

**FOOD AND DRUG ADMINISTRATION (FDA)
Center for Biologics Evaluation and Research (CBER)
173rd Vaccines and Related Biological Products Advisory
Committee (VRBPAC) Meeting**

OPEN PUBLIC MEETING

**Web-Conference
Silver Spring, Maryland 20993**

June 7, 2022

This transcript appears as received from the commercial transcribing service after inclusion of minor corrections to typographical and factual errors recommended by the DFO.

ATTENDEES

COMMITTEE MEMBERS	
Arnold Monto, M.D. (Chair)	University of Michigan
Paula Annunziato, M.D.	Merck
Archana Chatterjee, M.D., Ph.D.	Rosalind Franklin University
CAPT Amanda Cohn, M.D.	National Center for Immunizations and Respiratory Diseases Centers for Disease Control and Prevention
Adam C. Berger, Ph.D.	National Institutes of Health
Henry H. Bernstein, D.O., MHCM, FAAP	Cohen Children's Medical Center
David Kim, M.D., M.S., M.H.A.	U.S. Department of Health and Human Services
Eric J. Rubin, M.D., Ph.D.	Brigham and Women's Hospital
Paul Offit, M.D.	The Children's Hospital of Philadelphia
Steven A. Pergam, M.D., M.P.H., FIDSA	Seattle Cancer Care Alliance
Jay Portnoy, M.D.	Children's Mercy Hospital
TEMPORARY VOTING MEMBERS	
A. Oveta Fuller, Ph.D.	University of Michigan
Bruce Gellin, M.D., M.PH.	The Rockefeller Foundation
Michael Nelson, M.D., Ph.D.	UVA Health & UVA School of Medicine
Jeannette Lee, Ph.D.	University of Arkansas for Medical Sciences
Ofer Levy, M.D., Ph.D.	Massachusetts Institute of Technology
Pamela McInnes, D.D.S., M.Sc.	National Institutes of Health
Wayne A. Marasco, M.D., Ph.D.	Harvard Medical School

Cody Meissner, M.D.	Tufts University School of Medicine
Stanley Perlman, M.D., Ph.D.	University of Iowa
Mark Sawyer, M.D., F.A.A.P.	Rady Children's Hospital San Diego
Arthur Reingold, M.D.	University of California, Berkeley
Melinda Wharton, M.D, M.P.H.	Centers for Disease Control and Prevention
SPEAKERS AND GUEST SPEAKERS	
CDR Heather Scobie, Ph.D., M.PH.	Centers for Disease Control and Prevention
Tom Shimabukuro, M.D., M.PH., M.B.A.	Centers for Disease Control and Prevention
Filip Dubovsky, M.D. MPH, FAAP	Novavax, Incorporated
Raburn Mallory, M.D.	Novavax, Incorporated
Denny Kim, M.D., MPH	Novavax, Incorporated
Gregory A. Poland, M.D., FIDSA, MACP, FRCP	Mayo Vaccine Research Group
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Doran Fink, M.D., Ph.D.	Food and Drug Administration
Goutam Sen, Ph.D.	Food and Drug Administration
Peter W. Marks, M.D., Ph.D.	Food and Drug Administration
Celia M. Witten, Ph.D., M.D.	Food and Drug Administration
Jerry Weir, Ph.D.	Food and Drug Administration
Lucia Lee, M.D.	Food and Drug Administration
FDA ADMINISTRATIVE STAFF	
Prabhakara Atreya, Ph.D.	Food and Drug Administration

Mr. Michael Kawczynski	Food and Drug Administration
Karen Thomas	Food and Drug Administration
Sussan Paydar, Ph.D.	Food and Drug Administration
Lisa Wheeler	Food and Drug Administration
Joanne Lipkind, M.S.	Food and Drug Administration
PUBLIC COMMENTERS	
Benjamin Newton	
Cathy Keaveney	
Mitchell Goldstein	Loma Linda University Children's Hospital
David Charles, M.D.	Practicing Physician
Chad Rittle	Chatham University
Sophia Phillips	National Center for Health Research
Martha Dawson	National Black Nursing Association
Kermit Kubitz	

1 Pergam. I'm a professor at the Fred Hutchinson Cancer
2 Center. And I focus on adult infectious diseases,
3 specifically in the immunosuppressed host.

4 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
5 Jay Portnoy, our consumer representative. Mike, is he
6 available? If not, we'll move on to Dr. Eric Rubin.

7 **DR. ERIC RUBIN:** Good morning, Praba, I'm Eric
8 Rubin. I'm at Harvard, the Brigham and Women's
9 Hospital, and the *New England Journal of Medicine*.

10 **DR. PRABHAKARA ATREYA:** Thank you. Next, we
11 will do the roll call for our temporary voting members.
12 Dr. Fuller.

13 **DR. A. OVETA FULLER:** Good morning, I'm Oveta
14 Fuller, I'm Dr. Oveta Fuller. I'm at the University of
15 Michigan African Studies Center and Department of
16 Microbiology/Immunology. I'm a virologist by training,
17 and I do implementation science in the community.

18 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Fuller.
19 Next is Dr. Bruce Gellin.

20 **DR. BRUCE GELLIN:** Hi, I'm Bruce Gellin. I'm
21 currently the chief of global public health strategies

1 for the Rockefeller Foundation. I'm honored to be back
2 as a temporary member of the committee. For 15 years I
3 was the director of what was then called The National
4 Vaccine Program Office at HHS. Thanks.

5 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Gellin.
6 The next one is Dr. Jeannette Lee.

7 **DR. JEANNETTE YEN LEE:** Yes, good morning, I'm
8 Jeannette Lee. I'm a professor of biostatistics and a
9 member of the Winthrop P. Rockefeller Cancer Institute
10 at the University of Arkansas for Medical Sciences. My
11 area is multicenter clinical trials. Thank you.

12 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
13 Ofer Levy.

14 **DR. OFER LEVY:** Hi, good morning, my name is
15 Ofer Levy. I'm a physician scientist and pediatric
16 infectious disease specialist at Boston Children's
17 Hospital. I'm professor of pediatrics at Harvard
18 Medical School, and I direct the precision vaccines
19 program, which conducts research by applying precision
20 medicine concepts to vaccinology.

21 **DR. PRABHAKARA ATREYA:** Thank you. Dr.

1 Marasco, Wayne Marasco. We can't hear you, Dr.

2 Marasco.

3 **DR. WAYNE MARASCO:** Sorry, wrong button. I'm
4 Wayne Marasco, professor of medicine at Dana Farber
5 Cancer Institute at Harvard Medical School. I study
6 antiviral antibody immunity to vaccines and natural
7 infection.

8 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
9 Pamela McInnes. We can't hear you, Dr. McInnes.

10 **DR. PAMELA MCINNES:** Good morning --

11 **MR. MICHEAL KAWCYNski:** Give me one second,
12 there we go.

13 **DR. PAMELA MCINNES:** -- Pamela McInnes.
14 Retired deputy director of the National Center for
15 Advancing Translational Sciences at the U.S. National
16 Institutes of Health. Good morning.

17 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
18 Cody Meissner.

19 **DR. CODY MEISSNER:** Thank you, Praba. Good
20 morning. My name is Cody Meissner. I'm a professor of
21 pediatrics at Tufts University School of Medicine in

1 today's meeting.

2 Today on June 7, 2022, the Committee will meet
3 in open session to discuss Emergency Use Authorization
4 request by Novavax for a vaccine to prevent COVID-19 in
5 individuals 18 years of age and older. This topic is
6 determined to be of particular matter involving
7 specific parties. With the exception of the industry
8 representative members, all standing and temporary
9 voting members of the VRBPAC are appointed special
10 government employee (SGEs) or regular government
11 employees (RGEs) from other agencies and are subjected
12 to federal Conflicts of Interest laws and regulations.

13 The following information on the status of
14 this Committee's compliance with the federal Ethics and
15 Conflict of Interest laws including, but not limited
16 to, 18 U.S. Code Section 208 is being provided to
17 participants in today's meeting and to the public.

18 Related to the discussions at this meeting,
19 all members, RGE and SGE consultants of this Committee
20 have been screened for potential financial conflicts of
21 their own as well as those imputed to them, including

1 those of their spouse or minor children and, for the
2 purpose of U.S. 18 Code 208, their employers.

3 These interests may include investments,
4 consulting, expert witness testimony, contracts and
5 grants, cooperative research and development agreements
6 or CRADAs, teaching, speaking, writing assignments,
7 patents and royalties, and also their primary
8 employment. These may include interests that are
9 current or under negotiation.

10 FDA has determined that all members of this
11 Advisory Committee, both regular and temporary members,
12 are in compliance with federal Ethics and the Conflict
13 of Interest laws. Under the 18 U.S. Code Section 208,
14 Congress has authorized FDA to grant waivers to special
15 government employees and/or regular government
16 employees who have financial conflicts of interest when
17 it is determined that the Agency's need for a special
18 government employee's services outweighs the potential
19 for a conflict of interest created by the financial
20 interest involved. Or when the interest of a regular
21 government employee is not so substantial as to be

1 deemed likely to affect the integrity of the services
2 which the government may expect from the employee.
3 Based on today's agenda and all financial interests
4 reported by Committee members and consultants, there
5 have been no Conflicts of Interest waivers issued under
6 18 U.S. Code 208 in connection with this meeting.

7 We have the following consultants service as
8 temporary voting members. Dr. Oveta Fuller, Dr. Bruce
9 Gellin, Dr. Jeannette Lee, Dr. Ofer Levy, Dr. Wayne
10 Marasco, Dr. Pamela McInnes, Dr. Cody Meissner, Dr.
11 Michael Nelson, Dr. Stanley Perlman, Dr. Art Reingold,
12 Dr. Mark Sawyer, and Dr. Melinda Wharton.

13 Dr. Paula Annunziato of Merck will serve as
14 the industry representative for today's meeting.
15 Industry representatives are not appointed as special
16 government employees and serve as non-voting members of
17 the Committee only. Industry representatives act on
18 behalf of all the regulated industry and bring general
19 industry perspective to the Committee. Dr. Jay Portnoy
20 is serving as the consumer representative for this
21 Committee. Consumer representatives are appointed

1 special government employees and are screened and
2 cleared prior to their participation in the meeting.
3 They are voting members of the Committee.

4 The guest speakers for today's meeting are the
5 following: Dr. Heather Scobie, Deputy Team Lead,
6 Surveillance and Analytics Epidemiology Task Force
7 COVID Emergency 19 Emergency Response Team at CDC,
8 Atlanta and Dr., and CAPT. Tom Shimabukuro, Director in
9 the Immunization Safety Office at the Centers for
10 Disease Control and Prevention in Atlanta, Georgia.
11 They are the guest speakers for today.

12 Disclosure of conflicts of interest for
13 speakers and guest speakers follow applicable federal
14 laws, regulations, and FDA guidance. FDA encourages
15 all meeting participants, including open public hearing
16 speakers, to advise the Committee of any financial
17 relationships that they may have with any affected firm
18 and product and, if known, if direct competitors.

19 We would like to remind the standing and
20 temporary members of the Committee that if the
21 discussions involve any of the products or firms not

1 already on the agenda for which an FDA participant has
2 a personal or imputed financial interest, the
3 participants need to inform the DFO and exclude
4 themselves from the discussion and their exclusion will
5 be noted for the record.

6 This concludes the reading of my Conflicts of
7 Interest statement for the public record. At this time
8 I would like to hand over the meeting back to our
9 chair, Dr. Arnold Monto. Thank you very much and, Dr.
10 Monto, take it away.

11 **DR. ARNOLD MONTO:** Thank you very much, Praba.
12 First, we're going to hear from the director of CBER,
13 Dr. Marks. Take it away, Dr. Marks.

14

15 **FDA INTRODUCTION**

16

17 **DR. PETER MARKS:** Thank you very much. So I
18 just wanted to welcome everyone to today's VRBPAC
19 Meeting. I'm not going to say very much right now,
20 except to welcome everyone. This is our first meeting
21 of a series of several this month to take up some

1 important topics. We'll look forward to working
2 through these meetings.

3 We believe that we have done a fair amount of
4 work to solve some of the technical glitches that have
5 essentially haggled us in the past when we've had these
6 meetings, and they hopefully will not be an issue today
7 and we'll hopefully have a very good meeting today. I
8 really look forward to and thank our advisors for their
9 engagement and for our staff's hard work preparing for
10 the meeting, and for everyone's participation today. I
11 will turn it back over to Dr. Monto.

12 **DR. ARNOLD MONTO:** Thanks, Dr. Marks, first
13 we're going to be going to hear some presentations from
14 CDC, which will serve as background for our further
15 deliberations. First, we hear from Dr. Heather Scobie,
16 who's going to talk about the current epidemiology of
17 COVID-19 and COVID-19 vaccination rates in the United
18 States. Dr. Scobie.

19 **DR. PRABHAKARA ATREYA:** Dr. Monto, I think we
20 need to allow Dr. Sen to speak from FDA before we hear
21 from CDC.

1 **DR. ARNOLD MONTO:** Oh, excuse me, I jumped
2 ahead. Thank you, Praba. We hear next from Dr. Sen.
3 Dr. Sen is going to be telling us why we're here and
4 the rules for Emergency Use Authorization. My
5 apologies, Dr. Sen.

6

7 **EMERGENCY USE AUTHORIZATION (EUA) REQUEST BY NOVAVAX**
8 **FOR A VACCINE TO PREVENT COVID-19 IN INDIVIDUALS 18**
9 **YEARS OF AGE AND OLDER**

10

11 **DR. GOUTAM SEN:** Good morning, Dr. Monto, and
12 good morning, everybody. I would like to thank the
13 Committee members for your time to convene here this
14 morning to discuss Novavax COVID-19 vaccine Adjuvanted
15 request for Emergency Use Authorization. My name is
16 Goutam Sen, I'm from Office of Vaccine at CBER FDA.
17 I'll give an overview of the product and today's
18 agenda.

19 Here is my outline. I'll discuss about SARS-
20 CoV-2 pandemic, then I'll discuss about Novavax COVID-
21 19 vaccine, Adjuvanted and their EUA request for

1 immunization as a primary series two doses three weeks
2 apart; considerations for EUA of a COVID-19 vaccine;
3 COVID-19 vaccines available for use in the U.S.;
4 overview of today's agenda; voting questions for the
5 Committee.

6 Since the beginning of the pandemic in early
7 2020, SARS-CoV-2 has caused over half a billion
8 confirmed cases of COVID-19 worldwide, including over
9 six million deaths. In the United States, SARS-CoV-2
10 has caused over 84 million reported COVID-19 cases and
11 over one million deaths. Surges in SARS-CoV-2
12 transmission and COVID-19 cases, hospitalizations, and
13 deaths have been associated with emergence of SARS-CoV-
14 2 variants. For example, Beta, Delta and, more
15 recently, the Omicron, that are more infectious, more
16 virulent, and are more resistant to natural or vaccine-
17 elicited immunity than the prototype strain.

18 Each 0.5 mL dose of Novavax COVID-19 vaccine,
19 Adjuvanted contains 5 micrograms of recombinant viral
20 spike protein from SARS-CoV-2.1 strain expressed in Sf9
21 cells co-formulated with Novavax saponin-based Matrix-M

1 adjuvant 50 micrograms. Proposed use under the EUA:
2 active immunization to prevent COVID-19 caused by SARS-
3 CoV-2 in individuals 18 years of age and older. The
4 dosing regimen is a two series of two doses of 0.5 mL
5 each, administered intramuscularly three weeks apart.
6 Novavax COVID-19 vaccine also referred to at NVX-
7 CoV2373 during clinical development.

8 On February 1, 2022, FDA received Novavax's
9 request for Emergency Use Authorization of their COVID-
10 19 vaccine. EUA of Novavax COVID-19 vaccine,
11 Adjuvanted would depend on clinical data to inform
12 benefits and risks; manufacturing and product
13 information to ensure the vaccines quality and
14 consistency. The manufacturing process for Novavax
15 COVID-19 vaccine, Adjuvanted has changed over time, and
16 submission to FDA of complete manufacturing and product
17 information to support the vaccine product intended for
18 use under EUA is ongoing.

19 Novavax EUA request clinical package includes
20 safety, immunogenicity, and efficacy data from a Phase
21 3 study protocol 2019nCoV-301 conducted in the U.S. and

1 Mexico with approximately 30,000 participants. FDA
2 will be able to determine compatibility of the vaccine
3 product evaluated in this study to the vaccine product
4 intended for use under EUA. Novavax clinical package
5 also includes safety data from approximately 10,000
6 subjects who received Novavax COVID-19 vaccine across
7 three clinical studies worldwide: a Phase 3 Study 302
8 conducted in United Kingdom; a Phase 2 Study 501, which
9 was conducted in South Africa, and a Phase 1 Study 101
10 conducted in Australia and U.S.

11 Available manufacturing and product
12 information does now allow for a determination of
13 compatibility between the vaccine product used in these
14 three studies and the vaccine product intended for use
15 under EUA. Therefore, FDAs review of these studies was
16 limited to safety evaluation.

17 We would request the Committee members to
18 focus their applications of clinical package only.
19 Criteria for Emergency Use Authorization. FDA may
20 issue an Emergency Use Authorization of an unapproved
21 medical product following an EUA declaration if the

1 following statutory requirements' are met: the agent
2 referred to in the EUA declaration can cause a series
3 or life-threatening disease or condition; the medical
4 product may be effective to prevent, diagnose, or treat
5 the serious or life-threatening condition caused by the
6 agent; the known and potential benefits of the product
7 outweigh the known and potential risk of the product;
8 there is no adequate, approved, and available
9 alternative to the product for diagnosing, preventing,
10 or treating the disease or condition.

11 Currently, there are three COVID-19 vaccines
12 available in the U.S. for use in individuals 18 years
13 of age and older: Pfizer-BioNTech's COVID-19 vaccine, a
14 mRNA vaccine, licensed as COMIRNATY; Moderna's COVID-19
15 vaccine, another mRNA vaccine, licensed as SPIKEVAX;
16 Janssen's COVID-19 vaccine, not licensed, but available
17 under EUA. Use of Janssen COVID-19 vaccine is limited
18 to individuals for whom other FDA-approved or
19 authorized COVID-19 vaccines are not accessible or
20 clinically appropriate, and individuals who elect to
21 receive the Janssen COVID-19 vaccine because they would

1 otherwise not receive a COVID-19 vaccine.

2 So, here is today's agenda, after my
3 introduction Dr. Heather Scobie from CDC will give you
4 an overview of current epidemiology of COVID-19 and
5 COVID-19 vaccination rates in the United States.
6 Followed by Dr. Tom Shimabukuro from CDC will give you
7 an overview of COVID-19 vaccine-associated myocarditis,
8 followed by sponsors presentation: Emergency Use
9 Authorization request by Novavax for a vaccine to
10 prevent COVID-19 in individuals 18 years of age and
11 older.

12 There is a short break followed by Dr. Lucia
13 Lee, the Lead Medical Officer from Office of Vaccine
14 Research for FDA, will present FDA's Review of
15 Effectiveness and Safety of Novavax COVID-19 Vaccine,
16 Adjuvanted in Individuals 18 Years of Age and Older.
17 Then we have 45 minutes lunch break, followed by open
18 public hearing. Then a short break, and then
19 additional question and answering session regarding the
20 Sponsor and FDA's presentation. Followed by Committee's
21 discussion and voting, and then meeting will be

1 adjourned.

2 Here is the voting question for the Committee.
3 Based on the totality of scientific evidence available,
4 do the benefits of Novavax COVID-19 vaccine,
5 Adjuvanted, when administered as a 2-dose primary
6 series, outweigh its risk in individual 18 years of age
7 and older under EUA? Thank you for your attention.

8 **DR. ARNOLD MONTO:** Thank you, Dr. Sen, you've
9 given us a good overview of the entire day's
10 proceedings. We have a few minutes now and if the
11 Committee has any questions about the guidance, about
12 EUAs and the rationale for Emergency Use Authorization,
13 you can raise your hands now. Okay, Dr. Rubin, is that
14 your hand raised? I'm not seeing it in green here.

15 **DR. ERIC RUBIN:** Yeah, that's me, Doctor.

16 **DR. ARNOLD MONTO:** Okay. Go ahead.

17 **DR. ERIC RUBIN:** I know that it isn't our
18 mission to interpret statute, but I am curious about
19 the EUA justification. As you stated, Dr. Sen, there
20 are three, two approved and one authorized vaccine out
21 there so I'm curious as to how this meets the criteria

1 for a product for which there is a necessity given the
2 existing products.

3 **DR. GOUTAM SEN:** Dr. Marks, would you like to
4 respond?

5 **DR. PETER MARKS:** Yeah. I'm happy to, or Dr.
6 Fink can. I'm trying to get my camera on here, there
7 we go. Thanks very much for that question, Dr. Rubin.
8 The statute says, it allows us some leeway because it
9 gives us the ability to have products that are either,
10 they would fulfill some unmet need. And, in this
11 particular case, although we have mRNA vaccines out
12 there, we have the Janssen vaccine out there, the
13 Janssen vaccine is currently not being used as a
14 frontline vaccine the same way as the mRNA vaccines.

15 Which leaves the issue of vaccines for those
16 who might not want to take an mRNA vaccine because of
17 concerns they might have with an mRNA vaccine. As
18 needing potentially an alternative, having a protein-
19 based alternative may be more comfortable for some in
20 terms of their acceptance of vaccine. I will use this
21 as a moment on the bully pulpit to say that we do have

1 a problem with vaccine uptake that is very serious in
2 the United States. And anything we can do to get
3 people more comfortable to be able to accept these
4 potentially life-saving medical products is something
5 that we feel we are compelled to do. Does that answer
6 your question?

7 **DR. ERIC RUBIN:** That does, that's great.
8 Thank you very much.

9 **DR. GOUTAM SEN:** Thank you, Dr. Marks.

10 **DR. ARNOLD MONTTO:** Thank you. Dr. Levy.

11 **DR. OFER LEVY:** Hello, thank you for that
12 helpful introduction. If I understood correctly, there
13 have been some concerns with the manufacture of the
14 protein that is the basis of this Novavax vaccine, and
15 for that reason some of the data from some of the other
16 international studies will not be considered with
17 regards to vaccine efficacy and immunogenicity today.

18 My question is this, could FDA say a few words
19 about what the nature of the manufacturing process was?
20 And also, are we as a Committee to assume that these
21 issues are completed solved now and that the latest

1 version of the way the protein is manufactured will not
2 lead to any manufacturing problem?

3 **DR. ARNOLD MONTA:** Dr. Sen, I don't know if
4 you would like to answer those questions or wait until
5 later on because they are about the substance, so it's
6 your choice.

7 **DR. GOUTAM SEN:** No, Dr. Monta, thank you. I
8 think we'll discuss that during question and answer
9 session. We can discuss a little more about that, so
10 I'll pass it on now.

11 **DR. ARNOLD MONTA:** Okay, thank you. Dr.
12 Gellin. We can't hear you.

13 **DR. PRABHAKARA ATREYA:** Dr. Gellin, muted.

14 **MR. MICHAEL KAWCYNKI:** You're muted, sir, on
15 your phone.

16 **DR. BRUCE GELLIN:** Okay, got it. Thanks,
17 sorry. About dosing, we're asked to review the safety
18 and efficacy of a two-dose schedule. If you wind back
19 the clock that's how this all began, and we learned
20 subsequently that two doses was not really the full
21 need. And then, with this confusion about what's a

1 booster versus a third dose, we're likely to get into
2 this later, but what are we going to be doing about
3 more than a second dose?

4 And then a related piece is that this is
5 entering a marketplace with other vaccines and while
6 there may be some who've been waiting for this as their
7 only vaccination, there are others who might want to
8 think about how they optimize their own immunity with
9 mixing/matching with other things, so hopefully we can
10 hear something and learn something about that. Thank
11 you.

12 **DR. ARNOLD MONTO:** Again, it's up to you
13 whether you want to answer these questions now or
14 later.

15 **DR. GOUTAM SEN:** Dr. Monto, Novavax has
16 completed the booster dose data and once we complete
17 these primary series, FDAs going to review those data
18 and we'll discuss that in future.

19 **DR. ARNOLD MONTO:** Finally, Dr. Marasco, a
20 very short question. We've run out of time.

21 **DR. WAYNE MARASCO:** Yes, it's really a

1 question to Dr. Marks and CBER really. It's a follow-
2 up to Dr. Rubin's question. This vaccine that we're
3 going to hear about today is Adjuvanted and I'm curious
4 in terms of CBER have you guys really considered what
5 the public is hearing and seeing, which is waning
6 immunity. And is there any emphasis in this particular
7 vaccine on the fact that it's Adjuvant and may change
8 the durability of the response?

9 **DR. ARNOLD MONTO:** Dr. Marks?

10 **DR. PETER MARKS:** Yeah, no, thanks for that
11 question. I think that'll be something for the
12 Committee to discuss today and I think the Sponsor may
13 be presenting some information on that as well.
14 There's the issue of durability of response as well as
15 the breadth of protection, which I think are both
16 things that will be open for discussion.

17 **DR. ARNOLD MONTO:** Thank you, all. We've
18 heard some questions which we need to park, and we can
19 bring these up later on as we get into discussions of
20 the substance that we're going to be handling today.
21 Now, let's get back to the background, which I jumped

1 to before, and I'd like to reintroduce Dr. Scobie. Dr.
2 Scobie, tell us about COVID vaccination rates in the
3 United States.

4

5 **CURRENT EPIDEMIOLOGY OF COVID-19 AND COVID-19**

6 **VACCINATION RATES IN THE UNITED STATES**

7

8 **DR. HEATHER SCOBIE:** Good morning, can you
9 hear me?

10 **DR. ARNONLD MONTO:** We can.

11 **DR. HEATHER SCOBIE:** Great. The Omicron
12 variant has been shown to have increased
13 transmissibility, a decreased severity relative to
14 previous lineages. Omicron has many mutations in the
15 spike gene, including 15 mutations in the receptor
16 binding domain, as shown in the picture on the right.
17 These mutations are associated with reduction and
18 efficacy of some monoclonal antibody treatments. And a
19 reduction in neutralization by sera from vaccinated or
20 convalescent individuals.

21 This is a graph of the number of SARS-CoV-2

1 sequences submitted globally to the GISAID Public
2 Genomic Data Repository since Omicron was first
3 detected at the end of November 2021. The blue color
4 shows the Delta variant being displaced as the Omicron
5 BA.1 sub-lineages, in salmon color, quickly rose to
6 predominance followed by the rise of the Omicron BA.2
7 sub-lineages in peach. The other Omicron sub-lineages
8 like BA.4 and BA.5 are not readily apparent in the
9 figure because they are still a relatively low
10 proportion of submitted sequences. The total number of
11 submitted sequences globally has shown a declining
12 trend since January of 2022.

13 This stacked bar shows recent U.S. trends and
14 the national weighted estimates of variant proportions
15 and Nowcast projections of circulating SARS-CoV-2
16 lineages by week of specimen collection date from CDCs
17 COVID data tracker. Omicron sub-lineage's depicted in
18 different purple and pink shades have been over 99
19 percent predominant since late January.

20 The BA.1.1 sub-lineage in dark purple was
21 gradually displaced by the BA.2 sub-lineage shown in

1 lavender and, more recently, the BA.2.12.1 sub-lineage,
2 in pink, which was 59 percent of circulating lineages
3 as of the week ending May 28th. BA.4 and BA.5 are not
4 shown in this graph because they were less one percent
5 for this period. But these sub-lineages will be shown
6 in the variant proportion estimates released later
7 today.

8 This map shows the relative proportions of
9 BA.2.12.1 in pink, BA.2 in lavender, and other Omicron
10 sub-lineages in the darker purple shade across the 10
11 health and human services subregions. You can see that
12 BA.2.12.1 is at least 50 percent predominant in all
13 regions, except region 10 in the northwest.

14 This graph shows the trends in daily numbers
15 of COVID-19 cases reported in the United States since
16 the beginning of the pandemic. The number of cases
17 associated with the Alpha variant were relatively small
18 compared with the Delta variant and then the Omicron
19 variant. Nationally reported cases show increasing
20 trends in April and May. Those trends may be starting
21 to turn in the last week or so.

1 Reported cases still remain relatively high.
2 I notice that the number of reported cases is likely
3 underestimated due to the increased use of at-home
4 tests whose reports are mostly unreported to public
5 health departments. As of June 5th there have been
6 over 84 million cases of COVID-19 reported in the U.S.

7 This is a graph from a recent MNWR on CDCs
8 National Commercial Laboratory Seroprevalence Study and
9 shows trends of infection-induced SARS-CoV-2 antibodies
10 by age group. These results do not include anti-spike
11 antibodies from vaccination, nor do they reflect the
12 percentage of the population that might have sufficient
13 antibodies to be protected from reinfection.

14 The percentages of people with previous
15 infection noticeably increased following the rise of
16 the Omicron variant. Greater seroprevalence was noted
17 in younger age groups likely related to these groups
18 being eligible for vaccination in later months and
19 different exposure risk compared to older age groups.
20 National seroprevalence during February 2022 was 58
21 percent.

1 This graph shows the trends in the daily
2 number of reported COVID-19 deaths in the United States
3 since the beginning of the pandemic. Including during
4 the waves associated with the Alpha, Delta, and Omicron
5 variants. Even though the Omicron infection is less
6 severe overall relative to Delta, the number of deaths
7 related to Omicron was relatively high because Omicron
8 case numbers were very high. As of June 4th there have
9 been over one million deaths due to COVID-19 reported
10 cumulatively in the U.S.

11 These are the weekly trends in COVID-19
12 associated mortality rates by age group. The data show
13 that higher mortality rates are consistently observed
14 in older age groups. Most notably on this graph among
15 ages 75+, 65 to 74, and 50 to 64, as shown in the
16 purple and pink colors. These are the weekly trends in
17 the rates of new COVID-19 in-patient admissions by age
18 group. Similar to the previous graph, you can see
19 higher hospitalization rates in the older age groups.
20 With patients 70+ in purple, 65 to 74 and 50 to 64
21 years in the pink colors having the highest admission

1 rates, followed by other adult age groups in shades of
2 blue.

3 As of June 2nd more than 221 million people in
4 the U.S. have been vaccinated with a primary vaccine
5 series, which is 71 percent of the eligible population
6 aged five years and older. There are also over 103
7 million people, or 49 percent of the population, aged
8 12 years or older who have also received the first
9 booster dose. And about 15 million people, or 23
10 percent of the population, aged 50 years and older who
11 have also received a second booster dose.

12 This graph shows trends over time and by age
13 group, and the percentage of people who have received
14 at least a primary series on the left and a booster a
15 dose on the right. In both figures vaccination
16 coverage is higher in older age groups, indicated in
17 the purple and pink colors. We can also see that
18 coverage with the primary series for ages 5 to 11
19 years, shown with the yellow dotted line on the left,
20 is still relatively low at 29 percent. Booster dose
21 coverage on the right remains' under 50 percent for age

1 groups less than 50 years, shown in blues and yellows.

2 From data reported to COVID Data Tracker, over
3 230 million, or 89 percent, of U.S. adults ages 18
4 years and older have received at least one COVID-19
5 vaccine dose. Using these data and Census data, we can
6 estimate that there are about 27 million adults who
7 have not yet received a vaccine at this time. I'll
8 also note that most adults aged 65 years and older have
9 already received at least COVID vaccine dose.

10 This is data from the National Immunization
11 Survey on adults who have not received a COVID-19
12 vaccine by age group, race and ethnicity. Across the
13 age groups we can see that people of non-Hispanic,
14 other, or multiple races, and non-Hispanic white people
15 have the highest percentages remaining unvaccinated.
16 While Hispanic and non-Hispanic black people have the
17 lowest percentages remaining unvaccinated.

18 Next, we're going to shift to consider
19 surveillance monitoring of rates of cases,
20 hospitalizations, and deaths by vaccination status.
21 CDC collaborates with 31 public health jurisdictions

1 representing 70 percent of the U.S. population. These
2 jurisdictions actively link case surveillance,
3 immunization registry, and vital registration data to
4 monitor rates of COVID-19 cases and deaths by
5 vaccination status. CDC also track's rates of COVID-19
6 hospitalizations by vaccination status using COVID-NET,
7 which is a population-based sentinel surveillance
8 system in 99 counties and 14 states representing 10
9 percent of the U.S. population.

10 In addition, CDCs vaccine effectiveness
11 studies allow for more robust analyses as compared with
12 surveillance, and a better understanding of how well
13 vaccines are working. We also have detailed data on
14 serious illnesses in vaccinated persons through COVID-
15 NET, as well as electronic health record and vaccine
16 effectiveness platform.

17 This slide shows the age-adjusted rates of
18 COVID-19 associated deaths by vaccination status and
19 receipt of booster doses. Unvaccinated people in all
20 age groups have had higher mortality rates than people
21 who received a primary series alone, and people who

1 also received a booster dose. Including after Omicron
2 became the predominant variant. In March, unvaccinated
3 people ages 12 years and older had 17 times the risk of
4 dying from COVID-19 compared with people vaccinated
5 with a primary series and booster dose.

6 This graph shows age-adjusted rates of COVID-
7 19 associated hospitalizations by vaccination status
8 and receipt of a booster dose. Hospitalizations for
9 COVID-19 were higher among unvaccinated than vaccinated
10 people over time. Including after Omicron became the
11 predominant variant. In March, unvaccinated adults
12 ages 18 years and older had five times higher risk of
13 COVID-19 associated hospitalization compared to those
14 fully vaccinated with a booster dose.

15 This slide shows age-adjusted rates of COVID-
16 19 cases by vaccination status. In April, unvaccinated
17 people ages five years and older had a two times higher
18 risk of testing positive for COVID-19 compared to full
19 vaccinated people overall.

20 Various studies have shown that severe COVID-
21 19 illness is relatively rare among vaccinated people

1 compared with unvaccinated people. Compared with
2 unvaccinated people, fully vaccinated people with
3 severe COVID-19 illness are more likely to be older, be
4 long-term care facility residents, and have underlying
5 medical conditions, including immunosuppression,
6 diabetes, and chronic kidney, lung, cardiovascular, and
7 neurologic diseases. More than 75 percent of people
8 who are fully vaccinated and get severe COVID-19
9 illness have multiple risk factors.

