

**FOOD AND DRUG ADMINISTRATION (FDA)  
Center for Biologics Evaluation and Research (CBER)  
174th Vaccines and Related Biological Products Advisory  
Committee (VRBPAC) Meeting**

**OPEN PUBLIC MEETING**

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

**June 15, 2022**

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

## ATTENDEES

<b>COMMITTEE MEMBERS</b>	
Arnold Monto, M.D.	University of Michigan
Hayley Altman-Gans, M.D.	Stanford University Medical Center
Paula Annunziato, M.D.	Merck
Adam C. Berger, Ph.D.	National Institutes of Health
Henry H. Bernstein, D.O., MHCM, FAAP	Cohen Children's Medical Center
Archana Chatterjee, M.D., Ph.D.	Rosalind Franklin University
CAPT Amanda Cohn, M.D.	National Center for Immunizations and Respiratory Diseases Centers for Disease Control and Prevention
David Kim, M.D., M.S., M.H.A.	U.S. Department of Health and Human Services
Paul Offit, M.D.	The Children's Hospital of Philadelphia
Steven A. Pergam, M.D.	Seattle Cancer Care Alliance
Jay Portnoy, M.D.	Children's Mercy Hospital
<b>TEMPORARY VOTING MEMBERS</b>	
A. Oveta Fuller, Ph.D.	University of Michigan
Randy Hawkins, M.D.	Charles Drew University and Private Practice
James Hildreth, Sr., Ph.D., M.D.	Meharry Medical College
Jeannette Lee, Ph.D.	University of Arkansas for Medical Sciences
Ofer Levy, M.D., Ph.D.	Massachusetts Institute of Technology
Wayne A. Marasco, M.D., Ph.D.	Harvard Medical School
Pamela McInnes, D.D.S., M.Sc.	National Institutes of Health

Cody Meissner, M.D.	Tufts University School of Medicine
Michael Nelson, M.D., Ph.D.	UVA Health & UVA School of Medicine
Arthur Reingold, M.D.	University of California, Berkeley
Mark Sawyer, M.D., F.A.A.P.	Rady Children's Hospital San Diego
Melinda Wharton, M.D, M.P.H.	Centers for Disease Control and Prevention
<b>GUEST SPEAKERS</b>	
Carla Vinals, Ph.D.	ModernaTX, Inc.
Evan Anderson, M.D., FAAP	Emory University School of Medicine
Jacqueline Miller, M.D., FAAP	ModernaTX, Inc.
Rituparna Das, M.D., Ph.D.	ModernaTX, Inc.
William C. Gruber, MD, FAAP, FIDSA, FPIDS	Pfizer Inc.
<b>FDA PARTICIPANTS/SPEAKERS</b>	
Peter W. Marks, M.D., Ph.D.	Food and Drug Administration
Sudhakar B. Agnihothram, Pharm., Ph.D.	Food and Drug Administration
Doran Fink, Ph.D.	Food and Drug Administration
Ramachandra Naik, Ph.D.	Food and Drug Administration
Jerry Weir, Ph.D.	Food and Drug Administration
Robin Wisch, M.D.	Food and Drug Administration
Ceila M. Witten, Ph.D., M.D.	Food and Drug Administration
Susan Wollersheim, M.D.	Food and Drug Administration
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Prabhakara Atreya, Ph.D.	Food and Drug Administration
Lisa Wheeler	Food and Drug Administration
Joanne Lipkind, M.S.	Food and Drug Administration
Sussan Paydar, Ph.D.	Food and Drug Administration
Christina Vert	Food and Drug Administration
Karen Thomas	Food and Drug Administration
Mr. Michael Kawczynski	Food and Drug Administration
<b>PUBLIC SPEAKERS</b>	
Jasmine King	
Dr. Ashley Serrano	
Michael Baker	
Fatima Khan	
Nicholas Giglia	
Lauren Dunnington	
Kathlyn Hinesley	
Melissa Braveman	
Congressman Louie Gohmert	
Dr. Harvey (Heshie) Klein	
Dr. Kailey Soller	
Shae Lynn	
Kate Schenk	

Tamara Thomson	
Sam Dodson	
Donna Treubig	
Catharine Diehl	
Jessica Nehring	
Dr. Katarina Lindley	
Dr. Caroline Bishop	

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1

**DAY 2**

2

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

3

4

**MR. MICHAEL KAWCZYNSKI:** Good morning and

5 welcome to the day two of the 174th meeting of Vaccines

6 and Related Biological Products Advisory Committee.

7 I'm Mike Kawczynski, and I, along with the DFO Dr.

8 Prabha Atreya and our Chair Arnold Monto -- we will be

9 running today's meeting. We look forward to your

10 participation as the public.

11 Please note this is a live public meeting, so

12 we do have presenters and responders and all that from

13 around the world joining us. If at any time we run

14 into any technical difficulties, we may take a

15 momentary break just to make sure that we can get

16 everything squared away so that you don't miss any of

17 the content in today's meeting.

18 So, with that being said, I'm going to hand it

19 off to our Chair Dr. Monto. Dr. Monto, are you ready?

20 **DR. ARNOLD MONTO:** I'm ready. And it's my

21 pleasure to open the second day of the 174th meeting of



1 the Vaccines and Related Biological Products Advisory  
2 Committee. Our topic for today -- and we have a double  
3 topic -- the Committee will meet in open session to  
4 discuss amending the EUA of the Moderna COVID-19  
5 vaccine to include the prevention of COVID-19 in  
6 infants and children six months through five years of  
7 age, and the second topic, also to discuss amending the  
8 EUA of Pfizer BioNTech COVID-19 vaccine to include the  
9 prevention of COVID-19 in infants and children six  
10 months through four years of age.

11 We next will have Prabha Atreya, the  
12 Designated Federal Officer, open the meeting on her  
13 side, introduce the members, and go through the  
14 housekeeping issues. Over to you, Prabha.

15

16 **ADMINISTRATIVE ANNOUNCEMENTS, ROLL CALL, INTRODUCTION**  
17 **OF COMMITTEE, CONFLICT OF INTEREST STATEMENT**

18

19 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Monto.  
20 Good morning, everyone. This is Prabha Atreya, and I'm  
21 the Designated Federal Officer for this 174th Vaccines

1 and Related Biological Products Advisory Committee  
2 meeting. And it is my great honor to serve as the DFO  
3 for this meeting. On behalf of the FDA, the Center for  
4 Biologics Evaluation and Research, and also the  
5 Vaccines Advisory Committee, I'm very happy to welcome  
6 everyone for today's virtual meeting.

7 Today, the Committee will meet in open session  
8 to discuss amending the emergency use authorization of  
9 the Moderna COVID-19 mRNA vaccine to include the  
10 administration of the primary series to infants and  
11 children from six months through five years of age and  
12 also to discuss amending the emergency use  
13 authorization of the Pfizer BioNTech COVID mRNA vaccine  
14 to include the administration of the primary series to  
15 infants and children six months through four years of  
16 age.

17 Today's meeting and the topic were announced  
18 in the federal register notice that was published on  
19 May 31, 2022. At this time, I would like to introduce  
20 and acknowledge the excellent contributions of the  
21 staff and the great team I have in my division in

1 preparing for today's meeting. Dr. Sussan Paydar is my  
2 alternate DFO, who will read the Conflicts of Interest  
3 statement for the public record. Ms. Christina Vert,  
4 my backup DFO, will be conducting the voting process  
5 later on today.

6 In addition to Sussan and Christina, the other  
7 staff who contributed significantly are Ms. Joanne  
8 Lipkind and members Karen Thomas, Lisa Wheeler, and Ms.  
9 Viola Sampson for this meeting. I would also like to  
10 express our sincere appreciation to Mike Kawczynski in  
11 facilitating today's meeting. Also, our sincere  
12 gratitude goes to many CBER and FDA staff working hard  
13 behind the scenes trying to ensure that today's virtual  
14 meeting will also be a very successful one like all the  
15 previous Vaccines Advisory Committee Meetings.

16 Please direct any press and media questions  
17 for today's meeting to FDA's office of the media  
18 website, [FDAOMA@FDA.hhs.gov](mailto:FDAOMA@FDA.hhs.gov). The transcriptionist for  
19 today's meeting is Ora Giles.

20 We'll begin today's meeting by taking a formal  
21 roll call for the Committee members and the temporary

1 members. When it was your turn, please turn on your  
2 video camera, unmute, and state your first and last  
3 name, and when finished you can turn your camera off so  
4 we can proceed to the next person. Please see the  
5 meeting member roster slides in which we will begin the  
6 chair Dr. Arnold Monto. Dr. Monto, can you start,  
7 please?

8 **DR. ARNOLD MONTO:** Yes, thank you, Prabha.  
9 I'm Arnold Monto. I'm at the University of Michigan  
10 School of Public Health where I have been involved in  
11 research on prevention and control of respiratory  
12 infections, flu, and COVID-19 for a number of years.  
13 Back to you, Prabha.

14 **DR. PRABHAKARA ATREYA:** Thank you. Next, is  
15 Dr. Paula Annunziato who will be joining a few minutes  
16 later. And we can proceed with Dr. Adam Berger.

17 **DR. ADAM BERGER:** Hi, I'm Adam Berger. I'm a  
18 geneticist by training. I am also the director of  
19 clinical and healthcare research policies at the  
20 National Institute of Health where I oversee all of our  
21 clinical research and clinical trial policies. Thanks.

1           **DR. PRABHAKARA ATREYA:** Thank you. Next, is  
2 Dr. Hank Bernstein.

3           **DR. HENRY BERNSTEIN:** Good morning, I'm Hank  
4 Bernstein. I'm a professor of pediatrics at the Zucker  
5 School of Medicine in Hofstra/Northwell. I'm a general  
6 pediatrician with special interests in vaccines and  
7 public health.

8           **DR. PRABHAKARA ATREYA:** Thank you. Next is  
9 Dr. Archana Chatterjee.

10          **DR. ARCHANA CHATTERJEE:** Good morning. My  
11 name is Archana Chatterjee. I have the privilege to  
12 serve as the dean of Chicago Medical School and vice  
13 president for medical affairs at Rosalind Franklin  
14 University in North Chicago. I'm a pediatric  
15 infectious disease specialist with expertise in the  
16 field of vaccines. Thank you.

17          **DR. PRABHAKARA ATREYA:** Thank you. Next is  
18 Captain Amanda Cohn.

19          **CAPT. AMANDA COHN:** Good morning. I'm Amanda  
20 Cohn. I'm a pediatrician and a public health expert at  
21 the Centers for Disease Control and Prevention with

1 expertise in vaccine preventable diseases. Thanks.

2 **DR. PRABHAKARA ATREYA:** Thanks. Next is Dr.  
3 Offit -- Paul Offit.

4 **DR. PAUL OFFIT:** Good morning. I'm Paul  
5 Offit. I'm an attending physician in the Division of  
6 Infectious Diseases at the Children's Hospital of  
7 Philadelphia and a professor of pediatrics at the  
8 University of Pennsylvania School of Medicine. My area  
9 of research interest is mucosal vaccines. Thank you.

