

**FOOD AND DRUG ADMINISTRATION (FDA)
Center for Biologics Evaluation and Research (CBER)
170th Vaccines and Related Biological Products Advisory
Committee (VRBPAC) Meeting**

OPEN SESSION

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

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1 **OPENING REMARKS: CALL TO ORDER AND WELCOME**

2

3 **MR. MICHAEL KAWCZYNSKI:** Good morning. I'm
4 Mike Kawczynski, and welcome to the 170th meeting of
5 the Vaccines and Related Biological Products Advisory
6 Committee.

7 Today, please note that we are having some
8 weather issues with much of our members because this is
9 a broad panel, so there may be periodic changes and
10 pauses just in case any of those have any difficulty
11 staying in the meeting.

12 But, just like always, I'd like to right away
13 hand it off to my colleague and the chair, Dr. Arnold
14 Monto, so he can take it away.

15 Dr. Monto, are you ready?

16 **DR. ARNOLD MONTO:** Thank you, Mike.

17 Good morning, everybody. I think we're all at
18 least in the U.S. time zones this time. I'd like to
19 welcome everybody to the 170th meeting, as you've
20 heard, of the Vaccines and Related Biological Products
21 Advisory Committee of the FDA. We're going to be

1 discussing a very important topic today, on which we
2 are going to have a vote. And we are going to be
3 discussing in open session the Pfizer-BioNTech request
4 for an emergency use authorization for administration
5 of their COVID-19 mRNA vaccine to children 5 to 11
6 years of age.

7 As usual, I want to welcome everybody, the
8 participants, including the members and our speakers
9 and everybody online all over, because there's been a
10 lot of interest in this subject. So, welcome to our
11 discussion. And we are going to review the science
12 here and make a decision that I know affects a lot of
13 people.

14 So, first of all, I'd like to turn the meeting
15 over to our designated federal officer, Prabha Atreya,
16 who is going to go over some of the housekeeping
17 issues, tell you all about how the meeting is going to
18 work, and then introduce the Committee.

19 Over to you, Prabha.

20

1 **ADMINISTRATIVE ANNOUNCEMENTS, ROLL CALL, INTRODUCTION**
2 **OF COMMITTEE, CONFLICT OF INTEREST STATEMENT**

3

4 **DR. PRABHAKARA ATREYA:** Good morning. Thank
5 you, Dr. Monto.

6 Good morning, everyone. This is Prabha
7 Atreya, and it is my great honor to serve as the
8 designated federal officer -- that is DFO -- for
9 today's 170th Vaccines and Related Biological Products
10 Advisory Committee meeting.

11 On behalf of the FDA's Center for Biologics
12 Evaluation and Research and the Vaccines Advisory
13 Committee, I would like to welcome everyone for today's
14 virtual meeting. The topic of today's meeting is to
15 discuss in open session Pfizer-BioNTech's emergency use
16 authorization, EUA, request for administration of their
17 COVID-19 mRNA vaccine to children 5 to 11 years of age.

18 Today's meeting and this topic were announced
19 in the *Federal Register* notice that was published on
20 October 13th, 2021. I would like to now introduce and
21 acknowledge the excellent contributions of the staff in

1 my division and the great team that I have in preparing
2 for this meeting.

3 Can we have the staff slide, please?

4 Ms. Kathleen Hayes is my co-DFO providing
5 excellent support in all aspects of preparing for this
6 meeting and conducting this meeting as well. Other
7 staff who have contributed significantly are Ms.
8 Monique Hill, Ms. Karen Thomas, Ms. Christina Vert, who
9 also provide excellent administrative support.

10 I would also like to express our sincere
11 appreciation to Mr. Mike Kawczynski, who is
12 facilitating the meeting today. I also offer kudos to
13 many FDA staff working very hard behind the scenes
14 trying to ensure that today's virtual meeting will also
15 be a successful one like all the previous VRBPAC
16 meetings on COVID topics.

17 Please direct any press or media questions for
18 today's meeting to FDA's Office of Media Affairs at
19 FDAOMA -- one word -- @fda.hss.gov. The
20 transcriptionists for today's meeting are Ms. Linda
21 Giles and Erica Dunham.

1 We will begin today's meeting by taking a
2 formal roll call for the Committee members and
3 temporary voting members. When it is your turn, please
4 turn on your camera, unmute your phone, and then state
5 your first and last name. And then, when finished, you
6 can turn your camera off so we can proceed to the next
7 person.

8 Can we have the member slide, please?

9 Okay. Let's start today with the chair, Dr.
10 Arnold Monto. Can we start with you, Dr. Monto,
11 please?

12 **DR. ARNOLD MONTO:** Yes, Prabha. And, again,
13 we've been doing this for a couple of times recently,
14 and I will introduce myself again. I'm Arnold Monto.
15 I am professor of epidemiology and public health at the
16 University of Michigan School of Public Health.

17 I've been working for many years on vaccines,
18 on disease occurrence in populations, and particularly
19 respiratory infections, including coronaviruses. And I
20 want to welcome, again, everybody to this meeting. I
21 know there is a great deal of interest.

1 Back to you, Prabha.

2 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Monto.
3 Next, Dr. Annunziato.

4 **DR. PAULA ANNUNZIATO:** Good morning. My name
5 is Paula Annunziato, and I lead vaccine global clinical
6 development at Merck. My training is in pediatric
7 infectious diseases, and I'm here today as the non-
8 voting industry representative.

9 **DR. PRABHAKARA ATREYA:** Thank you, Dr.
10 Annunziato. Next, Dr. Cohn.

11 **CAPT. AMANDA COHN:** Good morning. My name is
12 Amanda Cohn. I am a pediatrician at the Centers for
13 Disease Control and Prevention with expertise in
14 vaccine-preventable diseases.

15 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Cohn.
16 Dr. Gans?

17 **DR. HAYLEY GANS:** Good morning. I am Dr.
18 Hayley Gans. I am professor of pediatrics at Stanford
19 University, and I have trained in pediatric infectious
20 disease. My research focus is on how individuals
21 respond to pathogens. Thank you very much.

1 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
2 Kurilla.

3 **DR. MICHAEL KURILLA:** Thank you, Prabha.
4 Good morning. Michael Kurilla. I'm the
5 Director of the Division of Clinical Innovation at the
6 National Center for Advancing Translational Sciences
7 within the National Institutes of Health. I'm a
8 pathologist by training with a background in infectious
9 disease and vaccine and other interventional
10 development. Thank you.

11 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
12 Meissner.

13 **DR. CODY MEISSNER:** Good morning. My name is
14 Cody Meissner. I'm a professor of pediatrics at Tufts
15 University School of Medicine and the Tufts Pediatric
16 Children's Hospital at Tufts Medical Center.

17 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
18 Paul Offit.

19 **DR. PAUL OFFIT:** Good morning. I'm Paul
20 Offit. I'm a professor of pediatrics at Children's
21 Hospital of Philadelphia and the Perelman School of

1 Medicine at the University of Pennsylvania. My
2 expertise is in pediatric infectious disease and
3 vaccines. My specific interest was in coronavirus
4 vaccines. Thank you.

5 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Offit.
6 Next, Dr. Pergam.

7 **DR. STEVEN PERGAM:** Hello, everyone. I'm
8 Steve Pergam. I am an adult infectious disease
9 physician at Fred Hutchinson Cancer Research Center and
10 the University of Washington Medical Center in Seattle,
11 Washington. And my interest is in infections in
12 immunocompromised patients. Thanks.

13 **DR. PRABHAKARA ATREYA:** Thank you. Next, we
14 will introduce our temporary voting members.

15 Dr. Fuller?

16 **DR. OVETA FULLER:** Thank you. Good morning.
17 I am Oveta Fuller. I am an associate professor of
18 microbiology and immunology at the University of
19 Michigan Medical School. I am a virologist scientist,
20 and I work with implementation of science in the
21 community.

1 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
2 Hildreth.

3 **DR. JAMES HILDRETH:** Good morning. I'm Dr.
4 James Hildreth. I'm the president and CEO of Meharry
5 Medical College and professor of internal medicine.
6 I'm an immunologist by training, and I do research on
7 pathogenic viruses. Thank you.

8 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
9 Jeannette Lee.

10 **DR. JEANNETTE LEE:** Good morning. My name is
11 Jeannette Lee. I'm a professor of biostatistics and a
12 member of the Winthrop P. Rockefeller Cancer Institute
13 at the University of Arkansas for Medical Sciences.
14 Thank you.

15 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
16 Ofer Levy.

17 **DR. OFER LEVY:** Good morning. My name is Ofer
18 Levy, and I'm a professor of pediatrics at Harvard --

19 **DR. PRABHAKARA ATREYA:** You're breaking up,
20 Dr. Levy.

21 **DR. OFER LEVY:** Oh. Can you hear me now?

1 **DR. PRABHAKARA ATREYA:** Yes. Thank you.

2 **DR. OFER LEVY:** Okay. My name is Dr. Ofer
3 Levy. I'm a professor of pediatrics at Harvard Medical
4 School and director of the Precision Vaccines Program.
5 Our research program applies precision medicine
6 principles to understand age-specific effects of
7 vaccines.

8 **DR. PRABHAKARA ATREYA:** Thank you very much.
9 Now, Dr. Patrick Moore.

10 **DR. PATRICK MOORE:** Good morning. I'm Pat
11 Moore. I'm at the University of Pittsburgh Hillman
12 Cancer Center. My expertise is in molecular biology
13 and in epidemiology, and my interests are looking at
14 tumor viruses and at epidemics.

15 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
16 Michael Nelson.

17 **DR. MICHAEL NELSON:** Good morning. Thank you.
18 I'm Mike Nelson, professor of medicine at the
19 University of Virginia and chief of the Asthma, Allergy
20 and Immunology Division there, also president of the
21 American Board of Allergy and Immunology. And my

1 expertise is in allergic reactions to vaccines and
2 severe adverse events.

3 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
4 Perlman.

5 **DR. STANLEY PERLMAN:** Good morning. I am
6 Stanley Perlman. I am a professor of microbiology and
7 immunology and a pediatric infectious diseases
8 specialist at the University of Iowa. I have a long-
9 term interest in coronaviruses spanning almost four
10 decades.

11 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
12 Portnoy.

13 **DR. JAY PORTNOY:** Good morning. I'm Jay
14 Portnoy. I'm a professor of pediatrics at the
15 University of Missouri-Kansas City School of Medicine,
16 and I'm an allergist immunologist at Children's Mercy
17 Hospital in Kansas City.

18 **DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.
19 Eric Rubin. Dr. Rubin?

20 **MR. MICHAEL KAWCZYNSKI:** You're unmuted, Dr.
21 Rubin.

1 **DR. ERIC RUBIN:** I don't know if you can hear
2 me, but I can't turn my phone --

3 **DR. PRABHAKARA ATREYA:** Yes. Now we can hear
4 you.

5 **MR. MICHAEL KAWCZYNSKI:** Yes, we can hear you.

6 **DR. ERIC RUBIN:** Okay. I'm Eric Rubin. You
7 can't see me, but I'm really here. I'm at the Harvard
8 TH Chan School of -- well, there it is -- Harvard TH
9 Chan School of Public Health, the Brigham and Women's
10 Hospital, where I'm an infectious disease physician,
11 and the *New England Journal of Medicine*.

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

14 **DR. MARK SAWYER:** Good morning. I'm Mark
15 Sawyer. I'm a professor of pediatric infectious
16 disease at the University of California San Diego and
17 Rady Children's Hospital, San Diego. And my area of
18 expertise is vaccines.

19 **DR. PRABHAKARA ATREYA:** Thank you. Last, but
20 not least, Dr. Melinda Wharton.

21 **DR. MELINDA WHARTON:** Good morning. I'm

1 Melinda Wharton. I'm an adult infectious disease
2 physician at the Centers for Disease Control and
3 Prevention.

4 **DR. PRABHAKARA ATREYA:** Thank you.

5 Today, we have total 19 participants, with 18
6 voting members and one non-voting industry
7 representative. Now I will proceed with the reading of
8 the Conflicts of Interest statement for the public
9 record.

10 The Food and Drug Administration is convening
11 virtually today, October 26th of 2021, the 170th
12 meeting of the Vaccines and Related Biological Products
13 Advisory Committee, VRBPAC, under the authority of the
14 Federal Advisory Committee Act of 1972. Dr. Arnold
15 Monto is serving as the acting chair for today's
16 meeting.

17 Today, on October 26th, 2021, the Committee
18 will meet in open session to discuss Pfizer-BioNTech's
19 emergency use authorization request for administration
20 of their COVID-19 mRNA vaccine to children 5 to 11
21 years of age. The topic is determined to be of

1 particular matter involving specific parties.

2 With the exception of the industry
3 representative, all standing and temporary voting
4 members of the Vaccines Advisory Committee are
5 appointed special government employees, SGEs, or
6 regular government employees, RGEs, from other agencies
7 and are subjected to federal conflicts of interest laws
8 and regulation.

9 The following information on the status of
10 this Committee's compliance with federal ethics and
11 conflicts of interest laws, including but not limited
12 to 18 U.S. Code Section 208, is being provided to
13 participants in today's meeting and to the public.

14 Related to the discussions at this meeting,
15 all members, RGE and SGE consultants of this Committee
16 have been screened for potential conflicts of interest
17 of their own as well as those imputed to them,
18 including those of their spouse or minor children and,
19 for the purpose of 18 U.S. Code 208, their employers.

20 These interests may include investments,
21 consulting, expert witness testimony, contracts and

1 grants, cooperative research and development
2 agreements, or CRADAs, teaching, speaking, writing,
3 patents and royalties, and their primary employment.
4 These may include interests that are either current or
5 under negotiation. FDA has determined that all members
6 of this Advisory Committee, both regular and temporary
7 members, are in compliance with federal ethics and
8 conflicts of interest laws.

9 Under 18 U.S. Code 208, Congress has
10 authorized the FDA to grant waivers to special
11 government employees and/or regular government
12 employees who have financial conflicts of interest when
13 it is determined that the agency's need for a special
14 government employee's services outweighs the potential
15 for a conflict of interest created by the financial
16 interest involved or when the interest of a regular
17 government employee is not so substantial as to be
18 deemed likely to affect the integrity of the services
19 which the government may expect from the employee.

20 Based on today's agenda and all financial
21 interests reported by the Committee members and

1 consultants, there has been one conflict of interest
2 waiver issued under 18 U.S. Code 208 in connection with
3 this meeting.

4 We have the following consultants serving as
5 temporary voting members. They are Dr. Fuller, Dr.
6 Hildreth, Dr. Lee, Dr. Levy, Dr. Monto, Dr. Moore, Dr.
7 Nelson, Dr. Perlman, Dr. Portnoy, Dr. Rubin, Dr.
8 Sawyer, and Dr. Wharton. Among these consultants, Dr.
9 James Hildreth, a special government employee, has been
10 issued a waiver for his participation in today's
11 meeting. That waiver was posted on the FDA website for
12 public disclosure.

13 Dr. Paula Annunziato of Merck will serve as
14 the industry representative at today's meeting.
15 Industry representatives are not appointed as special
16 government employees and will only serve as non-voting
17 members of the Committee. Industry representatives act
18 on behalf of all regulated industry and bring general
19 industry perspective to the Committee. Industry
20 representatives on this Committee are not paid, does
21 not participate in any closed sessions we have, and do

1 not have the voting privileges.

2 Dr. Jay Portnoy is serving as a temporary
3 consumer representative for this Committee. Consumer
4 representatives are appointed special government
5 employees and are screened and cleared prior to their
6 participation in the meeting. They are voting members
7 of the Committee.

8 The guest speakers for this meeting are Dr.
9 Matthew Oster, an associate professor of pediatrics at
10 Emory University School of Medicine and a pediatric
11 cardiologist at the Sibley Heart Center at Children's
12 Healthcare of Atlanta -- and he's also a medical
13 officer for CDC COVID-19 response at the Center for
14 Disease Control and Prevention, Atlanta.

15 Dr. Fiona Havers is a medical officer in the
16 Division of Viral Diseases, National Center for
17 Immunizations and Respiratory Diseases at CDC in
18 Atlanta, Georgia.

19 Disclosure of conflicts of interest for
20 speakers and guest speakers follow applicable federal
21 laws, regulations, and FDA guidance. FDA encourages

1 all meeting participants, including open public hearing
2 speakers, to advise the Committee of any financial
3 relationships they may have with any affected firms,
4 its products, and if known, its direct competition.

5 We would like to remind the standing and
6 temporary members that if the discussions involve any
7 of the products or firms not already on the agenda for
8 which an FDA participant may have a personal or imputed
9 financial interest, the participant needs to inform the
10 DFO and exclude themselves from the discussion, and
11 their exclusion will be noted for the record.

12 This concludes my reading of the Conflicts of
13 Interest statement for the public record. At this
14 time, I would like to hand over the meeting back to our
15 chair, Dr. Arnold Monto.

16 Dr. Monto, take it away. Thank you so much.

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

18 First, I would like to introduce Dr. Peter
19 Marks, the Center Director of CBER, who is going to add
20 his welcoming comments to what we've already heard and
21 give us a little bit of the background for the meeting.

1 Dr. Marks?

2

3 **FDA INTRODUCTION: WELCOME**

4

5 **DR. PETER MARKS:** Thanks very much, Dr. Monto.

6 Welcome to this 170th meeting of the Vaccines
7 and Related Biologics Advisory Committee. I want to
8 thank the speakers, the sponsor, our open public
9 hearing speakers, our Advisory Committee members, and
10 the FDA staff for their participation today, as well as
11 our virtual audience for joining us.

12 I'd like to take a moment to provide an
13 overview of today's discussion. We'll be considering
14 the proposed amendment to the emergency use
15 authorization of Pfizer-BioNTech's COVID-19 vaccine for
16 use in children ages 5 to 11 years of age.

17 Far from being spared from the harm of COVID-
18 19, in the 5- to 11-year-old age range, there have been
19 over 1.9 million infections, over 8,300
20 hospitalizations, about a third of which have required
21 intensive care unit stays, and over 2,500 cases of

1 multisystem inflammatory disorder from COVID-19. And
2 there have also been close to a hundred deaths, making
3 it one of the top ten causes of death in this age range
4 during this time. In addition, infections have caused
5 many school closures and disrupted the education and
6 socialization of children.

7 Following a few introductory presentations,
8 Pfizer will present their data in support of their
9 emergency use authorization amendment, and this will be
10 followed by FDA's presentation, including our benefit-
11 risk assessment. There will then be an open public
12 hearing followed by discussion of the application and a
13 vote on this topic.

14 Before we get started, I want to acknowledge
15 the fact that there are strong feelings that have
16 clearly been expressed by members of the public both
17 for and against the use of the Pfizer-BioNTech vaccine
18 under emergency use authorization for this age group of
19 5- to 11-year-old children.

20 To be clear, today's discussion is going to be
21 about the scientific data that are presented, and it's

1 not about vaccine mandates, which are left to other
2 entities outside of FDA. I ask that we keep our
3 discourse today civil and focused on the science
4 related to this issue so that we can get through a
5 productive discussion.

6 Thank you again, and I'll now turn it over
7 back to Dr. Monto.

8 **DR. ARNOLD MONTO:** Thank you, Dr. Marks.

9 We're going to get into the meat of our
10 discussion right now. First, we're going to hear from
11 FDA about the topic and also the background so that we
12 will learn what we are going to be voting on.

13 And before I turn over to Dr. Fink, I want to
14 thank FDA for providing us with an agenda which has
15 plenty of time for discussion and to air all of the
16 issues that face us today. Often, we have to compress
17 some of our discussion because of issues of time.
18 That's not the case today. We're going to have a lot
19 of time to discuss these important issues.

20 Over to you, Dr. Fink.

21

1 **FDA'S INTRODUCTION OF THE TOPIC PRESENTATION: PFIZER-**
2 **BIONTECH COVID-19 VACCINE: REQUEST FOR EMERGENCY USE**
3 **AUTHORIZATION (EUA) AMENDMENT, USE OF A 2-DOSE PRIMARY**
4 **SERIES IN CHILDREN 5-11 YEARS OF AGE**

5

6 **DR. DORAN FINK:** Thank you, Dr. Monto.

7 Good morning. I'm Doran Fink. I'm the Deputy
8 Director for Clinical Review in the Division of
9 Vaccines and Related Products Applications in the
10 Office of Vaccines at CBER, FDA. I'll be introducing
11 today's topic, Pfizer-BioNTech's request for emergency
12 use authorization of their COVID-19 vaccine for use of
13 a two-dose primary series in children 5 through 11
14 years of age.

15 As we all know, the Pfizer-BioNTech COVID
16 vaccine is authorized for use under EUA in individuals
17 12 years of age and older and additionally is approved
18 under the trade name COMIRNATY for use in individuals
19 16 years of age and older for active immunization for
20 prevention of COVID-19 caused by the SARS-CoV-2 virus.

21 Pfizer-BioNTech has now submitted a request

1 seeking an amendment to their EUA for use of a two-dose
2 primary series in children 5 through 11 years of age.
3 This request includes use of a lower mRNA content --
4 ten micrograms -- than authorized for use in older age
5 groups, 30 micrograms. That is, we are considering the
6 use of an age-appropriate dose level because, as we
7 pediatricians are fond of saying, children are not
8 simply small adults.

9 The VRBPAC is convened today to discuss
10 whether available data support that the benefits of the
11 Pfizer-BioNTech COVID-19 vaccine outweigh its risks
12 when administered as a two-dose primary series to
13 children 5 through 11 years of age.

14 We'll hear a more detailed update on the
15 status of the COVID-19 pandemic from our colleagues
16 from CDC a little bit later this morning.

17 But just to touch on some high points, more
18 than 45 million COVID-19 cases, including more than
19 700,000 COVID-19-associated deaths, have been reported
20 to date in the U.S. The Delta variant surge that began
21 during this summer has been associated with increased

1 SARS-CoV-2 transmission and disease, with the most
2 severe outcomes being predominantly among unvaccinated
3 individuals.

4 The effectiveness of currently available
5 COVID-19 vaccines has been both demonstrated in
6 clinical trials and further confirmed in real-world
7 observational studies. While the Delta variant surge
8 is now on a downward trajectory, the current number of
9 COVID-19 cases reported daily in the U.S. remains at
10 approximately 70,000.

11 As we head toward the winter months where
12 people will be forced to go more inside, and as we
13 continue to adhere to a national priority of getting
14 life back to normal as much as possible, which includes
15 keeping children in schools and involved in their
16 activities, it is likely, because we have not reached
17 herd immunity, that transmission of the virus will
18 continue.

19 Children 5 through 11 years of age have
20 accounted for approximately nine percent of the
21 reported COVID-19 cases in the U.S. overall.

1 Currently, they account for approximately 40 percent of
2 all pediatric COVID-19 cases. The current case rate in
3 children 5 through 11 years of age is near the highest
4 of any age group.

5 Clinically significant sequelae of COVID-19,
6 such as long COVID, hospitalizations, and deaths, are
7 less frequent in children than in adults, but
8 nonetheless, these sequelae account for substantial
9 morbidity and mortality in pediatric age groups.

10 Sequelae of particular concern in children include
11 COVID-19-associated myocarditis and multisystem
12 inflammatory syndrome in children, or MIS-C.

13 So, now, we have in front of us an EUA request
14 for use of a COVID vaccine in children 5 through 11
15 years of age. I've lost track of the number of times
16 that I've presented this slide, but just as a reminder,
17 here are the statutory criteria for issuance of an EUA.

18 FDA may issue an EUA of an unapproved medical
19 product following an EUA declaration if the following
20 statutory requirements are met. First, the agent
21 referred to in the EUA declaration can cause a serious

1 or life-threatening disease or condition. We know this
2 to be the case for SARS-CoV-2. Second, the medical
3 product may be effective to prevent, diagnose, or treat
4 the serious or life-threatening condition caused by the
5 agent.

6 Third, the known and potential benefits of the
7 product outweigh the known and potential risks of the
8 product. And, fourth, no adequate, approved, and
9 available alternative to the product is available for
10 diagnosing, preventing, or treating the disease or
11 condition.

12 The balance of benefits and risks is central
13 to any EUA request and decision, and no more so than in
14 today's discussion.

15 Benefit/risk considerations and considerations
16 on data to support emergency use authorization of
17 COVID-19 vaccines for use in pediatric age groups were
18 discussed at the June 10th, 2021, VRBPAC meeting. As
19 discussed in that meeting, the benefits of vaccination
20 in pediatric age groups can be assessed via a clinical
21 endpoint efficacy trial that generates data to directly

1 demonstrate prevention of SARS-CoV-2 infection, or
2 COVID-19 disease.

3 Alternatively, or in addition, we can rely on
4 established regulatory approach called immunobridging,
5 in which immune response biomarkers elicited by the
6 vaccine in a pediatric age group are compared to those
7 elicited in a reference group, or comparator group, for
8 which clinical endpoint efficacy of the same vaccine
9 was previously demonstrated, for example, younger
10 adults who were enrolled in a clinical endpoint
11 efficacy trial.

12 In terms of risks, these are assessed in
13 pediatric age groups by safety evaluation in
14 preauthorization clinical trials enrolling participants
15 of that age. Also, these risks are considered in the
16 context of the safety profile and risks described in
17 older age groups.

18 During the June 2021 VRBPAC meeting, we
19 discussed that the safety database size for pediatric
20 age groups to support an EUA of a COVID-19 vaccine
21 would generally be in the same range as prelicensure

1 safety databases that have supported approval of other
2 preventive vaccines for infectious diseases, provided,
3 of course, that no safety concerns are identified that
4 could reasonably be evaluated in larger
5 preauthorization clinical trials.

6 There was some discussion in June about
7 exactly what that size should be, with some VRBPAC
8 members thinking that it should really be toward the
9 upper end of that range. Of course, no matter what the
10 size of the safety database, there will always be
11 uncertainties regarding benefits and risks, including,
12 for example, the risk of vaccine-associated myocarditis
13 or pericarditis. These uncertainties must be addressed
14 through post-authorization safety surveillance and
15 observational studies.

16 But, going back to today's VRBPAC meeting, as
17 has been mentioned several times, the potential
18 emergency use authorization of COVID-19 vaccines for
19 use in younger children has been a topic of intense
20 anticipation and public debate going back well before
21 we had any age-appropriate data to inform safety or

1 effectiveness.

2 But today, data to inform the benefits and
3 risks of the Pfizer-BioNTech COVID vaccine manufactured
4 to provide for an age-appropriate mRNA content are now
5 available for children 5 through 11 years of age. FDA
6 has conducted a comprehensive and independent review of
7 the data, and the input provided by the VRBPAC today
8 will be considered in FDA's assessment of the data and
9 decision regarding regulatory action.

10 I'd like to close by thanking the VRBPAC for
11 your tireless efforts, critical appraisal of the data,
12 and advice over the many meetings that we've had, in
13 particular over the past month. And I would also like
14 to thank the small army of FDA review staff who has
15 also worked tirelessly, working nights, weekends, and
16 holidays for longer than I can remember, and in
17 particular over the last month literally working around
18 the clock at times to ensure that the information that
19 we present, we are as certain as possible about its
20 accuracy and that we are as transparent as possible in
21 the areas where we have uncertainty.

1 There are too many FDA staff to put their
2 photos up, but please know that you are appreciated.
3 And I look forward to an objective discussion today.
4 Thank you.

5 **DR. ARNOLD MONTO:** Thank you, Dr. Fink. And I
6 want to add my appreciation and that of the Committee
7 to all the work that the FDA staff has done in
8 reviewing the submissions so that we have a fully
9 vetted dossier to work with here as we continue our
10 discussions.

11 And to continue the background from an FDA
12 standpoint, I'd like now to introduce Dr. Ramachandra
13 Naik, the review committee chair of the Division of
14 Vaccines and Related Products Applications.

15 Dr. Naik?

16

17 **FDA'S BACKGROUND PRESENTATION - PFIZER-BIONTECH COVID-**
18 **19 VACCINE EMERGENCY USE AUTHORIZATION AMENDMENT**
19 **REQUEST FOR USE IN CHILDREN 5 THROUGH 11 YEARS OF AGE**

20

21 **DR. RAMACHANDRA NAIK:** Good morning. I'm Ram

1 Naik from the Division of Vaccines and Related Products
2 Applications in the Office of Vaccines, and I'm the
3 review committee chair for this EUA amendment. I'm
4 going to provide a brief background for today's
5 Advisory Committee meeting regarding Pfizer-BioNTech's
6 EUA amendment request for the Pfizer-BioNTech COVID-19
7 vaccine for use in children 5 through 11 years of age.

8 This is the outline of this background talk.
9 I will briefly describe the currently available COVID-
10 19 vaccines and their uses in different populations,
11 provide overview of the EUA amendment request for use
12 of the Pfizer-BioNTech COVID-19 vaccine in children and
13 the clinical package, briefly describe the Pfizer-
14 BioNTech COVID-19 vaccine formulation requested for
15 EUA, an overview of today's agenda, and finally the
16 voting question to the Committee.

17 Regarding the currently available COVID-19
18 vaccines for prevention of COVID-19 caused by SARS-CoV-
19 2, there are three COVID-19 vaccines available under
20 EUA and one licensed vaccine in the U.S.

21 Pfizer-BioNTech COVID-19 vaccine is authorized

1 under EUA for use to provide two-dose primary series
2 three weeks apart in individuals 12 years of age and
3 older; third primary series dose at least one month
4 after the second dose in individuals 12 years of age
5 and older who have been determined to have certain
6 kinds of immunocompromise; a single booster dose at
7 least six months after completing a primary series of
8 Pfizer-BioNTech COVID-19 vaccine in individuals 65
9 years of age and older, 18 through 64 years of age and
10 at high risk of severe COVID-19, 18 through 64 years of
11 age with frequent institutional or occupational
12 exposure to SARS-CoV-2; a single booster dose to
13 eligible individuals who have completed primary
14 vaccination with a different authorized COVID-19
15 vaccine, also called a heterologous booster or mix-and-
16 match booster.

17 Each 0.3 mL dose of Pfizer COVID-19 vaccine
18 contains 30 micrograms of mRNA encoding the viral spike
19 glycoprotein of SARS-CoV-2. The licensed vaccine
20 COMIRNATY was approved on August 23rd, 2021, for use in
21 individuals 16 years of age and older. Each 0.3 mL

1 dose contains 30 micrograms of mRNA, the same amount as
2 that in the Pfizer-BioNTech COVID-19 vaccine.

3 As currently authorized, COMIRNATY can be used
4 interchangeably with the Pfizer-BioNTech COVID-19
5 vaccine to provide doses for COVID-19 primary
6 vaccination or a booster dose.

7 Moderna COVID-19 vaccine is authorized under
8 EUA for use to provide two-dose primary series one
9 month apart in individuals 18 years of age and older,
10 third primary series dose in certain immunocompromised
11 individuals, a single homologous and heterologous
12 booster dose. Please note that the booster dose use
13 population and interval for the Moderna COVID-19
14 vaccine is the same as for the Pfizer-BioNTech COVID-19
15 vaccine or COMIRNATY.

16 The Janssen COVID-19 vaccine is authorized
17 under EUA for use to provide a single-dose primary
18 vaccination in individuals 18 years of age and older, a
19 single booster dose administered at least two months
20 after the primary vaccination to individuals 18 years
21 of age and older, a single heterologous mix-and-match

1 booster dose.

2 Topic for today's Advisory Committee meeting,
3 the EUA amendment request for children 5 through 11
4 years of age. The EUA amendment was submitted on
5 October 6th, 2021. The Pfizer-BioNTech COVID-19
6 vaccine is proposed to be administered as a primary
7 phase of two doses, 0.5 [sic] mL each, containing 10
8 micrograms mRNA, three weeks apart in individuals 5
9 through 11 years of age.

10 The clinical package includes safety and
11 immunogenicity data. Safety data included are from
12 approximately 1,500 vaccine recipients with two months
13 or more safety follow-up post-dose 2 and from
14 approximately 1,600 vaccine recipients with about two
15 weeks safety follow-up post-dose 2. Breakdown of this
16 subject and details of the data will be provided in the
17 later presentation by FDA and Pfizer.

18 Regarding the Pfizer-BioNTech COVID-19 vaccine
19 formulation requested for EUA, the formulation of the
20 Pfizer-BioNTech COVID-19 vaccine for which the EUA is
21 being requested is a modified formulation that is

1 called the Tris/Sucrose formulation. Although the EUA
2 is being requested for the Tris/Sucrose formulation,
3 the vaccine formulation that was used in Study C4591007
4 in children 5 through 11 years of age was the
5 PBS/Sucrose formulation but diluted to adjust the
6 dosage to ten micrograms.

7 The Tris/Sucrose formulation uses tris buffers
8 instead of the phosphate-buffered saline, or PBS, used
9 in the previous formulation. Tris and PBS are
10 buffering agents that help maintain the pH and
11 stability of the product.

12 While PBS/Sucrose formulation of the vaccine
13 indicated for individuals 12 years of age and older
14 uses 0.3 mL dose containing 30 microgram mRNA, the
15 Tris/Sucrose formulation of the vaccine indicated for
16 children 5 to 11 years of age uses 0.2 mL dose
17 containing ten micrograms mRNA.

18 Pfizer has switched to the Tris/Sucrose
19 formulation because it has an improved stability
20 profile. For example, the Tris/Sucrose formulation of
21 the vaccine can be stored at refrigerator temperature

1 that is 2 degrees Celsius to 8 degrees Celsius for up
2 to ten weeks. PBS/Sucrose formulation must be stored
3 frozen at minus 80 degrees Celsius until expiry date or
4 minus 20 degrees Celsius for up to two weeks prior to
5 use.

6 As I stated earlier in Study C4591007 in
7 children 5 to 11 years of age, the PBS/Sucrose
8 formulation was used but diluted to adjust the mRNA
9 content to ten micrograms per dose and 0.2 mL. FDA
10 agreed with Pfizer that an analytical comparability
11 strategy was suitable for evaluation and authorization
12 of the Tris/Sucrose formulation.

13 In the EUA amendment, Pfizer submitted the
14 required chemistry, manufacturing, and controls data
15 supporting analytical comparability of the Tris/Sucrose
16 formulation to the current PBS/Sucrose formulation.
17 The results of the in-process tests, drug product
18 release tests, product characterization data, and
19 ongoing stability studies were submitted for FDA to
20 review, and manufacturing consistency was established.

21 This is an overview of today's agenda. After

1 this FDA introduction, there will be two presentations
2 by CDC. The first one is from Dr. Fiona Havers on
3 epidemiology of COVID-19 in children. Dr. Matthew
4 Oster will present on known safety signals, myocarditis
5 in adolescents and young adults, followed by a five-
6 minute break.

7 Later, Dr. Bill Gruber from Pfizer will
8 provide the sponsor presentation. After that, there
9 will be three presentations by FDA. Clinical
10 presentations will be provided by Dr. Leslie Ball,
11 followed by Hui-Lee Wong, who is going to present on
12 post-market surveillance of COVID-19 vaccines in the
13 pediatric population in the FDA BEST System. Dr. Hong
14 Yang will present the benefit-risk analysis.

15 There will be a lunch break for 35 minutes;
16 followed by open public hearing, about 60 minutes;
17 followed by break; and question and answer session
18 later regarding the applicant and FDA presentations;
19 followed by Committee discussion and voting and the
20 adjournment of the meeting.

21 This is the question to the review Committee:

1 "Based on the totality of scientific evidence
2 available, do the benefits of the Pfizer-BioNTech
3 COVID-19 vaccine when administered as a two-dose
4 series, ten micrograms each dose, three weeks apart,
5 outweigh its risks for use in children 5 through 11
6 years of age? Please vote yes or no."

7 That's the end of this background. Thank you.

8

9

Q&A SESSION

10

11 **DR. ARNOLD MONTO:** Thank you, Dr. Naik.

12 We do have several minutes of time for the
13 Committee to question the FDA representatives about any
14 of the items that they have presented already. We
15 don't want to go into the substance of our discussion
16 yet because we will have plenty of time for that, but
17 mainly the process. So, questions from the Committee,
18 please raise your hands.

19 Dr. Meissner?

20 **DR. CODY MEISSNER:** Thank you, Dr. Naik, for
21 that presentation. And maybe this is a better question

1 for Pfizer, but why does changing the buffer from
2 phosphate-buffered saline to tris change the stability
3 in such a dramatic way? Do we know?

4 **DR. PETER MARKS:** Dr. Meissner, I will let
5 Pfizer respond to that later on. I think I can tell
6 you from my knowledge of chemistry what I believe the
7 answer is, having to do with keeping stability of pH
8 and buffering of solution. But let me defer that to
9 them.

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

11 **DR. ARNOLD MONTO:** I see no further hands
12 raised, so we are in the unusual position of being a
13 little ahead of schedule. It's my pleasure to
14 introduce the CDC presentations. We're going to be
15 hearing first about the epidemiology of SARS-CoV-2 in
16 children and then some of the issues about myocarditis
17 and other potential side effects of the vaccines and
18 also of SARS-CoV-2 infection.

19 So, I hand over to Dr. Fiona Havers, who will
20 be telling us about the epidemiology of COVID-19 in
21 children. Dr. Havers?

1

2 **CDC PRESENTATION: EPIDEMIOLOGY OF COVID-19 IN CHILDREN**

3

4 **AGED 5-11 YEARS**

5

6 **DR. FIONA HAVERS:** Great. Thank you, Dr.
7 Monto. Appreciate the introduction.

8 So, my name is Fiona Havers, and I'm a medical
9 officer in the Division of Viral Diseases and also
10 currently on the Epidemiology Task Force in the CDC
11 COVID-19 public health response.

12 In this presentation, I'm going to give an
13 overview of the epidemiology of COVID-19 in children
14 aged 5 to 11 years, covering incidence and burden
15 estimates, COVID-19-associated hospitalization rates
16 and mortality, multisystem inflammatory syndrome in
17 children, or MIS-C, and post-COVID conditions. I will
18 also talk briefly about transmission and lost in-person
19 learning and other impacts.

20 As of October 22nd, there have been over 45
21 million cases of COVID-19 reported in the U.S. The
22 majority of these have been in adults, as have most

1 hospitalizations and deaths due to COVID-19 illness.
2 However, children have been greatly impacted by the
3 pandemic.

4 Here are the reported cases by age group, with
5 children 5 to 11 years of age in dark blue. In total,
6 there have been more than 1.9 million cases of COVID-19
7 reported in this age group. Starting in July and
8 August of this year, there was a sharp increase in
9 cases in this age group.

10 Over the past two months, we are seeing that
11 children 5 to 11 years, shown here again in dark blue,
12 are making up a greater proportion of total cases,
13 representing 10.6 percent of all cases reported to the
14 CDC the week of October 10th, 2021, while making up 8.7
15 percent of the population in the 2020 census.

16 While the data I showed on the previous two
17 slides were on cases reported to the CDC, many
18 infections are asymptomatic or result in mild illness
19 and are not tested and reported. As one way of
20 assessing the full spectrum of disease burden, CDC
21 conducts an ongoing nationwide seroprevalence study

1 done in collaboration with commercial laboratories. A
2 screenshot of the results on the CDC Data Tracker is
3 shown on the right.

4 Every two weeks, approximately 50,000 people
5 are tested for SARS-CoV-2 antibodies using de-
6 identified residual sera collected by commercial
7 laboratories. While this is a large-scale study, many
8 jurisdictions have a limited availability of pediatric
9 specimens.

10 In the age-stratified analysis I will show you
11 on the next slide, this is restricted to 15
12 jurisdictions that included a hundred or more specimens
13 from children aged 5 to 11 years per two months. We
14 were also limited to a total antibody anti-nucleocapsid
15 assay, which is one that maintains high sensitivity
16 over time and assesses infection-induced antibodies
17 only.

18 This slide here are the weighted infection-
19 induced seroprevalence estimates from November 20th to
20 June 2021. The estimates are aggregated into two-month
21 time periods to increase precision of the estimates.

1 In the figure, time is on the X-axis, and
2 seroprevalence is on the Y-axis. Each color represents
3 a different age group.

4 Children, shown in red, olive, and green,
5 consistently have higher seroprevalence estimates than
6 adults, displayed in blue and purple. The
7 seroprevalence point estimates for ages 5 to 11 are the
8 highest, but the confidence intervals overlap with
9 other pediatric age groups.

10 For ages 5 to 11, shown in the olive line on
11 the top, the seroprevalence increased from 12 percent
12 in November/December 2020 to 42 percent in May/June
13 2021. Investigators also used seroprevalence to
14 estimate the cumulative number of infections and
15 compared that with the number of reported cases by age.

16 Overall, for the general population, the
17 jurisdiction-level infections-to-case ratio had a
18 median of 2.4, with a range of 2.0 to 3.9. For
19 children, the infection-to-case ratio was substantially
20 higher with a median of 6.2 cases for every one
21 infection, with a range of 4.7 to 8.9.

1 These seroprevalence data suggest that
2 infections in children are less likely to be reported
3 compared with adults, but the children are at least as
4 likely as adults to be infected with SARS-CoV-2.
5 Seroprevalence in children continues to increase with
6 estimated more than 40 percent in children 5 to 11 in
7 May and June 2021. Note that the residual sera
8 assessments collected from children through routine
9 clinical care may not be representative of the general
10 population.

11 I'm now going to switch and focus on pediatric
12 hospitalization using data from the COVID-19-associated
13 Hospitalization Surveillance Network, or COVID-NET,
14 which is a population-based surveillance system that
15 collects data on laboratory-confirmed COVID-19-
16 associated hospitalizations among children and adults
17 for a network of over 250 acute-care hospitals in 14
18 states.

19 Cases are identified in COVID-NET if they test
20 positive for SARS-CoV-2 through a test ordered by a
21 healthcare professional and are hospitalized within 14

1 days of the positive test. This chart illustrates the
2 weekly rates of COVID-19-associated hospitalizations by
3 pediatric age group, with children aged 5 to 11 years
4 in red.

5 The cumulative hospitalization rate was 30.1
6 per 100,000 population for this age group as of October
7 2nd. As you can see, rates for this age group have
8 been consistently lower than other pediatric age
9 groups. However, note that in September, population-
10 based hospitalization rates were higher in this age
11 group than at any other previous point during the
12 pandemic.

13 We also do see variations in hospitalizations
14 by race and ethnicity, like American Indian and Alaska
15 Native, Hispanic, and Black non-Hispanic children
16 having cumulative hospitalization rates that were more
17 than three times as high as the hospitalization rates
18 in non-Hispanic white or non-Hispanic Asian children.
19 The disparate impact of the pandemic, including rates
20 of hospitalizations, on these groups is similar to what
21 we have seen in other age groups.

1 To further put the burden of COVID-19 illness
2 in context, we examined rates of COVID-19 versus
3 influenza-associated hospitalization rates among
4 children ages 5 to 11 years using data from COVID-NET
5 and the Influenza Hospitalization Surveillance Network,
6 or FluSurv-NET.