10 In summary, CDC continues to monitor emerging
11 variants, like the BA.2 sub-lineage of Omicron,
12 including their prevalence and impact on disease
13 incidents and severity over time. Monitoring trends
14 and rates of cases, hospitalizations, and deaths by
15 vaccination status has been helpful for monitoring the
16 impacts of different variants. And, finally, currently
17 authorized vaccines offer protection against infection,
18 severe illness, and death so it's important to stay up-
19 to-date with vaccinations, including receipt of first
20 and second booster doses in eligible populations.
21 Thank you, and I'd like to acknowledge those people for

1 their contributions.

2 **DR. ARNOLD MONTO:** Thank you, Dr. Scobie. We
3 have a few minutes for questions specifically
4 concerning the presentation about where we are with
5 COVID, with the variants, and with vaccination. Let's
6 stick to those topics. Dr. Chatterjee.

7 **DR. ARCHANA CHATTERJEE:** Thank you, Dr. Monto.
8 Dr. Scobie, my question is in regard to long COVID and
9 whether you have any data to share with us on the
10 impact of the vaccines on long COVID?

11 **DR. HEATHER SCOBIE:** No, unfortunately I don't
12 have data on that today, but I might ask Lieutenant
13 Commander Ruth Link-Gelles, so she's on the line, if
14 she has any data from vaccine effectiveness studies or
15 any other related data that she wants to share. Are
16 you there Dr. Link-Gelles?

17 **MR. MICHAEL KAWCZYNSKI:** I'm sorry, who are
18 you looking for, Heather?

19 **DR. HEATHER SCOBIE:** Ruth Link-Gelles, do you
20 see her on the line?

21 **MR. MICHAEL KAWCZYNSKI:** No. Go ahead, Praba.

1 **DR. ARNOLD MONTO:** Okay, I think we'll just
2 move on. Sorry, Dr. Chatterjee, but this'll probably
3 come up later today. Dr. Perlman.

4 **DR. STANLEY PERLMAN:** Yeah, I just had a
5 question about one of the first figures that you
6 showed. The data showing the high mortality in people
7 over 75 with the Omicron. Do you know if those people
8 were vaccinated? Would this be justification for
9 different vaccines? Or were those people mostly
10 unvaccinated? Or were they just people that had many,
11 many comorbidities? Do we know about antibody titers
12 in them? Trying to get a sense for how the Novavax
13 vaccine could fit in this.

14 **DR. HEATHER SCOBIE:** Yeah, that's an
15 interesting question. The data I showed are actually
16 surveillance data, so we don't have detailed
17 information in that system on vaccination status. And
18 we don't have titers, like you were asking about.
19 There are studies, like vaccine effectiveness studies,
20 that would have more detailed information. And the
21 data that I showed you on vaccine breakthrough

1 surveillance, the rates of cases, hospitalizations, and
2 deaths by vaccination status, those data are collected
3 by age groups. And even in the older age groups we do
4 see a very large disparity in unvaccinated people
5 having higher rates of hospitalization and death
6 regardless of age group.

7 Although it may be true that, as I was saying,
8 that if you are of older age and you have underlying
9 conditions and you happen to have a breakthrough
10 infection, you will be more likely to have a serious
11 event compared to people who don't have those risk
12 factors. It's still very much the case that adults and
13 children alike are protected against serious illness
14 with these vaccines.

15 **DR. STANLEY PERLMAN:** Thank you.

16 **DR. ARNOLD MONTO:** Thank you. Dr. Reingold.

17 **DR. ARTHUR REINGOLD:** Can you hear me?

18 **DR. ARNOLD MONTO:** Yes.

19 **DR. HEATHER SCOBIE:** Yes.

20 **DR. ARTHUR REINGOLD:** Thanks' for that.

21 Arthur Reingold. Quick question, I know you depressed

1 the most recent data, you don't have quantified yet,
2 but the eyeball test looking at those graphs of rates
3 of either hospitalizations or deaths by vaccination
4 status would suggest they're converging more recently.
5 And that the VE is in fact shrinking in the most recent
6 time period. I'm just curious if you have any thoughts
7 about that of whether the eyeball test --

8 **DR. HEATHER SCOBIE:** Yeah, I mean -- so the
9 eyeball test is challenging in this situation because
10 the Omicron peak at the beginning of the year was so
11 high, so it's really throwing the Y axis off. It's
12 scaling everything down. And then, in the data that I
13 showed you on more serious outcomes, that was during a
14 period of relatively low incidents in the U.S. so it's
15 pretty hard to see what's going on in those graphs.

16 But it is true what you're saying, that as
17 different variants have come through, notably the Delta
18 variants and then the Omicron variants, we have seen
19 evidence in our rate data that suggests a decrease in
20 vaccination effectiveness. We don't choose to
21 calculate vaccine effectiveness using those data

1 because of our inability to control for other factors
2 besides age.

3 It's definitely true what you're saying that
4 vaccine effectiveness has been reduced related to
5 different variants. I don't, Ruth Link-Gelles, I don't
6 know if you're able to connect her now, but she was my
7 expert that I had on about VE if she wants to say more.

8 **DR. ARNOLD MONTO:** Let's, for technical
9 reasons I think it's very difficult to link other
10 people on, so --

11 **DR. HEATHER SCOBIE:** Okay.

12 **DR. ARNOLD MONTO:** -- let's go on and Dr.
13 Gellin has his hand raised.

14 **DR. BRUCE GELLIN:** Heather, thanks' for that,
15 can you hear me?

16 **DR. HEATHER SCOBIE:** Yes.

17 **DR. BRUCE GELLIN:** Two things, you used the
18 term fully vaccinated several times, I wanted to know
19 how you define that. And maybe this is for later when
20 we think about epidemiology of COVID infection, will we
21 be hearing either now or later background rates of

1 myocarditis from natural infection? Thanks.

2 **DR. ARNOLD MONTO:** We have a talk coming up,
3 Bruce, on myocarditis.

4 **DR. HEATHER SCOBIE:** Yes, that's the next talk
5 about myocarditis. Let's see, and fully vaccinated is
6 a term that still exists that's defined as vaccinated
7 with a primary series. And it's challenging to
8 understand, so we make attempts to not use it, but for
9 whatever -- it still exists in the literature, and it
10 still exists on my slides, so apologies for that. But
11 it means vaccinated with a primary series.

12 There's another term called up-to-date that
13 means vaccinated with a primary series and whatever
14 booster doses were indicated for the particular
15 individual according to minimal intervals specified in
16 the guidance. That term is challenging to implement
17 from a surveillance and monitoring perspective. It's
18 often not what's used in our measurements for
19 surveillance data.

20 **DR. ARNOLD MONTO:** Thank you, and Dr. Nelson,
21 final question in this series.

1 **DR. MICHAEL NELSON:** Thank you, Commander
2 Scobie, for that great overview and very informative
3 presentation. One of our considerations for an EUA
4 authorization is the availability of treatments for the
5 disease in which we are trying to prevent with the
6 vaccine. So, in scouring the agenda today, I didn't
7 really see the impact of available treatments for
8 disease on the epidemiology of the disease itself. And
9 I wonder if you care to comment at this time or save it
10 for later discussion. Thank you.

11 **DR. HEATHER SCOBIE:** Yeah, so unfortunately,
12 so I have a variant's expert also on the line, but I'm
13 not sure that that person could be connected, Dr.
14 Natalie Thornburg, so I didn't prepare for certain
15 questions because I believed they would be able to be
16 connected. It's true what you're saying that this is
17 definitely a concern when we're talking about
18 vaccination and these variants.

19 Whether there are other treatments that can be
20 used when people become infected to protect them
21 against serious illness. And it's definitely true that

1 when Omicron became predominant this was a major thing
2 that the healthcare system had to deal with because
3 there was essentially only one monoclonal antibody that
4 was effective against Omicron. And there wasn't enough
5 of it, and it was a major problem. Natalie is writing
6 me now. But --

7 **DR. PRABHAKARA ATREYA:** Dr. Monto can we have
8 Dr. Natalie speak?

9 **DR. HEATHER SCOBIE:** Were you able to connect
10 her?

11 **DR. ARNOLD MONTO:** Well, yes, if she's
12 available.

13 **DR. PRABHAKARA ATREYA:** Yes, she is available,
14 thank you.

15 **DR. ARNOLD MONTO:** Then we'll have to move
16 ahead. And, Dr. Nelson, this is an important point
17 which I think you may wish Dr. Mark's group to weigh in
18 on, but later on this afternoon.

19 **DR. MICHAEL NELSON:** Understood. Thank you.

20 **DR. ARNOLD MONTO:** Is Natalie available?

21 **DR. HEATHER SCOBIE:** Dr. Thornburg, are you

1 there?

2 **DR. PRABHAKARA ATREYA:** Yes, Mike, can you
3 connect Natalie please?

4 **DR. ARNOLD MONTO:** Let me suggest --

5 **DR. HEATHER SCOBIE:** She said she is muted.

6 **DR. ARNOLD MONTO:** -- that we not have too
7 many link-ins. The technology is not all that able to
8 handle this.

9 **MR. MICHAEL KAWCZYNSKI:** Natalie, hold on a
10 second, I will unmute you right now. Hold on, I just
11 had to know who it was. Thank you. Go ahead, Natalie,
12 take it away.

13 **DR. HEATHER SCOBIE:** I believe you may have
14 unmuted Dr. Link-Gelles, it's Natalie Thornburg.

15 **DR. NATALIE THORNBURG:** I am unmuted now,
16 thank you.

17 **DR. HEATHER SCOBIE:** Oh, you're there. Okay,
18 great.

19 **DR. NATALIE THORNBURG:** Yes, I'm here. Yeah,
20 so I believe the question was use of therapeutics. You
21 sort of summarized the question, it was use of

1 therapeutics and how that has impacted the variants,
2 with variants circulating, is that the correct
3 question?

4 **DR. HEATHER SCOBIE:** Concerns about Omicron
5 probably specifically, and the use of monoclonal
6 antibodies and other treatments.

7 **DR. NATALIE THORNBURG:** Yeah, on the
8 monoclonal antibodies, use of those treatments and
9 those prophylaxis, because there's so many changes in
10 the receptor binding domain of Omicron, Heather said
11 there's 15 in the receptor binding domain, that's the
12 part of the spike protein that binds to the cell and,
13 therefore, that is also the same region that
14 neutralizing monoclonal antibodies bind. So Omicron
15 has indeed lost activity, or the monoclonal antibody
16 therapeutics, several of them have lost potent activity
17 against Omicron.

18 And we don't have as many of those available.
19 Those same problems won't exist for small molecule
20 inhibitors, fortunately. And new monoclonals can be
21 developed, but when a variant emerges like Omicron,

1 that have a lot of changes in the receptor binding
2 domain, it does reduce the toolbox clinicians have to
3 use when people get infected.

4 **DR. MICHAEL NELSON:** And I guess for
5 Committee's consideration and one clarifying question,
6 would it be fair to state that the availability of
7 these various treatments have had little impact on the
8 overall course of the epidemiology of the disease in
9 the U.S. at this time?

10 **DR. NATALIE THORNBURG:** Well, I think that the
11 transmission of the virus, most people are most
12 transmissible in the day or two leading up to symptom
13 onset, and a few days after symptom onset. Often, they
14 can't get access to treatment until their
15 transmissibility is already beginning to wane. And
16 therefore, vaccines are a really key tool in reducing
17 transmission. But we have to use all of the tools in
18 our toolbox.

19 **DR. ARNOLD MONTTO:** Right, thank you. Dr.
20 Marks, for a final comment before we go on to the next
21 presentation.

1 **DR. PETER MARKS:** I think it's very important
2 for us to step back here for a moment and just
3 recognize that vaccines are a unique public health tool
4 that is relatively inexpensive. The safety of vaccines
5 in terms of the benefit/risk is often much better than
6 the safety of some of the therapeutics that might be
7 used post-facto after one is infected. And so, one of
8 the really important things here about vaccines is they
9 have been wonderful public health interventions, and
10 that's why we use them.

11 They can give protection to many, many, many
12 more people than we can come up with courses of oral
13 therapies or intravenous therapies. And the cost of
14 actually, and the complexity and the potential
15 complications of delivering intravenous therapies or
16 even some of the oral therapies are much greater than
17 the simplicity of giving vaccines. Not that vaccines
18 have zero risk associated with them; we'll hear about
19 potential side effects of vaccines later today. But
20 that overall the benefit/risk is quite favorable as a
21 public health intervention.

1 **DR. ARNOLD MONTO:** Thank you, Dr. Marks. Now
2 we are moving ahead to the next discussion, which is
3 about myocarditis. We will hear Captain Shimabukuro
4 from CDC giving us this update. Thank you.

5

6 **OVERVIEW OF COVID-19 VACCINE ASSOCIATED MYOCARDITIS**

7

8 **DR. TOM SHIMABUKURO:** Hi, can you hear me
9 okay?

10 **MR. MICHAEL KAWCZYNSKI:** Yeah, you're fine.

11 **DR. TOM SHIMABUKURO:** All right. Next slide,
12 please, or, I'm sorry, I'll control. So today topic
13 I'm going to cover is a background on classic
14 myocarditis and myocarditis associated with mRNA COVID-
15 19 vaccination. And then I'll give an update on
16 myocarditis following mRNA COVID-19 vaccination with a
17 focus on people ages 18 and older that will include
18 data from the Vaccine Adverse Event reporting system,
19 or VAERS, and the Vaccine Safety Datalink, or VSD.

20 Classic myocarditis usually has an infectious
21 cause, typically viral or presumed to be viral.

1 Although infection with a pathogen is frequently not
2 identified. It can be due to direct microbial
3 infection of the myocardial cells. I'm having some
4 technical difficulties with the slides. They keep on
5 reversing order here. I don't know if that's on my end
6 or your end.

7 **MR. MICHAEL KAWCZYNSKI:** We're not touching
8 your slides, so go ahead, sir.

9 **DR. ARNOLD MONTO:** We're okay.

10 **DR. TOM SHIMABUKURO:** Okay. It can also be
11 toxin-mediated or in a setting in systematic infection
12 or infection of non-cardiac tissue. Rarer causes
13 include autoimmune, hypersensitivity, or giant cell
14 myocarditis. Incidence is higher in males compared to
15 females starting after age five years. And, as I
16 mentioned, it's common to not identify a pathogen or
17 possible infectious etiology for myocarditis. And some
18 studies, when they do testing in a minority of cases do
19 they find a possible infectious etiology.

20 These are graphs showing the epidemiology of
21 myocarditis with children on the righthand side, and

1 adults on the lefthand side. This is from the
2 published literature. If you focus on the lefthand
3 side, with the exception of very early in childhood
4 when there may be factors like genetic factors in play
5 incidence is relatively low in early childhood. And
6 then begins to increase in adolescence. And if you
7 move over to the right graph, you can see peaking in
8 adolescence and then gradually decreasing incidence
9 with age. Most of these cases are male, and by the
10 time you hit middle age the male to female predominance
11 goes away.

12 This is a table showing the characteristics of
13 myocarditis associated with mRNA COVID-19 vaccination
14 in a comparison with viral myocarditis. For vaccine
15 associated myocarditis, mRNA COVID-19 vaccination is
16 the inciting exposure. And then, for viral
17 myocarditis, it's viral, although many of these cases
18 can be asymptomatic. For vaccine associated
19 myocarditis, most cases have been in adolescence and
20 young adults, with more cases in males compared to
21 females. Then for viral myocarditis incidents in males

1 greater than females. Male incidence peaking in
2 adolescence and then gradually declining. Onset for
3 vaccine associated myocarditis has typically been
4 within a few days after vaccination, with most cases
5 occurring within a week. And then, for viral
6 myocarditis, onset is typically one to four weeks after
7 viral illness.

8 The next set of characteristics get at
9 clinical severity, but just in general vaccine
10 associated myocarditis following mRNA COVID-19
11 vaccination has been relatively mild when compared to
12 viral myocarditis which can frequently be severe.

13 So, now I'm going to move on to data from the
14 Vaccine Adverse Event Reporting System, which is the
15 national spontaneous reporting system that's comanaged
16 by CDC and FDA. The key limitation, VAERS is a passive
17 surveillance system. We generally cannot determine
18 cause and effect from VAERS data alone. This is a flow
19 diagram showing U.S. reports to VAERS of myocarditis
20 after mRNA COVID-19 vaccination among people 18 and
21 older following primary series and first booster. We

1 have observed 1,836 reports in this age group. Eleven
2 remain under review, 504 did not meet case definition,
3 and that leaves us with 1,321 reports in this age group
4 that met CDC case definition. To put that number in
5 context, there's been an estimated 491.9 million
6 primary series and first booster doses administered in
7 this age group.

8 This is a figure showing time to onset of
9 these cases. And you'll notice that there appears to
10 be clustering within a few days after vaccination.
11 Many of these cases occurring in the one to four day
12 period. When we get to the vaccine safety data link,
13 I'll show you some additional data that also supports
14 this clustering of onset within a few days of
15 vaccination.

16 Of these 1,321 verified reports that met CDC
17 case definition, the median age in this age group 18
18 and older was 28 years. Median time to onset symptoms
19 after vaccination is three days. Most of these
20 occurred after dose two, and most occurred in males.
21 This is a table of VAERS reporting rates of myocarditis

1 per million doses administered after mRNA COVID-19
2 vaccination in the 0 to 7 and 8 to 21 days post-
3 vaccination.

4 I know this is a busy slide, but there's a few
5 key takeaway points from this. If you look, the peach
6 colored slides are where the observed reporting rates
7 to VAERS exceed the expected background rates based on
8 what's in the published literature. So you can use
9 that as a proxy of risk, that's where the O to E ratio
10 exceeds background. If you look in the 8 to 21 days,
11 you'll see that there are no peach shaded cells, and
12 that reinforces that the risk is concentrated primarily
13 in the zero to seven days.

14 If you look at males versus females you see
15 that reporting rates are generally higher in females,
16 and reporting rates for both males and females are
17 higher after dose two compared to dose one. I have the
18 children in there for reference, but if you start at
19 the 18 to 24 year old age group you see that the
20 reporting rates decrease with time. And, at least for
21 males, by the time you hit 50 years old we do not see

1 an increased risk.

2 So, of these 1,321 reports, where we had
3 information on healthcare utilization most were
4 hospitalized. And most of these reports that were
5 hospitalized had a known outcome at the time of the
6 report. And 73 percent of these had recovered from
7 symptoms at the time of the last follow-up, according
8 to the VAERS report. There were 21 reports of death
9 involving myocarditis. When we evaluated the reports
10 and accompanying records, in one report myocarditis was
11 attributed to causes other than vaccination, and four
12 potential alternate etiologies were present. In 15,
13 cause of death was not attributed to myocarditis, and
14 then one adequate information was not available to
15 fully evaluate the case.

16 So I just want to spend a little bit of time
17 talking about CDCs enhanced surveillance of myocarditis
18 outcomes. And this is currently in an age 12 to 29
19 years. The purpose was to assess functional status and
20 clinical outcomes among individuals reported to have
21 developed myocarditis after mRNA COVID-19 vaccination.

1 And it's a two component survey conducted at least 90
2 days after the onset of symptoms. It included a
3 patient survey and a healthcare provider survey.

4 When the analytic period close in November
5 2021 VAERS had received 852 reports in this age group
6 that were at least 90 days that met case definition.
7 They were at least 90 post-myocarditis diagnosis.
8 We're able to complete 360 patient surveys and 398
9 cardiologist or other healthcare provider surveys that
10 these patients were seeing in aftercare. The main
11 finding from the cardiologists or healthcare provider
12 survey was that based on the provider assessment most
13 patients appeared to have fully or probably fully
14 recovered from their myocarditis.

15 Roughly 82 percent of patients, according to
16 the cardiologist, were classified as fully recovered or
17 probably fully recovered, but pending more information.
18 The majority of the remainder had improved but did not
19 report being fully recovered. So some key findings
20 from this enhanced surveillance activity. On patient
21 follow-up with the patient surveys at least 90 days

1 after diagnosis, most patients who were reached
2 reported no impact on their quality of life and most
3 did not report missing school or work. As I mentioned,
4 82 percent of healthcare providers indicated that the
5 patient was fully recovered or probably fully
6 recovered.

7 Notably there was substantial heterogeneity in
8 the initial and follow-up treatment and testing of
9 these patients. And there did not appear to be a
10 single test that was indicative of recovery. Some
11 additional next steps we're doing is we're going to
12 follow-up on patients who were not yet fully recovered
13 at the time of the survey to further assess the
14 recovery status at least 12 months after myocarditis.
15 And we're also following up on children and evaluating
16 myocarditis cases in children ages 5 to 11 years.

17 So now I'm going to move on to data from our
18 Vaccine Safety Datalink system, which is our electronic
19 health record-based system for surveillance and
20 research. We conduct rapid cycle analysis in the
21 Vaccine Safety Datalink. The aims are to monitor the

1 safety of COVID-19 vaccines weekly using pre-specified
2 outcomes and to describe the uptake of COVID-19
3 vaccines over time among eligible VSD members.

4 Here's a table of the pre-specified outcomes
5 that we are monitoring in VSD and the settings in which
6 we are monitoring them. I'm not going to go through
7 this slide, this is methods. I'll just mention that
8 the primary analytic method for VSD rapid cycle
9 analysis is a vaccinated concurrent comparator
10 analysis. It basically compares vaccinated individuals
11 to other vaccinated individuals looking at cases in a
12 risk interval compared to cases in a comparison
13 interval. For the outcome of myocarditis and
14 pericarditis, all cases were chart confirmed and
15 verified using the CDC case definition.

16 Here's the mRNA COVID-19 vaccine doses
17 administered in VSD in the age group 18 to 39 years
18 old, which is the age group that I'll be presenting
19 data for. There were about 950 patients who received a
20 primary series dose one and dose two for Moderna. And
21 about 1.5 million who received a primary Pfizer series.

1 There's about 574 million people who received a Moderna
2 booster dose one and about 812,000 people who received
3 a Pfizer booster dose one.

4 This is a figure showing the day of onset of
5 verified myocarditis and pericarditis cases in the age
6 group. And you can see similar to what I showed in
7 VAERS, these cases following vaccination tend to
8 cluster shortly after vaccination. In this case,
9 statistically significant clustering in the day zero to
10 three and zero to four. Reinforcing the biological
11 plausibility of this zero to seven day risk interval
12 that we use for our main analyses for myocarditis after
13 mRNA COVID-19 vaccination.

14 This is a table showing verified myocarditis
15 and pericarditis cases in the zero to seven day risk
16 interval compared to outcome events in vaccinated
17 comparators and risk. This is basically looking at the
18 risk in the risk interval compared to the comparison
19 interval. This statistic is the adjusted rate ratio,
20 and this table is for males 18 to 39 years old. And
21 you can see whether it's a combined analysis of both

1 vaccines or looking at the Pfizer vaccine or looking at
2 the Moderna vaccine, the adjusted rate ratios are all
3 elevated. Many of them statistically significantly
4 elevated with the dose two rate ratios tending to be
5 the highest. And then you see, on the far righthand
6 side there, how that translates into the excess cases
7 in the risk period per million doses, which, depending
8 upon the analysis, range from about 40 to 60 additional
9 cases in the risk period per million doses
10 administered.

11 This is the same table, but for females. And
12 you can see that the case counts are substantially
13 lower. The adjusted rate ratios tend to be elevated,
14 some statistically significantly elevated. And some of
15 these adjusted rate ratios are comparable to those
16 observed for males, but I want to caution you, this is
17 based on relatively small numbers. And so, these can
18 be impacted by those small number effects, and then you
19 see the excess cases in the risk period on the
20 righthand side there. I'm going to go back to the
21 previous slide, you'll see that the excess cases in the

1 risk period there. Like I said, in the highest risk
2 strata ranging from about 40 to 60, and you'll see
3 they're substantially lower here for females. So even
4 though some of the adjusted rate ratios may be elevated
5 in females, because of the lower case counts the excess
6 risk tends to be quite lower in females compared to
7 males.

8 This is a table showing the level of care and
9 status of the cases in VSD. And these are the cases
10 after a primary series dose of mRNA COVID-19 vaccine.
11 Most of these cases are admitted to the hospital. A
12 relatively small minority are treated in the emergency
13 department. The length of stays tends to be short.
14 The median length of stay is one. The overwhelming
15 majority of these cases have stays of three days or
16 less. And 100 percent of these case patients were
17 discharged home.

18 This is the same slide, it's a similar table,
19 but it's showing the cases following the first booster
20 dose of an mRNA COVID-19 vaccine. And this, I think,
21 just demonstrates that the level of care and status is

1 similar for the cases following the booster dose
2 compared to the cases following the primary series.

3 So, just to sum up, the current evidence
4 supports a causal association between mRNA COVID-19
5 vaccination and myocarditis and pericarditis. Cases
6 following vaccination cluster within the first week of
7 vaccination. The risk is greatest in adolescents and
8 young adults, higher after dose two compared to dose
9 one of the primary series. And higher in males
10 compared to females. Some risk estimates for females
11 in VSD are comparable to males, but case counts are
12 small and excess risk in females is substantially lower
13 than for males.

14 The risk appears to decrease with age and the
15 male to female predominance of cases attenuates with
16 age. Reporting rates in VAERS are highest following
17 dose two, reporting rates following dose one and first
18 booster dose tend to be lower. Incidence rates in VSD
19 of verified myocarditis and pericarditis zero to seven
20 days following vaccination are generally highest
21 following dose two. In a minority of age and sex

1 strata, notable males aged 16 to 17 years, the
2 incidence is highest following the booster dose.

3 And, based on our follow-up of VAERS cases
4 reports, available information suggests that most
5 persons with myocarditis after mRNA COVID-19
6 vaccination recover from myocarditis by three to eight
7 months after diagnosis. I'd like to acknowledge the
8 following groups for their contributions. And I'll be
9 happy to answer questions.

10 **DR. ARNOLD MONTO:** We have only a few minutes
11 for questions right now. I'm sure that the topic will
12 come back. Remember, to our Committee, that this is
13 background information on mRNA vaccines in basically
14 observational studies. I see a lot of hands raised and
15 we're not going to be able to get all of them. I'm
16 going to have a couple of questions, maybe two or
17 three, and then we're going to be going on to the
18 Sponsor presentation. If you are disappointed, my
19 apologies. Dr. Rubin.

20 **DR. ERIC RUBIN:** Hi, sorry about that. Thanks
21 Dr. Shimabukuro. One of the hypotheses is that the

1 antigen itself and cross reactivity that's leading to
2 myocarditis, is there any evidence, and I realize a lot
3 of it might be international, of an association between
4 myocarditis and the viral vectored vaccines?

5 **DR. TOM SHIMABUKURO:** I don't know if anyone
6 could hear me.

7 **DR. ARNOLD MONTO:** No, I couldn't.

8 **MR. MICHAEL KAWCZYNSKI:** Tom just disconnected
9 his audio inadvertently, so I'm just going to reconnect
10 Tom's audio here. Here he comes. There he comes.
11 There you go. Tom, you there?

12 **DR. TOM SHIMABUKURO:** Sorry, I lost audio
13 there for a second and missed --

14 **DR. ERIC RUBIN:** That's okay.

15 **DR. TOM SHIMABUKURO:** -- the questions.

16 **MR. MICHAEL KAWCZYNSKI:** Go ahead, Eric, will
17 you repeat that quick?

18 **DR. ERIC RUBIN:** The quick version, is there
19 evidence that this is the antigen rather than the
20 method of delivery? In other words, do you see the
21 same thing with viral vectored vaccines?

1 **DR. TOM SHIMABUKURO:** There have been case
2 reports after the Janssen vaccine, but the data are
3 pretty sparse. There hasn't been much vaccine
4 administered, and there hasn't been much vaccine
5 administered in these high risk groups, namely
6 adolescents and young adults. So I don't think we have
7 sufficient evidence to rule out or establish a risk.
8 And I'm not aware of any surveillance or epi data from
9 the Astra-Zeneca vaccine that would indicate a risk,
10 but I think right now the data are really not
11 sufficient for Janssen to draw hard conclusions on
12 that.

13 **DR. ERIC RUBIN:** Thank you.

14 **DR. ARNOLD MONTO:** Thank you. Dr. Gellin. We
15 can't hear you.

16 **MR. MICHAEL KAWCZYNSKI:** You have your phone
17 muted again, Dr. Gellin.

18 **DR. BRUCE GELLIN:** Sorry. This is about
19 natural history of myocarditis and recovery from it.
20 You talked about recovery in the vaccine associated
21 cases. Does that mean in the natural history, is fully

1 recovered meaning people don't have to worry about it
2 ever again, or are there long-term consequences that
3 might come up later? Over.

4 **DR. TOM SHIMABUKURO:** I'm probably not the
5 best person to talk about the natural history of
6 myocarditis. I think that there can be long-term
7 effects, residual effects of myocarditis. There is
8 not, as I said, there appears to be a lot of
9 heterogeneity, both in the treatment and in the follow-
10 up care, and not really a standard to determine whether
11 a patient has recovered. There's a bit of a lack of
12 standardization.

13 What I can say about the cases that we have
14 followed up on is that overwhelming, either when you
15 survey the patient or you survey the healthcare
16 provider, they report generally having favorable
17 outcomes. There's a small number which have improved
18 but have not fully recovered, and that's why we're
19 going to follow-up on these case patients at 12 months
20 or more to try to get a better idea of the recovery
21 status of these vaccine associated cases.

1 **DR. ARNOLD MONTO:** Thank you. Dr. Meissner.

2 **DR. CODY MEISSNER:** Dr. Shimabukuro, thank you
3 so much for your work in this area over the past year
4 or two, it's been very helpful. The question I have
5 for you first is a follow-up to Dr. Gellin's question,
6 and that is, gadolinium uptake of children or
7 adolescents who have had myocarditis has been a helpful
8 marker to address this question of longer term
9 inflammation in the heart muscle.

10 Do you have any more data regarding, in the
11 groups that your following, regarding results of
12 studies to look at gadolinium uptake? If I may, a very
13 quick question, the numbers from Israel regarding
14 myocarditis following the mRNA vaccines is a little bit
15 different than from VAERS. Probably reflecting the
16 means by which the data is collected. Can you comment
17 on that? Over.

18 **DR. TOM SHIMABUKURO:** I'm don't think I'm
19 going to be able to comment on the comparison between
20 the Israel data and the U.S. data because I'm not, at
21 least off the top of my head, not as familiar with the

1 Israeli data. To get to your question on the recovery
2 status. For patients that we followed up on that did
3 receive an MRI during outpatient follow-up, some of
4 those patients did have this late gadolinium
5 enhancement on cardiac MRI. And from speaking to our
6 cardiologist consultants, the clinical significant of
7 the late gadolinium enhancement, especially in patients
8 who report having recovered their cardiac function and
9 are otherwise feeling well, is unclear. So I think
10 there still needs to be some more work in that area
11 about what is the significant of that finding in these
12 patients months after the initial diagnosis.

13 **DR. CODY MEISSNER:** Has it been --

14 **DR. ARNOLD MONTO:** Thank you.

15 **DR. CODY MEISSNER:** -- possible to collect the
16 figures?

17 **DR. ARNOLD MONTO:** We're going to have to move
18 ahead, Cody. Dr. Bernstein, the final question.

19 **DR. HENRY BERNSTEIN:** Yeah, Tom, a very clear
20 presentation, as always. I was interested to know
21 whether the number of cases following booster doses

1 appeared to be notably lower than after dose two. Can
2 you comment about the length of interval between doses
3 as possibly further lowering the rate of myocarditis in
4 patients?

5 **DR. TOM SHIMABUKURO:** In many cases the rate
6 of myocarditis after the booster dose is lower than
7 after dose two, although I would say not in all age and
8 sex strata. I believe there is some evidence in other
9 countries where they have had some different
10 recommendations or at least operationalized the
11 vaccination program so there were longer spacing
12 between vaccines. Maybe not necessarily the booster,
13 but maybe the primary series. And some evidence that
14 that spacing may mitigate the risk of myocarditis. In
15 the United States, there tends to be a fairly close
16 following of the immunization schedule, so we don't,
17 unfortunately, we don't have that kind of data.

18 But, I mean, it is an interesting finding that
19 when you have that longer interval between that booster
20 dose, we tend to see lower reporting rates or lower
21 risk. I would just caution that it's possible that

1 there could be some self-selecting out of the
2 population. For example, if a person got myocarditis
3 after dose two, they may not get a booster dose. So
4 that may also be impacting the findings as well.

5 **DR. HENRY BERNSTEIN:** Yeah. I just mention
6 that because of the 21 days between the doses of
7 Novavax as well.

8 **DR. ARNOLD MONTO:** Right, thank you. We're
9 going to have to move ahead. Dr. Shimabukuro, I'm sure
10 we're going to be coming back to these issues and
11 ascertainment and rates later on, so please stick with
12 us to the afternoon. Now I'd like to turn the floor
13 over to the Sponsor, to Dr. Dubovsky, who is going to
14 take the lead in the presentations on the Emergency Use
15 Authorization by Novavax for a vaccine to prevent
16 COVID-19 in individuals 18 years of age and older.
17 Over to you.

18

19 **EMERGENCY USE AUTHORIZATION (EUA) APPLICATION FOR NVX-**

20 **CoV2373 INTRODUCTION**

21

1 **DR. FILIP DUBOVSKY:** Thank you, and I'll just
2 wait for the slides to load up.

3 **MR. MICHAEL KAWCZYNSKI:** Are you sharing on
4 your end?

5 **DR. FILIP DUBOVSKY:** It should be coming from
6 --

7 **MR. MICHAEL KAWCZYNSKI:** Yep, we gave the
8 share to Justin.

9 **DR. FILIP DUBOVSKY:** Justin.

10 **MR. MICHAEL KAWCZYNSKI:** There you go, sir.

11 **DR. FILIP DUBOVSKY:** I'm still seeing a lag
12 here.

13 **MR. MICHAEL KAWCZYNSKI:** They're up on our
14 end, sir.

15 **DR. FILIP DUBOVSKY:** Excellent. Good morning,
16 after that delay, my name is Filip Dubovsky, and I'm
17 the chief medical officer at Novavax. We're pleased to
18 have this opportunity to present our data for NVX2373.
19 Our vaccine provides an important new approach in the
20 fight against COVID-19. We believe its authorization
21 will improve vaccine availability and accessibility,

1 with the ultimate goal of increasing vaccination rates
2 in the U.S. and throughout the world.

3 As we will show you today, NVX2373 leverages a
4 well-defined platform offering a different vaccine
5 option to fulfill an unmet need within the U.S. and
6 globally. Our vaccine is a recombinant protein subunit
7 vaccine formulated with a natural malleable adjuvant.
8 It induces robust immune responses and provides high
9 levels of protection against mild, moderate, and severe
10 COVID-19. The vaccine is proven to be generally well-
11 tolerated and has a positive benefit/risk profile
12 across a large and diverse patient population.