10 **DR. PRABHAKARA ATREYA:** Thank you. Next is  
11 Dr. Steve Pergam.

12 **DR. STEVEN PERGAM:** Thanks, Prabha. I'm Steve  
13 Pergam. I'm an adult infectious disease physician at  
14 the Fred Hutchinson Cancer Center in Seattle,  
15 Washington and primarily focused on infections in  
16 immunosuppressant patients.

17 **DR. PRABHAKARA ATREYA:** Thank you. Next is  
18 Dr. Jay Portnoy.

19 **DR. JAY PORTNOY:** Good morning, I'm Jay  
20 Portnoy. I'm a professor of pediatrics at the  
21 University of Missouri, Kansas City School of Medicine.

1 I'm an allergist/immunologist in the division of  
2 allergy and clinical immunology at Children's Mercy  
3 Hospital in Kansas City.

4 **DR. PRABHAKARA ATREYA:** Thank you. Next is  
5 Dr. Eric Rubin.

6 **MR. MICHAEL KAWCZYNSKI:** Dr. Rubin is running  
7 a little late, so we're going to move on to the next  
8 one, Prabha.

9 **DR. PRABHAKARA ATREYA:** Okay. So next we  
10 introduce our temporary voting members. Dr. Oveta  
11 Fuller.

12 **DR. OVETA FULLER:** Good morning, I'm Oveta  
13 Fuller. I'm in the microbiology and immunology  
14 department at the University of Michigan Medical  
15 School. I'm a virologist who studies viral entry and  
16 community engagement.

17 **DR. PRABHAKARA ATREYA:** Thank you. Next is  
18 Dr. Jim Hildreth.

19 **DR. JAMES HILDRETH:** Good morning. I'm James  
20 Hildreth, the President and CEO of Meharry Medical  
21 College, a professor of internal medicine. I'm an

1 immunologist, and I study viral pathogenesis. Thank  
2 you.

3 **DR. PRABHAKARA ATREYA:** Thank you. Next is  
4 Dr. Jeannette Lee.

5 **DR. JEANNETTE LEE:** Good morning, my name is  
6 Jeannette Lee. I'm a professor of biostatistics and a  
7 member of the Windsor P. Rockefeller Cancer Institute  
8 at the University of Arkansas for Medical Sciences.  
9 Thank you.

10 **DR. PRABHAKARA ATREYA:** Thank you. Next is  
11 Dr. Ofer Levy.

12 **DR. OFER LEVY:** Hi, good morning. My name is  
13 Dr. Ofer Levy. I'm a physician scientist and attending  
14 physician in pediatric infectious diseases at Boston  
15 Children's Hospital where I direct the precision  
16 vaccines program, bringing precision medicine  
17 principles to vaccine research. I'm also professor of  
18 pediatrics at Harvard Medical School. Thank you.

19 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Levy.  
20 Next is Dr. Wayne Marasco.

21 **DR. WAYNE MARASCO:** Good Morning. My name is



1 Wayne Marasco. I'm a professor of medicine at Dana  
2 Farber Cancer Institute at Harvard Medical School. I'm  
3 a practicing adult infectious disease expert. I'm also  
4 a research scientist, and the work that I specialize in  
5 is antiviral immunity in vaccine responses. Thank you.

6 **DR. PRABHAKARA ATREYA:** Thank you. Next is  
7 Dr. Pamela McInnes.

8 **DR. PAMELA MCINNES:** Good morning. I'm Pamela  
9 McInnes. I am a retired deputy director of the  
10 National Center for Advancing Translational Sciences,  
11 one of the U.S. National Institutes of Health  
12 institutes.

13 **DR. PRABHAKARA ATREYA:** Thank you. Dr.  
14 Meissner. Cody Meissner.

15 **MR. MICHAEL KAWCZYNSKI:** Just one second. And  
16 Prabha we also forgot a member. We have to go back to  
17 -- I just thought I'd share that with you. So.

18 **DR. PRABHAKARA ATREYA:** Okay.

19 **MR. MICHAEL KAWCZYNSKI:** Go ahead, Dr.  
20 Meissner.

21 **DR. PRABHAKARA ATREYA:** We are getting a lot

1 of background, Mike.

2 **MR. MICHAEL KAWCZYNSKI:** Yup, I took care of  
3 it.

4 **DR. PRABHAKARA ATREYA:** Okay. Thank you. Go  
5 ahead, Dr. Meissner. We can't hear you. You are  
6 muted, I think.

7 **MR. MICHAEL KAWCZYNSKI:** I got it.

8 **DR. CODY MEISSNER:** Thank you. Thank you,  
9 Mike and thank you, Prabha. And good morning to  
10 everyone. My name is Cody Meissner. I'm a professor  
11 of pediatrics and pediatric infectious disease at Tufts  
12 University School of Medicine. The Children's Hospital  
13 will soon close, and I will have a new address. But I  
14 appreciate the opportunity to participate in this  
15 meeting this morning. Thank you.

16 **DR. PRABHAKARA ATREYA:** Thank you. Next is  
17 Dr. Michael Nelson.

18 **DR. MICHAEL NELSON:** Thank you, Dr. Atreya.  
19 I'm an allergist/immunologist. I'm professor of  
20 medicine and chief of the Division of Asthma/Allergy  
21 and Immunology at the University of Virginia. I also

1 serve as the president of the American Board of  
2 Allergy/Immunology. Thank you.

3 **DR. PRABHAKARA ATREYA:** Thank you so much.  
4 Dr. Art Reingold.

5 **DR. ARTHUR REINGOLD:** Good morning. My name  
6 is Art Reingold. I'm an infectious disease  
7 epidemiologist at the School of Public Health at the  
8 University of California, Berkeley.

9 **DR. PRABHAKARA ATREYA:** Thank you. Next is  
10 Dr. Mark Sawyer.

11 **DR. MARK SAWYER:** Good morning. This is Mark  
12 Sawyer. I'm a professor of pediatric infectious  
13 disease at University of California, San Diego and Rady  
14 Children's Hospital. My expertise is in the area of  
15 public health implementation of vaccine policy.

16 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Sawyer.  
17 Last but not least, Dr. Melinda Wharton.

18 **DR. MELINDA WHARTON:** Good morning. I'm  
19 Melinda Wharton. I'm an adult infectious disease  
20 physician by training, and I work at vaccine policy in  
21 the Centers for Disease Control and Prevention.

1           **DR. PRABHAKARA ATREYA:** Thank you. Thank you,  
2 Dr. Wharton. Now I will call Dr. Sussan Paydar to read  
3 the Conflicts of Interest statement for the public  
4 record. Thank you. Sussan.

5           **MR. MICHAEL KAWCZYNSKI:** Prabha. Prabha, we  
6 have one more -- Prabha, we have one more member. Dr.  
7 Gans.

8           **DR. PRABHAKARA ATREYA:** Okay. Okay. She has  
9 joined. Thank you. Sorry, Dr. Gans. Go ahead,  
10 please.

11           **DR. HALEY ALTMAN-GANS:** Thank you. This is  
12 Dr. Haley Gans, pediatric infectious disease at  
13 Stanford University. Relevant to our conversation  
14 today, my research focuses on immune response to  
15 vaccines and those immunocompetent and also those  
16 children with suppressed immune systems. And I sit on  
17 many committees looking at adverse events. Thank you.

18           **DR. PRABHAKARA ATREYA:** Thank you, Dr. Gans.  
19 Okay. Mike, do we have anybody else joining now?

20           **MR. MICHAEL KAWCZYNSKI:** No, we're good now.  
21 Thank you.

1           **DR. PRABHAKARA ATREYA:** Okay. Okay. Thank  
2 you. So, Sussan, go ahead please and review our  
3 conflicts of interest statement for public record.

4           **DR. SUSSAN PAYDAR:** Good morning, everyone.  
5 My name is Sussan Paydar. It is my honor and pleasure  
6 to serve as the alternate Designated Federal Officer  
7 for today's VRBPAC meeting. Thank you for your  
8 attention as I proceed with reading the FDA conflict of  
9 interest disclosure statement for the public record.

10           "The Food and Drug Administration, FDA, is  
11 convening virtually today, June 15th, 2022, the 174th  
12 meeting of the Vaccines and Related Biological Products  
13 Advisory Committee, VRBPAC, under the authority of the  
14 Federal Advisory Committee Act, FACA, of 1972. Dr.  
15 Arnold Monto is serving as the acting voting chair for  
16 today's meeting.

17           "Today on June 15, 2022, under topic two, the  
18 Committee will meet in open session to discuss amending  
19 the EUA of the Moderna COVID-19 mRNA vaccine to include  
20 the administration of the primary series to infants and  
21 children six months through five years age and to

1 discuss amending the EUA of the Pfizer BioNTech COVID-  
2 19 mRNA vaccine to include the administration of the  
3 primary series to infants and children six months  
4 through four years of age.

5            "This topic is determined to be a particular  
6 matter involving specific parties CMISB (phonetic).  
7 With the exception of industry representative member,  
8 all standing and temporary voting members of the VRBPAC  
9 are appointed special government employees, SGEs, or  
10 regular government employees, RGEs, from other agencies  
11 and are subject to federal conflicts of interest law  
12 and regulation.

13            "The following information on the status of  
14 this Committee's compliance with federal ethics and  
15 conflicts of interest laws, including but not limited,  
16 to 18 U.S.C. Section 208 is being provided to  
17 participants in today's meeting and to the public.  
18 Related to the discussions of this meeting, all  
19 members, RGE and SGE consultants, of this Committee,  
20 have been screened for potential financial conflicts of  
21 interest of their own, as well as those imputed to

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

4           “These interests may include, investment,  
5 consulting, expert witness testimony, contracts and  
6 grants, cooperative research and development  
7 agreements, CRADAs, teaching, speaking, writing,  
8 patents and royalties, and primary employment. These  
9 may include interests that are current or under  
10 negotiation. FDA has determined that all members of  
11 this Advisory Committee, both regular and temporary  
12 members, are in compliance with federal ethics and  
13 conflicts of interest laws.

14           “Under 18 U.S.C. Section 208, Congress has  
15 authorized FDA to grant waivers to special government  
16 employees and regular government employees who have  
17 financial conflicts of interest when it is determined  
18 that the Agency’s need for special government employees  
19 services outweighs the potential for a conflict of  
20 interest created by the financial interest involved or  
21 when the interest of the regular government employee is

1 not so substantial as to be deemed likely to affect the  
2 integrity of the services which the government may  
3 expect from the employee.

4           "Based on today's agenda and all financial  
5 interests reported by Committee members and  
6 consultants, there have been one conflicts of interest  
7 waiver issued under 18 U.S. Code 208 in connection with  
8 this meeting. We have following consultants serving as  
9 temporary voting members: Dr. Oveta Fuller, Dr. James  
10 Hildreth, Dr. Jeannette Lee, Dr. Ofer Levy, Dr. Wayne  
11 Marasco, Dr. Pamela McInnes, Dr. Cody Meissner, Dr.  
12 Michael Nelson, Dr. Art Reingold, Dr. Mark Sawyer, and  
13 Dr. Melinda Wharton.