7 FluSurv-NET is a long-standing influenza
8 hospitalization surveillance platform that was
9 leveraged to create COVID-NET. It conducts population-
10 based surveillance for influenza-associated
11 hospitalizations from October 1 through April 30th
12 every year. FluSurv-NET has a similar catchment area
13 to that of COVID-NET and uses similar methods for case
14 ascertainment and data extraction.

15 To compare COVID-19 and influenza-associated
16 hospitalization rates, the COVID-19-associated
17 hospitalization rate was calculated for a one-year
18 period of October 1, 2020, to September 30th, 2021.
19 This annual rate was compared with influenza-associated
20 hospitalization rates from October 1 through April 30th
21 during the 2017/'18 season through the 2020/2021

1 season.

2 Influenza-associated hospitalizations occur
3 seasonally with very low influenza detection during
4 most of September, suggesting that few influenza-
5 associated hospitalizations are missed outside the
6 October through April surveillance window. The
7 FluSurv-NET rates from October through April were used
8 to approximate the annual influenza hospitalization
9 rate.

10 The gray shaded area indicates weeks
11 during which influenza hospitalization surveillance was
12 not conducted. For ease of comparison, influenza-
13 associated hospitalization rates were extended out in a
14 dashed line. The COVID-19-associated hospitalization
15 rates in this age group are shown in yellow, and the
16 influenza-associated hospitalization rates in the three
17 pre-pandemic influenza seasons are shown in red, blue,
18 and green, and the 2020/2021 season is shown in black.

19 Annual COVID-19-associated hospital rates in
20 children ages 5 to 11 is similar to influenza-
21 associated hospitalization rates for 2017/'18 and the

1 2018/'19 season, and they were lower than the
2 influenza-associated hospitalization rates for the 2019
3 and 2020 season.

4 Notably, influenza hospitalization rates for
5 the 2020/'21 season were exceedingly low. There were
6 only nine hospitalizations being reported across all
7 pediatric age groups for the entire season. During
8 this season, mitigation measures such as school
9 closures and mask-wearing were in place. This suggests
10 that the annual rate of COVID-19 hospitalizations would
11 have been much higher than those for influenza during
12 typical influenza seasons had these mitigation measures
13 not been in place.

14 I am having a connectivity issue, so I --

15 **MR. MICHAEL KAWCZYNSKI:** Yeah, we're bringing
16 you back in right now, Fiona. There you go.

17 **DR. FIONA HAVERS:** Great. Thank you. All
18 right. Sorry about that.

19 **MR. MICHAEL KAWCZYNSKI:** You should be able to
20 turn your camera back on again.

21 **DR. FIONA HAVERS:** All right. There we go.

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

2 **DR. FIONA HAVERS:** Great. All right. So,
3 going on to the next slide, we also compared outcomes
4 and interventions in children hospitalized with COVID-
5 19 or influenza in the three pre-pandemic influenza
6 seasons.

7 The median length of stay among children
8 hospitalized with influenza was two days versus three
9 days for children with COVID-19. 21.2 percent of
10 children hospitalized with influenza versus 32 percent
11 of children with COVID-19 required ICU admission. 4.6
12 percent of children with influenza versus 7.2 percent
13 of children with COVID-19 required invasive mechanical
14 ventilation, and a similar proportion of children ages
15 5 to 11 with influenza versus COVID-19 died in the
16 hospital at about 0.6 percent.

17 These data suggest that among hospitalized
18 children, the severity of influenza and COVID-19 in
19 this age group is similar or maybe slightly worse for
20 COVID-19.

21 These next results are from an investigation

1 to identify underlying medical conditions associated
2 with increased risk of severe COVID-19 among children
3 aged 5 to 11 who were hospitalized with COVID-19 from
4 March 2020 through August 2021. All children had a
5 primary reason for admission that was related to COVID-
6 19. This investigation identified underlying medical
7 conditions as risk factors for severe disease, defined
8 as requiring ICU admission or invasive mechanical
9 ventilation during hospitalization.

10 Of 562 children 5 to 11 years, 36 percent had
11 severe disease per this definition, and 0.2 percent
12 died during hospitalization. Approximately two-thirds
13 of the children were Hispanic or non-Hispanic Black.
14 Sixty-eight percent of children had at least one
15 medical condition, with the most common being chronic
16 lung disease, primarily asthma; obesity; neurologic
17 disorders; and cardiovascular disease.

18 This investigation modeled underlying
19 conditions associated with severe disease among
20 children aged 5 to 11 hospitalized with COVID-19 using
21 multivariable generalized estimating equations.

1 Estimates are adjusted for sex and race and ethnicity
2 groups and account for geographic clustering of
3 hospitalizations. As shown in the figure, the adjusted
4 relative risk of severe COVID-19 was statistically
5 significantly higher among children with a history of
6 obesity and feeding tube dependence.

7 As noted previously, during recent months in
8 which the Delta variant has been circulating, there has
9 been an increase in rates of pediatric-associated
10 hospitalizations. However, it was unclear if clinical
11 outcomes were more severe or if the increase in
12 hospitalizations was due to increased community
13 transmission.

14 This slide here compares outcomes from mid-
15 June through the end of August, a period in which the
16 Delta variant was predominant, to pre-Delta period.
17 Hospital length of stay and proportion admitted to ICU
18 and the proportion requiring vasopressor support or who
19 died during hospitalization were similar in both
20 periods. There was a slightly higher proportion of
21 children who required invasive mechanical ventilation

1 during the Delta period, but note that the numbers are
2 relatively small, and we're still continuing to monitor
3 these outcomes.

4 Next, moving to COVID-19 mortality, as of
5 October 22nd, there have been over 730,000 COVID-19
6 deaths reported in the U.S., the vast majority in
7 adults. However, there have been deaths in children.

8 Here are the counts of reported COVID-19
9 deaths by pediatric age. Between January 1st, 2020,
10 and October 16th, 2021, there were 94 COVID-19-
11 associated deaths reported among children 5 to 11 years
12 of age. COVID-19-associated deaths accounted for 1.7
13 percent of all deaths in this age group. Also note
14 that there is a lag in death reporting, and these
15 numbers may increase.

16 To put this in context, this table is showing
17 the top-ten causes of death for children 5 to 11 years
18 of age for the year 2019, the most recent year that
19 complete NCHS mortality statistics are available. In
20 the one-year period of October 3rd, 2020, to October
21 2nd, 2021, there were 66 COVID-19-associated deaths

1 reported for this age group, which would be equal to
2 the eighth leading cause of death.

3 I'm now going to move on from mortality to
4 discussing multisystem inflammatory syndrome in
5 children, or MIS-C. This is a severe hyperinflammatory
6 syndrome typically occurring two to six weeks after
7 acute SARS-CoV-2 infection, resulting in a wide range
8 of manifestations and complications. Approximately 60
9 to 70 percent of patients are admitted to intensive
10 care, and one to two percent die.

11 There have been 5,217 MIS-C cases reported
12 nationally as of October 4th, 2021. Children aged 5 to
13 11 is the age group most frequently affected by MIS-C.
14 The median age of cases is 9 years with 39 percent of
15 cases occurring in children 6 to 11 years old. Sixty-
16 one percent of children with MIS-C are Hispanic/Latino
17 or Black non-Hispanic. Adjusted incidence estimates
18 that 100 to 600 cases per million SARS-CoV-2 infections
19 result in MIS-C, varying with race, ethnicity, age, and
20 region.

21 I'm now going to talk about post-COVID

1 conditions in children. These encompass a wide range
2 of new, returning, or ongoing health problems,
3 including physical and mental health consequences
4 experienced by patients four or more weeks after
5 initial infections with SARS-CoV-2.

6 Data on post-COVID conditions are still
7 lacking. However, it does appear that, while less
8 common in an adult, post-COVID conditions do occur in
9 children. In published reports, frequency of their
10 occurrence have varied depending on the characteristics
11 of children studied and other factors.

12 Further investigation is needed to better
13 characterize post-COVID conditions in children, but a
14 national survey in the U.K. found that seven to eight
15 percent of children with COVID-19 reported continued
16 symptoms 12 or more weeks after their initial
17 diagnosis.

18 Post-COVID conditions in children appear after
19 both mild and severe infections and after MIS-C.
20 Symptoms are similar to those seen in adults and
21 include fatigue, cough, muscle and joint pain,

1 headache, insomnia, and trouble concentrating. It's
2 important also to consider the impact of post-COVID
3 conditions on quality of life, which include
4 limitations of physical activity, feeling distressed
5 about symptoms, mental health challenges, and decreased
6 school attendance and participation.

7 I'm now going to switch gears and talk briefly
8 about children and transmission of SARS-CoV-2.

9 Multiple factors impact the transmission of SARS-CoV-2
10 virus. They include the presence and type of symptoms
11 of the index case, type and timing of exposure, viral
12 load, and variant.

13 Some studies have observed similar secondary
14 infection rates between children and adults, and others
15 have found lower infection rates among children
16 compared with adults, although some of those are
17 earlier studies that likely underestimated infections
18 in children.

19 However, what is clear is that secondary
20 transmission from children both to other children and
21 to adults can and does occur, with data from household

1 and school settings. Multiple household studies,
2 outbreak, and contact-tracing investigations have
3 demonstrated efficient transmission among children and
4 adults in multiple settings.

5 Here is a recent MMWR describing transmission
6 of the Delta variant within a classroom setting in an
7 elementary school with an attack rate of 50 percent
8 among students too young to be vaccinated. You can see
9 from the figure on the right that some students, in
10 blue, were links in transmission to other students,
11 siblings, and their parents.

12 In addition to the severe outcomes of
13 hospitalization, ICU admission, and death and the
14 potential for MIS-C and post-COVID conditions, there
15 are many other adverse outcomes on children from the
16 pandemic, including worsening emotional and mental
17 health, decreased physical activity, and loss of
18 caregivers.

19 Lost in-person learning is another potential
20 outcome of COVID-19 illness and exposure among
21 children. I'm not going to talk about this or other

1 adverse outcomes at length. However, numerous reports
2 have described the negative impact of lost in-person
3 learning on social, emotional, and physical health of
4 children, with disproportionate impacts on children of
5 color.

6 We are showing data from the School Dismissal
7 Monitoring System, which performs daily systematic
8 searches of Google, Google News, and Google Alerts to
9 assess information on unplanned school disclosures
10 [sic], including the number of districts, individual
11 schools, and students and teachers impacted.

12 In this school year to date, more than 2,000
13 schools had unplanned closures, impacting more than a
14 million students. You can see from the map on the
15 right the range of school closures by state.

16 In summary, children ages 5 to 11 are at least
17 as likely to be infected with SARS-CoV-2 as adults.
18 There have been more than 1.9 million reported cases
19 and seroprevalence estimates of more than 40 percent in
20 May and June 2021. Seroprevalence data is consistent
21 with the realization that younger children are less

1 likely to be recognized and tested and reported as
2 cases than adults.

3 Children 5 to 11 years of age are at risk for
4 severe illness from COVID-19. There have been more
5 than 8,300 hospitalizations to date, the
6 hospitalization rates three times as high for non-
7 Hispanic Black, non-Hispanic American Indian and Alaska
8 Native, and Hispanic children as for non-Hispanic white
9 children.

10 Cumulative hospitalization rates are similar
11 to pre-pandemic influenza-associated hospitalization
12 rates despite the mitigation measures put in place
13 during the pandemic. Severity is comparable among
14 children hospitalized with influenza and COVID-19, and
15 approximately a third of the children ages 5 to 11 who
16 are hospitalized require ICU admission.

17 In addition, MIS-C, a serious complication, is
18 most frequently seen among children ages 5 to 11 years,
19 and post-COVID conditions have been seen in children in
20 this age group. Secondary transmission from young
21 school-aged children can and does occur in both

1 household and school settings. And COVID-19 in
2 children leads to lost in-person learning and other
3 adverse outcomes.

4 There have been a lot of people involved in
5 the research included in this presentation and in the
6 development of this talk, and I'd like to thank all of
7 them. And now I am happy to take questions. Thank you
8 very much.

9

10

Q&A SESSION

11

12 **DR. ARNOLD MONTO:** Thank you, Dr. Havers. We
13 now have some time for questions. And we want to be
14 able to examine the epidemiology and impact of this
15 SARS-CoV-2 in the age group in question, so please
16 raise your hands.

17 I see Dr. Kurilla.

18 **DR. MICHAEL KURILLA:** Thank you, Arnold.

19 Thanks for that presentation, Fiona. Two
20 questions, one related to MIS-C. My impression is that
21 the median age is somewhere around 12 or 13 for MIS-C?

1 **DR. FIONA HAVERS:** I believe it's around 9 was
2 what I -- I think it's around 9. And we do see it in
3 older children as well.

4 **DR. MICHAEL KURILLA:** Okay. What I'm trying
5 to get a sense of, is there any evidence in the 12
6 crowd and older as to whether or not vaccination has in
7 fact impacted MIS-C? That's my first question.

8 My second question is -- and I'll just say
9 both at the same -- is, with regard to
10 hospitalizations, there's been some reports that being
11 hospitalized with COVID versus hospitalized for COVID -
12 - that hospitalized with COVID may be on the order of
13 40 to 45 percent for kids.

14 Is your hospitalizations -- do you distinguish
15 that, or any child in the hospital for any reason, if
16 they have a positive COVID test, then they are a COVID
17 hospitalization?

18 **DR. FIONA HAVERS:** That's a great question.
19 So, I do want to clarify that the median age for MIS-C
20 is 9, but we do see it in older children. I don't know
21 yet that we have seen the impact on -- there is a lag

1 in MIS-C reporting, and so I'm not sure that we would
2 necessarily tease out if there has been a decrease in
3 rates of MIS-C in older children who are eligible for
4 vaccine and adolescents. We have seen it slightly
5 decrease in proportion of hospitalizations for children
6 ages 12 to 17 relative to what they had been before
7 when you compare it to other pediatric age groups.

8 Coming to your second question regarding the
9 proportion of children that are hospitalized, in COVID-
10 NET, we do have the ability to see kind of what their
11 primary reason for admission was. For the rate
12 population, we include all children that have a
13 positive SARS-CoV-2 regardless of the reason for
14 admission.

15 But, when we're doing further analyses like
16 the ones where I presented with underlying conditions
17 and the outcomes, we remove the children that were
18 admitted for other reasons. And those are primarily
19 things like -- in this age group, in the 5- to 11-year-
20 olds, it was like planned surgeries, trauma,
21 psychiatric admissions requiring medical care.

1 In this age group, in 5- to 11-year-olds, we
2 had about, I think, 19 percent of children who were
3 admitted with a positive SARS-CoV-2 test were probably
4 admitted primarily for other reasons. It's not always
5 totally clear cut, and sometimes the reason for
6 admission then develops into a more COVID-19 illness-
7 related admission. But we thought it was about 20
8 percent.

9 But, in terms of the outcomes, the 36 percent
10 that I presented that ended up in the ICU in this age
11 group, those were all just among children who were
12 primarily admitted for COVID-related illness.

13 **DR. MICHAEL KURILLA:** Okay. And then, last
14 question, what percentage of the deaths in this age
15 group is MIS-C related?

16 **DR. FIONA HAVERS:** That's a great question,
17 actually. These deaths are reported through two
18 different systems. And of the deaths that I noted
19 there in this age group, about 23 of them -- or about
20 20 or so; we actually looked up these numbers yesterday
21 to see what the overlap was -- about 20 of them were

1 related to MIS-C. However, there have been 44 deaths
2 total for MIS-C that have been reported in children
3 under 18. So, that's actually among all children.

4 So, I think a proportion of them, but there's
5 two slightly different reporting systems, and there is
6 a lag for both death-reporting for COVID-associated
7 deaths and then for MIS-C deaths, which are reported
8 separately. So, the numbers that I included for the 5-
9 to-11 age group does include some MIS-C deaths but not
10 all of them.

11 **DR. MICHAEL KURILLA:** All right. Thank you.

12 **DR. ARNOLD MONTO:** Thank you. Dr. Hildreth?

13 **DR. JAMES HILDRETH:** Thank you, Dr. Monto.

14 Thank you, Dr. Havers, for your very informative
15 presentation.

16 I just want to clarify a couple of things that
17 you referenced in your talk: that if I understand it,
18 the prevalence of COVID-19 among -- or at least
19 infection by SARS-CoV-2 among children this age is 42
20 percent as of early summer. Is that correct?

21 **DR. FIONA HAVERS:** That was what we were

1 seeing in the seroprevalence studies, yes.

2 **DR. JAMES HILDRETH:** And do you have any data
3 as to whether or not that prevalence is uniform across
4 the racial groups? Is it higher in some than others?

5 **DR. FIONA HAVERS:** The residual clinical sera
6 that's used in these studies I don't think has complete
7 race and ethnicity data, so I don't think that we would
8 know that. I do think that we know from other studies
9 and also from the studies that have data on
10 hospitalizations that the incidence, as I mentioned,
11 among non-Hispanic Black and Hispanic and AI/AN
12 children is much higher in terms of hospitalization.

13 So, I imagine that we've seen a greater impact
14 on communities of color in general, so I would imagine
15 the prevalence is probably likely higher in children of
16 color, as well, for seroprevalence.

17 **DR. JAMES HILDRETH:** Okay. Thank you.

18 **DR. ARNOLD MONTA:** Thank you. Dr. Levy?

19 **DR. OFER LEVY:** Thank you, Dr. Havers, for an
20 excellent presentation.

21 I wanted to ask a few questions regarding

1 obesity. Clearly, obesity has been well established as
2 a risk factor for severe COVID in adults. Obesity
3 rates have been increasing among children in the United
4 States. You highlighted in your presentation some
5 analyses that suggested obesity is also a risk factor
6 for severe COVID in children.

7 As you know, many factors impact obesity,
8 including regional factors, racial/ethnic factors, and
9 others. And I'm just wondering -- it went by a little
10 quickly -- what kind of adjustments did you make to
11 make sure that wasn't confounded in the pediatric case?
12 How well can we hang our hat on obesity in children, in
13 5- to 11-year-olds, as a risk factor here? Thank you.

14 **DR. FIONA HAVERS:** No, thank you for that.
15 The multivariable model that I showed adjusted for age.
16 It also adjusted for geographic clustering of
17 hospitalizations within the COVID-NET system, and we
18 also adjusted for race and ethnicity as well as other
19 underlying medical conditions. And we have very
20 complete race and ethnicity data within that system.

21 So, I think that -- I mean, there's obviously

1 a lot of factors that go into it, but I think that it
2 did seem to be an independent risk factor. Those were
3 only among children that were already hospitalized for
4 COVID-19 illness, and so I think that you should keep
5 that in mind when looking at the data. But that was
6 among severe outcomes among already-hospitalized
7 children.

8 **DR. OFER LEVY:** But you do believe that's an
9 independent risk factor, then, for severe outcomes?

10 **DR. FIONA HAVERS:** I think so, yes.

11 **DR. OFER LEVY:** Yeah. Thank you.

12 **DR. FIONA HAVERS:** Yeah.

13 **DR. ARNOLD MONTTO:** Thank you. Dr. Gans?

14 **DR. HAYLEY GANS:** Thank you, Dr. Havers. I
15 really appreciate the information you provided to us
16 today.

17 I had a couple of questions about long-term
18 effects because I think those are very important. And
19 I realize this is a new virus; we haven't had it for
20 that long. But there's been at least a year for some
21 of the studies, particularly relating to some of the

1 long-term outcomes with MIS-C.

2 And I'm particularly interested in some of the
3 data that is looking at the cardiac effects of long
4 term, particularly because we know that this virus has
5 receptors on the heart, and so even less symptomatic
6 disease could lead to scarring and electrical
7 abnormalities. So I'm particularly interested in
8 breaking that down a little further.

9 And I know we're going to have a talk on
10 myocarditis/pericardi- -- I don't know if that's going
11 to be covered there. But since you talked about MIS-C,
12 there are some studies looking particularly long term
13 (audio skip) wondered if you had any further breakdown
14 of the data.

15 And then, related to Dr. Hildreth's, the long-
16 term outcomes in children, since there does seem to be
17 health disparities in illness and hospitalizations,
18 have people looked at the long-term outcomes (audio
19 skip) in those, (audio skip) well, to see (audio skip)
20 they're at higher risk for some of the adverse (audio
21 skip)?

1 **DR. ARNOLD MONTO:** And, as we discuss this,
2 Dr. Havers, I'm being reminded we're going to be
3 hearing about this again in the next presentation.
4 Please go ahead.

5 **DR. FIONA HAVERS:** Yeah. I'm going to defer
6 all of the questions about myocarditis to Dr. Oster,
7 who's a pediatric cardiologist and I think will
8 probably have the best data available on that question.

9 In terms of the long-term outcomes, I don't
10 know that this is as well studied as we would like yet.
11 I mean, I think there are studies going on that are
12 looking at long-term outcomes in different groups, but
13 I don't necessarily think -- we don't have a lot of
14 good data or very concrete data on that yet. But I
15 definitely think it has been a very active research
16 area.

17 **DR. ARNOLD MONTO:** Thank you. Dr. Perlman?

18 **DR. STANLEY PERLMAN:** Yes. So, this is
19 actually a continuation of the questions that were just
20 asked because one of the things in thinking about the
21 cost-benefit ratio of this vaccine is its effects on

1 long-term disabilities. And it sounds like a lot of
2 what we're hearing is that these children are
3 developing something that looks like chronic fatigue
4 syndrome or some version of that.

5 And do we have any idea, is this behaving like
6 chronic fatigue and not disappearing, or is it going
7 away after a few months? Do you have any information
8 about the duration of how long those symptoms last?

9 **DR. FIONA HAVERS:** I think that it does go
10 away in some children, but I think that this research
11 is still ongoing. I don't have great answers to that
12 right now. I mean, I think that the studies that have
13 come out have shown that there has been some fairly
14 durable symptoms and that people several months out of
15 their infection are still having symptoms.

16 But I think, in terms of much longer effects,
17 we don't have a lot of great data in the pediatric age
18 population. And then Dr. Oster, I think, is going to
19 be also talking about some of the longer-term cardiac
20 side effects of MIS-C in his presentation as well. So,
21 he may have some more information to share there.

1 **DR. STANLEY PERLMAN:** Okay. Thank you.

2 **DR. ARNOLD MONTO:** Thank you. Dr. Wharton?

3 **DR. MELINDA WHARTON:** Fiona, great
4 presentation. Do we know anything about the frequency
5 of reinfection or second infections in children?

6 **DR. FIONA HAVERS:** The question of reinfection
7 and second infection is definitely an area of active
8 interest. I think that we don't have great data on
9 that at this point. I do think that we are seeing more
10 and more second infections just in the population in
11 general, but I don't have any data on this right now.

12 **DR. ARNOLD MONTO:** Dr. Portnoy?

13 **DR. JAY PORTNOY:** Thank you, Dr. Havers, for
14 that presentation. It obviously took a lot of effort
15 to accumulate all of that information. I have two
16 quick questions. First one is about the seroprevalence
17 surveillance that you're doing. Do you have the
18 ability to separate recent infections from infections
19 that happened a long time ago, perhaps by looking at
20 IgM and IgG antibody types?

21 **DR. FIONA HAVERS:** For the data that I

1 presented here, I think that they don't have a sense of
2 the timing of infection. Also note that of the
3 residual sera specimens that they have, they exclude
4 people that have sort of an ICD-10 code or something
5 that indicates that they were being evaluated for a
6 recent SARS-CoV-2 infection.

7 So we don't have good information on the
8 timing of it. I mean, I do think that the change in
9 time in seroprevalence does sort of give some idea kind
10 of on a general population level, but we don't have
11 good individual-level data on symptoms that go in with
12 the seroprevalence studies.

13 **DR. JAY PORTNOY:** And given the fact that
14 there's likely to be an underestimate of the prevalence
15 of COVID-19 in young children because many of them are
16 asymptomatic, how do you adjust for the hospitalization
17 rate given the fact that you're likely underestimating
18 the total number of people who have the disease?

19 **DR. FIONA HAVERS:** Well, I think for
20 hospitalizations, it's a little bit different. I
21 think, generally speaking, you're totally right. I

1 think that cases and infections are definitely
2 underestimated in kids because they are not being
3 tested, and many of them are asymptomatic or have mild
4 illness or don't seek medical care.

5 For hospitalizations, I think many of the
6 children, when they're being admitted and meet the bar
7 for hospitalization, they generally are being tested
8 for SARS-CoV-2. And so, for the COVID-NET data that we
9 presented, those are all based on clinician-driven
10 testing. And so, a child did have to have -- it wasn't
11 surveillance testing. A child had a clinician order a
12 SARS-CoV-2 test.

13 So, it is possible that we are
14 underestimating, a little bit, the hospitalization
15 rates. But I think, generally speaking, for
16 hospitalizations, we feel pretty good that we have good
17 case ascertainment within COVID-NET and that we're not
18 missing a lot of pediatric hospitalization cases with
19 more serious illness.

20 **DR. JAY PORTNOY:** But when you express it in
21 terms of --

1 **DR. ARNOLD MONTO:** Thank you. We're --

2 **DR. JAY PORTNOY:** Okay.

3 **DR. ARNOLD MONTO:** -- going to have to move
4 on. We have more hands, and we're going to be having
5 lots more time for discussion.

6 Dr. Moore?

7 **DR. PATRICK MOORE:** Thank you. That was a
8 really nice presentation. It really helped a lot. Do
9 you have any data from COVID-NET or other places that
10 tells us more about whether there's vaccine efficacy or
11 effective vaccines on, for instance, nucleocapsid
12 antibodies through a conversion, particularly among 12-
13 to 18-year-olds, getting at does the vaccine look like
14 it's inhibiting transmission, particularly asymptomatic
15 transmission, which is so critical to this epidemic?

16 **DR. FIONA HAVERS:** I am not aware of data,
17 particularly in the adolescent age group, that shows
18 that in terms of its impact on seroprevalence. We
19 don't have that in COVID-NET. I can certainly check
20 with my CDC colleagues and perhaps get back to you on
21 that later today.

1 **DR. PATRICK MOORE:** It's such a (audio skip)
2 question.

3 **DR. FIONA HAVERS:** Yeah.

4 **DR. ARNOLD MONTO:** Thank you. One more
5 question because we're going to be circling back again
6 in a more general discussion after the next
7 presentation.

8 Dr. Sawyer, final question.

9 **DR. MARK SAWYER:** Thanks, Arnold.

10 So, we just discussed that a fair number of
11 children will have been infected and not tested and
12 recognized at the time. In the 12- to 16-year-old age
13 group, do we have information about receipt of vaccine
14 in close proximity to prior infection and what that
15 does to the safety profile of the vaccine? Because
16 inevitably, as we start rolling out this vaccine in
17 younger kids, we're giving it to some children who may
18 have been recently infected. And I'm wondering if you
19 have that data, or are we going to get to that point
20 sometime today?

21 **DR. FIONA HAVERS:** That's a great question.

1 I'm going to defer vaccine safety questions to Dr.
2 Oster and his presentation, and I think he'll be in a
3 better position to answer that than I will because I
4 think you're certainly going to address, potentially,
5 vaccination close to the time of natural infection.
6 So, (audio skip) question to him.

7 **DR. ARNOLD MONTO:** Thank you. That's a nice
8 segue into the next presentation, "Known safety signals
9 (Myocarditis in adolescents and young children)," Dr.
10 Matthew Oster. He's from the Center of Disease Control
11 COVID Response. He's also a pediatric cardiologist at
12 Sibley Heart Center, the Children's Healthcare of
13 Atlanta, Emory University.

14 Dr. Oster?

15

16 **CDC PRESENTATION: mRNA COVID-29 VACCINE-ASSOCIATED**

17 **MYOCARDITIS**

18

19 **DR. MATTHEW OSTER:** Great. Thank you very
20 much for having me. The usual CDC disclosures.

21 Today, I was asked to talk about three areas,

1 really, as it pertains to myocarditis, but first to
2 give a brief update on cases of myocarditis after
3 COVID-19 vaccine -- and some of this will be
4 information you may have seen previously -- but then
5 talking a little bit more about the different types of
6 myocarditis that we have seen, especially in the COVID
7 era, and then what do we know so far about outcomes
8 following myocarditis?

9 So, first, I'd like to present some
10 information from the Vaccine Adverse Event Reporting
11 System, or VAERS. This graph shows the estimates of
12 reports of myocarditis among males. This is per one
13 million doses administered with a seven-day risk period
14 with an estimated background incidence rate of about
15 0.2 to 1.9 per million.

16 The shaded areas shown show a reporting rate
17 that exceeded the background incidence. As you can
18 see, for those receiving Pfizer, following dose 1, it
19 exceeded background for ages 12 to 24, and then for
20 dose 2 for ages 12 to 49 with peaks in adolescents.

21 For Moderna, similarly, there was an excess

1 risk noted after dose 1 in young adults, as well in
2 dose 2 in young adults from 18 to up to 49 with the
3 peak again in the 18-to-24 age range.

4 For females, the rates were much lower,
5 although there were some areas where there was an
6 excess risk. This was following dose 2 primarily, both
7 for Pfizer in females ages 12 to 24 and for Moderna in
8 females ages 18 to 29.

9 Before the VAERS reports, I wanted to touch a
10 moment on what we know about those less than 29 years
11 of age. CDC has been reaching out to reporters to find
12 more information and to investigate these cases. Of
13 about 1,600 total preliminary reports, 877 were able to
14 be adjudicated as meeting case definition.

15 There was a small number that were able to be
16 determined not meeting case definition per myocarditis.
17 There are 637 that are still under review, meaning
18 there was not enough information given at the time of
19 the VAERS reports to truly confirm the case, but
20 investigations are ongoing to gather more information.

21 Of those meeting case definition, 829 were

1 hospitalized, and, at the time of their report, 789 had
2 been discharged with 77 percent of those reported to
3 have recovered from their presenting symptoms at the
4 time of the report. Thirty-four were not hospitalized
5 and were seen in outpatient settings.

6 This is data from Vaccine Safety Datalink, an
7 ongoing project to evaluate health records from a
8 number of different health systems to look for active
9 signals of safety risks following vaccine
10 administration. Vaccine Safety Datalink, I'm going to
11 present the data for just the adolescents here, ages 12
12 to 17 years. This is only those receiving Pfizer-
13 BioNTech. And they looked at not only a 0- to 7-day
14 interval but also a 0- to 21-day interval.

15 But, as you can see, the primary events were
16 in the zero- to seven-day interval, similar to what was
17 seen in VAERS, with no events in the comparison
18 interval. Thus, rate ratios were not able to be
19 computed, but, as you can see, the risk was high.

20 They also reported excess cases per risk
21 period per one million doses, with the highest being

1 after dose 2 with an estimate in the zero-to-seven
2 group about 54. And those numbers are very similar to
3 what was seen in the VAERS data.

4 But now I'd like to speak a little bit,
5 though, about the different types of myocarditis.
6 Myocarditis, put simply, is inflammation of the
7 myocardium, or heart muscle. But when we talk about
8 myocarditis, there can be different etiologies,
9 presentations, and outcomes.

10 So, classic myocarditis, for lack of a better
11 term -- when I say that, I'm going to be speaking about
12 myocarditis in the pre-COVID-19 era. But, since the
13 onset of the pandemic, we have noticed some other types
14 of myocarditis, namely COVID-19-related myocarditis,
15 that is, acute COVID-19 infection leading to myocardium
16 inflammation. MIS-C myocarditis, which you heard a
17 little bit in the earlier presentation, I'm going to
18 expand upon. And then COVID-19 vaccine-related
19 myocarditis is one of our very concerning adverse
20 events.

21 So, first, our classic or pre-COVID

1 myocarditis is thought to have a number of different
2 etiologies. Most are thought to be due infectious when
3 a cause is found, but often, a cause is not necessarily
4 identified. We'll call that idiopathic myocarditis.

5 But there can be a number of non-infectious
6 etiologies as well, and these types of myocarditis are
7 still around in our background, right? So, we need to
8 remember to be checking for these and to be conscious
9 of those in patients.

10 This slide shows the epidemiology of
11 myocarditis in pre-COVID era with children on the left
12 and adults on the right. And you'll notice a couple of
13 things here. In children, there was a peak kind of in
14 the first year of life, and many of these cases are
15 thought to have a genetic component. And then, at
16 least among children, it starts to peak around
17 adolescence.

18 In adults, again, peaks start in adolescence
19 and young adulthood and then slowly comes down over
20 time, particularly for males. Females seem to have a
21 more constant rate over time with maybe a slight uptick

1 in the 50s.

2 So, two things to note about these graphs.
3 So, first, at least for the 12-and-older range, these
4 patterns seem very similar to what we were seeing for
5 the vaccine-related myocarditis. And I think these are
6 different entities, but it is interesting that the
7 epidemiology in terms of incidence and some of the sex
8 distribution seem to have a very similar pattern.

9 And then, second, I know we're talking about
10 children 5 to 11 years today. If that pattern holds,
11 then we would expect that the rates of myocarditis in
12 the 5- to 11-year-old group, even if they were given
13 the same dose in the lower group, would be less. But,
14 again, this is comparing two diseases which may not be
15 exactly similar.

16 The pre-COVID-era myocarditis in children can
17 have a very severe outcome, especially in the younger
18 children. But overall mortality is about four to seven
19 percent, with heart transplant four to nine percent of
20 cases.

21 What about MIS-C myocarditis, or myocarditis-

1 associated multisystem inflammatory syndrome? In data
2 reported to CDC from states on case report forms,
3 myocarditis was indicated as occurring in 17 percent of
4 cases. In early reports from COVID-NET, cardiovascular
5 involvement overall was quite common, about 80 percent
6 of children having some sort of cardiovascular
7 involvement, with elevated troponin in about 50
8 percent. Those cases would -- combination of elevated
9 troponin and symptoms would be case definition for
10 myocarditis as per the CDC definition.

11 And what about myocarditis due to COVID-19?
12 In this MMWR, we looked at the association between
13 COVID-19 and myocarditis, and this is using hospital
14 administrative data from March of 2020 through January
15 of 2021. As you'll see here, one of the highest areas
16 for risk, at least for myocarditis due to COVID, was in
17 the less-than-16-year age group.

18 However, it is unclear in looking just at this
19 data how much of that myocarditis was due to acute
20 COVID infections versus how much was due to cases of
21 MIS-C. Prior to January 2021, there was not a specific

1 ICD-10 code for MIS-C, and so, many cases had COVID
2 classified as part of their disease illness.

3 This is data from two large
4 administrative -- and some other -- health records data
5 sets. This is very preliminary data that these
6 entities shared with us.

7 So, first, using EPIC data -- this is
8 including over about 700 hospitals with primarily
9 inpatient. There are some outpatients in here. But in
10 looking at cases of COVID-19 without MIS-C -- there was
11 no codes for MIS-C; this is since January this year --
12 myocarditis was diagnosed in 0.02 percent. But in MIS-
13 C, myocarditis was diagnosed in about eight percent.
14 So, most of the myocarditis seems to be due to MIS-C.

15 Looking at data from Children's Hospital
16 Association with their Pediatric Hospital Information
17 System, we see a similar trend where the acute cases of
18 COVID-19 -- this is only inpatient admission from their
19 data -- myocarditis was diagnosed in 0.08 percent of
20 COVID-19 admission but nine percent of MIS-C
21 admissions, with MIS-C myocarditis outnumbering the

1 COVID-19 myocarditis in both base systems.

2 So, it appears that a lot of the myocarditis,
3 at least associated with COVID, in kids seems to be due
4 to MIS-C, although there are certainly some cases due
5 to COVID-19, but it was much rarer.

6 Now I'd like to present some early data from a
7 paper published on medRxiv. This is actually a report
8 from my role at Children's Healthcare of Atlanta, where
9 I supervised one of our cardiology fellows to look at
10 what was our single-center experience with the
11 different types of myocarditis. We did not include
12 acute COVID-19 myocarditis because we really hardly had
13 any cases.

14 So, this graph, it seems busy, but I'm going
15 to show you just a highlight here, though, is that for
16 a number of different laboratory measures -- which are
17 troponin, B natriuretic peptide, lymphocytes, white
18 blood cells, C-reactive protein, and platelets -- the
19 classic myocarditis, which is the leftmost group in
20 each panel, and the vaccine-related myocarditis, which
21 is the rightmost group in each panel, seem quite

1 similar in their presentation. And the MIS-C group in
2 the middle is very different, at least in their
3 presentation.

4 This makes us think that, again, not all these
5 types of myocarditis are the same. When we looked at
6 acute outcomes -- and so, for this one, we looked
7 primarily at ejection fraction echocardiogram -- there
8 were no deaths in any of these groups. So, first,
9 let's look at the blue and the red groups.

10 So, the blue is the classic or pre-COVID-19
11 myocarditis group, and the red is the MIS-C myocarditis
12 group. Both of these groups, on presentation, at
13 least, had a fair number of patients, so about two-
14 thirds of their patients, who had decreased ejection
15 fraction by echocardiogram.

16 But as you'll see, whereas previously the
17 classic myocarditis group, by about 10 to 15 days,
18 about 30 percent of children still had decreased
19 ejection fraction, by that same period in the MIS-C
20 group, nearly all had returned to normal ejection
21 fraction, so normal function by their echocardiogram.

1 In the vaccine-related myocarditis group --
2 and this is just in our first nine patients --
3 decreased function, decreased ejection fraction, was
4 rare, in about two of the nine patients. It was not
5 nearly as common. And those patients had full
6 resolution back to normal function within a few days.

7 Now let's move to some of the longer-term
8 outcomes. So, what do we know about the pre-COVID era
9 for outcomes? First, we know that myocarditis portends
10 a risk of sudden death in children and adolescents. In
11 a paper published last year, it was noted that five to
12 ten percent of sudden death in adolescents and young
13 adults was attributable to myocarditis.

14 And I want to make clear that's not saying
15 that five to ten percent of those with myocarditis are
16 at risk for sudden death. It's saying that five to ten
17 percent of sudden death on autopsies were found to have
18 myocarditis, usually not previously diagnosed. And it
19 is findings like this that help inform the latest
20 guidelines in the American Heart Association/American
21 College of Cardiology.

1 These were published in 2015, and their
2 approach to myocarditis is that children, before
3 returning to competitive sports for children and
4 adults, should basically have a full cardiac evaluation
5 to look for any evidence of decreased function,
6 myocardial information, or arrhythmias.

7 Many kids have abnormalities on their MRI in
8 myocarditis. I didn't show it here, but in the VAERS
9 reports, about 72 percent who had an MRI had some
10 inflammation or other findings consistent with
11 myocarditis on their MRI. But it's unclear whether
12 resolution of late gadolinium enhancement -- and you'll
13 see that come up later -- should be required in MRI.
14 This is still under research and trying to figure out
15 the meaning of this.

16 But the important thing to note, also, is that
17 this recommendation from American Heart
18 Association/American College of Cardiology specifically
19 mentioned that it is independent of age, gender, and
20 left ventricular function. So having normal function
21 does not necessarily mean that you're out of the woods

1 from a risk standpoint.

2 So, what are risk factors, though, for
3 myocarditis outcomes? Again, in the pre-COVID era --
4 and this paper was recently published, which had a good
5 summary of factors and variables that can lead to a
6 good outcome or poor outcome.

7 So, as it relates to vaccine-associated
8 myocarditis, I put in a box some of their features,
9 which are very similar or might portend a good outcome.
10 So, first, chest pain and Class New York Heart
11 Association I and II, this is a very common
12 presentation of vaccine-associated myocarditis.
13 They're not presenting, typically, with some of the
14 other features that you'd see that portend a bad
15 outcome.

16 Electrocardiogram -- many of the vaccine-
17 associated myocarditis cases have ST elevation with
18 myocarditis, but other findings are rare. Troponin --
19 early rise and fast decline associated with a good
20 outcome, and that is the typical story that we see with
21 vaccine-associated myocarditis, although occasionally

1 there can be some persistent abnormal levels.

2 And then echocardiogram, preserved LV ejection
3 fraction at onset or early improvement of that, that
4 seems to be the typical finding with vaccine-associated
5 myocarditis.

6 And, again, here we'll see cardiac magnetic
7 resonance imaging. This is the area that we need to
8 follow and see in these kids because presence of late
9 gadolinium enhancement or persistence of this over time
10 can be associated with a poor outcome. And, as I
11 mentioned, on presentation, a fair number of those with
12 vaccine-associated myocarditis did have some of these
13 findings despite having all the other factors
14 associated with a good outcome.

15 What are some of the long-term outcomes of
16 pre-COVID myocarditis? This is a paper from 2004, so
17 it is from a couple of decades ago, looking at
18 myocarditis in children. And they broke these up into
19 three groups and looked at them over about 14 years.
20 Top group is the acute myocarditis group. Second is
21 borderline myocarditis, and third is groups of dilated

1 cardiomyopathy that wasn't inflammatory, so not really
2 an acute myocarditis picture.

3 And it showed that those in acute myocarditis
4 actually did quite well over time. So, once you get
5 over the acute phase, the long-term outcomes tended to
6 be quite good in children. In adults, the picture is a
7 little bit different. Again, this is an older study,
8 from 1995.

9 This study was comparing immunosuppressive
10 therapy for myocarditis and showed no difference in
11 long-term outcomes. But the long-term outcomes in this
12 group -- and in total, there were 111 patients with a
13 mean age of 42 years -- at about five years, cumulative
14 mortality is about 50 percent.

15 What do we know about the three- to six-month
16 outcomes for multisystem inflammatory syndrome in
17 children? This question came up earlier. So, this is
18 looking first just at ejection fraction, so the cardiac
19 function, the red line being normal ejection fraction.
20 And, as you can see in that first blue box, a number of
21 kids had an abnormal ejection fraction on presentation

1 or during their lowest EF during their course of their
2 illness.

3 But, by discharge, most have reached normal
4 ejection fraction, and by two weeks, almost all had
5 normal, with then all having normal at six months. And
6 this was in 50 children of a median age of about 8.5
7 years.

8 What about the cardiac magnetic resonance
9 imaging? So, this is in about 19 kids, and this group
10 did follow-up MRIs, and they found no persistent
11 cardiac changes in cardiac MR at follow-up. There have
12 been some other reports here, some smaller changes, but
13 it is quite rare in kids.

14 Not shown here, because I was asked to speak
15 primarily on myocarditis, but this question did come up
16 -- concerns about other factors. There was a paper
17 published in the U.K. looking at some six-month
18 outcomes for kids with MIS. They had similar findings
19 from some of the cardiac findings, but they also looked
20 at some quality-of-life questions.

21 I will point out about 20 to 30 percent of

1 children and their parents reported either mild or
2 severe impairment on at least one scale with the
3 highest being an emotional scale, having some
4 difficulties with the emotional level. There was no
5 control group, so it's hard to determine how much of
6 that was due to just the COVID pandemic setting versus
7 their own personal illness. But it is interesting to
8 continue to follow.