13 Our COVID-19 vaccine is based on Novavax's
14 platform technology. A recombinant protein antigen
15 formulated as a particle and our Matrix-M adjuvant,
16 which is a saponin-based adjuvant. Our recombinant
17 proteins represent a tested and well-understood vaccine
18 technology. Currently approved examples include
19 influenza, hep-B, HPV, MenB, and shingles. There are
20 also approved vaccines for malaria and shingles that
21 includes saponin-based adjuvants.

1 Here's a brief overview of our vaccine. The
2 NVX2373 antigen is a recombinant SARS-CoV-2 spike
3 protein. The spike protein is based on the following
4 sequence from the original strain, including a
5 transmembrane domain. We've engineered changes into
6 the sequence to inactivate the (inaudible) and
7 stabilize its structure. It's manufactured in the
8 baculovirus SS9N60 expression system, a well-defined
9 approach which has been used for decades. And then the
10 full length protein is expressed and self-assembled
11 into a trimer, which is locked into a state of
12 confirmation.

13 These recombinant protein trimers are purified
14 and further processed to form nanoparticles around a
15 polysorbate core, shown on the slide in blue. The
16 adjuvant, Matrix-M, is purified from the Soapbark tree
17 grown in South America. During processing and
18 purification, the saponin forms cage-like structures.
19 The antigen and adjuvant are co-dispensed into a vial
20 where they form a ready-to-use suspension.

21 Let's talk a bit about the mechanism of

1 action, or the Matrix and adjuvant. The mechanism of
2 action of saponin-based adjuvants has been evaluated in
3 a number of animal models. Matrix-M is just a
4 transient effect at the injection site and a more
5 sustained immunostimulatory effect in the draining
6 lymph nodes. It does not contain alum, it does not
7 form a depo at injection site, nor does it engage the
8 total (inaudible) receptor pathways. Injection of
9 Matrix-M increases the magnitude and breadth of immune
10 response. It induces a rapid transient activation of
11 innate immune cells and increases cytokine and
12 chemokine production at the injection site.

13 This peaks at 5 to 48 hours after injection
14 and rapidly drops by 72 hours. This results in a local
15 influx of activated antigen-presenting cells, which the
16 antigen is delivered and triggers and antigen specific
17 immune response. Subsequently, there's enhanced
18 antigen presentation by MHC class one and MHC class two
19 molecules in the draining lymph nodes. The result is
20 the induction of high levels of neutralizing antibody,
21 polyfunctional CD4 T cells, and a TH1 biased cell-

1 mediated immune response.

2 Now let's shift to the vaccines presentation
3 and profile. Our vaccine has key attributes that
4 support the increased access and ease of use. It's
5 dispensed in a 10-dose vial as a preservative-free,
6 ready-to-use liquid suspension. It can be transported
7 and stored through refrigerator temperatures, making it
8 easy to ship, store, and administer. Each dose
9 contains 5 micrograms of antigen and 50 micrograms of
10 Matrix-M adjuvant. Two doses are administered 21 days
11 apart of a 0.5 mL intramuscular injection using
12 standard needles and syringes. The proposed medication
13 under discussion for today's meeting is for adults 18
14 years of age and older.

15 Our clinical development program includes four
16 studies. These studies constitute the body of data
17 used for global regulatory approvals. The initial
18 Phase 1/Phase 2 Study established the 5 microgram dose
19 level, confirmed the total of the adjuvant, and a two-
20 dose schedule in both younger and older adults. The
21 study also defined the immunologic phenotype and

1 described the preliminary safety profile.

2 Subsequently, our Phase 2 Study in South Africa did
3 include a small subset of medically-stable participants
4 living with HIV evaluated preliminary efficacy and
5 safety.

6 Pivotal safety and efficacy was initially
7 evaluated in a Phase 3 Study in the UK followed by an
8 even larger study in the U.S. and Mexico to (inaudible)
9 within the U.S. As part of the U.S./Mexico Phase 3
10 Study effectiveness and clinical efficacy was
11 established in adolescents 12 to 17 years of age. Now,
12 after discussion with the FDA, today's efficacy
13 presentation will focus on our largest study in the
14 U.S./Mexico Phase 3 Study, Study 301.

15 Study 301 is most relevant for today's
16 discussion because it was conducted in a diverse U.S.
17 population and the vaccine used in the study was
18 manufactured in the commercial scale that's consistent
19 with the vaccine we are distributing globally.
20 Relevant safety data from all studies will be
21 discussed.

1 Okay, let's briefly review the 301 topline
2 results. Our U.S./Mexico Phase 3 Study met it's
3 prespecified primary efficacy endpoint. Study 301
4 demonstrated an overall efficacy of 9.4 percent against
5 protocol-defined symptomatic disease. And achieved 92
6 percent efficacy in the highest populations with
7 medical comorbidities, and 100 percent efficacy against
8 moderate and severe disease. All events of moderate
9 and severe disease, and hospitalizations occurred in a
10 placebo group.

11 Additionally, matched strain efficacy was 97
12 percent. Matched strains are strains that are
13 considered genetically similar to the original virus on
14 which the vaccine is based. As far as variants go, our
15 vaccine demonstrated high levels of protection against
16 the Alpha variant, as well as against all of the
17 variants of interest and concern that circulated at
18 that time. And a number of variants circulated and
19 caused disease during our study. In fact, the majority
20 of cases were caused by variants of concern and
21 variants of interest. The most commonly observed were

1 Alpha, Epsilon, and Iota.

2 Displayed here are our global regulatory
3 approvals. As of today our vaccine has been granted
4 authorization for use in over 40 countries for
5 individuals 18 years of age and older, including those
6 over 65. In December 2021, we received our first
7 authorization in the European Union granting access to
8 all 27 countries. This was followed by the World
9 Health Organization granting Emergency Use, listing for
10 global use. Subsequently approval was achieved in the
11 countries listed on the slide. I should note that the
12 indication in India and Thailand includes adolescents
13 and adults, and our vaccine has been approved as a
14 booster dose in Japan.

15 Our clinical development plans are ongoing and
16 will continue following EUA. We've submitted the
17 results from the adolescent expansion of Study 301 and
18 are completing safety follow-up in our Phase 2 and
19 Phase 3 studies to support whole BLA. And we have
20 additional ongoing studies in adolescents, and soon we
21 will initiate a pediatric HDS (inaudible) study

1 beginning in school-aged children. We believe one
2 approach to optimizing protective efficacy may include
3 the use of vaccines engineered against emerging
4 variants.

5 We're collecting data on homologous and
6 heterologous boosting for continued vaccine use. And,
7 finally, we have post-authorization plans which include
8 additional studies for real-world effectiveness and
9 safety monitoring. Here's the agenda for the remainder
10 of our presentation. Dr. Raburn Mallory will review
11 the immunogenicity and efficacy data. Dr. Denny Kim
12 will present the safety data, followed by Dr. Gregory
13 Poland with the Mayo Clinic to provide his clinical
14 perspective for NVX2373.

15 I will then return to conclude the
16 presentation, and my colleagues and I will be available
17 to answer questions from the Committee. We also have
18 additional experts with us today. All outside experts
19 have been compensated for their time to prepare for
20 today's meeting. Thank you. I'll turn this
21 presentation over to Dr. Mallory to review the

1 immunogenicity and efficacy data.

2

3

IMMUNOGENICITY AND EFFICACY

4

5 **DR. RABURN MALLORY:** Thank you, Dr. Dobovsky.

6 I'm the senior vice president and head of clinical

7 development at Novavax, and I'm pleased to review our

8 FDA data for the EUA application today. As I'll share

9 with you, our data demonstrates the vaccine induced

10 high levels of neutralizing antibodies in both younger

11 and older adults. Vaccine was highly efficacious in

12 preventing COVID-19 illness and showed a high level of

13 efficacy for the variants of concern and variants of

14 interest that circulated during our Phase 3 Study.

15 Vaccine also completely prevented moderate and

16 severe COVID-19 in the study. Before I describe our

17 clinical data, I'd like to briefly summarize our non-

18 clinical results. We conducted a number of non-

19 clinical studies during the development of the vaccine.

20 In immunogenicity studies, the vaccine induced high

21 levels of functional antibodies and induced a strong

1 TH1 virus and cellular immune response. In animal
2 challenge studies, the vaccine effectively suppressed
3 viral replication in both the upper and lower airways.
4 And this was an important milestone because it suggests
5 that the vaccine could be highly protective in human's.

6 In addition, reassuringly, there was no
7 evidence of enhanced disease in these studies. We
8 performed a comprehensive toxicology program, and there
9 were no adverse findings seen in these studies. There
10 were also no adverse findings in our developmental and
11 reproductive toxicity study. These results combined
12 with the absence of the safety findings in all of the
13 studies supported moving the vaccine into clinical
14 development.

15 Turning next to the results from our
16 U.S./Mexico 301 Study. The results are called PREVENT-
17 19. This was a randomized, observer-blinded, placebo
18 controlled study. We randomized participants in a 2 to
19 1 ratio to receive vaccine or placebo. And we did this
20 so that we could gather additional safety data on the
21 vaccine from a larger number of participants. The

1 study initially enrolled adults 18 years of age and
2 older, but we then amended it to also include
3 adolescents 12 through 17 years of age.

4 About four months after the initial
5 vaccination period, participants remained blinded and
6 were crossed over to the opposite treatment arm. And
7 we did this so that all participants in the study could
8 receive active vaccine. Participants are now being
9 followed for up to two years following primary
10 vaccination. The primary endpoint of the study was
11 mild, moderate, or severe disease occurring seven days
12 or more after the second dose of vaccine. The terms of
13 the definition of success: in order to meet the primary
14 endpoint for vaccine efficacy, the lower limit of the
15 95 percent confidence interval needed to be greater
16 than 30 percent.

17 One of the main secondary endpoints we were
18 interested in was how effective the vaccine would be in
19 preventing the more concerning cases of moderate and
20 severe COVID-19. As Dr. Dobovsky mentioned, a large
21 number of variants of interest and variants of concern

1 circulated during the study. Sequenced data were
2 available for 75 of the endpoint cases and 61 of these,
3 or about 80 percent, were due to variants of concern or
4 variants of interest, with the Alpha variant being the
5 most common and isolated.

6 These strains are now classified as variants
7 being monitored, but they aren't circulating to a large
8 extent. However, efficacy for these variants remains
9 relevant as some of them contain those (inaudible)
10 mutations, like the L452R being the Omicron subvariant
11 that could also be seen in future variants. Turning
12 now to the results. Demographics and baseline
13 characteristics were well-balanced between the two arms
14 as shown. Thirteen percent of participants were 65 or
15 older. It's important to note that enrollment of older
16 adults was somewhat limited. This is because COVID-19
17 vaccines became authorized and recommended for those
18 over 65 while we were enrolling.

19 Black or African American participants made up
20 about 12 percent of the study population. Seven
21 percent were American Indian, and 22 percent were

1 Hispanic or Latino, representative of the overall U.S.
2 population. BMI was one of our study goals. About 95
3 percent of participants were considered at increased
4 risk of COVID-19. Either due to underlying medical
5 conditions, their occupations, or living conditions.
6 About seven percent were seropositive at baseline, and
7 we excluded these individuals from the immunogenicity
8 and efficacy analyses.

9 In terms of immunogenicity, in Study 301 there
10 was a robust neutralizing antibody response on day 35,
11 14 days after the second dose of vaccine. Now, as you
12 can see, this was true for both younger and older
13 adults. In fact, there was 123-fold increase for
14 younger adults and an 87-fold increase in older adults
15 from baseline. Turning to the efficacy results.

16 (Audio skipped)

17 **DR. PRABHAKARA ATREYA:** Dr. Raburn, we can't
18 hear you.

19 **DR. RABURN MALLORY:** Sorry about that, I
20 appear to have been muted. I'll start this slide
21 again. Looking at the Kaplan-Meier curve, we can see

1 that cases began to diverge between the placebo and
2 vaccine arms at around the time of the second dose, the
3 day 21. And that there were very few cases in the
4 vaccine arm through day 98. We achieved our primary
5 efficacy endpoint in the study with 90 percent
6 protection from mild, moderate, and severe disease. In
7 fact, there were only 17 cases in the 17,000 or so
8 vaccine recipients, compared to 79 cases in the 8,000
9 placebo recipients. And, as a reminder, we randomized
10 participants 2 to 1 to receive vaccine. We also
11 observed 100 percent protection against moderate or
12 severe illness, a key secondary endpoint.

13 As I showed previously, a number of different
14 variants of interest and variants of concern were
15 circulating during the study. And were responsible for
16 about 80 percent of the cases where sequence data are
17 available. Our vaccine showed 93 percent efficacy
18 against these PCR-confirmed variants of interest and
19 variants of concern. Including the Alpha variant. All
20 of our cases that did occur in the vaccine arm were
21 mild in severity. Notably efficacy was 97 percent for

1 strains that would be considered more closely matched
2 to the vaccine.

3 When we look at vaccine efficacy based on
4 race, the vaccine provided a consistently high level of
5 protection across all groups. The efficacy estimate
6 for Hispanic or Latino participants was somewhat lower
7 than that seen for the overall study. Though with
8 broad confidence intervals. In order to evaluate this
9 in more detail we looked to see if lower immune
10 responses might have contributed to this finding.
11 However, what we found was that ITG and neutralizing
12 antibodies in Hispanic and Latino participants were
13 actually slightly higher than those seen in non-
14 Hispanic/Latino participants.

15 As a result, this efficacy estimate may
16 reflect the (inaudible) finding. However, we will
17 continue to gather additional information about the
18 effectiveness of our vaccine in this subgroup in our
19 planned, U.S. post-marketing effectiveness study. The
20 vaccine also provided a very high level of protection
21 against severe disease, and for individuals who had

1 baseline comorbidities that puts them at increased risk
2 from COVID-19. As you can see, the number of cases in
3 older adults was limited. As you may recall older
4 adults made up 13 percent of the overall study
5 enrollment, but they were clearly practicing social
6 distancing measures during this time. But they only
7 made up six percent of the cases in the study. The
8 estimate for vaccine efficacy in older adults was 79
9 percent, so this was based on a total of six cases.
10 And we believe that that's likely attributable to the
11 very small number of cases that occurred.

12 On the next slide I'll provide some additional
13 data on vaccine immunogenicity and efficacy by age that
14 indicates the vaccine continues to be immunogenetic and
15 efficacious in older adults. On this slide I'm showing
16 the relationship between geometric mean neutralizing
17 antibody titers, efficacy, and age. When we look at
18 adults 18 to 64 years of age, they had a neutralizing
19 antibody titer of approximately 1300. And this was
20 associated with 91 percent efficacy. Within this
21 group, we then evaluated whether vaccine efficacy might

1 be decreasing with age.

2 However, this did not appear to be the case
3 because vaccine efficacy remained high at 91 percent
4 for the 50 to 64-year-olds, even though their antibody
5 titer was somewhat lower at 979. We also saw an
6 efficacy estimate of 89 percent for adults 50 or older,
7 with a corresponding neutralizing antibody titer of
8 922. Finally, for those 65 or older, the efficacy
9 estimate was 79 percent, but with a broad confidence
10 interval that overlaps with the primary efficacy
11 endpoint.

12 When we looked at the neutralizing antibody
13 titer for this group, which was 900, it is quite
14 similar to and, in fact, non-inferior to the titers for
15 the 50 to 64-year-olds and for those 50 or older that
16 were associated with around 89 to 90 percent efficacy.
17 These data, along with supportive efficacy data in
18 older adults from a large Phase 3 Study conducted in
19 the U.S. in the UK, not presented today, provided
20 assurance the vaccine is efficacious in older adults.
21 Supporting this indication in all countries in which

1 the vaccine has been approved to date.

2 So, to conclude, our vaccine was highly
3 efficacious in preventing COVID-19 in a large Phase 3
4 Study. This efficacy was demonstrated against all the
5 variants that circulated during the study. The vaccine
6 also provided complete protection for moderate or
7 severe COVID-19 in our pivotal study. Our vaccine also
8 demonstrated consistently high efficacy across
9 subgroups, including race, gender and in individuals
10 with comorbidities. I'll now turn the presentation to
11 my colleague, Dr. Kim, to present the safety results.
12 Thank you.

13

14

SAFETY

15

16 **DR. DENNY KIM:** Thank you, Dr. Mallory. I'm
17 the chief safety officer at Novavax. And it really is
18 a pleasure for me to be able to present the safety
19 results for our Novavax COVID-19 vaccine. While our
20 presentation will focus on the U.S./Mexico Phase 3
21 Study 301, we will also take into consideration the

1 other studies from our clinical development when there
2 are safety data that adds additional insights.

3 The total safety database includes nearly
4 50,000 people enrolled across four studies. More than
5 30,000 received our vaccine and more than 19,000 of
6 these individuals received the vaccine in our Phase 3
7 U.S. and Mexico Study 301 in the pre-crossover portion
8 of the study. This is a large data set that can
9 provide us confidence that we have a well-characterized
10 safety profile that supports positive benefit/risk and
11 a favorable reactogenicity profile across the diverse
12 populations that Dr. Mallory described.

13 Now, taking into account follow-up time,
14 during the placebo controlled period of Study 301 we
15 have more than 5,500 person-years of follow-up in the
16 vaccine arm alone. The median follow-up was 89 to 92
17 days. Our study compliance was high, actually more
18 than 96 percent of study participants received two
19 doses. I'd like to briefly review now how our safety
20 follow-up was conducted.

21 Beginning in the pre-crossover phase

1 participants received two doses 21 days apart at day
2 zero and day 21. On the day of each vaccination in the
3 pre-crossover phase participants recorded local and
4 systemic reactions using an electronic diary for seven
5 days. Unsolicited adverse events were collected
6 through day 49. Approximately four months after
7 initial vaccination, participants entered a blinded
8 crossover and received two doses 21 days apart.

9 Local and systemic solicited reactions were
10 not recorded post-crossover. However, unsolicited
11 adverse events were collected through day 49.

12 Participants were then followed by visits occurring at
13 six month intervals in person or by phone until the end
14 of study. In addition to the nasal swab that was
15 collected prior to each vaccination, continued
16 monitoring for COVID-19 was ongoing with active and
17 passive surveillance, and prompt PCR testing when
18 warranted.

19 This study includes long-term follow-up with
20 SAEs and AEs of special interest collected through two
21 years following initial vaccination. Let me begin with

1 a summary of our solicited adverse events collected
2 through e-diary entries for seven days following each
3 vaccinations. Shown here are the local reactogenicity
4 events after the first dose. Participants 18 to 64
5 years of age are represented in the top panel. And
6 those 65 and older in the bottom panel.

7 Within each of that column, on the left are
8 vaccinated participants and placebo participants are on
9 the right. Pain and tenderness were the most commonly
10 reported events. And those 65 years of age and older
11 experienced fewer local events compared to those 18 to
12 64 years of age. While many participants did not
13 report reactogenicity events, those who did mostly
14 reported events that were grade one or two, which is
15 mild to moderate in severity, shown in blue. Grade
16 three and higher, shown in yellow, occurred at low
17 rates.

18 Overall, these events resolved quickly with a
19 median duration of one to two days. As expected,
20 events occurred more frequently following the second
21 dose. And again, as expected, more participants in

1 the vaccine group experienced these symptoms. And most
2 events remain grade one or two in severity with low
3 numbers of grade three and higher events.

4 Now, I'd like to turn to systemic
5 reactogenicity. On this slide are systemic events
6 after the first dose. Malaise, fatigue, muscle pain,
7 and headache were the most commonly reported. And as
8 well for systemic events, we also see lower frequencies
9 in those 65 years of age and older. Again, events were
10 reported as grade one or two, and resolved quickly with
11 a median duration of one to two days. Notably the
12 rates of fever were quite low in less than one percent
13 of participants.

14 Following the second dose, while higher
15 overall, most systemic events remained mild to moderate
16 in severity as grade one or two. Rates of grade three
17 and higher events were low and occurred in relatively
18 few participants. And even after the second dose,
19 participants reporting fever continued to remain low.
20 Moving to an overview of unsolicited adverse events.
21 Overall the frequency of unsolicited adverse events was

1 comparable between vaccine and placebo groups. And
2 severe adverse events are reported in few participants.
3 Both pre- and post-crossover.

4 Medically attended adverse events as well as
5 potential immune-mediated conditions were similar
6 between groups. SAEs were also balanced across vaccine
7 and placebo groups. And, as you can see in the last
8 row, that's also occurred at similar rates between
9 treatment arms. This figure shows pre-crossover
10 unsolicited AEs by system organ class occurring at a
11 frequency of at least one percent through day 49. This
12 was our primary safety collection window through four
13 weeks after receiving the second dose.

14 Frequency between treatment groups was similar
15 and the overall percentage of participants reporting
16 adverse events remained low. Here, we see more data on
17 potential immune-mediated conditions. These all
18 occurred with low frequency. Individual events
19 occurred with less than one percent incidence and
20 without any obvious patterns that would suggest
21 associations with vaccination. There's a lot of data

1 on this slide, so let me give you a moment to review
2 the table.

3 And, as you'll note, overall events were
4 balanced between both vaccine and placebo arms. Shown
5 here are pre-crossover serious adverse events by system
6 organ class with frequency of at least 0.1 percent.
7 SAEs by system organ class were infrequent and
8 comparable between vaccine and placebo groups with the
9 exception of the infection system organ class due to
10 COVID-19 cases in the placebo arm.

11 When we looked at individual preferred terms
12 there was a numerical imbalance driven by events
13 reported as cholecystitis. And I'd like to provide you
14 a little more of our analysis on this topic. Because
15 we saw an imbalance in cholecystitis cases, we looked
16 at the totality of the data, including a deep dive into
17 individual cases. We do believe that the weight of
18 evidence does not suggest a causal link. In Study 301,
19 the overall frequency of cholecystitis in the vaccine
20 group is low, 0.05 percent, which is consistent with
21 the expected background rate.

1 In the UK Study 302, there was one additional
2 event in the vaccine arm as well as another in the
3 placebo arm. No events occurred in Studies 501 and
4 101. All these events occurred in participants with
5 known risk factors for cholecystitis. And all
6 participants had gallstones at the time of event onset.
7 A broader look at related terms with a standard Medrol
8 search did not reveal any additional findings.
9 Importantly there was no clustering or temporal
10 relation to treatment, and we have not received and
11 post-authorization reports with more than 740,000 doses
12 administered.

13 On this slide we've plotted time to onset of
14 cholecystitis following vaccination. The Y axis is the
15 patient's age, and the X axis represents the number of
16 days from the first dose to when the event was
17 reported. As you can see, we did not observe any
18 temporal patterns and see a pretty random spread over a
19 long period following vaccination.

20 Because of the importance of
21 myocarditis/pericarditis we wanted to provide you a

1 complete summary of our clinical data. For this
2 analysis we will be presenting from our entire pool of
3 safety database for a little context. And, as Dr.
4 Shimabukuro reviewed in detail, with the numerous
5 investigations into the myocarditis findings of the
6 past year with messenger RNA vaccines I think we've
7 learned that we can expect to see natural background
8 events of myocarditis in any sufficiently large
9 database.

10 We've also learned that young males are at
11 higher risk for both vaccine-induced myocarditis and
12 other forms of myocarditis. Most often caused by non-
13 specific infections. COVID infections can also cause
14 myocarditis. It's important to note that our studies
15 were largely conducted during this time of heightened
16 awareness for myocarditis. And so, for our data,
17 overall in our placebo-controlled phase of our clinical
18 development program the rates of myocarditis were
19 balanced between the vaccine and placebo arms at 0.007
20 percent for vaccine and 0.005 percent for placebo. No
21 pericarditis was reported. In Study 301 one case

1 occurred in the active arm and one case in the placebo
2 arm.

3 As a reminder, there was a 2 to 1
4 randomization in Study 301 in order to increase the
5 sample size of vaccinees. And one case occurred in the
6 active arm of Study 302. Of the two cases in vaccine
7 recipients, one 67-year-old male also had a concurrent
8 severe COVID infection after dose one. The other cases
9 from Study 302 occurred in a 19-year-old male three
10 days after the second dose of vaccine and was without a
11 definitive alternative cause. In the post-crossover
12 portion of Studies 301 and 302, where all participants
13 had been exposed to our vaccine, events of myocarditis
14 or pericarditis occurred within the expected background
15 rates as determined by the EMA Access Study.

16 This study was specifically designed to
17 determine background rates of interest for COVID
18 vaccines. There were three reports of myocarditis or
19 pericarditis, and all had plausible infectious
20 alternative causes. One notable case occurred in a 16-
21 year-old male two days after the second crossover dose

1 of vaccine with a viral diagnosis that was diagnosed by
2 a healthcare provider. One 20-year-old male had strep
3 throat preceding the events of pericarditis diagnosed
4 by EKG findings and normal troponin levels.

5 While the cases in the two teenage males, one
6 during the placebo-controlled phase and one post-
7 crossover, have characteristics of vaccine-induced
8 myocarditis we believe that the totality of the
9 clinical evidence here is not enough to establish an
10 overall causal relationship with the vaccine. I wanted
11 to mention that we did not include here a case that the
12 FDA has included in their briefing document of a 28-
13 year-old male who had features of myocarditis but was
14 diagnosed by a cardiologist with non-ST elevation
15 myocardial infarction. We also, a few days ago,
16 received a follow-up report of a cardiac MRI that did
17 not show evidence of a recent episode of myocarditis.

18 Our latest monthly summary safety report with
19 post-authorization data includes more than 740,000
20 doses administered and was submitted in May with a data
21 cutoff of April 30th. We analyzed a cumulative 35

1 spontaneous reports of potential myocarditis or
2 pericarditis received from passive surveillance
3 systems. These reports often come with very limited
4 information. Because of the general limitations of
5 spontaneous reports, we carefully adjudicated these
6 reports and applied the Brighton Collaboration case
7 definition.

8 Out of the 35 potential reports none met a
9 definitive case definition. One report was a probable
10 case of myocarditis in a 47-year-old male with an
11 unknown time to onset. There were 10 reports of
12 probably pericarditis. Of these, seven were in males
13 and three were females with a median age of 42 years.
14 The time to onset was 2 to 14 days from vaccination.
15 One of the 10 probable cases of pericarditis was in a
16 participant with a history of messenger RNA vaccines
17 and pericarditis.

18 Illustrating the limitations of this type of
19 spontaneously reported data we just recently received
20 confirmation by the Australian Health Authority that
21 two pairs of pericarditis cases are duplicate reports

1 bringing the 10 reports of probable pericarditis down
2 to 8. It's worth noting that as of April 30th all of
3 the probable cases were reported from Australia despite
4 the fact that the doses administered in Australia
5 account for only 17 percent of global administration of
6 the 744,000 doses administered worldwide. No reports
7 of probable cases have been received from other
8 regions, including the EU and South Korea, which also
9 have robust surveillance systems. And those regions
10 also account for the majority of doses administered.

11 We take all reports of adverse events
12 seriously. As we examine the accumulating data and
13 continue our collaborations and discussions with global
14 regulators, we will get a better understanding of the
15 nature of the cases and a more precise and stable
16 estimate of the rates. We then expect to have more
17 clarity on whether or not this important safety risk is
18 related to the vaccine. We do consider myocarditis an
19 important potential risk and we are very carefully
20 monitoring our post-authorization data. Additionally,
21 we attempt to follow-up each reported case with

1 targeted questionnaires and these data are being
2 communicated in our analyses in our monthly summary
3 safety reports.

4 Our close monitoring will also include safety
5 studies which will cover large populations and
6 administrative claims databases and electronic health
7 records. For these other specific events of interest
8 in our clinical development program there were no
9 reports of anaphylactic reactions, or TTS, in our
10 integrated safety data. While our integrated safety
11 data from our EUA submission did not have any cases of
12 Guillain-Barré, a recent update to an SAE of neuropathy
13 from Study 302 has provided information that meets the
14 Brighton Collaboration case definition for Guillain-
15 Barré Syndrome.

16 We will of course continue to carefully
17 monitor for these events in our post-authorization
18 surveillance activities. Because pregnant women were
19 excluded from all our studies there is limited
20 information on pregnancy. For all women of
21 childbearing potential a negative urine pregnancy test

1 was required at screening and prior to vaccination.
2 But as it occurs for all large studies with long
3 follow-up, we did have some reports of pregnancies. As
4 of March 15, 2022, a total of 147 pregnancies were
5 reported across the entire clinical program. Fifty-six
6 of the pregnancies were still ongoing and 41 resulted
7 in live birth. Twenty-five experienced miscarriages,
8 13 women elected to have voluntary terminations, and
9 one had an ectopic pregnancy. There were no fetal
10 deaths or stillbirths reported.

11 Because pregnancy data was systematically
12 collected and there are inherent reporting and
13 ascertainment biases, you can't make direct comparisons
14 to background rates and draw definitive conclusions.
15 But overall this data does not indicate a potential
16 risk for the mother or fetus and there are no specific
17 restrictions for pregnant women in our global labels.
18 In order to continue safety surveillance for very rare
19 events that may not have been seen in clinical
20 development we also have plans and strategies in place
21 to address potential safety concerns following

1 Emergency Use Authorization.

2 Our post-authorization pharmacovigilance
3 investigates potential risks, such as vaccine
4 associated enhanced disease and myocarditis. Novavax
5 supplements our routine monitoring with monthly summary
6 safety reports and targeted follow-up questionnaires.
7 Qualitative and quantitative reviews using multiple
8 data sources for signal detection are conducted on a
9 daily, weekly, and monthly basis. Additionally, we
10 plan to conduct five post-authorization studies. They
11 include two effectiveness studies and two safety
12 studies using administrative claims and electronic
13 health record databases to robustly characterize the
14 safety profile in the post-marketing setting.

15 And Study 405 is a global registry that will
16 provide us with important data in pregnant women who
17 receive our vaccine. So, in summary, the Novavax COVID
18 vaccine safety data supports positive benefit/risk and
19 a favorable reactogenicity profile. Our vaccine is
20 well-characterized with exposure in more than 30,000
21 recipients across the entire clinical program in the

1 pre-crossover placebo-controlled portion of the
2 studies. Local and systemic reactogenicity events were
3 generally grade one to two in severity and resolved
4 within one to two days. Grade three and higher events
5 were infrequent.

6 Importantly, we saw low rates of fever post-
7 vaccination and most AEs were mild to moderate in
8 severity. When we look at our long-term post-crossover
9 follow-up where more than 40,000 recipients received
10 the vaccine rates of SAEs were low and comparable to
11 placebo. And for the important potential risks we will
12 continue to monitor for these events with our ongoing
13 and future safety studies. Thank you. I'd like to
14 invite now Dr. Greg Poland to share his clinical
15 perspective on the Novavax COVID vaccine.

16

17

CLINICAL PERSPECTIVE

18

19 **DR. GREG POLAND:** Thank you. Good morning,
20 everybody, I'm very pleased to be here to provide my
21 clinical perspective on the Novavax vaccine. I've been

1 a practicing internist for 40 years and have served as
2 a PI of over 40 vaccine clinical trials. And I'm the
3 editor-in-chief of the *Journal Vaccine*. I've spoken to
4 this Committee before about the need for COVID
5 vaccines, and I'm here today to discuss why the Novavax
6 vaccine is an important addition to what is already
7 authorized.

8 As we are all well-aware two years into this
9 pandemic the SARS-CoV-2 variants continue to challenge
10 and re-challenge us. And a major reason for the
11 continuing pandemic is that despite the availability of
12 safe and effective COVID-19 vaccines and the constant
13 efforts of our public health officials to increase
14 vaccination rates, millions of Americans today are
15 still unvaccinated, as we've heard.

16 While I expected some of the challenges, we're
17 seeing today with this pandemic I am still surprised to
18 see how this virus continues to unfold and what we're
19 learning about the long-term and multidimensional
20 impact the virus is having on individuals and the
21 public health. There's no question that our ability to

1 quickly develop vaccines has been impressive, however,
2 the complexity and dynamic nature of this virus
3 emphasizes the need to have multiple vaccine platforms
4 to fight it.

5 For those individuals who are not fully
6 vaccinated and waiting for another option, having a
7 vaccine platform that multiple stakeholders, including
8 regulators, physicians, and the public are familiar
9 with, can help mitigate some of the challenges we're
10 facing today. Indeed a recent Ocugen/Harris Poll found
11 that 73 percent of Americans would like additional
12 COVID-19 vaccines developed from a more traditional
13 method.

14 Perhaps this is no surprise considering what
15 we've witnessed during the pandemic when people become
16 concerned about vaccine safety or tolerability. The
17 latest CDC data reports that 89 percent of the U.S.
18 population over the age of 18 have received one dose.
19 And then we see the uptake of a second dose and booster
20 shot fall precipitously. Only 77 percent have gotten a
21 second dose, and only 50 percent the first booster.

1 There are many indications that decrease is
2 linked in part to concerns people have about vaccine
3 safety, reactogenicity, and efficacy. I certainly see
4 that in my own practice. In the last year I've
5 received innumerable requests from physicians asking
6 how to treat patients who've had a reaction to one of
7 the currently available COVID-19 vaccines.
8 Reactogenicity is a real problem, and one that prevents
9 a significant number of people from being fully
10 vaccinated.

11 So what is the benefit of the Novavax vaccine
12 platform? The data shows that combining the SARS-CoV-2
13 spike protein with an immune-enhancing adjuvant
14 stimulates robust antigen-specific immune responses and
15 provides high efficacy. Importantly, the vaccine is
16 not highly reactogenic and compares favorably with
17 other vaccines. We saw that borne out in the Sponsor's
18 clinical trials, where most events were mild to
19 moderate and resolved in just a day or two. And, as a
20 reminder, the vaccine was able to deliver 90 percent
21 efficacy with this favorable reactogenicity profile.

1 This well-defined recombinant protein platform
2 demonstrated safety and efficacy in two large Phase 3
3 clinical trials against numerous variants. The
4 combination of the immunogenicity data showing robust
5 antibody responses across multiple variants with
6 clinical efficacy data from the Phase 3 trials signals
7 broad cross-protection. This will be vital as we head
8 into an era where we simply don't know what the next
9 variant will be. Simply put, it's important to have
10 choices in vaccine platforms in a pandemic that is
11 constantly evolving.