14           "Among these consultants, Dr. James Hildreth,  
15 a special government employee, has been issued a waiver  
16 for his participation in today's meeting. The waiver  
17 was posted on the FDA website for public disclosure.  
18 Dr. Paula Annunziato of Merck will serve as the  
19 industry representative for today's meeting. Industry  
20 representatives are not appointed as special government  
21 employees and serve as non-voting members of the



1 Committee.

2 "Industry representatives act on behalf of all  
3 regulated industry and bring general industry  
4 perspective to the Committee. Dr. Jay Portnoy is  
5 serving as the consumer representative for this  
6 Committee. Consumer representatives are appointed  
7 special government employees and are screened and  
8 cleared prior to their participation in the meeting.  
9 They are voting members of the Committee.

10 "FDA encourages all meeting participants,  
11 including open public hearing speakers, to advise the  
12 Committee of any financial relationship that they may  
13 have with any affected firms, its product, and if  
14 known, its direct competitors. We would like to remind  
15 standing and temporary members that if the discussions  
16 involve any other products or firms not already on the  
17 agenda for which an FDA participant has a personal or  
18 imputed financial interest, the participants need to  
19 inform the DFO and exclude themselves from the  
20 discussion, and their exclusion will be noted for the  
21 record."



1 vaccines to include the younger pediatric populations  
2 of six through five and six through four years,  
3 respectively.

4           If I could have the slide, Mike, that I sent  
5 you, just to remind people of why we're here. It's  
6 because even though there is a very high seroprevalence  
7 rate of the SARS Coronavirus 2 in the pediatric  
8 population, there still was during the Omicron wave a  
9 relatively high rate of hospitalization during this  
10 period. If one looks at that grey period there towards  
11 the right of this slide, that was the Omicron period,  
12 and you can see a very sharp wave.

13           That rate of hospitalization actually is quite  
14 troubling, and if we compare this to what we see in a  
15 terrible influenza season, it is worse. And the same  
16 way as the number of deaths in the zero to four age  
17 range during the two years of the pandemic in total, as  
18 of May 28th as we were reminded of yesterday by our CDC  
19 colleagues, the total number of deaths as of May 28th  
20 was 442 in the under four age range. That also  
21 compares quite terribly to what we've seen with

1 influenza in the past.

2           If one goes back to the H1N1 influenza season  
3 of 2009/2010, the number of deaths in that age range  
4 reported was 78, and we consider that pretty terrible.  
5 So, we are dealing with an issue where I think we have  
6 to be careful that we don't become numb to the number  
7 of pediatric deaths because of the overwhelming number  
8 of older deaths here. Every life is important, and  
9 vaccine preventable deaths are ones that we would like  
10 to try to do something about. We routinely give  
11 influenza vaccines across a broad age spectrum in order  
12 to help prevent deaths in precisely this kind of  
13 manner.

14           So, I just wanted to set the context here that  
15 the intervention we're talking about here is one that  
16 is something that we have accepted in the past to try  
17 to prevent deaths from influenza. Here we have a  
18 different pathogen but one that has created a lot of  
19 havoc just the same. And so, as we move today, I think  
20 we can kind of help -- just wanted to help frame this  
21 in terms of the magnitude of the issue of COVID-19 in

1 the youngest population.

2           Granted, it's a population that has been much  
3 less affected than the older populations, particularly  
4 the oldest population, but one nonetheless that has  
5 also been affected, and I think for those who have lost  
6 children to COVID-19, our hearts go out to them because  
7 these are the -- each child that's lost essentially  
8 fractures a family.

9           So, with that said, we'll look forward to I  
10 think a very good series of presentations, some  
11 excellent discussion, and wish everyone a very  
12 successful meeting today. Thank you. And I'll turn it  
13 back to Dr. Monto.

14           **DR. ARNOLD MONTO:** Thank you, Dr. Marks.  
15 You've set the scene for what our obligation is today  
16 to look at the problem in the youngest of our  
17 population and to keep them as protected as possible  
18 using available vaccines.

19

20           **MODERNA COVID-19 VACCINE: REQUEST FOR EMERGENCY USE**  
21 **AUTHORIZATION (EUA) AMENDMENT, USE OF A 2-DOSE PRIMARY**

1 **SERIES IN INFANTS AND CHILDREN 6 MONTHS THROUGH 5 YEARS**  
2 **OF AGE**

3  
4 **DR. ARNOLD MONTO:** Now I'd like to turn the  
5 floor over to Dr. Sudhakar Agnihothram from FDA. He is  
6 going to walk us through the agenda, tell us what we  
7 are going to be doing today, specifically, and what the  
8 voting questions are going to be. This is a little  
9 unusual kind of meeting where we are looking at two  
10 different products, and he'll tell us how we're going  
11 to be managing going in and out of each with our  
12 discussions and then our voting questions. Sudhakar.

13 **DR. SUDHAKAR AGNIHOTHRAM:** Thank you very  
14 much, Dr. Monto. Good morning, everyone. Can you all  
15 hear me okay?

16 **MR. MICHAEL KAWCZYNSKI:** Yes, sir. Go ahead.

17 **DR SUDHAKAR AGNIHOTHRAM:** Okay, thank you very  
18 much, Mike. Good morning, everyone, and welcome to the  
19 second day of the Advisory Committee Meeting for  
20 discussion of pediatric EUAs. Just a quick thing, this  
21 will be a co-presentation with Dr. Ramachandra Naik,

1 Committee chair for Pfizer BioNTech COVID-19 EUA  
2 request. So, I will be co-presenting this presentation  
3 with Ramachandra Naik.

4           So, with that said, I'm Sudhakar Agnihothram,  
5 primary reviewer and committee chair for Moderna COVID-  
6 19 vaccine EUA amendment, and I would like to begin my  
7 talk by thanking the FDA EUA review committee for  
8 Moderna COVID-19 vaccine, supervisors, management for  
9 all their hard work that went into this and also the  
10 Advisory Committee for their time in this valuable  
11 discussion. I will be providing an overview of the  
12 request from Moderna on amending their EUA for use of  
13 Moderna COVID-19 vaccine as a two-dose primary series  
14 in children six months to five years of age.

15           Here is the outline of my talk and then I will  
16 be providing a refresher on the currently available  
17 COVID-19 vaccine for use for primary vaccination in  
18 children. This will be followed by an overview of the  
19 request from Moderna on amending their EUA for use of  
20 Moderna COVID-19 vaccine as a two-dose primary series  
21 in children six months through five years of age and

1 the clinical package that supports this EUA request.

2           Then, I will be handing over the presentation  
3 for Dr. Ramachandra Naik, and he would be taking about  
4 the overview of the request from BioNTech manufacturing  
5 GmbH (phonetic) on amending their EUA for use of Pfizer  
6 BioNTech COVID-19 vaccine as a three-dose primary  
7 series in individuals six months through four years of  
8 age and the clinical package that supports this EUA  
9 request.

10           He will also be providing a refresher on the  
11 statutory requirements for emergency use authorization,  
12 and Dr. Naik will also provide an overview of today's  
13 agenda, followed by presentation of the voting  
14 questions for both the Moderna COVID-19 vaccine and the  
15 Pfizer BioNTech COVID-19 vaccine EUA request.

16           To give an overview of the currently available  
17 COVID-19 vaccine for primary vaccination in pediatric  
18 population, Pfizer BioNTech COVID-19 vaccine is  
19 available under the EUA for use as a two-dose primary  
20 series given three weeks apart in individuals five  
21 years of age and older. Pfizer BioNTech COVID-19



1 vaccine is also available under the EUA for use as a  
2 third primary series dose given at least 28 days after  
3 the second dose in individuals five years of age and  
4 older who have been determined to have certain kinds of  
5 immunocompromise.

6 Comirnaty is FDA approved for use as a two-  
7 dose primary series in individuals 16 years of age and  
8 older and can be used interchangeably with Pfizer  
9 BioNTech COVID-19 as currently authorized. To provide  
10 an overview of the request from Moderna for amending  
11 their EUA for use of Moderna COVID-19 vaccine as a two-  
12 dose primary series in individuals six through five  
13 years of age, Moderna submitted this amendment request  
14 on April 30, 2022, and then the proposed dosing regimen  
15 includes a primary series of two doses, 0.25 ml each  
16 containing 25 micrograms of mRNA given one month apart  
17 administered intramuscularly in individuals six months  
18 through five years of age.

19 The clinical package that supports this EUA  
20 request includes safety, efficacy, and immunogenicity  
21 data from approximately 1,800 vaccine recipients in

1 children 6 to 23 months of age and approximately 3,000  
2 vaccine recipients in children two through five years  
3 of age. You will be hearing a breakdown and much  
4 detailed presentation on this from both the FDA and the  
5 sponsors today. I will hand it over to Dr. Ramachandra  
6 Naik now. Thank you very much.

7

8 **PFIZER-BIONTECH COVID-19 VACCINE: REQUEST FOR EUA**  
9 **AMENDMENT, USE OF A 3-DOSE PRIMARY SERIES IN INFANTS**  
10 **AND CHILDREN 6 MONTHS THROUGH 4 YEARS OF AGE**

11

12 **DR. RAMACHANDRA NAIK:** Thank you, Dr.  
13 Agnihothram. Good morning, everyone. So, my name is  
14 Ramachandra Naik from the Divisions of Vaccines and  
15 Related Products Applications in the Office of Vaccine,  
16 and I am the review committee chair for this EUA  
17 amendment. I'm going to provide the background  
18 regarding Pfizer BioNTech's EUA amendment request for  
19 the Pfizer BioNTech COVID-19 vaccine for use in  
20 children six months through four years of age.

21 Pfizer submitted an EUA amendment request on

1 May 27th. The Pfizer BioNTech COVID-19 vaccine is  
2 proposed to be administered as a primary series of  
3 three doses, 0.02 ml each dose containing three  
4 micrograms mRNA plus two doses administered three weeks  
5 apart followed by a third dose administered at least  
6 eight weeks after the second dose administered  
7 intramuscularly in individuals six months through four  
8 years of age.

9           The clinical data package includes safety and  
10 effectiveness data from about 3,000 vaccine recipients  
11 six months through four years of age. Details on this  
12 data will be provided in the later presentations by  
13 Pfizer and the FDA. As today's meeting is about  
14 discussions of amending emergency use authorization  
15 from the COVID-19 vaccine, I'm going to reiterate the  
16 statutory requirements for issuing an EUA.

17           FDA may issue an EUA of an unapproved medical  
18 product following an EUA declaration by the secretary  
19 of the U.S. Department of HHS if the following  
20 statutory requirements are met: the agent referred to  
21 in the EUA declaration can cause a serious or life-

1 threatening disease or condition; the medical product  
2 may be effective to prevent, diagnose, or treat serious  
3 or life-threatening condition caused by the agent; the  
4 known and potential benefits of the product outweigh  
5 the known and potential risks of the product; no  
6 adequate, approved, and available alternative to the  
7 product for diagnosing, preventing, or treating the  
8 disease or condition.

