, in general, giving quite
9 low titers when we do this sort of analysis compared with the
10 reference virus raised in eggs.

11 So our next slide. So, in summary, I've told you that
12 H3N2 viruses predominated in many countries and caused severe
13 epidemics, for example, in Hong Kong and in Australia in recent
14 months. I didn't show you, but we did discuss at the meeting
15 there were interim Southern Hemisphere vaccine effectiveness
16 estimates provided to the group. And these were quite low, in
17 the order of about 20% for Australia. And this is quite a bit
18 lower than what we've seen for H3N2 viruses even in other
19 Southern Hemisphere seasons. So there was a general sense that
20 for H3N2, the vaccine effectiveness was below par.

21 The majority of influenza viruses collected belonged to
22 the phylogenetic clade 3C.2a and the subclade 3C.2a1. And when
23 we used ferret antisera raised against cell-propagated 3C.2a
24 viruses, such as the Hong Kong/4801/2014, we saw that most
25 viruses were well inhibited in both the HI and the virus

1 neutralization test. And this included multiple genetic
2 subgroups within the 3C.2a and 2a1 viruses.

3 And this data suggested that there's no true antigenic
4 drift amongst these viruses occurring at this time. However,
5 if we used ferret antisera raised to the egg-propagated Hong
6 Kong/4801 virus, then this antisera poorly inhibited many of
7 the viruses tested. In HI, it's close to 50% and well over 50%
8 by the virus neutralization, signaling that there's a problem
9 with the egg-adapted virus.

10 So next slide, please. So as you know, egg propagation is
11 known to introduce additional changes that can affect
12 antigenicity, and this is particularly problematic, as I've
13 just demonstrated, for the H3N2 viruses. And it's becoming
14 increasingly more problematic with recent circulating viruses.

15 And so we've found that the ferret antisera raised to a
16 new virus, the egg-propagated Singapore/INFIMH-16-0019,
17 provided broader coverage against recently circulating viruses
18 from both 3C.2a and 2a1 groups compared with antisera raised to
19 the former 3C.2a Hong Kong/4801-like.

20 And, in addition, sera obtained from post-influenza-
21 vaccinated human serum panels failed to inhibit a number of
22 circulating viruses when we looked at the cell-propagated
23 viruses compared with the cell-propagated reference, Hong
24 Kong/4801-like virus. And I didn't show you the data, but this
25 was also true when we looked at virus neutralization tests.

1 So next slide, please. So I'll try and wrap this up and
2 talk a little more quickly about the influenza B viruses.

3 Next slide, please. So, again, although there was fairly
4 wide circulation of influenza B viruses globally in the
5 reporting period, influenza B viruses were invariably
6 subdominant to the influenza A viruses that were circulating in
7 particular regions, mostly the H3N2s.

8 Next slide, please. And you can see here shown in the red
9 line, which represents the influenza B viruses for 2017, that
10 the number of viruses actually detected by GISRS were lower
11 than what we've seen in previous seasons.

12 Next slide, please. This is showing data from WHO looking
13 at the proportion of the different lineages, either the
14 B/Yamagata and B/Victoria lineage. The actual numbers are
15 shown in that small table in blue. And as you can see, only a
16 subset of viruses are actually -- we actually have the lineage
17 determination. But we feel that this is probably generally
18 representative of different regions.

19 And you can see there that the B/Yamagata lineage
20 predominated globally and primarily in Europe, Oceania, and
21 North America, while the B/Victoria was a little less
22 prevalent. But in regions in Asia and Africa, B/Victoria was
23 predominant.

24 Next slide, please. And so we'll talk about the
25 B/Victoria lineage viruses.

1 Next slide. And so, again, this is one of the large trees
2 which shows all of the phylogenetic HA gene data that is
3 available at this time in GISAID. Again, we've color coded the
4 viruses by distinct little bars on the right-hand side by the
5 month in which the virus was collected and by the region it was
6 collected in.

7 All of the B/Victoria lineage viruses currently still
8 belong to the V1A clade, and that's the clade that's circulated
9 for a number of years now. And overall, there's not a lot of
10 genetic diversity, but there's a couple of exceptions that have
11 become notable in this past reporting period.

12 The first is a group of viruses that have acquired a
13 substitution at 180V. And then you can see them highlighted
14 there. There's a little bar indicating deletion 162/163.
15 These are viruses that really largely circulated in the U.S. in
16 the Northern Hemisphere season particularly at the end of the
17 season. And these are viruses that have actually acquired a
18 sixth nucleotide deletion, which results in two amino acids at
19 residues 162 and 163 being deleted.

20 Independently, we also saw if you look further up in the
21 tree, there's another very small group of viruses. These are
22 only three viruses, in fact. It's this DEL 162/163/164. This
23 is an independent introduction because these are viruses from
24 Hong Kong. They acquired a different change at residue 180,
25 from an I to a T, and then they acquired a three amino acid

1 deletion in the HA protein. These viruses, we only have three
2 examples of these, and they have not been seen further.

3 Next slide, please. So this just shows the global
4 distribution of the B/Victoria deletion viruses. First of all,
5 if you look over on the right-hand side, there's a circle that
6 says 3. There's a triple deletion viruses that were seen in
7 Hong Kong. And even though they had quite a large, robust
8 season, albeit it was predominantly H3N2, these viruses did not
9 appear to be spreading anywhere in the region and were quite
10 localized.

11 For the double deletions, and these are the ones that are
12 shown in the various shades of pink and red, you can see that
13 the vast majority of these came from the United States, in
14 fact, with small numbers in other Northern Hemisphere regions,
15 a couple in Canada, a few in Mexico, and very small numbers in
16 some Central and South American countries. One virus only was
17 seen in Australia. And a small cluster of five viruses of
18 these double deletions was seen in Norway during the Northern
19 Hemisphere season but nowhere else in Europe or other regions
20 of the world, suggesting that these viruses are really not
21 spreading very widely at this time.

22 So next slide, please. So this is again antigenic
23 characterization of B/Victoria lineage viruses. This is some
24 HI data from CDC. All of the viruses highlighted in yellow are
25 viruses of the V1A group. So the test viruses are the

1 circulating viruses. And you can see that compared with
2 antisera raised to either cell- or egg-propagated Brisbane/60
3 -- this is the far left-hand side -- you can see that these
4 antisera generally react well with the circulating viruses
5 highlighted in yellow. But the viruses that are not
6 highlighted, these are antigens like 14 through 18, these are
7 the viruses that have the double deletion in the hemagglutinin.
8 And here we're seeing eightfold or greater reductions with
9 antisera raised to the reference vaccine viruses,
10 Brisbane/60/2008.

11 If you look over at the right-hand side of the column, of
12 the table, we have some viruses highlighted in green. And
13 antigens 5 and 6 are our reference viruses that represent --
14 this is Maryland/15/2016 viruses, one isolated in eggs, one
15 isolated in cells. And when we raise antisera to these
16 viruses, we can see that the deletion viruses now are generally
17 better recognized by this antisera than they are by antisera
18 raised to the Brisbane/60.