12 It's also important to make it as easy as
13 possible to get vaccines to the people who need them.
14 While many of us think of logistics in the cold chain
15 and increased access is an issue in the developing
16 world, there are also many healthcare providers in the
17 United States who will find the ease of storage and
18 administration of the Novavax vaccine to be a
19 significant benefit over current vaccines. Every day
20 we're learning more about just how important it is to
21 remain vigilant about trying to control this pandemic

1 in the longer term for both the individual and the
2 public health.

3 Someone who is unvaccinated has a four-fold
4 greater chance of getting infected, is 23 times more
5 likely to be hospitalized, and has a 20-fold higher
6 chance of dying than a vaccinated person. The fact
7 that we're still seeing more than 300 people die every
8 day in American from COVID-19 is simply unfathomable to
9 me. In fact, there are four more than the 100,000 new
10 cases being reported each day. This is clearly an
11 undercount due to the amount of home testing.

12 These cases are resulting in almost 3,000 new
13 hospitalizations per day. And this represents a
14 significant opportunity to protect health with
15 vaccines. And this is just the impact from the
16 immediate acute infection. One aspect of this pandemic
17 that is just starting to be understood is the long-term
18 impact. And this includes both the individual and our
19 healthcare system. A study published in *Nature* this
20 February showed that one year after recovery people
21 with COVID, whether mild or not, had a substantially

1 higher risk of 20 different cardiovascular conditions
2 than those who did not have COVID.

3 These conditions, like heart disease, vascular
4 disease, and heart failure are likely to negatively
5 affect the health and life expectancy of people for
6 years, if not decades, to come. In addition to
7 physical ailments the new research is also documenting
8 the mental COVID is having on people. A study also
9 published this February, this one in the *BMJ*, reported
10 that people who had COVID and were hospitalized were
11 more likely to experience anxiety, depression, suicidal
12 thoughts, and to experience opioid disorders.

13 And these physical and mental health issues
14 due to COVID are preventable if we get a handle on this
15 pandemic and offer people choices that they may be more
16 likely to use. Thereby encouraging them to get
17 vaccinated. In summary, as a clinician, I believe the
18 Novavax vaccine offers benefits to multiple
19 stakeholders. Patients and providers will find the
20 Novavax vaccine an easy and logical option based on its
21 efficacy, safety, and tolerability, especially the

1 millions of Americans who say they are waiting for
2 another option.

3 Pharmacies and distributors will find this an
4 easy and logical option for logistical reasons because,
5 as we've heard, it's easier to ship, store, and
6 administer. Employers will find this an easy and
7 logical option to encourage people to get vaccinated.
8 And, finally, policymakers will find this an easy and
9 logical option because it's a vaccine that's easy for
10 people to access, easy to explain, and a choice that
11 people want. One last note, while we're here today to
12 discuss only the COVID vaccine, the clinician in me is
13 also hopeful about the continued potential of this
14 vaccine platform.

15 By design it's inherently amenable to
16 combination vaccines, including influenza, RSV, and
17 other respiratory illnesses. We've had remarkable
18 success increasing vaccine compliance utilizing
19 combination vaccines in children. And, ultimately,
20 this can be true in adolescents and adults. As I
21 conclude, I want you to understand that speaking to you

1 today is both personal and professional for me. I've
2 dedicated my career to researching and fighting
3 infectious diseases. I've taken care of patients for
4 over 40 years, and I've seen firsthand the miracle of
5 what vaccines can do.

6 We have an opportunity and a need to be
7 proactive and continuously vigilant as the challenge
8 and the fight against COVID is likely to continue for
9 the foreseeable future. Authorizing an effective
10 vaccine with a different mechanism of action is not
11 only important for Americans but will have an impact on
12 global health. Our goal should be to have the right
13 vaccine for the right person for the right purpose at
14 the right time. And having more vaccine options with
15 different platforms is a key component of achieving
16 just that. Thank you for your attention, I'll now turn
17 the presentation over to Dr. Dubovsky to conclude.

18

19

SPONSOR PRESENTATION CONCLUSION

20

21

DR. FILIP DUBOVSKY: Thank you, Dr. Poland.

1 The results from our clinical development program
2 strongly support Emergency Use Authorization for people
3 18 years of age and older. Our vaccine is based on the
4 differentiated platform that is well-understood.

5 Recombinant protein vaccines have been used globally
6 for decades. Our adjuvant, Matrix-M, is a natural
7 saponin product and saponin-based adjuvants are used
8 globally.

9 Importantly, our vaccine achieved 90 percent
10 efficacy in our Phase 3 Study in the U.S. and Mexico
11 despite the majority of cases been attributed to
12 variants. Our vaccine offers a favorable
13 reactogenicity profile with most symptoms resolving
14 after one or two days. And our safety data, that was
15 collected in a diverse American population, supports a
16 positive benefit/risk profile.

17 In summary, NVX2373 can be a useful tool in
18 addressing the ongoing pandemic, providing a different
19 option, and may be helpful in increasing the incomplete
20 vaccination rates in the U.S. Thank you, and I'll turn
21 it over to Dr. Monto.

1 **DR. ARNOLD MONTO:** Thank you. We have just a
2 few minutes for some specific questions. I want to
3 remind the Committee that we will have a much more,
4 less time-constrained discussion after we hear the FDA
5 presentation. And I want to remind you that yes, we do
6 know there have been other variants, yes, we know there
7 are booster shots being given, and there are mix and
8 match strategies. But that's not what we're going to
9 be talking about in the next few minutes of questions.
10 We're going to be talking about the presentation of the
11 data on the clinical trial that is being considered for
12 our evaluation right now. Dr. Levy.

13 **DR. OFER LEVY:** Hello, thank you for that
14 presentation which was very interesting. I had two
15 quick questions. One is regarding the apparent lower
16 vaccine efficacy, or VE, in Hispanic or Latino
17 individuals. The presentation pointed out that this
18 was puzzling because the immunogenicity appeared to be
19 similar to other groups. And that maybe this was a
20 chance observation. Another interpretation may be that
21 we don't understand the correlative protection well

1 enough.

2 And that's what's being measured for the
3 immune response doesn't capture what is protecting. So
4 does Novavax have a comment on that? The other
5 question regarding safety, are there any lessons to be
6 learned from looking at safety data of other studies
7 with other saponin-based adjuvants? Thank you.

8 **DR. FILIP DUBOVSKY:** Yeah, so as far as your
9 first question goes, there's emerging data now from our
10 Phase 3 Study, 301 Study, that was supported by the
11 U.S. government. And there's a close-up protection
12 analysis that's emerging now. And the best correlative
13 that was in fact identified appears to be looking into
14 neutralization (inaudible) antibodies. Now we looked
15 at those patients, the Hispanic participants, very
16 closely.

17 We were interested to know if they were from
18 the U.S. or Mexico, in fact all the cases were in the
19 U.S. And when we looked carefully at their other risk
20 factors, we didn't identify anything specifically which
21 seemed to have pointed to an increased risk. So right

1 now our best estimate is that may be a chance finding
2 alone.

3 As far as other saponin-based vaccines, the
4 largest database for our particular version of saponin
5 is clearly the studies we presented today. We have
6 data from multiple antigens that we've tested
7 previously in pre-live interest studies. And that
8 includes influenza, which we took through a Phase 3
9 Study. And the reactogenicity profile looks
10 comparable. And certainly, we didn't see anything that
11 looks like any of the events of concern that we talked
12 about previously.

13 The other saponin-based vaccines are largely,
14 well, they're distributed both in the U.S. as well as
15 globally. And I'm not sure that there's anything
16 specific we can learn from them because clearly, they
17 are given with different antigens. So that leads to a
18 different biological profile.

19 **DR. ARNOLD MONTTO:** Thank you. Dr. Pergam.

20 **DR. STEVEN PERGAM:** Okay, I think I was
21 unmuting, and somebody unmuted me, I apologize. I had

1 a question just about the incidence of COVID. It
2 seemed as though the benefit was primarily after the
3 second dose of the vaccine, which was around three
4 weeks that second dose was given. Does the company
5 have any data on antibody responses following the first
6 dose knowing that the data that Dr. Poland presented?
7 Not everyone does get a second dose of vaccine, and is
8 there evidence, or do they have additional data on
9 those who only received one dose of vaccine and the
10 antibody responses in those?

11 **DR. FILIP DUBOVSKY:** Yeah, so the Kaplan-Meier
12 that Dr. Mallory showed, showed the rates diverging on
13 day 21, which was the day the second dose was
14 administered. So, obviously it takes time for that
15 second dose immune response to mature, so we would
16 posit that some of that benefit we're seeing is really
17 from the first dose. We have looked at efficacy
18 following the first dose, and I think I'll need to
19 bring that data to you after the lunch break. I don't
20 seem have it readily available right now.

21 **DR. ARNOLD MONTTO:** That's perfect.

1 **DR. STEVEN PERGAM:** Okay, thank you.

2 **DR. ARNOLD MONTO:** Looks go on to Dr. Berger.

3 **MR. MICHAEL KAWCZYNSKI:** You don't have to
4 wait till your camera pops up to speak, go ahead, Dr.
5 Berger.

6 **DR. ARNOLD MONTO:** We see you.

7 **MR. MICHAEL KAWCZYNSKI:** Dr. Berger, did you
8 mute your phone? Yeah, did you mute your own phone?
9 There you go, sir.

10 **DR. ADAM BERGER:** Okay, sorry. I just wanted
11 to come back to the question around vaccine efficacy in
12 Hispanic populations again. And just see if you've
13 been able to conduct any sub-group analyses to look at
14 the 18 to 64 range and the 65+ to evaluate vaccine
15 efficacy in each of those sub-populations by
16 themselves.

17 **DR. FILIP DUBOVSKY:** Yeah, there were very few
18 number of cases, if you remember. There were a total
19 of 27 cases. In the elderly there were really very few
20 cases, as Dr. Mallory presented, there were only six
21 cases total. So, I'm not sure that would be an

1 informative analysis to look at, but we can try to do a
2 2 by 2 table over the break.

3 **DR. ARNOLD MONTO:** Thank you. Dr. Meissner.

4 **DR. CODY MEISSNER:** Thank you, Dr. Monto. I
5 have one comment which will lead into my question.
6 That is there's an interesting editorial this week in
7 the *New England Journal* about whether the world needs
8 additional vaccines. And the article points out that
9 there have been 11.5 billion doses of COVID vaccines
10 that have been distributed, which sounds like a big
11 number until you remember there are almost eight
12 billion people on the planet that we need to vaccinate.

13 And the distribution obviously of those
14 vaccines have been unequal between high income, middle
15 income, and low income countries. Clearly there's a
16 need for additional vaccines. And, furthermore, it may
17 be that a protein platform vaccine such as the one
18 you're using offers advantages over the messenger RNA
19 vaccine, which is what leads to my question. And that
20 is, Dr. Mallory mentioned that there was a reduction in
21 upper airway viral numbers among people who had

1 received the vaccine.

2 Suggesting that there may be some mucosal
3 impact from this vaccine, and it might have perhaps
4 better effectiveness at reducing infection in addition
5 to severe illness. Can you quantify that? Have you
6 looked at IG, mucosal IGA or do you have a sense of how
7 well this vaccine might protect against infection
8 versus severe disease? Over.

9 **DR. FILIP DUBOVSKY:** Yeah, the data that Dr.
10 Mallory referenced was primate work and there, what we
11 demonstrated and is published now, is that the vaccines
12 capable of generating sterile immunity in the upper and
13 lower airway. We don't have IGA data from the studies
14 to collect, and during the pandemic we weren't actually
15 able to do that. What we do know is the vaccine is
16 capable of preventing infection from our clinical
17 studies. And we measured this by looking at zero
18 conversion to N, at the N protein as well as being PCR
19 positive.

20 Perhaps I'll be able to briefly share that
21 data with you, but what we saw is that in the UK study,

1 we were able to prevent infection in 82 percent of the
2 people who were vaccinated. And, obviously, if you
3 don't get infected you can't transmit, you can't
4 develop the emergence of variants, and you can't have
5 long COVID because you're not infected.

6 **DR. ARNOLD MONTO:** Thank you. Finally, Dr.
7 Marasco.

8 **DR. WAYNE MARASCO:** Yes, thank you, Dr.
9 Mallory. So I have a -- Dr. Mallory's, I have a
10 comment on Dr. Mallory's presentation and a question on
11 Study 301. If I have the data right, you looked at
12 neutralizing antibody responses 35 days after their
13 second boost. And you followed the patients for
14 roughly 50 days.

15 Is there a time dependence for breakthrough
16 infection? Do you have enough data to know that?
17 Because with your high neutralizing antibody titers
18 that were measured at day 35, and then your follow-up
19 period, is there a time dependent risk in acquiring
20 infection?

21 **DR. FILIP DUBOVSKY:** Right. It's an excellent

1 question. As we described, for all of our studies we
2 had to institute a crossover into the design, and
3 that's because Emergency Use vaccines became available
4 and to maintain integrity of the study, we had to
5 provide everyone a vaccine. What that did is it took
6 away our ability to have placebo-controlled data beyond
7 the crossover period.

8 The issue with looking at the breakthrough
9 cases for our specific vaccine in Study 301 is there
10 were very, very few cases. So you could see from the
11 Kaplan-Meier curve kind of where they fell out. And
12 there wasn't a specific uptick as time went on, it was
13 relatively flat, if you remember the data that Dr.
14 Mallory showed.

15 **DR. ARNOLD MONTTO:** Thank you. We're going to
16 try to catch up by taking a break now. Why don't we
17 stick with the 15 minutes we had before, so we will
18 reconvene at 11:30 Eastern Time. And then we're going
19 to shorten our lunch to half an hour so that we can
20 fully catch up and start the oral public hearings on
21 schedule. So, break until 11:30 Eastern, 15 minutes.

1

2

[BREAK]

3

4

FDA REVIEW OF EFFECTIVENESS AND SAFETY OF NOVAVAX

5

COVID-19 VACCINE IN INDIVIDUALS 18 YEARS OF AGE AND

6

OLDER

7

8

MR. MICHAEL KAWCZYNSKI: All right. Welcome

9 back from that quick break. Just to keep us on time,

10 I'm going to hand it over to our Chair. Dr. Monto, are

11 you ready?

12

DR. ARNOLD MONTO: I am ready. We have one

13 presentation before our lunch break from the FDA

14 presenting the review of effectiveness and safety of

15 Novavax COVID-19 vaccine in individuals 18 years of age

16 and older. Dr. Lucia Lee will be our presenter. Dr.

17 Lee.

18

DR. LUCIA LEE: Good morning. I'll now

19 present the FDA review of clinical data submitted in

20 the Novavax COVID-19 emergency use authorization

21 request. I'll start with the regulatory background and

1 the overview of clinical studies followed by the design
2 of Study 301, the main source of efficacy and safety
3 data to support the EUA request, additional safety data
4 from other studies, and then a summary of risks and
5 benefits and the VRBPAC question.

6 The Novavax COVID-19 vaccine contains five
7 micrograms of recombinant spike protein and 50
8 micrograms of Matrix-M adjuvant. The proposed primary
9 series is two doses given three weeks apart. This
10 slide presents an overview of clinical studies and the
11 number of vaccine recipients in the safety population
12 during the pre-crossover period.

13 The primary source of clinical data to support
14 the EUA request is Study 301, which provides the safety
15 and efficacy data in approximately 20,000 vaccine
16 recipients who were initially randomized to receive the
17 vaccine. Additional safety data from approximately
18 10,000 additional vaccine recipients were provided from
19 three studies conducted with the vaccine produced by an
20 earlier manufacturing process than the vaccine
21 evaluated in Study 301.

1 In Study 301, an ongoing, randomized,
2 observer-blind, placebo-controlled Phase 3 efficacy,
3 safety, and immunogenicity study, a total of
4 approximately 30,000 participants 18 years and older in
5 the U.S. and Mexico included adults who, by virtue of
6 age, race, ethnicity, or life circumstances, were
7 considered at substantial risk for exposure to SARS-
8 CoV-2.

9 These participants were stratified by age
10 groups 18 to 54 and 65 years and older. During the
11 course of the study, COVID-19 vaccines authorized for
12 emergency use became available, and participants who
13 ineligible for vaccination per national and local
14 public health prioritization recommendations were
15 offered the opportunity to cross over from the
16 originally assigned study treatments to the other study
17 treatment, the vaccine to placebo and placebo to
18 vaccine.

19 The primary efficacy endpoint was assessed
20 until the participant received the first blinded
21 crossover vaccination or until the data cutoff of

1 September 27th, 2021, whichever came first. And there
2 was also an assessment of humoral antibody responses
3 assessed in a subset of participants.

4 The safety assessments concluded the
5 following: the solicited, systemic, local and systemic
6 adverse reactions during the seven days after each
7 vaccination, unsolicited adverse events and medically-
8 attended adverse events through 28 days following a
9 second vaccination in both the pre-crossover and the
10 post-crossover period, and through the duration of the
11 study, medically-attended adverse events attributed to
12 study vaccine, serious adverse events, and adverse
13 events of clinical interest.

14 Efficacy was assessed through daily
15 surveillance of symptoms suggestive of COVID-19
16 throughout the study follow up. Symptoms of COVID-19
17 experienced by participants during the post-vaccination
18 follow up prompted an unscheduled illness visit in
19 person. A nasopharyngeal swab was collected and sent
20 to the central lab for processing.

21 Additionally, participants were also given a

1 kit to begin a daily self-nasal swabbing within three
2 days of symptom onset and collected for a total of
3 three days. The swabs were also sent to the central
4 lab for processing. Molecular confirmation of SARS-
5 CoV-2 infection by the central laboratory was required
6 to meet primary and secondary efficacy endpoint case
7 definitions.

8 The primary efficacy objective was to prevent
9 PCR-confirmed symptomatic COVID-19 illness diagnosed
10 seven or more days after completion of the primary
11 series. Primary efficacy endpoint was the first
12 episode of PCR-confirmed mild to moderate or severe
13 COVID-19 assessed up until the blinded crossover
14 period. The primary objective would be met if the
15 point estimate of the vaccine efficacy was 50 percent
16 or more and the lower bound of the 95 percent
17 confidence interval was greater than 30 percent.

18 And below, some of the secondary and
19 exploratory efficacy objectives are also shown on this
20 slide. These are the case definitions for mild,
21 moderate, and severe COVID-19 and the dataset to

1 support the EUA. The FDA conducted independent
2 analyses of datasets with different cutoff and
3 extraction dates. These included efficacy and safety
4 data with the data cutoff of September 27th, 2021.
5 These were cleaned datasets.

6 And then safety data was requested from FDA to
7 review clinically important safety events with an
8 extraction date of February 17th, 2022. And these were
9 from datasets that were not fully cleaned. This slide
10 presents disposition of all randomized participants as
11 of the data cutoff, September 27th, 2021. A total of
12 29,945 participants were initially randomized in a two-
13 to-one ratio with 19,963 vaccine participants and 9,882
14 placebo participants who received saline.

15 96.8 percent of the vaccine group and 95.7
16 percent of the placebo group completed the two-dose
17 primary series. Then, 77.7 percent of participants who
18 were initially randomized to the vaccine group and 64.8
19 percent in the placebo group elected to participate in
20 the crossover portion of the study. This slide
21 presents the efficacy analysis population.

1 Per protocol, population for efficacy was
2 comprised of participants who received two doses of the
3 vaccine or placebo at the pre-specified time points and
4 had no major protocol deviations prior to the first
5 COVID-19-positive episode, no confirmed SARS-CoV-2
6 infection during the surveillance period, or prior
7 infection due to SARS-CoV-2 at baseline and were not
8 censored prior to the start of the observational
9 period.

10 Seventy-eight percent of vaccine participants,
11 recipients and 73.1 percent of placebo recipients
12 completed at least two months of follow up after Dose
13 2. And then the second per-protocol efficacy sets
14 included all participants regardless of baseline SARS-
15 CoV-2 status. Here's the pre-protocol efficacy
16 population. They were balanced in terms of percentage
17 of male and female. The median age was 47 years with
18 12 percent of participants 65 years and older.

19 In terms of race and ethnicity, 11 percent of
20 participants were African American. Six percent were
21 American Indian or Alaskan native. Four percent were

1 Asian, and 22 percent were Hispanic. The main
2 comorbidities were obesity and chronic lung disease.
3 The primary efficacy endpoint was assessed until the
4 participant received the first blinded crossover
5 vaccination or until the data cutoff of September 27th,
6 2021, whichever came first.

7 In the per-protocol efficacy set, during the
8 pre-crossover period, 21.7 percent of participants who
9 received the placebo were unblinded with the intention
10 to receive a COVID-19 vaccine under EUA as compared to
11 13.2 percent of participants who received the vaccine.
12 These participants were censored for the primary
13 efficacy analyses at the time of unblinding.

14 For the results, the primary endpoint for 18
15 years and older as a whole was met. The vaccine
16 efficacy for the first episode of PCR-confirmed mild,
17 moderate, or severe COVID-19 was 90.4 percent. And of
18 the 17 cases of COVID-19 in the vaccine group, all were
19 mild in severity. In the placebo group, there were 66
20 cases which were mild, 9 which were moderate, and 4
21 cases that were severe.

1 There were no hospitalizations or deaths due
2 to COVID-19 among the 96 primary endpoint cases. In
3 the analysis of the primary efficacy endpoint provided
4 for participants who were SARS-CoV-2 positive at
5 baseline, among the 3,300 participants who were SARS-
6 CoV-2 positive at baseline, there were no COVID-19
7 cases that occurred at least seven days after the
8 second dose. So the vaccine efficacy, regardless of
9 baseline SARS-CoV-2 status, was 89.8 percent.

10 And in the age group 65 years and older, the
11 lowered limit of the 95 percent confidence interval for
12 the vaccine efficacy estimate was negative 16.6. There
13 were six cases, two in the vaccine group and four in
14 the placebo group. And the 95 percent confidence
15 interval for the estimate was wide. To provided
16 supportive data for the effectiveness in adults 65
17 years and older, a post-hoc analysis of the vaccine
18 efficacy among participants 50 to 64 years of age was
19 conducted at FDA's request.

20 The neutralizing antibody titers in this age
21 group was compared descriptively to those participants

1 65 years of age and older. The table on the left
2 summarizes the results of the immunogenicity comparison
3 between the two age groups. The GMT for the
4 participants 65 years of age and older was a little
5 lower than the GMT for the age group 50 to 64 years of
6 age, but the GMT ratio was 0.91 with the lower bound of
7 the 95 percent confidence interval that would've met
8 FDA's usual success criterion for immunoprotein.

9 On the right, the vaccine efficacy estimate
10 for age groups 50 to 64 years of age was 90.7 percent,
11 which was comparable to the overall vaccine efficacy
12 for ages 18 years and older, which was 90.4 percent,
13 and for the age group 18 to 64 years of age, which was
14 90.1 percent. These are the results of the secondary
15 and exploratory efficacy analysis. First, the efficacy
16 against COVID-19 for variants.

17 Of the 96 cases in the primary efficacy
18 analysis, 75 cases has sequencing data available, which
19 were mainly the Alpha variant. These were classified
20 in the sponsor's presentation according to the CDC
21 classification during May 2021. Currently, as of June

1 2022, none of the variants identified in the primary
2 efficacy analysis were considered variants of concern
3 or variants of interest. The second analysis was
4 vaccine efficacy against moderate to severe COVID-19.

5 There was a total of 13 cases in placebo arm
6 and none in the vaccine group, resulting the vaccine
7 efficacy estimate of 100 percent. Third, the vaccine
8 efficacy by race was comparable to the overall study
9 population. And, as discussed previously, there was a
10 lower vaccine efficacy estimate for participants of
11 Hispanic ethnicity. The participants in the safety
12 analysis, these participants were enrolled from a total
13 of 119 sites in the U.S. and Mexico.

14 In the pre-crossover period, as of the cutoff
15 date, September 27th, 2021, the median duration of
16 follow up during the pre-crossover period was 2.5
17 months. In the safety analysis, that included 19,111
18 participants in the vaccine group and 9,416
19 participants in the placebo group. And 77.8 percent in
20 the vaccine group and 72.8 percent of placebo
21 recipients completed at least two months of safety

1 follow up after the second dose.

2 In the post-crossover period, the median
3 duration of follow up after the fourth dose was 4.4
4 months, and 99 percent of participants in each study
5 group were followed for at least 2 months after the
6 second crossover dose. Third, the Sponsor provided, at
7 FDA's request, additional safety data through the
8 extraction date to February 17th, 2022, to assess
9 clinically important adverse events.

10 And at the time of the extraction date, the
11 median duration of follow up was 8.4 months after the
12 completion of the crossover series. The demographics
13 for the safety analysis population in the vaccine group
14 and the placebo group were similar.

15 (technical difficulties 03:14:21)

16 **MR. MICHAEL KAWCZYNSKI:** Go ahead with your
17 microphone.

18 **DR. LEE:** Thank you. Can you still hear me
19 now?

20 **MR. MICHAEL KAWCZYNSKI:** Yep. I can here you
21 now. Go ahead.

1 **DR. LUCIA LEE:** Okay. The safety analysis
2 population -- okay. The demographic and baseline
3 characteristics -- I think I'm hearing an echo.

4 **MR. MICHAEL KAWCZYNSKI:** Yeah. Go ahead and
5 turn off your speaker -- turn down your speaker.
6 Again, if you want to just reconnect your audio, ma'am.
7 Right now you're on speaker but on your microphone on
8 your computer. If you want dial back in, it's up to
9 you. otherwise you can continue but just turn your
10 volume down. I'll help you.

11 **DR. LUCIA LEE:** Okay.

12 **MR. MICHAEL KAWCZYNSKI:** Yeah. Ma'am, I'm
13 going to dial you in a different way real quick. If
14 you could, look at the chat pod. Just give us a quick
15 momentary break, and I'm going to help our speaker
16 here. Again, just give us a minute while we help out
17 Dr. Lee. Dr. Lee, you with us?

18 **DR. LUCIA LEE:** Yes. Can you hear me now,
19 Mike?

20 **MR. MICHAEL KAWCZYNSKI:** Yes, I can. Just go
21 ahead and mute your speakers then continue, okay? On

1 the top of your screen, just go ahead and mute the
2 speaker symbol, and you can continue. Okay, ma'am?

3 **DR. LUCIA LEE:** Okay.

4 **MR. MICHAEL KAWCZYNSKI:** All right. Take it
5 away.

6 **DR. LUCIA LEE:** Okay. So the demographic
7 baseline characteristics in the safety analysis
8 population in the vaccine group and placebo group were
9 similar in the pre-crossover period. Also, the pre-
10 crossover period the demographic and baseline were
11 similar to the post-crossover period and the safety
12 analysis set was similar to the per-protocol efficacy
13 set.

14 This slide shows the overall rates of
15 reactogenicity.

16 (technical difficulties 03:19:51)

17 **MR. MICHAEL KAWCZYNSKI:** You still there,
18 ma'am? Lucia, you still there? Ma'am, did you mute
19 your own phone? Oh, you dialed back in. Here we go.

20 **DR. LUCIA LEE:** Okay?

21 **MR. MICHAEL KAWCZYNSKI:** There you go. There

1 you go, ma'am. Go ahead.

2 **DR. LUCIA LEE:** So the solicited adverse
3 reaction were reported in higher proportion of the
4 vaccine recipients than the placebo recipients and more
5 frequent after vaccine Dose 2 than Dose 1. In the
6 interest of time, I'm going to skip the details of
7 this. In general, the local and systemic adverse
8 reactions were mild to moderate and lasted about one to
9 three days.

10 This slide shows unsolicited adverse events.
11 The frequency of nonserious unsolicited adverse events
12 occurring through 28 days after Dose 2 by time period
13 are shown here. In the pre-crossover period, the
14 percentages of participants reporting at least one
15 nonserious unsolicited adverse events were comparable
16 between the vaccine and placebo groups. In the post-
17 crossover period, the percentage of participants
18 reporting at least one unsolicited adverse events was
19 lower than the pre-crossover period and slightly higher
20 than the vaccine group and placebo group.

21 In terms of Grade 3 reactions and Grade 3

1 reactions considered by the investigator as related to
2 the study product, all those percentages in both the
3 vaccine group and the placebo group were low. The key
4 findings in the pre-crossover period included that
5 there were no adverse events by preferred term reported
6 by more than one percent of participants in either
7 study group.

8 There were imbalances in the system organ
9 class of general disorders and administrative site
10 conditions and blood and lymphatic system disorders,
11 which were largely due to reactogenicity and
12 lymphadenopathy, respectively. Lymphadenopathy was
13 reported by a higher proportion of participants in the
14 vaccine arm for Dose 1 and Dose 2, which was 0.06
15 percent and 0.2 percent, respectively, than in the
16 placebo group.

17 The most commonly reported severe unsolicited
18 adverse event in the vaccine group was fatigue. The
19 percentage of participants reporting serious adverse
20 events was similar in the placebo group and the vaccine
21 group in both the pre-crossover and the post-crossover

1 period and range from one percent to 1.4 percent across
2 study groups. The percentage of participants reporting
3 SAEs related to study vaccination was 0.1 percent in
4 both the vaccine group and the placebo group and in
5 both time periods.

6 The percentage of deaths reported in the
7 vaccine and placebo groups was less than 0.1 percent in
8 both time periods. This slide shows the number and
9 percentage of deaths reported in the pre- and post-
10 crossover periods by study group and the causes of
11 death. For participants with fatal cardiac arrest,
12 there were five in the vaccine group during the pre-
13 crossover period compared to three in the placebo group
14 and one in the post-crossover period in the vaccine
15 group.

16 For most of these participants, they had
17 underlying factors and conditions which were risk
18 factors for cardiac arrest. However, at this time,
19 there is limited information available to assess the
20 cause of death as some of the autopsy data were not
21 available. Participants in this study were randomized

1 in a two-to-one ratio which could account for more
2 events in the vaccine group. Additional data presented
3 through the February 17th, 2022, extraction date: all
4 of these deaths had a time onset of 140 days or more
5 following the Dose 4 in the crossover period.

6 None of these deaths were considered by the
7 investigator or FDA as related to vaccination. In the
8 pre-crossover period, the most common serious adverse
9 events that occurred at higher rates in the vaccine
10 group than the placebo group were cerebrovascular
11 accident, acute cholecystitis, atrial fibrillation,
12 aspiration pneumonia, and spontaneous abortion.

13 In the post-crossover period, the most common
14 SAEs occurring at higher rates in the vaccine group
15 versus the placebo group were ischemic cardiac events,
16 which included myocardial infarction, cholecystitis,
17 both chronic and acute, and pneumonia. In terms of
18 events of clinical interest, which included potentially
19 immune-mediated medical conditions, there were
20 numerical imbalances observed in the following
21 categories of cardiac, neurovascular, embolic and

1 thrombotic, and biliary events.

2 In terms of cardiac events, there was an
3 imbalance of events of cardiac failure and
4 cardiomyopathy with 0.5 percent in the vaccine group
5 and 0.02 percent in the placebo group. Almost all of
6 these participants had underlying conditions that were
7 risk factors, and the time to onset is comparable
8 between the two groups. In the post-crossover period
9 there was imbalance events consistent with myocardial
10 infarction.

11 The time to onset was comparable between the
12 two groups. In terms of neurovascular events, in the
13 pre-crossover period there was an imbalance in events
14 consistent with stroke, and three of the events
15 occurred within 15 days of the most recent vaccine
16 dose. And both events in the placebo group occurred
17 within 15 days of the most recent placebo dose.
18 Cumulatively through February 17th, 2022, there were a
19 total of 19 neurovascular events consistent with stroke
20 that were reported in the vaccine group in the pre-and
21 post-crossover period.

1 The time to onset from last vaccine dose for
2 11 of the 19 cases occurred greater than 61 days after
3 the last vaccination. In terms of thrombotic and
4 embolic events, in the pre- and post-crossover period,
5 the noncardiac non-neurovascular thrombotic and embolic
6 events were balanced in the pre- and post-crossover
7 periods. However, there were 8 participants in the
8 vaccine group that experienced events within 21 days of
9 the most recent vaccine dose without plausible
10 alternative etiologies.

11 And cumulatively through February 17th, 2022,
12 there was an imbalance of pulmonary embolisms that
13 occurred during the post-crossover period. However,
14 most of the events in both study groups had an onset of
15 greater than 90 days after the most recent dose, and
16 the proportion of events with onset less than two weeks
17 were comparable.

18 In terms of biliary events, in the pre- and
19 post-crossover period, there was an imbalance in
20 cholecystitis. And the 18 events in the vaccine
21 recipients in both time periods, 6 of those had an

1 onset within 30 days of the vaccine dose. In terms of
2 other events of clinical interest, those included
3 Bell's palsy, and these were all in the pre-crossover
4 period.

5 There was 1 case of Bell's palsy within 30
6 days of vaccination in each of the placebo and vaccine
7 groups. In terms of uveitis, there were three
8 participants in the vaccine group with new-onset
9 uveitis within three weeks of vaccination, one of which
10 recurred with rechallenge.

11 In the placebo group, there were two events of
12 uveitis, one of which had onset within one week of
13 placebo in a participant that had a history of uveitis.
14 Lastly, there was one event of angioedema and urticaria
15 that occurred two days after Dose 2 in the vaccine
16 group, which was potentially related, but the
17 participants also started an antibiotic concomitantly.

18 In review of the additional safety data from
19 Studies 101, 301, and 501, which were conducted in
20 Australia and the U.S., 302 was in the United Kingdom,
21 and 501 was in South Africa, the FDA reviewed serious

1 adverse events and adverse events of clinical interest.
2 These studies were conducted with a vaccine produced by
3 an earlier manufacturing process than the vaccine
4 evaluated in 301.

5 Out of the three studies, there was one event,
6 Guillain-Barre syndrome, that was reported by a 65-
7 year-old female in the vaccine group who experienced
8 progressive neuropathy starting at 9 days after Dose 1.
9 Other than this event, there were no new serious
10 adverse events, adverse events of special interest, or
11 potentially immune-mediated conditions in these studies
12 that were considered at least possibly related by FDA
13 that were not already previously identified in Study
14 301.

15 In a total clinical safety database of about
16 40,000 vaccine participants to date, 6 vaccine
17 recipients reported myocarditis and/or pericarditis,
18 including 5 events that occurred within 20 days after
19 the Novavax vaccine. These are the cases, a little bit
20 more detail. These cases were concerning for the
21 following reasons. The temporal relationship for 5 of

1 the cases occurred within 20 days after vaccination.

2 And only one of the events among the vaccine
3 group had a clearly identified alternative etiology
4 associated with myocarditis. And the other events had
5 only circumstantial evidence of potentially plausible
6 alternative etiologies. Four of the events occurred in
7 young men, which is a subject population known to be at
8 high risk for mRNA COVID vaccine-associated
9 myocarditis.