9 What do we know about COVID-19 vaccine-
10 associated myocarditis in adolescence? We don't know a
11 whole lot yet. This paper, looking at 54 patients, a
12 mean of 15 years, again 92 percent male -- this was
13 looking really at about one month since vaccination for
14 a mean of 35 days. About 13 percent still had
15 persistent symptoms despite all of them having normal
16 echocardiograms. Eighty percent had normal EKGs, but
17 about 20 percent obviously still had some abnormality.

18 Troponin, when it was checked, was usually
19 normal, although a few had borderline findings. And
20 only two had had MRI by this time, at about two months
21 and two and a half months -- did show improvement in

1 myocardial edema but some persistence of late
2 gadolinium enhancement.

3 Vaccine Safety Datalink is also following up
4 the cases that have been identified. They're doing
5 chart review to look at their follow-up. As of earlier
6 this month, they had done reviews of 47 cases, and 37
7 of whom had had at least one follow-up visit. And, of
8 those, some of them had had a follow-up visit at least
9 three months since their initial encounter.

10 And I'll point out down this slide, any new or
11 worsening symptoms, present down about 20 to 50
12 percent. And this did vary by age. Troponin levels,
13 EKG, and echocar- -- often had some abnormalities,
14 again in about 20, 50 percent. Echocardiograms were
15 typically normal when they were performed. Only one
16 MRI had been completed in this group to date.

17 I classified these groups as their current
18 status, and these are not mutually exclusive groups.
19 But, by age, about 30 percent of those 12 to 17 have
20 been given a status of recovered, meaning no
21 medications, no exercise restrictions, no ongoing

1 symptoms, and about 50 percent of those in the 18- to
2 39-year age.

3 CDC is also doing an investigation to
4 investigate the long-term effects of myocarditis, and
5 CDC is reaching out to patients who have been
6 identified in VAERS case reports. And the purpose is
7 to assess their functional status and clinical outcomes
8 long term.

9 There's a two-part component to the survey:
10 first, contacting the patients themselves or their
11 parents to assess functional status, clinical symptoms,
12 quality of life, and other ongoing clinical needs; and
13 to ask them to identify a healthcare provider that
14 they're seeing, which is usually a cardiologist, to try
15 to gather information on their cardiac health and
16 functional status.

17 So, to date, about 680 patients have reached
18 the 90-days-post-myocarditis diagnosis. About 41
19 percent of these have received one phone call. About
20 60 percent of those have completed the survey, and
21 about 168 patients were able to identify -- 132 of them

1 were able to identify a cardiologist or healthcare
2 provider. About 26 of them had completed the survey.
3 So, more data on this will be forthcoming.

4 In summary, myocarditis is a rare but
5 important adverse event following COVID-19 vaccination,
6 and not all myocarditis is the same. There may be some
7 similarities in presentation with some or in acute
8 outcomes with others, so it's hard to do straight
9 comparisons. So, that's sometimes just the best that
10 we have.

11 And we really need to see what the long-term
12 outcomes for these kids will be. So far, the data for
13 follow-up results is sparse, but ongoing follow-up is
14 in progress.

15 Thank you very much, and I'd specifically like
16 to thank Tom Shimabukuro, John Su from the Vaccine Task
17 Force, and Niki Klein from Vaccine Safety Datalink for
18 sharing some slides, Sam Butler from EPIC, and Matt
19 Hall and Cary Thurm from the Children's Hospital
20 Association, for sharing some very preliminary data.

21 Thank you. I'm happy to take any questions.

1

2

Q&A SESSION

3

4 **MR. MICHAEL KAWCZYNSKI:** Arnold looks like
5 he's reconnecting his audio here momentarily, so we'll
6 just give him a moment. There we are.

7 Arnold, are you back?

8 **DR. ARNOLD MONTA:** Am I on?

9 **MR. MICHAEL KAWCZYNSKI:** Yes, you are, sir.

10 Take it away.

11 **DR. ARNOLD MONTA:** Okay. Somebody sent me a
12 FaceTime call and knocked me off.

13 Dr. Pergam?

14 **DR. STEVEN PERGAM:** Thanks, Dr. Oster. I
15 think this was a fantastic presentation to review. I
16 have two questions, and hopefully, they'll be brief
17 answers.

18 One is, in the distribution epidemiologically
19 of myocarditis in kids, interestingly, that 5-to-11
20 group is the lowest rates in general with myocarditis.
21 Can you speculate sort of the reason why that is

1 specifically that that's lower in the general
2 population with standard, sort of typical myocarditis?

3 And then number two is I just want to be
4 clear: you're talking about myocarditis, and then
5 there's this sort of subgroup of pericarditis. For the
6 discussion that you're bringing up for us, are you
7 bringing those two together? Are the reviews including
8 both of those, or is that a separate entity in terms of
9 how you all look at this?

10 **DR. MATTHEW OSTER:** Great. Okay. So, first,
11 for the epidemiology in kids, there's lots of
12 different, I guess, theories as to why that can be. I
13 think one of the biggest theories is that their
14 testosterone and hormones play a big level in this,
15 which is part of the reason why you may see a really
16 high peak in adolescence and young adulthood,
17 especially among males.

18 So, I think people still want to learn that,
19 and does that differ also for the different types of
20 myocarditis?

21 In terms of myocarditis and pericarditis, yes,

1 both have been reported, and sometimes the symptoms and
2 presentation can overlap. So, we tried to come up with
3 some definition. Certainly, sometimes someone will
4 meet definition for both, and, in which case, we'll
5 call them myopericarditis, inflammation of both areas.

6 For these numbers, though, we included those
7 who had myocarditis or myopericarditis, and not just
8 pericarditis. But pericarditis numbers are not nearly
9 -- they don't jump out nearly as much for the young
10 adults, and as a safety signal, most certainly some
11 cases for sure. But it doesn't have the same impact in
12 terms of numbers, nor for the long-term outcomes. But
13 it is important to keep in mind that that has been seen
14 as well.

15 **DR. ARNOLD MONTA:** Thank you. Dr. Meissner?

16 **DR. CODY MEISSNER:** Thank you, Dr. Monto.

17 And thank you, Dr. Oster, for this
18 presentation because I think this is a principal
19 concern that people have regarding use of these mRNA
20 vaccines in children. So, your presentation was very
21 clear, and it was very helpful.

1 I would like to go back to the issue of late-
2 phase gadolinium uptake on the MRI scan. My
3 understanding is gadolinium is very sensitive for any
4 inflammation in the heart. But the adult cardiologists
5 say that a late-phase uptake, as you pointed out, is
6 associated with further complications in life or, as
7 you noted, sudden cardiac failure and death.

8 So, my question is do we have any experience
9 with late-phase gadolinium uptake in children from
10 other types of myocarditis and what sort of a prognosis
11 that affords us in terms of what might be expected?
12 And then, secondly, in adults who have late-phase
13 uptake, how long is the interval of time before they
14 begin to run into problems with heart failure? Thank
15 you.

16 **DR. MATTHEW OSTER:** Sure. So, yes, you've
17 touched upon a field that I can't even get all the
18 cardiologists in my practice to agree on, and it's
19 definitely a controversial field in the -- what is the
20 meaning of the finding that we see? And I can tell you
21 a couple of things about it.

1 So, first, yes, especially in adults -- not so
2 much in kids -- it's been studied well in terms of its
3 impact on longer-term outcomes. One thing, though,
4 that people do like to see is improvement in this and
5 resolution of this.

6 We often see, even still, a little bit of
7 uptake, but everything else is normal; there's no
8 active inflammation. The function is normal. You
9 know, kids, their exercise test can be normal. Their
10 (inaudible) are normal. Everything else will be
11 normal, and all we have is this little signal that you
12 see in the MRI that's there but, comparing to prior
13 MRIs, isn't as impressive. So, what do we make of all
14 that? And I think that's an area still ripe for
15 investigation.

16 In terms of progressing and progression, I
17 will say I hesitate a little bit to compare everything
18 and say what those are because I really think of these
19 diseases as same name but maybe different kind of
20 entities and mechanisms. Certainly, some of the data I
21 showed there for longer-term outcomes, adults have the

1 higher mortality when you have acute myocarditis,
2 whereas kids tend to bounce back a bit better.

3 Will we continue to see that with others?
4 Probably. I will say, you know, I showed you the MIS-C
5 outcomes. We, as a field, have all been very
6 pleasantly surprised to see how well these MRIs have
7 looked in the kids after MIS-C. We'll see what we find
8 after the vaccine-associated myocarditis.

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

10 **DR. ARNOLD MONTO:** Thank you. Dr. Rubin?

11 **DR. ERIC RUBIN:** Thanks. That was
12 fascinating, Dr. Oster. And maybe this is a little bit
13 of a follow-up on Dr. Meissner's question, but you were
14 comparing classic myocarditis and its outcomes with
15 what might be happening with vaccine-associated
16 disease. And classic myocarditis, I know, in adults is
17 often associated with direct viral infection of the
18 myocardium or rheumatologic diseases and inflammatory
19 (audio skip).

20 What do we know from the small amount of
21 biopsy and pathology materials from the cases in

1 children that might tell us anything about underlying
2 mechanism and might make us more comfortable with the
3 predictions that you can make from the classic
4 myocarditis cases?

5 **DR. MATTHEW OSTER:** Yeah, I wish I could give
6 you a good answer to that. But what I can tell you is
7 -- and I just looked at this yesterday -- of those
8 about 800 or so, 800 to 900 cases, that we've called
9 myocarditis, I think, like, one or two have actually
10 had biopsies. Biopsy is not routinely used, especially
11 in younger adults and in this population.

12 So, unfortunately, I can't talk about that. A
13 number of the adults at least went to CAF to rule out a
14 myocardial infarction, but they didn't necessarily grab
15 a biopsy, or at least if they did, it wasn't reported
16 to CDC. So, I think we don't know yet, but it'll be
17 fascinating to learn more about it.

18 **DR. ARNOLD MONTO:** Thank you. Dr. Kurilla?

19 **DR. MICHAEL KURILLA:** Thank you, Arnold.

20 Yeah, Matthew, while we seem to see the most
21 of the myocarditis after the second dose, I'm curious

1 about if there's been any close examination of those
2 individuals experiencing myocarditis after their first
3 dose of the vaccine. Do they have evidence of prior
4 COVID infection, and specifically a recent COVID
5 infection?

6 And then, related to that, do we have any data
7 coming out of, let's say, the U.K., where they've
8 played with a longer dosing interval between the first
9 and the second dose? Is it the closeness of the dosing
10 interval, the shorter dosing interval, that actually
11 influences that rate of myocarditis that we see after
12 the second dose?

13 **DR. MATTHEW OSTER:** Yeah, those are both
14 excellent questions. For the VAERS data, we did not
15 specifically separate out exactly the dose 1 or dose 2
16 yet. When we briefly looked, we didn't see a huge
17 difference in their basic demographics. And we didn't
18 feel like we had good information about whether there
19 was actually a prior COVID infection.

20 That data is just not routinely reported to
21 us, or it's not known. As you heard earlier, large

1 number of this population who have COVID-19 infection
2 didn't know. Some places are starting to try to
3 collect, for instance, nucleocapsid antibody when those
4 kids come in, and try to look at that and figure out
5 some more.

6 There have been some anecdotal reports that
7 yes, maybe there was a prior infection. Of course,
8 that doesn't give us any information about the timing
9 whatsoever. But I know there are some more rigorous
10 and robust studies that are being planned, so
11 hopefully, we can answer some of those questions. And
12 then I think your other question was prior --

13 **DR. ARNOLD MONTO:** Okay.

14 **DR. MATTHEW OSTER:** -- the timing? Yeah, we
15 really don't have much information on the timing of the
16 prior -- oh, and in the U.K., there has not been much
17 released yet, but we are very interested to learn it.
18 Most of the stuff that's come out for myocarditis
19 that's not from the United States has been from Israel,
20 but also some other countries as well. But they didn't
21 necessarily have different dosing regimens. But it

1 will be interesting to see.

2 **DR. MICHAEL KURILLA:** Okay. Thank you.

3 **DR. ARNOLD MONTTO:** Thank you. Dr. Gans?

4 **DR. HAYLEY GANS:** Thank you very much. I
5 really appreciated that, obviously, because I had my
6 previous question. My question this time -- because
7 you did a very nice job in answering. Thank you very
8 much.

9 My real question this time is -- this age
10 group that we're considering right now, the younger age
11 group, are the highest risk for MIS-C as opposed to the
12 myocarditis. We saw that there is a drop in all the
13 things that you explained to us.

14 So, there seems to be a very phenotypic
15 difference between the MIS-C cardiac effects versus the
16 post-vaccine cardiac effects, which you related mostly
17 to the pre-COVID myocarditis. And I'm wondering --
18 this goes to the pathophysiology question that was
19 already asked and what we can predict from vaccination
20 in this particular age group. What would be their risk
21 in terms of the cardiac effects?

1 So, I'm wondering if you could think through a
2 little bit of that in terms of the different phenotypes
3 of the post-vaccine myocarditis, which seems to be very
4 different, and we know MIS-C itself has a particular
5 phenotype. But that's what this age group is
6 particularly high risk for, and how that could be
7 impacted by vaccination.

8 I think (audio skip). I get we don't have
9 data on that, but we do have some speculation about the
10 differences about the physiology of those.

11 **DR. ARNOLD MONTO:** Yes, please. Can you
12 speculate?

13 **DR. MATTHEW OSTER:** I will try my best while
14 staying in whatever bounds I can. So, yes, you're
15 right. We do think there are some differences, and
16 it'll be hard to predict what we will see here. We'll
17 certainly be watching it closely.

18 Regarding MIS-C, I will say, since there's
19 some overlap in this age group -- there's been over
20 5,000 cases of MIS-C, and CDC is certainly monitoring
21 for all vaccine safety efforts. And something when

1 vaccines first came out, that question that you posed
2 was certainly of interest. And so, CDC has been
3 actively looking for, are there cases of MIS-C that are
4 associated all with vaccination? What do we see?

5 And we're not really seeing a big signal yet,
6 at least in the 12-and-older group. CDC has
7 identified, to date, 24 persons who received COVID-19
8 vaccine and then had an illness that met the CDC MIS-C
9 case definition. Eighteen of these had evidence of
10 past or recent SARS-CoV-2 infection, so follow-up from
11 the question earlier. Six didn't.

12 And the definition for MIS-C is very broad.
13 But important to note is there's no pattern that's
14 really emerged either in the clinical features or the
15 timing of onset or some of the demographics. So, we're
16 still watching it and seeing it, but no patterns
17 emerged like those for myocarditis where the very early
18 pattern quickly emerged.

19 What's going to happen in the younger age
20 group? We're going to be very active and very
21 interested in learning that. But I'm reassured that we

1 haven't seen high rates of MIS-C associated with
2 vaccine in any of the older kids.

3 **DR. ARNOLD MONTTO:** Thank you. Dr. Nelson for
4 the final question before our shortened break.

5 **DR. MICHAEL NELSON:** Thank you, Dr. Monto.

6 And thank you, Dr. Oster, for an outstanding
7 presentation really acknowledging the complexities and
8 really the data gaps with respect to the long-term
9 outcomes of individuals affected. I have, hopefully,
10 two quick questions for you.

11 One is, are there any ethnicity or social
12 determinant-of-health trends with respect to the
13 outcomes and timing of presentations for these patients
14 affected either by COVID-19 disease or vaccination?
15 The second one has to do with looking at the degree or
16 type of data that's been acquired. From my
17 observation, most of this data appears to be passively
18 acquired through VAERS and other reports or active
19 surveillance of codes for acute presentations.

20 And I do have a concern that there are many
21 cases that are milder forms of myocarditis disease that

1 don't make it to the hospital and are not reported.
2 So, my question for you is are there any -- speculating
3 again -- differences that you would expect with COVID-
4 19 disease and/or vaccination pre-hospital or milder
5 forms of disease, and are there any data with respect
6 to longer-term outcomes for these milder forms that
7 could pose a concern for this age group?

8 **DR. MATTHEW OSTER:** Okay. Excellent question.
9 So, first, yes, at some of the race and ethnicities and
10 what are we seeing, you heard earlier about differences
11 in COVID-19 and MIS-C. And I will say we published a
12 paper looking at MIS-C and found that those higher
13 risks in non-Hispanic Blacks actually exceeded what we
14 would expect their numbers to be if it was all
15 attributable to just their increased numbers of COVID-
16 19.

17 So, it's almost like a double hit. It's the
18 higher numbers amongst the non-Hispanic Black
19 population, but then, even so, a higher risk of
20 developing MIS-C. Obviously, the etiologies of that
21 are unclear. For Hispanics, with the higher rates of

1 MIS-C, it seemed to be explainable by their higher
2 numbers of COVID-19 that then led to higher rates of
3 MIS-C.

4 For post-vaccine myocarditis, the data on race
5 and ethnicity is not as complete as we would like it to
6 be. I will say that the largest percent of people that
7 have been reported have been white, but we need to take
8 that in the context of what vaccination numbers are.

9 So, I think it's too early to say risks
10 associated -- racial and ethnic disparities until we
11 eliminate first some of the racial and ethnic
12 disparities in terms of just overall vaccination
13 because we can't really look at the outcomes until we
14 cross that barrier.

15 In terms of identifying cases and how their
16 cases are identified -- so, yes, VAERS is passive
17 reporting. So, there's always a risk and concern for
18 overreporting and underreporting. I will say I don't
19 think overreporting is a big issue, because about 90
20 percent of the cases, with the information, they're
21 able to be fully adjudicated. Underreporting can

1 certainly be a concern.

2 But there are other systems, and they all kind
3 of work in tandem to look at it from different aspects.
4 Vaccine Safety Datalink, from the data I showed, does
5 do pretty active surveillance and looking at charts.
6 It's not just ICD codes or discharge numbers. Some of
7 the other systems, as well, try to incorporate that as
8 much as able. So, each different way of looking at it
9 has their advantages and disadvantages.

10 In terms of the milder cases, though, that
11 don't present to care, for sure, that is a worrying
12 concern. And I can say just in my own practice,
13 though, once this all came up, we had a few kids
14 referred to us who -- the parents said, oh, wow, they
15 may have had something right after this. Was this
16 myocarditis? And then we did an evaluation for them in
17 the office and even did some other testing where there
18 was any abnormalities noted.

19 So, could that be happening? Potentially, but
20 I think now, at least it's on people's radar. And at
21 least if the pediatrician or healthcare provider

1 becomes aware of it, they're trying to refer the kids
2 to the appropriate care and evaluation.

3 But what do the outcomes mean in terms of a
4 mild case versus not? I don't know. I don't think we
5 have good information on that. I know, certainly, some
6 of the other larger studies that are planned will try
7 to get at that as much as possible. In kids, it can
8 sometimes be a little bit harder even to identify it
9 because they don't often identify chest pain. Case
10 definition does allow for other symptoms to be present.

11 But we'll need to watch and see how they look
12 and how they do.

13 **DR. MICHAEL NELSON:** I think that's been part
14 of my frustration is that the clinical studies do not
15 solicit the exact symptoms associated with myocarditis
16 and pericarditis, and we're relying on patients
17 presenting. It is an area for future study. Thanks
18 again for your (audio skip).

19 **DR. ARNOLD MONTTO:** Okay. Thank you very much.
20 Very important discussion and questions.

21 We're going to take a 12-minute break. We're

1 going to start five minutes late at 10:50 Eastern Time,
2 and I think we'll make up for the time by cutting into
3 our lunch a little bit.

4 Okay. Ten-minute break now.

5 **MR. MICHAEL KAWCZYNSKI:** All right. Just a
6 ten-minute break.

7

8 **[BREAK]**

9

10 **SPONSOR PRESENTATION: BNT162b2 (PFIZER-BioNTech COVID-**
11 **19 VACCINE) - REQUEST FOR EMERGENCY USE AUTHORIZATION**
12 **FOR INDIVIDUALS 5 TO < 12 YEARS OF AGE**

13

14 **MR. MICHAEL KAWCZYNSKI:** Good morning. Good
15 afternoon depending upon where you are and welcome back
16 from that break. I am Mike Kawczynski, and this is our
17 170th meeting of the VRBPAC. Now, just as a reminder
18 to everybody, momentarily we may -- because we do have
19 a lot of members that are in some areas that are having
20 some different weather conditions, so please know we
21 may have to do some unscheduled pauses if that does

1 happen. That being said, so far things have been
2 running pretty well. I'm going to now hand it back to
3 our chair, Dr. Monto. Dr. Monto, are you ready?

4 **DR. ARNOLD MONTO:** I am. I'm going to
5 introduce Dr. Bill Gruber, who is the senior vice
6 president for Vaccine Clinical Research and Development
7 at Pfizer who will give the sponsor presentation. Dr.
8 Gruber.

9 **DR. WILLIAM GRUBER:** Thank you, Dr. Monto and
10 members of the Committee. Good morning. I'm pleased
11 to present to you today the Pfizer-BioNTech BNT162b2
12 vaccine request for emergency use authorization in
13 individuals 5 to less-than-12 years of age. My name is
14 Bill Gruber, and I head the Vaccine Clinical Research
15 and Development group at Pfizer.

16 My presentation this morning will be brief and
17 to the point. Although I will touch on each of the
18 topics shown here, I will focus primarily on the
19 clinical data that demonstrates clear and compelling
20 vaccine safety and efficacy and supports an emergency
21 use authorization in 5- to less-than-12-year-olds.

1 Pfizer-BioNTech are seeking emergency use
2 authorization of a 10-microgram dose of BNT162b2 for
3 use in children 5 to less-than-12 years of age. A
4 lower dose of 10 microgram was selected as the optimum
5 dose for 5 to less-than-12 years of age based on the
6 favorable reactogenicity profile and robust
7 immunogenicity results from a dose finding in Phase 2/3
8 study. The proposed indication is for the active
9 immunization to prevent COVID-19 caused by SARS-CoV-2
10 in individuals 5 to less-than-12 years of age
11 administered as a primary series of two doses of 0.2
12 milliliters each, three weeks apart.

13 I will share information with you today that
14 the vaccine meets emergency use authorization guidance
15 for children 5 to less-than-12 years of age. You will
16 see that the vaccine meets all safety data expectations
17 and meets immunobridging criteria and that 90.7 percent
18 efficacy was observed. Plans are established for
19 active follow-up of safety under emergency use
20 authorization, and the vaccine's benefits outweigh its
21 risks.

1 There's an unmet medical need for a safe and
2 effective COVID-19 vaccine in children 5 to less-than-
3 12 years of age. This was reviewed extensively by the
4 CDC and will only be covered briefly on this slide.

5 In this age group, the cumulative burden of
6 COVID-19 to date is at least 1.8 million cases. You've
7 heard a figure of 1.9 million from the CDC
8 presentation. With over 8,600 hospitalizations and 143
9 deaths, children of color are particularly vulnerable
10 to COVID-19. COVID-19 causes additional long-term
11 sequelae in children. There have been over 5,000 cases
12 of multisystem inflammatory syndrome in children, or
13 MIS-C, reported. Fifty percent of which have been in
14 5- to 13-year-olds. Sixty-seven percent of children
15 experience symptoms greater than or equal to 60 days
16 after COVID-19 diagnosis.

17 Severe outcomes are unpredictable and can
18 occur in healthy children, prompting need for broad
19 age-based vaccination. In fact, one in three
20 hospitalizations occur among children without
21 comorbidities, and you heard some of this again from

1 the CDC earlier.

2 MIS-C is unpredictable and can affect healthy
3 children. Vaccinating children has other large
4 societal benefits. For example, children likely play
5 an important role in transmission, and vaccinating
6 children can help reach herd immunity. Vaccination
7 will help ensure in-person learning, which is critical
8 for childhood development, by limiting community spread
9 and school outbreaks. The need for a safe and
10 effective vaccine for children 5 to less-than-12 years
11 of age is clear.

12 I will share with you today clinical data that
13 supports emergency use authorization for children 5 to
14 less-than-12 years of age. I will highlight key
15 points. Additional details are included in the
16 briefing document.

17 We'll begin by looking at the experimental
18 design of the vaccine study. This began with Phase 1
19 to identify a preferred dose level based on immune
20 response and a safety profile. The 10-microgram dose,
21 one-third the adult dose, was chosen because it had the

1 right balance between immune response and a
2 satisfactory reactogenicity profile.

3 This 10-microgram dose was advanced into Phase
4 2/3 with a randomization scheme of two to one. Please
5 keep this in mind when looking at both the safety as
6 well as efficacy results. First group of safety
7 information includes approximately 1,500 individuals
8 that received the vaccine versus 750 that received
9 placebo. At the request of the FDA, we've also
10 enrolled approximately 1,500 additional individuals who
11 received vaccine and 750 placebo receipts, most of whom
12 have at least two weeks of safety data after dose 2.
13 Non-inferior immune responses have been established
14 comparing responses in children 5 to less-than-12 years
15 of age to individuals 16 to 25 years old from the
16 pivotal Phase 3 study.

17 Although not required for emergency use
18 authorization, COVID-19 surveillance was conducted
19 permitting evaluation of vaccine efficacy.

20 This represents the Phase 2/3 timeline of
21 participants in this age group. This scheme is similar

1 to the scheme for other populations in which the doses
2 were administered 21 days apart. Reactogenicity data
3 was captured for seven days. Non-serious adverse
4 events were captured for a month. Serious adverse
5 events were captured for six months.

6 To enhance possible detection of the rare
7 event of myocarditis observed in adolescents and young
8 adults should it occur, specific instructions were
9 provided to investigators to be vigilant for symptoms
10 and signs of this condition, including chest pain, and
11 to perform work up in the event of suspected
12 myocarditis. Blood draws are obtained as shown to
13 measure immune response.

14 As for nearly all our trials, we continue to
15 obtain surveillance on the populations to look for the
16 potential to demonstrate efficacy, and that proved
17 possible in this particular trial.

18 This slide represents the two datasets that
19 have been submitted to support emergency use
20 authorization application. One is the initial cohort
21 of 2,268 participants, for which the median follow-up

1 time is 2.3 months, shown as the top blue bar. In the
2 later submission, follow-up of this group has been
3 extended as shown in light blue. Findings did not
4 differ appreciably and will not be discussed further in
5 this presentation.

6 Additionally, later and represented by the
7 lower bar graph, we also enrolled an additional cohort
8 of 2,379 participants. In conjunction with the
9 original cohort, this permits evaluation of a total of
10 approximately 3,000 vaccine recipients to define rare
11 events for at least two weeks for most of the 3,000
12 vaccine recipients and for two to three months for over
13 1,500 vaccine recipients in this submission.

14 I will first describe safety in the initial
15 safety enrollment group.

16 Here are the demographics for the 5- to less-
17 than-12-year-olds in the initially enrolled safety
18 population. Demographics for the additional safety
19 group and efficacy population are similar. You can see
20 there was good representation in terms of gender, race,
21 and ethnicity. The mean age of vaccination was in the

1 middle of the age span between 5 to 11 years of age at
2 8 years of age. More than 11 percent of the population
3 had obesity as an underlying condition and
4 comorbidities, including obesity, were represented in
5 approximately 20 percent of the population.

6 Here are local reactions by maximum severity
7 within seven days after each dose. Dose 1 is at the
8 top. Dose 2 is at the bottom. You can see the
9 reactions in the 5- to less-than-12-year-old age group
10 compared to 16- to 25-year-olds. There is some
11 increase in mild to moderate redness and swelling, both
12 after dose 1 and dose 2, in the 5- to less-than-12-
13 year-old age group. Pain at the injection site was
14 comparable between the two age groups. In general, the
15 local reactions meet a satisfactory safety profile.

16 Systemic events are shown on this slide by
17 maximum severity within seven days after dose 2 in
18 children 5 to less-than-12 compared to 16- to 25-year-
19 olds. Reactions were typically higher in vaccine
20 recipients. Dose 1 reactions tended to be less
21 frequent and are not shown here.

1 The vaccine group is shown at the top part of
2 the graph and the placebo group at the bottom. I draw
3 your attention particularly to fever and chills. You
4 can see that, if anything, the incidence of fever was
5 lowered and mostly mild to moderate in individuals who
6 were 5 to less-than-12 years old compared to the older
7 age group. That was true for chills as well.

8 Likewise, across the other systemic event
9 parameters, you can see that responses were comparable
10 or less to those seen in 16- to 25-year-olds, again
11 representing a satisfactory systemic reaction profile
12 for 5- to less-than-12-year-old children.

13 Now let me review unsolicited adverse events.
14 This graphic represents overall adverse events from
15 dose 1. The initial enrollment group is shown at the
16 top, and the safety expansion group is shown at the
17 bottom. In both groups, you can see comparable levels
18 of any adverse events or related adverse events.

19 There were very few serious adverse events and
20 no related serious adverse events and no deaths. One
21 female participant was withdrawn from the study due to

1 a fever of 40 degrees centigrade on day 2 after dose 1
2 accompanied by neutropenia. The fever resolved in one
3 day. This child carries a preexisting diagnosis of
4 benign neutropenia followed by a hematologist. She
5 recovered uneventfully.

6 This represents adverse events occurring at an
7 instance of greater-than-one percent by system organ
8 class for this age population in the initial enrollment
9 group. You can see comparable rates between vaccine
10 receipts and placebo recipients whether we're talking
11 about any adverse events or the categories specified
12 underneath. This again reflects a satisfactory safety
13 profile and events common to this age group.

14 Lymphadenopathy has been infrequently observed in other
15 populations after vaccine and was observed in 0.9
16 percent of vaccine recipients in this enrollment group.

17 This represents comparable analysis of adverse
18 events in the safety expansion enrollment group. You
19 can see similar rates between vaccine and placebo
20 groups. Again, this reflects a satisfactory safety
21 profile.

1 Serious adverse events from dose 1 to the
2 cutoff date are shown here for both safety groups. All
3 SAEs were considered unrelated. Three events are
4 related to trauma and one related to ingestion of a
5 foreign body. In the expansion safety group, one
6 participant reported infective arthritis of undiscerned
7 etiology 15 days after dose 1. It resolved 21 days
8 later.

9 We followed participants for adverse events of
10 special interest as designated by either the FDA or the
11 CDC. Summaries for both enrollment groups are shown
12 here. For FDA adverse events of special interest, no
13 anaphylaxis, no myocarditis, no Bell's palsy, and no
14 appendicitis were reported.

15 For CDC adverse events of special interest,
16 angioedema and hypersensitivity were uncommonly seen,
17 observed in both vaccine and placebo recipients, and
18 were short lived. Rashes tended to be more after
19 vaccine, uncommon overall, mild and short lived. One
20 case of arthritis is the infective arthritis already
21 described. The case of vasculitis is a reported case

1 of Henoch-Schonlein purpura considered unrelated that
2 occurred 21 days post-dose 1. Follow-up is ongoing.

3 Safety conclusions for 5- to less-than-12-
4 year-olds. Reactogenicity was mostly mild to moderate
5 and short lived. Observed mild to moderate local
6 reactions, redness, swelling captured by eDiary were
7 more common, and systemic reactions including fever,
8 less common than those in 16- to 25-year-olds. The
9 observed AE profile in this study did not suggest any
10 safety concerns for vaccination in children 5 to less-
11 than-12 years of age. The database of approximately
12 3,000 enrolled BNT162b2 recipients provides a high
13 degree of confidence for the following: rare events
14 approximate to vaccination, such as myocarditis or
15 anaphylaxis, are unlikely to occur at a rate of 1 in
16 1,000 or higher.

17 Now I'd like to turn to the examination of the
18 immune response to the vaccine. Immunobridging
19 criteria comparing the 5- to less-than-12-year-olds to
20 16- to 25-year-olds were met both for the geometric
21 mean ratio and for seroresponse as shown on this slide.

1 At the top is represented SARS-CoV-2 neutralizing
2 antibody titer. You can see the geometric mean titers
3 represented after the second dose in the middle two
4 columns in blue. The geometric mean ratio of 1.04 is
5 shown on the right-hand side with a lower bound of the
6 confidence interval well above the 0.67 criterion.

7 The observed GMR was above the prespecified
8 criteria of 0.8 and also above the GMR of one requested
9 post hoc by the FDA. In addition, seroresponse rates
10 are shown at the bottom. You can see the seroresponse
11 rates were virtually identical in 5- to less-than-12-
12 year-olds compared to the 16- to 25-year-olds at 99.2
13 percent a piece. This criterion was also met with a
14 lower confidence bound of minus 2 percent, well above
15 the minus 10 percent that was required.

16 It was also important and requested by the FDA
17 for us to look at responses to the Delta variant given
18 its prominence as a cause of COVID-19. Much as we have
19 seen in older populations, the responses were quite
20 robust, not only to the wild type, shown on the left
21 side but also to the Delta variant on the right in the

1 subpopulation of 34 individual study. Note the
2 comparable postvaccination titers at one month for
3 wild-type vaccine strain and for the Delta variant with
4 high geometric mean fold rises shown at the top. This
5 comparable response predicts efficacy for 5- to less-
6 than-12-year-olds during a time when the Delta variant
7 is prominent.

8 High efficacy against COVID-19 was in fact
9 overserved when examining COVID-19 occurrence from
10 seven days after dose 2. Remembering that the
11 randomization in this study was two to one vaccine
12 versus placebo, the case split of 3 to 16 with
13 surveillance times shown yields an efficacy of 90.7
14 percent with a high degree of confidence shown. No
15 severe cases of COVID-19 or multisystem inflammatory
16 syndrome in children were reported in either group.
17 Note that cases occurred in July through September,
18 when the Delta variant was the most prominent variant
19 in circulation.

20 At this time, 14 of 19 samples have been
21 successfully sequenced, and all yielded the Delta

1 variant, confirming high efficacy against this highly
2 transmissible strain of SARS-CoV-2. This data is yet
3 to be submitted to the FDA.

4 This curve shows the cumulative incidence of
5 all available COVID-19 cases beginning after dose 1.
6 The mean length of follow-up time after dose 2 is 3.3
7 months. Placebo cases are in red, vaccine cases in
8 blue. Efficacy was durable for this period of follow-
9 up to date, and surveillance is continuing.

10 Let me summarize the immunogenicity and
11 efficacy conclusions. Immunobridging success criteria
12 were met for 5- to less-than-12-year-olds compared to
13 16- to 25-years-olds. Vaccine-immune sera effectively
14 neutralized both the wild-type vaccine virus as well as
15 the highly transmissible Delta variant of concern.
16 BNT162b2 as a two-dose series demonstrated high
17 efficacy against COVID-19 in this population of 5- to
18 less-than-12-year-olds when the Delta variant was
19 prominent.

20 Pharmacovigilance activities are a critical
21 component of activities to detect unexpected safety

1 events rapidly. Pfizer continues to conduct robust
2 pharmacovigilance activities and collaborate with
3 regulators and international groups. Proactive risk
4 mitigation activities, such as labeling, educational
5 materials, and bio differentiation will continue.
6 Pharmacoepidemiology studies will include children 5
7 years and up to evaluate for myocarditis occurrence and
8 sequelae as well as other possible rare adverse events.
9 This includes one study that will follow up identified
10 U.S. postvaccination myocarditis/pericarditis cases for
11 five years within the Pediatric Heart Network.

12 What are some of the key things that have been
13 learned about myocarditis that inform the positive
14 benefit-risk of the Pfizer-BNT vaccine? As we have
15 learned from publications, government public health
16 websites and the previous presentations from the CDC,
17 myocarditis is typically caused by viral infections.
18 SARS-CoV-2 is one such example. COVID-19 patients have
19 nearly 16 times the rate of myocarditis compared to
20 individuals without COVID-19. In rare cases,
21 myocarditis is observed after COVID-19 vaccination in

1 children and adolescents.

2 This occurs more frequently after the second
3 dose and in males. The acute clinical course is
4 generally mild, resolving with conservative treatment.
5 Rates of post-vaccination myocarditis in 12- to 15-
6 year-olds appear lower relative to older adolescents in
7 both the United States and Israel.

8 In this context, benefit-risk assessments
9 supports a revision to the emergency use authorization
10 for the vaccine to include children 5 to less-than-12
11 years of age. This is based on model-predicted
12 benefit-risk outcomes per million children vaccinated
13 over six months.

14 You've heard some of this from the CDC, and
15 information is also included in the Pfizer and FDA
16 briefing documents. Please keep in mind that this
17 projection of benefit-risk assumes the rate of
18 myocarditis in 5- to less-than-12-year-olds that is
19 equal to that of 12- to 15-year-olds, which may be an
20 overestimate. Why? Rates trend downward in younger
21 adolescents compared to older adolescents. This

1 downward trend may extend to children less than 12. In
2 addition, the lower 10-microgram dose and lower common
3 systemic reactions in children 5 to less than 12 may
4 also result in a lower risk of rare adverse events like
5 myocarditis.

6 This table displays FDA Scenario 4 which
7 appears to better match, given the 90.7 percent
8 observed clinical trial efficacy in 5- to less-than-12-
9 year-olds. This scenario assumes the COVID-19
10 incidence rate of September 11th, 2021. This incidence
11 rate is a good choice because we may see it yet again
12 if children are not vaccinated due to the looming
13 winter respiratory disease season and unpredictable
14 nature of pandemic spread. COVID-19 outcomes prevented
15 versus excess myocarditis case risks are displayed.
16 The CDC VAERS and VSD myocarditis case estimates have
17 been described previously.

18 Note that the VSD result may be inflated by
19 virtue of including 16- to 17-year-olds at the peak of
20 myocarditis incidence compared to lower rates seen in
21 younger adolescents. VSD rates are based on cases

1 observed in a network of health systems where case
2 confirmation is performed via medical chart review.
3 VAERS included cases reported to the FDA that have, at
4 least to some extent, been medically confirmed. This
5 confirms some specificity to the diagnosis of
6 myocarditis.

7 In contrast, the FDA briefing document model
8 relied on a non-chart-confirmed cases from a U.S.
9 healthcare claims database, OPTUM, as a worst-case
10 scenario. This, therefore, lacks potential
11 specificity, and the FDA document acknowledges that the
12 106 value may be an overestimate.

13 However, even if myocarditis rates in children
14 5 to less than 12 are the same as younger adolescents
15 regardless of which adolescent myocarditis rates we
16 choose, the corresponding benefits exceed the risks.
17 For every one million children vaccinated, the number
18 of cases and hospitalizations prevented exceed any of
19 the myocarditis estimates.

20 ICU admissions prevented exceed both CDC
21 myocarditis estimates. Vaccination is also likely to

1 confer additional benefits, including reduced
2 transmission, improved herd immunity, and increased in-
3 person learning, supporting child development. In such
4 a case, the benefit becomes all that more substantial
5 compared to the risk.

6 Hence, Pfizer-BioNTech requests emergency use
7 authorization of BNT162b2 for active immunization of
8 individuals 5 to less-than-12 years of age administered
9 intramuscularly as a series of 2-microgram doses, three
10 weeks apart.

11 We want to thank all of those who made this
12 possible, the clinical trial participants and their
13 families foremost, sites, investigators, CRO, our
14 partners and their staff, and the FDA guidance to help
15 us assess and address this urgent medical need. Thank
16 you and I'm now prepared to respond to questions.

17 With the indulgence of the chair, we might
18 begin with the first question that Dr. Meissner asked
19 about the use of buffer. But I defer to the chair.

20

Q&A SESSION

1

2

3 **DR. ARNOLD MONTA:** Go ahead and answer it,
4 Bill.

5 **DR. WILLIAM GRUBER:** Thank you, Dr. Monta.
6 Also, I'll start and then I'm going to ask Nick Warnie
7 to provide some of the details. As indicated in, I
8 think, the FDA presentation, the buffer was changed to
9 confer additional stability as a minor change that will
10 also actually improve shelf life. I think Dr. Meissner
11 had asked the question, actually how does the buffer
12 work and perhaps how it was chosen. Nick Warne will
13 provide some of the details. Nick?

14 **DR. NICK WARNE:** Thank you, Dr. Gruber. My
15 name is Nick Warne, and I'm in biotherapeutics and
16 pharmaceutical sciences.

17 We've explored a number of alternate buffer
18 systems to enhance the stability of the RNA LNP product
19 as well as to allow for lower concentrations to be made
20 available. The switch from phosphate to tris
21 demonstrated better refrigerated stability and

1 increased from 31 days out to 10 weeks as well as it
2 enabled us to dilute the product from 0.5 milligrams
3 per mL to 0.1 milligrams per mL, making it easier to
4 prepare the dose.

5 Tris is a precedented buffer in biotechnology
6 and has been used in at least three vaccines. Our
7 decision was based on empirical stability data,
8 manufacturability, and ease of use for pharmacists and
9 healthcare professionals. We prefer not to speculate
10 about the underlying chemistry. We have performed an
11 extensive comparability evaluation comparing the two
12 formulations and have found them to be biochemically
13 and pharmaceutically comparable.

14 Please note that the manufacturing process of
15 the RNA active ingredient and the lipid nanoparticle is
16 completely unchanged. The only change is in the
17 formulation, which is the last step of the product
18 manufacturer. Again, there is no change to the active
19 ingredient.

20 **DR. ARNOLD MONTO:** Thank you. We'll go on to
21 Dr. Offit.

1 **DR. PAUL OFFIT:** Thank you, Dr. Gruber. One
2 of the questions already starting to come up were -- if
3 this vaccine were to be authorized -- from parents of,
4 say, children who are 11 years old, they have been
5 asking, should we just wait until they're 12 and get
6 the larger dose?

7 My question to you is, did you break down sort
8 of the geometric mean titer for neutralizing antibodies
9 in, say, the 10- to 11-year-old versus 5- to 6-year-
10 old? Was there any difference there? And then does it
11 correlate to that of the three children who, despite
12 getting vaccinated, still developed mild COVID? What
13 were their ages? Thank you.

14 **DR. WILLIAM GRUBER:** Let me address the first
15 question about the nature of the antibody responses
16 based on age. If we can bring up Slide number 1,
17 please. While I'm doing that, if we can address the
18 ages of the -- some of the notes on the individuals
19 that we had breakthrough infection. I think you can
20 see represented here. This represents geometric mean
21 titers by age subgroup in the subjects 5 to less-than-

1 12 years of age. On the left-hand side, you see the
2 entire group. Then as you walk through, you see the
3 individual groups by very narrow age breakdown.

4 I think it's easy to appreciate, recognizing
5 that the left bars represent preimmunization, right
6 bars represent one month post-dose 2, that there really
7 is a comparable response across the age groups that we
8 are confident that the dose works well across the
9 entire age group. The three cases in the BNT162b2
10 group that you asked about were 10 and 11 years old. I
11 am mindful of, actually, the highest tack rate in the
12 placebo group was also, I think, over 50 percent in
13 cases as I recall were in that age group.