19 However, antisera raised to these viruses, these deletion
20 variants, do not cover the other circulating viruses very well.
21 So the majority of viruses in this table are not well inhibited
22 by this antisera, suggesting that we have this two-way
23 antigenic difference.

24 Next slide, please. So this is a little more data from
25 the London collaborating center. And they were able to raise

1 antisera also to a representative virus of the triple deletion
2 viruses from Hong Kong. This is the Hong Kong 269 virus.

3 If you'll look at the titers that are highlighted in that
4 salmony pink color, these are the homologous titers to the Hong
5 Kong/269 virus, which is the triple deletion virus. And you
6 can see that they give good homologous titers, but the sera are
7 reacting poorly with any other viruses, including a virus below
8 that, the Norway/2409, which is a double deletion.

9 So this data is telling us not only are these deletion
10 viruses distinct from the Brisbane/60 vaccine viruses or
11 reference viruses, the triple deletion virus is also
12 antigenically distinct from the double deletion virus.

13 So next slide, please. So the HI data I just talked to
14 you about is presented graphically here. This is the CDC data
15 where we tested a larger number of the double deletion viruses.
16 So you can see that the majority of viruses are still tightly
17 clustered around the red Brisbane/60/2008 vaccine virus, with
18 the viruses in yellow representing the more recent 2016 and '17
19 viruses, but that there's a sub-cluster of viruses that are
20 more closely clustered around the light blue large dot, which
21 represents the Maryland/15, so this is our reference deletion
22 virus. So you can see very clearly the antigenic difference
23 between the double deletion and the other majority of
24 circulating viruses that fall into the V1A clade.

25 Next slide, please. So if we look at the data taken from

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1 all collaborating centers and just remember that most
2 collaborating centers had no deletion variant viruses to
3 assess, and if we focus on the right-hand side of this table
4 and look at the proportion of viruses that were well inhibited
5 by antisera raised to cell-propagated Brisbane/60/2008, we see
6 that the vast majority, 91% of over 1300 viruses tested were
7 well inhibited by the Brisbane/60/2008-like reference virus.

8 In general, there's a lower proportion if we look at the
9 left-hand side of the table and compare with antisera raised to
10 egg-propagated Brisbane/60. The proportion of viruses, it's
11 still a majority, but it's reduced to 66%. And that's because
12 for a couple of collaborating centers, primarily the CRICK, so
13 the London and Australian collaborating centers, their
14 proportions using the antisera that they produced are
15 particularly low.

16 But overall, if we compare to the cell-propagated
17 reference vaccine virus, the data suggests that these viruses
18 are not -- by and large are not antigenically different, with
19 the exception of the deletion viruses I've mentioned.

20 Next slide, please. So this is looking at some human
21 serology studies similar to what I've shown you for the
22 influenza A viruses. We had panels of sera from individuals
23 that were vaccinated either with the 2016-17 Northern
24 Hemisphere or 2017 Southern Hemisphere quadrivalent vaccines.
25 So these all contained the Brisbane/60/2008 component.

1 And you can see when we compare on the left-hand side
2 here, comparing the geometric mean titers of the test viruses
3 compared to the egg-propagated B/Brisbane/60/2008 reference
4 virus set at 100%, and all of the panels are giving titers that
5 are above that 50% reduction, suggesting that the geometric
6 mean titers took different circulating viruses similar to the
7 B/Brisbane/60/2008.

8 Children's panels in green, there's some that look like
9 they're 0, but they were actually not tested because of the
10 limited amounts of children's sera available in different
11 institutions to test.

12 So, interestingly, the viruses that gave good geometric
13 mean titers post-vaccination included the double deletion
14 viruses that were tested. And this is shown by the Colorado/6
15 and the Maryland/15 viruses. And if you look at the far
16 right-hand side of this first figure, it says double deletion
17 egg. You can see that the geometric mean titers of all these
18 viruses collectively are above the 50% line.

19 So at CDC, we're a little surprised by this because we can
20 see clear antigenic difference using ferret reference antisera.
21 And previously, in the Northern Hemisphere season, in February,
22 we had a virus, a representative double deletion virus grown in
23 cells, the New York/52, and that gave geometric mean titers
24 compared with the vaccine virus.

25 So we went back and did some additional testing. And

1 that's shown on the panels on the right-hand side. We're now
2 comparing these viruses compared with the cell-propagated
3 Brisbane/60/MDCK virus set at 100%. But again you can see that
4 the more recent viruses, the Maryland/15 and the Colorado/6,
5 these are all double deletion viruses. The majority of them
6 are giving titers that are similar and are not substantially
7 reduced compared with the titer to the vaccine reference virus.

8 So next slide, please. Just briefly I'll turn to the
9 B/Yamagata lineage viruses.

10 Next slide. And here, this is again a very high-level
11 phylogenetic tree that shows all of the data available. And I
12 just really want to point out that the recently circulating
13 viruses, which you can see if you look at the bars on the
14 right-hand side of this figure, the viruses circulating, say,
15 from February 2017 to August 2017, are all in the Y3 clade. So
16 that hasn't changed much. And really there's very limited
17 genetic diversity in the B/Yamagata viruses at the moment. All
18 of the more contemporary Y3 viruses have substitutions at 173Q
19 and 252V, and that hasn't changed from the previous reporting
20 period.

21 Next slide, please. So just one quick hemagglutination
22 inhibition test. This is from the Melbourne collaborating
23 center. So the Phuket/3073 is the reference virus. This is
24 the cell-propagated, and it's highlighted in yellow. It has a
25 homologous titer of 160. And if you look at all the test

1 antigens, and these are viruses from New Zealand, Australia,
2 and a couple from Asia, you can see that all of the circulating
3 viruses are well inhibited by antisera raised to the reference
4 B/Phuket/3073 cell-propagated virus.

5 And this is also true if you look at the column on the
6 left of that, column F. This is antisera raised to egg-
7 propagated B/Phuket/3073. And again, the majority of viruses,
8 with just one exception there or a couple of exceptions, are
9 well inhibited by this antisera, indicating that the
10 circulating viruses are antigenically similar to the
11 B/Phuket/3073 reference viruses representing the vaccine
12 viruses.

13 Next slide, please. And this is shown with some
14 additional data, which is shown in antigenic cartography. This
15 is HI data from the collaborating center in Tokyo. And you can
16 see, with the big bull's-eye being in red, the Phuket/3073/2013
17 reference virus and the more contemporary 2016 and '17 viruses,
18 shown in yellow, are generally closely surrounding that red
19 spot, representing the vaccine virus.