9           Next slide is about the overview of today's  
10 agenda. After this FDA introduction, Moderna will  
11 provide the sponsor presentation followed by FDA  
12 presentation by Dr. Robin Wisch on FDA review of  
13 effectiveness and safety of Moderna COVID-19 vaccine in  
14 infants and children six months through five years of  
15 age.

16           After the 15-minute break, Pfizer will provide  
17 the sponsor presentation followed by FDA presentation  
18 by Dr. Susan Wollersheim on the FDA review of  
19 effectiveness and safety of the Pfizer COVID-19 vaccine  
20 in infants and children six months through four years  
21 of age. After the lunch break there will be one hour

1 open public hearing followed by additional question and  
2 answer for FDA and sponsor presenters and Committee  
3 discussion and voting on Moderna COVID-19 vaccine and  
4 after the break, additional question and answer for FDA  
5 and sponsor presenters and Committee discussion and  
6 voting on Pfizer BioNTech COVID-19 vaccine. After  
7 that, the meeting will be adjourned.

8           Next slide is -- this is the question to the  
9 Committee regarding the Moderna COVID-19 vaccine.  
10 "Based on the totality of the scientific evidence  
11 available, do the benefits of the Moderna COVID-19  
12 vaccine when administered as a two-dose series 25  
13 micrograms each dose, outweigh its risk for use in  
14 children six months through five years of age? Please  
15 vote yes or no."

16           This is a question to the Committee regarding  
17 the Pfizer BioNTech COVID-19 vaccine. "Based on the  
18 totality of the scientific evidence available, do the  
19 benefits of the Pfizer BioNTech COVID-19 vaccine when  
20 administered as a three-dose series, three micrograms  
21 each dose, outweigh its risk for use in infants and

1 children six months through four years of age? Please  
2 vote yes or no." Thank you.

3 **DR. ARNOLD MONTTO:** Thank you both for your  
4 description of our activities today. Next, we go to  
5 the Moderna presentation and the FDA presentation  
6 concerning -- excuse me, we have questions and answers.  
7 I just realized -- a few minutes of questions and  
8 answers about the substance of our discussions today --  
9 I mean, the process, not the substance. A few minutes  
10 to talk about the process before we get into what I was  
11 thinking about going to.

12 So, questions and answers about the process.  
13 Again, this is a little unusual because we are  
14 switching from one product to the other. The reason  
15 behind this is that the oral public hearing has to be  
16 held at the time it is being held. So, we're going to  
17 be doing this switch from one product to the other and  
18 going back. So, we're going to have to pay attention  
19 to what we are going to be discussing. Any questions  
20 about the process right now? I'm looking to see if I  
21 have any raised, and I do not. So, I was right in

1 going ahead and jumping ahead to the presentations.

2

3 **SPONSOR MODERNA PRESENTATION: MRNA-1273 (MODERNA COVID-**  
4 **19 VACCINE) - REQUEST FOR EMERGENCY USE AUTHORIZATION**  
5 **FOR USE IN INDIVIDUALS 6 MONTHS THROUGH 5 YEARS OF AGE**

6

7 **DR. ARNOLD MONTO:** Let's do that now. I'd  
8 like to call on Dr. Vinals again who spoke to us  
9 yesterday about the other approach to use of the  
10 Moderna vaccine, and she's going to lead, as she did  
11 yesterday, her team. Dr. Vinals.

12 **DR. CARLA VINALS:** Good morning. My name is  
13 Carla Vinals, and I'm the Vice President of Regulatory  
14 Affairs Strategy for Infectious Diseases at Moderna.  
15 Thank you, again, to the FDA and VRBPAC for the  
16 opportunity to present today our safety,  
17 immunogenicity, and efficacy data for mRNA-1273, the  
18 Moderna COVID-19 vaccine.

19 We're here today requesting emergency use  
20 authorization of mRNA-1273 as a two-dose primary series  
21 for the prevention of COVID-19 in young children two to

1 five years of age and infants and toddlers 6 to 23  
2 months of age. The proposed two-dose, 25 microgram  
3 primary series is to be administered one month apart.  
4 The totality of safety, immunogenicity, and efficacy  
5 data from our clinical development program supports  
6 that the benefits of mRNA-1273 in young children  
7 outweigh the known and potential risks.

8 mRNA-1273 was generally well tolerated, and  
9 the safety profile is consistent with that observed in  
10 older adult age groups. No new safety concerns have  
11 been identified. Our pediatric studies were designed  
12 to meet FDA recommendations for emergency use  
13 authorization to infer vaccine effectiveness based on  
14 immunogenicity compared to young adults as the efficacy  
15 in adults has already been demonstrated. In both age  
16 groups, the core primary immunogenicity objectives were  
17 met.

18 In addition, there was evidence of efficacy  
19 against COVID-19 confirmed by mRNA-1273 in both age  
20 groups, and the rates were comparable to the  
21 effectiveness observed in adults during the Omicron



1 period. Our clinical trials enrolled more than 6,600  
2 participants across the two age groups, and more than  
3 5,000 have received at least one dose of mRNA-1273.

4           The median duration of follow-up in each study  
5 cohort is greater than two months, which again meets  
6 the requirements outlined in the guidance. The dose  
7 selected met all immunogenicity objectives compared to  
8 young adults, and vaccine efficacy is consistent with  
9 what was observed with adults. We have also  
10 established plans for extensive follow-up post  
11 authorization to ensure that the long-term safety and  
12 effectiveness of mRNA-1273 is closely monitored.

13           Based on this information, we will demonstrate  
14 today that the benefits of mRNA-1273 in infants,  
15 toddlers, and young children outweigh the potential  
16 risks. Here's now the agenda for the rest of our  
17 presentation. And I'll now turn the presentation over  
18 to Dr. Anderson who will review the unmet medical need  
19 for COVID-19 vaccines in young children.

20           **DR. EVAN ANDERSON:** Thank you and good  
21 morning. My name is Dr. Evan Anderson. I'm a

1 professor of pediatrics and medicine and a practicing  
2 physician at Emory University and Children's Healthcare  
3 of Atlanta. I'm grateful for the opportunity to  
4 present today the burden of COVID-19 in infants and  
5 young children and the need for vaccines.

6           This slide lists my conflicts of interest,  
7 which have not changed since yesterday. I have been  
8 intricately involved with the clinical trials of COVID-  
9 19 vaccines including the Moderna and Pfizer vaccines.  
10 As a father of four, I have a vested personal interest  
11 in seeing children protected against COVID. Early in  
12 the pandemic, there were several common misperceptions  
13 about COVID-19 in infants and young children and its  
14 associated risks as well as the potential need for  
15 vaccination. Today, I will review the data that  
16 demonstrate that these were clearly misperceptions.

17           First, infants and young children do, in  
18 fact, get infected with SARS-CoV-2. This slide shows  
19 the incidence of SARS-CoV-2 infections per 100,000  
20 population over time as reported by CDC. Infants and  
21 young children are represented with the yellow solid

1 line. Adults and seniors are shown with the grey  
2 dashed and solid lines, respectively.

3           While very few diagnosed cases of SARS-CoV-2  
4 infection were observed early in the pandemic,  
5 beginning with the Delta wave, and now during the  
6 Omicron wave, we have seen a substantial increase in  
7 the number of infections among these children. Next,  
8 we also know that these infants and young children do  
9 get hospitalized with COVID. Again, looking at CDC  
10 data, we see a substantial increase in the number of  
11 hospitalizations during the Omicron surge among infants  
12 and young children less than five years of age.

13           Recent data have also shown that there is a  
14 substantial burden of hospitalizations in young  
15 children. This slide shows the outcomes of COVID  
16 related hospitalizations. Roughly one in four infants  
17 and young children hospitalized with COVID require ICU  
18 admission.

19           In addition, while we often hear that  
20 hospitalizations among healthy children are uncommon,  
21 data demonstrate that over 60 percent of children zero

1 to four years of age hospitalized with COVID have no  
2 underlying medical conditions. Unfortunately, infants  
3 and young children can and do die with COVID. As of  
4 June 2nd, more than 440 infants and young children,  
5 aged zero through four, have died with COVID as  
6 documented by CDC. This is a tremendous burden of  
7 disease and 74 deaths in 2020, more than 200 in 2021,  
8 and almost 150 in the first five months of 2022.

9           What is even more striking is when we place  
10 the number of deaths due to COVID into perspective. If  
11 we think back to the pre-vaccine era, for vaccines that  
12 we are now routinely using -- such as rotavirus,  
13 hepatitis A, rubella, and varicella -- the number of  
14 deaths that were occurring in children with these  
15 pathogens before implementation of routine vaccination  
16 were all less than 60 per year.

17           Flu in the current era ranges up to about 87  
18 deaths per year in children less than five years of  
19 age. For COVID, since the beginning of the pandemic,  
20 we've seen 74 to 221 deaths per year among infants and  
21 young children zero to four years of age. As Dr. Marks

1 has already highlighted, what we saw with COVID last  
2 year alone was more than double the deaths associated  
3 with the 2009 H1N1 influenza pandemic.

4           This is a tremendous burden. Having cared for  
5 many children that have been in the ICU on ventilators  
6 for COVID and with MISC and having cared for several  
7 children that have died of COVID, we need to be able to  
8 prevent COVID-19. Finally, although the focus is most  
9 often on the morbidity and mortality associated with  
10 infection, COVID has dramatically impacted children in  
11 many other ways.

12           Masking and social distancing of young  
13 children is difficult. Almost 60 percent of children  
14 zero to five years of age not enrolled in kindergarten  
15 are routinely cared for in part by individuals other  
16 than their parents, such as their family members or by  
17 day care. Frequent, unexpected disruptions in  
18 childcare and schooling have significantly contributed  
19 to the daily burden for these families during COVID.  
20 COVID crisis family related hardships have adversely  
21 impacted the well-being of our children.

1           Finally, concerns have arisen regarding the  
2 narrow development of children born during the pandemic  
3 and increases have been observed in child abuse and  
4 mistreatment. So, in summary, infants and young  
5 children do get infected with SARS-CoV-2. I'd also  
6 like to highlight that these infants and children are a  
7 continuously renewing population. We now have two-  
8 year-olds that were born after the onset of the  
9 pandemic.

10           Over three and a half million infants are born  
11 each year in the U.S., and by six months of age, these  
12 infants are all fully susceptible to COVID. Infants  
13 and young children do get hospitalized with COVID, and  
14 the surge in hospitalizations with the emergence of the  
15 Omicron variant was prominent in our youngest children  
16 who have no access to a COVID vaccine.

17           Unfortunately, data also show that infants and  
18 young children do get hospitalized with COVID;  
19 approximately one in four of these will require ICU  
20 level care. Infants and young children do, on  
21 occasion, die with COVID. In fact, we have seen 442

1 deaths with COVID since the start of the pandemic in  
2 this age range. These deaths far exceed that for many  
3 other pathogens for which vaccines are now available  
4 and recommended.