10 Now, I'm continuing to the Sponsor-submitted
11 post-marketing safety data. As of April 30th, 2022,
12 there are about 700,500 doses administered in
13 Australia, Canada, the European Union, New Zealand, and
14 South Korea. The Sponsor reported a potential safety
15 signal for myocarditis and pericarditis listed here.
16 The observed-to-expected rate ration for all doses was
17 4.95.

18 In summary, the known potential benefits
19 include that the vaccine was efficacious with an
20 estimate of 90.4 percent and the efficacy estimates
21 from Study 301 were generally consistent among some

1 groups stratified by demographic variables and for the
2 risk of severe COVID-19. The uncertainty in the
3 benefits include vaccine effectiveness against
4 currently circulating SARS-CoV-2 variants, long-term
5 effects of COVID-19 disease, effectiveness in certain
6 populations at higher risk of severe COVID-19, and the
7 duration of protection.

8 The known and potential risks associated with
9 vaccination include local and systemic reactogenicity,
10 myocarditis and pericarditis and Guillain-Barre
11 syndrome. And there are uncertainties in the risk in
12 certain populations and for adverse reactions that are
13 uncommon and that require longer follow up, which
14 include biliary events, neurovascular events, cardiac
15 events, and uveitis.

16 Sponsor submitted a pharmacovigilance plan to
17 monitor safety concerns that could be associated with
18 the Novavax COVID-19 vaccine. The FDA recommended
19 adding myocarditis and pericarditis as an important
20 identified risk. And the Sponsor considered as
21 important potential risk vaccine-associated enhanced

1 respiratory disease, myocarditis and pericarditis and
2 anaphylaxis. The Sponsor will conduct several post-
3 marketing activities, which include active and passive
4 surveillance activities, periodic aggregate safety
5 review of safety data, and five planned surveillance
6 studies.

7 So the pharmacovigilance activities include
8 adverse event reporting, which come from vaccine
9 recipients, vaccine providers, or the Sponsor themself.
10 First, the vaccine participants will be notified that
11 adverse events can be reported to VAERS through the
12 vaccine for recipients and health care providers or
13 from the V-SAFE program, and this reporting is
14 voluntary.

15 For the vaccine provider and the Sponsor,
16 these adverse event reporting is mandatory. For both
17 the vaccine providers and the Sponsor, they report to
18 VAERS the following information; serious adverse events
19 irrespective of attribution to vaccination, cases of
20 multisystem inflammatory syndrome in adults, and cases
21 of COVID-19 that result in hospitalization or death.

1 In addition, the Sponsor will also conduct
2 periodic aggregate safety review of safety data and
3 report newly identified safety concerns. Both the FDA
4 and CDC take a collaborative and complementary approach
5 to reviewing adverse events. In the initial stage of
6 post-authorization surveillance, FDA will individually
7 review all serious adverse events on a daily basis.

8 FDA will also examine other sources of AE,
9 such as in the literature, and perform data mining to
10 determine if the adverse events are disproportionately
11 reported for the candidate vaccine compared to other
12 vaccines in VAERS. And other potential safety signals
13 will also be investigated. In addition to passive
14 surveillance, FDA will also perform active surveillance
15 studies for safety outcomes.

16 These studies will be conducted using the
17 Biologics Effectiveness and Safety System which obtains
18 safety outcomes from various health care settings.
19 Active surveillance will also be performed using data
20 from the centers for Medicare and Medicaid services.
21 The Sponsor also proposed five post-authorization

1 surveillance studies.

2 The first is a Pregnancy Exposure Registry,
3 and the second and third are two active follow-up
4 safety studies, one in the U.S. and one in the U.K.
5 And the last two are real-world effectiveness studies,
6 one in the U.S. and one in Europe. Lastly, the Sponsor
7 was requested to include certain safety outcomes in
8 active surveillance studies, which includes the
9 basement of cardiac, neurovascular, embolic and
10 thrombotic, and biliary events.

11 The Sponsor will also perform enhanced
12 pharmacovigilance activities for safety outcomes of GBS
13 and uveitis. This concludes my presentation.

14 **DR. ARNOLD MONTO:** Thank you, Dr. Lee, and
15 apologies for the interruption. You did very well
16 considering. We do have a few minutes for questions
17 now before the lunch break. I don't see any hands
18 raised. Is that the system's fault?

19 **MR. MICHAEL KAWCZYNSKI:** No, no. There's no
20 hands raised at the moment. I was looking too.

21 **DR. ARNOLD MONTO:** No hands raised? I can't

1 believe it.

2 **MR. MICHAEL KAWCZYNSKI:** No. Oh, wait. Here
3 we go. We got out first one.

4 **DR. ARNOLD MONTO:** There we go. Okay, Dr.
5 Gellin.

6 **DR. LUCIA LEE:** I also wanted to mention that
7 Dr. Brandon Day will answer questions pertaining to the
8 pharmacovigilance plan.

9 **DR. ARNOLD MONTO:** Thank you. Dr. Gellin.

10 **DR. BRUCE GELLIN:** Okay. Thanks. Maybe we're
11 going to get into later. Thank you for that great
12 presentation. It's a lot of detail, and you had to
13 deal with the system. None of that is easy, so thanks
14 for that. Are we going to get into sort of the real-
15 world part of this? We heard the study data is through
16 the end of September. A lot has happened since then.
17 I'm guessing study participants have had real lives and
18 done other things, like gotten other vaccines from
19 whomever, maybe had other experiences. Is that going
20 to come into play at some point?

21 **DR. LUCIA LEE:** Dr. Day, do you want to take

1 that question?

2 **MR. MICHAEL KAWCZYNSKI:** Who did you want to
3 take that question again?

4 **DR. LUCIA LEE:** Brandon Day.

5 **MR. MICHAEL KAWCZYNSKI:** Brandon go ahead and
6 unmute yourself.

7 **DR. ARNOLD MONTO:** Or anybody else who wants
8 to answer that question.

9 **MR. MICHAEL KAWCZYNSKI:** I don't see Brandon
10 in here right now. I'll call Brandon back in just to
11 be safe. Go ahead. Let's go to the next question real
12 quickly.

13 **DR. ARNOLD MONTO:** I don't see another
14 question. Can't believe this.

15 **MR. MICHAEL KAWCZYNSKI:** If you give us a
16 moment, we'll bring Mr. Day back in here.

17 **DR. ARNOLD MONTO:** Or anybody else who can
18 answer that question. It might Dr. Fink or Dr. Marks.

19 **MR. MICHAEL KAWCZYNSKI:** Here we go. There's
20 Brandon. Brandon, are you there? Brandon, go ahead
21 and answer that question.

1 **DR. BRANDON DAY:** I'm reconnected. Can you
2 restate the questions?

3 **MR. MICHAEL KAWCZYNSKI:** Hi. We hear you. Go
4 ahead.

5 **DR. BRUCE GELLIN:** Want me to go again?

6 **DR. ARNOLD MONTO:** Bruce, why don't you go
7 again.

8 **DR. BRUCE GELLIN:** All right. Thank you.

9 **DR. ARNOLD MONTO:** Dr. Fink's here as well.

10 **DR. LUCIA LEE:** I also wanted to mention that
11 we did review the safety data through February 2022.

12 **DR. BRUCE GELLIN:** So that's the good news,
13 that somebody's continued to follow these patients, as
14 you said, for safety past the end of the study. The
15 questions is what else are we going to learn about the
16 trial participants since the study, durability, other
17 vaccines that they may have received. Did they get
18 boosters of Novavax as well? This is entering into the
19 real world of other vaccines.

20 While it's not our purview to figure how
21 they're going to be used if and when they're available,

1 that's going to be an important consideration. So any
2 data about that and including any data about Omicron,
3 which is missing from this discussion because it wasn't
4 present in September, but it's quite present now. And
5 hopefully people are still being followed in an Omicron
6 environment. Thank you.

7 **DR. LUCIA LEE:** The study was conducted quite
8 a while ago, and so the cases that accrued were not
9 during the time that Omicron was circulating. We tried
10 to focus mainly on the primary series, which is the
11 topic of this VRBPAC. We were not prepared to further
12 discuss the topics of participants who got boosters and
13 those related topics.

14 **DR. ARNOLD MONTO:** Dr. Fink, are you in the
15 position to straighten things out?

16 **DR. DORAN FINK:** I will try. Although I have
17 to admit, I'm having a lot of problems on my end with
18 the system figuring out --

19 **DR. ARNOLD MONTO:** We hear you.

20 **DR. DORAN FINK:** -- on or not. Can you hear
21 me?

1 **DR. ARNOLD MONTO:** Yes, we hear you.

2 **DR. DORAN FINK:** Yes. Okay. Great. I think
3 that the main points, as Dr. Lee summarized, are that
4 we do have rather long-term safety follow up that we
5 were able to review in detail for all of these study
6 participants. There has been some use of the vaccine
7 worldwide in post-authorization settings. Although, we
8 really don't have much data to report on that beyond
9 what is summarized in the slides.

10 If this vaccine is authorized for use in the
11 U.S., clearly we will need to have the same intense
12 level of post-authorization safety surveillance as we
13 have had for the other COVID-19 vaccines that have been
14 authorized, some of which have gone on to be approved
15 and fully licensed. Again, I just have to reiterate.
16 I know that there is intense interest in the potential
17 for using this vaccine as a booster dose in individuals
18 who might have received a primary vaccination with some
19 other COVID-19 vaccine.

20 We don't have the capacity to discuss that
21 potential use today or data related to that use. If

1 this vaccine were to be authorized for use as a primary
2 series, we could take an approach similar to what we
3 have for the other authorized COVID vaccines who are
4 considering use as a booster dose, and we would
5 evaluate study data to inform the safety and
6 effectiveness as a booster dose as it comes to us.

7 **DR. ARNOLD MONTO:** Thank you.

8 **MR. MICHAEL KAWCZYNSKI:** We have Brandon Day
9 (phonetic) also on as well. Brandon, did you have
10 anything to add?

11 **DR. BRANDON DAY:** No. I think they covered
12 it. Thanks.

13 **DR. ARNOLD MONTO:** Okay. This will be a
14 persistent item of discussion as we go through the rest
15 of the day is my humbled prediction. Dr. Lee.

16 **DR. JEANETTE LEE:** Yes. Thank you for that
17 presentation. I think one of the questions that I have
18 -- and I don't know if you're exactly the person to
19 ask. This actually was designed as a crossover so that
20 individuals were randomized to either receive the
21 vaccine first followed by placebo and then placebo

1 followed by vaccine. So far, obviously, the primary
2 endpoint was based on the original randomization of
3 vaccine versus placebo before the crossover, although
4 we have seen some safety data after the crossover
5 period.

6 Is there any plan to analyze -- typically in a
7 crossover, you have a wash out period, and then you do
8 the second comparison. The reason I ask that is it
9 would seem as though those that have started with a
10 vaccine and then went to placebo -- that there might
11 actually be a carry-over effect that might actually
12 give us some indication as to waning immunity or not.
13 I didn't know if there were any plans for that analysis
14 to be done to separate the pre- and post-crossover in
15 terms of efficacy not just safety.

16 **DR. LUCIA LEE:** I think the Sponsor can add.
17 But since the study is still ongoing, there are
18 provisions to collect samples to look at the duration
19 of protection.

20 **DR. JEANNETTE LEE:** Okay. All right. Thank
21 you.

1 **DR. ARNOLD MONTO:** Why don't we park that
2 question, Dr. Lee, and this is something we can come
3 back to when we have a broader discussion with the
4 Sponsor online as well after lunch?

5 **DR. JEANNETTE LEE:** Okay. Thanks.

6 **DR. ARNOLD MONTO:** Dr. Meissner.

7 **DR. CODY MEISSNER:** Dr. Lee, thank you for the
8 presentation. I would like to ask you about the FDA's
9 experience with baculovirus, insect cell protein
10 expression systems. I don't think it's been used very
11 often. Do you have any other specific issues regarding
12 safety with that eukaryotic protein expression system
13 that the FDA worries about?

14 **DR. LUCIA LEE:** I'd have to defer this
15 question to Dr. Fink or others from the FDA.

16 **DR. DORAN FINK:** Hi. So we do have an example
17 of a recombinant protein-based seasonal influenza
18 vaccine, Flublok, that has been approved and is
19 manufactured using a similar expression system. We
20 don't have any safety concerns attached to that vaccine
21 specific to that manufacturing platform.

1 **DR. CODY MEISSNER:** Thank you.

2 **DR. ARNOLD MONTO:** Not seeing any further
3 hands raised to my amazement. We will be able to start
4 lunch a few minutes early. Thank you, Dr. Lee for your
5 careful presentation and handling the technical issues
6 in the middle. Back for the open public hearing at
7 1:00.

8 **DR. LUCIA LEE:** Thank you.

9 **MR. MICHAEL KAWCZYNSKI:** All right. So
10 everyone, just give us a moment as we pull up the
11 lunch. Nobody log off and take break yet.

12

13 **[LUNCH BREAK]**

14

15 **MR. MICHAEL KAWCZYNSKI:** Welcome back to the
16 173 meeting for Vaccines and Related Biological
17 Products Advisory Committee meeting. I will now hand
18 the meeting over to our chair, Dr. Monto, and our DFO,
19 Dr. Prabhakara Atreya. Take it away.

20

1

OPEN PUBLIC HEARING

2

3

DR. ARNOLD MONTO: Thanks, Mike. Welcome

4

everybody to the open public hearing session. Please

5

note that both the Food and Drug Administration and the

6

public believe in a transparent process for information

7

gathering and decision making. To ensure such

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transparency at the open public hearing session of the

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Advisory Committee meeting, FDA believes that it is

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important to understand the context of an individual's

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presentation.

12

For this reason, FDA encourages you, the open

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public hearing speaker, at the beginning of your

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written or oral statement, to advise the Committee of

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any financial relationship that you may have with the

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Sponsor, the product, and, if known, its direct

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competitors. For example, this information may include

18

the Sponsor's payment of expenses in connection with

19

your presentation in this meeting.

20

Likewise, FDA encourages you, at the beginning

21

of your statement, to advise the Committee if you do

1 not have any such financial relationships. If you
2 choose not to address the issues of financial
3 relationships at the beginning of your statement, it
4 will not preclude you from speaking. Prabha, over to
5 you.

6 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Monto.
7 Before I begin calling on the registered speakers, I
8 would like to add the following FDA guidance. FDA
9 encourages participation from all public stakeholders
10 in its decision-making process. Every Advisory
11 Committee meeting includes an open public hearing
12 session, during which interested persons may present
13 relevant information of use.

14 Participants during the open session are not
15 FDA employees or members of this Advisory Committee.
16 FDA recognizes that the speakers may represent a range
17 of viewpoints. The statements made during this open
18 public hearing can reflect the viewpoints of the
19 individual speakers and of their organizations only,
20 and they're not meant to indicate Agency's agreement
21 with the statement made.

1 With this guidance provided, I'm going to call
2 on the first registered speaker, Mr. Benjamin Newton.
3 You have five minutes to speak. Thank you.

4 **MR. BENJAMIN NEWTON:** Thanks so much for your
5 time. I really appreciate it. The question we have
6 here -- and it is always the question -- is how can we
7 save the most lives. This is the question that
8 constantly chases this Committee and all of the FDA.
9 The question before VRBPAC today is easy to answer:
10 authorize Novavax's vaccine. It's highly effective.
11 It's something we knew more than a year ago. Plus, it
12 hurts less than the mRNA vaccines.

13 It appears, from the limited data that the FDA
14 has shared, the myocarditis issues are likely a result
15 of data mining errors, but we will only know with more
16 data. From my view, there's a clear benefit to a
17 vaccine that hurts less. For example, I have an
18 acquaintance who recently got sick with COVID because
19 he didn't want to get boosted because the mRNA vaccines
20 hurt too much. All of this is really an aside to the
21 rest of my presentation.

1 Next slide. Really the thrust here is about
2 how we can better protect people, right? the question
3 we have to ask ourselves as a regulatory body is how
4 best can we serve the people of this nation? Should we
5 provide people with options, or should we stand in the
6 way of people protecting themselves? Today, children
7 under five still have no access to vaccines nearly a
8 year after the American Academy of Pediatrics
9 recommended approval using sero-bridging data.

10 Today, Omicron-specific boosters have not yet
11 been approved six months after we knew that they were
12 required. Today, we all suspect that antibody half-
13 life long term would be about 90 days. So we will need
14 boosters about every six months. However, it is very
15 challenging for people to get access to needed
16 boosters. The question we are trying to answer is not
17 if these vaccines are safe, but rather are they safer
18 than the alternative. They are clearly safer than
19 COVID. Next slide.

20 So why was Novavax delayed? Novavax's vaccine
21 demonstrated efficacy superior to J&J's vaccine before

1 J&J was approved. Instead of approving Novavax in
2 January of 2021, the FDA required a second Phase 3
3 trial for one of the best vaccines, delaying approval.
4 At this point, Novavax's vaccine has been authorized
5 for use in more than 100 countries, courtesy of the
6 WHO. Like all approved vaccines, this could've been
7 approved sooner.

8 What went wrong at the FDA? What can we do
9 better next time? These are questions that only the
10 FDA can answer. Next slide. The FDA prevents access
11 to life-saving medicines. Why? In fact, that is the
12 entire point of the FDA: block access to drugs to
13 prevent dangerous drugs from entering the marketplace.
14 This is a constant balancing act, one that is
15 impossible to get right but that the FDA must
16 constantly work to improve.

17 Some reasons for delayed approval are likely
18 to be incentives. No one gets fired for being
19 conservative with drug approval. FDA Committee members
20 derive revenue from illness and/or clinical trials.
21 This is to be expected as it's populated by doctors.

1 You are all likely familiar with the trolley problem.
2 People feel differently about having agency in an
3 outcome versus just letting people die by preventing
4 access to medicines.

5 The FDA does not quantify the mortality and
6 morbidity associated with both action and inaction. We
7 count the people injured taking bad medicines. We
8 don't count the people injured by lack of access to
9 good medicines. Diversity matters, and it's highly
10 important for effective decision making. There is
11 almost no diversity on VRBPAC, partially by design.
12 Someone is not on mute.

13 We know that there are problems; it would be
14 surprising if there were not. So what can the FDA do
15 to improve? You can set clear guidelines for approval
16 of vaccines for all known pathogens today. You can
17 create data standards and automated data feeds for
18 clinical trials. You can publish this data in real
19 time, redacted of personal and identifiable
20 information, allowing for real-time analysis. You can
21 quantify and assess the risks of both action as well as

1 the cost of inaction.

2 You can increase diversity on FDA committees.

3 You can create a process to authorize vaccines in 30

4 days for all ages, then name a pathogen and let the FDA

5 and the industry practice. We are going to have

6 another pandemic; it's only a matter of time. And this

7 group is the group that can best prepare us for that

8 eventuality. Next slide. On slide six, our future is

9 bright. So this may have seemed like all doom and

10 gloom, but it's not.

11 We have this bright future. There are a few

12 hundred viruses that cause disease in humans. It's a

13 trackable problem. What is nice is that vaccine

14 development is actually very cheap, less than a million

15 dollars per vaccine. Unfortunately, clinical trials

16 cost hundreds of millions of dollars, with most of the

17 cost occurring during phase three. With modern

18 statistics and a highly effective vaccine, phase three

19 trials are a measure of how effective and safe a

20 vaccine is, not if it is safe and effective.

21 This allows regulators the ability to

1 streamline and standardize trials and dataflows,
2 reducing cost, increasing the speed of innovation. If
3 we want people to stop getting sick and dying from
4 viruses, the safest course of action today is
5 vaccination, a process impeded by a current regulatory
6 environment. I really thank you for your time and
7 attention to this matter. You've done so much work over
8 the last couple of years getting these vaccines
9 approved. Thank you.

10 **DR. PRABHAKARA ATREYA:** Thank you. The next
11 speaker is Ms. Cathy Keaveney.

12 **MS. CATHY KEAVENEY:** My name is Cathy
13 Keaveney. Thank you for the opportunity to speak.
14 (Inaudible) Japan, Australia, New Zealand, India,
15 Switzerland, Thailand, Indonesia, the Philippines, The
16 United Arab Emirates, 4 countries of the United
17 Kingdom, 27 countries of the European Union, Canada,
18 and the World Health Organization have all approved the
19 Novavax vaccine, a vaccine developed by a company in
20 Maryland, funded with \$1.8 billion of United States
21 citizens' hard-earned taxpayer money.

1 And yet, it has still not been approved for
2 the American citizens who paid for it. Why not? Why,
3 in the United States, bastion of freedom of personal
4 choice, are Americans served up only one type of
5 vaccine option, mRNA, while the rest of the world gets
6 choice? When Operation Warp Speed was initiated,
7 (inaudible) companies. Practically speaking, we are
8 now down to two, Moderna and Pfizer, and both are mRNA
9 platforms.

10 The FDA's response to (inaudible) delay in
11 approving Novavax has seemingly been two issues: the
12 amount of trial data to be reviewed and the need to
13 inspect Novavax's manufacturing. I question both.
14 Your (inaudible) and review boards across the world
15 have managed to review Novavax's (inaudible) data and
16 expeditiously approved this vaccine. What is it about
17 this data that is somehow more onerous for the FDA to
18 interpret?

19 A *Wall Street Journal* article attributed the
20 delay to manufacturing inspections, quoting a source as
21 saying, "Pandemic safety protocols made it more

1 difficult for FDA inspectors to get to Novavax's
2 overseas manufacturing sites." I fail to see why, in
3 the midst of a global pandemic with millions dying, the
4 FDA couldn't put on a mask, get on a military plane,
5 and fly to India to inspect Novavax's one manufacturing
6 site.

7 Certainly, many inspectors from other
8 countries did. Throughout the last two years, I've
9 learned a great deal about why others want Novavax.
10 I've learned that there are American citizens who,
11 after two years, still haven't left their homes because
12 they have medical reasons that won't allow them to take
13 mRNA vaccines. I've learned that many Americans have
14 been fired or quit their jobs rather than be forced to
15 take the one type of vaccine that their employers
16 mandate.

17 I've learned that many have had adverse
18 reactions to the mRNA vaccines. At this same meeting
19 two months ago, this very Committee heard from American
20 citizens, many in tears, who described their adverse
21 reactions to mRNA and pleaded with you to help. I've

1 learned that Americans with dual citizenship have
2 resorted to going to other countries in hopes of
3 receiving the Novavax vaccine where it has been
4 approved.

5 Americans paying to go to other countries to
6 get a vaccine that's headquartered 20 minutes from your
7 office. I've learned that, while we deny our own
8 citizens the Novavax vaccine, we allow citizens from
9 other countries who have been vaccinated with Novavax
10 there to freely travel here. I've learned that
11 Americans who want Novavax choice are not vaccine-
12 hesitant or anti-vax or afraid or whatever other terms
13 the media likes to use to marginalize us.

14 We are simply informed Americans who believe
15 that this is a better, safer vaccine, and we want what
16 our \$1.8 billion paid for. And where is America's
17 leadership on this? Full disclosure, I voted for
18 President Biden, but I don't understand how a country
19 can evoke the Defense Production Act to manufacture and
20 import baby formula, yet, in a time when millions are
21 dying, can't figure out how to get Novavax from India

1 or, better yet, help them produce it in the United
2 States.

3 I year ago, President Biden was quoted as
4 saying, "The problem right now is that we have to make
5 sure we have other vaccines like Novavax and others
6 coming on." Also a year ago, Ashish Jha, Biden's COVID
7 czar, had this to say about Novavax: "I realize that
8 the Novavax vaccine results won't get the same
9 attention that we heard from Moderna, Pfizer, and
10 Johnson & Johnson. But, for vaccinating the world,
11 this is huge, very, very good news. Novavax is
12 essential to vaccinating the globe. The fact that
13 Novavax has 90 percent efficacy is awesome."

14 And yet, still nothing. Awesome news for the
15 globe, just not for the United States. An emergency
16 use authorization based on today's meeting will
17 certainly be a step in the right direction, but it
18 would be largely meaningless if you do not follow
19 quickly behind that with a EUA to allow people to
20 choose Novavax as a booster to the Moderna and Pfizer
21 mRNA vaccine they have already received.

1 A week from now, on June 14th and 15th, the
2 same Committee will review Moderna and Pfizer's
3 applications for immunizing six months to four-year-old
4 children. For some Byzantine reason, Novavax can't
5 advertise in any other countries where it's already
6 been approved until it's approved by the FDA. Without
7 advertising or marketing or media coverage or
8 governmental promotions, parents aren't informed.

9 Many don't know that out there in the world
10 vaccine choice exists, and it should exist for they and
11 their children. Parents don't have the time or energy
12 to sit around and read up (inaudible). Instead, they
13 will rely on your recommendations. Because they are
14 scared and wanting to protect their kids, they will
15 rush to vaccinate our most vulnerable with the only
16 option you've allowed them.

17 (Inaudible) on them but you should until
18 they're given a choice. Parents should be able to make
19 informed decisions about their children's health, and
20 you should inform them. Which brings me to the media;
21 you are complicit. I'm a mother, not an investigative

1 reporter and have eight-grade math homework to focus
2 on. Do your job. Ask questions. Quit regurgitating
3 what you were fed.

4 I challenge you to verify or discount every
5 detail of what I've said here today. You have one week
6 until this Committee meets again to determine approval
7 in mRNA in infants and toddlers. Again, parents should
8 be informed; you should inform them. Members of this
9 Committee, you were charged with evaluating the
10 benefits of this vaccine. But you also have the
11 awesome responsibility of ensuring American citizens
12 continue to have freedom of choice. Thank you for
13 allowing this mom for Novavax to speak.

14 **DR. PRABHAKARA ATREYA:** Thank you. The next
15 speaker is Mr. Mitchell Goldstein.

16 **DR. MITCHELL GOLDSTEIN:** Yes. I'm Dr.
17 Mitchell Goldstein. I'm a professor of pediatrics at
18 Loma Linda University Children's Hospital. The
19 emergency use authorization request by Novavax for a
20 vaccine to prevent COVID-19 in individuals 18 years of
21 age and older should be granted. As reported by Dunkel

1 et al. in the *New England Journal of Medicine*, data
2 from two separate studies involving over 30,000
3 participants demonstrated a composite efficacy of
4 approximately 90 percent in preventing significant
5 infection.

6 Although this data was collected prior to the
7 presence of Omicron and other subvariants, this vaccine
8 product is the first traditional protein-based vaccine
9 to achieve this level of protection. The vaccine has
10 been authorized for emergency use by the World Health
11 Organization and can be used in over 170 countries
12 worldwide. Current mainstream United States
13 immunization regimens for COVID-19 involve the use of
14 mRNA technologies.

15 These immunizations have resulted in decreased
16 morbidity and mortality when measured against the
17 demographic considerations of an unprotected
18 population. However, the frequent need for boosters
19 and the broad public perception of these technologies
20 as untested, and thus untrusted, demonstrates the need
21 for a traditional protein-based technology that mirrors

1 those of the more trusted traditional vaccine products
2 currently on the market for other viral diseases.

3 Further, the need to provide effective
4 protection to pregnant women and their particular
5 concerns regarding the use of mRNA immunizations and
6 potential consequences to their unborn babies, as
7 described by Hageman and Goldstein in *Neonatology*
8 *Today*, provides further corroboration of the need for
9 an effective, traditional, protein-based vaccine
10 product.

11 Please make this vaccine available to provide
12 additional protection for those most at-risk groups.
13 Thank you.

14 **DR. PRABHAKARA ATREYA:** Thank you for your
15 comment. The next speaker is David Charles.

16 **MR. MICHAEL KAWCZYNSKI:** David, you're
17 unmuted. Make sure your own phone isn't muted.

18 **DR. DAVID CHARLES:** Thank you and good
19 afternoon. Thank you for allowing me to address
20 today's Food and Drug Administration Vaccines and
21 Related Biologics Product Advisory Committee. My name

1 is David Charles. I'm a practicing physician in
2 Tennessee, and I'm here today on behalf of my role as
3 founding member and chief medical officer of the
4 Alliance for Patient Access.

5 The Alliance for Patient Access is a national
6 network of policy-minded health care providers who
7 advocate for patient-centric care. The Alliance is
8 supported through associate memberships, grants, and
9 donations from a diverse group of organizations,
10 including Novavax and other vaccine manufacturers. The
11 Alliance supports health policies that reinforce
12 clinical decision making, promote personalized care,
13 and protect the physician-patient relationship.

14 Motivated by these principles, Alliance
15 members participate in clinical working groups,
16 advocacy initiatives, stakeholder coalitions, and the
17 creation of educational materials. On behalf of the
18 Alliance for Patient Access, we would like to commend
19 the FDA and the Advisory Committee on the important
20 work that you have done in ensuring safety and the
21 efficacy of COVID-19 vaccines throughout the pandemic.

1 As we know, access to FDA-approved vaccines
2 has slowed the spread of COVID and undoubtedly saved
3 the lives of untold numbers of Americans. However,
4 despite the work that the FDA and the emergency use
5 authorization process has done in approving COVID-19
6 vaccines, there continues to be vaccine hesitancy among
7 the American population. The World Health Organization
8 has listed vaccine hesitancy as one of the top threats
9 to global health.

10 They further noted that the reasons some are
11 choosing not to vaccinate are complex, but a lack of
12 confidence in the vaccine is a concern. This lack of
13 confidence can stem from a lack of understanding about
14 the newer or unknown vaccine designs and technologies.
15 While the mRNA and viral-vector vaccine designs are
16 available, they're still not well known to the general
17 population, which makes additional vaccine options
18 valuable.

19 Having another vaccine design introduced, such
20 as a recombinant-based design, may encourage those who
21 are vaccine hesitant to finally become vaccinated.

1 There continues to be many unknowns about the virus,
2 variants, and long-term effects of contracting COVID-
3 19. It is imperative that Americans have access to a
4 variety of safe and effective vaccines to ensure
5 greater uptake and to protect individuals and the
6 public.

7 As the virus evolves, additional vaccine
8 options are important to meet the needs in keeping the
9 Americans safe. The benefits of more COVID-19 vaccine
10 availability, especially with those who are vaccine
11 hesitant, greatly outweighs the risk of declining to
12 authorize the use of safe and effective vaccines.
13 We're asking the Committee to strongly consider
14 emergency use authorization of safe and effective
15 COVID-19 vaccine applicants that use different,
16 historically well understood vaccine designs.

17 It is to the benefit of every American to have
18 additional vaccine options other than mRNA, including
19 protein-based vaccines if available. Thank you very
20 much for allowing me to participate.

21 **DR. PRABHAKARA ATREYA:** Thank you for your

1 comments. The next speaker is Chad Rittle.

2 **MR. CHAD RITTLE:** Okay. Thank you very much.
3 My name is Chad Rittle. I am a professor of nursing at
4 Chatham University in Pittsburgh and have been
5 promoting public health and universal vaccination of
6 adults for many years. Thank you for this opportunity
7 to address the Vaccines Related Biological Products
8 Advisory Committee meeting today to discuss the issue
9 in emergency use authorization request for the Novavax
10 vaccine to prevent COVID-19 infection in individuals 18
11 years of age and over.

12 I would like to put forward three reasons to
13 support this EUA. First, there are currently
14 approximately 258 million Americans who have received
15 at least one dose of vaccine and two-thirds of the
16 population can be considered fully vaccinated. That's
17 221 million. Accepting these statistics, that
18 approximately one-third of the population is still
19 skeptical of the COVID-19 vaccine, how can we persuade
20 those reluctant Americans to get vaccinated?

21 The Novavax vaccine produces an exact replica

1 of a spike protein of the COVID-19 virus that prompts
2 our immune system to produce antibodies against the
3 virus. This may help those who are hesitant, who are
4 not supportive of the messenger-RNA technology that
5 comprised the first two vaccines currently under EUA.
6 This vaccine does not involve utilizing any of the
7 genetic functions in the human cell.

8 Specifically, there is no production of
9 messenger-RNA to make new proteins within the cell.
10 The vaccine uses proven technology by presenting
11 antigens to the immune system resulting in production
12 of antibodies. Additionally, the Novavax COVID-19
13 vaccine includes a special adjuvant, Matrix-M1, bonded
14 to the particles in the vaccine. This Matrix very
15 strongly boosts immune responses similar to the
16 adjuvant used in the SHINGRIX Zoster vaccine.

17 With this boost, even people over 80 years of
18 age who typically have weak immune responses to
19 vaccines can respond. Secondly, I have been actively
20 working to promote vaccines to enhance public health in
21 America for close to 20 years. My first publication

1 promoted universal vaccination against pertussis -- was
2 the result of my doctoral research project addressing
3 an outbreak within a school district that resulted in
4 over 70 cases in multiple age groups.

5 The paper was published in 2010. Vaccines
6 have been proven to help to prevent disease in all age
7 groups. And the meta-analysis describes the
8 effectiveness of pertussis vaccines, showing that
9 patients were more than twice as likely to contract
10 pertussis if vaccine doses containing pertussis antigen
11 were missed or administered late.

12 Third, during the past two years, I have been
13 closely monitoring the COVID-19 pandemic while
14 attending ACIP meetings as the ANA liaison
15 representative and conducting research doing an
16 academic sabbatical in fall of 2021. One result of
17 that study was publication of an article titled "COVID-
18 19 Vaccine Hesitancy and How to Address it," published
19 early this year.

20 Points discussed included, vaccine hesitancy
21 described an unwillingness of citizens to accept

1 vaccines that are accessible and available. Currently,
2 one-third of the population has not received any dose
3 of vaccine and are at risk for significant disease,
4 hospitalization, and death. We need another tool in
5 the arsenal to address the concerns of this significant
6 segment of the population. Secondly, not all health
7 care workers are acceptant of COVID-19 vaccine.

8 A *Relias Media* report documents that 20
9 percent of nurses refused the initial vaccines due to
10 questions about safety and efficacy. A proportion of
11 the population, a third point, are grouped as in-
12 betweeners, those adults who have taken a wait-and-see
13 attitude. This group typically includes women, younger
14 adults, and an ethnic minority background with less
15 education.

16 Common concerns include vaccine safety and
17 skepticism about the risk of COVID-19, belief they are
18 already immunized from prior exposure, and reservations
19 about efficacy. There are many approaches to educating
20 this hesitant population. It is key that we make
21 another effective vaccine available, that they'd be

1 more acceptable to this broad and complex population --
2 as you can see crosses many boundaries between gender,
3 ethnic group, and socioeconomic classification.