20 Next slide, please. And so, just again showing you the
21 breakout of this data for the different collaborating centers.
22 Again, if you look at the antisera raised to the cell-
23 propagated Phuket/3073 on the right-hand side of the table,
24 we've tested over 1300 viruses, and 97% of them overall were
25 characterized as being Phuket/3073-like. And if we compared

1 with antisera raised to the egg-propagated Phuket virus, we get
2 a very similar result, with 95% of the viruses being well
3 inhibited by this antisera.

4 Next slide, please. And finally, looking at the human
5 serology data, this is again individuals that were vaccinated
6 either with the 2016-17 Northern Hemisphere or 2017 Southern
7 Hemisphere vaccines. These are quadrivalent vaccines with the
8 B/Yamagata lineage. And you can see again that we're not
9 seeing any significant trend that any of the circulating
10 viruses are reacting less well or giving -- the human sera is
11 yielding geometric mean titers against the circulating viruses
12 that are similar and not less than 50% compared with the
13 Yamagata B/Phuket reference viruses.

14 So next slide, please. So, finally, just to summarize the
15 B/Victoria and B/Yamagata lineages, overall they circulated at
16 varying levels and in different proportions in most countries.
17 The B/Victoria lineage viruses predominated in Asia and Africa.
18 B/Yamagata lineage viruses predominated globally and
19 predominated in Europe, Oceania, and the Americas.

20 The B/Victoria lineage viruses all belonged to the genetic
21 clade 1A. We're not seeing a lot of genetic or antigenic
22 diversity except for the subset -- a small group of viruses
23 with amino acid deletions in the HA proteins. And these
24 viruses were poorly inhibited by ferret antisera raised against
25 the cell culture-propagated reference virus,

1 B/Brisbane/60/2008, although as I showed you in the map showing
2 the circulation, these viruses really haven't taken off and are
3 not spreading globally at this point.

4 For the human serology studies, I showed you that the HI
5 geometric means against representative recent B/Victoria
6 lineage viruses were similar to the HI titers against the
7 B/Brisbane/60 reference viruses.

8 Next slide, please. And for the B/Yamagata lineage
9 viruses, all of the HA genes belonged to the genetic clade 3.
10 There was very limited genetic diversity among the B/Yamagata
11 lineage viruses at this time. And recently circulating viruses
12 are well inhibited by ferret antisera raised against the
13 B/Phuket/3073/2013 reference viruses, representing the vaccine
14 viruses.

15 Similarly, the human serology studies show that the HI
16 GMTs against most representative recent Yamagata lineage
17 viruses were similar against the cell-propagated
18 B/Phuket/3073/2013 virus.

19 Next slide, please. So based on these data, as Jerry has
20 already mentioned, the recent consultation made the following
21 recommendations for the 2018 Southern Hemisphere influenza
22 season:

23 It was recommended for the (H1N1)pdm09 virus that a
24 Michigan/45/2015-like virus be included; for H3N2 viruses, a
25 Singapore/INFIMH-16-0019/2016-like virus be included; and for

1 the trivalent inactivated vaccine, that the Yamagata lineage
2 B/Phuket/3073/2013-like virus be included. For quadrivalent
3 vaccines that contain two components, they would contain the
4 above or just mentioned three components as well as the
5 B/Victoria lineage virus, B/Brisbane/60/2008-like virus.

6 Next slide, please. So that wraps up my presentation.
7 I'd just like to acknowledge the huge amount of work that was
8 made by all of the collaborating centers as well as the
9 headquarter staff in Geneva and our other colleagues, the
10 national influenza centers, that play a very important part in
11 GISRS, our University of Cambridge partners, the essential
12 regulatory labs, and in the U.S., our collaboration with the
13 Association of Public Health Laboratories and our USAFSAM
14 partners. Also, at this time we included fitness forecasting
15 from our predictive modelers in Europe and the U.S. And
16 finally, I'd just like to acknowledge all of our staff at the
17 flu division at CDC.

18 I'll take questions. Thank you. That's it.

19 CAPT HUNTER-THOMAS: Thank you, Dr. Katz.

20 DR. KATZ: Okay.

21 CAPT HUNTER-THOMAS: Dr. Sawyer?

22 DR. SAWYER: Are you able to hear me?

23 CAPT HUNTER-THOMAS: Yes, we are.

24 DR. SAWYER: Great. I would like to, first of all, thank
25 Dr. Katz for, as usual, an amazing ability to take us through a

1 very complex set of data very quickly and that we appreciate
2 that very much, those of us who don't live in the influenza
3 world on a daily basis. So thank you very much for that.

4 So, again, let's ask the Committee if there are questions
5 for Dr. Katz?

6 DR. MOORE: Yes, Mark, I have a question. This is Patrick
7 Moore.

8 DR. SAWYER: Please go ahead.

9 DR. MOORE: Jackie, first, I've been on this Committee for
10 4 years, and you always amaze me by being able to go through
11 this talk, similar talk, extremely complicated, and you do such
12 a good job. And I want to thank you for that.

13 I want to go, I want to -- I actually have two questions,
14 one about the H1N1, and then the second, a little more
15 elaborate question, will be on the H3N2 vaccine components.

16 First, I wanted to go to slide 12, which is the H1N1.

17 DR. KATZ: Right.

18 DR. MOORE: And it shows the low titer responses from the
19 different centers. And it looks like everything is fine except
20 for CNIC, which is in China. And also, I noticed in an earlier
21 slide, I think it's slide -- oh, it's slide number 7 -- that
22 China is a hotspot, according to this graph for H1N1. So I'm
23 wondering, going back to 12, whether you're worried if there's
24 a Michigan escape -- starting to come out of China, or does
25 that concern you at all?

1 DR. KATZ: Yeah, thanks, Patrick. That's a good eye. So,
2 first of all, just with respect to slide 7, which is the
3 activity, this needs to be taken with a little bit of --
4 because China did not report a predominant (H1N1)pdm09 season.
5 The way this is reported, it's reported to WHO by their
6 regional epidemiologists. And so if they see any H1N1
7 activity, it can be marked as widespread. That means they saw
8 it in many places. It didn't mean for China in particular that
9 the activity was high.

10 In other regions in Asia that are shown as regional, I
11 would say that they did have a predominant H1N1 season. But
12 yeah, we did all notice that -- now turning to slide 12 -- that
13 there was a slight up-tick of viruses from China. And we're
14 keeping a close eye on this. There was nothing genetically
15 different about these viruses.

16 So you'll remember that in order that we really believe
17 there's a drifted virus occurring, we want to see both
18 antigenic changes and then signature genetic changes. And so
19 at this point, we haven't seen signature genetic changes, the
20 genetic variability that was -- or diversity that was seen
21 globally was also seen in China. And so there wasn't a lot of
22 evidence that a new genetic group is emerging. But we are
23 keeping our eye on that very closely. Over.