5           Finally, these children and their families  
6 have been profoundly impacted in many other ways by  
7 COVID. All of this taken together is why a safe and  
8 effective vaccine for COVID-19 is needed specifically  
9 for infants and young children. Thank you very much  
10 for the opportunity to present to you today. I'll turn  
11 the presentation over to Dr. Das.

12           **DR. RITUPARNA DAS:** Good morning. My name is  
13 Rita Das, and I'm the vice president of COVID-19  
14 vaccines at Moderna. I'm pleased to present the  
15 safety, immunogenicity, and efficacy data from Study  
16 204 in young children six months through five years of  
17 age. Our development program includes more than 5,000  
18 young children who received at least one 25 microgram  
19 dose of mRNA-1273. Overall, this represents a  
20 substantial pre-licensure safety database in these age  
21 groups.

1           Study 204 was conducted in two parts. Part  
2 one was the open label dose escalation study, and it  
3 was conducted to select a dose level for further  
4 testing in part two which was the placebo-controlled  
5 portion of the trial. Both 25 and 50 micrograms were  
6 studied in two- to five-year-old children. The 25  
7 microgram dose was chosen for the older children, so  
8 the 50 microgram then was not investigated in the  
9 younger children.

10           The 25-microgram dose was chosen for both age  
11 groups because it showed an acceptable tolerability  
12 profile and demonstrated a high likelihood of meeting  
13 the prespecified immunogenicity success criteria.  
14 After part one was completed, a DSMB meeting occurred  
15 to ensure the Committee's concurrence with the selected  
16 dose. Part two randomized children in a three to one  
17 ratio to receive either mRNA-1273 or saline placebo.

18           The children will be boosted and followed for  
19 an additional 12 months. The data we will present  
20 today focus on part two, which evaluated the two dose  
21 25 microgram primary series against placebo. The



1 median safety follow-up meets the EUA recommendation of  
2 at least two months after the final dose. The part one  
3 cohorts had seven to eight months of follow-up, and the  
4 part two cohorts had median safety follow-up of two  
5 months post dose two.

6 Safety endpoints included solicited local and  
7 systemic adverse reactions which were collected seven  
8 days post vaccination. All unsolicited events were  
9 captured for 28 days after each vaccination, and SAEs,  
10 medically attended AEs, and adverse events of special  
11 interest were followed throughout the entire study.  
12 Vaccine effectiveness was a primary objective, and it  
13 was successfully inferred by meeting the predefined  
14 immunogenicity criteria which were agreed with the FDA.

15 There were two non-inferiority criteria.  
16 First, the lower bound of the GMC ratio had to be at  
17 least 0.67, and the point estimate had to be at least  
18 0.8. The FDA requested that, if we selected doses  
19 lower than 100 micrograms, we ensure that the point  
20 estimate of the GMC ratio be at least 1.0. Second, the  
21 lower bound of the difference in seroresponse rates,

1 which were defined as a four-fold rise from baseline  
2 titers, had to be greater than minus 10 percent with a  
3 point estimate greater than minus five percent.

4 Evaluation of efficacy was pre-specified as a  
5 secondary objective. As in the 301 study, there were  
6 two case definition applied. The CDC definition, which  
7 requires one systemic or respiratory symptom, and the  
8 301 definition which requires two systemic or a single  
9 respiratory symptom. Both case definition require a  
10 nasal swab positive by RT-PCR for SARS-CoV-2. The CDC  
11 case definition was considered primary since children  
12 tend to have less severe symptoms of COVID than adults.

13 Turning to results, overall, the demographics  
14 were well balanced between vaccine and placebo in both  
15 age groups. The mean age in the youngest group was  
16 about 11 months, and it was 3 years in the older group.  
17 Gender, race, and ethnicity also were well balanced.  
18 Next, I'll review the safety findings starting with  
19 solicited local reactions in children two to five.

20 In this figure, mRNA 1273 is shown in blue,  
21 and placebo is shown in grey. Pain was the most common

1 event, with similar rates in severity following dose  
2 one and dose two. Most local AEs, including pain, were  
3 Grade 1 to Grade 2 with few Grade 3 reactions. The  
4 median duration of local adverse reactions for this age  
5 group was two to three days. Looking at infants and  
6 toddlers, pain was again the most common local adverse  
7 reaction. Although, reports of pain in this youngest  
8 group were very similar to placebo and much more  
9 similar than the older age groups.

10           Next, turning to systemic reactions. Systemic  
11 adverse reactions were evaluated according to age.  
12 Young children's events included fever, headache,  
13 fatigue, myalgia, arthralgia, nausea, vomiting, and  
14 chills. For infants and toddlers events included,  
15 fever, irritability and crying, sleepiness, and loss of  
16 appetite. Headache and fatigue were the most common  
17 systemic adverse reactions among children 37 months to  
18 5 years. Among vaccine recipients systemic adverse  
19 reactions were more frequent post dose two compared to  
20 post dose one, although this difference now was less  
21 pronounced than in the older age groups.

1           Duration was two to three days, very  
2 consistent with the older age groups. In this slide  
3 we're showing the systemic adverse reactions collected  
4 for infants and toddlers. On the top are the toddlers  
5 aged 24 to 36 months, and on the bottom are the infants  
6 and toddlers aged 6 to 23 months. Here, reporting  
7 rates of systemic adverse reactions were similar  
8 between dose one and dose two. Also, these systemic  
9 events were reported at similar rates among vaccine and  
10 placebo recipients.

11           I will discuss fever separately since this is  
12 particularly important in the assessment of pediatric  
13 vaccines. This slide shows fever by increment among  
14 children six months through five years. Overall, fever  
15 after any dose occurred in about a quarter of the  
16 children. The distribution of temperatures was similar  
17 between the two age groups. Reports of fever greater  
18 than 40 degrees Celsius were rare. And over the next  
19 few slides I will provide a detailed assessment of all  
20 the fevers.

21           In this slide we have maximum temperatures

1 post dose one and post dose two according to  
2 temperature ranges. First, we look at the fevers in  
3 children two to five years. We see that fevers  
4 occurred more frequently following the second dose.  
5 It's important to note that most reports of fever were  
6 less than 39 degrees Celsius.

7           Here are the fevers for infants and toddlers.  
8 Again, fevers are reported more commonly post dose two.  
9 The rates of fever greater than 39 degrees in this  
10 youngest age group are very similar to placebo. This  
11 figure shows fever by day after the second dose in  
12 children two to five years of age. Most events of  
13 fever occurred within two days following vaccination.  
14 Beyond day two, we see that fever rates in the children  
15 receiving mRNA-1273 are similar to placebo.

16           The median duration of fever in this age group  
17 was one day. It's important to note that this study  
18 was conducted during the winter months when respiratory  
19 infections are prevalent, and this is evidenced by the  
20 relatively higher rates of fever in the placebo group  
21 as well. We see a similar pattern in infants and

1 toddlers with the peak of fever again occurring on days  
2 one and two after vaccination.

3           On subsequent days, fevers look similar among  
4 the vaccine and placebo groups. The higher background  
5 rate of fever is even more prominent in the infants and  
6 toddlers. There were 15 children with fever greater  
7 than 40 degrees Celsius in the mRNA group and three in  
8 the placebo group. The peak temperature of greater  
9 than 40 degrees Celsius had a duration of less than one  
10 day. Of the 15 events in vaccine recipients, six of  
11 the children also had symptoms of concurrent viral  
12 infections.

13           Since febrile seizures can occur in up to five  
14 percent of young children, next I will talk about the  
15 febrile seizures that were reported in children six  
16 months to five years. There were four episodes of  
17 febrile seizures overall in study 204. One was  
18 proximal to vaccination and considered related by the  
19 investigator. This child also had a maculopapular rash  
20 onset two days after the seizure and then went on to  
21 have a subsequent seizure associated with another fever

1 approximately six weeks later.

2           The child has remained in the study and  
3 received dose two of the vaccine without event. The  
4 other three events occurred 10 to 66 days after  
5 vaccination and were not considered related by the  
6 investigators. All three events occurred in children  
7 with other symptoms of either concurrent viral  
8 infections or one child who had a periodic fever  
9 syndrome.

10           Next, I will discuss unsolicited adverse  
11 events. Presented here are the events reported after  
12 28 days after any injection in children two to five  
13 years. The incidence of unsolicited AEs was similar  
14 among vaccine and placebo recipients. There were no  
15 SAEs considered to be related by the investigator.  
16 Incidents of MAAEs were similar, and there were no AEs  
17 which led to discontinuation of the vaccine or from the  
18 study.

19           After the data cut, there was one event of  
20 urticaria reported on day one post vaccination that did  
21 lead to discontinuation. There were no deaths or

1 adverse events of MIS-C or myocarditis. Among the  
2 infants and toddlers, the incidence of unsolicited AEs  
3 overall and MAAEs were again similar among vaccine and  
4 placebo recipients. There was one SAE within 28 days  
5 which was considered related to vaccination which I  
6 already described in the fever discussion.

7           Since the data cut of our submissions in late  
8 February, we pulled the SAEs from our live database in  
9 early May to provide further reassurance of mRNA-1273's  
10 safety. This updated analysis did not identify any new  
11 safety signals, and there were no SAEs which were  
12 considered by the investigator to be related to  
13 vaccination.

14           Next, we'll turn our attention to the  
15 immunogenicity data. The two-fold primary  
16 immunogenicity objectives were met for children two to  
17 five years old after the two-dose primary series. The  
18 ratio compared to young adults was 1.01 with a lower  
19 bound of 0.88. Seroreponse rates were close to 100  
20 percent in both groups with a difference of minus 0.4  
21 percent and a lower bound of minus 2.7 percent.



1           Next, looking at infants and toddlers 6 to 23  
2 months of age, we see again that both co-primary  
3 immunogenicity endpoints were met after receiving the  
4 two-dose primary series of mRNA-1273. The ratio  
5 compared to young adults was 1.28 with a lower bound of  
6 1.12. In addition, the seroresponse rate was 100  
7 percent. A group difference of 0.7 percent and a lower  
8 bound of minus 1.0 percent was observed.

9           Next, I'll review the efficacy assessment  
10 which was a secondary objective. I'd like to highlight  
11 that our pediatric studies were conducted and efficacy  
12 follow-up was performed throughout a time when  
13 predominant SARS-CoV-2 strains were changing. And this  
14 is important to context when interpreting the efficacy  
15 results in the two youngest cohorts. As shown in this  
16 slide, the enrollment and efficacy follow-up in young  
17 children was conducted during the Omicron variant wave.

18           The impact of the Omicron daily incidence is  
19 apparent from the curve shown in red. From December  
20 2021 through March 2022, the daily U.S. incidence of  
21 SARS-CoV-2 infections rose from fewer than 200,000 per

1 day to a peak of 1.4 million cases per day indicating  
2 that the SARS-COV-2 epidemiology changed significantly  
3 when these youngest cohorts were followed.