4 Let's not forget the social determinants of
5 health can also influence vaccine acceptance. Some of
6 those factors include political belief, education, low
7 trust in scientists, where they live, where they work,
8 where they get their news information, and how they
9 evaluate health risk. Just because someone in the
10 family had COVID would not necessarily influence
11 acceptance of the vaccine.

12 I strongly urge the Vaccines and Related
13 Biological Products Advisory Committee to approve this
14 emergency use authorization to make another vaccine
15 tool available to help achieve universal vaccination
16 against COVID. With another choice available to
17 doctors and nurses, we will have a better change of
18 convincing adult citizens to accept COVID-19 vaccine
19 more readily.

20 The Novavax COVID-19 vaccine could help break
21 down some of those barriers of which many of us are

1 aware and help achieve the World Health Organization's
2 goal of 70 percent coverage with COVID-19 vaccines
3 throughout the world. Thank you very much.

4 **DR. PRABHAKARA ATREYA:** Thank you. Thank you
5 for your comments. The next speaker is Ms. Sophia
6 Phillips.

7 **MS. SOPHIA PHILLIPS:** Hello. Thank you for
8 the opportunity to speak today on behalf of the
9 National Center for Health Research. My name is Sophia
10 Phillips, and I am a fellow at the center. We analyze
11 scientific data to provide objective health information
12 to patients, health professionals, and policy makers.
13 We do not accept funding from drug or medical device
14 companies, so I have not conflicts of interest.

15 Today, the panelists were asked to evaluate if
16 the benefits of the Novavax COVID-19 vaccine outweigh
17 its risks for youths and individuals 18 years of age
18 and older. While this vaccine demonstrates similar
19 levels of efficacy as compared to vaccines approved for
20 COVID-19, the data suggests additional safety risks.
21 As was stated in the FDA materials, there was an

1 elevated risk of myocarditis and pericarditis
2 demonstrated in Study 301.

3 Further, this risk could be higher in the
4 Novavax vaccine compared with mRNA COVID-19 vaccines.
5 There were six cases identified pre-authorization of
6 Novavax, while no cases were identified before the
7 authorization of mRNA COVID-19 vaccines. Although
8 these serious complications were also identified for
9 mRNA vaccines, that was only when the much larger
10 numbers of people were vaccinated, not the original
11 mRNA study participants.

12 Data from passive surveillance in other
13 countries where the Novavax vaccine is authorized also
14 indicate a higher-than-expected rate of myocarditis and
15 pericarditis associated with the vaccine. As a result,
16 the FDA requested that the Sponsor change myocarditis
17 and pericarditis to important identified risk on the
18 pharmacovigilance plan.

19 The design of Study 301, which is the basis
20 for today's discussion, initially resembled that of the
21 three COVID-19 vaccines granted in EUA. They were

1 similarly Phase 3, randomized placebo-controlled trials
2 with a similar number of vaccinated participants.
3 However, when the study design transitioned to a
4 blinded crossover due to the availability of EUA
5 vaccines for certain populations, it weakened the value
6 of the data.

7 Efficacy of the drug compared to placebo could
8 only be determined in the pre-crossover period after
9 Dose 2 for approximately two months before the opposite
10 treatment was given to each participant. Therefore, it
11 is not possible to assess sustained efficacy over a
12 longer period of time. It remains unclear how long
13 protection lasts. While the FDA remains hopeful that
14 Novavax will provide some meaningful protection against
15 Omicron, that is also uncertain since the vaccine was
16 primarily studied on the Alpha variants.

17 Additionally, very few of study participants
18 were immunocompromised, pregnant or lactating, or at
19 risk of severe COVID because of cardiovascular, chronic
20 renal, and chronic liver disease. That made it
21 impossible to meaningfully evaluate the vaccine's

1 efficacy for those populations. Few cases of PCR-
2 confirmed COVID-19 were analyzed for participants over
3 65 years of age, limiting the value of the efficacy
4 data for that age subgroup.

5 For those that were studied, there was a 12.5
6 percent dip in vaccine efficacy for individuals 65 or
7 older, which is also typical for the mRNA COVID-19
8 vaccines. What would be the value of this vaccine
9 compared to the three COVID vaccines that have already
10 been approved? If it is less safe than the other three
11 vaccines, it does not provide additional benefit to
12 make up for that.

13 Even if it not proven to be less effective
14 than the other COVID vaccines, it lacks long-term,
15 placebo-controlled efficacy data. And there is very
16 little safety or efficacy data for the most at risk
17 patients. When we already have vaccines on the market
18 that are FDA approved and based on much better data,
19 why would the FDA authorize this vaccine? Wouldn't it
20 just add to the controversy surrounding COVID-19
21 vaccines? Thank you.

1 **DR. PRABHAKARA ATREYA:** Thank you for your
2 comments. The next speaker is Martha Dawson. Ms.
3 Dawson.

4 **MS. MARTHA DAWSON:** Good afternoon, everyone.
5 Thank you so much for allowing me to speak today. I'm
6 here today to support another technology to fight
7 COVID-19 and the many growing variants. When one is at
8 war, many different approaches are used by land, air,
9 and water. Although the public is exhausted and ready
10 for this pandemic to end, there really is no light at
11 the end of the tunnel.

12 As a nurse for 45 years and the current
13 president and CEO of the National Black Nursing
14 Association, representing over 500,000 registered
15 nurses, licensed, practical, and vocational nurses, and
16 nursing students nationwide, I am also fatigued from
17 educating, testing, vaccinating, and addressing other
18 health and social determinants that place black and
19 brown population at risk during this pandemic. And we
20 know that more of them have died.

21 In addition, NBNA nurses have been on the

1 frontline. We have been serving every day from March
2 the 20th, when the first variant of COVID hit our
3 nation. Therefore, I encourage the FDA to give us
4 another, more traditional medical innovation in this
5 fight and approve this vaccine. African Americans and
6 black nurses that I represent and give voice to are on
7 the frontline of this pandemic, and they continue to
8 watch more of our population die.

9 They have lost colleagues, spouses, partners,
10 parents, children, and other relatives and friends.
11 Let us be very clear, COVID-19 is a public health
12 crisis. However, it has been politicized with mis- and
13 disinformation. Therefore, some people will never
14 become vaccinated, putting others at risk.
15 Unfortunately, people are not following public health
16 policies and best practices.

17 It appears that the world is just tired of
18 wearing masks and washing their hands, isolating and
19 being social distanced. However, through the lens of
20 public health, this is exactly what is still needed
21 today. But, again, since the majority of the

1 population is not leaning in that preventive and
2 health-promotion direction, we have to look for other
3 measures.

4 I do believe that having another vaccine will
5 give people options. Maybe some of those that are
6 still sitting on the sideline saying, "Well, let's just
7 wait until a few more are vaccinated." But that put us
8 at risk, and it brings to mind of me talking to a close
9 friend this week, I mean just this week, with another
10 under-40-year-old relative ended up with COVID
11 pneumonia.

12 How many of our young people are we going to
13 allow to die or who we're going to allow to become
14 sick? Again, it's unfortunate that people are not
15 following public health policies and best practices, so
16 we have to look for other options and give people more
17 options. Many believe that these measures did not work
18 and are not going to work. However, we see cases still
19 increasing. Yes, again, we have a breather. It's now
20 summertime; we can be out.

21 We can have more fresh air. But make no

1 mistake, within another eight to ten weeks, we're going
2 to move back into our kids going into the school
3 system. And we will probably see another spike if we
4 don't do something. As I stated, I represent nurses
5 and nursing students, and the future workforce for this
6 profession is not good. It is projected that over one
7 million nurses will be needed in the United States and
8 over six million will be needed worldwide by 2030.

9 My colleagues, it takes three to four years
10 just to educate one nurse. So, if we continue to lose
11 nurses because they are fatigued and they're tired and
12 they just can't see one more patient expire from this
13 COVID pandemic, then we're going to continue to have
14 them leave the occupation and look for other things to
15 do. So I want to just say let's think about this
16 because, yes, I know nurses and physicians and others
17 in the health care space; they are also refusing to be
18 vaccinated.

19 But we need to continue to provide option to
20 reduce excuses and as many excuses as we possibly can.
21 This is why I strongly support and encourage the FDA to

1 approve the Novavax vaccine. I would like to close
2 with this; in the art of humanity and public safety,
3 since we as a country have not been able to lean in and
4 accept that this a public health crisis and that we
5 should not only protect ourselves but those around us,
6 then we need to have other options.

7 So let's look at this and say is it going to
8 do more harm, or do we lean that pendulum towards it?
9 It could be the next thing that saves your life or your
10 loved one's life. Thank you.

11 **DR. PRABHAKARA ATREYA:** Thank you for your
12 comments. Last but not least, Mr. Kermit Kubitz.

13 **MR. KERMIT KUBITZ:** Hello, can you hear me?

14 **DR. PRABHAKARA ATREYA:** Yes, we can. Go ahead
15 please.

16 **MR. KERMIT KUBITZ:** Okay. Thank you. I'm a
17 graduated of Caltech, Harvard Law School, and the
18 Harvard Business School. I have participated in VRBPAC
19 and ACIP meetings, including the October 22nd, 2020,
20 VRBPAC meeting on developing and licensing vaccines,
21 the December 20th Pfizer EUA meeting, and the September

1 17th, 2021, VRB meeting on boosters.

2 And I have no conflicts and no fiscal interest
3 in the company being considered. The question to the
4 ACIP is do the benefits outweigh the risk of a two-dose
5 series of vaccination for persons 18 years and older
6 for NVX-CoV2373. I look at this and the evidence in
7 the form of a structured benefit-risk table of the form
8 previously adopted by the FDA: one, the condition to be
9 treated, two, available alternative therapies, three,
10 the benefits of the proposed drug, including
11 uncertainties, four, the risks of the proposed drug,
12 including uncertainty, and five, the summary conclusion
13 in view of all available evidence, including
14 uncertainty, about the benefit-risk, and is it
15 positive?

16 Point five is similar to the question
17 presented to the ACIP meeting. In my analysis, the
18 condition to be treated is prevention of COVID-19 mild,
19 moderate, or severe, including hospitalization and
20 death. The alternatives are other vaccines, Moderna,
21 Pfizer, as well as Jansen and AstraZeneca, and

1 treatments such as Paxlovid. As one of the initial
2 questioners on this panel asked, why EUA if there are
3 other available vaccines?

4 As other speakers before me have discussed,
5 vaccine hesitancy is a serious problem. Some people
6 may not be able to take mRNA vaccines, and we need as
7 many tools as we can get to control and eliminate this
8 pandemic. The benefit of the Novavax vaccine is
9 elimination in the treatment arm of 17,000 patients of
10 moderate to severe COVID-19.

11 The risks of the Novavax vaccine are
12 significant adverse events of about one percent for
13 Novavax and one percent for placebo. The Novavax
14 vaccine versus the placebo showed about no moderate or
15 severe cases versus 11 percent moderate cases and 5
16 percent severe, or about 16 percent severe or moderate
17 COVID-19 cases which were not occurring with the
18 Novavax vaccine.

19 This demonstrates significant efficacy. In
20 addition, the Novavax vaccine has now been administered
21 to hundreds of thousands of patients outside the U.S.,

1 so there is available data on its effectiveness. See
2 the study published in *Cell* (phonetic) by the La Jolla
3 Institution of Immunology professor, Daniela Weiskopf
4 and Shane Crotty, who found antibodies after six months
5 were highest with the Moderna, Pfizer, and Novavax
6 vaccine.

7 All participants retained a similar percentage
8 of memory CD4+ helper T cells. It's important to have
9 multiple vaccines ready and approved to fight COVID-19
10 to provide initial protection, to provide protection
11 against variants, and to provide protection against
12 boosters. As the CDC has noted, heterologous booster
13 vaccinations may provide significant benefits even if
14 mixing and matching vaccines.

15 Finally, I'd like to thank the ACIP and the
16 FDA. You have saved a million lives by you providing
17 vaccinations through all the vaccines despite all the
18 time its cost you to attend these meetings. Thank you
19 very much.

20 **DR. PRABHAKARA ATREYA:** Thank you for your
21 comments and the presentations. This concludes the

1 open public hearing session. We're going to be moving
2 onto the next items of the agenda as we are finished
3 with the public comment speakers. Thank you, and I
4 hand over the meeting to Dr. Monto. Monto, take it
5 away please.

6 **DR. ARNOLD MONTO:** Thank you, Prabha.

7

8 **ADDITIONAL Q & A REGARDING SPONSOR AND FDA**

9 **PRESENTATIONS**

10

11 **DR. ARNOLD MONTO:** Thank you, Prabha.

12 Question is, do we -- we have a break scheduled and
13 reconvening at ten minutes past 2:00. Is it possible
14 to begin the meeting at 2:00 instead? Prabha? Dr.
15 Marks? Or should we go to 2:10 as we are scheduled?

16 **DR. PETER MARKS:** Let me just check with our
17 technical people. But as long as they say we can move
18 ahead; we will move ahead.

19 **MR. MICHAEL KAWCZYNSKI:** Yep, we're ready. We
20 can move ahead if you'd like to.

21 **DR. PETER MARKS:** I believe then that would be

1 wise to do. Thank you, Dr. Monto. Go ahead and
2 proceed.

3 **DR. ARNOLD MONTO:** Okay. Well, we're moving
4 ahead now to the additional question and answer
5 session, which is regards of both the presentations of
6 the sponsor and the FDA. And, Dr. Marks, would you
7 like to say a few comments before we go ahead with this
8 session?

9 **DR. PETER MARKS:** Yes, thank you. Thanks very
10 much. So, there have been some questions about how the
11 Novavax vaccine will fit into the other vaccines. And
12 I think what we need to say here is that we are here to
13 consider the authorization for the primary series right
14 now, and that means that this is the initial step.
15 There will be additional submissions, I am sure, and
16 additional consideration by FDA of both booster doses,
17 additional populations, as well as potentially the
18 activity of this vaccine or variant vaccines using this
19 technology that will be submitted or considered in the
20 coming weeks to months.

21 So I think we need to, just so the Advisory

1 Committee members think about this, there will
2 obviously be some evolution of this. I believe it's
3 fair to say that and you can certainly feel free to ask
4 the company that question as well over the coming weeks
5 to months to essentially make it consistent with the
6 vaccine paradigms that we are using now.

7 Dr. Monto, is that helpful to the Committee?

8 **DR. ARNOLD MONTO:** That's very helpful, and
9 perhaps I could start the discussion by asking the
10 sponsor if there is anything further that they would
11 like to tell us which might help in our deliberations
12 given the fact that all the testing was done in the era
13 of Alpha, and we're now preparing to launch a vaccine
14 in the era of various Omicrons. So, does the sponsor
15 want to give us any additional information that might
16 be valuable to us?

17 **DR. FILIP DUBOVSKY:** Sure. And, Dr. Monto,
18 should I start off with that topic, or do you want me
19 to cover some of the questions that we deferred from
20 previously today?

21 **DR. ARNOLD MONTO:** It's up to you. We have

1 more time than I anticipated, so we can an in-depth
2 discussion. This is very helpful.

3 **DR. PETER MARKS:** Can I make a suggestion?
4 Why don't we stick to that? Since I just mentioned
5 that, maybe it'd be good -- if you don't mind -- just
6 to address that question now so we take care of that
7 issue before moving on.

8 **DR. ARNOLD MONTA:** Okay.

9 **DR. FILIP DUBOVSKY:** Okay, sounds good. So,
10 let me parse it apart. So, a couple things we talked
11 about. One of them was expanding our indication beyond
12 adults greater than 18 years of age and as we've
13 already talked about, we've completed studies in
14 adolescents 12 to 17 years of age, and those studies
15 have been the basis of approvals in other territories.
16 And certainly, as soon as we reach the EUA in the U.S.,
17 our intent is to file that and to seek regulatory
18 approval to expand that indication.

19 We also have data on boosting, both homologous
20 and heterologous boosting, and once again that's the
21 sort of data which we are going to bring to the FDA to

1 seek approval for the booster indication as well.

2 So, it's true that the efficacy studies we
3 conducted were conducted in the era before Omicron
4 emerged. What we do know is the data that we've shown
5 you is the vaccine works well against the variants that
6 have circulated during the conduct of the study, and
7 there were a broad number of variants. And this is a
8 feature we think of our technology.

9 So, the recombinant proteins are made in six
10 cells, which give benefit to antigenic spread along
11 with the adjuvant system and this is proved to be true
12 in our influenza vaccine where which the immune
13 responses were shown to recognize a broad array of H3N2
14 drift as well as ancestral strains. And it's true in
15 efficacy data we showed you that showed that the
16 vaccine worked well against the variants that
17 circulated.

18 We additionally have data, immunologic data,
19 from our studies which look at how they respond to the
20 Omicron variant, and perhaps we can show some of that
21 now. This is data from the U.S. Adolescent Study, and

1 I bring this up because we don't have the comparable
2 data for the adult data. What you can see is the
3 immune response against the original prototype on the
4 left-hand side and the immune responses against the
5 various variants that circulated, including Omicron on
6 the far right-hand side, and this is the VA1 version.

7 Now, what we can also look at is data from our
8 previous study, our 101 Study. Once again, what this
9 is looking at is immune responses IgG after two doses
10 and after three doses: two doses in dark blue, three
11 doses is in light blue. And you can see we've got a
12 nice boost against all those variants with a third
13 dose.

14 Importantly, if you look at Omicron and look
15 at the values achieved after three doses, it's really
16 comparable to what we saw for two doses to the
17 original. And those were the kinds of immune responses
18 that were comparable with 90 percent protection in our
19 efficacy study. This is binding. We'll have our
20 neutralization responses.

21 Here what I'm showing is a comparable graph:

1 original on the left-hand side, Omicron on the right.
2 And you can see there's a good boost once again between
3 two doses and three doses. But importantly between
4 Omicron after two doses, there's only a 3.6-fold
5 difference than from the original. And this is data
6 generated by the Matt Frieman lab at the University of
7 Maryland, and so we have good confidence that not only
8 are we sharing binding antibody, but at least in this
9 assay, induction of neutralizing responses.

10 So, overall, it's factual that we don't have
11 efficacy data against Omicron, but what we do have is
12 the technology that we think generates a broad immune
13 response demonstrated against a broad array of
14 variants.

15 **DR. ARNOLD MONTTO:** Thank you. And now that
16 we've had that question answered, you had some other
17 information that you wanted to give us. So let's go
18 onto that, and then we've got hands raised. We've got
19 questions from the members.

20 **DR. FILIP DUBOVSKY:** Okay. So, there was a
21 question asked by Dr. Meissner about IgA responses.

1 And what I'm showing you here now is data from rhesus
2 macaques, and what we're looking at is IgA titers in
3 the vaccine group versus placebo group. And on the
4 left-hand side of the panel, we're looking at upper
5 airway, so these are nasal IgA. And on the right-hand
6 side, lower airway, so bronchial airway lavage. And
7 you can see that the vaccine does in fact induce IgA in
8 both the upper and lower airway, and this was
9 associated with sterilizing protection in this animal
10 model in both the upper and lower airway system.

11 Now, I mentioned some data earlier about the
12 ability that we have to stop infection, whether it be
13 symptomatic or asymptomatic infection, and I wanted to
14 bring complete a read of that. What I'm showing you
15 here is the 302 data from the U.K. on the left-hand
16 side, I mentioned, and comparable data in the U.S. on
17 the 301 study. So, this is the ability for the vaccine
18 to block all infection, whether it be symptomatic or
19 asymptomatic, and the only difference between the 302
20 and the 301 study is the time. The meeting time of
21 surveillance in the U.K. study was longer; it was a

1 hundred days versus 60 days in the U.S. study.

2 And the point, once again, being is the
3 sterilizing protection and the IgA that we saw in the
4 animal models may be a signal this is what we're seeing
5 as far as the ability for the vaccine to protect
6 against all infection. I'd like to mention that,
7 obviously, we stopped infection by the ability to
8 prevent long COVID and transmission.

9 There was a question asked by Dr. Pergam about
10 efficacy after Dose 1. And what I'm showing here is
11 data from the U.S. study -- the 301 study -- and you
12 can see that after Dose 1, the totality of 133 cases in
13 the vaccine group and 156 in the placebo group, two to
14 one amortization, and that gave an efficacy of almost
15 59 percent. And after Dose 2, it was 86 percent in
16 this analysis. And this is an FAS analysis, so it's
17 like an ITT analysis, so it doesn't take into account
18 the observation window which starts seven days after
19 post-Dose 2 in seronegative alone.

20 Now, the efficacy that you see at 58 percent,
21 that includes the timeframe after Dose 2, so a lot of

1 that efficacy is attributed to the time period after
2 the second dose is administered.

3 There was a third question asked about the
4 Latinos and the proportion that was in those greater
5 than 65 years of age. In fact, there were no cases in
6 the Latino group in those that were greater than 65
7 years of age.

8 And I think that's what -- I did think perhaps
9 you'd be interested in the immune responses we talked
10 about during the main presentation. On the left-hand
11 side, you see the Day 0 values; on the right-hand side,
12 you see the Day 35 values. In dark blue are the
13 Hispanic/Latino participants, and in light blue are the
14 non-Hispanics. And you can see the Hispanic
15 population, in fact, had a slightly higher IgG titer
16 than those in the non-Hispanics. And when we look at
17 neutralizing responses, we see a very similar pattern,
18 once again, a slight increase in the dark blue
19 representing the Hispanic population at the peak immune
20 response at Day 35.

21 So, I think those tidy up the questions that

1 were asked prior to the break.

2 **DR. ARNOLD MONTO:** All right, and now we're
3 going to be moving into the discussion, and I want to
4 remind the members that not only is the sponsor here to
5 answer questions but also the FDA representatives. So,
6 Dr. Offit, you're up next.

7 **DR. PAUL OFFIT:** Yeah, thank you, Arnold.
8 This is directed, I guess, to both the FDA and CDC
9 presenters. I agree with the FDA's assessment that
10 that handful of cases of myocarditis that occurred
11 within three or four days of receiving the second dose
12 of vaccine in young men is consistent with what was
13 seen with the mRNA-induced myocarditis. So, I think
14 that is likely a causal and not coincidental
15 association.

16 It's also interesting in the document that the
17 FDA handed us, or handed out to us, that they referred
18 to a 2020 paper where there was suspected molecular
19 mimicry between SARS-CoV-2 spike protein and the heavy
20 chain of (audio skip) on cardiac muscle cells.

21 If that's true, then you would argue that

1 really all COVID vaccines, as well as COVID itself
2 should cause myocarditis, but that may well not be
3 true. And this gets to Dr. Rubin's question, we really
4 need to know whether or not this is true for the
5 vectored virus vaccines like J&J or AstraZeneca. We
6 really may need to know whether this is true for a
7 whole and activated viral vaccine-like (inaudible)
8 vaccine which has now been administered to millions of
9 people, or whether it's true -- I think is most
10 interesting -- for the Covovax vaccine which is a
11 receptor-binding domain vaccine. In other words, a
12 truncated protein vaccine that's been given out to many
13 people in India.

14 I think it's incumbent upon us to know this,
15 to know whether it's about the protein itself or
16 whether it's about the way the protein is being
17 processed, so that we can use that knowledge to make
18 safer vaccines for a disease that is going to be with
19 us for decades, if not longer.

20 So, I think that this is a real opportunity to
21 learn something. I hope that it's not lost. We need

1 to get the data -- the kind of data that Dr. Rubin was
2 referring to earlier. Thank you.

3 **DR. ARNOLD MONTO:** Who's up to answer this
4 rather critical question? I think the FDA, I think in
5 the briefing document you raised the issue of mimicry,
6 though it's -- why don't you try to answer it first?

7 **MR. MICHAEL KAWCZYNSKI:** I'm sorry, who are
8 you calling upon, Andrew? I mean, Arnold?

9 **DR. ARNOLD MONTO:** I'm calling on FDA, since
10 it was in the briefing document, the reference to the
11 issue of mimicry.

12 **MR. MICHAEL KAWCZYNSKI:** There's Doran.
13 Doran, I'll unmute you. There you go.

14 **DR. DORAN FINK:** Okay, thank you. Yeah. So,
15 Dr. Offit, I couldn't agree with you more that this is
16 a critical question to understand whether vaccine-
17 associated myocarditis is a class effect related to S-
18 protein antigen and if so whether there are other
19 features of specific vaccine platforms that mitigate
20 either positively or negatively toward a risk of
21 vaccine-associated myocarditis.

1 I think the situation is clear for mRNA
2 vaccines. We have some preliminary evidence from the
3 clinical trials of this vaccine from Novavax that
4 raises this concern. Although I think we need more
5 data from post-authorization use in larger numbers of
6 individuals to really get at what the rate of
7 myocarditis associated with this vaccine is and what
8 exactly the risk is.

9 As you heard earlier from Tom Shimabukuro from
10 CDC, as we accumulate more experience with the Janssen
11 vaccine which has been used to a much lesser extent
12 than the mRNA vaccines here, as well as outside the
13 U.S., we are continuing to evaluate the occurrence of
14 myocarditis after that vaccine, and, of course, there's
15 the AstraZeneca vaccine and other platforms that you
16 mentioned as well. I couldn't agree with you more that
17 we really need to look closely at these events and also
18 to do the work necessary to understand what the
19 mechanism might be.

20 And so, I guess here from an FDA perspective,
21 we would endorse that viewpoint strongly and, of

1 course, are here to assist vaccine manufacturers in the
2 research community in addressing this very important
3 issue.

4 **DR. ARNOLD MONTO:** Any further comments from
5 CDC on this or from the sponsor? Dr. Filip Dubovsky.

6 **DR. FILIP DUBOVSKY:** Yeah. A couple points to
7 what Dr. Offit said. I mean, it's curious in the data
8 we saw. There's the third boosting dose. There wasn't
9 as big an increased risk after Dose 2, and that makes
10 me wonder if there are other mechanisms at play that
11 wasn't proposed. And we also know about other vaccine-
12 associated myocarditis from the smallpox/monkeypox, and
13 they don't even have the spiked antigen.

14 So, I think the story's incompletely written
15 here, and we do need to more fully understand what's
16 going on before we can think about a class.

17 **DR. ARNOLD MONTO:** Thank you.

18 **DR. TOM SHIMABUKURO:** Hi, this is Dr.
19 Shimabukuro from CDC. Can you hear me?

20 **DR. ARNOLD MONTO:** We can.

21 **DR. TOM SHIMABUKURO:** Dr. Offit, I would just

1 reinforce what Dr. Fink said about the importance of
2 getting the data that you mentioned, and I'm not so
3 familiar with some of the other vaccines that are used
4 outside of the United States. But I'm not aware of a
5 similar association observed with the AstraZeneca
6 vaccine which was widely used in Europe similar
7 association as seen with the mRNA vaccines.

8 And with respect to disease, my understanding
9 is that isolated myocarditis following COVID disease is
10 pretty rare and the adverse cardiac outcomes that you
11 see after disease are often in association with MIS
12 which may be a different mechanism altogether.

13 But with respect to disease and just pure
14 myocarditis or isolated myocarditis, it's a fairly rare
15 occurrence after COVID.

16 **DR. ARNOLD MONTO:** Thank you. And thank you
17 all for a discussion of an important topic that we need
18 more information about. Dr. Levy.

19 **DR. OFER LEVY:** Yes, I wanted to thank the
20 sponsor for showing the additional data a few moments
21 ago with some slides about antibody responses. And I

1 wanted to note, those data were elegant, they were
2 helpful, and yet, without knowing what level or
3 concentration of antibody correlates with protection,
4 it's a little hard to draw any conclusions as to
5 whether this vaccine -- how it would perform against
6 Omicron.

7 I mean, it seems like there were lower
8 responses -- lower binding and neutralization of
9 Omicron than the other variants, yet there were some.
10 But without -- maybe I'm stating the obvious -- without
11 a correlate of protection, it's hard to draw a
12 conclusion one way or another.

13 The sponsor made some comments about their
14 impression of the correlate of protection earlier in
15 the day, and I'm wondering if they can make some
16 further comments in terms of where they would see the
17 correlate of protection to be on those graphs and does
18 Omicron reach up. I realize there's an element of
19 speculation here, but it is the elephant in the room, I
20 think.

21 **DR. FILIP DUBOVSKY:** Yeah.

1 **DR. ARNOLD MONTO:** Dr. Dubovsky, do you care
2 to speculate?

3 **DR. FILIP DUBOVSKY:** I will always speculate,
4 but I agree that, without definitive data, we won't
5 know. Listen, we think that -- we simply don't know if
6 an Omicron-based vaccine is required, right. Those
7 studies are ongoing. They're ongoing, and we sponsored
8 a study in Australia, but we're looking both at an
9 Omicron vaccine as well as the bivalent form. I have
10 to see if that offers any advantage.

11 What we do know is what we've showed you as
12 this technology, in general, does a good job with
13 antigenic spread and having a broad response, and we do
14 know that the binding and immune responses we see are
15 relatively favorable. The best I can do to compare --
16 and I understand this is very, very fraught with
17 potential error -- is to try to compare back to the
18 levels we saw after Dose 2 to prototype, and as you saw
19 for prototype in U.S. study, we had 97 percent
20 protection.

21 So where is the cutoff isn't clear. The

1 signals we're getting right now is, in our view,
2 favorable, but we'll know for sure when the study reads
3 out in Australia.

4 **DR. ARNOLD MONTA:** Thank you. Dr. Pergam.

5 **DR. STEVEN PERGAM:** Thanks, Arnold. I had a
6 question about the adjuvant in particular. I know that
7 the adjuvant comes from a particular tree; I believe
8 it's in South America. My understanding is that's a
9 highly regulated supply chain. Do you guys have any
10 comments about the ability to get this on a regular
11 basis to make the vaccine available because I know that
12 is an issue?

13 **DR. FILIP DUBOVSKY:** So, we took steps early
14 on to secure the supply chain. There is zero supply
15 problem with the adjuvant.

16 **DR. STEVEN PERGAM:** Okay, thanks.

17 **DR. ARNOLD MONTA:** Thank you. Dr. Lee.

18 **DR. JEANNETTE LEE:** So, thank you for that
19 presentation. I think one of the questions I had
20 earlier -- and I think this is really for the sponsor --
21 -- had to do with the current design is that protocol

1 which was actually a crossover. Most of the data we're
2 seeing for efficacy is obviously related to the first
3 random -- the first part with the randomized obviously
4 with the vaccine and placebo. And I do understand the
5 study is ongoing so the crossover part from vaccine to
6 placebo and placebo to vaccine.

7 And I think the comparison of the second part
8 after the crossover would be very illustrative in terms
9 of what kind of carry-over effect it might have from
10 those that started with a vaccine and then were getting
11 placebo. Do you have that data, or when do you
12 anticipate we would be able to see that?

13 **DR. FILIP DUBOVSKY:** Yeah, so you're right;
14 the crossover complicated, or eliminated, our ability
15 to look at placebo control data at this crossover time.
16 Furthermore, we've taken the opportunity to boost those
17 participants with both Dose 3, and some with Dose 4,
18 which complicates the story even more.

19 **DR. JEANNETTE LEE:** Yeah.

20 **DR. FILIP DUBOVSKY:** Now without a good
21 comparator and with new variants emerging and the

1 different course of infections across time, it becomes
2 extremely difficult to do anything but make model-based
3 assumptions.

4 Now that work is ongoing, and we'll have that
5 available in due course. I'm not sure how trustworthy
6 it is because I'm convinced we know how to guess the
7 efficacy against the variants until we get real data on
8 that.

9 **DR. JEANNETTE LEE:** Okay, thank you.

10 **DR. ARNOLD MONTO:** Thank you. Dr. Gellin.

11 **DR. BRUCE GELLIN:** Thanks. So, thanks for all
12 this. I want to start by thanking the public who
13 commented, and then the many, many more of the public
14 who commented in writing that didn't get a chance to
15 speak. This is an important part of these
16 conversations.

17 Filip mentioned a couple times something that
18 doesn't always get mentioned about sterilizing
19 immunity, so I'd like to hear some more about that. He
20 showed us a little bit of data about it but the grade
21 of which you believe this vaccine can lead to

1 sterilizing immunity and any data that you have from
2 anywhere that might have insights about its limited or
3 its ability to dampen transmission.

4 And then finally, we hear a lot about its
5 authorization in other countries. It'd be interesting
6 to know, A, to know about how much it's being used in
7 other countries and what other data you might have
8 that's relevant to these discussions today from other
9 country experiences.

10 **DR. ARNOLD MONTO:** A very broad question.

11 **DR. FILIP DUBOVSKY:** I think I got these, so
12 we'll see. So, as far as the sterilizing protection
13 data, it's a broad leaf feature we've seen in animal
14 models we've tested, and our best data for what we saw
15 in humans is the data I showed you. So, there's no
16 direct measurement that we have in hand of a
17 transmission. You need to make that leap of faith of
18 logic that, if you don't get infected, you can
19 transmit.

20 The durability of that period where you're
21 protected from infection is also variable. In any case

1 study, like I mentioned, that was measured across --
2 those cases were accrued over six months with a median
3 of about 101 days observation in those groups. So, I
4 think it's speculative, frankly, but we're hopeful.

5 As far as real-world evidence from the doses
6 that are administered, it's still early days for us.
7 We're shipping doses; they're being used. Right now,
8 you heard from Dr. Kim from the pharmacovigilant side,
9 we have good line of sight to about 770,000 doses
10 having been administered. We have imperfect visibility
11 into this. Our customer is the governments; the
12 governments deploy those. So we to a certain degree
13 rely on the governments to feed that data back to us,
14 so we understand how many are used.

15 For us to get into real-world effectiveness,
16 which we want to do, and we will do -- we're committed
17 to doing it -- we need to get the vaccine usage up
18 enough in certain areas where we can do a test study or
19 a controlled design. Without adequate doses being
20 deployed, we can't do those studies.

21 **DR. ARNOLD MONTO:** Does that answer all your

1 questions, Bruce?

2 **DR. BRUCE GELLIN:** It did. Thank you.

3 **DR. ARNOLD MONTO:** Okay, I just wanted to
4 interject a question of my own for Dr. Dubovsky, and
5 that is we've heard that there are differences in the
6 vaccines that are being authorized for use in other
7 countries versus the vaccine that we're now considering
8 for the United States. Would you speak about that and
9 how different are they would suggest the question of
10 where they were manufactured? What's the story there?

11 **DR. FILIP DUBOVSKY:** Right. So, all vaccines
12 are being distributed globally/commercially, are being
13 made in a single facility in bio partners in
14 (inaudible). That includes the vaccines which are
15 being deployed around the world as well as the ones
16 that'll be initially deployed in the U.S.