24 DR. MOORE: Great. Just one real quick question on H1N1,
25 and that's going to slide 10 and, in fact, all of the

1 phylogenetic analyses. You know, it seems like it would be
2 very helpful if, since you have the virus and you actually got
3 the virus from someone, if some of your centers could try to
4 also identify evidence for serologic, evidence for vaccination,
5 let alone epidemiologic evidence for vaccination so that it
6 would be -- if we knew all of these viruses were in vaccine-
7 positive persons, then that would suggest that there is vaccine
8 antigenic escape rather than just natural drift in
9 transmission, in mutation in the virus --

10 DR. KATZ: Right, yeah. Understood. And we try and do
11 that in the U.S. and some other countries, but our ability to
12 catch that because these viruses are coming from different
13 surveillance systems compared to -- and although we ask for
14 that information in the metadata that is provided with the
15 virus, we don't uniformly get it unless we're doing, for
16 example, like a vaccine effectiveness trial or something like
17 that in the U.S.

18 But yeah, your point is taken, and I think we can all try
19 and do a better job on that. Over.

20 DR. MOORE: Yeah. I mean, it's a tremendous job that
21 you're doing. It's just we might -- that might be one way to
22 put together both the genetics and the immunology.

23 I wanted to go to slide 23, I think it is.

24 DR. KATZ: Um-hum.

25 DR. MOORE: So this is back in March, I abstained from the

1 Hong Kong antigen. And the reason I think that maybe we're
2 seeing this, it's not that I was really smart on this, but it's
3 just that it was very frustrating to know the low efficacy that
4 seemed to be occurring with the Hong Kong antigen. And it
5 looks like we're seeing that on 23 and 24. And also the
6 differences between the egg-based and the cell line-based virus
7 neuts are pretty striking.

8 And we now have the Hong Kong-based antigen as our
9 Northern Hemisphere vaccine for the upcoming season for H3N2,
10 and most of the manufacturers are egg-based vaccines. And so
11 do you have any comments? Do you -- is there any way that the
12 approval of the Southern vaccine, which will be changed to a
13 Singapore that's likely to be more efficacious, can be used in
14 the Northern Hemisphere? I know that may not -- you may not
15 know the regulatory aspects of that, but would you at least
16 recommend that?

17 And, secondly, there is at least one cell-based
18 manufacturer that is using the Hong Kong antigen. Does your
19 data suggest that we might publicly describe that as a vaccine
20 that we as a Committee think might be more efficacious than the
21 egg-based antigen?

22 DR. KATZ: Okay. Nice easy questions. Thank you.

23 (Laughter.)

24 DR. KATZ: So, yeah, first of all, I'd just like to say
25 that the -- so the HI data, it's suggestive of how the vaccine

1 effectiveness may be, but we actually need studies to determine
2 the effectiveness to really demonstrate that.

3 So just to back up, in our Northern Hemisphere season, the
4 final results for the H3N2 effectiveness from the U.S. was 34%,
5 and this was in a season where we know we had both 3C.2a and a
6 larger extent of 3C.2a1 viruses circulating. Now, we all agree
7 34% isn't great, but it is within sort of the average range of
8 the H3N2s at the moment.

9 So, yes, we're going to have Hong Kong/4801. It's going
10 into people's arms right now. It's hard to say what will
11 happen. We never know what virus is going to predominate in
12 the upcoming season, but if it is H3N2 viruses, it could be
13 that the Hong Kong/4801 vaccine virus that's in the Northern
14 Hemisphere in the U.S. vaccines being administered at the
15 moment will do less well than they did in the past season.

16 I think -- I don't believe we can make any recommendations
17 to provide the Southern Hemisphere vaccine. I'll defer to
18 Jerry Weir and others at the FDA, but my understanding is that
19 what needs to be administered is a Northern Hemisphere
20 recommendation composition vaccine.

21 With respect to the cell-based vaccine that is being
22 produced in smaller numbers, I believe around 20 million doses
23 for the U.S. this year, and it's only licensed in the U.S.,
24 they are for the first time, the H3N2 component is actually a
25 totally cell-based vaccine virus. It was isolated in cells and

1 then produced by the manufacturers in cells.

2 So we don't have direct evidence that vaccine
3 effectiveness would be better. We think it has the potential
4 because of all of the data I've shown you for the H3N2 to
5 provide better protection. But we still really need the data
6 to demonstrate that cell-based vaccines, particularly ones that
7 are totally cell-based like the H3N2 component of the cell-
8 based vaccine this season, is actually better than an egg-based
9 vaccine. And we're in discussions, and we think those studies
10 should be done.

11 DR. MOORE: Thank you.

12 CAPT HUNTER-THOMAS: Dr. Moore, I just wanted to confirm
13 for the record, was that you that's been speaking or asking
14 questions for Dr. Katz?

15 DR. MOORE: One and the same. That's me.

16 CAPT HUNTER-THOMAS: Okay. Thank you.

17 For the record, that was Dr. Moore. Thank you.

18 DR. SAWYER: Are there other questions for Dr. Katz from
19 the Committee --

20 DR. MONTO: Yes. This is Dr. Arnold Monto.

21 DR. SAWYER: Please go ahead.

22 DR. MONTO: Jackie, since we've got 23 and 24 up, I just
23 wanted to ask you about the results from the Tokyo lab, which
24 seem to be an outlier for the egg-based results, low reactors
25 again -- the H3N2 component was less of an outlier for the

1 egg-based than the -- the cell culture-based than the
2 egg-based.

3 DR. KATZ: Right.

4 DR. MONTO: Is there any explanation for that?

5 DR. KATZ: So the Tokyo collaborating center was the only
6 collaborating center that you can see that they're not listed
7 in the HI data. They're not performing HIs at all. They're
8 only performing a virus neutralization test for antigenic
9 characterization for the H3N2s. And the test that they use is
10 a little different from what the other centers are using. The
11 others are all basing their virus neutralization test on one
12 that was developed several years ago and was previously
13 referred -- or was referred to by the London group as a plaque
14 reduction. We refer to it as a focus reduction.

15 The Tokyo group are doing what we call a
16 microneutralization assay, the same neutralization assay that
17 we use for our human serology. And typically, in the antigenic
18 characterization, they can get titers, homologous titers that
19 are very high. And so it potentially could skew their results
20 a little more towards showing poor inhibition. And so that's
21 why some of their data could be -- I mean we need to really
22 evaluate that further if it's the difference in the assay, the
23 difference in the viruses they're testing, which are
24 predominantly from Japan, or a combination of things. Over.

25 DR. MONTO: A further question, Jackie, which you may or

1 may not know the answer to. The newspapers and some of the
2 publications we look at have been full of the outbreak of H3N2
3 in Australia. I know part of that was -- part of the mortality
4 was associated with not using antivirals in nursing homes. But
5 is there any evidence that there was further drift in late
6 specimens from Australia?

7 DR. KATZ: There's no evidence of drift as we define it
8 using -- evaluating circulating viruses compared to a cell-
9 propagated reference virus. They did see -- I mean, part of
10 their activity was due to quite a number of nursing home and
11 other institutional outbreaks primarily in older adults. And
12 they did see vaccine breakthroughs in that situation, but no
13 evidence, additional evidence of antigenic drift. Over.