14 That may be more a feature of the fact that
15 that group seemed to have more potential exposure,
16 which may make some sense given that these children
17 begin to socialize more as they get older. Did that
18 answer your question, Dr. Offit, and anything else?

19 **DR. PAUL OFFIT:** That answered my question.

20 **DR. ARNOLD MONTO:** I'll just turn that
21 question upside down and say, what would happen if you

1 gave a lower dose to a 12-year-old --

2 **DR. WILLIAM GRUBER:** I'm sorry. Could you
3 repeat that? You broke up.

4 **DR. ARNOLD MONTA:** -- in terms of antibody and
5 in terms of side effects?

6 **DR. WILLIAM GRUBER:** I'm can you just say that
7 again. I'm sorry. I'm not sure I completely
8 understood the question, Dr. Monto.

9 **DR. ARNOLD MONTA:** What would happen if you
10 gave the lower dose to the 12- to 15-year-olds in terms
11 of antibody response and perhaps reduction in side
12 effects?

13 **DR. WILLIAM GRUBER:** That becomes a logical
14 question. Obviously, based on the experience that we
15 now have in 5- to 11-year-olds, you'll recall that when
16 we presented the data to the FDA -- for those of you
17 that have reviewed that data -- we had higher antibody
18 responses at the 30-microgram dose in individuals who
19 were in the 12- to 15-year-old age group, and that
20 conferred a high level of efficacy. There is the
21 potential, although we don't have the data to show it,

1 for a 10-microgram dose to provide antibody response.
2 We have some possibility of looking at that in the
3 future, but we don't have that data today.

4 **DR. ARNOLD MONTO:** All right. You are
5 thinking about looking at that?

6 **DR. WILLIAM GRUBER:** Yes, we are thinking
7 about that as a potential option, particularly as we
8 move out of the pandemic period.

9 **DR. ARNOLD MONTO:** Right.

10 **DR. WILLIAM GRUBER:** The key goal right now is
11 obviously providing protection with a safe and
12 effective vaccine to get ahead of the pandemic.
13 Obviously, the 30-microgram dose has now been used.
14 (audio skip) to get evidence that it is working to
15 provide effectiveness.

16 **DR. ARNOLD MONTO:** Agreed. I violated a
17 principle of asking a question about something that
18 might be partially settled right now. Dr. Pergam.

19 **DR. STEVEN PERGAM:** Thanks, Dr. Gruber. A
20 couple of questions. Just to get back to the tris
21 versus the PDS in the study, was the actual study done

1 with the PDS version of the vaccine? Was the tris
2 version given in the actual trial? That's the first
3 question. The second question is I've seen some
4 images, but I just want you to clarify. For the
5 public, when these different dosing strategies are
6 being used, is the image or the look of the bottles
7 going to be different so that it's easier to assure
8 that there's not misdosing among children?

9 **DR. WILLIAM GRUBER:** Nick Warne's coming up,
10 and we actually have a slide to again represent the
11 image not only of the bottle but the nature of (audio
12 skip) the cap but also the label that I think will
13 answer that question.

14 The answer to your first question is that the
15 studies were done using the same volume, 0.2
16 milliliters, that is in the final presentation in terms
17 of the dose but contain the PDS buffer. We obviously
18 had extensive consultations with the FDA, and it was
19 determined that the clinical studies were not required,
20 again, because the LNP and mRNA are the same and the
21 behavior in terms of reactogenicity and efficacy are

1 expected to be the same. Let me ask Dr. Warne to
2 address the other question about the presentation.

3 **DR. NICK WARNE:** Thank you. If could have
4 Slide 2 brought up, please. In terms of vial
5 differentiation, we have made substantial efforts to
6 differentiate the pediatric 5- to 11-year-old vial from
7 the currently available vial. You can see the images
8 on your screen. On the left, you have the current vial
9 that's available with the purple cap, purple label.
10 It's quite distinct from the pediatric dosage form,
11 which has an orange cap and an orange label.
12 Similarly, the packaging, the actual cardboard box in
13 which the product will be received, is orange.

14 The large carton, the shipper carton, that is
15 received at the pharmacy will also have an orange label
16 on it. We have tried to maximize as best we can the
17 number of ways we can differentiate the pediatric
18 dosage form from the current dosage form.

19 In addition to product differentiation, the
20 instructions for use will be distinct. Also, you can
21 see on the screen we have a different dilution scheme

1 in the pediatric product versus the current product
2 which will allow ten doses per vial at ten micrograms.

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

4 **DR. OFER LEVY:** Thank you, Dr. Gruber, for
5 the presentation. An important element of
6 consideration is whether the Pfizer mRNA vaccine may be
7 able in some fashion to reduce transmission of
8 Coronavirus infection. It was alluded to in your
9 slides as likely. Maybe I'm paraphrasing something
10 along those lines. What data does Pfizer have, not
11 just in this age group but other age groups, at this
12 point in time to demonstrate an impact on transmission?

13 **DR. WILLIAM GRUBER:** Thank you, Dr. Levy.
14 Within the 1007 trial, we did not specifically look at
15 the potential for asymptomatic disease and therefore
16 the potential for transmission in that setting.
17 However, we are well aware, and I think the Committee's
18 well aware there's a great deal of real-world evidence
19 that supports that vaccination impacts transmission in
20 adults. The notation really is that, by virtue of
21 showing a non-inferior immune response from children to

1 adults where we demonstrated efficacy as well as the
2 high level of efficacy that we demonstrated in the 1007
3 study, that it's reasonable to expect that there'll be
4 some reduction in transmission for children having
5 asymptomatic disease or for the potential for
6 asymptomatic spread.

7 I think it's also worth remembering that just
8 prevention of symptomatic disease in its own right
9 prevents those children from potentially being in a
10 school-room setting and transmitting in that
11 circumstance. You heard from the CDC earlier that
12 children do appear to be an important mechanism of
13 transmission to other children as well as to the
14 community.

15 On balance, I think whether we're talking
16 about asymptomatic disease and transmission where we
17 can bridge to where that's proven to be the case or
18 just the nature of reducing symptomatic children from
19 ending up in the schoolroom (audio skip) potential for
20 affecting community spread seems very real.

21 **DR. OFER LEVY:** Thank you.

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

2 **DR. PATRICK MOORE:** Thank you. That was a
3 very nice, clear presentation. I'd like to follow up
4 on Dr. Levy's comment. As you said, if we have real,
5 clear data that this vaccine prevents transmission,
6 that would be a very important positive benefit in a
7 population that has a low risk of serious disease.
8 Also, the second point is your company, Pfizer, makes
9 the vaccine PREVNAR, which is a conjugate
10 polysaccharide vaccine as you know. The unconjugated
11 polysaccharide vaccine does not prevent transmission at
12 all. It's very effective at preventing invasive
13 disease, but it has no effect on transmission.
14 Conjugated vaccine does.

15 So where does this vaccine lie between those
16 two poles? And I think you have the data that you can
17 actually look at that. If you were to look at your
18 visit two, V2, and your visit five blood draws, you
19 would have a randomized, blinded controlled study that
20 would allow you to look at at least antibody titers
21 that would give you an idea as to whether there was

1 viral invasion let alone symptoms in the vaccinated
2 population. I'd urge you or perhaps request FDA to
3 urge you to make that test. Since you have those
4 blood, you have all the materials, it does not require
5 any additional visits, just a single blood test that
6 could potentially give us an answer.

7 **DR. WILLIAM GRUBER:** I thank you, Dr. Moore.
8 Let me deal with the last question first, and
9 obviously, we'll take that under advisement. I think
10 we've thought about doing that, not only in this
11 population but other populations as well, to look for
12 the potential for interference with asymptomatic
13 disease and then the potential for reduction in
14 transmission.

15 Regarding the first point, obviously, as
16 you're well aware, we are quite familiar with the
17 nature of the conjugated polysaccharide and what it
18 brings to the table in terms of immune response.
19 You're absolutely right. The polysaccharide vaccine
20 without conjugation to a protein essentially is a T
21 cell-independent antigen. It doesn't produce memory.

1 I think one of the things that is gratifying,
2 whether we'll actually impact transmission, I guess,
3 remains to be seen. But we have evidence that this
4 vaccine produces not only CMI but evidence that it
5 likely produces memory. Some of that's from the
6 laboratory studies but also from the fact that, I
7 think, there's at least supporting evidence that
8 although antibody declines, protection seems to persist
9 greater than the decline in antibodies.

10 If memory is important, which it may well be
11 on re-exposure to the virus in terms of preventing
12 transmission, then I think this comes closer in that
13 respect to the conjugate vaccine than it does the
14 polysaccharide.

15 **DR. ARNOLD MONTTO:** Thank you. Dr. Kurilla.

16 **DR. MICHAEL KURILLA:** Thank you, Arnold. This
17 is a two-parter. Don't know why my camera's not
18 working at the moment. I'll just reiterate some of the
19 previous comments related to the asymptomatic and
20 transmission. It's clear that the younger the infected
21 individual, the more likely they are to have an

1 asymptomatic infection. And I think, in terms of this
2 population, it's at least 50 percent. I would assume,
3 as we've seen with the adults, that, upon vaccination,
4 it's going to go higher than that. So you may be
5 actually missing, by just looking at symptomatic
6 disease, the degree of vaccine efficacy in terms of
7 preventing overall infection.

8 I think that's one major impact. The other
9 question I really wanted to pose to you is you have
10 very limited data at this point in time because of not
11 much follow-up. Is there any reason to believe that
12 the antibody decay kinetics in this population is going
13 to look any different from what we've seen in adults?
14 Is the expectation that these children are going to
15 need a boost in six months, and how do you think that's
16 going to play out with -- because, if the focus is on
17 immunobridging and the antibody response, then, if the
18 antibodies wane at the same level, then the argument
19 would be is we need to maintain their antibody levels.

20 Yet, we're seeing in younger populations
21 better holding up of protection for the serious disease

1 that's been commented on in terms of hospitalizations
2 and worse. Comments?

3 **DR. WILLIAM GRUBER:** Thanks, Dr. Kurilla. In
4 terms of your first question, obviously a good question
5 about the nature of being able to look at asymptomatic
6 infection. Like Dr. Moore's question before, we'll
7 look into the potential of looking serologically at
8 that.

9 As far as the second question in terms of
10 antibody decay, you may recall from the slide that I
11 showed that we intend to get antibody responses out at
12 six months, which maybe give us, of course, an early
13 clue as to the potential for waning immunity and
14 protection.

15 Much has existed for the other populations,
16 particularly adult populations. The real-world
17 evidence seems to be so robust and catches up so
18 quickly that my expectation is we'll gain information
19 from that as well to determine the durability of
20 response. I'm encouraged by the fact that we're
21 starting off, at least, essentially at the same point

1 that we do in adults with efficacy greater than 90
2 percent. So I'm expecting the given potential to
3 produce memory (audio skip) cell mediator even (audio
4 skip) that that will (audio skip) protection.

5 **DR. MICHAEL KURILLA:** But do you have any idea
6 if the lower dose you're giving the children provides
7 an equivalent stimulation to the memory as opposed to
8 just antibody levels?

9 **DR. WILLIAM GRUBER:** We don't have that
10 specific data. But again, I think the level of
11 efficacy certainly is comparable to what we've seen.

12 **DR. MICHAEL KURILLA:** Thank you.

13 **DR. ARNOLD MONTTO:** Dr. Hildreth. This is
14 going to be our last question before the FDA
15 presentation. I want to remind everybody that we will
16 have another question and answer period for both the
17 sponsor and the FDA after lunch. So this is not the
18 last question that you may receive, Dr. Gruber. Dr.
19 Hildreth.

20 **DR. WILLIAM GRUBER:** I'm ready for this
21 afternoon.

1 **DR. JAMES HILDRETH:** Thank you, Dr. Monto, and
2 thank you, Dr. Gruber.

3 When you did your risk-benefit assessment and
4 your bridging document, there were six scenarios that
5 you considered. It strikes me that Scenario 3, where
6 you have the incidence from, I think, it's, June of
7 2021 where the cases are low, the hospitalizations from
8 myocarditis actually exceeded hospitalization from
9 COVID-19.

10 As we get more adults vaccinated and we see
11 the Delta curve waning, isn't it likely that that's
12 going to be the more likely scenario versus the highest
13 incident that you have in your assessment?

14 Could you comment on that because, to me, the
15 single most important question is whether the benefits
16 outweigh the risk? In that scenario, they clearly
17 don't. Can you comment, please?

18 **DR. WILLIAM GRUBER:** Sure. We obviously
19 looked across all the six scenarios. You'll get a
20 chance to hear that in some detail from the FDA's
21 presentation. Our opinion in terms of Scenario Number

1 3 is it actually picked the lowest rate of disease,
2 which is actually lower than what's being experienced
3 now. And I think if you just look at our track record
4 in terms of predicting the epidemic, we've not done
5 particularly well. Given that the winter season is
6 coming, the Delta virus is still out there, you still
7 have a large number of susceptible children, there's
8 every reason to believe that the rate will not be at
9 the later.

10 Let's suppose that it is. Even in the FDA
11 briefing document, they talk about the fact that,
12 despite that difference where now the number of
13 myocarditis cases may exceed the benefits seen from the
14 vaccine, and of course in a circumstance where you're
15 assuming that that rate is the same as in 12- to 15-
16 year-olds, that the other benefits, and particularly
17 those societal benefits, obviously protecting
18 vulnerable populations and including populations of
19 color, the ability to get children back into the
20 schoolroom setting -- I think as you know, many
21 children depend on schools as a safe place as well as a

1 place to often get their meals.

2 All of those things I think have to enter into
3 the equation regardless of the rate that says (audio
4 skip). In our view, it's more realistic to think that
5 the rate is going to be higher than that very lowest
6 rate that's been (audio skip).

7 **DR. JAMES HILDRETH:** Thank you.

8

9 **FDA PRESENTATION: FDA REVIEW OF EFFECTIVENESS AND**
10 **SAFETY OF PFIZER-BioNTech COVID-19 VACCINE IN CHILDREN**
11 **5 THROUGH 11 YEARS OF AGE EMERGENCY USE AUTHORIZATION**
12 **AMENDMENT**

13

14 **DR. ARNOLD MONTTO:** Thank you. Now we move to
15 the FDA presentations. We have three parts to the
16 presentation. I'll introduce each of the speakers
17 individually. The first is Dr. Leslie Ball who will be
18 talking about the FDA review of the Pfizer-BioNTech
19 submission. She is a medical officer in the Division
20 of Vaccine and Related Products Applications. Dr.
21 Ball.

1 **DR. LESLIE BALL:** Hi, good morning. I'm Dr.
2 Leslie Ball, medical officer and pediatrician in the
3 Center for Biologics, Office of Vaccine Research and
4 Review, Division of Vaccines and Related Products
5 Applications at FDA.

6 I will be presenting FDA's review of the
7 effectiveness and safety of the Pfizer-BioNTech COVID-
8 19 vaccine in children 5 through 11 years of age
9 submitted under the Emergency Use Authorization
10 Amendment, or EUA.

11 I'd like to start off by acknowledging the
12 many contributions of my colleagues.

13 I will start with the regulatory background of
14 the product. I will next cover the design study
15 submitted to support EUA, review the immunogenicity,
16 supportive efficacy and safety results, and conclude
17 with an overall summary.

18 The EUA under discussion today is intended to
19 support the use of an intramuscular two-dose primary
20 series of the Pfizer-BioNTech COVID-19 vaccine, 10-
21 microgram mRNA each dose administered three weeks

1 apart. The vaccine composition is based on SARS-CoV-2
2 to spike glycoprotein (S) antigen encoded by RNA
3 derived from the Wuhan strain. It is formulated in
4 lipid particles.

5 COMIRNATY is the only vaccine that has FDA
6 approval for the prevention of COVID-19 in individuals
7 16 years of age or older. FDA has issued five related
8 EUAs previously, including the EUA for Pfizer-BioNTech
9 COVID-19 vaccine to individuals 12 years of age or
10 older with and without certain compromised immune
11 systems and as a booster dose. Each dose contains 30
12 micrograms of mRNA.

13 In August of this year, the Pfizer-BioNTech
14 COVID-19 vaccine, also known as its name during
15 development, BNT162b2, was approved under a biologics
16 license application. As I mentioned, the proprietary
17 name is COMIRNATY with an indication of active
18 immunization to prevent COVID-19 in individuals 16
19 years of age or older. The approved regimen is also a
20 two-dose primary series, three weeks apart.

21 I'll discuss the study design. Study

1 C4591007, hereafter referred to as Study 1007, is a
2 Phase 1/2/3 ongoing randomized, observer-blinded,
3 placebo-controlled study in children 5 through 11 years
4 of age. This slide provides an overview of the Phase
5 1, or dose-finding, portion of the study which
6 evaluated the safety and immunogenicity of three dose
7 levels at 10, 20, and 30 micrograms.

8 Formulation used in Study 1007 was the
9 currently authorized formulation, PBS sucrose
10 formulation, diluted with saline to the appropriate
11 dose levels to administer the 10-, 20-, and 30-
12 microgram dose levels. Phase 1 component took place in
13 the U.S. and enrolled children who were not at high
14 risk of SARS-CoV-2 exposure or severe disease and who
15 did not have evidence of prior SARS-CoV-2 infection.
16 Doses were evaluated sequentially with 16 participants
17 per dosage beginning with the 10-microgram dose. SARS-
18 CoV-2 50 percent neutralizing geometric mean titers, or
19 GMTs, were assessed at seven days after dose 2.

20 A total of 48 participants were enrolled in
21 this Phase 1 portion of the study. Safety review of

1 reactogenicity data from the initial four participants
2 who received the 30-microgram dose for both doses found
3 that all four participants developed mild to moderate
4 redness at the injection site and fever to 38.7 degrees
5 centigrade. The higher frequencies solicited adverse
6 events. Note there were no SAEs in the study.

7 In participants receiving the 30- and 20-
8 microgram doses, the favorable AE profile at the 10-
9 microgram dose and the immunogenicity results
10 demonstrating similar neutralizing antibodies at the
11 10- and 20-microgram doses informed the internal review
12 committee's decision to discontinue the 30-microgram
13 dosage and proceed to the Phase 2/3 study at the 10-
14 microgram dosage. There were no SAEs or deaths, and no
15 participants from Phase 1 withdrew or were discontinued
16 from the study.

17 This is Study 1007 Phase 2/3 as being
18 conducted in the United States, Finland, Poland, and
19 Spain. This portion of the study did not exclude
20 children with a history of prior SARS-CoV-2 infections,
21 children with known HIV, hepatitis B or hepatitis C, or

1 stable preexisting disease. Participants were
2 randomized two to one to receive two doses of 10-
3 microgram vaccine or saline placebo three weeks apart.

4 Phase 2/3 component of the study consisted of
5 two cohorts of equal size, approximately 22,250 each.
6 A second cohort was added at the request of FDA with
7 the intention of increasing the size of the safety
8 database in children 5 through 11 years of age. The
9 total size of the safety database consisted of
10 approximately 3,100 children in the vaccine group.
11 Immunogenicity was assessed in a subset of 322
12 participants in this study, and efficacy data was
13 obtained through continuous surveillance for potential
14 cases of COVID-19.

15 This slide depicts the timeline for Phase 2/3
16 Cohorts 1 and 2. Cohorts 1 and 2 vary by the duration
17 of follow-up. The data from an additional 2,369
18 participants in Cohort 2 were submitted during the EUA
19 review process. In Cohort 1, the first participant was
20 enrolled by June 7th, 2021. The data cutoff was
21 September 6th, 2021. This cohort included

1 approximately 1,500 vaccine recipients and 750 placebo
2 recipients, of whom 95 percent combined had at least
3 two months of safety follow-up after completing a two-
4 dose primary series. Safety data from this cohort
5 included solicited adverse events, unsolicited adverse
6 events, serious adverse events, and AEs of special
7 interest.

8 For Cohort 2, safety data from this cohort
9 included the safety monitoring as in Cohort 1 but, due
10 to the shortened follow-up time, focused on SAEs and
11 AEs of clinical interest. Cohort 2, the first
12 participant was enrolled on August 26th, 2021, and the
13 data cutoff was October 8th, 2021. The cohort was
14 approximately the same size as the Cohort 1, but the
15 median duration of follow-up here was 2.4 weeks post-
16 dose 2 at the time of data cutoff.

17 This slide depicts the study C4591001, or 1001
18 for short, which was used for the immunobridging
19 analysis to support vaccine effectiveness in a 5-
20 through 11-year age group. Study 1001 was the study in
21 which vaccine clinical efficacy against COVID-19 was

1 established for individuals 16 years of age or older.

2 The comparator group was a subset of 300
3 randomly selected participants enrolled in Study 1001
4 Phase 2/3 who received the vaccine at the 30-microgram
5 dose level in a two-dose primary series, 21 days apart.

6 This slide depicts the comparison that took
7 place in the immunobridging analysis. Effectiveness of
8 the Pfizer-BioNTech COVID-19 vaccine is being inferred
9 by comparing neutralizing antibody responses against
10 the Wuhan-like strain one-month post-dose 2 in children
11 5 through 11 years of age enrolled in the Study 1007
12 and comparing that to a subset of study participants 16
13 through 25 years of age enrolled in a separate study
14 1001. Participants in both studies had no evidence of
15 prior SARS-CoV-2 infection.

16 Immunobridging endpoints and statistical
17 success criteria will be discussed in the next two
18 slides. There were two immunobridging endpoints. The
19 first endpoint was GMT ratio. The important thing to
20 note here was that that immunobridging success criteria
21 consisted of the lower bound of the two-sided 95

1 percent confidence interval for GMT ratio with greater
2 than 0.67, and the point estimate was greater than or
3 equal to one.

4 The second immunobridging endpoint was
5 seroresponse. Immunobridging success criteria required
6 a lower limit of the 95 percent confidence interval for
7 the difference in seroresponse rates 5 to 11 years of
8 age minus 16 to 25 years of age of greater than or
9 equal to minus ten percent.

10 This slide provides an overview of the
11 analysis populations and the number of participants in
12 each. Safety populations consisted of all randomized
13 participants who received at least one dose of the
14 study intervention. The size of the safety populations
15 for Cohort 1 and 2 for the vaccine group are provided
16 near the top of the middle column in blue.

17 The population considered in the
18 immunobridging subset was the evaluable immunogenicity
19 population without evidence of prior SARS-CoV-2
20 infection by history or testing. Evaluable efficacy
21 population consisted of participants who received both

1 doses within a critical defined window.

2 This slide presents the demographics and
3 baseline characteristics of Study 1007 Phase 2/3 Cohort
4 1. Demographics of Cohort 2 were similar and will not
5 be shown. Overall, demographics included 52 percent
6 males and 48 percent females. The mean age was 8 years
7 in both groups. Regarding race, 78 percent were white;
8 seven percent were multiracial. Approximately 6
9 percent were African American, 6 percent Asian, and 21
10 percent were Hispanic.

11 Ninety-one percent were without evidence of
12 prior COVID-19 infection. Participants were enrolled
13 in four countries that I mentioned: U.S., Spain,
14 Finland, and Poland, with the U.S. contributing 71
15 percent of participants. Approximately 20 percent of
16 subjects had comorbidities which included obesity in
17 about 12 percent, asthma in approximately 8 percent,
18 neurologic disorders in about 1 percent, and congenital
19 heart disease in less than 1 percent.

20 Results for the GMT primary endpoint are
21 displayed here. The important thing to note is that

1 the success criteria for immunobridging based on a GMT
2 ratio were met as the lower bound of the 2-sided 95
3 percent confidence interval for GMT ratio was greater
4 than 0.67, and the point estimate was greater than or
5 equal to one.

6 Seroresponse rates among participants without
7 evidence of prior SARS-CoV-2 infection up to one month
8 after post-dose 2 were displayed here. The lower limit
9 of the 95 percent confidence interval for the
10 difference in seroresponse rate was minus 2 percent,
11 which was greater than the prespecified margin of minus
12 10 percent, and thus immunobridging based on
13 seroresponse rate was met.

14 In response to FDA's request for
15 immunogenicity data to support the effectiveness of the
16 10-microgram Pfizer-BioNTech COVID-19 vaccine primary
17 series against the Delta variant, Pfizer submitted
18 exploratory analyses from a randomly selected subset of
19 participants from the evaluable immunogenicity
20 population consisting of 34 vaccine and 4 placebo
21 recipients who did not have evidence of prior SARS-CoV-

1 2 infection. These data were generated using non-
2 validated SARS-CoV-2 plaque-reduction neutralization
3 assays with a reference strain and the Delta variant.
4 The relative sensitivity of the two assays is not
5 known.

6 This slide provides the results of the Delta
7 variant neutralization analysis which shows that a 10-
8 microgram primary series elicited PRNT neutralizing
9 titers against both the reference strain and the Delta
10 strain in participants 5 through 11 years of age with
11 no evidence of SARS-CoV-2 infection up to one-month
12 post-dose 2.

13 For your records, this slide provides the
14 definitions of the protocol-defined COVID-19 and severe
15 COVID-19 disease. COVID-19 was defined as the presence
16 of at least one of the listed symptoms, including
17 cough, shortness of breath, and chills, et cetera,
18 meaning that only one symptom was needed to meet that
19 definition and a confirmed SARS-CoV-2 PCR-positive test
20 during or within four days before or after the
21 symptomatic period.

1 In this descriptive analysis, vaccine efficacy
2 against symptomatic COVID-19 after seven days post-dose
3 2 up to the data cutoff was 90.7 percent in
4 participants without evidence of prior SARS-CoV-2
5 infection. A total of 3 cases of COVID-19 occurred in
6 the vaccine group, 16 in the placebo group, with most
7 cases occurring during July and August 2021 when the
8 Delta variant was prevalent in the U.S.

9 At the time of the data cutoff, none of these
10 vaccine cases met the criteria for severe COVID-19.
11 All cases occurred in children without a prior history
12 of COVID-19 infection. All cases of COVID-19 were
13 confirmed by the central lab PCR at least seven days or
14 more post-dose 2, and there were no cases of COVID in
15 participants with a prior history of SARS-CoV-2
16 infection.

17 In the COVID-19 cases, vaccinated participants
18 had less symptoms, one to three symptoms of COVID-19,
19 but approximately one-third of the placebo recipients
20 had more than five symptoms. No vaccinated
21 participants had fever, while 10 of 16, or 65 percent,

1 of the placebo recipients had fever. Only one case
2 occurred in a child with a predefined comorbidity,
3 asthma.

4 All confirmed COVID-19 cases occurred in the
5 U.S., except for one in Spain. No virus sequence
6 analyses had been provided to the FDA to determine
7 whether or not these cases were caused by the Delta
8 variant or another variant. It's important to note
9 that the study did not evaluate efficacy against
10 asymptomatic disease or transmission, so we made no
11 conclusions on that.

12 This slide provides a safety follow-up time
13 for Cohorts 1 and 2 post-dose 2. What's important to
14 note that, for Cohort 1, more than 95 percent had
15 safety follow-up data for two to three months after
16 dose 2.

17 For Cohort 2, 70 percent of the participants
18 had safety follow-up data for at least two to three
19 weeks after vaccination, which includes the timeframe
20 in which most cases of myocarditis after vaccination
21 have been observed. In both cohorts, over 3,000

1 participants were followed seven days or more.

2 Here we see the frequency of local reactions,
3 including injection site pain, redness, and swelling
4 within seven days after each dose, including the
5 frequency of Grade 3 reactions. In general, local
6 reactions occurred more frequently after dose 2.

7 Pain at the injection site was reported most
8 commonly in almost 75 percent of participants for dose
9 1. The frequency of Grade 3 reactions after
10 vaccination was low, seen in 0.3 percent of
11 participants for pain at the injection site following
12 either dose 1 or dose 2.

13 **DR. ARNOLD MONTO:** Dr. Ball, you're over time
14 already.

15 **DR. LESLIE BALL:** Okay. We will go through
16 this quickly. I think you've seen already the
17 frequency of solicited adverse events within seven days
18 after each dose. Systemic adverse events also
19 generally occurred more commonly after dose 2. In the
20 vaccine group, the most commonly observed systemic
21 events were fatigue, headache, and muscle pain. For

1 both the systemic and local reactions, most were mild
2 to moderate in severity.

3 This slide provides information on the onset
4 of duration of solicited local and systemic reactions.
5 The onset and duration for vaccine recipients were
6 similar with both dose 1 and 2 with a median time of
7 onset for local reactions of one day and for systemic
8 reactions of two days. Both local and systemic
9 reactions resolved within one to two days after onset.

10 The most common unsolicited adverse event was
11 lymphadenopathy which was reported in less than one
12 percent of the vaccine recipients. In both Cohort 1
13 and 2, there was only one participant that was
14 withdrawn due to an AE, a child with fever to 40
15 degrees centigrade two days after dose 1 and a
16 worsening of a preexisting neutropenia, the diagnosis
17 of benign transient neutropenia.

18 FDA conducted standardized MedDRA Queries, or
19 SMQs, to evaluate the constellation of unsolicited
20 adverse events. The SMQs that occurred more commonly
21 in the vaccine group than in the placebo, including

1 hypersensitivity reactions, consisting of primarily
2 rash and dermatitis. Angioedema was included as facial
3 swelling and urticaria cases. One participant, a 6-
4 year-old vaccine recipient, reported Henoch-Schonlein
5 purpura which was diagnosed 21 days after dose 1.

6 This was considered non-serious, and symptoms
7 resolved after one to three days with no laboratory
8 evaluations performed. All but one case event of rash
9 with onset 12 days post-dose 2 were considered resolved
10 at the time of data cutoff.

11 Chest pain was reported in six vaccine
12 recipients and also six placebo recipients. All
13 resolved without intervention and were considered
14 noncardiac in origin.

15 In Cohorts 1 and 2, the SAEs occurred at a
16 frequency of 0.1 percent and 0.2 percent, respectively,
17 in the vaccine recipients, and 0.1 percent and 0
18 percent in placebo recipients, respectively.

19 SAEs included common events that occurred in
20 this population, such as arthropod bite, knee
21 infection, and fractures, and were considered unrelated

1 to vaccination. There were no reports of myocarditis
2 or anaphylaxis and no participant deaths.

3 Here, I provide an overview of the
4 pharmacovigilance, or PV, plan for the Pfizer-BioNTech
5 COVID-19 vaccine. The plan includes monitoring for
6 important identified risks, including anaphylaxis and
7 myocarditis, and important potential risks, including
8 vaccine-associated enhanced disease.

9 Under the PV plan, four post-authorization
10 observational studies will be performed that includes
11 the 5- through 11-year age group. Each of these
12 studies involve monitoring for myocarditis and
13 pericarditis.

14 **MR. MICHAEL KAWCZYNSKI:** All right, Dr. Ball.
15 Because we didn't want to make sure we'd lose anything,
16 we paused right there. Go ahead and continue.

17 **DR. LESLIE BALL:** Okay. This slide presents
18 some key features for the two pediatric EUAs for the
19 Pfizer-BioNTech COVID-19 vaccine, the EUA currently
20 under consideration, 5 through 11 years of age, and the
21 EUA issued in May for adolescents 12 through 15. The

1 proposed EUA, 5 through 11, involves a 10-microgram
2 formulation while the 30-microgram formulation is
3 authorized for use in adolescents 12 through 15 years
4 of age. The clinical studies submitted to support the
5 EUAs for both age groups included similar endpoints,
6 similar immunobridging approaches, and similar
7 descriptive efficacy analysis.

8 The safety database for vaccine recipients was
9 approximately 3,000 in the 5- through 11-year age group
10 and 1,100 in the 12- through 15-year age group. At the
11 time of the data cutoff, the 5- through 11-year age
12 group had over 1,400 participants with two months or
13 more of safety data, and 12- to 15-year age group had
14 660 with 2 months or more of follow-up.

15 In summary, for immunogenicity and efficacy,
16 the immunobridging success criteria were met for GMT
17 and seroresponse rates at one-month post-dose 2.
18 Descriptive immunogenicity analyses in a small subset
19 of 34 vaccine recipients showed a 10-microgram primary
20 series-elicited PRNT 50 percent neutralizing titers
21 against both the reference and Delta strains.

1 Supplemental descriptive efficacy analysis
2 showed vaccine efficacy against symptomatic COVID-19
3 after seven days post-dose 2 was 90.7 percent in
4 participants without evidence of prior SARS-CoV-2
5 infection.

6 Regarding safety, local and systemic reactions
7 were more common after dose 2. The most frequent
8 reactions were injection site pain, fatigue, and
9 headache.

10 Most frequently reported unsolicited AE was
11 lymphadenopathy occurring in less than one percent of
12 vaccine recipients. More vaccine recipients reported
13 hypersensitivity-related events than placebo
14 recipients. No anaphylaxis cases were reported.

15 Of the combined safety database of over 3,100
16 vaccine recipients, 4 SAEs reported; all were
17 considered unrelated to vaccine. There were no reports
18 of myocarditis or pericarditis.

19 In closing, I'd like to acknowledge the
20 substantial contributions of my clinical colleagues,
21 Dr. Maria Allenda, Lucille Lee, Rebecca Reindel, and

1 Susan Wollersheim, and statistical colleagues Dr. Yang
2 and Lee Wong, as well as our many colleagues on the
3 multidisciplinary CB team. That concludes my
4 presentation.

5

6 **FDA PRESENTATION: POST-MARKET ACTIVE SURVEILLANCE OF**
7 **COVID-19 VACCINES IN THE PEDIATRIC POPULATION IN THE**
8 **FDA BEST SYSTEM**

9

10 **DR. ARNOLD MONTO:** Thank you, Dr. Ball. Now I
11 turn the floor over to Dr. Wong who is going to talk
12 about post-authorization evaluation briefly, I hope.

13 **DR. HUI-LEE WONG:** Indeed, it shall be brief
14 but informative. Thank you, Dr. Monto.

15 Today on behalf of our multiple partners in
16 the FDA BEST, we want to share one of the ways FDA
17 actively monitors the post-market safety of COVID-19
18 vaccines in children.

19 The active surveillance system for biologics
20 including COVID-19 vaccines is the FDA Biologics and
21 Effectiveness Safety. That's the BEST system.

1 Illustrated on this slide, there are the
2 multiple partners that we have. Our safety
3 surveillance for COVID-19 vaccines, these yellow
4 circles here is the large administrative claims
5 databases where collectively they represent claims from
6 each state in the United States.

7 In total here we see the pediatric population.
8 This is roughly, approximately the annual enrollees per
9 year breakdown by age. In total, that's around 20
10 million pediatric enrollees. That covers an estimated
11 percentage of around 25 to 30 percent of the U.S.
12 population.

13 While we generally use administrative claims
14 databases because this is very helpful for potentially
15 rare adverse events, BEST also has access to a number
16 of electronic health records databases. Shown here on
17 this slide are details of a pediatric EHR, or
18 electronic health records, from eight pediatric
19 hospitals.

20 I'll now move back to the database that we
21 generally use in general for the safety surveillance,

1 and that is the claims database. I just shared with
2 you four. Of these two of this year for the ages 12 to
3 17 Pfizer-BioNTech COVID-19 vaccine doses, we have
4 around 1.2 million. These are currently being used for
5 safety surveillance of COVID-19 vaccines.

6 FDA BEST monitors the safety of COVID-19
7 vaccines by monitoring the rate of outcomes. Here is a
8 working list of 16 outcomes. None of these have been
9 associated with COVID-19 vaccines based on
10 preauthorization evidence. Working lists are added on
11 as more information comes on.

12 What we do with that is that we monitor the
13 rates of these outcomes close as they occur, hence they
14 call it near real-time safety surveillance. For those
15 above 65 years, it's every week. For those under 65
16 years, it's from 12 to 64 years.

17 This slide shows you one of our latest results
18 that is for near real-time surveillance of Pfizer-
19 BioNTech COVID-19 vaccines in 12 to 64 years. Here you
20 can see that we did not detect any physical signals for
21 elevated risk of rates of these outcomes, except for

1 anaphylaxis, but there's mitigation strategies
2 currently in place.

3 While these are 12 to 64, for the pediatric
4 population, we monitor right now to see whether any of
5 the event occur, and then we do additional analysis.
6 We call those observed versus expected analysis. I'll
7 explain a little bit more of that, where we compare
8 with the rate that's observed after vaccination with
9 rates that is expected in the absence of vaccines, in
10 this case, background rates. We will focus on certain
11 age group of interest, for example where needed if it's
12 male 12 to 15, for example.

13 In summary, FDA BEST is monitoring the safety
14 of COVID-19 vaccines in near real-time surveillance.
15 Specifically for pediatric population, we will conduct
16 observed versus expected analysis for any of the
17 subgroups of interest when events sufficiently accrue.

18 We have conducted these for myocarditis and
19 pericarditis for males and female subgroups in
20 pediatric populations. One of these input actually
21 will be public input for the benefit-risk assessment

1 that our colleague, Dr. Hong Yang, will present.

2 I would like to thank the entire large, huge
3 cadre of persons working with us, our FDA staff, for
4 your dedication throughout weekends, throughout
5 holidays, for our collaborators, all the BEST
6 collaborators too numerous to be named here actually,
7 for keeping pace with us as we provide timely and yet
8 rigorous data in terms of COVID-19 vaccine
9 surveillance. Thank you. This concludes my remarks.

10

11 **FDA PRESENTATION: BENEFITS-RISKS OF PFIZER-BIONTECH**
12 **COVID-19 VACCINE FOR AGES 5 TO 11 YEARS**

13

14 **DR. ARNOLD MONTO:** Thank you, Dr. Wong. You
15 were indeed brief. Dr. Hong Yang is our next speaker
16 who will be talking about benefit-risk analysis. She's
17 from the Office of Biostatistics and Epidemiology,
18 CBER. Dr. Yang.

19 **DR. HONG YANG:** Hi. Thank you. My name is
20 Hong Yang. I'm senior advisor for benefit-risk
21 assessment, Office of Biostatistics and Epidemiology in

1 CBER.

2 Today, I'm presenting a benefit-risk
3 assessment for use of Pfizer-BioNTech COVID-19 vaccine
4 for age 5 to 11 years.

5 To authorize use of a drug or biologic
6 product, FDA need to determine whether the benefit
7 outweigh the risk. For COVID vaccine, the key benefits
8 are preventing of COVID-19 cases, hospitalization, ICU
9 stays and death due to COVID-19. The key risks are
10 myocarditis, pericarditis cases attributable to vaccine
11 or related hospitalization, ICU stays, and death.

12 Throughout the rest of the presentation, I
13 will use myo cases to represent both myocarditis and
14 pericarditis. FDA conducted analysis to assess the
15 benefits and risks per one million individuals who
16 received two dose of Pfizer vaccine. Analysis was
17 conducted first by male, female, and both sex combined.
18 For (inaudible) purpose, FDA's approach is purposefully
19 conservative.

20 FDA assessed the benefit of vaccine within six
21 months post second dose. This slide shows the model

1 assumption and input for Scenario 1 or we call base
2 scenario.

3 Two general assumptions were made. First,
4 duration of vaccine protection is six months post
5 second dose of vaccine, efficacy remained constant.
6 The second is incidence of COVID cases,
7 hospitalizations, ICU stays, and death are stable over
8 the period. To estimate the benefit of vaccine, we
9 used the COVID incidence data available from COVID NET
10 of the week of September 11, 2021. We took an average
11 of four weeks prior to September 11 for incidence of
12 hospitalization and historical average rate for ICU
13 stays and death. We assumed vaccine efficacy 70
14 percent against cases and 80 percent against
15 hospitalization.

16 This is of CDC vaccine effectiveness study
17 which monitoring the Pfizer vaccine recipients age 20-
18 to 64-years-old for both pre-Delta and Delta period.
19 To estimate the risk, we used the myo incidence data
20 age 12 to 15 years from OPTUM. That is the healthcare
21 data, a part of FDA's Sentinel BEST system. We used

1 this 12- to 15-years data because the data for 5 to 11
2 years age is not available. The rate of
3 hospitalization and ICU stays due to vaccine-related
4 myocarditis cases were obtained from Vaccine Safety
5 Datalink.

6 They found no death was determined to be
7 associated with vaccine-related myo cases. The
8 majority of the vaccine-related myo cases are in mild
9 conditions, and they resolved in a short period of
10 time. This base scenario is a temporary (inaudible) of
11 our modeling. It does represent the most likely
12 scenario. There are major uncertainty associated with
13 model assumption and the incurred. On the next two
14 slides, I will discuss the uncertainties and the
15 alternative model scenario used to evaluate the impact
16 of those uncertainties.

17 One of the key uncertainties is the future
18 dynamic of the pandemic. The COVID-19 incidence has
19 great influence on the benefit of the vaccine. The
20 higher the incident, the greater the benefit, vice
21 versa. We use the recent peak incidence and the lowest

1 incidence in Scenario 2 and 3 to represent the bound of
2 future pandemic with a caveat that incidence may but
3 are less likely (inaudible) response. Another issue is
4 inconsistency in COVID death rate derived from CDC Data
5 Tracker compared to COVID NET. We use Scenario 5 to
6 (inaudible) the impact of these inconsistencies.

7 In the death scenario, we use vaccine efficacy
8 of 70 percent against cases and 80 percent against
9 hospitalization based on CDC Vaccine Effectiveness
10 Study. Recently, a sponsor submitted a supportive
11 efficacy analysis which suggests 90.7 percent efficacy
12 against COVID-19 among age 5 to 11 years. We used this
13 higher efficacy in Scenario 4. Last, there is great
14 uncertainty on incidence of excess myo cases among the
15 age 5 to 11 years. There are two layers of
16 uncertainties. First, no data available for age 5 to
17 11 years old.

18 We used the rate for age 12 to 17 years.
19 However, historical data on classical myo cases suggest
20 that the risk among age 5 to 11 years may be lower than
21 the age 12 to 17 years. In addition, the incidence

1 (inaudible) of proposed vaccine for 5 to 11 years of
2 age is lower than the vaccine for 12 to 15 years for
3 the use under the EUA.

4 The observed systemic reactogenicity in
5 clinical trial is lower accordingly. There is
6 speculation that the incidence of excess myocarditis
7 cases may be lower in age 5 to 11 years. Second, both
8 Vaccine Safety Datalink data and Vaccine Adverse Event
9 Reporting System suggested a lower excess myocarditis
10 case rate among (inaudible).

11 Even though we believe OPTUM data fit best for
12 the purpose of this study, there may be uncertainty due
13 to limited sample size and limitation of the healthcare
14 data. Also, the case is not reviewed in depth, so that
15 may cause the overestimate of the myocarditis case
16 rate. We use Scenario 6 to represent a potential 50
17 percent lower incidence for excess myo case. Sorry. I
18 forgot to advance slide.

19 Next, I will present the benefit-risk
20 assessment results. Scenario 1, here I will remind you
21 this is the key assumption and model input used in this

1 scenario, COVID-19 incidence at the week of September
2 11, 2021.