4           Moving now to the efficacy results. We took a  
5 comprehensive approach to capturing cases. All  
6 children with symptoms were requested to come into the  
7 clinic for illness visits where a nasal swab was  
8 collected for RT-PCR. Efficacy estimates in the  
9 children two to five years were based on 180 cases  
10 captured over 71 days post dose two. There was a lower  
11 incidence of COVID-19 by both case definitions in  
12 children who received vaccine compared to those who  
13 received placebo.

14           Statistically significant efficacy of 36.8  
15 percent was observed using the CDC definition. When we  
16 get to the 301-case definition, we see that the number  
17 of cases is reduced, and the efficacy is 46.4 percent.  
18 Next, looking at efficacy among infants and toddlers 6  
19 to 23 months. Efficacy estimates here are made using  
20 85 cases captured over 71 days post dose two. We again  
21 see statistically significant efficacy of 50.6 percent

1 when using the CDC definition.

2           When we get to the 301 definition, the point  
3 estimate is directionally similar, but the confidence  
4 intervals are wider due to the drop in the number of  
5 cases. To that end, at the start of the Omicron wave,  
6 we noticed that parents were reluctant to bring the  
7 youngest children into the site for illness visits.  
8 Instead, they were calling in results of positive home  
9 antigen tests. Since we captured results from the home  
10 antigen tests as well, we did a sensitivity analysis  
11 defining COVID-19 by either positive PCR or home test.

12           With the increased number of cases captured,  
13 the confidence intervals narrowed and the point  
14 estimates for efficacy were now 53.5 percent and 43.7  
15 percent with confidence intervals excluding zero. For  
16 context, we will now look at real world effectiveness  
17 in adults during the Omicron surge to help interpret  
18 the vaccine efficacy from our pediatric program.

19           Presented on this slide on the left are real  
20 world effectiveness data against Omicron among adults.  
21 These data are from our collaboration study with the

1 Kaiser Permanente health system. Vaccine effectiveness  
2 of mRNA-1273 against infection was 44 percent when the  
3 Omicron variant was predominant. Now, on the right are  
4 the estimates of efficacy from study 204 in infants and  
5 young children. Efficacy of mRNA-1273 was consistent  
6 with the effectiveness seen in adults.

7           While vaccine effectiveness against any  
8 infection was lower during Omicron, we continued to see  
9 the benefits of mRNA-1273 against hospitalization. Two  
10 doses of mRNA-1273 was shown to be 84 percent effective  
11 against hospitalization during the Omicron period.  
12 This is important because we would expect the same  
13 level of protection in children given the consistency  
14 of the immune response and efficacy with adults.

15           Study 204 is ongoing, and safety follow-up  
16 will continue for all participants. Children will be  
17 offered a booster at least four months after the second  
18 dose. They will be boosted either with mRNA-1273 or  
19 our bivalent Omicron containing vaccine.

20           In summary, mRNA-1273 was well tolerated.  
21 Local and systemic reactions were seen less frequently

1 in these youngest groups. Solicited adverse reactions  
2 were mostly Grade 1 to 2 and slightly more common after  
3 dose two. Fever was most commonly reported in the  
4 first two days after vaccination and resolved in one  
5 day. No deaths, myocarditis, pericarditis, or MIS-C  
6 were reported among vaccine recipients. There was one  
7 related SAE of fever febrile seizure within 28 days of  
8 any vaccination.

9           The primary immunogenicity objectives were  
10 met. Two doses of mRNA-1273 were shown to be  
11 immunogenic. GMCs and seroresponse rates were non-  
12 inferior to young adults. Vaccine efficacy can  
13 therefore be successfully inferred based on  
14 immunogenicity. In both age groups, direct efficacy  
15 against COVID-19 was observed during the Omicron  
16 period, again, consistent with the effectiveness  
17 observed in adults. And now I'll turn the presentation  
18 over to Dr. Miller to summarize.

19           **DR. JACQUELINE MILLER:** Thank you, Dr. Das.  
20 Good morning to the Committee members. My name is  
21 Jacqueline Miller, and I'm the Senior Vice President

1 and Therapeutic Area Head for Infectious Diseases at  
2 Moderna. And I'd like to summarize our presentation  
3 for children six months to five years of age. Dr.  
4 Anderson reviewed a significant unmet medical need  
5 remains for pediatric vaccines against SARS-CoV-2 and  
6 hospitalizations due to COVID-19 disease have increased  
7 amongst the youngest age cohort during the Omicron  
8 period.

9           Of these children, approximately one in four  
10 will be admitted to the ICU. Since the beginning of  
11 the pandemic, 442 deaths involving SARS-CoV-2 have been  
12 reported in children up to four years of age, and this  
13 exceeds the number of deaths due to other vaccine  
14 preventable diseases in their respective pre-vaccine  
15 eras.

16           Vaccine effectiveness has been demonstrated in  
17 children six months through five years of age via  
18 immunobridging of the young adult cohort from the 301  
19 study which demonstrated vaccine efficacy against any  
20 and severe COVID-19 disease. The immune response has  
21 been remarkably consistent across age groups in a two-

1 dose primary series with lower doses administered to  
2 younger children. This slide depicts the immune  
3 responses ranging from young adults to children in all  
4 age cohorts and across the pediatric age groups. The  
5 ratio after the second dose ranged from 1.01 through  
6 1.28, successfully meeting all primary immunogenicity  
7 hypotheses.

8           Additional support for this EUA submission was  
9 provided through the secondary assessments of efficacy  
10 which were comparable with effectiveness in adults for  
11 the same variant of concern. Although we did not  
12 observe severe cases of COVID-19 in children at the  
13 time of the data cutoff, this consistency leads us to  
14 believe that efficacy against severe disease will be  
15 similar to adults, and this will be evaluated in our  
16 ongoing post authorization study.

17           We plan to administer booster doses with our  
18 Omicron containing bivalent vaccine to the six-month to  
19 five-year-old cohort which will generate the safety and  
20 effectiveness data. Children will be followed for 12  
21 months after boosting. The ongoing post authorization

1 studies we described yesterday will also be extended to  
2 the youngest age cohorts. So, in summary, our  
3 pediatric development program meets all FDA  
4 recommendations for EUA in children six months to five  
5 years of age.

6           Our clinical trials enrolled more than 6,600  
7 participants across these two age groups, and more than  
8 5,000 participants have received mRNA-1273 with more  
9 than two months of follow-up. The 25-microgram dose  
10 has met all prespecified immunogenicity objectives, and  
11 vaccine efficacy is consistent with what was observed  
12 with adults during the Omicron period, allowing the  
13 initiation of protection in infants and young children  
14 as of six weeks after initiating the vaccination  
15 schedule.

16           Our long-term safety and effectiveness studies  
17 will continue to evaluate the impact of mRNA-1273 in  
18 infants, toddlers, and young children. Based on this  
19 information, we have demonstrated that the benefit-risk  
20 profile of mRNA-1273 is strongly favorable in children  
21 six months to five years of age. And so, we are



1 requesting emergency use authorization of a 25  
2 microgram two-dose primary series in children six  
3 months to five years of age. This proposal is the  
4 result of careful dose selection and the optimization  
5 of the immunogenicity and reactogenicity profile in  
6 this age group, and the proposed dosing schedule is  
7 consistent with our approved dosing schedule in adults.

8           We have heard the feedback from the Committee  
9 yesterday and want to assure you that all children  
10 enrolled in these studies are being boosted and  
11 followed for safety, immunogenicity, and disease  
12 incidence for 12 months afterwards. And of these, a  
13 cohort will contain our Omicron containing booster  
14 since the data over time indicates that Omicron  
15 represents a step change in the evolution of this  
16 virus.

17           These booster data will roll out over the  
18 summer, and we will be submitting them for FDA review  
19 as soon as possible. However, as children under four  
20 have had the greatest increase in their risk of  
21 hospitalization due to COVID-19 during the Omicron

1 surge, initiating this vaccination series now is vital  
2 to start protecting children this summer. Thank you  
3 very much to the FDA and this Committee, as well as all  
4 of our collaborators and particularly to the children  
5 and parents in our summer. We heard from one of those  
6 parents yesterday and her story was quite compelling.

7 I'd be happy to take any questions from you  
8 now.

9

10

#### Q&A SESSION

11

12 **DR. ARNOLD MONTO:** Thank you to the Moderna  
13 team. Very clear presentations. I'd like to ask the  
14 Committee to come up with some questions on the  
15 specifics. We're going to have a much broader  
16 discussion this afternoon after we hear the FDA  
17 presentations. So, this should be mainly for  
18 clarification of questions in the short time we have  
19 available right now. Dr. Gans.

20 **DR. HALEY ALTMAN-GANS:** Thank you very much  
21 for that presentation. I appreciate also your

1 information about the boosters. I did have a question  
2 just to clarify on maternal antibodies. Are you  
3 collecting the leads for the youngest babies at that  
4 six-month mark?

5 I noticed that in some of the immunogenicity,  
6 at least on the slides that I looked at, there were  
7 several infants that had preexisting antibodies, and so  
8 I'm wondering about are you collecting information on  
9 the mothers' immunization status during pregnancy? And  
10 are you looking at a pre -- I'm imagining a pre-vaccine  
11 antibody so that's how you're getting the group that  
12 had a preexisting? And are we looking for the  
13 distinction between infection and maternal antibodies  
14 in those?

15 So, the maternal antibody question continues.  
16 Are those children that are seeing breakthrough  
17 disease, or are there any differences in that group  
18 moving forward?

19 **DR. JACQUELINE MILLER:** Thank you for that  
20 question, Dr. Gans. So, this particular study did not  
21 collect maternal antibodies. However, we're initiating

1 a study in infants that are at birth to six months of  
2 age, and that study is called Baby-CoV is initiating  
3 now. And our intent is to stratify our results by  
4 immunogenicity. Sorry, by maternal antibodies.

5 **DR. HALEY ALTMAN-GANS:** Okay. And this group  
6 you didn't collect that data even if the mother got  
7 immunized or not?

8 **DR. JACQUELINE MILLER:** Yes.

9 **DR. HALEY GANS:** Thank you.

10 **DR. ARNOLD MONTO:** Thank you. Dr. Portnoy,  
11 followed by Dr. Chatterjee. Dr. Portnoy.

12 **DR. JAY PORTNOY:** Great. Thank you. I  
13 learned the trick that you hit the raise your hand  
14 early, and that way you can get your question in in  
15 advance.

16 **DR. ARNOLD MONTO:** That's right.

17 **DR. JAY PORTNOY:** Exactly. I was just  
18 wondering about infants and children who -- in your  
19 study who had been previously infected with COVID and  
20 whether there was any effect of a previous COVID  
21 infection on immunogenicity and effectiveness of the

1 vaccine. How many of the patients in your study were  
2 previously infected and already had some immunity going  
3 into the trial?

4 **DR. JACQUELINE MILLER:** Yeah, so we actually  
5 do have information on those that were previously  
6 infected, and previously infected is defined as having  
7 either a positive RT-PCR swab or a nucleocapsid protein  
8 antigen pre-vaccination. And can you please put up the  
9 slide first for children two to five years of age?  
10 It's IM4.