17 As far as the previous studies that were done,
18 all the clinical and commercial lots were released
19 after being tested to assure they met a set of critical
20 quality attributes. This includes the lots that were
21 used in the early studies in Australia, U.S., U.K.,

1 South Africa, as well as in the U.S./Mexico study.

2 And it's normal for these specifications to
3 tighten as experience is gained with the manufacturing
4 process. Now we've completed a comparability program
5 that we believe demonstrates the comparability between
6 the early lots and the lots used in Study 301 and the
7 commercial lots. And we acknowledge the FDA has a
8 perspective on this that's different from ours, but the
9 quality of that material and the results of all those
10 studies are really the basis of our global licensure.
11 So, I think that's where we stand.

12 But importantly, all the vaccine which is
13 being deployed commercially comes from a single
14 facility.

15 **DR. ARNOLD MONTTO:** Thank you. Dr. Meissner.

16 **DR. CODY MEISSNER:** Thank you, Dr. Monto, and
17 thank you, Dr. Dubovsky. I feel like you're carrying a
18 heavy load here. You're facing all of these questions.
19 But let me -- I have a question about the adjuvant --
20 two questions about the adjuvant. The first one, and
21 it may be you simply don't know, but what happens if a

1 person gets at the same visit or the same day two
2 saponin-containing adjuvants? For example, if someone
3 were to get the shingles vaccine that contains AS01 on
4 the same day that your vaccine is administered, are you
5 worried about an increased risk of adverse events that
6 might occur?

7 And then secondly, a little bit -- one of your
8 earlier studies with respiratory syncytial virus that I
9 thought was very interesting because you really broke
10 new ground with that publication and -- but during the
11 study with the same platform I think using RSV fusion
12 glycoprotein, used a different adjuvant. You used an
13 absorbed aluminum adjuvant, and I think that was
14 because there was some concern about using the saponin-
15 based adjuvant during pregnancy -- in a person who
16 might be pregnant -- and so I'm assuming you no longer
17 feel that's a concern and that's why you haven't
18 expressed any reservation in that setting. Over.

19 **DR. FILIP DUBOVSKY:** Yeah, so the RSV maternal
20 program, which was a study done before my time, was
21 also a study done before the company had the Matrix-M

1 adjuvant in its portfolio. The immune responses
2 induced by alum were probably quite good at that time.
3 We don't have any specific concern with saponin; the
4 reproductive tox studies have been clean, and certainly
5 in the data that Dr. Kim presented, we didn't see
6 anything that looked concerning to us. I'll remind you
7 that the amounts of -- just back to your previous
8 question -- the amounts of adjuvant we were deploying
9 were very low, at 50 micrograms.

10 We've previously tested doses that are higher,
11 up to 75 micrograms for a quadrivalent influenza
12 vaccine program. We know that there are a small number
13 of people who received Shingrix in our study -- less
14 than ten -- those probably weren't co-administered,
15 those were just given close by, but certainly we didn't
16 see any concerns with that.

17 **DR. CODY MEISSNER:** Thank you.

18 **DR. ARNOLD MONTO:** Thank you. Dr. Perlman.

19 **DR. STANLEY PERLMAN:** Yes, so I just have two
20 questions. One, what will it take for this to obtain a
21 full licensure as opposed to an EUA because we keep

1 hearing about why it should be an EUA instead of a full
2 licensure? But what more would be needed to obtain
3 full licensure? The other thing is what's the
4 adjuvant? I know you looked for things related to
5 autoimmune disease, but was there any hints of
6 exacerbation of preexisting autoimmune disease with
7 this adjuvant?

8 **DR. FILIP DUBOVSKY:** Okay, I'll handle the
9 first question, and perhaps I'll turn it to Dr. Kim to
10 talk about the second question. The long pull in the
11 tent, the thing that takes the longest to get a BLA is
12 through a lot-to-lot consistency study, and this is a
13 requirement that's unique in the U.S. And to do that
14 study, we need to generate lots which are deemed to be
15 comparable and appropriate for such a study by the FDA
16 before we do the study.

17 So that's really the thing which is going to
18 take the longest. We have some additional data
19 requirements for length of follow-up, and those we'll
20 come to terms with, in discussions with the FDA before
21 we bring it to them for the full BLA. Dr. Kim, do you

1 have a perspective on enhancement of autoimmune
2 disease?

3 **DR. DENNY KIM:** Yes, can you hear me?

4 **MR. MICHAEL KAWCZYNSKI:** Yes, we can.

5 **DR. ARNOLD MONTA:** Yes.

6 **DR. DENNY KIM:** It seems like my camera's not
7 on.

8 **MR. MICHAEL KAWCZYNSKI:** There you go. I'll
9 turn it on for you sir. I'll turn it on for you sir.
10 There you go.

11 **DR. DENNY KIM:** All right. Thank you. Yeah,
12 so we've seen very low frequencies of potential immune-
13 mediated conditions, and so whether it's new onset or
14 potentiation of existing comorbidities that some
15 participants had in our study population, we didn't
16 really see any patterns that suggested a worsening of
17 conditions.

18 **DR. STANLEY PERLMAN:** Thank you.

19 **DR. ARNOLD MONTA:** Dr. Sawyer?

20 **DR. MARK SAWYER:** The point has been made that
21 one of the main audiences for this being are vaccine-

1 hesitant people who, by now, many of whom have been
2 infected with natural disease because of their
3 reluctance to get vaccinated. And we've also discussed
4 the fact that this vaccine has been used in other
5 countries for quite some time.

6 Perhaps I missed it in the presentation, but I
7 don't think we heard much data about vaccine reaction
8 in people who had prior exposure to the natural virus.
9 I think the 301 study specifically was in seronegative
10 individuals. So, I'm wondering if you could either
11 remind me, or share, any information that we have about
12 the experience with the vaccine in people who've
13 already had infection.

14 **DR. ARNOLD MONTO:** You might as well stay on,
15 Dr. Dubovsky. I think that you're in the hot seat.
16 Please, go ahead.

17 **DR. FILIP DUBOVSKY:** I mean, you remember
18 correctly that seven percent of the people in Study 301
19 were positive in baseline. And while they were
20 excluded from the efficacy analysis, we do have data
21 both immunologic as well as safety data on what the

1 vaccine does. Let me see if I can get that data pulled
2 up. But in general, if I were to summarize, what we
3 see is we see really quite a nice boost of the immune
4 response in people who are previously vaccinated.

5 Let me start with a slide that shows you what
6 the neutralizing responses were by age group in those
7 that were seronegative. And you can see overall in
8 those that were greater than 18 is the value of about a
9 thousand, and those greater than -- the younger group,
10 18 to 64, it was 1,200. When you compare it to the
11 values that we see in those that were seropositive,
12 what you see is an increase of roughly three to four-
13 fold. So, they're getting a nice priming response from
14 a natural infection, those vaccines boost through it
15 quite well.

16 From a safety perspective, we didn't really
17 see any difference in the reactogenicity of the vaccine
18 when it was delivered in the seropositives versus the
19 seronegatives.

20 **DR. ARNOLD MONTA:** Thank you. Doctor --

21 **DR. MARK SAWYER:** Sorry. Could you quickly

1 tell us how many people -- I know it was seven percent,
2 but what was that total that you had experience with?

3 **DR. FILIP DUBOVSKY:** So, in this particular
4 study, it was 7 percent in both groups so 7 percent of
5 30,000. So, I've got to do that math.

6 **DR. MARK SAWYER:** Thank you.

7 **DR. ARNOLD MONTA:** Dr. Fuller, did you have
8 your hand raised?

9 **DR. FILIP DUBOVSKY:** We have additional
10 exposure data in people who were seropositive in our
11 other studies. That attack rate was very, very high in
12 South Africa, for instance, where a much larger portion
13 were seropositive, and we see the same pattern. We
14 don't see increased safety signals, but we do see an
15 increased immune response.

16 **DR. ARNOLD MONTA:** Thank you. Dr. Fuller, did
17 you have your hand raised? I thought you did.

18 **DR. JAY PORTNOY:** Hi there. So, I have two
19 questions. Can you hear me? Okay.

20 **DR. ARNOLD MONTA:** Yep.

21 **DR. JAY PORTNOY:** I have two questions. As an

1 allergist, I would be remiss if I didn't ask whether
2 you observed any allergic reactions to the vaccine?
3 After all, it was a protein-based vaccine rather than
4 mRNA, so the risk of having an allergic reaction might
5 be higher. I guess you can answer that one first, and
6 then I have one more question.

7 **DR. FILIP DUBOVSKY:** Yeah, I'll give a
8 scientific spin to it, and then I'll pass it off to Dr.
9 Kim, actually. So, our adjuvant is the Th1-biased, so
10 in a sense, it's tightly antiallergic as far as that
11 goes, so I think that plays in our favor. Dr. Kim, do
12 you want to review the hypersensitivity? And there's
13 no anaphylaxis as has been mentioned in the pre-
14 licensure database. Dr. Kim?

15 **DR. DENNY KIM:** Yes. So, as to confirmed
16 anaphylaxis, we had no cases of anaphylaxis in our
17 clinical development program pre-crossover or post-
18 crossover. Certainly, we do a broad search to look for
19 any type of allergic-type reactions or
20 hypersensitivity-type reactions, and I can show you
21 some of that data here.

1 And so, as you can see, the pre-crossover --
2 and we use a standard metric query, and that's a very
3 broad search and so, any sort of events that could
4 possibly be related to allergic-type reactions. And we
5 saw a minor imbalance and numerical imbalance. And so,
6 you can see a 0.77 percent in the active arm compared
7 to 0.57 percent in the placebo arm.

8 And the most frequent preferred terms or
9 events were rash, as you can see there, and we had that
10 in exposure-adjusted incidents. So, 0.93 events per
11 hundred person-years versus 0.90 events per hundred
12 person-years. That's fairly balanced, and the reason
13 we did that is because there's differential follow-up
14 oftentimes, especially when you consider post-crossover
15 between placebo and active arms or those who'd receive
16 vaccines because everyone will eventually receive --
17 will have received vaccine.

18 That small numerical difference is mostly
19 driven by urticaria and dermatitis. And so, we didn't
20 see clinically significant sort of patterns and
21 associations here.

1 **DR. JAY PORTNOY:** So presumably all the
2 patients would be advised to do the standard 15-minute
3 wait after the vaccine and not a prolonged wait or
4 anything like that. My other question is you're
5 playing for emergency use authorization -- this is kind
6 of a continuation of Dr. Perlman's question -- and yet
7 we already have two vaccines available that are highly
8 effective and relatively safe.

9 I haven't seen -- your vaccine seems to be
10 comparably effective and comparably safe to the other
11 ones, but you didn't show that it was superior in any
12 particular way. And, since so many people in the
13 United States have already been vaccinated, I assume
14 that the large -- it's going to be promoted largely to
15 the vaccine-hesitant individuals who might adopt a more
16 conventional vaccine that's protein-based rather than
17 these other technologies.

18 Do you have any information from vaccine-
19 hesitant individuals suggesting that they might be more
20 willing to consider getting this vaccine as opposed to
21 one of the other vaccines? Have you talked to vaccine-

1 hesitant people or have any sense of whether they would
2 be willing or more interested in using this vaccine
3 than one of the others?

4 **DR. FILIP DUBOVSKY:** Yeah, so I'm going to ask
5 Dr. Poland to step in and give his perspective. But I
6 have to say one in ten Americans has yet to be
7 vaccinated, and we haven't given up on them. We heard
8 in the open public comment period that there seems to
9 be a desire to use this product, and that's why --
10 that's what we want to bring to the U.S. population is
11 another option, a choice.

12 Now whether the proportion that choose to be
13 vaccinated from a primary series? That isn't clear;
14 we'll find out. We do know that, in countries where
15 the vaccine is being deployed, it is being used both as
16 a primary series as well as a booster and are the
17 choices that people are making in those countries -- to
18 choose our vaccine.

19 Dr. Poland, do you have any other perspective?

20 **MR. MICHAEL KAWCZYNSKI:** Arnold?

21 **DR. ARNOLD MONTTO:** Hello.

1 **MR. MICHAEL KAWCZYNSKI:** Yeah. Are we waiting
2 on somebody?

3 **DR. ARNOLD MONTA:** We're waiting on Dr. Poland
4 who was called on.

5 **MR. MICHAEL KAWCZYNSKI:** Oh, there we go.

6 **DR. FILIP DUBOVSKY:** No, I don't know that if
7 he's even coming on, so maybe we'll take that as the
8 sponsor's answer for the time being.

9 **DR. ARNOLD MONTA:** Okay, I see Dr. Reingold.
10 He's not on my regular list. He's up among the
11 presenters, so I don't know how long he's been waiting.

12 **DR. ARTHUR REINGOLD:** Hi, can you hear me?

13 **DR. ARNOLD MONTA:** We can.

14 **DR. ARTHUR REINGOLD:** Good. So, that's one of
15 the problems with coming late is lots of questions that
16 have been answered; particularly, the ones Dr. Sawyer
17 asked. But I do have one other question building on
18 what Dr. Meissner mentioned. It will be fall soon;
19 we'll be giving a lot of flu vaccine to people. And I
20 don't know about other people, but I got my flu shot
21 and my booster dose of COVID in different arms on the

1 same day. I'm just curious what you know about the
2 administration of this vaccine at the same time people
3 get a flu shot.

4 **DR. FILIP DUBOVSKY:** Yep, I'd say a question
5 that we have also been very curious about. In the U.K.
6 study, we actually included a cohort of participants
7 who received the first dose -- a dose of licensed
8 influenza vaccine -- and what we saw there is that it
9 didn't negatively impact the hemagglutinin responses.
10 However, what we did see is a decrease in the anti-
11 spike responses in that cohort. We still maintain
12 efficacy. Efficacy was maintained at pretty much
13 exactly the same rate as the overall population, but it
14 did drive the anti-spike response.

15 This isn't unique to our platform. There are
16 publications that show that, with other platforms when
17 you give flu vaccine, it tends to drop those responses,
18 including against mRNA vaccines. We've furthermore
19 conducted a combination study with our flu vaccine and
20 our COVID vaccine, and this was made public a few
21 months ago. We capitulated the same finding. We do,

1 in fact, impact the anti-spike response, but we can
2 overcome this response by minimally decreasing the
3 hemagglutinin while increasing the spike antigen. And
4 that's a combination product that we're taking forward
5 as well.

6 **DR. ARNOLD MONTA:** Thank you. Dr. Marasco.

7 **DR. WAYNE MARASCO:** This is a question for Dr.
8 Dubovsky. So, I wanted to follow up on a question I've
9 asked before in a different way, and it has to do with
10 your comments about antigenic spread.

11 So, your titers look pretty reasonable going
12 across the lineages, but there is some drop-off. So,
13 my question -- it's really two questions. One, do you
14 know that the vaccine is not -- just because you're
15 adjuvanted, and that's going to have some impact on
16 this. Do you know that you're not getting epitope
17 shift? I mean some of the more conserved regions of
18 the spike are in the S2 domain, for example. So do you
19 know that the reason you're getting less of a
20 particular drop-off is because there's a difference in
21 the antibody response that you're eliciting?

1 And relating to that, the other -- when you
2 look at the studies that have been published on immune
3 serum from people that have been vaccinated with the
4 Wuhan strain versus hybrid immunity, it's pretty clear
5 that it's both your -- and Dr. Marks comment on this --
6 it's both your peak response, your breadth of response,
7 and the sort of rate of decay. So, do you know, for
8 example, that the rate of decay is not lower because
9 you're adjuvanting?

10 I mean, this would be a very important point
11 for the public who recognizes now that the vaccine
12 responses wane, and my real question is, because this
13 is adjuvanted, do you know anything more about your
14 rate of decay? I mean, it would really take you three
15 time points to know that, or antigenic shifts in terms
16 of subdomains of the spike that you may be eliciting
17 the antibodies to.

18 **DR. FILIP DUBOVSKY:** Yep, so, let me show you
19 the data we have on decay, and, since it takes time to
20 develop those studies, they are from our earlier
21 studies, although this is data that we're developing in

1 the 301 study as well. What I'm showing here is IgG
2 responses in the first instance. We see that they peak
3 at Day 35, they decay in the subsequent six months, and
4 then they take a nice boost up to four or five-fold
5 higher with the boost.

6 So, when I look at the comparable data, I'm
7 not seeing there's any specific advantage in the length
8 of decay. The IgG seems to be dropping at about the
9 same rate. Just as far as the boosting, what we do
10 know is that those titers that were achieved are quite
11 high.

12 So what I'm showing you here is that same IgG
13 with the third dose and showing you that the levels we
14 achieve are much higher that's achieved in the two
15 Phase 3 studies, and that gives us some assurance that
16 a third dose boost is going to be quite efficacious.
17 And, if you prefer neuts, although our neuts in IgG
18 correlate extremely well, once again you can see a 5.5-
19 to-5.6-fold increase in neuts with a third dose
20 compared to the levels achieved in the two Phase 3
21 studies. So that's as far as decay and boosting.

1 I, as far as your question about what parts of
2 the antigen we see or don't see. So, we know we
3 recognize parts of this by domain that are distant from
4 the RVD, right. We've mapped that out, and some of the
5 common epitopes, including the original SARS epitope,
6 are found by this vaccine and are utilized. The extent
7 of that and how they've matured is something we're
8 working on right now.

9 And maybe I'll stop there, and, if there are
10 further questions, I'll need to call into my bench and
11 perhaps I'll call on my colleagues if you have further
12 questions.

13 **DR. WAYNE MARASCO:** No, that's good. Thank
14 you.

15 **MR. MICHAEL KAWCZYNSKI:** Who would you like to
16 call on?

17 **DR. ARNOLD MONTA:** Dr. Bernstein.

18 **MR. MICHAEL KAWCZYNSKI:** There we go.

19 **DR. HENRY BERNSTEIN:** Thank you, Arnold. So,
20 I just had two questions. One is, can you remind me of
21 Novavax study plans in the pediatric population and

1 specifically what experience do you have with the use
2 of the adjuvant in the pediatric population in younger
3 age groups? That's that the first question.

4 **DR. FILIP DUBOVSKY:** So, we've concluded the
5 study in adolescents 12 to 17 years of age and that was
6 in 3,000 adolescents in the U.S., and that's the basis
7 of the licensure we're going to be requesting from the
8 FDA subsequent to our EUA. Our further plans -- we
9 have further plans to study this vaccine in first
10 school-age children and then age deescalating down to
11 children as young as six months of age in the first
12 study.

13 Our colleagues in serum have done this study
14 down to two years of age, taking the same adult vaccine
15 dose, and what they've found in that study is that the
16 reactogenicity profiles stayed very solid. The only
17 small uptick they saw was in fevers, but less than one
18 percent were a Grade 3 fever, and the immune responses
19 were favorable. They were much higher than was seen in
20 adults.

21 This adjuvant is in a Phase 3 study being

1 studied in West Africa for Malaria. And, in that
2 study, the doses have been taken down to children as
3 young as five months of age and, once again, they're
4 not seeing a safety problem, although it is a different
5 antigen, obviously, since it's against malaria. But
6 overall, this appears to be quite favorable, and we'll
7 know more as we develop more data.

8 **DR. HENRY BERNSTEIN:** Thank you and my second
9 --

10 **DR. FILIP DUBOVSKY:** And I should say we have
11 agreed upon a pediatric investigational plan and a
12 specific study planned with the FDA, as well as the
13 E.U.

14 **DR. HENRY BERNSTEIN:** Thank you. My second
15 question is --

16 **DR. ARNOLD MONTO:** Thank you.

17 **DR. HENRY BERNSTEIN:** -- and I may have missed
18 this, but can you explain -- you published the U.K.
19 data in September of 2021 and the U.S./Mexico data in
20 February of 2022. Is there a reason that we're talking
21 about this in June of 2022 as opposed to earlier

1 request for EUA?

2 **DR. FILIP DUBOVSKY:** Yeah, so our first
3 approval was in December of last year, but, when the
4 pandemic started, this company didn't have a
5 manufacturing base, so we had to build it from scratch
6 and build a manufacturing network from ground up. What
7 really took the longest time, however, wasn't the
8 manufacturing of the product; it was the generation of
9 the assays to demonstrate that we could make the
10 product over and over again the same way and to deploy
11 those assays against the multiple lots. All of them
12 need to achieve those critical quality attributes.

13 So, our approach then was to settle on a
14 single facility in India because they're the world's
15 largest vaccine manufacturer by dose and that's the
16 single process we've taken forward and that's the one
17 that's the basis of licensure globally as well as a EUA
18 request here in the U.S.

19 **DR. HENRY BERNSTEIN:** And do you have a
20 concern about having a single manufacturing plant?

21 **DR. FILIP DUBOVSKY:** There's always a risk

1 there and we have a network and the subsequent sites
2 are being brought on now. They're going to be
3 variations, so first, you need to be approved with one
4 -- in the instance, with serum -- and we're bringing on
5 our sites one that we own in Europe and then one of our
6 partners in South Korea. Those are being now applied
7 for in various locations globally.

8 **DR. HENRY BERNSTEIN:** Thank you.

9 **DR. FILIP DUBOVSKY:** I would say that also
10 Takeda and SK are licenses of ours, and they have a
11 different relationship. They're not manufacturing for
12 us; they're manufacturing for themselves, and they're
13 licensed in Korea and Japan, respectively.

14 **DR. HENRY BERNSTEIN:** Thank you.

15 **DR. ARNOLD MONTO:** Thank you. That helps in
16 some of our considerations. Dr. Fuller.

17 **DR. OVETA FULLER:** Yes. Thank you. Yes, so a
18 question that I think the public will ask and trying to
19 ask it in a way that the public will understand. For
20 those who have not been vaccinated, as well as those
21 who may want to use this in some other way, this

1 baculovirus-expressed protein in an adjuvant, we get
2 asked all the time with other vaccines. Well, how long
3 does it stay in my system? Could you just share in
4 sort of general language for people who may be
5 listening, how long this -- they can expect this
6 particular baculovirus with adjuvant of the S protein
7 to be in the system to get the response that we want
8 from the immune system?

9 And secondly, if they get this, how long will
10 it take you to make something else, if indeed something
11 else is going to be needed later as far as a strain of
12 SARS virus. Just some practical questions in a way
13 people can understand.

14 **DR. FILIP DUBOVSKY:** Right. And just to be
15 clear, even though we use baculovirus virus in the
16 manufacturing process, the vaccine contains no virus
17 whatsoever. In fact, the process has been specifically
18 designed to eliminate all virus from a final product we
19 generate. All that it's in there is the viral spike
20 protein. Now, what we've talked about is that the
21 adjuvant effect seems to peak right about 72 hours

1 locally with a longer protracted effect in the lymph
2 nodes later on. What we saw from our immunogenicity
3 data is it generally kind of peaks at two weeks and
4 then goes lower after that.

5 I guess as far as the variants question, we're
6 manufacturing Omicron right now. It isn't clear to us
7 it'll be needed. It isn't clear to us what the public
8 health agencies and the customers and the people will
9 want; we just want to be ready to have that vaccine in
10 hand should it be needed. I know there's a VRBPAC
11 coming up later this month to decide or help decide on
12 what kinds of vaccines we should be asking for in the
13 fall.

14 **DR. OVETA FULLER:** So, in general with the
15 side effects, the 72 hours expression -- or not
16 expression, but presence of the vaccine -- does that
17 prolong the time of side effects that people see or the
18 appearance of the time of those side effects? You had
19 data on that, but could you just restate that, please?

20 **DR. FILIP DUBOVSKY:** Yeah. No, it's an
21 excellent question. So, the major side effects, you

1 know we follow very, very closely for the first seven
2 days, and the vast majority were either mild or
3 moderate. Actually, many people had no side effects
4 whatsoever, and the side effects that did occur will
5 resolve after one or two days. Those are both the
6 local ones, things like pain and tenderness, as well as
7 the broader ones like fatigue.

8 **DR. OVETA FULLER:** Okay, so those side effects
9 that can be seen in many vaccines --

10 **DR. FILIP DUBOVSKY:** Two days.

11 **DR. OVETA FULLER:** -- yeah. They're from the
12 actual injection versus from the 72 long-term hours of
13 antigen being present?

14 **DR. FILIP DUBOVSKY:** What it is, it's they're
15 likely to be caused by the immune response against the
16 vaccine. Right, so now the act of the vaccine being
17 delivered into your arm versus the immune response of
18 inflammation which comes along with the body reacting
19 to the vaccine and generating the protective immune
20 response.

21 **DR. OVETA FULLER:** All right. Thank you.

1 **DR. ARNOLD MONTO:** Thank you. Dr. Nelson.

2 **DR. MICHAEL NELSON:** Thank you very much for a
3 very thorough presentation and lineup this morning. I
4 wanted to follow up a little bit on the durability
5 question. I'm intrigued by the possibility that it may
6 last longer.

7 To date, the data that has been shown has been
8 with respect to clinical efficacy, as well as the
9 humoral immune response. So, what I haven't seen is
10 whether you're generating any cellular immune response
11 data with respect to generation of memory B-cells and
12 others; it might also provide an explanation. And is
13 there anything unique about your vaccine that is
14 inducing a different cellular response that may impact
15 durability and memory response?

16 **DR. FILIP DUBOVSKY:** Yeah, let's talk about a
17 slow immune response for a bit. Although, I don't have
18 kinetic data on that, so I think I'll disappoint you in
19 being able to look at it over time. But this is --
20 oops, that's not what I wanted. Let's try this one.
21 This is data that we published in the *New England*

1 *Journal* by P. Chid Aoh (phonetic), and what it's
2 looking at is the intracellular cytokine profile after
3 vaccination on Day 28. On the left-hand side, we
4 stained against Th1 cytokines, and, in this case, IL2
5 TNF alpha and interferon-gamma, and what you can see is
6 we got a really nice bump at Day 28.

7 On the right-hand side, you can see the Th2
8 profiles. We look at IL5 and IL13 which is a lesser
9 bump. Importantly -- at least we think importantly --
10 when we looked at those that were polyfunctional to
11 those that either stained for two Th1 cytokines or
12 three Th1 cytokines comparing to those that stained for
13 two Th2 cytokines, we saw this polyfunctionality. And
14 we think that's important as far as effective memory
15 cells go. Although we don't have the kinetic data to
16 demonstrate that fully.

17 **DR. MICHAEL NELSON:** Is that being required?
18 And certainly, does -- Th1 skewing may impact on the
19 observation of lower immediate systemic effects with
20 respect to anaphylaxis and other immediate type of
21 responses, which is favorable with your platform.

1 **DR. FILIP DUBOVSKY:** Right.

2 **DR. MICHAEL NELSON:** My second question is
3 related to the distinction between your Hispanic and
4 Latinx efficacy response. I thought I heard this
5 morning that certainly it's been acknowledged that the
6 difference -- no obvious explanation to date. I
7 wondered if you wanted to clarify a little bit more as
8 to what your plans are to tease out whether those
9 differences were indeed due to chance versus something
10 else.

11 **DR. FILIP DUBOVSKY:** Yeah. So, we've
12 obviously been very interested in understanding what
13 this data is trying to tell us, and what's even more
14 interesting is when we looked at the racial profile of
15 the Hispanics, they were all identified as Caucasian
16 and not black Hispanics. So, there is something quirky
17 happening in the data.

18 Well really, our best chance to understand
19 this data is in our effectiveness studies. Those are
20 planned for the U.S. where we'll obviously have the
21 ability to probe that in the Hispanic population to

1 understand if it was a real difference over this chance
2 finding. I'm a believer in immune responses, and the
3 immune responses in the Hispanic population give me a
4 lot of comfort that it's going to be a chance finding.
5 I have to say in all the moderate and severe cases,
6 there weren't any. So even in that population, all the
7 cases were mild.

8 **DR. MICHAEL NELSON:** Acknowledged. Thank you
9 very much.

10 **DR. ARNOLD MONTTO:** Thank you. Dr. McInnes.

11 **DR. PAMELA MCINNES:** Hello.

12 **MR. MICHAEL KAWCZYNSKI:** Yep, we can hear you.
13 Take it away.

14 **DR. PAMELA MCINNES:** Hi. Okay. I have a very
15 simple question. It's for Filip. Hi, I searched these
16 briefing documents, but I can't seem to find out what
17 the placebo was, and it's important to me because I'm
18 measuring a delta between that and the activation. Can
19 you tell me what the placebo is?

20 **DR. FILIP DUBOVSKY:** Sure, it's normal saline.

21 **DR. PAMELA MCINNES:** Could you hear me?

1 **DR. FILIP DUBOVSKY:** Yep. Normal saline.

2 **DR. PAMELA MCINNES:** Normal saline. Okay,
3 thank you.

4 **DR. ARNOLD MONTO:** Dr. Meissner.

5 **DR. CODY MEISSNER:** Thank you, Dr. Monto. And
6 again, thanks for your persistence because I appreciate
7 it. The question I have is you hadn't -- there was an
8 earlier study, and I might've missed this this morning
9 during some of the clinical trials, but it was done in
10 South Africa, and it included HIV-positive subjects.
11 And I think the vaccine efficacy was reported as 50
12 percent -- or something around that -- in the HIV-
13 positive population, which seems pretty good in view of
14 their degree of immunocompromise, I guess, depending on
15 their reconstitution.

16 But can you provide any further data regarding
17 that group and how this vaccine might work in
18 individuals who are immunocompromised for other
19 reasons?

20 **DR. FILIP DUBOVSKY:** Yeah, and maybe if I
21 could have the immune responses in people with HIV in

1 Study 301, please? We can start there. Yeah, here we
2 go. So, what I'm showing you here is IgG responses,
3 and, on the left-hand side, you see those that are
4 seronegative. So, meaning seronegative, meaning
5 baseline seronegative against SARS, and you can see the
6 HIV levels are higher than those that were living with
7 HIV, although broadly the confidence intervals overlap.

8 Now in the U.S., these are people who are well
9 controlled (inaudible), and they were immunologically
10 reconstituted. We had a small number of individuals,
11 that I'm showing on the right-hand side, who came in
12 previously exposed, and you can see they boosted
13 extremely well with the vaccine, so they achieved
14 titers many-fold higher than was associated with
15 protection in the HIV negative group.

16 Now our data so far on various levels of
17 immunocompromised individuals is somewhat limited, and
18 we're going to be gathering that data in due course.
19 We've completed enrolling a study in South Africa where
20 we looked at giving three doses and giving doses on
21 different schedules to see if we can get an advantage -

1 - an immunologic advantage -- by delivering it in that
2 manner.

3 Now, as far as the results in South Africa,
4 Dr. Mallory, do you want to give a crack at reviewing
5 the South African results for what our findings were?

6 **MR. MICHAEL KAWCZYNSKI:** Sorry, who would you
7 like to call on?

8 **DR. FILIP DUBOVSKY:** Dr. Mallory.

9 **DR. RABURN MALLORY:** Can you hear me?

10 **MR. MICHAEL KAWCZYNSKI:** Yes, we can. Take it
11 away.

12 **DR. ARNOLD MONTO:** We can. Yes, go ahead.

13 **DR. RABURN MALLORY:** I just wanted to clarify,
14 Dr. Meissner, that I'm showing the results of the South
15 Africa study here, and we did show a notable efficacy
16 of around 50 percent. Remember, this study was
17 conducted when the beta antigenic escape mutation was
18 circulating. The efficacy in individuals without HIV
19 was 55 percent. However, we had a very small number of
20 individuals involved in this study who were living with
21 HIV, and, in that group, we were not able to

1 demonstrate efficacy, but it was not powered for it.

2 So, I think maybe there's some
3 miscommunication. The 55 percent is in individuals who
4 were HIV negative in that study.

5 **DR. CODY MEISSNER:** Oh. Thank you.

6 **DR. RABURN MALLORY:** In all cases, again,
7 there were no severe cases in this study, so the
8 vaccine protected all participants enrolled from severe
9 disease in that study.

10 **DR. CODY MEISSNER:** Okay. Thank you for that
11 clarification.

12 **DR. ARNOLD MONTO:** Yes, thank you.

13

14 **COMMITTEE DISCUSSION AND VOTING**

15

16 **DR. ARNOLD MONTO:** Seeing no further hands
17 raised, we're able to move to our next phase of our
18 discussion, and that is the Committee looking at the
19 question that we are going to have to vote on shortly.
20 And that is whether we recommend emergency use
21 authorization for the Novavax vaccine, and there is the

1 voting question. I'm going to be officially reading it
2 later on, but just to remind you this is for the two-
3 dose series, and it's based on whether the risks
4 outweigh the benefits.

5 So, any of you who would like to start the
6 discussion please raise your hands. We don't have to
7 fill the full two hours in if a lot of our questions
8 have already been answered. Dr. Rubin.

9 **DR. ERIC RUBIN:** I don't want to fill the two
10 hours.

11 **DR. ARNOLD MONTO:** You don't have to.

12 **DR. ERIC RUBIN:** Very simply then, I think
13 that the data that were presented looks very similar to
14 the data that were presented for the mRNA vaccines that
15 we approved a long time ago and, in fact, that's in
16 part because those trials were done at the same time.
17 But I think that the efficacy is quite similar --

18 **DR. ARNOLD MONTO:** I had the same feeling, Dr.
19 Rubin. It was déjà vu.

20 **DR. ERIC RUBIN:** And if we're going to use the
21 same criteria that we did then, I think that it's not

1 that difficult a decision now. It is disappointing --
2 and we've discussed this already -- that we don't have
3 more updated information because we're looking at the
4 efficacy against strains that don't exist any longer.
5 Nevertheless, I think that the argument made earlier by
6 Dr. Marks, and for EUA, if there really is a population
7 of patients who are willing to take this and not
8 willing to take existing vaccines, I think it's pretty
9 compelling.

10 **DR. ARNOLD MONTO:** Thank you. I'm amazed. I
11 see no hands raised. Anybody who doesn't feel that
12 this is compelling? Dr. Sawyer.

13 **MR. MICHAEL KAWCZYNSKI:** Go ahead, Mark.

14 **DR. MARK SAWYER:** Yeah, I'd just like to sort
15 of reiterate the previous comment. It is quite
16 disappointing that we don't have any data in the
17 Omicron era. Clearly, such data could have been
18 presented, but I will follow what I understand is the
19 FDA guidance which is we're supposed to evaluate this
20 vaccine based on the data presented to date and leave
21 it up to them whether they actually issue the EUA given

1 the lack of data about Omicron effectiveness, at least
2 as presented on the Committee.

3 So, I do agree with the previous conclusion
4 that the data that was presented is quite similar to
5 what we've approved in the past with other vaccines.