14 DR. MONTO: Thanks.

15 CAPT HUNTER-THOMAS: And the name of the Committee member
16 who just spoke for the record, please?

17 DR. MONTO: Arnold Monto.

18 CAPT HUNTER-THOMAS: Thank you, Dr. Monto.

19 DR. SAWYER: Are there additional questions for Dr. Katz?

20 MR. TOUBMAN: Yes. This is Sheldon Toubman. I have a
21 question about how you get to the recommendation from the
22 summary that states on slide 54 that B/Victoria viruses
23 predominated in Asia and Africa and B/Yamagata lineage viruses
24 predominated in Europe, Oceania, and the Americas. How do you
25 get to preferring the Yamagata lineage vaccine for trivalent

1 and only recommending the Victoria in quadrivalent?

2 And by the way, I have to say that, you know, I'm really,
3 really ignorant. I mean, I don't -- I'm not a medical person
4 at all, so you have to -- in answering my questions, you have
5 to, you know, start from square one. But I guess the basics
6 here are just what's the selection process?

7 I looked at the maps on slide 42 and 49. And we are
8 talking about the Southern Hemisphere. And I can't quite tell,
9 you know, where it's worse there, but I'm just trying to figure
10 out what the thinking is in preferring the Victoria -- excuse
11 me -- the Yamagata lineage.

12 DR. KATZ: Right, right. That's a great question.

13 I think it was twofold. One, that B/Yamagata was still
14 predominating globally. And I think also the fact that we'd
15 had the B/Victoria as the recommendation for the trivalent
16 vaccine in the past year. So individuals that would have been
17 vaccinated in this Southern Hemisphere season would have
18 received B/Victoria. And I think it was felt that it was time
19 to switch over to the B/Yamagata particularly for young
20 children who may be receiving vaccine for the first time.
21 Over.

22 MR. TOUBMAN: So does that mean that if they're vaccinated
23 from a previous time, that we expect the protective effect to
24 continue for a period of time, for a period of years?

25 DR. KATZ: Well, it's not for a period of years, but the

1 individuals have at least seen that lineage before. And we
2 know for the B viruses, there is some broader cross-reactivity
3 between the two different lineages than what we see for
4 influenza A subtypes, particularly in individuals who've
5 probably had natural infection with one or both and then would
6 get vaccinated.

7 MR. TOUBMAN: Okay. Thank you.

8 DR. SAWYER: Additional questions?

9 (No response.)

10 DR. SAWYER: Okay. Are we ready to move to the Open
11 Public comment, Serina?

12 CAPT HUNTER-THOMAS: Yes, Dr. Sawyer. Thank you.

13 DR. SAWYER: Okay. I would like to now turn to the Open
14 Public Comment session and welcome you to that session. Please
15 note that both the Food and Drug Administration and the public
16 believe in a transparent process for information gathering and
17 decision making. To ensure such transparency of the Open
18 Public Hearing session of the Advisory Committee meeting, FDA
19 believes that it is important to understand the context of an
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21 you, the Open Public Hearing speaker, at the beginning of your
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6 relationships at the beginning of your statement, it will not
7 preclude you from speaking.

8 And I believe we have one registered speaker for Open
9 Public comment, Dr. Megan Polanin from the National Center for
10 Health Research.

11 Is Dr. Polanin available?

12 CAPT HUNTER-THOMAS: Dr. Sawyer, Dr. Polanin is not in the
13 room, and so at this point, we can invite anyone else who is
14 available or interested in providing a public comment.

15 (No response.)

16 CAPT HUNTER-THOMAS: And hearing none, seeing none, we can
17 then move on to the committee discussion, voting, and
18 recommendations.

19 But before we do that, Dr. Sawyer, I would like to take a
20 poll again -- I mean, excuse me -- a roll call of the Committee
21 members again starting with Dr. Edwards.

22 Dr. Edwards, can you hear us?

23 (No response.)

24 CAPT HUNTER-THOMAS: Dr. Edwards has been communicating
25 via e-mail, and she may submit her vote via e-mail, which will

1 be read aloud for the record.

2 Dr. Janes?

3 DR. JANES: Yes, I'm here.

4 CAPT HUNTER-THOMAS: Dr. El Sahly?

5 (No response.)

6 CAPT HUNTER-THOMAS: Dr. Long?

7 DR. LONG: Here.

8 CAPT HUNTER-THOMAS: Dr. McInnes? Dr. McInnes?

9 DR. McINNES: Yes.

10 CAPT HUNTER-THOMAS: Thank you.

11 Dr. Moore?

12 DR. MOORE: Here.

13 CAPT HUNTER-THOMAS: Dr. Monto?

14 DR. MONTO: Here.

15 CAPT HUNTER-THOMAS: Dr. Sawyer, I know you're there.

16 DR. SAWYER: Yes.

17 CAPT HUNTER-THOMAS: Mr. Toubman?

18 MR. TOUBMAN: Present.

19 CAPT HUNTER-THOMAS: Dr. Wharton?

20 DR. WHARTON: Present.

21 CAPT HUNTER-THOMAS: Dr. Levy?

22 DR. LEVY: I'm here.

23 CAPT HUNTER-THOMAS: Thank you.

24 Dr. Greenberg, I just want to check if you're present. I

25 know you're not voting.

1 DR. GREENBERG: Yes, I'm here. Thank you.

2 CAPT HUNTER-THOMAS: Okay. Thank you.

3 Okay. If everyone would please stand by, we are going to
4 post the screen with the voting questions.

5 DR. SAWYER: And, Serina, we'll then have a chance to have
6 discussion around the questions?

7 CAPT HUNTER-THOMAS: Yes, absolutely. Thank you.

8 Okay. Dr. Sawyer, I give you the floor again for
9 continued committee discussion.

10 DR. SAWYER: So I think we've heard a lot of information
11 today as is usual for this meeting and have had some excellent
12 questions already. I'd like to open it up for any further
13 discussion before we vote on these two questions.

14 MR. TOUBMAN: There is one more from Sheldon Toubman here.
15 Again, since this is so all new to me, what's the basis for
16 determining whether a trivalent or quadrivalent inoculation is
17 going to be provided? Is there -- is that completely out of
18 the hands of recommendations from FDA, and those decisions are
19 made by other entities?

20 DR. SAWYER: This is Mark. I can comment that the ACIP,
21 which makes recommendations about the use of vaccines, has not
22 stated a preference of quadrivalent over trivalent. I don't
23 know if anyone from FDA would like to further comment?

24 DR. GRUBER: No, we don't. This is Marion Gruber. We
25 were going to say the same thing, that the United States is

1 actually the ACIP will make the recommendations on use of the
2 vaccine. We do license the vaccines. We have both trivalent
3 as well as quadrivalent formulations licensed, but we don't,
4 you know, make recommendations as to the use of these products.