3 We used vaccine efficacy 70 percent against
4 cases and 80 percent against hospitalization. The rate
5 of excess myocarditis is coming from OPTUM's data for
6 age 12 to 15 years old.

7 This bar chart from top down present model-
8 perceived benefit-risk assessment for male age 5 to 11,
9 12 to 15, and 16 to 17 years. The vaccine has been
10 authorized under EUA for later two age group. The
11 benefit-risk of these two groups were for past year for
12 comparison.

13 On the left side of each bar chart are four
14 benefit endpoints. From bottom up, prevented COVID
15 cases, hospitalization, ICU stays, and death.

16 On the right side of the bar chart are four
17 risk endpoints. From bottom up, excess myo cases,
18 hospitalization, ICU stays, and death. When we compare
19 the benefit and risk side by side, we need to keep in
20 mind that the clinical implication of hospitalization
21 and ICU stays due to COVID-19 are very different from

1 those due to vaccine-related myocarditis. The former
2 require much more extensive clinical care and later
3 typically to monitor patients' condition as a
4 precaution.

5 Looking at the chart on the top, for male age
6 5 to 11 years, model predicts vaccine prevent about
7 45,000 COVID cases, 203 hospitalization, 57 ICU stays,
8 and 1 death among 1 million fully vaccinated
9 individuals.

10 In the meantime, this vaccine may cause 179
11 excess myo cases, 98 hospitalizations and 57 ICU stays.
12 The benefit appear to outweigh the risks. There're
13 similar result for the other two age group.

14 This bar chart for female under base scenario.
15 For all three age groups from top down, the benefits
16 clearly outweigh the risk. The benefit-risk are
17 clearly more favorable compared to the benefit-risk for
18 male presented on the previous slide.

19 These are bar chart for male and female
20 combined. Similarly, we can see for all age group the
21 benefit clearly outweigh the risks.

1 Scenario 2 with peak incidence. On this
2 slide, there are three bar chart, top down, for age 5
3 to 11 years, male, female, and male-female combined.
4 For sake of time, from now on, I will focus on the
5 result for 5 to 11 years old, male only. This is the
6 group with the highest risk. The female and two sets
7 combined always have more favorable benefit-risk
8 compared to the male group. For Scenario 2 with peak
9 incidence for age 5 to 11 years male, model predicts
10 vaccine prevents about 54,000 COVID cases, 250
11 hospitalization, 82 ICU stays, and 1 death while
12 vaccine may cause 179 excess myo cases, 98
13 hospitalizations, and 57 ICU stays. The benefit
14 appears to outweigh the risk.

15 Scenario 3 with the lowest COVID-19 incidence.
16 For male 5 to 10 years old, the chart on the top, the
17 model predicts much lower benefit, which is prevention
18 of 2,639 COVID cases, 21 hospitalizations, and 7 ICU
19 stays. However, the vaccine may cause 179 excess myo
20 cases, 98 related hospitalizations, and 57 related ICU
21 stays. Where the benefit of vaccine outweighs the risk

1 under this scenario, this may require a (inaudible).
2 Considering the clinical implications and the length of
3 stay for COVID-19 versus myo-related hospitalization
4 and ICU stays and the benefit of preventing COVID-19
5 (inaudible) morbidity. So overall, benefit of the
6 vaccine may still outweigh the risk.

7 Scenario 4 with higher vaccine efficacy. For
8 male 5 to 10 years, the model predicts vaccine will
9 prevent about 58,000 COVID cases, 254 hospitalizations,
10 83 ICU stays, and 1 death, while cause 179 excess myo
11 cases, 98 hospitalizations, and 57 ICU stays. The
12 benefit appears to outweigh the risk.

13 Scenario 5 with the higher COVID death rate.
14 For Scenario 5, the male 5 to 10 years, the model
15 predicted prevention of about 45,000 COVID cases, 203
16 hospitalizations, 67 ICU stays, and 3 deaths. However,
17 vaccine may cause 179 excess myo cases, 98
18 hospitalizations, and 57 ICU stays. So overall,
19 benefit appear to outweigh the risk.

20 The last, Scenario 6, with 50 percent lower
21 myocarditis case rate. For male 5 to 10 years, the

1 model predict about 45,000 COVID cases, 203
2 hospitalizations, 57 ICU stays, and 1 death. However,
3 it may cause 89 excess myo cases, 49 hospitalizations,
4 and 29 ICU stays. The benefit clearly outweigh the
5 risks.

6 This is the results slide. The greatest
7 uncertainty of this analysis is associated with the
8 assumption that the pandemic remains stable over the
9 next six months, which leads to great uncertainty on
10 the prediction of vaccine benefit.

11 Vaccine efficacy may change due to emerging of
12 new variants. Hospitalization and ICU stays from
13 COVID-19 or vaccine-related myocarditis have bigger
14 clinical implications in comparison (inaudible).

15 FDA's assessment is conservative. The benefit
16 of reducing COVID-related multisystem inflammatory
17 syndrome may not fully capture this by the full benefit
18 endpoint used in this analysis. This benefit-risk
19 assessment does not consider potential long-term
20 benefits and risk. This benefit-risk assessment does
21 not include secondary benefits and risks such as

1 prevention of disease transmission, in-person learning
2 of the children, socioeconomic impact, and so on.

3 In conclusion, in the five out of six model
4 scenarios, model predict favorable benefit-risk for the
5 Pfizer vaccine. Under Scenario 3, the model predicts
6 more excess than prevented hospitalizations and ICU
7 stays in male and both sexes combined. However,
8 considering the difference in the clinical implications
9 and the length of the stay for hospitalization and ICU
10 stays due to COVID-19 versus vaccine-related myo cases
11 and the benefit of preventing COVID-19 with significant
12 morbidity, the overall benefit of the vaccine may still
13 outweigh the risk.

14 Finally, I would like to acknowledge the
15 member of FDA benefit-risk assessment team, Dr. Patrick
16 Funk; Osman Yogurtcu for their excellent contributions
17 to the benefit-risk modeling; and to Dr. Rich Forshee,
18 his leadership. We thank CDC Vaccine Task Force for
19 sharing initial benefit-risk assessment model also the
20 data on COVID-19 pandemic. We thank Acumen and OPTUM
21 team for providing myocarditis incidence data. We also

1 thank many of our FDA colleagues for their input
2 through their analysis.

3 **DR. ARNOLD MONTO:** Thank you, Dr. Yang. We're
4 running a bit late, so that we are not going to be able
5 to entertain questions now. What I think we will do
6 when we resume after lunch and the open public hearing
7 is to ask Dr. Yang to put up her conclusion slide
8 again, and then we will have our question and answer
9 period from the members because this is an important
10 presentation. We really need time to discuss the
11 presentation before we go into our general question and
12 answer period. So break now until the open public
13 hearings at 1:00. Then we resume questions and answers
14 at 2:10, I believe, all Eastern Time.

15

16

[LUNCH BREAK]

17

18

OPENING PUBLIC HEARING

19

20

21 **MR. MICHAEL KAWCZYNSKI:** All right. Good
afternoon and welcome back from that lunch break to the

1 170th VRBPAC meeting. We are now going to go into our
2 afternoon portion of today's activities. So, Dr.
3 Arnold Monto, are you there?

4 **DR. ARNOLD MONTO:** I am. And I'd like to
5 welcome everybody to the open public hearing session.
6 Please note that both the Food and Drug Administration
7 and the public believe in a transparent process for
8 information gathering and decision-making. To ensure
9 such transparency at the open public hearing session of
10 the Advisory Committee meeting, FDA believes that it is
11 important to understand the context of an individual's
12 presentation.

13 For this reason, FDA encourages you, the open
14 public hearing speakers, at the beginning of your
15 written or oral statement, to advise the Committee of
16 any financial relationship that you may have with the
17 product, the sponsor, and if known, its direct
18 competitors. For example, this financial information
19 may include the sponsor's payment of expenses in
20 connection with your participation in this meeting.
21 Likewise, FDA encourages you, at the beginning of your

1 statement, to advise the Committee if you do not have
2 any such financial relationship.

3 If you choose not to address this issue of
4 financial relationships at the beginning of your
5 statement, it will not preclude you from speaking.
6 Over to you, Prabha.

7 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Monto.
8 Before I begin calling on the registered speakers, I
9 would like to add the following guidance. FDA
10 encourages participation from all public stakeholders
11 in its decision-making process. Every Advisory
12 Committee meeting includes an open public hearing
13 session, OPH session, during which interested persons
14 may present relevant information or views.
15 Participants during the OPH session are not FDA
16 employees or members of this Advisory Committee.

17 FDA recognizes that the speakers may present a
18 range of viewpoints. The statements made during this
19 open public hearing session reflect the viewpoints of
20 the individual speakers or their organization and are
21 not meant to indicate the agency's agreement with the

1 statements made. With this guidance, I would like to
2 move forward with the registered speakers. The first
3 speaker is Dr. David Burger.

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

6 **DR. DAVID BURGER:** My name is Dr. David
7 Burger. I have no financial conflicts of interest.

8 Slide number 2. I am a board-certified
9 pediatrician with more than 25 years of clinical
10 experience. I practice primary care with a focus on
11 optimizing nutrition and lifestyle. I offer vaccine
12 consultations for all ages.

13 Slide 3. I serve a diverse patient population
14 and am hearing more COVID-19 vaccine hesitancy for the
15 5 to 11 age group than I did for adolescents. People
16 with vaccine questions often look to me as a trusted
17 source of information. I explain that for most people
18 immunity will develop following vaccination or natural
19 infection, but the strength and duration of immunity
20 varies. I suggest that they make a benefit versus risk
21 list for both getting the vaccine as well as catching

1 the virus. I am glad I can share the Pfizer briefing
2 data and let parents know that the safety and efficacy
3 studies will be ongoing for two years.

4 Slide 4. My approach to vaccine hesitancy is,
5 rather than expel families from my practice as many
6 pediatricians do, I find that having patience,
7 acknowledging concerns, and educating in a non-
8 threatening way allows people to make the best choices
9 for themselves, including deciding whether to vaccinate
10 their children. A number of them eventually choose to
11 vaccinate; some do not.

12 Slide 5. According to the Pfizer data, 3,750
13 children were given 10-microgram doses of the vaccine,
14 750 received a placebo. The antibody response using
15 the lower dose was similar to that found in older
16 children who were given 30 micrograms. This is
17 promising data. If authorized, I am glad parents will
18 have the choice to give this lower dose product.

19 Slide 6. Parents are asking many questions,
20 including whether the vaccine will likely result in a
21 significant reduction of pediatric hospitalization or

1 death especially since these outcomes are already rare
2 in young children. The Pfizer data shows a 90 percent
3 reduction of symptomatic disease among this population.

4 They ask if a reduction of pediatric long-haul
5 incidents can be expected. We have seen cases of long-
6 haul COVID in our practice but not among the young
7 children. Parents want to know if the vaccine is
8 expected to reduce family and community spread. I
9 explain that the more people who have immunity, the
10 more protected those are around them.

11 Slide 7. Parents are asking if the sample
12 size was adequate. Assuming an approximate number of
13 children at each age, the study included an estimated
14 1,600 children vaccinated age 5 to 7 and 1,100 children
15 in the 8 to 9 and 10 to 11 age groups.

16 Slide 8. Parents want to know about
17 myocarditis and if there could be side effects specific
18 to this age group that are not seen in older people.
19 They ask how to optimize nutrition and moderate
20 inflammation. I explain that having good vitamin D and
21 zinc levels, adequate sleep, and physical fitness are

1 all beneficial.

2 Slide 9. It's important to recognize that
3 parents make decisions that they think are best for
4 their children. Many will vaccinate right away, some
5 will wait, and some will choose not to vaccinate. Even
6 vaccinated parents may be uncomfortable vaccinating
7 their young children, especially at the beginning. I
8 find most people with hesitancy about the COVID
9 vaccines are not who are often labeled anti-vaxxers. I
10 would like to take this opportunity to call for
11 understanding, civility, and respect. No one benefits
12 if we judge and ridicule each other.

13 Slide 10. Thank you for allowing me this
14 opportunity to present to you.

15 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Burger.
16 The next speaker is Steve Kirsch.

17 **MR. STEVE KIRSCH:** Hi, I'm Steve Kirsch,
18 Executive Director of the COVID-19 Early Treatment
19 Fund. I have no conflicts of interest.

20 Slide 2. Why are kids dropping like flies
21 right after getting vaccinated? If they didn't die

1 from the vaccine, then what killed these kids?

2 Next slide. How can a healthy 16-year-old boy
3 die in the middle of a Zoom math class? He was fine 20
4 minutes before he died.

5 Next slide. The doctor's found nothing, what
6 did the CDC find?

7 Next slide. Why did this 15-year-old die in
8 his sleep just two days after getting vaccinated?

9 Slide number 6. How did you miss all of these
10 safety signals?

11 Slide number 7. If the vaccines are so safe,
12 how come Taiwan officially admits that the vaccines
13 killed more people than the virus?

14 Slide 8. Do you find this recent U.K.
15 headline troubling?

16 Slide 9. How are Germany and Norway both able
17 to determine causality in sample sizes of 100 or less,
18 but the CDC can't determine causality in over 16,000
19 deaths it has investigated?

20 Slide 10. How come deaths in Israel go up
21 when vaccinations go up and go down when vaccinations

1 go down?

2 Slide 11. What is the VAERS under-reporting
3 factors? How can you do a risk-benefit analysis if you
4 don't know the URF? This is extremely, extremely
5 important. You've been assuming it's been one, it is
6 not one.

7 Slide 12. Using a URF of 41 which is
8 calculated using the CDC methodology, we find over
9 300,000 excess deaths in VAERS. If the vaccine didn't
10 kill these people, then what did?

11 Slide number 13. Is there any stopping
12 condition to these experiments? How many Americans
13 have to die before you pull the plug? How many kids
14 have to die before you yell, stop?

15 Slide 14. Why are there no autopsies for
16 deaths after vaccination?

17 Slide 15. Why didn't the highly unusual
18 causes of deaths in these kids raise any red flags in
19 the CDC 12 to 17 safety study? They didn't even
20 comment, they said just move on, nothing to see here.

21 Slide 16. How many months do troponin levels

1 stay elevated after vaccination?

2 Slide 17. Of the over nearly 140,000 comments
3 have been posted against the vaccines in kids, I found
4 only one comment in favor. How many did you find?

5 Slide 18. Did you ever read the Kostoff
6 paper? It says that five times as likely to die from
7 the vaccine as from COVID. And it's even worse if
8 you're younger.

9 Slide 19. Why was this paper removed over the
10 objections of the editors?

11 Slide 20. They found 19 times the expected
12 number of myocarditis cases and a 5-fold increase on
13 dose 2.

14 Slide 22. Is this what you mean by slightly
15 elevated risk?

16 And let's skip to Slide 26. How can a kid who
17 was in the Pfizer 12- to 15-year-old trial be paralyzed
18 and not have that reported to the FDA? How can you
19 approve a vaccine for under 12 when you haven't
20 investigated this study?

21 Let's skip to the end here, Slide number 30

1 which is the complete list of my questions are posted
2 on "TrialSiteNews" today. Just search for VRBPAC.

3 There are too many unanswered questions for
4 you to approve the vaccine for 5- to 11-year-olds.
5 Thank you.

6 **DR. PRABHAKARA ATREYA:** Thank you. The next
7 speaker is Dr. Andrea Kline-Tilford.

8 **DR. ANDREA KLINE-TILFORD:** Greetings. I'm
9 Andrea Kline-Tilford. I have no conflicts of interest.

10 I'm a pediatric nurse practitioner and
11 president of the National Association of Pediatric
12 Nurse Practitioners, a professional organization
13 representing more than 8,000 pediatric-focused advanced
14 practice registered nurses. We support the timely and
15 complete immunization of all infants, children, and
16 adults in an attempt to maximize the health and well-
17 being of all people. The last 20 months have brought
18 immense strain to the world, including our nation's
19 more than 20 million children 5 to 11 years of age.
20 Our children have been pivoting in all areas of life.

21 Slide 2. The strain has been immense and has

1 resulted in physical and mental health challenges that
2 will undoubtedly have lasting impacts on social,
3 emotional, and mental health. In a poll conducted by
4 researchers in Chicago, 71 percent of parents or
5 caregivers believe the pandemic impacted their child's
6 mental health.

7 Pediatric nurse practitioners are on the front
8 line in primary and acute settings encountering these
9 challenges in our children each and every day. There
10 has been an alarming increase in child and adolescent
11 anxiety, depression, and suicide. According to the
12 CDC, mental health-related emergency department visits
13 by adolescents increased by 31 percent in 2020. And at
14 one point during the pandemic, emergency department
15 visits for suspected suicide attempts in girls was up
16 51 percent from 2019.

17 Additionally, eating disorders, sometimes
18 deadly, increased 62 percent during the pandemic and an
19 estimated 140,000 children have lost parents and
20 caregivers due to COVID-19. Let's not forget the
21 physical ramifications of COVID-19. Children can and

1 do suffer acute illness, multi-system inflammatory
2 syndrome, and long-haul physical symptoms. Over the
3 last several months the number of COVID cases in
4 children has substantially increased.

5 Data from October of 2021 reveals more than
6 630 pediatric deaths from COVID-19 and at least 46
7 pediatric deaths associated with MIS-C. Children have
8 paid a significant toll, and we have the ability to
9 alter this trajectory. Right now, we rely on masking,
10 physical distancing, hand hygiene, and surrounding
11 children with adolescents and adults that are
12 vaccinated. Without other options, these strategies
13 were acceptable but are not a solution and leave a
14 tremendous gap in protection for our children.

15 Slide 3. NAPNAP urges the FDA to authorize
16 the Pfizer-BioNTech COVID-19 vaccine for children 5 to
17 11 years and supports widespread equitable rollout to
18 every eligible child in the U.S. using all possible
19 vaccination sites, including primary care offices,
20 schools, health centers, pharmacies, popup sites, and
21 mobile units. COVID-19 vaccination is safe and

1 effective, and, with the adjusted dosing for children 5
2 to 11, we can protect our school-aged children
3 immediately and further shield them from short and
4 long-term physical and mental health consequences.

5 Let's use the newly provided data on the
6 Pfizer vaccine to deliver comprehensive, equitable
7 immunization to all children 5 to 11 years of age.
8 Thank you for this time to share the views of the
9 National Association of Pediatric Nurse Practitioners
10 and my own views as a mother of two children under 12
11 years of age.

12 **DR. PRABHAKARA ATREYA:** Thank you. The next
13 speaker is Dr. Jessica Rose.

14 **DR. JESSICA ROSE:** My name is Dr. Jessica
15 Rose, and I'm a virtual immunologist and computational
16 biologist. I have no conflicts of interest.

17 Note number 1. Emergency use authorization of
18 biological agents requires the existence of an
19 emergency and the non-existence of alternate
20 treatments. There is no emergency, and COVID-19 is
21 exceedingly treatable.

1 Note number 2. Individuals with resolved
2 COVID-19 infection are potentially pathogenically
3 primed for subsequent CH2 immunopathology. If injected
4 with a targeted immune stimulant in the form of a host-
5 run spike protein manufacturing system, this could
6 trigger subsequent inflammation, immune complex
7 formation, and over-activation of the complement system
8 leading to myocarditis and other immunopathologies that
9 are in fact being prolifically reported to VAERS.
10 VAERS reports must include prior COVID-19 infection
11 status in order to make it possible to assess the
12 potential relationship between immuno-related
13 pathologies including myocarditis and the injections.

14 Slide 1. On the left is a bar plot from a
15 recently accepted for publication peer-reviewed paper
16 showing the absolute numbers of VAERS reports of
17 myocarditis according to age group. Myocarditis rates
18 were significantly higher and used age 13 to 23.
19 Within eight weeks of the COVID-19 roll out for ages
20 12- to 15-year-olds, 19 times the expected number of
21 myocarditis cases were reported over background rates

1 for this age group. In an act of censorship, this
2 paper was temporarily removed and has now been killed
3 without criticism of the work.

4 Considering the relevance of the confines of
5 this paper to many, it seems not only strange but
6 irresponsible to censor this paper at this point in
7 time. The paper is being relied upon by many for the
8 information therein, and you and the public at large
9 deserve an opportunity to read it.

10 Slide 2. On the left is a bar plot showing
11 myocarditis reports from the VAERS domestic datasets
12 according to age and dose. The data is skewed in a
13 statistically significant way towards children.

14 The reporting rate for boys aged 15 years is
15 6-fold higher for the second dose, which makes it
16 plausible that the products are causing the adverse
17 events and subsequent reporting. On the right is a
18 similar bar plot according to age and gender. Of the
19 reports, 80 percent of the gender classification was
20 male. And in general, 70 percent of all VAERS reports
21 are made by females, so this statistic is particularly

1 telling. What will happen in children ages 5 through
2 11?

3 Slide 3. Tens of thousands of reports have
4 been reported to VAERS for children aged 0 through 18.
5 In this age group, 60 children have died, 23 of them
6 were less than 2 years old. Of the metric host listed,
7 it is disturbing to note that products administered to
8 patients of inappropriate age was filed 5,510 in this
9 age group. This means that two children were
10 inappropriately injected, presumably by a trained
11 medical professional, and subsequently died.

12 Slide 4. This is a table showing several
13 examples of VAERS reports for children between the ages
14 of 5 and 11 who died. They died within zero, five, and
15 an unknown number of days following the injection. The
16 11-year-old shown here was injected despite being too
17 young. This is malfeasance. I implore you all to
18 empathetically cast your votes using both your hearts
19 and your minds. Thank you very much for this
20 opportunity to speak.

21 **DR. PRABHAKARA ATREYA:** The next speaker is

1 Josh Guetzkow.

2 **DR. JOSH GUETZKOW:** My name's Josh Guetzkow.
3 I'm a senior lecturer at the Hebrew University and have
4 no conflicts.

5 Expanding the EUA to children is unnecessary,
6 premature, and will do more harm than good.

7 Slide 2. There is no emergency for children,
8 especially healthy ones whose risk of severe illness or
9 death is almost nil. Kids with preexisting conditions
10 and prior COVID infections were not included in
11 Pfizer's study so including them in the EUA is
12 negligence.

13 Slide 3. Correction, the 2268 number is for
14 all subjects. Pfizer's trial is woefully underpowered
15 to detect specific safety concerns such as myocarditis,
16 just like the adolescent study was. And, if they
17 weren't able to detect an unexpected safety concern
18 there, they wouldn't be able to here. In Pfizer's
19 study, only 0.5 percent of controls were dropped due to
20 important protocol violations versus 3 percent in the
21 treatment group. The odds of that happening by chance

1 are one in 10,000. This deviation is poorly explained
2 with no (audio skip) wait.

3 Slide four. From CDC reports, we can expect
4 that for every 18 child hospitalizations prevented at
5 least 43 will end up in the hospital for all causes
6 following vaccination. FDA's risk-benefit analysis
7 only counts myocarditis hospitalization. Why ignore
8 the V-Safe data? And shouldn't FDA verify Pfizer's
9 efficacy and immunobridging analyses first?

10 Slide 5. VAERS shows alarming safety signals
11 which we have shown cannot be attributed to increased
12 vaccinations, stimulated reporting, or COVID
13 infections.

14 Slide 6. We calculated the ratio of adverse
15 events reported per million Pfizer vaccinations to
16 reports per million flu vaccinations among teenagers to
17 see what to expect in children. Serious events are
18 reported 61 times more often for Pfizer, deaths 47
19 times, and life-threatening conditions 49 times.

20 Slide 7. Here are the Pfizer flu reporting
21 ratios for some adverse event categories. Look at the

1 box on the left. What are we doing to their
2 reproductive organs? How can you expect young children
3 to take these risks to protect adults?

4 Look at myocardial disorders on the right and
5 ask yourself why Pfizer's briefing document didn't
6 mention their child sub-study on troponin levels. You
7 should demand to see those results.

8 Slide 8. There are over 900 types of adverse
9 events reported in teens from Pfizer vaccination that
10 has never been reported for flu vaccines including 11
11 cases of MIS-C with no COVID infection. And that's
12 before correcting for under-reporting. If you were
13 hoping to prevent MIS-C, time to reconsider.

14 Slide 9. The fact is, your approval today
15 means mandates tomorrow for healthy children who don't
16 need it and for those who weren't studied. If you have
17 even the slightest doubt about safety, you must vote
18 against forcing these and unknown long-term risks on
19 young children. So, in the name of millions of parents
20 around the world, I implore you, hold the line. You
21 won't be able to say you didn't know. Thank you.

1 **DR. PRABHAKARA ATREYA:** Thank you. The next
2 speaker is Ms. Shoshana Fishbein.

3 **MS. SHOSHANA FISHBEIN:** Hi, this is Shoshana
4 Fishbein. I have no conflicts of interest. Next
5 slide, please.

6 Thank you to VRBPAC for all your hard work
7 during the COVID-19 pandemic and also every year to
8 ensure that our vaccines are safe and effective. It's
9 fitting that I'm speaking today on behalf of Families
10 Fighting Flu as you discuss vaccines for children. Our
11 organization was founded when all children six months
12 and older were not recommended to receive annual flu
13 vaccines.

14 The founders of our organization are parents
15 who lost healthy children to what they thought was just
16 the flu. I'm here today to thank you for your hard
17 work in ensuring children have access to safe and
18 effective vaccines because our organization uses
19 stories to show how vaccines can save lives.

20 Slide 3, please. We want to recognize the
21 important work VRBPAC does every single year to make

1 recommendations about flu vaccine formulations.
2 Although flu vaccines are not perfect, this Committee
3 helps to ensure that the supply in America matches the
4 strains most likely to circulate. Our stories are a
5 cautionary tale of what happens when people do not take
6 the flu seriously, and we've seen many parallels with
7 COVID-19 and in children. We thank you for this
8 important work that often goes unnoticed.

9 Lastly, we want to acknowledge the work that
10 went into the last pandemic, H1N1, in formulating
11 pandemic vaccines over a decade ago. Many of our
12 stories are people who were hospitalized, on life
13 support, or died from H1N1 flu, many of whom were
14 children. And we know it's important that COVID-19
15 vaccines are safe and effective for children 5 to 11
16 years old because children can and do spread COVID-19
17 and flu. The work that VRBPAC does is meaningful and
18 necessary. Families Fighting Flu is just one of many
19 examples of why prioritizing science and evidence-based
20 practices is literally lifesaving. Thank you for your
21 time and commitment to science.

1 **DR. PRABHAKARA ATREYA:** Thank you. The next
2 speaker is Dr. Robert Edmonds.

3 **DR. ROBERT EDMONDS:** Dear Committee, I have no
4 financial conflicts of interest to disclose.

5 Previously, I have reviewed the latest
6 statistics of tinnitus with the Johnson and Johnson
7 trial data as seen on the slide. While my main goal is
8 simply to encourage early and appropriate treatment for
9 this rare event and support continued COVID
10 vaccination, I have also encouraged investigations into
11 this matter because I have hope that there would
12 eventually be study into the process that results in
13 this condition.

14 Why? Because in early January, I got my first
15 shot from a different vaccine and yes, a different
16 platform, Moderna. Two to three weeks later, I
17 developed tinnitus on the right side. I then received
18 a second dose in early February. As with what happens
19 to many who develop tinnitus after dose 1, I then
20 worsened. The tone became louder, and I developed
21 near-constant headaches, right side facial pressure,

1 numbness, paresthesia.

2 A few days after my second dose, my wife then
3 received her first dose of Moderna. By early March, my
4 wife received a second dose, but she then too developed
5 tinnitus about a week later as well. While my other
6 symptoms later resolved, both my wife and I continue to
7 experience constant tinnitus. At the time of onset, we
8 had no close contact and I later had a negative
9 nucleocapsid test. I have also had normal scans and
10 two normal hearing tests, something that appears unique
11 but common to many with this adverse event.

12 Because of the staggered vaccination timing
13 for us as a couple, but with symptom onset still
14 coincidental with vaccination, it is hard to shake that
15 this is not somehow a related difficult to detect, low-
16 frequency adverse event despite not appearing in the
17 trial data. Something even my providers work under the
18 assumption of as described in their notes.

19 It leaves my wife and I in a challenging
20 position. For one, is there some shared environmental
21 exposure that increases the correlated risk to our

1 young daughter for experiencing this event in the
2 future? Something I would never have dreamed of
3 worrying about prior to this.

4 I know tinnitus is not considered serious, but
5 this may be a permanent, lifelong condition. Also, it
6 has led some who have developed tinnitus after COVID
7 vaccination to thoughts of suicide due to the severity
8 of the constant sound. I can also say that one
9 individual, Dr. Timothy Boreing, completed suicide
10 after battling tinnitus for seven months after a COVID
11 vaccination. His daughter gave me permission to mention
12 his struggle here today.

13 As I have mentioned in other comments,
14 severity needs to be considered when determining a
15 background rate of tinnitus to compare against. In
16 Phoenix, ABC 15 ran a story discussing how there are
17 10,000 reports mentioning tinnitus in VAERS. The story
18 highlighted me and two others that developed tinnitus.
19 One, a member who once sat on this very committee, a
20 little detail not widely known.

21 All three of us are a part of a tinnitus

1 adverse event pair. I know of many other tinnitus
2 pairs not in the story as well, another unique
3 curiosity that's gone unstudied. I know we are a small
4 number in a sea of misery in this pandemic, but we
5 rolled up our sleeves, defended our communities, and
6 now we are asking for study into this issue. Thank you
7 for this time.

8 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Edmond.
9 The next speaker is Dr. Beatrice Setnik.

10 **DR. BEATRICE SETNIK:** Good afternoon. My name
11 is Beatrice Setnik. I'm a clinical pharmacologist and
12 consultant to various pharmaceutical and biotech
13 companies.

14 Slide 1 shows the total number of daily COVID
15 cases and the current downward trajectory. Pfizer
16 stated that most of the COVID cases observed in their
17 study were during the July to August period, a time
18 when the Delta variant was predominant and now makes up
19 more than 99 percent of the tested strains. Despite
20 this, the immunogenicity of the vaccine against the
21 Delta strain was only tested in 38 children, using a

1 non-validated assay as an exploratory measure.

2 To date, Pfizer has not disclosed any
3 biodistribution data for this vaccine. There is
4 evidence that biodistribution and mRNA expression in
5 these vaccine technologies are not limited to
6 localization at the site of injection and may
7 potentially cause safety implications for other organs
8 and tissues.

9 On slide 2, the figure shows the number of
10 COVID cases stratified by age group. COVID cases among
11 5- to 11-year-olds represent 5.3 percent of all COVID
12 cases.

13 Five- to 11-year-olds have one of the lowest
14 COVID case percentages in relation to their percentage
15 in the U.S. population despite not having current EUA
16 access to the vaccine. Furthermore, the 0- to 11-year-
17 olds consistently have the lowest percent emergency
18 department visits with diagnosed COVID.

19 On the next slide, Slide 3, COVID-19 deaths
20 are reported by age group. Fortunately, there were few
21 deaths reported for 0- to 17-year-olds. When we

1 examined the age groups 5 to 11 years, 156 deaths
2 occurred, which represent 0.03 percent of the total
3 COVID deaths.

4 The majority of COVID deaths were attributed
5 to other comorbidities in the presence of COVID. COVID
6 deaths in 5- to 11-year-olds were at 0.008 percent by
7 total numbers of COVID cases. When deaths were
8 examined on the whole population of 0- to 17-year-olds,
9 these compromised -- and please note the correction on
10 the slide, the correct number is 0.014 percent deaths
11 relative to the total COVID-19 cases reported in this
12 age group. The overwhelmingly high likelihood of
13 survival rate up to 99.99 percent in children is not a
14 justification for emergency use.

15 We can skip to Slide 5 which shows the adverse
16 events reported to the VAERS database following
17 exposure to the Pfizer vaccine with 25 deaths reported
18 for the 6- to 17-year-old age group, and 245 life-
19 threatening events. VAERS is notoriously under-
20 reported. In Canada, 206 reports of Bell's Palsy
21 recently warranted an update to the COMIRNATY Product

1 Monograph. Canada has one-tenth of the U.S.
2 population. In addition, there have been increasing
3 reports of menstrual irregularities following COVID
4 vaccination, to the point that the NICHD recently
5 awarded \$1.67 million in research funds to further
6 explore this.

7 Yet this does not even appear as an adverse
8 event of special interest in this study. What impact
9 does this vaccine have on our vulnerable pre-pubescent
10 and developing girls? What increased risks will occur
11 in children with the clearly short-lived and waning
12 effects of the vaccine that will require an unknown
13 number of booster shots in the future? The risk-
14 benefit analysis presented today does not account for
15 any of this. We know the risks of myocarditis and
16 pericarditis are a real risk, particularly for young
17 boys.

18 Slide 6 shows the post-approval requirements
19 that the FDA mandated to Pfizer on August 23rd. This
20 demonstrates that many years of additional studies are
21 required to establish the safety and efficacy of

1 COMIRNATY in both children and adults. Long-term
2 complications of myocarditis after vaccination will not
3 have final reports until May of 2027.

4 On the next slide, Slide 7, the guidelines for
5 emergency use authorization clearly state that the
6 known and potential benefits must outweigh the known
7 and potential risks of the vaccine. Pfizer makes
8 assumptions that vaccinations may cause a substantial
9 reduction in virus transmission. However, the CDC
10 citation Pfizer provided clearly states that more
11 studies are needed, and that transmission does in fact
12 occur with the vaccinated.

13 Finally, on Slide 8, Health Canada is
14 reporting a high number of reported rates of serious
15 adverse events following administration of the Pfizer
16 COMIRNATY vaccine with a majority appearing after the
17 first dose. Assuming drug safety has had devastating
18 consequences, Thalidomide being one such example that
19 caused deformities in newborn children.

20 In the 1990s, the FDA assumed that oxycontin
21 had less abuse potential compared to other opioids,

1 making a false claim that helped fuel the opioid
2 epidemic that still ravages our children in communities
3 to this day.

4 Please do not assume that this vaccine is safe
5 in our children until all data, including long-term
6 data, has been carefully evaluated. Thank you.

7 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Setnik.
8 The next speaker is Ms. Amy Alvo.

9 **MS. AMY ALVO:** Hello, my name is Amy Alvo. I
10 have no conflicts of interest.

11 I am here on behalf of my daughter, Abigail
12 Alvo. At age 17, she was a perfectly healthy teenager,
13 played softball since she was 5 years old, and was
14 cheer captain of her high school cheer team. Thinking
15 I was protecting my daughter as she would be traveling
16 for summer vacation, I allowed her to receive the
17 vaccine. I couldn't be more wrong.

18 On March 31, 2021, Abby was given the first
19 dose of the Pfizer vaccine. This was the only vaccine
20 approved for her age group. After the vaccine was
21 administered, Abby felt faint. She slept the rest of

1 the day. The following morning, April 1st, Abby woke
2 up not feeling well but she insisted on going to work.

3 A few hours into her shift, we received a
4 phone call from HR that Abby had fainted and was
5 shaking uncontrollably to the point she couldn't walk.
6 Abby was taken to the ER and rushed in. They
7 immediately started running tests. She was given an IV
8 with a cocktail of drugs until she was heavily sedated.
9 She was having a neurological reaction and no one had
10 answers.

11 Her final diagnosis was an adverse effect of
12 the coronavirus COVID-19 vaccine. All of our questions
13 and concerns were met with uncertainty. The doctors
14 did not know. They couldn't answer any of our
15 questions. Could Abby's injuries get better? Could
16 they get worse as she ages? Is this the early stages
17 of Parkinson's? No one knows. There are no long-term
18 studies available. Abby is the study and collateral
19 damage. All of our children will be the study.

20 Within a few weeks of Abby's hospital
21 discharge, we received a check from the hospital paying

1 us back for our copay from our ER visit. Never have I
2 received money back from a hospital.

3 It has almost been seven months since Abby
4 received the vaccine. Her right arm continues to shake
5 uncontrollably. California is now mandating the
6 vaccine, and Abby's school is requiring her to be fully
7 vaccinated by November. We thought we would easily get
8 a medical exemption due to having a documented adverse
9 reaction to the Pfizer vaccine. We requested the
10 medical exemption. It was denied not once, but twice.
11 We were told there are two other vaccines that Abby
12 could try.

13 I am asking all of you today. Do not allow
14 our children to be experiments. Children are at
15 extremely low risk of having severe reactions from
16 COVID. The Pfizer vaccine has no health benefit to
17 this age group. In fact, the vaccine causes
18 catastrophic side effects, particularly heart
19 inflammation and neurological damage. The long-term
20 studies are not there. It is too soon. We are causing
21 more harm to our children.

1 As parents and lawmakers, it is our job and
2 duty to protect our children. I failed my daughter in
3 allowing her to get this vaccine. Now she has
4 neurological damage.

5 Don't allow the same thing to happen to other
6 children. Please do not pass the emergency use
7 authorization of Pfizer's vaccines for kids 5 to 11.
8 Thank you.

9 **DR. PRABHAKARA ATREYA:** Thank you, Ms. Alvo.
10 The next speaker is Ms. Belinda Macauley.

11 **MS. BELINDA MACAULEY:** Good morning from
12 Thousand Oaks, California. My name is Belinda
13 Macauley. I'm an attorney and a nonprofit executive
14 but, for today's purposes, a parent. I have no
15 conflicts of interest.

16 I'm here to speak in strong support of
17 approval of the COVID vaccine for ages 5 to 11. As a
18 family who has taken COVID seriously and tried to
19 sensibly manage risk, the expansion of the vaccine to
20 younger kids represents a welcome and critical next
21 step in keeping ourselves and our community safer.

1 My husband and I have an 8-year-old daughter.
2 We were fortunate to have the resources to keep her
3 remote for last school year as cases surged in our
4 region. We sent her back in person this year for third
5 grade, and she had a COVID positive classmate on the
6 first and second days of school. Fortunately, no other
7 kids in her small classroom became ill, thanks in part,
8 I'm sure, to masks.

9 But the risk of exposure remains, including
10 from unvaccinated volunteers that our state and school
11 board allow in classrooms. In fact, I received a
12 notice of another case on campus last night as I was
13 finalizing these remarks. I am aware that my healthy
14 daughter's odds of becoming very ill with COVID-19 are
15 quite low. Our concerns are primarily broader.

16 What if she inadvertently gets someone more
17 vulnerable sick? We have friends and family members
18 who are high risk. My mother is in hospice nearby, so
19 staying COVID negative so that we can visit her in the
20 care facility is extremely important to us. And, if
21 COVID continues to widely circulate, all of us are

1 impacted. We haven't taken our daughter to eat inside
2 at a restaurant, to the movies, or on a plane since
3 COVID began. She wears KN95 masks anytime she's
4 indoors in public.

5 I share this not to complain but to say that
6 we are doing what we can. But we welcome the
7 additional protection of vaccines to help her and other
8 kids return to more of a normal life. If the data
9 shows the vaccine is safe and helps prevent
10 transmission and severe disease, my family is
11 enthusiastically in favor of our prompt approval and
12 our daughter will get it the first day it's authorized.

13 My friends with young kids look forward to
14 your approval of this vaccine and tellingly, those who
15 have experienced COVID-19 and its effects on a daily
16 basis are the most supportive. One friend said, "My
17 husband is an ER physician, and I am immune-
18 compromised. Needless to say, we are eagerly awaiting
19 the vaccine approval for our 5-year-old daughter and
20 will be first in line once it is approved."

21 A friend who teaches elementary school shared,

1 "Teachers are on the front line of keeping our children
2 and their families safe in their school environment.
3 The emotional stress of thinking that you are the one
4 responsible for the health and safety of families is
5 overwhelming. Knowing that these children could have
6 protections outside" (audio skip) "teach parents and
7 students."

8 When I was growing up, my mom had a framed
9 newspaper clipping of my grandfather from the 1950s.
10 He was a doctor and administering polio vaccines.
11 There was a line extending beyond the picture of kids
12 waiting to be vaccinated.

13 I regret that the understanding of vaccine
14 necessity is not as broad as it was then. Those who
15 believe in science and public health should have the
16 opportunity to give our kids a safe and effective
17 vaccine that helps protect them, their schools, and our
18 larger communities.

19 I hope this Committee will provide that chance
20 soon.

21 **DR. PRABHAKARA ATREYA:** Thank you. The next

1 speaker is Ms. Kim Witczak.

2 **MS. KIM WITCZAK:** Good afternoon. My name is
3 Kim Witczak, and I am speaking on behalf of Woody
4 Matters, a drug safety organization started after the
5 death of my husband due to an undisclosed side effect
6 of antidepressants. We represent the voice of families
7 who live every day with the consequences of the current
8 drug safety system. You face a tough decision today,
9 whether or not you will authorize Pfizer's EUA
10 application for use in children 5 to 11 years old.

11 The outcome has the potential to force mandate
12 this experimental vaccine into the bodies of tens of
13 millions of children with limited evidence showing
14 benefit outweighs the harm. The current VAERS data
15 shows that COVID vaccines pose a significant risk to
16 teens and young adults with issues of myocarditis,
17 blood clots, and other neurological injuries. This is
18 in addition to all the unknown risks which will only be
19 discovered over time and in much larger numbers than
20 the 1,000 children in Pfizer's two-month trial.

21 Is there really an emergency with this age

1 group or is it being driven by a larger political
2 agenda? The Biden administration has already secured
3 millions of doses and has a distribution strategy ready
4 to roll. California Governor Newsome and other
5 governors have already indicated the intention to
6 mandate all school children K through 12 following FDA
7 approval. It must be exceedingly difficult to vote
8 your conscience when it seems that all the decisions
9 have already been made for you.

10 Are you aware that there are almost 140,000
11 comments from people across the country in the Federal
12 Register for today's meeting? As a member of another
13 FDA advisory committee, I have never seen this much
14 engagement from the public. I sure hope this
15 Committee, the FDA, and the Biden administration takes
16 time to read all the comments before making the
17 decision.

18 We live in a polarized society today. There
19 are two segments of American people: one that eagerly
20 awaits FDA authorization, and a large segment of the
21 American public that is not quite ready to inject their

1 children with an experimental product and certainly
2 don't want to be forced in order to go to school or
3 live-in society.

4 Let's be honest, an EUA will almost certainly
5 result in mandates across the country, regardless of
6 what the law says. One idea that was floated back in
7 December 2020 at the first EUA hearing was to consider
8 the expanded access program. This way it gives parents
9 who want the vaccine for their children to get it now,
10 but, for those who don't, they will not be mandated.
11 Everyone wins. Expanded access will allow parents to
12 make the best decision for their children instead of
13 taking that choice away through mandates.

14 After all, it will be the parents who will
15 have to live with the results of this decision, not
16 government officials or schools if something bad
17 happens to their child. And remember, even without an
18 expanded access program this particular Pfizer vaccine
19 is fully approved. So parents can already get this
20 vaccine off-label from their doctor. An EUA is not
21 necessary.