11 But the impact that we saw in both children  
12 two to four and infants and toddlers 6 to 23 months of  
13 age, we did see increases in antibody titers, and in  
14 fact evidence of previous infection actually lead to  
15 substantially higher antibody titers. And this is  
16 really consistent with data that other authors have  
17 published suggesting that a combination of a previous  
18 Omicron infection and vaccination actually leads to the  
19 longest protection against further Omicron infections.

20 **DR. JAY PORTNOY:** Okay. And were there any  
21 differences in adverse events from the vaccine in those

1 who had previously been infected?

2           **DR. JACQUELINE MILLER:** The difference was  
3 primarily in -- and I'm sorry, can you also put up the  
4 infants and toddlers, please? It's IM5 slide, please,  
5 thank you. Just to show you those while I talk through  
6 the safety data. We saw similar reactogenicity  
7 profile, but the timing of when those reactions  
8 happened is different. Um, so the reactions tended to  
9 happen more commonly at the higher rate post dose one  
10 versus post dose two.

11           **DR. JAY PORTNOY:** Great. Thank you.

12           **DR. ARNOLD MONTO:** Thank you. Dr. Chatterjee,  
13 followed by Dr. Cohn.

14           **DR. ARCHANA CHATTERJEE:** Yes, thank you. So,  
15 I have two questions if I may, Dr. Monto. The first  
16 one is related to slide 39, I believe. There was  
17 mention made of higher fever noted in some of the  
18 participants that had symptoms related to other viral  
19 infections -- potentially other viral infections. The  
20 question is were these participants tested for other  
21 viral infections, and do you have those data?

1           **DR. JACQUELINE MILLER:** Yeah, so if the  
2 children came into the office, the physician may have  
3 chosen to test for other viral infections. Because we  
4 were obtaining nasal swabs and not (audio skip) swabs,  
5 we don't have the BioFire results in this younger  
6 population as we do in the older population. But this  
7 just represents the concurrent symptoms because the  
8 parents report to the physician all of the AEs that are  
9 occurring simultaneously. We can say that there were  
10 multiple symptoms in those six participants.

11           **DR. ARCHANA CHATTERJEE:** Okay. My second  
12 question is with regard to concurrent administration of  
13 other vaccines, particularly for the six-month-old  
14 participants. Were the recipients of other vaccines  
15 simultaneously, or were those given at a different  
16 time?

17           **DR. JACQUELINE MILLER:** Yeah, so the  
18 administration of other vaccines was actually given at  
19 a separate time, and the reason for that was when we  
20 started this whole endeavor, there were actually a  
21 number of questions about the appropriate dose, the use

1 of the mRNA platform. And we really felt that it was  
2 important to first select the right dose and tease  
3 apart and fully describe that reactogenicity profile.

4           So, in the study that we're about to conduct  
5 in infants, we are going to be looking initially in  
6 infants for the right dose without concomitant  
7 vaccination, and then the intent is for those subjects  
8 -- because obviously as COVID continues with us the  
9 renewable cohort is the birth cohort -- we are also  
10 going to test (audio skip) versus non concomitant  
11 administration.

12           **DR. ARCHANA CHATTERJEE:** One last question, if  
13 I may, Dr. Monto. This is a follow up to the answer.

14           **DR. ARNOLD MONTO:** A very quick one.

15           **DR. ARCHANA CHATTERJEE:** Yeah, and that is in  
16 the children who received other vaccines, were vaccines  
17 given before or after the COVID vaccine?

18           **DR. JACQUELINE MILLER:** I think it is  
19 dependent on the physician's choice and how they wanted  
20 to administer the schedule. What we asked was that  
21 they separate the vaccinations by at least two weeks



1 for influenza and a month for the other vaccinations.

2 **DR. ARCHANA CHATTERJEE:** Thank you.

3 **DR. ARNOLD MONTO:** Thank you. Dr. Cohn,  
4 followed by Dr. Levy.

5 **CAPT. AMANDA COHN:** Thanks, Dr. Miller, for  
6 such a clear presentation throughout. I have a  
7 question about case ascertainment, and I was wondering  
8 if you had any data on the percent positives amongst  
9 the cases -- the vaccine recipients and placebos -- and  
10 if there was a difference in the number of parents who  
11 were bringing their kids in for testing between the two  
12 groups and if there was any -- and how often parents  
13 were bringing kids in for testing versus how often they  
14 were positive for COVID.

15 **DR. JACQUELINE MILLER:** Yeah. So, I should  
16 emphasize that parents were really encouraged by the  
17 staff to come in, and I think that was incredibly  
18 important to the investigators in the study. They did  
19 an amazing job, I think, at a difficult time. So, we  
20 did not analyze data based on whether they came in for  
21 or did a home test versus an RT-PCR. What I can show

1 you is the efficacy regardless of symptoms that were  
2 reported so that at least gets at some of the milder  
3 versus more serious symptoms. And so, first I'd like  
4 to share this slide, it's EF45. Could you put the slide  
5 up, please?

6 All right. So these are the results in the  
7 two- to five-year-olds, and as you can see, the case  
8 split is 120 versus 283. And there was a three to one  
9 randomization rate with vaccine effectiveness of 26.9  
10 percent and a lower limit above zero. And I'm going to  
11 have to check on the data for the other age group, and  
12 I'll bring that after the break.

13 **DR. ARNOLD MONTO:** Thank you. Dr. Levy  
14 followed by Dr. Bernstein, and unfortunately at that  
15 point we're going to have to cut off these questions.  
16 You'll have a chance later. Dr. Levy.

17 **DR. OFER LEVY:** Yes. Thank you for the  
18 presentation. If I understood correctly, there were  
19 four cases of febrile seizures, only one of which was  
20 attributed by the investigator as possibly related to  
21 the (audio skip). For that one case, can you please

1 let us know more about the current status of that  
2 infant and how it played out?

3 **DR. JACQUELINE MILLER:** Yeah. So, this infant  
4 was a 17-month-old female. She experienced her seizure  
5 two days after the first dose. Her maximum temperature  
6 was 103.1, and she was noted after that initial fever a  
7 day later to have a maculopapular rash covering her  
8 body. Her temperature actually reached a T-max of 104  
9 on day two, so the seizure happened with the 103  
10 temperature at approximately six hours after her  
11 vaccination.

12 She was treated with ibuprofen and  
13 paracetamol, was observed in the ER and then discharged  
14 to home. She did actually end up having a second  
15 febrile seizure, so that happened about six weeks later  
16 with other symptoms of fever respiratory infection.  
17 And then she actually did go on to stay in the study,  
18 receive the second dose without subsequent seizure.  
19 So, I think that's -- I mean, she continued in the  
20 study throughout; she's not a discontinuation.

21 **DR. OFER LEVY:** And the rash would be an

1 unusual finding after the vaccine, or you view that as  
2 potentially a different (audio skip)?

3 **DR. JACQUELINE MILLER:** I think it's hard to  
4 say. Fever and rash occurs with the vaccine. Fever  
5 and rash also occurs with viral syndromes. So  
6 certainly, something was happening, but she was noted  
7 to have an O2 stat of 97 percent. She was irritable  
8 when she got to the ER but otherwise was okay. And at  
9 the time of the seizure, she was noted to be limp with  
10 no purposeful movements, but the seizure was not  
11 observed by medical professionals.

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

13 **DR. ARNOLD MONTO:** Thank you. Dr. Bernstein.

14 **DR. HENRY BERNSTEIN:** Hi, thank you very much  
15 to you, Dr. Miller, and to your colleagues for very  
16 clear presentations. My question relates to the future  
17 studies that you're doing and your discussion about  
18 whether these are being termed as boosters or whether  
19 this will be a primary series. You're talking about a  
20 third dose, and I think it gets a little bit confusing  
21 to the public and to others about whether -- what a

1 primary series is versus a primary series and a so-  
2 called booster. And I was wondering how you're  
3 determining that or why you're labeling it as a  
4 booster?

5 **DR. JACQUELINE MILLER:** Yeah. Thank you for  
6 that question, Dr. Bernstein. I know this was a topic  
7 that came up yesterday, and so I would really like to  
8 show the RCC curves from our study in order to maybe  
9 discuss that further. But while the team pulls up  
10 those RCC curves -- so it's slide FF4 and FF5, please.  
11 I think the terminology, you can call it a primary  
12 series. You can call it a booster dose. I think all  
13 of us agree that these children are going to need a  
14 third dose at some moment in time.

15 But I think the point I would like to make is  
16 by administering these two doses on the schedule that  
17 we've shown, you begin to see separation of the RCC  
18 curve between the mRNA-1273 group in red and the  
19 placebo group in blue by day 40 in the modified intend  
20 to treat cohort. So, clearly the two-dose series is  
21 initiating protection early on after the schedule

1 administered at day zero and day 28, and certainly  
2 appreciate the points that are being made by the  
3 Committee and are really committed to not confusing the  
4 public.

5           But at this moment, our view is that it's just  
6 critically important to start vaccinating babies so  
7 that they can start benefitting from the same  
8 protection as other age cohorts. And can I also show  
9 FF5, please, just to be complete in the two different  
10 age cohorts?

11           **DR. ARNOLD MONTO:** Okay.

12           **DR. JACQUELINE MILLER:** Thank you.

13           **DR. HENRY BERNSTEIN:** Thank you.

14           **DR. ARNOLD MONTO:** We see it.

15           **DR. JACQUELINE MILLER:** Yup, thank you.

16           **DR. ARNOLD MONTO:** Okay. Did you have  
17 anything further to add about this second slide?

18           **DR. JACQUELINE MILLER:** No, no. Just to show  
19 that, again, by two weeks after the second dose we're  
20 beginning to see separation in those two RCC curves  
21 which, I think, ultimately is the objective of

1 initiating immunization in these children.

2 **DR. ARNOLD MONTO:** Thank you and apologies to  
3 those who we haven't had time to include in our  
4 questions session. We'll have much more time later  
5 after lunch.

6

7 **FDA PRESENTATION: FDA REVIEW OF EFFECTIVENESS AND**  
8 **SAFETY OF MODERNA COVID-19 VACCINE IN INFANTS AND**  
9 **CHILDREN 6 MONTHS THROUGH 5 YEARS OF AGE**

10

11 **DR. ARNOLD MONTO:** Now we go to the FDA  
12 presentation, the review of effectiveness and safety of  
13 Moderna COVID-19 vaccine in infants and children six  
14 months through five years of age. Dr. Wisch.

15 **DR. ROBIN WISCH:** Thank you. Good morning.  
16 I'm Robin Wisch. I'm a medical officer in the Center  
17 for Biologics, Office of Vaccine Research and Review,  
18 Division of Vaccines and Related Products Applications  
19 at FDA. I will be presenting FDA's review of the  
20 effectiveness and safety of the Moderna COVID-19  
21 vaccine in children six months through five years of

1 age submitted under an emergency use authorization  
2 amendment.