5 MR. TOUBMAN: So how -- sorry -- thank you for that
6 answer --

7 DR. SAWYER: This is Mark. I just wanted to add one other
8 additional point of information that might be relevant. You
9 know, the proportion of available vaccine that is quadrivalent
10 compared to trivalent has gradually been increasing over the
11 years since the quadrivalent vaccines became available. And I
12 believe this year, approximately 75% of the vaccine that's sold
13 in the U.S. is quadrivalent.

14 MR. TOUBMAN: And so the purchasers, I guess, of this,
15 they're the ones who are making the decision?

16 DR. SAWYER: Well, this is Mark again. I guess ultimately
17 the decision is made between the physician and the individual
18 patients based on available supply and perhaps other
19 considerations.

20 MR. TOUBMAN: Okay. Thank you.

21 DR. SAWYER: Are there any other discussion points that
22 anyone would like to raise before we vote?

23 DR. MOORE: Yeah. This is Pat Moore. If I could
24 reiterate some of the comments and concerns that I have for the
25 H3N2, I think that maybe it's -- I know that we're voting on a

1 Southern Hemisphere vaccine, and it's a little unclear whether
2 this new antigen for H3N2 will be available. I guess this
3 is -- to FDA to -- if we do start seeing a spike particularly
4 in 3C.2a cases that is dramatic in this upcoming winter,
5 then efforts should be made perhaps to think about how we could
6 get a licensed vaccine or a licensed management to try and --
7 that whether that's the Hong Kong-based cell-derived vaccine or
8 the Singapore antigen as a single antigen.

9 DR. SAWYER: Are there any comments in response?

10 DR. GREENBERG: This is David Greenberg as the Industry
11 Representative. The discussion I think that would take place
12 around addressing that topic would be between the manufacturers
13 and FDA. The manufacturing process for influenza vaccines is
14 some months long, and it does depend on some important aspects,
15 such as obtaining reagents for measuring the contents of
16 antigen in vaccines by each of the different manufacturers.

17 I personally don't know if those reagents are available
18 yet for the new strain. It usually comes along within a couple
19 of months after a WHO and FDA meeting such as this one. So
20 it's unclear whether a vaccine containing the new H3N2 strain
21 would be available for the winter season in the U.S. or
22 Northern Hemisphere. But that's something that would need to
23 be discussed between manufacturers and FDA.

24 DR. WEIR: Hi, this is Jerry Weir again. Can I just
25 interject one comment related to the last couple of comments in

1 this discussion?

2 From a practical matter, it's unlikely that anyone would
3 have a vaccine with the A/Singapore strain available for the
4 Northern Hemisphere. I mean, if you think about it, all of the
5 vaccine is now becoming available like last month, this month,
6 and being used between now and February. This recommendation
7 for the A/Singapore just came out last week, and any
8 manufacturer that wants to start working with it just begins
9 the process now with the anticipation that they would have a
10 vaccine made and formulated sometime next spring.

11 So I mean we've been through these scenarios before of how
12 late one could change a recommendation, and I don't think I've
13 ever seen a change -- anyone say that something as late as
14 October, now, much less any later, is at all practical to
15 change the vaccine for the Northern Hemisphere season. So I
16 just don't see how that actually could possibly work in just
17 terms of practically making a vaccine.

18 DR. LONG: This is Sarah Long. I thought that the
19 questioner was thinking about next October, 2018?

20 DR. WEIR: Well --

21 DR. LONG: Not this year.

22 DR. WEIR: This is Jerry again. Remember, we will go
23 through a strain selection process for the Northern Hemisphere
24 in early March of 2018, so we will all revisit this again based
25 on even more data at the time for the next -- not the current

1 but the next Northern Hemisphere season of '18, '19.

2 DR. LONG: No, for 2018 northern season, we will select in
3 March.

4 DR. WEIR: Correct.

5 DR. GRUBER: Well, yeah, that's correct. The VRBPAC will
6 meet in March of 2018 to make a recommendation as to the
7 components of the influenza vaccine for the '18-'19. This is
8 Marion Gruber, by the way.

9 Dr. Weir's comments that he just made, however, were
10 regarding -- and this -- that was our understanding that the
11 Committee members asked -- is it feasible to make the Southern
12 Hemisphere formulation that contains the Singapore available
13 sometimes during the current '17-'18 Northern Hemisphere
14 season, should there be need for it. In other words, should,
15 you know, should these strains start to circulate? So that was
16 the comment made in that regard. And that was the question,
17 how we understood it.

18 Thank you.

19 DR. MOORE: Let me just rephrase that. No, I actually
20 made two comments. One is that the FDA think about it a little
21 -- this is Pat Moore -- think about this as -- certainly, I
22 understand getting the Singapore antigen out is probably
23 impossible this late in the season, but we do have a licensed
24 cell-based Hong Kong vaccine. And although we don't have
25 vaccine efficacy data for it, I haven't seen any vaccine

1 efficacy data presented today. All we have are the
2 implications based on both the neutralizations and HI titers
3 and so forth that we have for the different viruses.

4 But it looks very much like if we base our judgment on a
5 vaccine being efficacious based on the ferret sera data, for
6 example, in the neuts, that the cell-based vaccine should
7 behave much better even with the Hong Kong antigen, and that is
8 a licensed vaccine. I guess the question is can that be
9 expanded if it's a very small production now, 20 million doses;
10 can it be expanded if we're facing a major epidemic of H3N2,
11 which we may not face this winter? Something to at least keep
12 under consideration.

13 DR. WEIR: This is Jerry again. I see your point, and
14 it's well taken. I actually don't know how to answer it. Part
15 of it would depend, of course, on the manufacturer when you
16 said could it be expanded. So I don't know the answer to that.
17 It's possible. My guess is that most vaccines have already
18 been purchased at this time, but again, I don't know. That
19 might be possible.

20 But the real question would be would anyone have the data
21 and the evidence to recommend it? And, for example, I don't
22 think the FDA would be making a recommendation like that. It
23 would all be based, theoretically, that it might be working
24 better, and I don't think we'd have any real-time data to know
25 that. So whether someone else, not the FDA, would make some

1 sort of recommendation like that, I don't know. It would be,
2 again, would not be based on real-time data, though.

3 DR. MOORE: Fair enough. Thank you.

4 DR. SAWYER: Okay. Are there other points of discussion
5 that anyone would like to raise? And at least on my WebEx
6 view, I've lost the questions on the screen. I don't know if
7 they're going to be back.

8 CAPT HUNTER-THOMAS: We're working on it on this end,
9 Dr. Sawyer.

10 DR. SAWYER: Okay.

11 CAPT HUNTER-THOMAS: In the meantime, instructions have
12 been sent to the Committee members that have logged into the
13 WebEx with their phone number instead of providing their name.
14 For those that we have just the phone number, if you could see
15 the instructions that Derek has sent so that you can change it
16 from a phone number to providing your name. Thank you.