1 In closing, all eyes are on you. If there is
2 any, any hesitation in a Committee member's mind about
3 this vote then, at the very least, you should state for
4 the record that you do not believe an EUA should lead
5 to mandates.

6 Our kids are not for sale. Leave parenting to
7 parents. Thank you for your consideration.

8 **DR. PRABHAKARA ATREYA:** Thank you for the
9 comment. Next speaker is Luke Yamaguchi.

10 **MR. LUKE YAMAGUCHI:** Hello, my name is Luke
11 Yamaguchi. I have no financial conflicts of interest
12 to disclose.

13 From March through October of last year,
14 children 5 to 14 years old had a one in a million
15 chance of dying with COVID-19 in the United States.
16 For perspective, children in this age group were about
17 ten times more likely to die from suicide than from
18 COVID-19.

19 A recent article in the *New York Times* cited
20 data showing that unvaccinated 5- to 11-year-old
21 children are actually at less risk of hospitalization

1 from COVID-19 than fully vaccinated older adults. For
2 children 5 to 11 years old, the weekly rate of COVID-19
3 associated hospitalization has ranged from 0 to a peak
4 of 1.1 per 100,000 population.

5 Regarding herd immunity, the state of Vermont,
6 despite having the highest COVID-19 vaccination rate in
7 the country is currently experiencing the highest
8 number of active COVID-19 cases they have ever had
9 during any point in the pandemic. Similarly, the
10 country of Singapore, with 84 percent of their
11 population fully vaccinated is now experiencing their
12 largest wave of COVID-19 cases and deaths since the
13 beginning of the pandemic.

14 With this in mind, I want to mention three
15 factors that must be taken into account when making a
16 risk-benefit analysis for COVID-19 vaccines in low-risk
17 pediatric populations. The first one I want to make is
18 that pediatric hospitalization rates are inflated by
19 the detection of mild or asymptomatic infection due to
20 universal COVID-19 testing procedures in hospitals.
21 One study out of Stanford found that 45 percent of

1 pediatric COVID-19 hospital admissions were not caused
2 by SARS CoV-2 infection. And so this must be accounted
3 for in your risk-benefit analysis.

4 Additionally, the risk of recommending COVID-
5 19 vaccines to children who already have natural
6 immunity against COVID must be taken into account.
7 Current estimates would suggest that almost 50 percent
8 of children have now recovered from COVID-19 and
9 acquired natural immunity. The research is abundantly
10 clear now that natural immunity to COVID-19 is vastly
11 superior to vaccine-induced immunity because COVID-19
12 vaccine-induced immunity rapidly wanes over time and
13 requires future booster doses, each of which carry
14 their own risk.

15 Furthermore, there is an additional risk with
16 vaccinating people who have previously had COVID-19.
17 Data out of the U.K. shows that prior COVID-19
18 infection is associated with increased risk of adverse
19 events from Pfizer's COVID-19 vaccine with young
20 individuals more likely to report adverse events. So
21 for about half the children in the United States who

1 have likely already acquired natural immunity, the
2 risks of COVID-19 vaccination almost certainly outweigh
3 any possible benefit. And this needs to be accounted
4 for in your risk-benefit analysis.

5 The last thing I'll say is that it's possible
6 that people who get a COVID-19 vaccine will need to get
7 another booster dose every six months, potentially for
8 the rest of their life. And with every additional
9 booster dose, there will be the risk of myocarditis
10 along with the risk of other adverse events. You can't
11 just look at a six-month risk-benefit analysis and say
12 that it's all good. You have to look at the long-term
13 risks versus benefits taking into consideration that
14 natural immunity is broad, robust, and long-lasting,
15 and vaccine-induced immunity is not.

16 And so I urge the Committee to exercise the
17 precautionary principle and withhold the EUA of
18 Pfizer's COVID-19 vaccine for children 5 to 11 years of
19 age. Thank you very much for your time and
20 consideration.

21 **DR. PRABHAKARA ATREYA:** Thank you. The next

1 speaker is Dr. Brian Dressen.

2 **DR. BRIAN DRESSEN:** My name is Dr. Brian
3 Dressen, a chemist who specializes in developing
4 protections for the warfighter and first response. I
5 have an extensive career background in thoroughly
6 researching and assessing the degree of safety and
7 efficacy of new technologies. My work saves lives. I
8 have no conflicts of interest.

9 I agree with doctors Rose, Guetzkow, and
10 Setnik in their assessment of the data from the
11 clinical trials. The Pfizer vaccine failed any
12 reasonable risk-benefit calculus in connection with
13 children.

14 Your decision is being rushed based on
15 incomplete data from underpowered trials insufficient
16 to predict rates of severe and long-lasting adverse
17 reactions. I urge the Committee to reject the EUA
18 modification and direct Pfizer to perform trials that
19 will decisively demonstrate that the benefits outweigh
20 the risk for children.

21 I understand first-hand the impact that you

1 will or will not have with the decision you are going
2 to make today. My wife was severely injured by a
3 single dose of COVID vaccine in a clinical trial here
4 in the United States last November. Because study
5 protocol requires two doses, she was dropped from the
6 trial and her access to the study app deleted. Her
7 reaction is not described in the recently released
8 clinical trials report.

9 Two hundred and sixty-six participants in that
10 trial are described as having an adverse event leading
11 to discontinuation, with 56 neurological reactions
12 being tallied. Since then, we have met trial
13 participants from the other vaccination trials,
14 including the Pfizer 12 to 15 age group trial, who have
15 suffered similar reactions and fate.

16 Injured support groups are growing.
17 Memberships numbering into at least the tens of
18 thousands. We must do better. Those injured in a
19 trial are a critical piece of vaccine safety data.
20 They are being tossed aside and forgotten.

21 The FDA has known firsthand about her case and

1 thousands of others. The FDA has also stated that
2 their own systems are not identifying this issue and
3 that theirs is not designed to identify any multi-
4 symptom signals. This system is broken. My family's
5 life is changed forever. The clinical trials are not
6 appropriately evaluating the data.

7 The FDA, CDC, and the drug companies continue
8 to deflect the persistent and repeated cries for help
9 and acknowledgment, leaving the injured as collateral
10 damage. Until we appropriately care for those already
11 injured, acknowledge the full scope of injuries that
12 are happening to adults, please do not give this to
13 kids. You have a very clear responsibility to
14 appropriately assess the risks and benefits to these
15 vaccines. It is obvious that isn't happening. I do
16 not wish this nightmare on my worst enemy, let alone a
17 child.

18 The suffering of thousands continues to
19 repeatedly fall on deaf ears at the FDA. Each of you
20 hold a significant responsibility today. And know that
21 without a doubt, when you approve this for 5- to 11-

1 year-olds you are signing innocent kids and uninformed
2 parents, who have faith that will undoubtedly rob some
3 of them of their life. With COVID, you get recognition
4 and help, with a vaccine injury you are completely on
5 your own. Thank you for your time.

6 **DR. PRABHAKARA ATREYA:** The next speaker is
7 Ms. Linda Mendonca.

8 **MS. LINDA MENDONCA:** Think you. I'm Linda
9 Mendonca, president of the National Association of
10 School Nurse, and I have no financial interests or
11 conflicts.

12 NASN is a nonprofit nursing organization with
13 a mission to optimize student health and learning by
14 advancing the practice of school nursing. In this
15 third school year affected by COVID-19 and following
16 the FDA's full approval of one COVID-19 vaccine, NASN
17 strongly urges all educators, school staff, and
18 eligible students be fully vaccinated. Vaccination is
19 the leading public health strategy to end the COVID-19
20 pandemic.

21 Today, this Committee considers extending

1 emergency use authorization of a vaccine for the
2 prevention of COVID-19 in children 5 to 11 years old.
3 NASN supports vaccination that provides an opportunity
4 to put an end to this pandemic that has resulted in
5 death, long-term ill health, economic hardship, loss of
6 educational progress, mental health challenges, and
7 more.

8 A recent survey revealed that parents have a
9 strong desire to protect their school-aged children
10 from COVID-19 and the need for increased efforts for
11 continued education about the benefits of vaccination.

12 As trusted health providers working directly
13 in communities where families live, learn, play, work,
14 and worship, school nurses provide culturally relevant,
15 factual education about the importance of vaccine
16 uptake. It is the position of the National Association
17 of School Nurses that immunizations inclusive of COVID-
18 19 vaccination are essential to primary prevention of
19 disease from infancy through adulthood. Thank you.

20 **DR. PRABHAKARA ATREYA:** Thank you. The next
21 speaker is Kermit Kubitz.

1 **MR. KERMIT KUBITZ:** I am Kermit Kubitz. I
2 have reviewed the FDA analysis of the Pfizer vaccine
3 for persons 5 to 11. I was a polio pioneer in 1955 and
4 am making these comments in memory of my friend, Tom
5 Schifelbein (phonetic), who had polio before that
6 vaccine and later died much too young as a result of
7 the after-effects of that disease.

8 The FDA analysis presents an adequate analysis
9 of the benefits and risks of lower dose 10-microgram
10 vaccination of young children with 90.7 efficacy. As
11 the FDA presentation notes, there have been more than
12 44 million COVID-19 cases, with 8.7 occurring among 5-
13 to 11-year-olds with 146 deaths. Hospitalized children
14 with chronic lung disease, obesity, and neurologic
15 disorders were at higher risk. The benefit-risk ratios
16 and comparative scenario analysis presented in Table
17 14, shown as my primary figure of merit, prevented
18 COVID-19 ICU admissions versus excess myocarditis ICU
19 admissions.

20 For the scenarios which I view as most
21 realistic, Scenario 2 with the Delta peak of August

1 2021, and Scenario 4, the 90 percent efficacy against
2 September 11th occurrence, approximately a four to
3 three ratio of ICU admissions, 77 to 80 per Scenarios 2
4 and 4 for vaccinated children versus 58 for the placebo
5 group. This positive benefit ratio supports
6 vaccination for 5- to 11-year-olds.

7 And other policy considerations also do,
8 including suppressing virus reproduction and variant
9 development, protecting the rest of the population
10 including immunosuppressed or unvaccinated individuals,
11 and reducing possible long-term effects, i.e., long-
12 term COVID, such as my friend Tom Schifelbein had from
13 polio.

14 I would have preferred a benefit-risk tabular
15 summary in the form used by the FDA for structured
16 benefit-risk with five questions and answers. One,
17 what is the medical condition? Two, what are the
18 available alternative treatments? Three, what are the
19 benefits of the treatment? Four, what are the risks of
20 the treatments? What is the summary benefit-risk?
21 Moreover, a structured benefit-risk table would have

1 been more informative and convincing to medical
2 professionals and families facing the decision to
3 vaccinate.

4 However, given the analysis presented,
5 vaccination of 5- to 11-year-olds is still supported.
6 Thank you.

7 **DR. PRABHAKARA ATREYA:** Thank you. The next
8 speaker is Ms. Kristi Dobbs.

9 **MS. KRISTI DOBBS:** Yes, hi. I want to
10 acknowledge to the Committee that I attest I have no
11 financial conflict of interest. And also, in my
12 speech, I want to note that I have permission to
13 discuss a minor patient from her mother.

14 My name is Kristi Dobbs. I'm a dental
15 hygienist, wife, and mother of four. I am pro-science
16 and I believe in good medicine.

17 I received my first and only dose of the
18 Pfizer COVID-19 vaccine on January 18, 2021. I had an
19 immediate reaction at the hospital clinic where I was
20 appointed. My initial reaction was a tingling
21 sensation in my left arm where I had just received the

1 shot. I felt as though water was dripping inside my
2 arm. I had barely sat down in the monitoring station
3 when I suddenly had a pre-syncopal episode. I couldn't
4 breathe, felt hot, I had increased pulse, respirations,
5 and heart rate, as well as a blood pressure reading
6 that was so high it was stroke worthy.

7 The next two days following my Pfizer vaccine,
8 my symptoms included sore arm, fatigue, swollen lymph
9 nodes, and a headache. These are all the normal side
10 effects I anticipated and was given as informed
11 consent.

12 However, on Day 3 after the inoculation, the
13 effects of the vaccine started to ravage my body. I
14 had sharp, stabbing pain in my left scapular region, as
15 well as paresthesias and tremors in my left arm and
16 hand. By day four I was having full body tremors and
17 paresthesias, as well as an internal electrical
18 vibration feeling, tinnitus, extreme fatigue, brain
19 fog, muscle pain and weakness, inability to sleep, and
20 multiple autonomic dysfunctions.

21 I have had over 22 different symptoms that

1 have plagued me over the last nine months. To date, I
2 have seen over 15 different medical providers and
3 specialists. Back in March, I even had a telehealth
4 visit with one of Dr. Naik's colleagues, Dr. Safavi, at
5 the NIH. And I have been specifically told not to
6 vaccinate my children. I have sent my blood to the NIH
7 as well as prestigious universities and private
8 researchers looking for answers.

9 My vaccine injury has been reported to Pfizer,
10 Bayer, CDC, FDA, NIH, and other prominent research
11 facilities. Messages and meetings have transpired
12 between the vaccine injured and top officials at the
13 CDC and FDA including Rochelle Walensky, Peter Marks,
14 Janet Woodcock, and Paul Richards. They have all known
15 about these COVID-19 vaccine injuries since at least
16 early this year.

17 I have met countless others that have been
18 injured by the COVID-19 vaccines. And, because of the
19 intentional suppression of these reactions, the injured
20 have been unable to get essential medical care,
21 research for treatment, and there is clearly no

1 recovery plan or financial support.

2 We are being silenced, abandoned, and cast
3 aside as collateral damage. I have met 13-year-old
4 Maddie de Garay who is severely injured and is now
5 confined to a wheelchair with a feeding tube after
6 receiving her Pfizer COVID-19 vaccine under clinical
7 trial. She has been given no real medical help,
8 abandoned by Pfizer, the test clinic, and the FDA. Her
9 adverse event was coded as nothing more than a
10 stomachache, and her mother fights every day for
11 answers and help while watching her child endure this
12 painful journey.

13 I accepted my vaccine as a personal
14 responsibility to my family, community, and country.
15 She chose to participate in the vaccine trial as a
16 brave 12-year-old child wanting to beat COVID and get
17 back to normal. We were wrongfully coerced into taking
18 this vaccine by prominent politicians, world health
19 leaders, and renowned medical directors of this
20 country. We were told that these vaccines are safe and
21 effective, but Maddie and I are living proof that these

1 vaccines are not safe nor effective.

2 If we impose these vaccines on our most
3 vulnerable, our children, it will be an absolute crime
4 against humanity. If this happened to us, it will
5 happen to more. We have got to protect our children.
6 They are our future. We are real, not rare.

7 **DR. PRABHAKARA ATREYA:** Thank you. The next
8 speaker is Dr. Dorit Reiss.

9 **DR. DORIT REISS:** Hello. Thank you for the
10 opportunity to comment. My name is Dorit Reiss, and I
11 am a professor of law at the University of California,
12 Hasting College of the Law. And I have no conflict of
13 interest.

14 I appreciate your careful analysis of the data
15 on this, and I want to add three points for your
16 consideration on top of everything you've already
17 heard. First, I want to remind you that the risk and
18 benefits of vaccines need to be considered in context.
19 In this case, I want to remind you that in 12 states,
20 there are prohibitions on requiring masks in school
21 either through the law or through executive order.

1 This includes large states such as Texas with
2 28 million or Florida with 20 million and many others.
3 In those states, there are battles around masks, but
4 the reality is that many parents just don't have the
5 option to send their children to school without taking
6 any precautions to reduce COVID-19. And, in several
7 states, they no longer have an online option. And this
8 is often on the background of high community
9 transmission rates and hospitals filling with children.
10 As we're seeing, and as was set out, cases in children
11 and hospitalizations of children have increased.

12 Authorizing vaccines for 5 to 11 would give
13 these parents the choice of vaccinating the children
14 and allow them to offer some protection, both for the
15 child and in families that have an immune-compromised
16 member to the immune-compromised member. Since
17 children bring back COVID-19 from school is a very
18 realistic option for some families. And it's the
19 hardest for families that don't have the resources to
20 pull their children out. Please give parents the
21 option to protect their children.

1 My next two points are as an administrative
2 law professor. I have studied advisory committees.
3 First, I want to remind you that as an expert advisory
4 committee, which is concerned to advise the FDA about
5 the data, your job is to provide an objective,
6 knowledgeable review of the information drawing on your
7 expertise. That means that when misinformation or
8 disinformation, such as the misuse of various reports
9 is raised before you, your job is to ignore it and
10 focus on the actual data. And you should also treat
11 unverified anecdotes with some caution because you
12 really need to focus on the data.

13 I expect you'll do it anyway, but thought it
14 worth reminding you that, when you are ignoring this
15 information and when you're cautious about unverified
16 stories, you are doing the right thing. Your decision
17 should be based on actual facts.

18 Finally, I want to say something about mass
19 commenting complaints. Yes, a lot of comments have
20 been submitted to the written comments. I want to
21 remind you that, although mass commenting complaints

1 are not usual for expert advising committees and they
2 are probably inappropriate for this Committee, they are
3 not unusual in rulemaking for some agencies.

4 And the way agencies usually treat them in
5 rulemaking is as if they were one big comment raising
6 the issues, if we're talking about form comments that
7 repeat the issue. Substantive and quality is what
8 matters, not the number of comments per se. It's not a
9 vote. Mass commenting complaints are not generally
10 representative, and the agency knows it. And agencies
11 are required to follow data, not votes. This is even
12 stronger for advisory committees. Advisory committees
13 are not a representative body; they're not there to
14 reflect community opinions, but to provide expert
15 input.

16 Even if the mass comments were representative,
17 and they're not, your job would be to provide
18 analytical input based on the data. We have other ways
19 to measure political will, and that's the job of the
20 political executive, not the Advisory Committee. Thank
21 you.

1 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Reiss.

2 The last speaker for the session is Ms. Brooklyn Aaron.

3 **MS. BROOKLYN AARON:** Hi, can everyone hear me?

4 **MR. MICHAEL KAWCZYNSKI:** Yes, we can. Go
5 ahead.

6 **DR. PRABHAKARA ATREYA:** Yes.

7 **MS. BROOKLYN AARON:** All right. My name is
8 Brooklyn. I am an ethics fellow at a health system but
9 I'm not speaking on the institution's behalf, and I
10 have no disclosures.

11 There's a reason we're focusing on a benefit-
12 risk analysis today. An ethical vaccine is one that is
13 anticipated, to the best of our knowledge, to result in
14 risks that are proportionate to the benefits provided
15 with the benefits outweighing the risk. I wanted to
16 draw a parallel to a widely accepted medical decision-
17 making model for minors, the best interest standard.

18 The right decision is the decision that best
19 promotes the interest of the child. This is how, if
20 approved for EUA, I am making the decision whether to
21 vaccinate my preschooler. COVID-19 vaccination for her

1 may not be justified on the sole basis of physiological
2 benefits given the low severity rates in her age group.
3 However, a study completed by the Leukemia and Lymphoma
4 Society demonstrated that one in four blood cancer
5 patients failed to produce detectible antibodies after
6 two doses of either Pfizer or Moderna.

7 Patients with these malignancies were least
8 likely to produce detectible antibodies, and common
9 treatments for those diagnoses target B cells
10 indiscriminately, resulting in the inability to produce
11 antibody responses to either vaccines or illness.

12 I am one of those patients, so I've had to
13 weigh for my child the extreme risk of losing a parent,
14 against the risk of not letting her leave the house.
15 Although we don't have full data on transmission, we do
16 know that transmission is less likely if more people
17 around an individual are vaccinated.

18 A vaccine is not going to be a hundred percent
19 effective at its aimed to prevent serious diseases.
20 It's not going to be 100 percent safe. But we have
21 taken steps to reduce already rare risk of the vaccine

1 such as reducing the dose of the vaccine.

2 The extreme isolation and stress and emotional
3 deterioration the world experienced for just a few
4 weeks of shutdown, there are children still
5 experiencing that. This vaccine adds another layer of
6 protection for us. For my preschooler, the risks of
7 being vaccinated don't come close to the risk of
8 continued isolation to the level she must adhere to
9 now.

10 For her, everything hinges on this vaccine.
11 It might not be worth the potential risk for every
12 child, and I accept that. But the data as presented,
13 the vaccine accomplished the aim unprecedentedly well.
14 To the best of our knowledge, it's safe. You should
15 now allow parents to weigh the benefits and risks for
16 their children and at least give us the option.

17 **MR. MICHAEL KAWCZYNSKI:** All right. Thank
18 you. Prahba?

19 **DR. PRABHAKARA ATREYA:** Thank you. We thank
20 all the OPH speakers who expressed their viewpoints
21 today. This concludes the open public sharing session.

1 And I will turn the meeting over to Dr. Monto, our
2 chair today. Thank you.

3 **DR. ARNOLD MONTO:** And I think we now have a
4 break which go on until 2:10 Eastern Time. So about
5 seven minutes until we reconvene.

6 **MR. MICHAEL KAWCZYNSKI:** All right. Thank
7 you, Dr. Monto.

8

9

[BREAK]

10

11

ADDITIONAL Q & A REGARDING SPONSOR AND FDA

12

PRESENTATIONS

13

14

MR. MICHAEL KAWCZYNSKI: Okay. Good afternoon
15 and welcome back to the 170th VRBPAC meeting. We are
16 now going to get into our -- this is our final session
17 run for the day. We are now going to go back to --
18 start with our Q&A in the afternoon. So, Dr. Monto,
19 are you there?

20

DR. ARNOLD MONTO: I am.

21

MR. MICHAEL KAWCZYNSKI: All right.

1 **DR. ARNOLD MONTO:** Since we ended abruptly
2 with Dr. Yang's presentation on the various risk-
3 benefit scenarios, I thought we'd start out by having
4 her and her colleague, Dr. Forshee, answer any
5 questions that the Committee has, and then move to a
6 more broad question and answer session involving both
7 FDA and the sponsors. So I see Dr. Offit has his hand
8 raised. Dr. Offit?

9 **DR. PAUL OFFIT:** Yes. First of all, thank
10 you, Dr. Yang, for a very thorough presentation. Let
11 me ask this question. Were you to include the data
12 that were presented by Dr. Havers, where she found that
13 40 percent roughly of 5- to 11-year-olds were
14 seropositive? Your analysis, and correct me if I'm
15 wrong, assume that all 5- to 11-year-olds were
16 susceptible to illness. She showed that many likely
17 weren't, or at least arguably were not susceptible to
18 serious illness.

19 So, a parent could reasonably say, my child is
20 seropositive. I think they're likely protected against
21 serious illness. There's much still not known about

1 myocarditis. I'm going to choose to wait. I mean, so
2 how would you -- first of all, how do you think it
3 would change your analysis, and what would you say to
4 that parent?

5 **DR. HONG YANG:** Yeah. Right. (Inaudible)
6 assumption, we do have a data balance. CDC consider
7 that that's imperative (inaudible) support these
8 groups. There's no vaccine for this group. So,
9 basically, we account for everyone in this group,
10 consider them susceptible to this disease.

11 Based it's on what you say, if it's 45 percent
12 of individuals in this group or they have immunity, and
13 then the cases that will be -- I don't know what about
14 the potential of those immunities because it depends on
15 -- we are not clear if someone tests positive how will
16 be the protection. So, if you assume those individuals
17 has immunity test positive in antibodies, they have the
18 same kind of the protection as the vaccine.

19 Then basically, you have 45 percent reduction
20 of the other benefit. We don't have that data. We
21 don't know if someone tests positive what would be

1 their antibody titer. How is the protection compared
2 to that vaccine? Because there is also some literature
3 based on -- for the adult population. Actually, if
4 someone got infected, they still are vulnerable to the
5 COVID infection. So we don't have the data for the
6 (inaudible).

7 **DR. PAUL OFFIT:** You're usually not as -- if
8 you can develop an antibody response, it's likely
9 you've developed a memory response, although you're
10 right. I think that you may not be protected against
11 asymptomatic or mildly symptomatic infection. You are
12 probably, likely protected against serious illness
13 after an actual infection, which would change your sort
14 of hospitalization rates, but you're right. I mean,
15 what one does, that's another piece of information
16 that's lacking, but thank you very much for that
17 answer.

18 **DR. ARNOLD MONTO:** Thank you, Dr. Offit. Dr.
19 Sawyer?

20 **DR. MARK SAWYER:** I'd like to call up Dr.
21 Offit's question and go back to a question Dr. Kurilla

1 asked at the very beginning that influences this same
2 issue of estimating hospitalizations prevented and ICU
3 stays prevented. That is the question of children who
4 are hospitalized for some other condition but just
5 happened to have a COVID test done as a part of the
6 routine testing of all admissions to the hospital.

7 I believe Dr. Havers estimated that only 20
8 percent of the patients in the COVID net data fit that
9 category. I'm wondering if you could address how you
10 dealt with this issue in making your estimates.

11 **DR. HONG YANG:** So --

12 **DR. RICHARD FORSHEE:** So, Hong, I'll take a
13 stab at that. I actually hoped that someone from CDC
14 might be able to comment a little bit more about how
15 they actually coded those cases because we don't have
16 the details. We were relying on the COVID-NET data.
17 So, I'm curious if anyone from the CDC can comment on
18 that.

19 **DR. ARNOLD MONTO:** Do we have anybody --

20 **DR. RICHARD FORSHEE:** Dr. Havers, I believe
21 you're on mute.

1 **DR. ARNOLD MONTO:** -- from the CDC in the
2 group? Another question I'd like to ask CDC is how
3 representative they believe the antibody prevalence is
4 in terms of past infections because from some of the
5 cohorts we work with, the antibody prevalence is far
6 lower, depending where you are and what the precautions
7 have been. So, Dr. Havers?

8 **DR. FIONA HAVERS:** Yeah. No. I'm happy to
9 take both of those questions. To answer the first
10 question regarding, how we determine the proportion of
11 patients that are actually determined? When they are
12 admitted with a positive SARS-CoV-2 test, if it's
13 primarily related to COVID-19 related illness, or
14 incidental on screening.

15 Again, in COVID-NET data, we have detailed
16 information on all of the pediatric admissions and
17 someone has -- a trained surveillance officer has
18 reviewed the medical chart, and, based on the reason
19 for admission, the chief complaints, and other
20 information, they determined whether or not it's COVID-
21 19 related illness. If there's any question about it,

1 they add in (inaudible) information, and then we have
2 two physicians that review the reason for admission and
3 other information.

4 We did find that for older children, for
5 adolescents, that the admission rate for probably nine
6 COVID-related reasons was higher. In adolescents, we
7 found that the proportion was higher than 20 percent
8 because there was a fair proportion of adolescents who
9 were admitted for, like, if they were pregnant and were
10 admitted for labor and delivery, caught on screening or
11 for mental health like suicide attempts or overdoses.

12 But any 5- to 11-year age group, we saw it was
13 about 18 or 19 percent that we think was most likely
14 related to something -- the primary information was not
15 a COVID-19 illness. Many of the children may have been
16 -- were symptomatic, even if they were categorized as
17 that if they were admitted for an elective surgery or
18 trauma or something else that was sort of more clearly
19 not COVID related. But it is sometimes difficult to
20 tell.

21 So, I would say that the rates are a little

1 bit higher. I mean, the rates include all of the
2 positive SARS-CoV-2 tests with children with positive
3 SARS-CoV-2 tests. But there is a proportion of
4 children that may not have been admitted for COVID-
5 related illness primarily.

6 Again, among the children that are admitted
7 and whose primary reason for admission is COVID-19, we
8 do see a fairly large proportion of patients that have
9 severe outcomes, at least a third of those are admitted
10 to the ICU. In relation to -- did I answer your first
11 question there?

12 **DR. MARK SAWYER:** Yes. Thank you.

13 **DR. FIONA HAVERS:** Okay. And then Dr. Monto,
14 you had a question about the seroprevalence studies
15 that we're looking at the antibodies in children.

16 **DR. ARNOLD MONTO:** Right. It was at 40
17 percent because I can tell you, from some of our own
18 populations that you know very well, it's far lower
19 than that.

20 **DR. FIONA HAVERS:** Yeah. No. I think that
21 those are good questions. I think the different

1 methodologies do yield different results. I think, as
2 I mentioned before, these were from national
3 seroprevalence studies that were -- we used select --
4 the investigators for this study did select
5 jurisdictions where they had a decent number of
6 pediatric specimens, that they are from residual
7 clinical specimens. So, it's children presenting for
8 clinical care.

9 Again, they may not be totally representative
10 of the general population. Most of them are probably
11 in this age group receiving cholesterol screenings,
12 which is recommended for children in this age group.
13 So, we don't know that that's that big of a limitation.
14 One, the other thing I would say is that seroprevalence
15 estimates vary a lot depending on the assay that is
16 used.

17 This is one that that, one, that they limited
18 this seroprevalence study too is one that has a pretty
19 high sensitivity and generally doesn't wane over time.
20 So, that may have given it higher estimates than you
21 would see in some other seroprevalence studies that use

1 different assays.

2 Again, I think there are other data out there,
3 and I would reemphasize that even when the results from
4 the study show that there was a 40 percent
5 seroprevalence in this particular population. That was
6 over the summer. Even since then, we saw the highest
7 hospitalization rates in the 5- to 11-year age group in
8 September during the Delta wave. So, there's clearly a
9 lot of susceptible children still out there that are
10 vulnerable to severe disease. So, I just wanted to
11 make that point as well. So, thank you.

12 **DR. ARNOLD MONTO:** Thank you. Dr. Meissner?

13 **MR. MICHAEL KAWCZYNSKI:** Dr. Meissner, you
14 don't have to wait for your camera to come up to start
15 speaking. Go ahead.

16 **DR. CODY MEISSNER:** All right. Thank you, Dr.
17 Monto. I have a question also for Dr. Yang. First of
18 all, I appreciate the model that you presented and the
19 sensitivity analysis that you included and -- because,
20 as we all know, it's the base case assumptions that are
21 made that determine the reliability of these sorts of

1 the model.

2 But the point that I wanted to make is that, I
3 believe you said you took data from the week ending
4 September 11, and I just want to point out that that
5 was the peak of the fourth or the fifth wave of this
6 pandemic. At that time, the rates of hospitalization
7 were in the 5- to 11-year-old group coming from the CDC
8 data was 1 per 100,000. Over the last few weeks, that
9 number has fallen to 0.4 per 100,000.

10 There's some suggestion that this pandemic may
11 be evolving into a pandemic as more and more people
12 acquire immunity from the vaccine and from infections
13 has been noted. So, in a way, you've taken the worst-
14 case scenario, and it is not really reflective of what
15 we're seeing at the present time. Obviously, it's very
16 hard to predict what's going to happen with this virus.
17 No one can say for sure.

18 I think it is important to look at your
19 analysis. I think you looked at a 10 or 20 percent
20 lower rate of disease, and that was just low. The
21 factors are it seems to be less than 50 percent

1 counting the numbers during the period that you took
2 your base case. Thank you.

3 **DR. ARNOLD MONTTO:** Response, please.

4 **DR. HONG YANG:** Yeah. So, our scenario, we
5 have Scenario 2 and 3. The reason we have that two
6 scenario is because we think that a future pandemic is
7 unsettling. So, the Scenario 2 is the peak. We take a
8 peak. So, actually, you are right. Our base of
9 Scenario, September 11, is close to the recent peak,
10 but we do have Scenario 3. We take the lowest point.
11 So, the lowest point, the incidence rate for the cases
12 is five percent for the September 11.

13 The incidence for hospitalization is a ten
14 percent of our base rate on September 11. So,
15 basically, we use these two scenarios, Scenario 2 and
16 3, as upper bar and lower bar. Of course, we still
17 cannot totally rule out the incidence can go beyond
18 these two bars, but we think it's less likely. So,
19 that is the way we try to see how the impact of the
20 future pandemic were of the benefit-risk of the
21 vaccine.

1 **DR. CODY MEISSNER:** Yes. I think that's a
2 very reasonable approach, and I certainly respect that
3 opinion. But I will just point out that the
4 hospitalizations are now 50 percent lower than they
5 were during that time period.

6 **DR. HONG YANG:** Right. So, the low --

7 **DR. ARNOLD MONTA:** Thank you, Dr. Meissner.
8 I'd like to go on to Dr. Fuller.

9 **DR. OVETA FULLER:** Thank you, Dr. Monta. This
10 was actually very informative with the modeling and the
11 FDA comments. I have a couple questions, but I'll
12 first ask the one of Dr. Yang. We know that parents
13 are wanting -- most parents want to do what's best for
14 their child and is going to make a decision should
15 these vaccines become available based on their
16 particular situation. So, I found that your scenarios
17 were very, very helpful.

18 We don't know what's going to happen. We're
19 in an unprecedented pandemic. We don't know if the
20 virus is going to go up or if the -- we just don't
21 know. So your scenarios were very helpful. My

1 question is, with other vaccines, such as HPV or
2 chicken pox or others that have been approved, have we
3 ever had the value of this sort of scenario predictions
4 before?

5 Then the other question is perhaps for Dr.
6 Wong about the BEST system, in terms of following long
7 term what happens. How long have we been doing that to
8 the degree that we can be able to pick up something
9 that is happening at a lower frequency, but at a longer
10 term? There's no precedence of this, but I really am
11 comforted by the fact that these are in place.

12 And my question is, have you done this
13 modeling with any other vaccines in terms of -- I know
14 we're not in a -- have not been in a global pandemic
15 with them, but has this sort of modeling scenario been
16 done before?

17 **DR. HONG YANG:** So, to answer your question,
18 FDA will really (inaudible). We always conduct the
19 benefit/risk assessment. For that kind of the formal
20 analysis is -- now, we don't do this for every
21 (inaudible) because it does take a lot of effort. So,

1 we usually only do this when there is a very
2 challenging issue, also of the important that is
3 difficult to speak to the (inaudible). Then we have
4 four more analyses.

5 **DR. OVETA FULLER:** I found it very (inaudible)

6 --

7 **DR. HONG YANG:** (Inaudible) --

8 **DR. OVETA FULLER:** -- so I wanted to thank
9 your team for doing this. Then my question, if I
10 might, Dr. Monto, to Dr. Wong, or do you want me to
11 hold it till later?

12 **DR. ARNOLD MONTO:** Let's come back to that.

13 **DR. OVETA FULLER:** Okay.

14 **DR. ARNOLD MONTO:** Because I just want to get
15 this clarified, and then we still have plenty of time
16 for a broadened discussion. Dr. Lee?

17 **DR. JEANNETTE LEE:** Yeah. So, thank you for
18 that presentation, Dr. Yang. I think one of the
19 questions I have, I think, what troubles some people
20 was the scenario 3, and the fact that what we've seen
21 was a pandemic as sort of a wave that sort of peaks,

1 and then there are valleys and so forth. The question
2 is, is there a point at which this would not really be
3 advised? I don't know that we can predict that.

4 I guess the other question I have related to
5 this, and I'm really very pleased to see this modeling,
6 is to what extent is there the potential for actually
7 sort of fine-tuning this, not necessarily in this
8 scenario, but in terms of stratification by age and
9 other demographic characteristics, as well as the fact
10 that I think we recognize that the incidence rates, the
11 vaccine efficacy, the death rates, and all of those
12 vary quite a bit regionally, and whether or not those
13 things can be used to sort of help make decisions.
14 Thank you.

15 **DR. HONG YANG:** Yeah. So that is a good
16 question. So, we understand a lot of benefit-risk
17 probably is not uniform. So, it depend on a lot of
18 comorbidity and also demographic characteristics. But
19 to test for modeling, we do need information. So a lot
20 of this kind of information, for example, efficacy. We
21 don't have the efficacy for (inaudible) in small

1 populations, and they may too have different
2 characteristics.

3 Also, a lot of (inaudible) for the model
4 enclosed, we were also (inaudible) that if we want to
5 do the (inaudible) analysis, we will need to have each
6 set by those subgroups. You will need to have efficacy
7 by those subgroups. So, that is really -- we have a
8 (inaudible) limitation on the data for that kind of the
9 more structural analysis.

10 **DR. JEANNETTE LEE:** Great. Thank you.

11 **DR. HONG YANG:** So I think that is a good
12 suggestion. Yeah.

13 **DR. ARNOLD MONTO:** Thank you. Dr. Cohn?

14 **CAPT. AMANDA COHN:** Thank you. Dr. Yang, I
15 just wanted to ask about your assessment of the
16 myocarditis cases, and I know that you mentioned
17 several times that it was the highest possible -- the
18 highest anticipated rate of myocarditis that you're
19 making in this age, but, based on the presentation from
20 earlier this morning, it seems like the likelihood of
21 this age group having even close to those same rates of

1 excess cases of myocarditis given they're receiving
2 both a third of the dose and they have such lower rates
3 of myocarditis in this age group, anyway.

4 It seems like the -- I believe it was the
5 fourth or fifth scenario where you used even the
6 Bayer's number of reports for the 12- to 15-year-olds
7 is a closer estimate of the number of cases of
8 myocarditis you would expect. So, I was wondering what
9 your thoughts were on that and how you determined which
10 data to use to support your rates of myocarditis.

11 **DR. HONG YANG:** So, to test for myocarditis,
12 we do look at different database, like the data from
13 vaccine safety data link, also VAERS, the Vaccine
14 Adverse Event Reporting System. For all those data, we
15 also have our own FDA symptom of BEST system.

16 So, for all those, they have limitations. But
17 for this purpose, we feel like the BEST system uses the
18 half-pan data (inaudible) because for VAERS system,
19 there's no denominator.

20 So, the reporting is a voluntary reporting.
21 That is not as we want (inaudible). Also, we don't

1 know what is the percentage. It's difficult. The
2 weight derived from the VAERS data, we still -- it's
3 likely under-reporting because --

4 **DR. AMANDA COHN:** But what about in comparison
5 to all the other countries that have reported rates of
6 myocarditis in younger adults or adolescents? Aren't
7 those also mostly lower than what the BEST data is
8 reporting?

9 **DR. HONG YANG:** Yeah. We do also look at the
10 other countries' data. So one thing is different
11 country have different populations. So that data
12 sometimes is not really representative. Also, we are
13 not very familiar and confident with the other
14 countries' recording system. We don't know what is
15 their limitations, how to really interpret the data,
16 how that will apply to our system. So, we feel like a
17 few -- yeah, maybe Dr. Rich Forshee may relate it more
18 about that.

19 **DR. RICHARD FORSHEE:** Yes. Dr. Cohn, I just
20 want to say that your basic point is correct. The
21 estimates that we're using are likely to be significant

1 overestimates, so what the myocarditis rate is likely
2 to be in the age groups that we're looking at. There
3 simply isn't any population levels data on this age
4 range since it hasn't been used in this age range yet.
5 So, there were very limited options for what we were
6 going to use to ground our analysis.

7 That's why we've tried to emphasize all of the
8 reasons that we do think it's likely to be the maximum
9 possible estimate and why we estimated scenarios to
10 reflect the possibility that we could have a 50 percent
11 lower myocarditis rate in this age group. We can
12 revisit this as more data are accumulated, but we chose
13 to use the closest age range for which we had national
14 level data to inform those rates and do sensitivity
15 analysis to assess the possibility of the likelihood
16 that the 5 to 11 age range would have a lower rate.
17 That was the approach that we chose.

18 **DR. ARNOLD MONTTO:** Thank you. Dr. Portnoy,
19 and, after this question, I'm going to try to open this
20 up. We'll continue with the people who had their hands
21 raised, but I'm going it up to more general questions.

1 You've been grilled for long enough. Dr. Portnoy?

2 **DR. JAY PORTNOY:** Thank you. Gosh, I'm a
3 little disoriented because the video is lagging behind
4 the audio. Can you hear me okay?

5 **DR. ARNOLD MONTO:** We can hear you. Go ahead.

6 **DR. JAY PORTNOY:** Okay. So I guess my
7 question -- I want to go back to the concept of
8 children already having been infected with the COVID
9 and having some immunity already. Do we know how good
10 that immunity is, how protective it is, and how quickly
11 the children who have had COVID before get reinfected?

12 We're giving vaccines to patients who are
13 likely to have been infected in the past. We're not
14 going to probably insist that serology be done before
15 we get these vaccines. So a lot of the people who get
16 the vaccine are likely to have already been infected.
17 Do we know how previous infection changed the response
18 to the vaccine, and in particular, how it changes the
19 likelihood of having adverse effects from the vaccine?
20 Do we have any information about that?

21 **DR. RICHARD FORSHEE:** So, Dr. Portnoy, I know

1 that we have some data on the effectiveness of the
2 vaccine when it's given to people who have previously
3 had a case of COVID-19, and the CDC has published in
4 MMWR showing that there is significantly reduced
5 likelihood of hospitalization when the vaccine is given
6 to people who have previously had the COVID-19
7 infection.

8 I'm not familiar with studies looking at
9 differences and the adverse event rates. Given that
10 myocarditis is a rare outcome, it may be difficult,
11 certainly using claim space systems. That would be
12 very difficult to reliably identify people who had
13 COVID-19 previously to see whether that was an effect
14 modifier for the adverse events. So that's what I can
15 add there. Maybe others who could add more as the
16 conversation goes on.

17 **DR. ARNOLD MONTA:** Thank you. Dr. Kurilla?

18 **DR. MICHAEL KURILLA:** Thank you, Arnold. Let
19 me just make one comment reflecting Dr. Portnoy and
20 actually getting back to Dr. Offit's comment about the
21 risk of reinfection and whether or not prior infection,

1 the degree of immunity. Pfizer does have in their
2 briefing package, they make a comment that in the
3 subset for immunobridging, that they saw no cases of
4 infection in any of that subset that had demonstrated
5 prior infection. So one could, if it's a small number,
6 say the prior infection was 100 percent efficacious.
7 At the very least, it's probably as good as
8 vaccination. So, that's just one little data point.

9 For Dr. Yang, you may have said this, and I
10 missed it, but your scenarios were done over what time
11 frame?

12 **DR. HONG YANG:** Six months, post second dose.

13 **DR. MICHAEL KURILLA:** Six months, okay. So,
14 did you assume that the efficacy of the vaccination
15 that they demonstrated at two months was going to be in
16 effect for the entire six-month period, or did you
17 actually use the Pfizer data on adults, which shows
18 waning immunity over that six-month time frame at least
19 for infection?

20 **DR. HONG YANG:** No. So, in our model, we did
21 not model the dynamic of the vaccine efficacy changes.

1 So, our one assumption is we keep the constant of
2 efficacy over the six months.

3 **DR. MICHAEL KURILLA:** So you assume that the
4 90 percent efficacy is going to hold up for six months?

5 **DR. HONG YANG:** No.

6 **DR. RICHARD FORSHEE:** Excuse me --

7 **DR. HONG YANG:** Our --

8 **DR. RICHARD FORSHEE:** -- Dr. Kurilla, that was
9 only one scenario that we used that. I'm sorry, Hong.
10 Please go ahead. I think you'll talk about the base
11 scenario.