6 **DR. ARNOLD MONTO:** Thank you. Dr. Reingold.

7 **DR. ARTHUR REINGOLD:** So, I agree with both of
8 those statements. I certainly will support
9 recommending FDA that they approve this vaccine.

10 I'm a little skeptical about how many of the
11 vaccine hesitant are just waiting for this vaccine and
12 are going to be convinced that this is better for them
13 than the vaccines that are currently available, so
14 obviously they're individuals who've testified to that.
15 But at a population level, I'm hoping to be proven
16 wrong that the large numbers of people who sign up for
17 this vaccine, who wouldn't take an mRNA vaccine, but
18 count me as skeptical about that.

19 And I do think that it remains to be seen just
20 what the risk of myocarditis is, but we know that that
21 certainly has dissuaded some individuals from getting

1 the mRNA vaccines, and it looks like it's likely to be
2 the case that we'll see at least comparable levels
3 following this vaccine.

4 **DR. ARNOLD MONTO:** Thank you. Dr. Gellin.

5 **DR. BRUCE GELLIN:** Thanks. So, having been in
6 these discussions before, I know the FDA selects their
7 words pretty carefully. Could you put it back on the
8 screen because I think the question about the totality
9 of the data available, we've only seen a subset of the
10 totality of the available data? And there's a lot of
11 other data that would help to inform this decision in
12 use currently and going forward that we haven't seen.
13 So maybe they want to talk about totality of evidence
14 available.

15 **DR. ARNOLD MONTO:** I can tell you, Dr. Gellin,
16 that that is the wording that's in the -- has been used
17 before, and I think is taken from the regulations, but
18 I'll let the FDA respond. Please.

19 **DR. DORAN FINK:** So, we would consider the
20 totality of data available to consist of the data that
21 had been presented and discussed at the meeting today,

1 and then primarily the data that have been reviewed and
2 independently verified by FDA as outlined in our
3 briefing document. I think it's important to make sure
4 that the Committee members and the public understand
5 that in response to some questions by Committee
6 members, Novavax has presented some additional data
7 that FDA has not covered in our briefing document, and
8 the reasons for this are several.

9 First of all, it has been mentioned several
10 times before, we view that there are important
11 manufacturing differences between the product that was
12 studied in the U.S./Mexico trial and the product that
13 was studied in previous trials in our assessments due
14 to inherent limitations in the product characterization
15 for this platform. We just cannot conclude
16 comparability of those products that would allow us to
17 consider those data.

18 That being said, I think we have laid out a
19 case in our briefing document to support why we think
20 that the available data from the U.S./Mexico trial
21 could meet the statutory criteria of -- may be

1 effective that is required to support emergency use
2 authorization. And that rests primarily on the
3 efficacy observed in Clinical Trial 301 that was
4 conducted in the U.S. and Mexico and considering those
5 data in the broader context of what we know about other
6 COVID-19 vaccines that were evaluated at the same time
7 and how they have performed in real-world use,
8 including against currently circulating variants.

9 There are additional immunogenicity data that
10 Novavax has presented as well that we did not review or
11 discuss. Some of these relate to binding assays, IgG
12 binding assays, that we have not used as the basis for
13 regulatory decision-making for any of our EUA decision,
14 and also come from clinical trials outside of the data
15 that we are really considering in support of this two-
16 dose series for use in adults 18 years of age and
17 older. And I see that with Dr. Marks has also turned
18 on his camera, and he might want to add some additional
19 context.

20 **DR. PETER MARKS:** I think that this issue of
21 why we're seeing a limited amount of the whole picture

1 presented is because we needed to feel comfortable that
2 the process that was used to make the product that was
3 studied was one that we were comfortable with and that
4 it was one where we felt that going forward, what you
5 would authorize as a committee would be what we would
6 expect to see. Now, granted, it will be in a different
7 era, perhaps, but what you're seeing is the product
8 that you're getting and that is the reason for focusing
9 on the manufacturing process that came from the
10 facility that is producing the product currently.

11 We take manufacturing very seriously. I think
12 it's very important for the public to understand that
13 we don't benchmark ourselves against other countries
14 when it comes to manufacturing. We consider that we
15 have a very high standard, and it's why we're often
16 considered a gold standard for our manufacturing. And
17 particularly in the area of vaccines, we owe it to the
18 American public to make sure that we have the highest
19 quality of vaccines. And that means that, whether it
20 be in any aspect of this including whether we will
21 allow release of lots of vaccines to be used, we will

1 need to see the data that supports that before that can
2 actually happen for any vaccine here in the United
3 States.

4 So, I think it's important to understand that
5 I fully respect the sovereignty of other countries to
6 release vaccines based on what they see as their
7 benefit/risk, but we have certain standards in the
8 United States that we hold to because that is the
9 expectation of the American public. Thanks.

10 **DR. ARNOLD MONTO:** Thank you. Dr. Chatterjee.

11 **DR. ARCHANA CHATTERJEE:** Thank you, Dr. Monto.

12 My question actually is for our FDA colleagues. With
13 regard to any kind of cautionary language that would be
14 included for this vaccine to be authorized with regard
15 to the risk for myocarditis, pericarditis,
16 cholecystitis, these quite rare but serious adverse
17 events that seem to be associated with this vaccine.

18 **DR. DORAN FINK:** Yes, thank you for that
19 question. So that is a question that we are discussing
20 as we have been reviewing the proposed EUA fact sheet
21 for this vaccine. So what I think you might be hinting

1 at is, do we include something along the lines of a
2 warning statement similar to what we have in the
3 currently authorized development of mRNA vaccines? And
4 so, the regulatory criteria for including a warning
5 statement is to have reasonable evidence of a causal
6 relationship.

7 Now, certainly, I think we can all agree that
8 the extent of evidence for myocarditis being causally
9 related to this vaccine is not at the same level as for
10 mRNA vaccines where we have many more cases described
11 among much more extensive use of the vaccine.

12 But I would actually like to get the
13 perspective of Committee members to weigh in. What do
14 you think based on the data that you've seen presented
15 of these myocarditis cases? Is your impression about
16 the likelihood of a causal relationship and whether you
17 would see a warning statement being appropriate in the
18 situation?

19 **DR. ARCHANA CHATTERJEE:** I actually would.

20 **DR. ARNOLD MONTO:** Dr. Chatterjee, if you're
21 there. Please answer.

1 **DR. ARCHANA CHATTERJEE:** Yes, yes. And you're
2 absolutely correct, Dr. Fink, that is what I was
3 alluding to. If we go back and recall the data that
4 were presented initially for authorization, we did not
5 have this concern. It really became evident after the
6 mRNA vaccines began to be used much more extensively,
7 so that often happens as we know with vaccines.

8 And so, in this instance, we have an
9 indication that there is a potential for these adverse
10 events to occur more as this vaccine gets utilized. So
11 I would be in favor of that type of language being
12 included so that the public is clear. Vaccine
13 providers are clear about the risk and can speak to
14 them with their patients.

15 **DR. ARNOLD MONTO:** And since my picture is up
16 there right now I will say that I agree as well. I
17 think there's question and there will be answers, but
18 we must be aware. Dr. Dubovsky.

19 **DR. FILIP DUBOVSKY:** Yeah, I just thought to
20 hear our perspective, honestly. It's important to
21 convey accurate level of risk for the available data.

1 We believe there's insufficient evidence to establish a
2 causal relationship, but we're not really that far from
3 where the FDA is. And, as we enter the final label
4 negotiations, I'm sure we're going to come to closure
5 on this. These regulatory agency reviews are clinical
6 in our post-marking data and come to their own
7 conclusions, and that's what informs their labels, so
8 we completely respect the approach that the FDA is
9 taking.

10 **DR. ARNOLD MONTO:** Any other questions? I see
11 a number of hands raised. I'd like to settle this
12 question at least in terms of the Committee's opinion
13 about the myocarditis issue. Dr. Levy, is that what
14 you're going to be talking about? You had your hand
15 raised before.

16 **DR. OFER LEVY:** Hello, can you hear me?

17 **DR. ARNOLD MONTO:** We can.

18 **DR. OFER LEVY:** Okay. I had a question for
19 FDA regarding the placement of this vaccine in the
20 broader context of the (inaudible).

21 **DR. ARNOLD MONTO:** Dr. Levy, we wanted to

1 settle the Committee's views of the -- okay, did you
2 have anything to say about that because then I'll come
3 back to you?

4 **DR. CODY MEISSNER:** Can I make a comment?

5 **DR. ARNOLD MONTTO:** Yes, please. Go ahead.

6 **DR. CODY MEISSNER:** Yes, on this risk, I have
7 such a hard time with this problem as we all do, and
8 there's been such variation in reports of the rates of
9 myocarditis following administration of these vaccines
10 that I think it's very hard to say that it occurs more
11 frequent. It would be, at this stage, difficult to say
12 that it occurs more frequently with one vaccine
13 platform than with another.

14 I mean, I think if because if you look at the
15 Israeli data, it's pretty high. It's higher than the
16 numbers we're seeing here, and they may have better
17 capture of rates of myocarditis to the messenger RNA
18 vaccine.

19 So, I don't think we can have enough
20 confidence in the rates because there's such a range,
21 and I think that any statement regarding the risk of

1 myocarditis should be standard between all of the
2 COVID-19 vaccine platforms. I think there is clearly
3 an association, but, to try and make a gradation as to
4 where the one platform is more likely to result in
5 myocarditis than another, I don't think we have the
6 numbers to make that statement. Over.

7 **DR. ARNOLD MONTO:** Thank you, Dr. Meissner.

8 **DR. DORAN FINK:** Thank you, Dr. Meissner.

9 Yes, I agree with you that at this point we don't have
10 enough information to really describe relative risk of
11 this event between different vaccines, but that's not a
12 requirement or a necessity to have a warning statement.
13 A warning statement is justified by -- and I'm going to
14 clarify what I said earlier here. A warning statement
15 is justified by reasonable evidence of a causal
16 association, and there does not need to be definitive
17 evidence of a causal relationship. It's reasonable
18 evidence of a causal association, and so that really is
19 the question that we're looking for input here. Based
20 on the information that you've heard today, do you
21 consider there to be reasonable evidence of a causal

1 association?

2 And, of course, it would be ideal if we could
3 describe the magnitude of the risk for each vaccine and
4 compare to the others, but we don't have the ability to
5 do that. At least not for this vaccine just yet.

6 **DR. CODY MEISSNER:** Thank you for that
7 comment, Dr. Fink, and I completely agree with what
8 you've said. But I think my point is, I think there
9 may be --

10 **DR. ARNOLD MONTO:** Is there anyone on the
11 Committee that does not agree with that comment? Dr.
12 Gellin, you have your hand raised. Do you disagree?

13 **DR. BRUCE GELLIN:** Well, my hand was up before
14 you changed the question, so I'm just going to give you
15 the answer from before.

16 **DR. ARNOLD MONTO:** You have to be nimble on
17 this Committee.

18 **DR. BRUCE GELLIN:** I got it. On this topic,
19 though, I want to support what Cody raised and what Dr.
20 Fink supported. But I think we also have to put this
21 in context that we talked about earlier about

1 myocarditis that comes from natural infection as well,
2 so people can look at that and weigh those as well.
3 And then most importantly what Paul Offit raised
4 earlier that this is a priority question to answer
5 mechanistically. Over.

6 **DR. ARNOLD MONTO:** Okay, I think you've got
7 the message, Dr. Fink, that there is a concern that the
8 topic be further investigated, and it's in your hands
9 in negotiations with the sponsor exactly how that is to
10 be done. But we do agree that there is a concern here.

11 **DR. DORAN FINK:** Thank you.

12 **DR. CODY MEISSNER:** Can I ask --

13 **DR. ARNOLD MONTO:** Okay. Do you think --

14 **DR. CODY MEISSNER:** Dr. Fink, don't you agree
15 that the likely association between the messenger RNA
16 vaccine and the Novavax vaccine -- and shouldn't it be
17 a standard statement?

18 **DR. DORAN FINK:** Well, what we say in product
19 labeling, including EUA fact sheets, needs to be
20 supported by available data and the level of evidence
21 is going to be different for different vaccines. I

1 think we're in a different place and can say more for
2 the mRNA vaccines at this point in time than what we
3 can say for this vaccine.

4 **DR. CODY MEISSNER:** Okay, thank you.

5 **DR. ARNOLD MONTO:** Okay. Moving on. Dr.
6 Levy, I interrupted you when you were ready to make
7 another point.

8 **DR. OFER LEVY:** Yeah, my question here -- can
9 you hear me?

10 **DR. ARNOLD MONTO:** We can.

11 **DR. OFER LEVY:** Yeah. My question here is to
12 FDA. In my view, we've seen great presentations today
13 establishing reasonable safety, demonstrating efficacy
14 at least against the variants that were circulating at
15 the time this vaccine was evaluated. Now, as we vote
16 to potentially recommend authorization of this vaccine,
17 where does the whole topic of how we place the vaccine
18 in a public health (audio skip) play into this? In
19 other words, it's a very different landscape now than
20 it was half a year or year ago. There are the well-
21 established mRNA vaccines, some of which are not just

1 authorized, but approved as this Committee knows very
2 well.

3 So, is there going to be a pecking order in
4 (audio skip) the mRNA vaccines where there's much more
5 data about the level of vaccine efficacy against
6 Omicron? Are those going to be the preferred first-
7 tier vaccines to use with the Novavax if and when it's
8 authorized being that we've heard a lot of talk about
9 people who might not want to trust or partake in the
10 mRNA platform; they might want to try a different
11 platform.

12 So, don't get me wrong, I'm a fan of this
13 vaccine. It has a lot of attractive features. It
14 doesn't require freezing. The adjuvant is intriguing.
15 We might get more bang for our buck with that. But
16 where does this get placed in the armamentarium?
17 Because in isolation, this vote would almost imply that
18 it just takes an equal spot on the shelf. But we know
19 that it's more complicated than that.

20 So, Peter, where does that stand, and does FDA
21 speak to that, or is that just a CDC matter?

1 **DR. PETER MARKS:** So I think we speak to
2 making available another option for those who might not
3 otherwise take a vaccine because, right now, any
4 vaccine, even one that may need to be updated for the
5 variants, right now getting that into someone's arm who
6 has no vaccine is probably going to prevent them from
7 having serious outcomes such as hospitalization and
8 death from COVID-19, even from Omicron, we hope at
9 least for a period of time. So, it's having additional
10 choice.

11 That said, my guess is that CDC will have some
12 discussion here around this as well about how they
13 might position this, and I can't say how they'll come
14 on this from ACIP.

15 **DR. OFER LEVY:** Of course.

16 **DR. PETER MARKS:** But from our perspective,
17 it's making available another option to hopefully get
18 some additional people vaccinated.

19 **DR. OFER LEVY:** Yes, it makes sense, but, in
20 the past, the committee has been asked to take votes on
21 very specifically worded for certain age groups, for

1 certain scenarios. This is a pretty broad statement.
2 You're not crafting a vote question that says, for
3 individuals who are reluctant to take mRNA. It's a
4 broader statement. That might be fine, but I'm
5 wondering, did you consider to phrase the question more
6 narrowly or you want this broad phrasing?

7 **DR. ARNOLD MONTO:** This is a question that we
8 voted on originally back in a year and a half ago.

9 **DR. PETER MARKS:** Yeah. I think the issue is
10 there were no data for us to suggest that there was a
11 reason to narrow this further at this point in time in
12 terms of adverse safety concerns that might want to
13 make one narrow this, and I certainly invite Dr. Fink
14 if he wants to add anything to that to add it. But I
15 think that, in the absence of data suggesting that a
16 narrowing was necessary, we have asked the broader
17 question here.

18 **DR. DORAN FINK:** Yeah, I'll just echo what Dr.
19 Marks said. The more restricted authorization for the
20 Janssen vaccine was participated by specific safety
21 concern related to thrombosis with thrombocytopenia

1 syndrome. Here we have a package of data to support
2 broad use in the general population of adults 18 years
3 of age and older. We did not identify a specific
4 safety concern that would cause us to think about a
5 more restricted use of this vaccine, and so that's why
6 the voted question was constructed, of course.

7 **DR. OFER LEVY:** No, I got that. (Audio skip)
8 true that all other things being equal, we know more
9 about the efficacy against Omicron of the mRNA than
10 this vaccine. I'm a supporter of this vaccine; I'm
11 just saying in terms of messaging, it's tricky, isn't
12 it?

13 **DR. ARNOLD MONTO:** We all agree that it's
14 tricky. Dr. Perlman, thank you.

15 **DR. STANLEY PERLMAN:** Yeah, I just have a
16 question about something we actually didn't talk about
17 much. So, this vaccine doesn't for the most part
18 induce CD8 T-cell response; it's mostly CD4 and
19 antibody and that's what was discussed. How does the
20 FDA take that laboratory information? Does it consider
21 that? The vaccine clearly works, so maybe it doesn't

1 matter, but I'm just curious how the FDA puts that into
2 its equation in going forward.

3 **DR. PETER MARKS:** I'm not sure there's really
4 a lot to say there. I mean, I think it's something
5 we're aware of, but, given the clinical data, that's
6 what we're hanging more of the hats on here. Doran,
7 I'll pass it over to you.

8 **DR. DORAN FINK:** Yeah, I think we really have
9 to look at the clinical data here. It's interesting to
10 see and discuss this data on cellular remediating
11 immunity to the extent that it is available. We don't
12 have a sufficient enough understanding of those data to
13 use it as the primary basis for making regulatory
14 decisions. And so really, I would ask the Committee to
15 focus on the clinical efficacy data that has been
16 presented.

17 **DR. STANLEY PERLMAN:** Right.

18 **DR. ARNOLD MONTO:** Thank you. Seeing no
19 further hands raised, I would like to turn the meeting
20 over to Christina Vert who will start the voting
21 process.

1 I'd like to remind the Committee that, after
2 the votes are completed and reread, we will allow time
3 for those who wish to explain their vote to do so. You
4 don't have to explain your vote if it's clear to you
5 and to the group, but that time will be made available
6 afterwards. So, we move to voting.

7 **MS. CHRISTINA VERT:** Thank you, Dr. Monto.
8 Can you hear me, okay?

9 **DR. ARNOLD MONTO:** We can.

10 **MS. CHRISTINA VERT:** Okay, great. Only our 10
11 regular members and 12 temporary voting members, a
12 total of 22, will be voting in today's meeting. With
13 regards to the voting process, Dr. Monto will read the
14 final voting question for the record, and, afterwards,
15 all regular voting members and temporary voting members
16 will cast their vote by selecting one of the voting
17 options which include yes, no, or abstain.

18 You will have one minute to cast your vote
19 after the question is read. Please note that once you
20 have cast your vote, you may change your vote within
21 the one-minute timeframe. However, once the poll has

1 closed, all votes will be considered final. Once all
2 of the votes have been placed, we will broadcast the
3 results and read the individual votes out loud for the
4 public record. Also wait until I say, start the vote.

5 Does anyone have any questions relating to the
6 voting process before I begin, and also do you feel you
7 need more than one minute to cast your vote? If you
8 need more time, or if I need more time to check things,
9 we will continue to keep the vote open for the two
10 minutes. Okay.

11 **DR. ARNOLD MONTO:** Okay, I'll read the
12 question. I'm sure that you will see everybody voting
13 within the minute and you'll know.

14 **MS. CHRISTINA VERT:** Yes, Dr. Monto, please
15 read the voting question.

16 **DR. ARNOLD MONTO:** "Based on the totality of
17 scientific evidence available, do the benefits of the
18 Novavax COVID-19 vaccine, when administered as a two-
19 dose series, outweigh its risks for use in individuals
20 18 years of age and older?" So, there is the pod.
21 Begin.

1 **MS. CHRISTINA VERT:** Please start voting at
2 this time. And set the timer. Yeah. Okay, I'm just
3 checking the votes. Okay, it looks like all the votes
4 are in. We can please end the vote, and then we can
5 broadcast the results. Okay. We'll close. Okay.
6 What is viewing? Okay, all right.

7 The majority -- so there's 22 total voting
8 members, again, today and we have 20 -- let's see here.
9 Oh, okay. We have 21 that have voted yes, zero have
10 voted no, and one has abstained. So, the majority have
11 voted yes, and I will read the voting responses of each
12 voting member for the record.

13 Okay. Dr. Fuller, yes; Dr. Berger, yes; Dr.
14 Cohn, yes. Okay. Dr. Chatterjee, yes; Dr. Monto, yes;
15 Dr. Reingold, yes; Dr. Gellin, abstain; Dr. Meissner,
16 yes; Dr. Kim, yes; Dr. Rubin, yes; Dr. Bernstein, yes;
17 Dr. Portnoy, yes; Dr. Lee, yes; Dr. Sawyer, yes; Dr.
18 Wharton, yes; Dr. Nelson, yes; Dr. Levy, yes; Dr.
19 McInnes, yes; Dr. Offit, yes; Dr. Perlman, yes; Dr.
20 Pergam, yes; Dr. Marasco, yes.

21 And that is everybody. Yes. Okay. That

1 concludes the voting portion of today's meeting, and I
2 will now hand the meeting over to Dr. Monto for asking
3 the Committee for their voting explanation. Thank you.

4 **DR. ARNOLD MONTO:** So, anybody who would like
5 to explain their vote please raise your hand now. I do
6 not see any hands raised.

7 **DR. BRUCE GELLIN:** Can you hear me?

8 **DR. ARNOLD MONTO:** Am I missing any?

9 **DR. BRUCE GELLIN:** I'm sorry. I got kicked
10 out of the -- can you hear me now?

11 **DR. ARNOLD MONTO:** I can hear you; I can't see
12 you.

13 **DR. BRUCE GELLIN:** I don't know -- something.
14 I got kicked out of the meeting, but you can still hear
15 me. I'm trying to get back in, but do you want me to
16 explain mine or how do you want to proceed?

17 **DR. ARNOLD MONTO:** I want to -- it's up to
18 you, if you want to explain your vote, please.

19 **DR. BRUCE GELLIN:** Yeah. Oh, I'd love to.
20 Let me just say that this is a conditional yes, and
21 I'll explain that. But conditional yes wasn't an

1 option.

2 I will say that this is a case study of
3 perseverance by the company, and there's nothing about
4 vaccine development that's easy. And the vaccine race
5 is inspired by COVID, and it was reported by Warp Speed
6 -- and I had nothing to do with that -- has brought us
7 vaccines that we didn't think we would have to have an
8 impact. That has been impressive.

9 And while global inequity remains, for which
10 additional platforms and more user-friendly
11 presentations will be welcomed, like this vaccine,
12 that's not why we're here. The data that we've heard
13 today and seen today has been impressive and support
14 the original vision for this vaccine from its
15 beginning. That it would provide safety and efficacy
16 in a presentation that didn't require extraordinary
17 logistics. With attribution to the novel adjuvant, the
18 lower amount of protein appears to make it even less
19 reactogenic.

20 With a focus on safety as we've discussed,
21 myocarditis is a signal that many are paying attention

1 to, and attention to this by the company and government
2 is critically important. As I said before,
3 highlighting Dr. Offit's intervention, that we need to
4 understand the mechanism here because this infection
5 and the vaccines against this are going to be with us
6 for the foreseeable future.

7 The question that we're asked is based on the
8 totality of the scientific evidence available. We've
9 already heard me ask about the availability word. And
10 as Dr. Marks reinforced, in looking at the totality of
11 the evidence presented, we can clearly say that it was,
12 in general, safe, including the long-term safety
13 follow-up in the study and because of its effectiveness
14 to prevent serious consequences of the viral infection.
15 But we don't know whether that attribute continues to
16 be relevant today.

17 Dr. Levy's important question about the
18 potential of cross-protecting immunity and the limited
19 data that we've seen in response to that are certainly
20 encouraging. But again, we don't really know whether
21 it's likely to be effective going forward and what the

1 duration of that protection might be.

2 In the flu world, we're always challenged by
3 mismatch; is the vaccine that's being made and
4 distributed likely to be a good match for the flu virus
5 that's likely to circulate? That's essentially the
6 question here. This vaccine has incredible potential,
7 and a lot has been learned about it that we didn't hear
8 about that's likely to inform the durability of
9 protection, transmission, the impact of boosting,
10 adjustments to the dosage interval, the impact of mix
11 and match, and its importantly impact against
12 circulating variants.

13 So therefore, I want to be clear that I'm not
14 voting against this vaccine because I did worry that
15 such a vote would be misinterpreted and hence this
16 conditional vote for it but as an extension. But as
17 this is a real product that, if authorized, would be
18 used, it would be important to evaluate whatever data's
19 available but can give us insights into its
20 performance, not just voting on the science that tells
21 us about its promise.

1 So, recognizing we're an advisory committee
2 and we're advising FDA and we know that FDA, as we
3 heard from Dr. Marks and others, will continue to work
4 with the company on some of the manufacturing issues,
5 then our discussions today are just part of what
6 they'll consider going forward in their decisions on
7 authorization.

8 So, my conditional vote, yes, is based on my
9 expectation that the FDA will review the totality of
10 the data that will be available to them, including the
11 data that we didn't see today to inform their
12 authorization decision. Thanks.

13 **DR. ARNOLD MONTA:** Thank you, Dr. Gellin. Dr.
14 Nelson.

15 **DR. MICHAEL NELSON:** Thank you, Dr. Monto.
16 And certainly, with the question posed before is, do
17 the benefits outweigh the risk? I'm entirely
18 supportive of a yes there. It does come with a little
19 bit of caveats because included in that question was
20 specific reference to the two-dose primary vaccines.

21 I think this group was in full recognition

1 that this is probably a three-dose series and that
2 they'll need to accumulate data supporting the need for
3 booster doses and subsequent doses to probably make it
4 a three-dose vaccine. But to address the question of
5 the table, certainly, the benefits outweigh the risk
6 for a primary series.

7 I also want to make reference to use Dr.
8 Marks' words from this morning that this vaccine does,
9 indeed, fill some unmet needs. So, he didn't ask us
10 specifically how to apply these to the EUA criteria,
11 but I'll offer my humble opinion, and that I do feel
12 that it does offer something for fulfilling unmet
13 needs, including those populations who have hesitancy
14 with regards to the messenger RNA vaccines.

15 As an allergist, it offers me an additional
16 tool for individuals who have hypersensitivity
17 responses to initial doses of the messenger RNA
18 vaccines, and there are other advantages that have been
19 referred to today including storage. Who knows, even
20 with supply chain challenges down the road, it will be
21 nice to have these options going forward.

1 I'll offer one additional word with respect to
2 myopericarditis. I've done some work in the Department
3 of Defense, and we'll be publishing our work on long-
4 term outcomes of myopericarditis with the smallpox
5 vaccine shortly. This is an important question and
6 should not be ignored. And I will say, Dr. Fink, with
7 utmost confidence, that it would be a travesty if we
8 didn't mention it in the EUA documentation for the
9 public to show the concern that we have.

10 Is there evidence that it's a true causal link
11 at a significantly higher relative risk? I have my own
12 doubts there, as we've heard from the sponsor as well,
13 but to be silent on the matter I think would be a
14 travesty. I also think we should be focusing on the
15 mechanism as has been discussed but also to put more
16 effort into identifying what happens with subclinical
17 appearance of myopericarditis. Our signals are those
18 who get admitted to the emergency room in the hospital.
19 I'm quite convinced that there are others who are
20 experiencing cardiac events of a lesser severity that
21 are worthy of being studied, both from a mechanistic

1 and outcome standpoint.

2 So, we have a lot of work to do, and I hope
3 this Committee and the focus of the FDA, and the NIH
4 remain on myopericarditis on all vaccine platforms, and
5 I appreciate the opportunity to express this opinion,
6 Dr. Monto.

7 **DR. ARNOLD MONTO:** Thank you, Dr. Nelson. Dr.
8 Portnoy.

9 **DR. JAY PORTNOY:** Thank you. Yeah, I was a
10 little bit torn when I first started the Committee this
11 morning. I was a little bit skeptical about the need
12 for an emergency use authorization of this vaccine
13 since we have two other vaccines that are highly
14 effective and relatively safe. So I was very skeptical
15 about that. We've had those vaccines for a year and a
16 half. If this vaccine had come up for discussion a
17 year and a half ago, there would've been no problem at
18 all getting it approved. I'm pretty sure that the
19 Committee would've just voted enthusiastically yes, but
20 now we've got these other vaccines. Is there really a
21 need for an additional vaccine?

1 So that's what I was torn about, but I realize
2 that this is a different technology; it's a more
3 traditional protein-based vaccine. I'm very skeptical
4 that vaccine-hesitant people will select to get this
5 vaccine because of that. I'm good friends with a
6 number of vaccine-hesitant people, and their hesitancy
7 is more ideological than technological. So I really
8 doubt that this vaccine is going to crack that nut, but
9 perhaps some individuals would get this when they
10 wouldn't get the other ones.

11 I see this as an opportunity to widely
12 vaccinate people with the protein vaccine and to
13 compare it with mRNA vaccines which are relatively new
14 technologies because we know how protein-based vaccines
15 work; we don't know how mRNA vaccines work. This is an
16 opportunity to find out how they compare to each other
17 over the long term when large numbers of people get
18 vaccinated. So, I see this as an opportunity.

19 I agree that the benefits definitely outweigh
20 the risks. Whether it meets the needs for emergency
21 use, I'm not totally convinced, but I feel that at

1 least it was worth voting yes in this case because the
2 vaccine deserves the opportunity to be given and
3 studied and used by individuals who wish to use this
4 vaccine.

5 Thank you for having such a transparent and
6 open meeting, and I do want to thank the organizers of
7 this meeting for holding it the way that you do. You
8 do an excellent job, so thank you.

9 **DR. ARNOLD MONTO:** Thank you. Dr. Meissner.

10 **DR. CODY MEISSNER:** Thank you, Dr. Monto. I
11 just want to note that the messenger RNA vaccines are
12 truly remarkable. I mean, they are a great gift to
13 humanity, and they were the first to cross the finish
14 line. But whether or not they will turn out being the
15 optimal vaccine for these viruses is not clear, and I
16 think it's -- I also want to recognize the perseverance
17 from the people at Novavax for developing this vaccine
18 with a novel platform because I think it's -- we still
19 need new vaccines.

20 I don't think we want to rest on just what we
21 have at this point because there's always an

1 opportunity to improve on a vaccine, and we've talked
2 about several of those issues such as sterilizing
3 immunity and the duration of the immune response and
4 the breadth of the immune response. And so I certainly
5 think we want to continue to encourage the development
6 of new vaccines despite the wonderful spot that we find
7 ourselves in today with the two messenger RNA vaccines.

8 And I would also, just in response to Dr.
9 Nelson's comment, again, just want to reiterate, I
10 agree there does appear to be a causal association with
11 the Novavax vaccine, but there's a causal association
12 with the messenger RNA vaccines also. So, my point is
13 I don't want to stigmatize this vaccine inappropriately
14 relative to the messenger RNA vaccines. Thank you.

15 **DR. ARNOLD MONTO:** Thank you, Dr. Meissner.
16 Dr. Marasco.

17 **DR. WAYNE MARASCO:** Yes, so I think to the
18 question posed today, I think that the benefits
19 certainly outweigh the risks. I voted yes because I
20 feel that that's really the question that we will pose.
21 I remain somewhat concerned about the timing of the

1 roll-out of this.

2 I know many of you have to be similar to me.

3 The public knows that there is talk amongst the FDA
4 about reformulating the vaccines in the fall to be more
5 Omicron-centric, if you will. And the real question
6 is, for the people that are vaccine-hesitant, are they
7 going to say, great, we finally have a protein-based
8 vaccine like we're familiar with? Or is the question
9 going to be, but should we do it now with an ancestral
10 strain or wait until the fall when the company itself
11 has said they're investigating it?

12 So, I think on balance, we need to get these
13 new vaccine platforms out there. I think there's some
14 certain advantages to the adjuvanted vaccine that I'd
15 like to see more about as we get more data, but it is a
16 concern that I have in my mind about we're rolling this
17 out, we're having a discussion two weeks before we're
18 having another discussion about formulations for the
19 fall. And although no decisions have been made, it'll
20 be an active topic of discussion.

21 So overall, I applaud the company for having

1 the perseverance to getting this platform and the
2 vaccine out, but there are some questions I think
3 remain in my mind.

4 **DR. ARNOLD MONTO:** Thank you, Dr. Marasco.
5 That's the last explanation of vote we have. I would
6 like to turn the meeting over to Prabha who will ask
7 Dr. Marks to give some closing remarks and thank you
8 all for a very vigorous and productive meeting. So,
9 over to you. I think you're muted.

10

11

MEETING ADJOURNED

12

13 **MR. MICHAEL KAWCZYNSKI:** Yep, Prabha, you're
14 double muted.

15 **DR. PRABHAKARA ATREYA:** Yes, I'm sorry. Thank
16 you, Dr. Monto. Dr. Marks, do you want to address the
17 Committee and make some closing remarks? And then we
18 can adjourn the meeting.

19 **DR. PETER MARKS:** Yeah, no, thank you very
20 much. First of all, I want to thank the Committee
21 members for a very good discussion today. Also want to

1 thank the sponsor, the open public hearing speakers.
2 Again, they all contribute to what is an important open
3 process -- transparent process here -- really
4 appreciate that, and we will do our best to continue to
5 work towards keeping technical glitches down to a
6 minimum. Thank you for your patience with those.

7 I also want to thank Dr. Atreya and the
8 Advisory Committee staff; they did a wonderful job
9 preparing things for this meeting. And then the entire
10 clinical team and the others that were involved from
11 the various offices in the Center preparing for this
12 advisory committee which took a lot of work. And as
13 you're aware, there are some coming attractions of
14 additional ones, so there's been a lot of work going
15 on. Thank you to everyone for that.

16 Thank you to those who have tuned in today, we
17 very much appreciate that. We will, again, look
18 forward to working through what's been said today and
19 moving forward and just appreciate everyone's input
20 today. Prabha, I can turn it back over to you. Thank
21 you, again, to everyone.

1 **DR. PRABHAKARA ATREYA:** Okay, thank you, Dr.
2 Marks. And I would also like to extend my thanks to
3 Dr. Arnold Monto for conducting the meeting very
4 smoothly, and then also all the members who have been
5 patiently working so that the (inaudible) such a
6 productive meeting; thank you so much. And I also
7 thank Michael Kawczynski for facilitating this meeting,
8 and Christina Vert for doing the voting process very
9 effectively. So, thank you and this meeting is
10 adjourned now and have a good evening.

11 **[MEETING ADJOURNED]**