17 And the questions are back up.

18 DR. SAWYER: So as people take a moment to read and follow
19 those instructions, let me again ask if there are any other
20 points people want to make before we actually undertake the
21 vote?

22 (No response.)

23 DR. SAWYER: Okay. It sounds like we're ready to vote
24 whenever we're technically ready to vote.

25 CAPT HUNTER-THOMAS: Okay. So we are going to --

1 actually, can you put the questions back up, the voting
2 questions back up for me?

3 Dr. Sawyer, if you could read for the benefit of the
4 Committee the first voting question, and then we will proceed
5 with the vote?

6 DR. SAWYER: Okay. So the first question we're asked to
7 vote on is for the composition of the trivalent 2018 Southern
8 Hemisphere formulations of influenza vaccine, does the
9 Committee recommend the inclusion of an A/Michigan/45/2015
10 (H1N1)pdm09-like virus; (b) the inclusion of an
11 Singapore/INFIMH-16-0019/2016 (H3N2)-like virus; and finally,
12 (c) the inclusion of a B/Phuket/3073/2013-like virus from the
13 B/Yamagata lineage?

14 CAPT HUNTER-THOMAS: Okay. Thank you. So, shortly, you
15 will receive the polling questions through the WebEx, and you
16 will submit your vote. Please stand by.

17 UNIDENTIFIED SPEAKER: How will we do that?

18 CAPT HUNTER-THOMAS: Please stand by. You'll see it.
19 You'll see it through the WebEx shortly. Okay.

20 UNIDENTIFIED SPEAKER: Got it.

21 CAPT HUNTER-THOMAS: The question is up. And if everyone
22 can proceed to submit your vote? Thank you.

23 MR. TOUBMAN: A quick question. This is Sheldon Toubman.
24 I did not get the instructions, and I'm using a different
25 computer and e-mail address. So when I vote, I just want to

1 make sure you know who I am.

2 CAPT HUNTER-THOMAS: Okay. If I don't see your name or
3 recognize your name, what we'll do is I'll call, I'll call you
4 verbally and request for you to respond with your vote.

5 MR. TOUBMAN: Okay. Thank you.

6 CAPT HUNTER-THOMAS: Thank you.

7 DR. LEVY: Point of clarification. This is Ofer Levy
8 speaking. Given that we're -- I'm using a lot of technologies
9 I haven't before and we're hearing both verbal information,
10 seeing slides that are changing, as I understand it, for
11 Question 1, the inclusion is coming up as one of the strains at
12 a time; is that correct?

13 DR. SAWYER: No. This is Mark. We're actually being
14 asked to vote on the combination of all three, unlike we do
15 typically for the Northern Hemisphere. This was to make this
16 simpler since this vaccine that we're recommending is just for
17 the Southern Hemisphere. So we're voting on the combination of
18 all three strains.

19 DR. LEVY: But what's showing up on my screen, it just
20 says inclusion of an A/Michigan/45/2015 (H1N1)pdm09-like virus.

21 DR. SAWYER: Ah, you need a bigger screen. No, I'm not
22 sure what's happening technologically there.

23 DR. LEVY: Oh, oh, here. Oh, yeah. I just adjusted my
24 screen. Now they all show up. Interesting. Okay, I'm sorry.
25 It sounds very silly, but I've seen mistakes made with this

1 kind of stuff.

2 Okay. And also, just another point of clarification, as I
3 understand it, this "package deal" of these three is
4 essentially the WHO recommendation?

5 DR. SAWYER: That is correct.

6 DR. LEVY: Yeah. Okay.

7 CAPT HUNTER-THOMAS: Thank you. Does anyone else have any
8 questions before you proceed to cast your vote?

9 (No response.)

10 CAPT HUNTER-THOMAS: Okay. So, please, Committee members,
11 go ahead and cast your vote at this time. Thank you.

12 (Committee vote.)

13 CAPT HUNTER-THOMAS: Okay. Does anyone need additional
14 time to submit their vote?

15 (No response.)

16 CAPT HUNTER-THOMAS: Has everyone submitted their vote?

17 DR. LEVY: This is Ofer Levy. I believe I have. It did
18 kind of gray out and seemed like it understood that I clicked
19 submit, but I'm not sure.

20 CAPT HUNTER-THOMAS: Okay.

21 DR. MONTO: Yeah. This is Arnold Monto. I think I've
22 submitted it as well.

23 CAPT HUNTER-THOMAS: Okay.

24 DR. MONTO: I had the same experience.

25 DR. LEVY: Hopefully, there are no hanging chads.

1 CAPT HUNTER-THOMAS: Okay. Stand by, please. Thank you.

2 (Pause.)

3 DR. SAWYER: This is Mark. We may have to put Dr. Katz in
4 charge of the voting process because she can dissect complex
5 processes and deliver them easily to us.

6 DR. LEVY: This is Ofer Levy speaking. I'm seeing a
7 screen now that seems to indicate that 73% voted yes, 27% voted
8 no --

9 CAPT HUNTER-THOMAS: Dr. Levy, thank you. Yes. We see
10 that screen, and we're going to do individual tabulations here.

11 So on behalf of Dr. Edwards, who has submitted her vote
12 via e-mail since we cannot hear her, but she can hear us, she
13 has voted -- for the first question, she has voted yes.

14 Dr. Janes, what is your vote, please? Dr. Holly Janes?

15 DR. JANES: I'm sorry. Can you hear me now? I voted yes.

16 CAPT HUNTER-THOMAS: Thank you.

17 Dr. Long, your vote, please?

18 DR. LONG: Yes.

19 CAPT HUNTER-THOMAS: Dr. McInnes, your vote, please?

20 Dr. McInnes?

21 (No response.)

22 CAPT HUNTER-THOMAS: Dr. Moore, your vote, please?

23 DR. MOORE: Yes.

24 CAPT HUNTER-THOMAS: Thank you.

25 Dr. Monto, your vote, please?

1 DR. MONTO: Yes.

2 CAPT HUNTER-THOMAS: Dr. Sawyer, your vote, please?

3 DR. SAWYER: Yes.

4 CAPT HUNTER-THOMAS: Mr. Toubman, your vote?

5 MR. TOUBMAN: Yes.

6 CAPT HUNTER-THOMAS: Dr. Wharton, your vote?

7 DR. WHARTON: Yes.

8 CAPT HUNTER-THOMAS: And --

9 DR. McINNES: Serina?

10 CAPT HUNTER-THOMAS: Yes?

11 DR. McINNES: This is Pamela McInnes. I did not have the
12 screen where I could do the unmute. I have it now, and I'm
13 confirming that my vote is yes.

14 CAPT HUNTER-THOMAS: Okay. Thank you very much. Thank
15 you, Dr. McInnes.

16 And finally, Dr. Levy, your vote, please?

17 DR. LEVY: Yes.

18 CAPT HUNTER-THOMAS: Okay. So, to summarize, we have
19 Dr. Edwards, yes; Dr. Janes, yes; Dr. Long, yes; Dr. McInnes,
20 yes; Dr. Moore, yes; Dr. Monto, yes; Dr. Sawyer, yes;
21 Mr. Toubman, yes; Dr. Wharton, yes; and Dr. Levy, yes. So
22 that's a total of 10 yes votes, 0 abstain, and 0 no votes for
23 Question No. 1.