12 **DR. HONG YANG:** Yeah. So the basis -- so,
13 basically, we did not use 90 percent. Ninety percent
14 is the higher efficacy based on the new supplemental
15 analysis submitted by the sponsor. Our base scenario
16 actually used 70 percent efficacy. So that data is
17 based on CDC's study of the vaccine. That (inaudible)
18 study, and they look at the period for (inaudible)
19 period of the Pfizer vaccine. So, we based scenario --
20 we used 70 percent again the cases, 80 percent again to
21 the hospitalizations.

1 **DR. MICHAEL KURILLA:** Well, no, but I'm
2 specifically talking about the cases, which by six
3 months, the Pfizer vaccine in adults at least is waning
4 significantly in terms of preventing infections and you
5 made no assumptions about asymptomatic infections in
6 this population at all either, correct?

7 **DR. HONG YANG:** No. So ours only look at the
8 systematic cases. Our assumption is 70 percent of
9 again the cases. We assume the efficacy, 70 percent,
10 is confident over six months.

11 **DR. MICHAEL KURILLA:** Okay. Thank you.

12 **DR. ARNOLD MONTO:** Okay. We're going to have
13 to move on. We've got a --

14 **DR. RICHARD FORSHEE:** Dr. Monto, could I make
15 one final point?

16 **DR. ARNOLD MONTO:** -- we're only (inaudible)
17 discussions -- I mean, our question time. Dr.
18 Hildreth, I think you've had your hand raised for a
19 while. Again, you can ask questions of anybody at this
20 point.

21 **DR. JAMES HILDRETH:** Thank you, Dr. Monto. My

1 question's related to something others have raised,
2 which is whether or not Scenario Number 3, which I
3 asked earlier, is the one that's most relevant to our
4 current situation. And, if the trends continue the way
5 they are going, the emergency for children is not what
6 we might think it would be, and that's just my main
7 concern is whether or not the scenario you used to
8 model this is the appropriate one for where we find
9 ourselves at right now? So that was it, Dr. Monto.
10 Thank you.

11 **DR. ARNOLD MONTO:** Okay. Would you like to
12 answer, or is that something --

13 **DR. RICHARD FORSHEE:** I can make a brief
14 response to that. This has been discussed a bit so far
15 that it is unpredictable, what the path of the COVID-19
16 pandemic is going to be from this point going forward.
17 We do recognize that the model is sensitive to the
18 incidence rate for COVID-19. So that is one of the
19 most important factors on what the benefit-risk balance
20 is going to look like.

21 I do want to say that when we built these

1 models, we were trying to make conservative assumptions
2 throughout. I think the one thing that's come up in
3 this discussion that we didn't add is an additional
4 conservative assumption is a natural immunity from
5 prior COVID infections. But we think that we're using
6 a very high rate for the risks of myocarditis,
7 pericarditis, and we are looking primarily at the
8 hospitalizations and ICUs for COVID-19.

9 This morning, there was discussion of many
10 other implications of the COVID-19, that there can be
11 other long-term effects that people in this age group
12 experience that were not included in the model. So,
13 overall, we think we used conservative assumptions, but
14 it is sensitive to the COVID-19 incidence rate. Thank
15 you.

16 **DR. ARNOLD MONTO:** Thank you. Just as a
17 parenthetical comment, we've been assuming that we're on
18 the descending slope of the curve previously and been
19 caught flat-footed as the rates again went up. So, I'm
20 thinking that this is going to be the end of the wave
21 permanently is maybe a little overly optimistic. Dr.

1 Perlman.

2 **MR. MICHAEL KAWCZYNSKI:** You're muted, Dr.

3 Perlman. Actually, Dr. Perlman, let's make sure you
4 reconnect your audio, and we're going to go to somebody
5 else at this time.

6 **DR. ARNOLD MONTO:** Okay. Dr. Rubin?

7 **DR. ERIC RUBIN:** Thank you. I actually went
8 to put my hand up for following discussion when you
9 said that (inaudible).

10 **DR. ARNOLD MONTO:** Well, we are in open. I'd
11 like to get off -- that's just the point. Let's open
12 up the question and answer.

13 **DR. ERIC RUBIN:** Well, if I could, and this
14 may be a question for Dr. Havers, who may be in the
15 best position to answer it if she's still around. In
16 the discussion --

17 **DR. ARNOLD MONTO:** Yeah. She was. But let's
18 hope.

19 **DR. ERIC RUBIN:** We have been talking about
20 the risk-benefit analysis, which is incredibly helpful,
21 by the way, for the vaccine. Obviously, there are some

1 close calls here using a population (audio skip).

2 **DR. ARNOLD MONTO:** I think you're breaking up.

3 **MR. MICHAEL KAWCZYNSKI:** Here, Dr. Rubin, I
4 unmuted you because you keep getting a -- there you go.
5 Go ahead.

6 **DR. ERIC RUBIN:** Okay. Yeah. I got muted
7 without touching anything.

8 **MR. MICHAEL KAWCZYNSKI:** Yeah. That's all
9 right. Take it away.

10 **DR. ERIC RUBIN:** Sorry. So, I don't know
11 where you lost me. I guess the question is, can we
12 identify a particularly at-risk population that we
13 should have a vaccine for right now among 5- to 11-
14 year-olds where it would be important to improve it
15 apart from a population level effect?

16 **DR. ARNOLD MONTO:** Dr. Havers, that's to you.

17 **DR. FIONA HAVERS:** Thanks for asking that
18 question. And may I say --

19 **DR. ARNOLD MONTO:** That's a tough call.

20 **DR. FIONA HAVERS:** That is a tough call. I
21 mean, I do think that we have identified that children

1 with underlying medical conditions are at higher risk
2 for hospitalizations and severe outcomes. Although
3 many of the underlying medical conditions that put
4 children at higher risk are very common in the
5 population. So I think that that would be very
6 challenging to sort out.

7 We are seeing higher rates of hospitalization
8 and severe outcomes among children of different ethnic
9 groups, as I said. Although once we adjusted for
10 underlying medical conditions, that they did not appear
11 to be at higher risk for severe outcomes conditional on
12 being hospitalized. So, I think it would be very
13 difficult to narrow it down to a specific population,
14 although we do know that children with underlying
15 medical conditions are at higher risk.

16 I will point out, though, that a third of the
17 children that are hospitalized do not have an
18 underlying medical condition that is identified prior
19 to hospitalization. And so there --

20 **DR. ARNOLD MONTO:** What proportion --

21 **DR. FIONA HAVERS:** -- are a lot of healthy

1 children. Pardon?

2 **DR. ARNOLD MONTO:** What proportion of those
3 hospitalized are previously healthy children? Can you
4 guess?

5 **DR. FIONA HAVERS:** Yeah. About 30 -- well, a
6 little bit over 30 percent of the children that are
7 hospitalized don't have any underlying medical
8 conditions in this age group.

9 **DR. ARNOLD MONTO:** Okay. Thank you. That's
10 very helpful. Dr. Perlman, can we connect you now?

11 **DR. STANLEY PERLMAN:** Can you --

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

13 **DR. STANLEY PERLMAN:** Okay. I just had some
14 questions for the sponsor, if I could.

15 **DR. ARNOLD MONTO:** Please. We've let them get
16 off so far.

17 **MR. MICHAEL KAWCZYNSKI:** All done.

18 **DR. WILLIAM GRUBER:** I'm back. I'm back.

19 **DR. STANLEY PERLMAN:** Okay. So, we heard
20 about some of the measurements of antibodies, and what
21 I was curious about is two or three things. One is, do

1 we have any information about T cell responses in these
2 children? And second, I know there's some samples
3 drawn at the six-month mark. Do we have any
4 information about the duration of the antibody? I
5 think that was answered earlier, but I just wanted to
6 confirm that.

7 The third question is, something that was
8 actually raised in the public discussion, which I had -
9 and I had the same question. Namely, what do we know
10 about the degradation of the RNA vaccine with time in
11 these younger children? Is it the same kinetics of
12 degradation as we see in older populations? Do we know
13 anything about that?

14 **DR. WILLIAM GRUBER:** Thanks, Dr. Perlman. Let
15 me sort of address the first question. I think the
16 first question was about the nature of antibody we have
17 -- are antibody response, one of the first two
18 questions about the length of antibody response.
19 Again, we have six months sera drawn, but we don't yet
20 have those data. Obviously, we'll be interested in
21 that.

1 As far as T cell responses, as you may recall,
2 we've done significant studies in adults, demonstrated
3 robust TH1, CD4 and CD8 T cell responses. We plan
4 additional analysis with our partner BioNTech in 5- to
5 less-than-12-year-olds. We've got about 30 of them.
6 The testing is being done at BioNTech, but we don't
7 have that data yet.

8 Then as far as the stability issue is
9 concerned or what happens to the mRNA, I don't know
10 that I can speak to anything in terms of the pediatric
11 population, but we know about animal studies where,
12 again, the safety profile was quite (audio skip).

13 **DR. ARNOLD MONTO:** Thank you. Dr. Nelson?

14 **DR. MICHAEL NELSON:** Thank you, Dr. Monto. As
15 a practicing allergist/immunologist caring for adults
16 and children with compromised immune systems, and in
17 light of the COVID-NET data this morning showing that
18 68 percent of the hospitalized patients have at least
19 one comorbidity, I have a couple questions about some
20 of our higher --

21 **DR. STANLEY PERLMAN:** Same here.

1 **DR. MICHAEL NELSON:** Is there any subset of
2 immunobridging or reactogenicity data for the 20
3 percent or 312 in the sponsor data set presented this
4 morning? And do the proposed sponsor post the EUA
5 authorization studies include proactive study of immune
6 responses for children with compromised immune systems
7 from underlying disorders or related treatment?

8 Lessons learned from the rollout in the older
9 age group demonstrated the value of additional doses as
10 early as two months after the primary series.
11 Hopefully, we won't need to wait six to eight months to
12 know that there are some high-risk patients with no
13 response.

14 **DR. ARNOLD MONTO:** And those that are given a
15 third of the dose. So, Dr. Gruber, do you have an
16 answer?

17 **DR. WILLIAM GRUBER:** Yeah. So let me address
18 the first one. I think the first question was focused
19 on the nature of antibody responses and those with
20 underlying comorbidity and we do have an analysis of
21 that. If we can bring Slide 1 up. This represents a

1 circumstance where we have individuals grouped together
2 as the entire group as well as those that have an
3 underlying comorbidity listed as yes and those that
4 don't listed as no.

5 And I think you can appreciate that the nature
6 of the response looks quite comparable whether we're
7 talking about the entire group, those with
8 comorbidities or those without. As I already
9 indicated, we'll obviously be monitoring real-world
10 evidence as well as antibody responses over time to see
11 about the potential for decline and when a boost might
12 be necessary.

13 **DR. MICHAEL NELSON:** Right. But any sense as
14 to within that comorbidity subset as those that
15 actually have comprised immune systems or were on
16 immunosuppressed treatment?

17 **DR. WILLIAM GRUBER:** No. No. Let me be clear
18 about that. These are individuals who did not have
19 immunosuppressive conditions. We do have additional
20 studies, actually, that have started in terms of
21 children with immunocompromising conditions, and

1 actually in all the age groups from greater than 2
2 years of age up to 18. This includes individuals that
3 are receiving immunomodulator treatment for autoimmune
4 disease.

5 That also includes individuals post solid
6 organ transplantation and those that are post-bone
7 marrow or stem cell translation. So we will have some
8 of that data to inform how best to use the vaccine in
9 those (audio skip).

10 **DR. ARNOLD MONTO:** Thank you. Dr. Gans?

11 **DR. HAYLEY GANS:** Thank you very much for this
12 opportunity. I had questions for both the CDC, the
13 FDA, and Pfizer. So I'm just going to try and
14 concentrate on some. So, one of the big questions that
15 I had related to this --

16 **DR. ARNOLD MONTO:** Oh, one or two, no more.

17 **DR. HAYLEY GANS:** Okay.

18 **DR. ARNOLD MONTO:** One or two questions.

19 **DR. HAYLEY GANS:** I'll concentrate and come
20 back if we have time.

21 **DR. ARNOLD MONTO:** No multiples questions.

1 Right.

2 **DR. HAYLEY GANS:** Okay. So, on Page 12 of the
3 FDA report out in 4.5 post-licensure vaccine doses. It
4 describes 125,000 children within this age group that
5 we're considering today. So below or less than 12
6 years of age who had received vaccination, I'm assuming
7 it was off-label use. We need to understand if there's
8 any safety data related to the doses that were given.
9 There's a lot of data being followed on vaccine status
10 and that faces hospitalizations, and I think it's very
11 important for us to understand those data. If they're
12 (audio skip).

13 **DR. WILLIAM GRUBER:** I think that's a question
14 maybe for the FDA since it's from their briefing doc.
15 I see Doran Fink coming up.

16 **DR. HAYLEY GANS:** Yeah.

17 **DR. DORAN FINK:** Hi. As far as I'm aware, we
18 don't have safety data for those individuals. Those
19 were numbers that we obtained from CDC. If there are
20 CDC staff who are on the line who might have
21 information about that safety data, they're welcome to

1 comment.

2 **DR. HAYLEY GANS:** And outcomes data, so the
3 CDC (audio skip) for that?

4 **CAPT. AMANDA COHN:** Hi. I'll respond on
5 behalf CDC. We do have reports of vaccinees who are
6 less than the age of 12 years. So (audio skip).

7 **DR. ARNOLD MONTO:** You're not -- we don't hear
8 you.

9 **DR. HAYLEY GANS:** Dr. Cohn, we can't hear you.

10 **DR. ARNOLD MONTO:** Mike, is there a problem?

11 **MR. MICHAEL KAWCZYNSKI:** Yeah. Dr. Cohn,
12 you're disconnected. Your audio is disconnected at the
13 moment. So she's going to have to reconnect. So we're
14 going to turn her off because we're not hearing her and
15 maybe she'll get the clue.

16 **DR. ARNOLD MONTO:** All right. She'll remember
17 the question. I'll call her back, Dr. Gans. Remember,
18 Committee members, we're going to have a general
19 discussion. These could be questions and answers and
20 not discussion. All right. So, Dr. Moore.

21 **DR. PATRICK MOORE:** Yeah. I'll just leave my

1 video off since we're having problems with that. But
2 this is for the sponsor mainly, perhaps for the FDA or
3 anyone else on the Committee here is that what -- this
4 is a new vaccine, and I'm not really certain -- I know
5 why it's being administered intramuscularly, but we're
6 seeing pericarditis or myocarditis as a consequence of
7 this in children.

8 I'm just wondering is there any effort to look
9 at either animal models or to look at clinical? Is
10 there data from clinical studies that suggest we could
11 give a intradermal injection of this and maybe reduce
12 these side effects? It's really an open question.

13 **DR. ARNOLD MONTO:** Well, since it's an open
14 question, let's have a short answer because this is not
15 the question that's in front of us today. So the
16 sponsor --

17 **MR. MICHAEL KAWCZYNSKI:** Dr. Cohn is back.

18 **DR. WILLIAM GRUBER:** Yeah. So I can give the
19 short answer. We have no data about intradermal
20 administration. Intramuscular administration is common
21 for most vaccines other than those that are given

1 (audio skip).

2 **DR. ARNOLD MONTO:** Okay. Dr. Cohn, let's have
3 your answer.

4 **CAPT. AMANDA COHN:** Apologies about that. I
5 have to admit, I was a little embarrassed that I made -
6 - I hung up on us. So we do have doses that have been
7 administered to less than 12-year-olds. I don't know
8 how much you hear me say before, but some of those may
9 have been off-label, but they also may have been
10 misclassified.

11 So somebody may have put the age wrong, and so
12 we need to go back and look at that data more closely,
13 which we can do. But we don't have any evidence of
14 adverse events being reported in that age group in
15 particular, and as well as no data on outcomes at this
16 time. We'll look at our data a little bit more closely
17 over the next week.

18 **DR. ARNOLD MONTO:** Okay. Thank you, Dr. Cohn.
19 I want to remind the Committee that these should be
20 questions for the presenters. We are over time now. I
21 do want to finish all the questions for those that

1 presented on this complicated topic. So I'm going to
2 go to the end of the list, but we're eating into our
3 general discussion on the voting question. Just be
4 aware. So, Dr. Rubin? Dr. Rubin, are you there?

5 **DR. ERIC RUBIN:** Sorry, my mistake. That's an
6 old hand.

7 **DR. ARNOLD MONTO:** Old hand, okay. That's a
8 good answer. Dr. Sawyer, is that a new hand?

9 **DR. MARK SAWYER:** And this is a question for
10 Pfizer. If I caught the numbers correctly, the
11 original immunobridging population was something over
12 300 and was whittled down to 264, and I'm assuming
13 there was -- people excluded were excluded because they
14 had pre-existing antibodies showing they had actually
15 been infected. And if so, that gives you a small
16 cohort of 50 or so kids in this age group who we could
17 look at side effects of vaccine after natural
18 infection. And I wonder if you have done that?

19 **DR. WILLIAM GRUBER:** Yeah. So, thanks for the
20 question. We actually, by virtue of having to test all
21 of the individuals even with prior evidence of

1 infection, either derived serologically or based on
2 having a PCR at the time of immunization. There
3 basically was little difference in terms of reaction
4 seen in those that were positive versus those that were
5 negative.

6 You may remember back to the adult data where,
7 if anything, individuals who had had prior
8 seropositivity might have a little bit of an increase
9 after their first dose, but interestingly enough, they
10 tended to have a lower response in terms of reactions
11 after the second. We saw much the same thing here, but
12 across the board really very little difference.

13 **DR. ARNOLD MONTTO:** Thank you. We have a few
14 more hands raised, and these are the same questions for
15 the presenters. Short questions. Dr. Meissner, your
16 question.

17 **DR. CODY MEISSNER:** Yes. A question for Dr.
18 Gruber, please. As a fellow pediatrician, Bill, I know
19 you understand the concern that people have about the
20 issue of myocarditis of that risk in the 6- to 11-year-
21 old children. And so the question I have for you, did

1 you, or is it possible, to look for troponin levels or
2 BMP levels in those samples that you've got from
3 participants after the vaccine, thinking about the
4 possibility of subclinical myocarditis?

5 **DR. WILLIAM GRUBER:** Thank you. As part of
6 the datasets that we provided to you today, we didn't
7 obtain samples proximate to vaccination when the risk
8 for myocarditis seems to be greatest, right, within the
9 first several days. However, we are taking a very
10 deliberate approach to try to determine whether
11 troponins, first of all, offer any value, in terms of
12 specificity.

13 So we're taking populations that have already
14 been studied to look at their baseline troponins. We
15 know that you can in some circumstances see false
16 positives. And, while we're doing that, we now are
17 enrolling some additional populations of children as
18 well as adolescents and young adults to then target
19 samples taken at four days after the second dose. Once
20 we define the nature of the specificity of the
21 troponins in this larger population, then we would use

1 that to inform how best to look at those troponins.

2 As of today, we don't have that data, and
3 again, I want to be careful in those circumstances.
4 I'm sure you can appreciate. We want to make sure we
5 have enough specificity around this so that we don't
6 end up having an erroneous result.

7 **DR. CODY MEISSNER:** But you can compare the
8 two groups obviously?

9 **DR. WILLIAM GRUBER:** Right. Right. I mean,
10 that's the idea that we basically -- once we have that
11 specificity and know the incidence with which we're
12 potentially seeing a spurious result, then we can
13 better decide the nature of what the data would -- how
14 the data would inform us from the troponins with the
15 samples that we're getting to test in troponins in the
16 vaccinated children.

17 **DR. ARNOLD MONTA:** Thank you. Very focused
18 questions now. Dr. Gans? Only one-part question.

19 **DR. HAYLEY GANS:** Thanks. I had a question
20 about the PRNTs (audio skip) our sponsor that were
21 reported, and they were reported against the Delta

1 strain, variant, and obviously, we have previous data.
2 So this was presented on the cohort that was studied
3 for their clinical trial for the 5211. I'm wondering
4 how that compares with the six-month data that we've
5 already collected on other individuals so that we can
6 start to understand how relevant that's going to be
7 going.

8 Then were any of the new variants of concern
9 tested even on an experimental basis? I realize these
10 are new tests. Because some of those are going to
11 start circulating.

12 **DR. ARNOLD MONTO:** That's the second part.

13 **DR. HAYLEY GANS:** Well, it's about variant
14 (audio skip).

15 **DR. ARNOLD MONTO:** No, that's okay.

16 **DR. WILLIAM GRUBER:** Yeah. So let me answer
17 the second part. We've not tested in the pediatric
18 population, the responses to new variants. But you may
19 recall from the discussions we had about the booster,
20 not that long ago at an EUA, we described how across
21 the board we've yet to find a variant that seems to

1 escape neutralization, and given -- again, let me just
2 show Slide 1 just to remind ourselves of what we've
3 seen with the Delta variant. Slide 1 up, please.

4 You can see here that we have very comparable
5 responses for the wild type versus the Delta strain in
6 the target population for this study, and we've shown
7 much the same thing in the circumstance where we've
8 looked adults. So, given this type of comparison, we
9 would expect the same thing to apply. So whether it's
10 the Delta variant or perhaps a variant in the future,
11 we would expect good coverage so far.

12 **DR. HAYLEY GANS:** But these were done shortly
13 after vaccinations, so I'm wondering how they compare
14 with the ones that we saw previously (audio skip)
15 level. So I'm looking at percent.

16 **DR. WILLIAM GRUBER:** Yes. I think the
17 circumstance where we saw some decrease in efficacy was
18 obviously in the circumstance where we were beginning
19 to get into a circumstance that you've seen with the
20 real-world evidence in the Delta variant phase. And
21 although there was some drop in overall real-world

1 effectiveness, it was generally well-maintained,
2 particularly for serious disease. And so we would
3 expect the same thing. But again, we'll need to study
4 this, and we'll be able to by virtue of having obtained
5 the specimens and obviously looking at real-world
6 evidence.

7 **DR. ARNOLD MONTO:** Two final questions, Dr.
8 Nelson?

9 **DR. MICHAEL NELSON:** Thank you. I do believe
10 this is a short one for the sponsor itself. Can you
11 provide us with any additional insight into dose
12 selection? So, very appropriately, the 10-microgram
13 dose was chosen based on the (inaudible) immunogenicity
14 and certainly the lowest reactogenicity. Were there
15 any lower doses checked, or was there pre-clinical data
16 suggesting that maybe lower doses would result in
17 suboptimal humoral cell-mediated responses or perhaps
18 even shorter durability of results?

19 **DR. WILLIAM GRUBER:** Yes. Thanks for that
20 question. Maybe we can show Slide 1? Again, the
21 details of how we went about dose ranging to some

1 extent are included in your briefing document. But you
2 see here represented what we were looking at when we
3 made the decision in Phase 1 to move forward with the
4 10-microgram dose, and that was based on coupling this
5 information where you can see on the left-hand side,
6 10-microgram neutralizing antibody responses, as well
7 as 20 micrograms.

8 First is what was seen in the 16- to 25-year-
9 olds, which was ultimately, of course, going to be the
10 comparison group for the non-inferiority trial. It was
11 in this circumstance where we saw the 10 micrograms
12 already was associated with a significant reduction
13 potentially in reactions in the setting where it was
14 already looking like it was going to exceed responses
15 in 16- to 25-year-olds.

16 Now, mind you, take note of what's on the X-
17 axis because this was seven days post-dose 2, and we
18 know that's the peak after two doses, and then there's
19 a decline within the first month. So we reckon that
20 there would be some decline. We reckon we already had
21 a good safety profile and that we would meet

1 noninferiority. As it turns out, we did.

2 So that's probably the best evidence that we
3 chose the optimum dose because we're at a geometric
4 mean ratio of 1.04 with a post hoc criteria from the
5 FDA to try to meet that number with reactions that are
6 below those for fever and chills and a number of
7 symptoms compared to 1625. So we think we have
8 optimized the immune response and minimized reactions.

9 **DR. ARNOLD MONTO:** Thank you. Dr. Kurilla,
10 you've got the last word in the questions.

11 **DR. MICHAEL KURILLA:** Thank you. Thank you,
12 Arnold. Yeah. One for the sponsor. I'm assuming that
13 based on the data you've presented that you have no
14 immunogenicity data just at the time of the second dose
15 being given. I'm wondering whether there's any
16 interest, or do you have anything ongoing that would
17 maybe inform whether or not someone who has had a prior
18 COVID infection can get by with a single dose.

19 The other question is, are you looking at
20 different dosing intervals? Because the three-week
21 dosing interval, quite frankly, seems to be suboptimal,

1 at least in terms of durability of the antibody
2 response.

3 **DR. ARNOLD MONTO:** I was going to disallow the
4 second part, but, since it's one of the questions I
5 have, I will allow it.

6 **DR. MICHAEL KURILLA:** Thank you, Arnold.

7 **DR. WILLIAM GRUBER:** All right. So let me
8 address the -- since both of you are interested in that
9 last question. Obviously, at the time of the pandemic,
10 we're trying to solve, first and foremost, for
11 providing protection in a short interval of time, and
12 that's why we were very pleased to be able to dose at a
13 21-day interval first in adults and then carry that
14 over into the pediatric population.

15 Obviously, as we think farther ahead to a
16 post-pandemic period, and particularly as we get into
17 very younger populations, it may be advisable and
18 probably will as we get particularly in that first year
19 of life to look at longer intervals as part of a
20 routine immunization series, but we don't have that
21 data now.

1 Then the first question, we don't have data
2 currently to describe on the immune responses after the
3 first dose, but I think you can get some sense of what
4 happened to adults after the first dose where we
5 typically did not see neutralizing antibody, except
6 potentially in the circumstance where individuals had
7 prior exposure. But we reckon that, again,
8 particularly given the importance of durability, that
9 two doses are likely going to be required to
10 essentially provide full protection.

11 **DR. ARNOLD MONTO:** Thank you and thank you to
12 the sponsors and to FDA for their presentation.

13

14 **COMMITTEE DISCUSSION AND VOTING**

15

16 **DR. ARNOLD MONTO:** We're now moving into the
17 general discussion leading up to the voting question.
18 Could you, Mike, put up the voting question? It is our
19 one and only discussion topic leading up to the vote.
20 So I think it --

21 **MR. MICHAEL KAWCZYNSKI:** Yeah. Give me a

1 moment here.

2 **DR. ARNOLD MONTO:** Okay.

3 **MR. MICHAEL KAWCZYNSKI:** I'll put it back up
4 in that sharing screen. We went back and forth.

5 **DR. ARNOLD MONTO:** All right.

6 **MR. MICHAEL KAWCZYNSKI:** We accidentally
7 pulled it out. So I'll put it back up. You are
8 looking for our community discussion, correct?

9 **DR. ARNOLD MONTO:** Well, this is a voting
10 question. You can find the voting question --

11 **MR. MICHAEL KAWCZYNSKI:** Yeah. It'll be in
12 there. It's in there.

13 **DR. ARNOLD MONTO:** Okay.

14 **MR. MICHAEL KAWCZYNSKI:** So I'll pull it up
15 right now.

16 **DR. ARNOLD MONTO:** Whatever it is (inaudible)
17 that has it.

18 **MR. MICHAEL KAWCZYNSKI:** No problem. Coming
19 in now. All right. There it is. So, let me just stop
20 touching the slide.

21 **DR. ARNOLD MONTO:** There it is. Okay.

1 **MR. MICHAEL KAWCZYNSKI:** There we go.

2 **DR. ARNOLD MONTO:** Now we won't have to read
3 it out to you. You can all read the voting question,
4 and this is what we are going to be discussing. This
5 is the overall voting question we're going to have to
6 vote on in a couple of hours or less than a couple of
7 hours since we've cut into the discussion time.

8 As a question of process, what we will do is
9 conclude the discussion. We will have the vote, and
10 then for anyone who wants to explain their vote, there
11 will be time to discuss and explain the vote. So you
12 can talk about the voting question and should talk
13 about the voting question as we go through the
14 discussion, but there will be additional time for those
15 who want to explain their vote. It's not mandatory,
16 but available. Okay. So Dr. Gans, are you up again?

17 **DR. HAYLEY GANS:** Thank you so much. I'll
18 just open up, I guess, this conversation with a couple
19 of points. For me, there's very intriguing data to --
20 regarding the disparities that we've seen in terms of
21 COVID disease and outcomes. For that, I think it's

1 very impressive that we need to provide some safety net
2 that isn't available otherwise without vaccination and
3 prevention of some of the outcomes we've seen.

4 I think very importantly are some of the
5 learning loss outcomes, not only as it would pertain to
6 loss of school time, which we know is very real in many
7 children's lives, but also in terms of outcomes and so
8 there's data that is being collected on memory loss and
9 other things as it relates to really the outcomes of
10 COVID disease and trying to prevent further loss in
11 these children.

12 The other things that I think are really
13 important for us to understand as we're moving forward
14 is that it's probably in this age group of people have
15 identified over analysis of the outcomes in terms of
16 the one thing that we're sort of looking at because it
17 was seen in the older children of the myocarditis or
18 any of the cardiac effects because those rates are
19 lower in this group anyway and the doses used here are
20 actually lower and more appropriate for these age
21 groups.

1 So I think those are important points for
2 conversation and I think for understanding what is
3 before us.

4 **DR. ARNOLD MONTO:** Thank you. Very good
5 opening to get us on track. Dr. Levy.

6 **DR. OFER LEVY:** Yeah. This has been a
7 fascinating day, and I'd like to thank FDA and the
8 sponsor and CDC and everyone for a very thoughtful
9 discussion. There were a number of broad-based
10 principles here that are converging. One of them was
11 touched on by Dr. Gans, which is the concept of
12 including children.

13 In fact, there's something called the
14 pediatric research initiative, or PRI, that was passed
15 on the federal level to include children in biomedical
16 research, and we're happy to see that studies are being
17 done because this pandemic is clearly affecting them
18 both directly and indirectly as we've heard today. So
19 I very much welcome these data, and in many ways,
20 they're promising.

21 Still, the challenge we face based on the

1 question that we're confronted with now with Committee
2 members is that the risk-benefit or benefit-risk
3 analysis and FDA has taken great effort and presented
4 to us today and taken a lot of questions about these
5 different models, and we see that we can reach
6 different conclusions to some extent based on the
7 assumptions that the models are built on.

8 One of the factors, of course, is how much
9 coronavirus is circulating in a community at a given
10 point in time and then other factors as well. What
11 will the actual myocarditis rate be in these younger
12 kids who may be less susceptible to myocarditis? But
13 right now, that's a speculation. We don't know that
14 for sure, and the studies were empowered really to
15 answer that question in the 5- to 11-year-olds.

16 So I'm just pointing out some broad-based
17 themes that are running through my mind as we're having
18 this conversation. It's a very meaningful one. I also
19 am wondering whether the prevailing conditions could
20 somehow work their way into our recommendations because
21 after all, that's the spirit of an EUA. It's

1 authorized in the setting of a public health emergency,
2 which we're in now, but one that is fluid. So I'm
3 going to leave my comments there, but I hope they're
4 helpful. Thank you, Dr. Monto.

5 **DR. ARNOLD MONTO:** Yes. Very helpful because
6 we are in a fluid situation, and that's why it's a good
7 thing we've got an emergency use authorization and not
8 an amendment or anything like that to do the license.
9 We are confronted with a binary choice as indicated in
10 the voting question. Keep that in mind as we move
11 ahead to Dr. Rubin.

12 **DR. ERIC RUBIN:** Thanks, Mr. Monto. This is a
13 much tougher one, I think, than we had expected coming
14 into it. Data show that the vaccine works and is
15 pretty safe, at least by immunobridging and even by
16 some real-world clinical data. Yeah, we're worried
17 about all of these -- we're worried about a side effect
18 that we can't measure yet, but it is probably real. We
19 see a benefit that isn't the same as it is in older age
20 groups.

21 So, for me, I think it's going to revolve

1 around two questions. First off, whether there is
2 going to be a use for this vaccine in this age group,
3 and then how the decision gets made to use it within
4 this age group. I think what sways me here is that
5 it's a very sort of personal choice. If I had a child
6 who was a transplant recipient, I would really want to
7 be able to use a vaccine like this. There are
8 certainly kids who probably should be vaccinated.

9 The question of how broadly to use it though,
10 I think, is a substantial one. I know it's not our
11 question, and I know we're kind of punting that to
12 ACIP, but I do think that it's a relatively close call.
13 And, as Dr. Levy just said, as Dr. Gans said, it really
14 is going to be a question of what the prevailing
15 conditions are.

16 We're never going to learn about how safe this
17 vaccine is unless we start giving it. That's just the
18 way it goes. That's how we found out about rare
19 complications of other vaccines, like the rotavirus
20 vaccine. I do think that we are going to -- I do think
21 we should vote to approve it.

1 **DR. ARNOLD MONTO:** Thank you. Dr. Hildreth?

2 **DR. JAMES HILDRETH:** Thank you, Dr. Monto.

3 Well, I have several thoughts here. One of the things
4 that's really been impactful for me is to learn that
5 the prevalence in children might already be 42 percent,
6 which means that 30 million of the 72 million children
7 in our country, they have some form of immunity to the
8 virus already.

9 The other thing is that I was disappointed
10 that the number of minorities in the Pfizer study got
11 such a small percentage of the total because they bear
12 the brunt of the disease and hospitalizations. It just
13 seemed to me that in some ways, we're vaccinating
14 children to protect the adults, and it should be the
15 other way around, that if 30 million children already
16 have some form of immunity, they've made their
17 contribution to herd immunity already, and our focus
18 should be to get the adults vaccinated to protect the
19 children.

20 So this is a really tough one for me, but I do
21 believe that children at highest risk do need to be

1 vaccinated but vaccinating all of the children to
2 achieve that just seems a bit much for me. So I'm
3 having some challenges with this one. Those are my
4 thoughts, Dr. Monto. Thank you.

5 **DR. ARNOLD MONTO:** Dr. Sawyer?

6 **DR. MARK SAWYER:** So I do -- we're all
7 concerned about the myocarditis issue, and I do think
8 the model has overestimated the hospitalizations
9 prevented because of prior immunity and the inclusion
10 of some kids who are hospitalized for reasons other
11 than COVID. I also think the high estimate of
12 myocarditis is probably too conservative based on the
13 natural history of myocarditis generally being less
14 common in this age group.

15 I'll paraphrase Dr. Fauchi who said models are
16 what you rely on until you get the data, and then you
17 throw out the model. So the models are the best we
18 have at the moment. As was just mentioned, we are not
19 going to get the data unless we start to use this
20 vaccine.

21 I do think we need it as a tool in our

1 armamentarium for high-risk children for equity issues,
2 for parents who really would like to protect their
3 children and because of the long-term, very profound
4 implications of schools being disrupted and the social
5 and educational impact that that's having.

6 So I agree that it's going to be a fluid
7 situation. A reminder that an EUA is not a permanent
8 situation, and that could change based on either
9 additional side effect data or depending on what
10 happens with the pandemic.

11 **DR. ARNOLD MONTTO:** Thank you. Dr. Offit?

12 **DR. PAUL OFFIT:** Thank you, Dr. Monto. So I
13 guess for me, it's always nerve-wracking. I think when
14 you're asked to make a decision for millions of
15 children based on studies of only a few thousand
16 children. So I mean, I guess the way I struggle are us
17 trying to deal with this is that it's never one you
18 know everything, you never know everything. The
19 question is, when do you know enough.

20 I think we certainly know that there are many
21 children between 5 and 11 years of age who are

1 susceptible to this disease who could very well be
2 sickened or hospitalized or die from it. Then
3 regarding the myocarditis issue, I think there were a
4 number of things that are reassuring. It is reassuring
5 to me that we're giving a lower dose.

6 It's reassuring that the incidence of
7 myocarditis in a 12- to 15-year-old is less than that
8 in the 16- to 29-year-old and that at least the general
9 classified myocarditis is not generally a phenomenon of
10 the prepubertal child, or at least much less so. We do
11 have efficacy data at 91 percent. I think that will
12 hold up. So I guess for me, I think I know enough to
13 move forward with a yes vote. It's always never when
14 you know everything; it's when you know enough. So
15 thank you.

16 **DR. ARNOLD MONTO:** Right. And it's a binary
17 choice that's put in front of us, which is always
18 difficult. Dr. Portnoy?

19 **DR. JAY PORTNOY:** Thank you for the discussion
20 and the opportunity to say this. Technically, I'm the
21 consumer representative, and I've had over 4,000 emails

1 from consumers asking me to vote no. Thank you for
2 those, but I feel like I need to also represent the
3 consumers' parents that I see every day in the clinic
4 who are terrified of sending their children to school
5 because they're not protected against COVID.

6 There's all this anti-mask rhetoric, parents
7 who don't want to get vaccines. Parents are just
8 terrified of sending their kids to school, and I feel
9 that they need a voice also because they're not being
10 represented. I've looked at the data, and I'm going to
11 use the data when making my decision because I think
12 that's what we have to do is to look at the cost and
13 the benefit of this vaccine.

14 I really appreciate the benefit and the risk
15 analysis that was done. It's extremely informative.
16 It really helps to center it. So I think that this
17 virus is just the beginning. Our kids are going to be
18 dealing with this virus for many years to come. It's
19 going to come repeatedly and getting this vaccine is
20 just the first step that they're going to take towards
21 being able to protect themselves from getting this

1 virus and having bad outcomes.

2 And so I really appreciate the opportunity to
3 participate in this activity. I think that the
4 information has been extremely helpful, but I think
5 that the evidence is pretty clear that this vaccine is
6 worthwhile. Thank you.

7 **DR. ARNOLD MONTO:** Thank you. Dr. Lee? And
8 please, members, check to see whether you still have
9 your hands raised.

10 **DR. JEANNETTE LEE:** So I would say I kind of
11 agree with Dr. Offit of how much -- do you know enough?
12 I would say that I was really sort of impressed with
13 the efficacy data, the immunobridging data. Obviously,
14 the adverse events are always a concern, but they don't
15 seem to be overwhelming really at this point. I will
16 say that the school closures and the disruption, I
17 think, has been enormous, and I think that we have to
18 weigh that against the benefits that we would see for
19 the vaccine.

20 I definitely think the benefits outweigh that.
21 But, obviously, we'll have to follow these kids for

1 some time to see how that happens. I mean, the reality
2 is, I think, at one point we thought if we vaccinated
3 enough people that the virus would go away. It's not
4 going away, and I think we're going to have to find a
5 way to live with it, and I think the vaccines kind of
6 give us a way to do that. Thanks.

7 **DR. ARNOLD MONTO:** Thank you. Dr. Gans. We
8 see you. We don't hear you.

9 **DR. HAYLEY GANS:** Yes. Yes, thank you.

10 **DR. ARNOLD MONTO:** Okay.

11 **DR. HAYLEY GANS:** As I was listening to my
12 colleagues, I greatly appreciate their viewpoints. I
13 just wanted to bring up one additional thought that
14 hasn't been raised. The current rates are still within
15 a great deal of mitigation for some of our populations,
16 most of our populations. We really can't continue to
17 do that.

18 The other thing that we have to realize is we
19 actually have to open back up. And, in order to do so,
20 we actually need to provide a way of allowing
21 individuals who are interested in preventive measures

1 and protecting individuals from actually seeing
2 disease, which again, even in asymptomatic individuals
3 who have experienced this disease, there are outcomes
4 that one would not necessarily want for their children.

5 So we do need to think about that and think
6 about the fact that we can't forever have mitigation
7 particularly in schools and children need to learn in
8 the more open life as we all do. So that's an
9 important thing to remember as we're considering those
10 models and rates that we're seeing in those models.
11 Those are with mitigation (audio skip) so it's
12 important to remember that it likely will go up and
13 we're heading into (audio skip).

14 **DR. ARNOLD MONTO:** Dr. Pergam?

15 **DR. STEVEN PERGAM:** Thanks, Dr. Monto. A
16 really great discussion by colleagues. I think the
17 thing that continues to stick in my head is, I'm trying
18 to put myself in the position of a parent who has a
19 child that's at particular risk, whether it's obesity,
20 whether it's immunocompromised position, lung disease,
21 that currently does not have the option to give their

1 children this vaccine.

2 Depending on how the ACIP votes on this, this
3 vote will really affect whether they can protect their
4 children. Those are kids that are being held out of
5 schools because masks are not being used in all
6 locations. I think we have to think beyond how this
7 would be used as a general group, but also to think
8 about those who are potentially at highest risk. I
9 think that's going to affect how I'm thinking about
10 this position to vote.

11 **DR. ARNOLD MONTO:** Dr. Kurilla?

12 **DR. MICHAEL KURILLA:** Thank you, Arnold.
13 Yeah. So, like my colleagues, I think this is probably
14 the toughest decision. I'll be honest and say I
15 actually resented this sort of binary presentation.
16 It's sort of like a take it or leave it. You must have
17 everything exactly the way the sponsor has presented it
18 and nothing else can be considered.

19 A few thoughts. The argument in favor of that
20 this will lead to herd immunity and a reduced
21 transmission, that's a theoretical possibility. I've

1 seen very little data. And in fact, most of what I see
2 right now is that regardless of the percentage in terms
3 of vaccination that the newer variants seem to be able
4 to pass through the population. So, if all we're
5 focused on is reducing cases in terms of a benefit, I
6 don't think that's likely to be realized.

7 I have a lot of issues with the immunobridging
8 because it's being based on an immunogenicity marker
9 that we know wanes and yet, continues in spite of the
10 waning of that antibody response, we continue to see
11 very good protection against the very things we want to
12 see protection against, hospitalizations, severe
13 disease, death.

14 But we're making an assumption that at a lower
15 dose in this pediatric population that it's just going
16 to pass -- that there's going to be equivalency in
17 terms of the overall protection because of the antibody
18 response.

19 So I have a lot of issues with that, and
20 particularly with the percentage of the population that
21 has already been infected previously with COVID, and I

1 think 40 percent is probably a lower limit. I think
2 the possibility that they likely only need one dose at
3 best is going to be very optimal, is probably going to
4 be more than sufficient for them.

5 So I think the idea of doing it under an
6 emergency use authorization two dose for everybody
7 without any flexibility around this, I think is going
8 to just not go over very well, and I don't think it's
9 going to give the healthcare community the options and
10 parents the options to choose what's best for their
11 children. There are high-risk individuals, and I think
12 they do need to be attended to, that we do need to
13 provide a vaccine for them, but, for many others, one
14 dose or no dose, even if they've had prior COVID
15 infection, I think they may not need anything more.

16 The last point I would make is that we are
17 vaccinating with a prototype spike protein that is no
18 longer circulating. So we have to go to higher and
19 higher levels in order to get efficient potency in
20 terms of neutralization. Everyone is focused on Delta
21 right now, but Delta is on the decline. We can

1 anticipate that the future variants are going to be
2 more distantly related and simply boosting, which we're
3 likely to need to do in this population in six months
4 if all we're relying on is neutralizing titers, is
5 going to become harder and harder to do.

6 So I think there are -- we need to more
7 carefully evaluate exactly the vaccination schemes that
8 we want going forward, and we simply don't have the
9 data right now to make those decisions.

10 **DR. ARNOLD MONTO:** Thank you. Dr. Levy?

11 **DR. OFER LEVY:** Yeah. I have another comment
12 that relates to how Dr. Marks framed our discussion
13 today. He was clear to say, "Look, our purpose today
14 is not to decide who exactly receives it within this
15 age range. Our purpose today as the VRBPAC Committee
16 is not to discuss or consider or consider mandates."
17 That's true, of course. Technically, that's not our
18 job right now.

19 Nevertheless, I'll speak for myself, and I
20 highly suspect the other Committee members as well. We
21 have in the back of our minds that after our vote how

1 this is used. This goes on -- could go on later on to
2 CDC depending on outcome and how it's implemented
3 across states and counties can vary, and we're hearing
4 from some of the Committee members some sympathy to the
5 view that, well, maybe it's good to make this available
6 to certain families, children at higher risk,
7 comorbidities.

8 There have been a number of publications
9 around comorbidities related to severe COVID in this
10 age group -- obesity, asthma, other conditions,
11 immunocompromised, et cetera -- and is that an option?
12 Typically, FDA wants us to vote on the question yes or
13 no, Dr. Monto, as you told us as phrased. But is there
14 the possibility, also, of considering rephrasing?
15 We've certainly done that as a Committee recently. So,
16 I just wanted to share that thinking. Thank you.

17 **DR. ARNOLD MONTO:** Dr. Marks, can I ask you
18 about this? In front of us, we have a binary choice.
19 That is the question for today.

20 **DR. PETER MARKS:** Yeah. I appreciate the
21 Committee's discussion very much here. I also

1 appreciate the fact that we did not present today the
2 emerging epidemiology of COVID across the globe,
3 including what's been happening with increases in
4 Europe and other areas and other concerns.

5 I would ask that we first vote on this
6 question, and then once have a vote on this question,
7 we can make a determination thereafter if we vote on --
8 if the Committee would like to explain their votes, ask
9 for something else, we could potentially either poll
10 the Committee or vote on something else. But I think
11 it would be helpful to have a vote on this question.

12 **DR. ARNOLD MONTO:** It was my understanding
13 this is the question for today. Is that the case?

14 **DR. PETER MARKS:** That is the case.

15 **DR. ARNOLD MONTO:** That is the case. Okay.
16 Let's see. Dr. Meissner?

17 **DR. CODY MEISSNER:** Thank you, Dr. Monto. An
18 awful lot has been said that's very, very interesting
19 and that I agree with, and I'd like to make a few
20 comments. I think the likelihood that this vaccine is
21 going to be effective is pretty likely in that the 6-

1 to 11-year-old age group. The issue is side effects or
2 adverse events that might be occurring after this
3 vaccine. I'm torn.

4 On one hand, we know that many mothers and
5 fathers and parents are eager to administer this
6 vaccine to children because they're so frightened,
7 perhaps overly so. They're so nervous about this
8 vaccine because of what's been stated that they really
9 are anticipating having access to this vaccine in
10 children.

11 On the other hand, I think we saw that
12 approximately 68 percent of the children who are
13 hospitalized with COVID-19 have underlying
14 comorbidities. So, that means about 32 percent do not.
15 Then, if we were to take 40 percent of that group that
16 may have immunity already, we're getting down to a very
17 small percent of otherwise healthy 6- to 11-year-old
18 children who might derive some benefit, and we simply
19 don't know what the side effects are going to be.

20 For example, it's not even clear that this
21 vaccine will reduce rates of transmission. We're

1 hoping that's the case, but we don't know. This
2 vaccine is probably not going to prevent infection.
3 It's going to prevent severe disease. So, my worry is
4 that -- I think my thought is that this vaccine should
5 be available to those parents who are very eager to get
6 it for their child and because their child has a
7 comorbidity, or they're concerned themselves.

8 I'm just worried that, if we say yes, that the
9 states are going to mandate the administration of this
10 vaccine to children in order to go to school, and I do
11 not agree with that. I think that would be an error at
12 this time until we get more information about the
13 safety. So I think I agree with what everyone is
14 saying here. We're in a very difficult decision-making
15 process.

16 **DR. ARNOLD MONTO:** Dr. Marks, can I ask you to
17 help us a little bit because we are hearing some
18 reservations about use? Also, the question of how
19 various groups that we have no control over will
20 further act.

21 Yet, if we do not approve, we will be denying

1 the vaccine to families that have a vulnerable member
2 present and who have been keeping their kids in because
3 they're concerned about infecting that individual, we
4 will be denying the vaccine to others who, for one
5 reason or another, want their child to be protected or
6 a risk, which we cannot really accurately estimate for
7 all the reasons we've heard up to now.

8 Help us out in terms of, if we vote yes, what
9 happens? Clearly, if we vote no, then the vaccine will
10 not be available to anyone. You're muted.

11 **DR. PETER MARKS:** Sorry. Double muted.

12 Thanks very much to the Committee and thanks for the
13 very thoughtful deliberations here. I just want to --
14 and before I get to answer that question, just remember
15 here, also, that we take measures to prevent influenza
16 in children in order to prevent about a hundred deaths
17 a year from influenza, and we're talking about having
18 this become more of a routine type of thing. So just
19 so we understand the order of what we're dealing with.

20 The other issue that I would just bring up
21 here is the issue of vaccine equity and that, if we try

1 to approve this for some subset of the group, that that
2 could potentially lead to a situation where this
3 becomes a vaccine that gets used more in those who are
4 of a socioeconomic status that they're able to maneuver
5 to receive the vaccine. That would put some at
6 disadvantage.

7 So, I think we just need to be careful about
8 where we go with that. At the end of the day, the way
9 this process has been set up is that it's this body's
10 decision to make sure that the data supports the safety
11 and effectiveness and that the Advisory Committee on
12 immunization practices then discusses the deployment of
13 the vaccine. I would suggest that we take a vote on
14 the question as it's written, and then, if the vote
15 fails, then we can tailor the vote to a subpopulation
16 at that point.

17 **DR. ARNOLD MONTO:** You feel -- okay. Let's
18 move on to -- since you mentioned ACIP, let's move on
19 to Dr. Cohn.

20 **CAPT. AMANDA COHN:** Hi. So, I'm reflecting a
21 little bit on the challenging discussion that we're

1 having as a Committee, and I think part of the problem
2 is that we're now talking about children. When we are
3 talking about children, we both don't accept deaths and
4 severe outcomes in the same way that maybe we accept to
5 some degree in older age groups, but we also don't
6 accept risks.

7 I guess, when I look at this question, it is
8 pretty clear to me that the benefits do outweigh the
9 risk when I hear about children who are being put in
10 the ICU, who are having long-term outcomes after their
11 COVID, and children are dying. As Dr. Marks just said,
12 we vaccinate routinely against several vaccine-
13 preventable diseases for which far fewer deaths and
14 hospitalizations and ICU admissions occur.

15 So, to me, the benefit is clear, even beyond
16 the direct benefit and the personal experience that I
17 know we're all having with children in our lives who
18 aren't able to go to school. So, then when I look at
19 the risk side of it, I see that the children in the
20 clinical trial, it's not substantially lower than other
21 clinical trials for vaccine-preventable diseases, which

1 have evaluated the safety, and we have this known rare
2 adverse event of myocarditis in an older age group with
3 a different formulation of the vaccine.

4 So, while I would not -- I don't want to
5 minimize the risk. I do think that you -- that we
6 could -- at this moment based on the totality of the
7 evidence, the benefits do outweigh the risk and as this
8 vaccine is used, which I think has been said before, we
9 have incredible safety systems in place to monitor the
10 potential for myocarditis in this age group, and we can
11 respond quickly as we've shown, we've done it for every
12 other rare adverse event that our safety systems have
13 identified.

14 So, to me, the question is pretty clear. We
15 don't want children to be dying of COVID, even if it is
16 far fewer children than adults and we don't want them
17 in the ICU.

18 **DR. ARNOLD MONTO:** Thank you. Dr. Lee?

19 **DR. JEANNETTE LEE:** Sorry. I needed to lower
20 my hand. Sorry.

21 **DR. ARNOLD MONTO:** Okay. Dr. Fuller?

1 **DR. OVETA FULLER:** Thank you, Arnold. So, I
2 want to -- I actually appreciate this question being
3 phrased the way it is. I'm not going to turn my camera
4 on for broadband purposes, but my question -- and I
5 agree with what Dr. Cohn just said, that the long-term
6 risk -- if I were a parent of a child in this age
7 group, I would want to have the choice. We can't have
8 the choice unless the vaccine is available.

9 So, rather than only the high-risk children,
10 and the question becomes, how do we know the risk for
11 any child, and how does the parent make that decision?
12 So, would Dr. Marks or someone remind me, please, of
13 the pharmacovigilant processes that will be done to
14 pick up things that that may not have shown up in the
15 children in the trial, but as a parent who's
16 considering this for my child, how will I know as it
17 rolls out in the real world if there's something that
18 does show up?

19 I know we have those. Just remind me and
20 everyone listening what those are so that we can feel
21 confident that should something come up, it will be

1 detected. I believe that's what happens, but just
2 remind me, please. Because I think, if we don't make
3 it available, we will never know what will happen with
4 a larger group of people. So, I just ask that of Dr.
5 Marks or maybe Dr. Cohn or someone who has that sort of
6 information, please.

7 **DR. PETER MARKS:** Dr. Fuller, thanks for that
8 question. I will start, and then if Dr. Forshee or
9 someone wants to jump in to augment what I'll say.
10 What we have done during this pandemic is we have an
11 overlapping safety surveillance system that is done in
12 collaboration with the Center for Disease Control and
13 Prevention, so FDA and CDC share this responsibility.
14 There is passive safety reporting as we've heard about
15 today multiple times through the Vaccine Adverse Event
16 Reporting System.

17 Moreover, there's active safety surveillance,
18 which is done by the CDC system using the vaccine
19 safety datalink, which has about, I think, 14 million
20 lives covered to be able to look in near real-time at
21 events that are coming up and then we have the Sentinel

1 BEST system, which is what we've done, used to evaluate
2 myocarditis in about 20 million vaccine recipients.
3 So, and that's even a larger system that continues to
4 grow.

5 So, we will continue to actively look for
6 adverse events, and I think the important thing here is
7 to say that the safety teams at -- and I can speak for
8 this in this case for CDC because I know them and at an
9 FDA -- are incredibly committed and devoted to making
10 sure that we understand the nature of the safety events
11 and then we catch these signals as soon as we possibly
12 can. So, that's what we're here to do. Does anyone
13 from my team or CDC want to add into that? You're
14 muted, Rich.

15 **DR. RICHARD FORSHEE:** Thank you very much, Dr.
16 Marks. This is Rich Forshee. I just wanted to
17 quantify a little bit what Peter said in terms of the
18 BEST system that we have in place, as Dr. Wong said in
19 her presentation earlier today. That covers somewhere
20 between about 25 percent to 30 percent of the people in
21 these age groups depending on which specific cut you're

1 looking at.

2 So, we have a substantial percentage of the
3 pediatric population that's included in our biologic
4 spectrum that's in safety system that we can use to
5 monitor for myocarditis or any other potential adverse
6 events that may come up. Thank you.

7 **DR. OVETA FULLER:** Just a quick follow-up in
8 this. I have a child that I get vaccinated, and I'm
9 really concerned about something happening with him or
10 her, I can go to my primary physician who then will
11 either comfort me or tell me I haven't seen that. They
12 will be basing that decision on what you are looking at
13 in those databases. I guess the question is, how
14 likely is something to get past or ignored by you?

15 I think that's been a lot of the questions
16 that have come up from other people. It's like all
17 these things are happening, but we have no data for
18 that. Are we missing it, or is there other things
19 happening that have nothing to do with the vaccine but
20 may just be coincidental? So, how would I as a parent
21 be comforted by the fact that I know I have a system

1 that is going to allow me to pick up on anything that
2 may be vaccine related.

3 **DR. RICHARD FORSHEE:** Yeah. Thank you. Go
4 ahead, Dr. Marks.

5 **DR. PETER MARKS:** Let me start by this, and
6 then I'll pass it over to Dr. Forshee. Obviously, it's
7 very challenging to figure out whether there are
8 emerging -- what an emerging safety signal is. It is
9 easiest when something is very unusual because it
10 didn't take very many cases of thrombosis or
11 thrombocytopenia syndrome to be able to pick that up.

12 We also are able to pick up things like
13 Guillain-Barre syndrome, but these systems do a -- our
14 statisticians are constantly looking at -- at this
15 point, I think it's 16 potential adverse events of
16 interest, and I'll let Dr. Forshee say more about that.
17 Those are events that have been seen with other
18 vaccines. In order to look for things that might come
19 up and then understand whether they are at a higher
20 rate with the vaccine than without. Rich, maybe I'll
21 pass it over to you to describe that more.

1 **DR. RICHARD FORSHEE:** Thank you, Dr. Marks.
2 So, I just want to build on what Dr. Marks said earlier
3 about the systems approach that we have here. The
4 vaccine adverse event reporting system is particularly
5 good at catching early, unexpected safety signals that
6 we may see. The BEST system and BFC provide us with
7 systems that are more robust in terms of conducting
8 statistical analyses.

9 One thing to keep in mind, however, is that
10 there is some lag with events appearing in these data
11 systems. Claims have to be filed. Claims have to be
12 made available in the data analysis files that we have.
13 So, we do have a robust system, and it has different
14 components to perform different functions. I think
15 I'll leave it there. Thank you.

16 **DR. OVETA FULLER:** All right. Thank you.

17 **DR. ARNOLD MONTTO:** Thank you. Dr. Cohn, and
18 when you're done talking about the systems, could you
19 also talk about what ACIP would do with the
20 recommendations because I think we don't want to
21 overlap the role of ACIP in fine-tuning the approvals

1 that we give and that the ACIP gives because I think
2 that's where I'm afraid we may be going in that
3 direction right now.

4 **CAPT. AMANDA COHN:** Sure. So, the first thing
5 I'll say is that whenever I -- we hear the parents
6 whose kids had medical events that occurred near the
7 timing of a vaccine, and it is really, really hard when
8 something devastating happens to your child, and you
9 want so badly to try to understand what's happened.
10 When a vaccine has occurred in that time frame, it can
11 be very -- I can see how easy it would be to connect
12 the vaccine with the adverse event. So, I definitely
13 don't want to diminish the way that any parent feels.

14 However, we do have several systems in
15 addition to what was just described. We also have
16 CISA, which is the Clinical Investigation Safety team
17 for which a physician can call on at any time, and they
18 have done dozens, if not, hundreds of clinical consults
19 over the past -- I guess, over the past ten months to
20 evaluate potential of an adverse event that is even so
21 rare that it wouldn't be picked up in our safety

1 systems being connected or related to the vaccine.

2 So, this is what has allowed us to really
3 review some of these very rare adverse events and to
4 look at them and to try to, first of all, find another
5 reason for that event to have occurred, which sometimes
6 nobody is able to do. So, you can't completely rule
7 out the possibility of a rare adverse event.

8 That being said, the combination of the safety
9 systems, especially as Dr. Marks was saying, in the
10 setting of a rare -- an event that occurs very rarely
11 in a population, such as myocarditis in these 5- to 11-
12 year-olds or any of the other adverse events that have
13 been detected. When we say we look at these 16 or 20
14 conditions regularly, it's called rapid cycle analysis.
15 The point of that is to look nearly every day at
16 whether or not these signals are being detected in our
17 active surveillance systems.

18 So, parents have the opportunity to enroll
19 their child -- they will have the opportunity to enroll
20 their child in V-safe and report symptoms and report
21 medical events. We have this group of experts to help

1 support clinical decision-making for providers who see
2 rare adverse events or concerns about an adverse event
3 that's related to a vaccine and in addition to our
4 large safety databases that we look at regularly.

5 In terms of HAP, I'd like to say that FDA has
6 the regularity decision-making over whether or not a
7 vaccine or another product is safe and effective and
8 can be used. The ACIP then takes those considerations
9 of use or that indication that FDA makes and looks at
10 other variables beyond just safety and effectiveness to
11 look at who would benefit from the vaccine and what --
12 who should get vaccinated.

13 So, that includes things like equity,
14 feasibility the indirect burden that we've talked about
15 from today. So, they look at the totality of the
16 evidence and don't just focus -- while safety and
17 effectiveness is an important component of that, they
18 look at potential impact of recommendations on a
19 population. So, I think -- if that helps clarify the
20 difference, I think that -- I can answer any other
21 questions.

1 **DR. ARNOLD MONTO:** What I'm really trying to
2 get at is a more broad approval or a more restrictive
3 approval because that is not traditionally what is done
4 in FDA during approvals. So, you're talking about
5 population groups to receive the vaccine. how would
6 our discussion that we are having right now impact -- I
7 know you can't predict, but how would that impact the
8 ACIP discussions?

9 **CAPT. AMANDA COHN:** Sure. So, if the FDA
10 limits an authorization to a population, as you saw
11 with the booster dose recommendations for the mRNA
12 vaccines, based on VRBPAC feedback, then ACIP could not
13 go beyond those conditions of use. So ACIP could limit
14 further, but they can't make the decision to expand the
15 (inaudible).

16 **DR. ARNOLD MONTO:** But they can limit?

17 **DR. AMANDA COHN:** They can limit further. So,
18 if FDA authorizes a product more broadly, then ACIP can
19 look at which specific populations may benefit and will
20 benefit from the vaccine and can make more focused or
21 nuanced recommendations if they choose, or they can

1 recommend that the entire population that FDA
2 authorized the product for is recommended to receive it
3 as you saw in December when we recommended all
4 individuals over the age of 16 or 18 be vaccinated.

5 **DR. ARNOLD MONTO:** Thank you, Dr. Cohn. Very
6 helpful. Dr. Levy?

7 **DR. OFER LEVY:** Sorry, that is an error.
8 Please go to the next.

9 **DR. ARNOLD MONTO:** Okay. Dr. Perlman?

10 **DR. STANLEY PERLMAN:** Yes. So, after
11 listening to all this discussion and thinking about the
12 ACIP, I'm going to vote in favor of this. (Audio skip)

13 **MR. MICHAEL KAWCZYNSKI:** We don't want to have
14 anybody thinking. So, all right. So, again, thank
15 you. We were holding off until -- we want to make sure
16 -- we're just going to make a quick announcement that
17 we do have some widespread power outages. So, we want
18 to make sure we didn't miss anything with Dr. Perlman.
19 So, now that we're reconnected, Dr. Perlman, take it
20 away with your question.

21 **DR. STANLEY PERLMAN:** Okay.

1 **DR. ARNOLD MONTO:** Please start from the
2 beginning.

3 **DR. STANLEY PERLMAN:** Okay. I'll see if I can
4 repeat that.

5 **DR. ARNOLD MONTO:** If you can try.

6 **DR. STANLEY PERLMAN:** Yeah. If I can remember
7 what I said, right. So, I was just going to say that
8 I'm going to vote in favor of this question. As I've
9 listened to all the discussion, all of which I
10 basically agree with, it occurs to me that not only are
11 we talking about acute disease, but we're also talking
12 about the other things that Amanda talked about, the
13 effects on families and transmissions to other people.
14 Then also, along COVID, which may be the biggest
15 problem that we have, certainly in adult populations,
16 maybe in pediatric populations.

17 So, I would want to give families the options
18 of getting their children vaccinated if they choose to.
19 The other thing is that even the shedding scenes are so
20 important for transmission. We don't really have data
21 that there is an effect on shedding, but, based on

1 other studies and other coronaviruses and even to
2 animal studies, it's likely that we will see an effect
3 on shedding. The problem with shedding is that we
4 almost have to do the transmission study to see if
5 people in the household get infected.

6 There may be virus left in the nasal cavity
7 after a vaccine, but the question is, is the shedding
8 is longer, the levels is high, and I think that we
9 don't really have very good data on that. I think it's
10 so important as it's been mentioned many times in this
11 discussion.

12 The final thing is that one of the things we -
13 - reasons we care so much about the risk-benefit ratios
14 is I think it's really been hard finding much of a
15 risk. Much of it so far has been more based on older
16 populations. So, I think the analyses that were done
17 by the CDC were great. But part of the issue is that
18 so far, the risk has not been very high in what we've
19 seen.

20 **DR. ARNOLD MONTA:** Thank you. Dr. Moore?

21 **DR. PATRICK MOORE:** Thank you. So, I found

1 the Committee discussion on this really, really
2 thoughtful. The way I'm thinking about this is that
3 there were -- what are the facts? We do know that
4 there were 94 children in this age group who died of
5 COVID. They all have names. All of them had mothers,
6 and these kids died of COVID.

7 In contrast, we're worried because we -- this
8 group has not been vaccinated before, we're very
9 worried about a side effect which is real. It cannot
10 be dismissed, but, on top of that, we're extrapolating
11 from higher risk boys and men in older age groups, the
12 side effect from a higher dose vaccine, and that's a
13 theoretical risk. It's an important one. Fortunately,
14 no one has died from that that fits that profile.

15 Now, if the surveillance systems do start
16 seeing severe outcomes and deaths from vaccination, I'm
17 quite confident that those surveillance systems will
18 tell us that we need to pause like we did with the J&J
19 vaccine to really have a good idea of what the effects
20 are of vaccinating this age group if we see that.

21 Two, it's also very hard for me to believe

1 that the risk for a severe outcome is going to come
2 close to the known risk that we've seen for this virus
3 in this age group, and to lay on top of that, thousands
4 of kids that have been hospitalized, some of them, no
5 doubt, disabled from that on top of the external costs
6 to parents, to society, to schools, and so forth. So,
7 to me, it seems like it's a hard decision but a clear
8 one. Just want to throw that out.

9 **DR. ARNOLD MONTO:** Thank you very much. Dr.
10 Pergam?

11 **DR. STEVEN PERGAM:** Yes. I keep coming back
12 to the thought that we're in a different situation than
13 we were before in the sense that one of the biggest
14 concerns and where there's a lot of hand wringing about
15 this is the issue of -- a question of myocarditis. We
16 didn't know about myocarditis when we talked about this
17 initially in the younger age group. We sort of learned
18 about this process through this becoming utilized much
19 more commonly.

20 I think we're going to be very tightly
21 following this. I think the guidelines that have been

1 set up by the FDA for pharmacovigilance are
2 specifically focused on this and other known outcomes.
3 And, to me, it feels like that's a really different
4 situation than we've been in when we've gone into
5 populations with basically no knowledge, and I think we
6 have this sort of warning.

7 I think, again, I keep thinking about what
8 Amanda said -- that Dr. Cohn -- specifically about what
9 pediatricians are going through and seeing children
10 dying of a disease that potentially could be
11 preventable and that, when we look at this data, the
12 data we have in front of us says that it can be quite
13 protective for individuals looking at antibody levels
14 as well as even some of the outcome data.

15 So, I think it's really important for us to be
16 thinking about this as we vote, and as well also
17 recognizing that some of the decisions about how this
18 was going to be used are somewhat out of our hands in
19 what happens in the communities and with the ACIP and
20 we should be voting on the question in front of us and
21 not trying to interpret what will happen with the data.

1 **DR. ARNOLD MONTO:** Thank you. Dr. Kurilla?
2 We have two more who are raised, and then we vote. Dr.
3 Kurilla?

4 **DR. MICHAEL KURILLA:** It looks like the camera
5 has burned out again. Yeah. I just wanted to make a
6 couple of additional comments. There's a lot of talk
7 about risks, and I think it's mostly been focused on
8 the myocarditis and that's appropriate, but I think one
9 of the other issues that's not discussed that much is
10 when you're doing a risk-benefit analysis, you have to
11 look at the benefit. And, while the benefit here is
12 assumed to be prevention of severe disease, which is
13 what we're all hoping for, one concern I have is that,
14 particularly for that population of children that has
15 experienced the previous infection -- which CDC
16 estimates is 40 percent of this population which I
17 think is probably a floor; I think it may actually be
18 higher than that -- the question really becomes, does
19 this vaccine offer any benefits to them at all?

20 Are they actually very well protected, and the
21 other aspect here is for children who have undergone,

1 for example, a Delta infection, does now vaccinating
2 them with a strain that goes back almost two years from
3 the vaccine there from the time they're getting the
4 vaccine, does that actually help or hurt their current
5 immune system with regard to ongoing variants? I don't
6 think we know that. We have no idea.

7 I think for many children who have experienced
8 COVID already, they're probably more than adequately
9 protected. One dose may be sufficient. I think for
10 the high-risk children, it's very different, but I will
11 emphasize again that this dosing interval, the way it
12 was put together, is suboptimal in terms of durability.
13 I think that there can't be any expectation that the
14 antibody decay rate is going to look any different from
15 the adults.

16 Then these children are going to be expected
17 to have a booster in another six months, and I think
18 the focus on cases, reducing cases, is really what's
19 going to confound us because I don't think we're going
20 to be able to do that. We're going to see vaccine
21 breakthroughs in this population, and it's going to

1 cause all the same problems that COVID does whether or
2 not they're vaccinated.

3 So, I think that we need to be a little more -
4 - we have to have a little more flexibility in how this
5 is implemented rather than add a single dosing primary
6 vaccination scheme that is one size fits all.

7 **DR. ARNOLD MONTO:** Dr. Nelson?

8 **DR. MICHAEL NELSON:** Thank you, Dr. Monto. I
9 understand why the question was asked the way it was,
10 but I certainly don't like it. Accordingly, almost
11 every vote casted today is probably going to be
12 caveated based on the discussion we've had today.

13 Personally, I see this as an access and really
14 a personal choice and equity question and not a mandate
15 for all in this age group. It had to come to that
16 decision, but certainly, that's where I centered, and
17 we'll probably be in favor of this particular question.

18 To me, we should certainly not underestimate
19 the knowledge and decision-making power of the public
20 as evidenced by the open public hearing comments today,
21 that content as well as, frankly, thousands of emails

1 some of us have received in the last couple of days.
2 Providing choice to a fully risk-informed public using
3 a shared decision-making model with their trusted
4 providers, to me, is a pretty reasonable way ahead.

5 There are millions of at-risk children, and
6 secondarily, family members needing risk-informed
7 access to this vaccine for this age group.

8 Unfortunately, I agree with Dr. Kurilla and the others
9 who were discussing the impact of prior infection and
10 probable existing immunity. Most families in the U.S.
11 are flying blind with respect to their individual
12 status.

13 So, in the absence of a testing strategy or
14 having that knowledge, I think we're stuck with where
15 we are and having to provide at least access to the
16 vaccine and giving families the choice to make that
17 vaccination. So, to me, depriving access to those with
18 the highest risk could have some very devastating
19 effects and hospitalizations and deaths that we'll
20 resolve.

21 So, I deeply appreciate the thoughtful

1 approach that the Committee has taken thus far and the
2 deliberation, I'll probably be supportive.

3 **DR. ARNOLD MONTO:** Thank you very much. Last
4 word to Dr. Fuller, please.

5 **DR. OVETA FULLER:** Thank you, Dr. Monto. I'm
6 just reminded from my infectious disease teaching that
7 we have had vaccines for children before. I'm reminded
8 of the polio vaccine campaign and Dr. Monto, you might
9 actually remember more, that people and children could
10 actually see the effects of polio on their classmates.
11 We cannot see the effects of COVID-19 so dramatically
12 on children, and thus, it weighs the question. Is it
13 worth the risk?

14 I certainly believe that in hindsight who can
15 look back on this decision giving parents the option to
16 make that decision for themselves will be something
17 that, in history, we will be glad that we were able to
18 do and to look at the risk-benefit ratio and say that
19 the benefits of this option far outweigh the known
20 risk. We can't see the disease, but we certainly
21 cannot anticipate all the risks ahead, but we have

1 systems in place that can help us do that.

2 So, I think we have to take a step and say we
3 want to make this option available for what it might do
4 to help the children as well as others in this
5 pandemic. Thank you.

6 **DR. ARNOLD MONTO:** Thank you, Dr. Fuller. So,
7 now we come to our vote. After the vote, we will have
8 for anyone who wants to talk about why they voted and
9 the caveats that are attached to their vote, we will
10 have a chance for anyone who wants to do that to do so.
11 Now, I think I have to read it for the record. Is that
12 correct, Kathleen?

13 **MS. KATHLEEN HAYES:** Yes, that is correct.

14 **DR. ARNOLD MONTO:** Okay. For the record,
15 "Based on the totality of scientific evidence
16 available, do the benefits of the Pfizer-BioNTech
17 COVID-19 vaccine when administered as a two-dose
18 series, 10 micrograms each dose, three weeks apart,
19 outweigh its risks for use in children 5 to 11 years of
20 age?"

21 **MS. KATHLEEN HAYES:** Thank you, Dr. Monto, for

1 reading that aloud and just to provide some guidance
2 before we bring up the voting poll. We do have 18
3 voting members today and 1 nonvoting industry
4 representative attending the meeting. So, only these
5 18 voting members, excluding the industry
6 representative, that's seen on this slide should be
7 voting. If you are not an official voting member,
8 please refrain as your vote will not be counted.

9 In regard to the voting process, Dr. Monto
10 already read the question aloud for the record. So,
11 all of the members and temporary voting members will
12 cast their vote by selecting one of the voting options,
13 yes, no, or abstain. You'll have two minutes to cast
14 your vote, and once all of the votes have been placed,
15 we will then broadcast the results, and I will read the
16 votes aloud for the record.

17 Please note that once you've cast your vote,
18 you may change it within the two-minute time frame.
19 However, once the poll has closed, all votes will be
20 considered final. So, unless anybody has any
21 questions, we can pull up the voting pod, please.

1 Great. So, the poll is up, and if you can please cast
2 your votes at this time.

3 Okay. Looks like all votes are in, so we can
4 now broadcast the results, and I will read the votes
5 aloud for the record. Dr. Moore voted yes. Dr.
6 Wharton voted yes. Dr. Perlman voted yes. Dr. Sawyer
7 voted yes. Dr. Nelson voted yes. Dr. Levy voted yes.
8 Dr. Fuller voted yes. Dr. Hildreth voted yes. Dr.
9 Cohn voted yes. Dr. Portnoy voted yes. Dr. Pergam
10 voted yes. Dr. Lee voted yes. Dr. Offit voted yes.
11 Dr. Monto voted yes. Dr. Kurilla abstained. Dr.
12 Meissner voted yes. Dr. Rubin voted yes. Dr. Gans
13 voted yes.

14 So, this concludes the vote. Out of 18 voting
15 members, 17 voted yes, and we had one abstain. Thank
16 you, Dr. Monto. I will turn it back to you for the
17 voting explanation.

18 **DR. ARNOLD MONTO:** Thank you. Anybody who
19 wants to further explain their vote, please raise your
20 hand. Dr. Meissner?

21 **DR. CODY MEISSNER:** Thank you, Dr. Monto. I

1 voted yes as has been stated, but I wanted to make a
2 point. I think that this is quite different than the
3 MMR vaccine, for example. People compare it as it's a
4 requirement to go to school to get the measles, mumps,
5 rubella vaccine, and that I don't think is a fair
6 comparison because we know that vaccine is safe. We
7 have tested that vaccine for decades. We have a very
8 good sense of what the adverse events are.

9 We do not have that with this particular
10 messenger RNA vaccine. I'm saying there are some
11 children that has been said in the 6- to 11-year-old
12 group who are deserving of this and may very well
13 derive benefit, but there are other children who may be
14 at increased risk of myocarditis. Dr. Yang gave a very
15 sophisticated mathematical model, but I just remind
16 people that the rates of hospitalization in this age
17 group of 6 to 11 is 0.1 per hundred thousand or less
18 than 10 per million.

19 The rates of myocarditis in older age groups
20 with a different vaccine from Israel, at least, were as
21 high as a hundred to 150 cases per million. So, I

1 think we have to very carefully monitor the safety
2 profile of this vaccine going forward if the ACIP does
3 recommend it. And hopefully, it'll be for those
4 children who have other risk factors.

5 **DR. ARNOLD MONTO:** Thank you, Dr. Meissner.
6 Dr. Portnoy?

7 **DR. JAY PORTNOY:** Great. First of all, I
8 wanted to thank you, Dr. Monto and the FDA, for holding
9 such transparent and scientifically valid committee
10 meetings like this. I think that having an open and
11 transparent discussion like we did today instills
12 confidence in the public so that they can see very
13 clearly that we were very careful in our deliberations,
14 and I think that the decision that we came to was
15 exactly the right one. I'm very pleased with that.

16 I work at a children's hospital. Our hospital
17 has been full for the last month or so with children
18 who have been critically ill. Not all of them have
19 COVID, but many of them do. We have a lot of them in
20 the intensive care unit. I'm looking forward to being
21 able to actually do something to prevent that. I'm

1 looking forward to seeing my patients tomorrow in the
2 clinic because they've been terrified that their
3 children are going to get COVID. Now I have some
4 really good news for them that they can look forward
5 to.

6 So, I want to thank the Committee for their
7 deliberations. I think we made the right decision, and
8 I look forward to telling my parents the good news.

9 **DR. ARNOLD MONTO:** Thank you, Dr. Portnoy.
10 Dr. Cohn?

11 **CAPT. AMANDA COHN:** Thanks. So, COVID-19 now
12 is a vaccine-preventable disease from my perspective,
13 and COVID is also the eighth highest killer of kids in
14 this age group over the past year. So, the use of this
15 vaccine will prevent deaths. It will prevent ICU
16 admission and will prevent significant long-term
17 adverse outcomes in children. We will monitor
18 myocarditis very carefully.

19 But I will also say that there have been no
20 deaths from myocarditis and nearly all of those cases -
21 - we were doing long-term outcomes -- have completely

1 recovered just weeks after the onset of their mild
2 cases of myocarditis. So, I just really am so grateful
3 that we had this discussion and that the Committee
4 voted to approve this because I think that the benefits
5 in this age group are really super important even if
6 they are lower, per se, than older age groups.

7 I think this is an age group that deserves and
8 should have the same opportunity to be vaccinated as
9 every other age.

10 DR. ARNOLD MONTO: Thank you, Dr. Cohn. Dr.
11 Levy?

12 DR. OFER LEVY: Thank you. I voted yes after
13 some deliberation and hearing the latest phase of the
14 discussion among the Committee members in FDA, which
15 was helpful to me. Severe pediatric COVID is not
16 nearly as common as an adult, but it does happen and
17 it's not negligible. It does seem to me that we do
18 need ongoing efforts by CDC and others to characterize
19 the disease in children and to measure and define long
20 COVID in children.

21 There's a lot of work to be done there. My

1 impression is not enough federal resources have been
2 invested in those directions, and I would encourage the
3 system to continue to do that. I think this vaccine
4 will likely be effective in reducing pediatric COVID in
5 this age group and may also help reduce transmission.

6 On the safety end, I'm encouraged by the lower
7 dose. The dose-finding, finding a dose that's
8 immunogenic and had not too much in terms of
9 reactogenicity.

10 Then in terms of the myocarditis, it will be
11 important to keep an eye on that as Dr. Cohn alluded to
12 given the surveillance and yet, a priority that seems
13 the 5- to 11-year age group may be less susceptible to
14 that. CDC, if FDA decides to proceed with this, CDC
15 will take it up and will consider the data with an
16 independent eye in terms of whether they need to direct
17 towards how this would be deployed and how it would be
18 used.

19 And I think that the surveillance systems are
20 going to be critical here, and I'm hoping that this
21 starts off as a campaign, if it moves forward, that

1 starts with choice and parents and their care providers
2 partnering in those decisions. Thank you.

3 **DR. ARNOLD MONTO:** Thank you. Dr. Rubin?

4 **DR. ERIC RUBIN:** (Audio skip) still get FDA
5 approved and it goes to ACIP, if they produce a
6 recommendation that says that there will be discretion
7 in how it's used as opposed to a mandate, which I think
8 we would all be concerned about at this point, we are
9 going to get plenty of experience with this, and the
10 good pharmacovigilance plans, I think, are going to be
11 very useful.

12 We will know how safe this is. I agree with
13 Dr. Cohn. You want to save because you can save. I do
14 think that it will be useful to have a lot more
15 information, though, to determine how best to deploy
16 the vaccine. So, I think that we ended up sort of in
17 between. We decided to go for it with a lot of heavy
18 conscious, but I'm hoping that this is the start of
19 learning more about it.

20 **DR. ARNOLD MONTO:** Dr. Wharton?

21 **DR. MELINDA WHARTON:** So, I think this is a

1 valuable tool for prevention of COVID. I know that
2 I've been very worried hearing about pediatric
3 hospitals and pediatric intensive care units being full
4 over the previous several months during the Delta surge
5 in so many communities. So, having this vaccine
6 available to prevent COVID in 5- to 11-year-olds seems
7 to me to be a really positive step.

8 Of course, we will learn more about safety as
9 things go forward, but I think, based on the lower
10 background rate of myocarditis in this age group, the
11 lower dose being used, and the evidence that risk is
12 lower in the younger adolescents than the older
13 adolescents, together, I think that I am not as
14 concerned about myocarditis in this age group as I am
15 in the older kids. So, I think it's a good move
16 forward for COVID prevention and for protecting our
17 kids.

18 **DR. ARNOLD MONTA:** Thank you, Dr. Wharton.
19 Dr. Pergam?

20 **DR. STEVEN PERGAM:** So, I really hope that as
21 we think about this, we focus similarly the way we did

1 on adults that mandates were not immediate after the
2 vaccine was approved, and we see sort of a delay in
3 that sort of approach because I think there is -- the
4 safety concerns are things that have been brought up by
5 Committee members, and there is some issues that folks
6 have, but we want to make sure that we're doing right
7 by children by giving them the opportunity to get
8 vaccinated as well.

9 So, I think that's going to be an important
10 piece as we move forward. You've heard that from
11 Committee members that there is some concern about
12 school mandates and such at the moment. So, I think
13 it's important to keep that in mind, at least in the
14 short term. I also think this sort of begs another
15 question that I think we haven't talked about enough is
16 that we don't do enough in early phases of vaccine
17 trials to include children.

18 Obviously, when they're pediatric vaccines,
19 that's different, but I think we need to rethink our
20 strategies and how we do this because having this data
21 a few months back would've been very valuable as we

1 think about this, and I think, yes, I'd love to see the
2 FDA rethink how they want to advise vaccine companies
3 about doing this kind of research because having this
4 in the earlier phase, and I think my pediatric
5 colleagues would agree with this, would be very
6 advantageous.

7 **DR. ARNOLD MONTO:** Thank you. Dr. Hildreth?

8 **DR. JAMES HILDRETH:** Thank you, Dr. Monto. I
9 voted yes primarily because I want to make sure that
10 the children who really need this vaccine, primarily
11 black and brown children in our country, get the
12 vaccine, but, to be honest, the best way to protect the
13 health of some kids would be to do nothing at all
14 because they're going to be just fine. There are lots
15 and lots of children who, for this vaccine, would be
16 the difference between health and even life.

17 So, my vote was primarily to make sure that
18 those who really need it can get it. I hope that the
19 ACIP will prioritize the vaccine in some ways to make
20 sure that that actually happens, but that's why I voted
21 yes, is to make sure that those who really need it can

1 get it. Thank you.

2 **DR. ARNOLD MONTO:** Thank you. Dr. Moore,
3 final comment.

4 **DR. PATRICK MOORE:** Thank you, Arnold. One
5 thing that I hope is that this is not a last step, but
6 just very, very tiny first step and that the -- I
7 really hope that Pfizer and that the national research
8 agencies -- NIH, FDA, CDC -- do put serious effort into
9 seeing how we can improve the use of this vaccine,
10 particularly in these younger age groups. Or the J&J
11 vaccine, for example, how can that be improved so that
12 the public has more confidence that we are authorizing
13 a vaccine that is as possibly safe and protective as we
14 can get?

15 I think it's too easy for these institutions
16 to simply say, well, we've gotten over the hurdle of
17 it. It's been accepted in this age group or this risk
18 group; let's move on to the next thing. I was a little
19 disappointed that the clinical trials for children
20 didn't start until June 1st of this year, whereas this
21 time last year, we were evaluating the clinical trials

1 for 18-year-olds and above for the Pfizer vaccine, and
2 then quickly thereafter for the Moderna vaccine.

3 So, I just hope that we can make a little bit
4 better progress on trying to find out how to optimize
5 our tools to fight against this virus.

6 **DR. ARNOLD MONTO:** Thank you very much, Dr.
7 Moore. Just to continue some of your thoughts, this
8 could be not the last step but the first step in
9 understanding the role of these vaccines in the
10 pediatric age group. We've identified a lower dose,
11 which we expect is going to decrease the frequency of
12 the rare side effect of myocarditis. We may want to
13 look at that dose in other age groups where myocarditis
14 is more frequent.

15 We have approved or recommended approval for a
16 three-week interval. That's something that we also
17 need to look at more closely, but this is what we have
18 to do now because we are in an emergency. I thank the
19 Committee for a very long and very deliberate and very
20 complete review of all of the elements that have gone
21 into our recommending approval of this vaccine for an

1 important age group of children. So, over to you,
2 Prabha, to close the meeting.

3

4

MEETING ADJOURNMENT

5

6 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Monto.
7 Actually, I will invite Dr. Marks to make the closing
8 remarks before I formally adjourn the meeting.

9 **DR. PETER MARKS:** Thank you very much to the
10 entire Committee for what were very, very thoughtful
11 deliberations today. I think it obviously is a
12 challenging thing, and I think it all shows how caring
13 the entire Committee is about our children. I think
14 everyone here is trying to weigh -- do their best to
15 weigh the benefits and risks here.

16 Just to reassure the Committee, because we are
17 taking an emergency use authorization rather than
18 approval, in general -- although it's possible that
19 mandates could be put in place, I suppose. In general,
20 people have not done mandates with emergency use
21 authorizations, and there are certain governors who

1 have already announced that they would not do a mandate
2 until there was an approval as opposed to an emergency
3 use authorization.

4 So, I really appreciate very much the concern
5 here. The other thing I would just like to just stress
6 is that the safety monitoring of this vaccine will
7 continue. It has actually been quite intense with a
8 small army of individuals who are very committed to
9 this, and they will continue this.

10 I do view this as one of our greatest
11 responsibilities to ensure that, as this vaccine is
12 deployed and as it continues to be deployed in both
13 adults, adolescents, and children, that we are very
14 actively looking for any safety signals and that we
15 take rapid action, and we do so in conjunction with our
16 colleagues at CDC.

17 So, thank you all again for what was a very
18 long day. We greatly appreciate your input and wish
19 you a very good rest of day.

20 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Marks.
21 This is now to formally adjourn the meeting. The

1 meeting is adjourned at 4:35 p.m. Eastern Time. Thank
2 you so much.

3

4

[MEETING ADJOURNED]