24 DR. SAWYER: Okay. We're ready to move to Question 2?

25 CAPT HUNTER-THOMAS: I believe so, Dr. Sawyer. Thank you.

1 Question No. --

2 DR. LEVY: Sorry. This is Ofer Levy. I just have a
3 process question. So it sounded like what you talked about was
4 a unanimous yes, but when I looked at the results, I guess what
5 it's reporting is not noes but abstentions? That's why there's
6 a 27% mark? Those are abstentions?

7 CAPT HUNTER-THOMAS: Yes. I did a verbal vote, Dr. Levy,
8 and the no answers are for individuals that are not present.

9 DR. LEVY: But no, it means they didn't vote, no? Or no,
10 their vote was no?

11 CAPT HUNTER-THOMAS: No. We have -- I just gave a verbal
12 tally, and we have 10 yeses from all of the members present,
13 including Dr. Edwards, who submitted her vote via e-mail.

14 DR. SAWYER: This is Mark.

15 DR. LEVY: Right, right, but -- this is Ofer Levy. I'm
16 sorry. I'm still trying to determine -- are you aware of any
17 no votes is what I'm asking?

18 CAPT HUNTER-THOMAS: Correct. We do not have any no votes
19 for Question No. 1, Dr. Levy.

20 DR. LEVY: Okay. Because the way it comes up on the
21 system, it makes it seem like there were three no votes. Okay.

22 CAPT HUNTER-THOMAS: Understood, but we have --

23 DR. SAWYER: All right. This is --

24 CAPT HUNTER-THOMAS: I'm sorry. Go ahead, Dr. Sawyer.

25 DR. SAWYER: Well, I was just going to attempt to clarify.

1 It sounds like the technology, for those of us who could not
2 vote, it may be registering as noes, which is why Ms. Hunter-
3 Thomas went to a verbal vote to make it clear.

4 UNIDENTIFIED SPEAKER: It doesn't register as noes; it
5 registers as no answer.

6 DR. SAWYER: Okay.

7 UNIDENTIFIED SPEAKER: It says yes, no, abstain, and no
8 answer on my screen.

9 DR. SAWYER: Are there any --

10 CAPT HUNTER-THOMAS: So please -- okay. Thank you.

11 DR. SAWYER: Does anyone else need clarification on the
12 voting process, or can we move to Question 2?

13 (No response.)

14 DR. SAWYER: Okay. Let's move to Question 2, then.

15 For the quadrivalent 2018 Southern Hemisphere formulations
16 of influenza vaccines, does the Committee recommend the
17 inclusion of a B/Brisbane/60/2008-like virus from the
18 B/Victoria lineage as the second influenza B strain in the
19 vaccine?

20 CAPT HUNTER-THOMAS: Thank you, Dr. Sawyer.

21 So what we're going to do for Question No. 2 is we're
22 going to forego the WebEx, and we're going to take a verbal
23 again. And I will start with Dr. Janes while I await for
24 Dr. Edwards to submit her response via e-mail.

25 Dr. Janes, your vote, please? Oh, sorry, sorry --

1 DR. JANES: Yes.

2 CAPT HUNTER-THOMAS: I'm sorry --

3 DR. JANES: Yes.

4 CAPT HUNTER-THOMAS: Dr. Janes, stand by one second while
5 they set up -- forgive me, excuse me.

6 UNIDENTIFIED SPEAKER: These things work when they work.

7 CAPT HUNTER-THOMAS: Okay. I have Dr. Edwards. Okay.

8 Dr. Edwards, I have received your vote via e-mail for a yes for
9 Question No. 2.

10 And now I would like to proceed with Dr. Janes, please?

11 DR. JANES: My vote is yes.

12 CAPT HUNTER-THOMAS: Thank you.

13 Dr. Long?

14 DR. LONG: Yes.

15 CAPT HUNTER-THOMAS: Thank you.

16 Dr. McInnes?

17 (No response.)

18 CAPT HUNTER-THOMAS: Dr. Moore, please?

19 DR. MOORE: Yes.

20 CAPT HUNTER-THOMAS: Thank you.

21 Dr. Monto?

22 DR. MONTO: Yes.

23 CAPT HUNTER-THOMAS: Dr. Sawyer?

24 DR. SAWYER: Yes.

25 CAPT HUNTER-THOMAS: Mr. Toubman?

1 MR. TOUBMAN: Yes.

2 CAPT HUNTER-THOMAS: Dr. Wharton?

3 DR. WHARTON: Yes.

4 CAPT HUNTER-THOMAS: And Dr. Levy?

5 DR. LEVY: Yes. And sorry, another process question. It
6 seems for the first question, we did some web-based voting as
7 well, but we're not doing that for Question No. 2?

8 CAPT HUNTER-THOMAS: Correct, Dr. Levy.

9 DR. LEVY: Okay.

10 CAPT HUNTER-THOMAS: We're doing a verbal.

11 DR. LEVY: Okay.

12 CAPT HUNTER-THOMAS: Thank you. Thank you.

13 And I would like to circle back to Dr. McInnes, please,
14 for your vote?

15 DR. McINNES: Yes.

16 CAPT HUNTER-THOMAS: Thank you. So I will read aloud for
17 a final count for Question No. 2.

18 Dr. Edwards, yes; Dr. Janes, yes; Dr. Long, yes;
19 Dr. McInnes, yes; Dr. Moore, yes; Dr. Monto, yes; Dr. Sawyer,
20 yes; Mr. Toubman, yes; Dr. Wharton, yes; and finally, Dr. Levy,
21 yes; for a total of 10 yes votes, 0 abstain, and 0 no,
22 unanimous vote of yes.

23 Thank you very much for your patience, and if there aren't
24 any other additional questions, Dr. Sawyer?

25 DR. SAWYER: Yes. Thank you. This is Mark. I would like

1 to thank the Committee for excellent questions and discussion,
2 thank Dr. Weir for providing us a review of the process by
3 which this information is gathered and reviewed, and again,
4 thanks to Dr. Katz for a clear presentation about the complex
5 data that's used to support the recommendation that we just
6 voted on. So thanks very much.

7 And I think with that, we can adjourn.

8 CAPT HUNTER-THOMAS: Thank you, Dr. Sawyer, for standing
9 in as chair. The meeting is adjourned. Thank you.

10 (Whereupon, at 3:30 p.m., the meeting was concluded.)

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C E R T I F I C A T E

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

149TH MEETING OF THE VACCINES AND RELATED BIOLOGICAL PRODUCTS
ADVISORY COMMITTEE

October 4, 2017

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.

MICHAEL McCANN
Court Reporter