3 I'd like to start off by acknowledging the  
4 many contributions of my colleagues in CBER. Here is  
5 the outline of my presentation today. I will start  
6 with regulatory background and then cover the design of  
7 the study submitted to support emergency use  
8 authorization for use of the Moderna COVID-19 vaccine  
9 as a two-dose series in children six months through  
10 five years of age. I will review the part one dose  
11 selection data and the part two immunogenicity,  
12 descriptive efficacy, and safety results. Then I will  
13 provide a summary of the planned pharmacovigilance  
14 activities and conclude with an overall summary of  
15 benefit-risk for the six-month through five years age  
16 group.

17 We'll start with background. The Moderna  
18 COVID-19 vaccine contains nucleoside modified mRNA that  
19 encodes for the full-length spike protein of SARS-CoV-2  
20 encapsulated in lipid particles. It was licensed as  
21 Spikevax for individuals 18 years of age and older on



1 January 31st, 2022. Data included in the EUA request  
2 for children six months through five years of age were  
3 from study P204, a Phase 2-3 study with an initial open  
4 label dose escalation and age de-escalation phase  
5 followed by a randomized observer blind placebo-  
6 controlled phase to evaluate the safety,  
7 reactogenicity, and effectiveness of mRNA-1273 vaccine  
8 in healthy children 6 months through 11 years of age.

9 Today, I will cover the six-month through five  
10 years age groups. This pediatric age group blinded  
11 follow-up was through the data cutoff of February 21st,  
12 2022. Data included in the EUA request for children  
13 six months through five years of age were from study  
14 P204. The phase 2-3 study was an initial open label  
15 dose escalation and age de-escalation phase followed by  
16 a randomized observer blind placebo-controlled phase to  
17 evaluate the safety, reactogenicity, and effectiveness  
18 -- excuse me, I'm so sorry. I'm off slides.

19 This slide provides an overview of the  
20 pediatric studies in age groups from 6 months through  
21 17 years of age. Yesterday, the age groups from 6

1 years through 17 years of age were discussed. Today, I  
2 will focus on the age groups from six months through  
3 five years of age, including approximately 1,700  
4 vaccine recipients in the 6 through 20 months age group  
5 which I will refer to as the infant/toddler group and  
6 3,000 vaccine recipients in the two through five years  
7 age group which I will refer to as the preschool group.

8           In part one of study P204, the open label dose  
9 escalation age group de-escalation phase, enrollment of  
10 participants two through five years of age began with a  
11 50-microgram dose level. Based on the observed rate of  
12 solicited adverse reactions, in particular the rates of  
13 fever after vaccination, the study proceeded to enroll  
14 the remaining part one participants into a lower 25  
15 microgram dose level. Based on the high rate of  
16 solicited adverse reactions in the preschool group at  
17 the 15-microgram dose level, all part one participants  
18 in the 6 through 23 months of age group received a 25  
19 microgram dose.

20           The immunogenicity results of the 25-microgram  
21 dose level and participants in the infant/toddler

1 group, along with the more tolerable reactogenicity  
2 profile at this dose level, supported the selection of  
3 25 micrograms as the dose for advancement into part two  
4 for both age groups.

5 Part two was the randomized placebo-controlled  
6 observer blind evaluation of a selected 25 microgram  
7 dose for each age group with just over 4,000  
8 participants randomized in the preschool group and  
9 approximately 2,300 participants randomized in the  
10 infant/toddler group. Participants were randomized  
11 three to one to receive two doses of 25 micrograms of  
12 mRNA-1273 or placebo given one month apart.

13 These are the study objectives and endpoints.  
14 The safety endpoints included solicited adverse  
15 reactions collected for seven days after each  
16 vaccination in an e-diary and collection of unsolicited  
17 adverse events for 28 days after each dose. Medically  
18 attended adverse events, serious adverse events, and  
19 adverse events with special interest were collected for  
20 the entire study duration. There was also active  
21 monitoring for myocarditis and pericarditis throughout

1 the study as described yesterday.

2           Using an immunobridging approach, GMCs and  
3 seroresponse rates one month post dose two were  
4 compared to young adults 18 through 25 years of age  
5 which demonstrated efficacy from study P301. There  
6 were also descriptive efficacy endpoints analyzed as  
7 secondary endpoints.

8           For the immunobridging analyses, participants  
9 in the per protocol immunogenicity subset were PCR-  
10 negative and/or seronegative for SARS-CoV-2 at  
11 baseline. Immunobridging to the young adult cohort in  
12 study P301 in whom vaccine efficacy was demonstrated  
13 during a time period when the original strain was  
14 predominant was based on comparisons of neutralizing  
15 antibody responses to the ancestral strain which  
16 carries a D614G mutation.

17           The first coprimary immunogenicity endpoint  
18 was GMC ratio of SARS-CoV-2 neutralizing concentrations  
19 in the specified age group either 6 to 23 months of age  
20 or two through five years of age, for those in young  
21 adults 18 through 25 years of age. The success

1 criteria required a lower limit of the two-sided 95  
2 percent confidence interval for the GMC ratio of  
3 greater or equal to 0.67 and a point estimate of the  
4 GMC ratio greater or equal to 0.8.

5           The second co-primary immunogenicity endpoint  
6 was difference in seroresponse rates between  
7 participants of the specified pediatric age group and  
8 the young adult age group where sero- (audio skip) was  
9 defined as greater than or equal to a four-fold rise  
10 from baseline.

11           The immunobridging success criteria required a  
12 lower limit of the 95 percent confidence interval for  
13 the difference in seroresponse rates for each of the  
14 two pediatric age groups minus the young adults age  
15 group of greater or equal to negative ten percent and a  
16 point estimate of difference in seroresponse rates of  
17 greater or equal to negative five percent.

18           For your reference this slide, again, provides  
19 the definitions in CDC defined COVID-19 and COVID-19 as  
20 defined in study P301, the two case definitions  
21 assessed in the descriptive efficacy analyses assessed

1 in study P204. Also, for your reference, as presented  
2 yesterday, these are the most pertinent pediatric  
3 analysis population views for evaluations of  
4 immunogenicity, efficacy, and safety.

5           This slide provides the follow-up time for  
6 study participants calculated from dose two to the  
7 cutoff date of February 21st, 2022. In the  
8 infant/toddler group on the top of the slide, the  
9 median follow-up time from dose two was 68 days. In  
10 the preschool group at the bottom of the slide, the  
11 median blinded follow-up time from dose two was 71  
12 days, and the median follow-up time from dose two,  
13 including both blinded and unblinded follow-up, was 74  
14 days.

15           The demographics and baseline characteristics  
16 of participants in the infant/toddler group are  
17 displayed in this slide. Demographic characteristics  
18 were comparable between the vaccine and placebo groups.  
19 The majority of study participants were white and non-  
20 Hispanic. Most participants in the study were enrolled  
21 in the U.S. Approximately 20 percent of study

1 participants were obese, and approximately six percent  
2 had evidence of prior SARS-CoV-2 infection at baseline.

3           The demographic from baseline characteristics  
4 of participants in the preschool group are displayed  
5 here. Similar to the previous slide, demographic  
6 characteristics were comparable between the vaccine and  
7 placebo groups. The majority of study participants  
8 were white and non-Hispanic, and most participants in  
9 the study were enrolled in the U.S. Approximately 11  
10 percent of the study participants were obese, and  
11 approximately nine percent have evidence of prior SARS-  
12 CoV-2 infection at baseline.

13           I'll now move on to discussing immunogenicity  
14 data. Shown here is the coprimary endpoints of a ratio  
15 of neutralizing antibody GMCs in the infant/toddler  
16 group compared to young adults at four weeks post dose  
17 two. The study met the prespecified success criteria  
18 of lower bound for GMC ratio for greater or equal to  
19 0.67 and point estimate greater or equal to 0.8 with a  
20 lower bound of 1.1 and a point estimate of 1.3.

21           This slide shows the coprimary endpoint of

1 difference in seroresponse rate in the infant/toddler  
2 group compared to young adults. The study met the  
3 prespecified success criteria of lower bounds greater  
4 or equal to negative ten percent and a point estimate  
5 greater or equal to negative five percent with a lower  
6 bound of negative one and a point estimate of 0.7.

7           The GMC ratio and difference in seroresponse  
8 rates across demographic subgroups were consistent  
9 where the results have changed based on the general  
10 study population, though some of these analyses were  
11 limited by small sub-group size. Results for subgroup  
12 analyses at the GMCs and the infant/toddler group by  
13 baseline SARS-CoV-2 status are displayed here. The  
14 small number of participants with positive baseline  
15 SARS-CoV-2 status in the immunogenicity subset had  
16 numerically higher GMCs at day 57 compared to those  
17 negative at baseline, consistent with the  
18 immunogenicity results observed in the 18 through 25  
19 years age group.

20           Now we move to the preschool group. Shown  
21 here is the coprimary end point of a ratio of



1 neutralizing antibody GMCs in the preschool group  
2 compared to the young adults at four weeks post dose  
3 two. The study met the prespecified success criteria  
4 of lower bounds for GMC ratio greater or equal to 0.67  
5 and point estimate of GMC ratio greater or equal to 0.8  
6 with a lower bound of 0.9 and a point estimate of one.

7           This slide shows the coprimary endpoint of  
8 difference in seroresponse rate in the preschool group  
9 compared to young adults. The study met the  
10 prespecified success criteria of lower bound greater or  
11 equal to negative ten percent and a point estimate  
12 greater or equal to negative five percent with a lower  
13 bound of negative 2.7 and a point estimate of negative  
14 0.4. The GMC ratio and difference in seroresponse rate  
15 across demographic subgroups in this age group were  
16 also generally consistent with the results of pain  
17 based on the general study population, though some of  
18 these analyses were also limited by small subgroup  
19 size.

20           Results for subgroup analyses on the GMCs on  
21 the children in the preschool group by baseline SARS-

1 CoV-2 status are displayed there. Again, participants  
2 with positive baseline SARS-CoV-2 status had  
3 numerically higher GMCs at day 57 compared to those  
4 negative at baseline, consistent with immunogenicity  
5 results observed in those 18 to 25 years of age.

6 I'll now move on to the descriptive efficacy  
7 data. Vaccine efficacy was descriptively analyzed as a  
8 secondary endpoint in the study with the data cutoff of  
9 February 21st, 2022, and during a period when the  
10 Omicron variant was the predominant circulating strain  
11 in the U.S. Shown here are vaccine efficacy results  
12 for first occurrence COVID-19 starting 14 days after  
13 dose two based on the CDC NP 301 case definitions.

14 No severe COVID-19 cases were reported in the  
15 study in the infant/toddler group. Among the  
16 approximately six percent of total study participants  
17 with evidence of prior SARS-CoV-2 infection at  
18 baseline, one placebo participant and no vaccine  
19 participants developed COVID-19 starting 14 days after  
20 dose two. Analysis of vaccine efficacy including a  
21 population of participants both with and without

1 evidence of prior SARS-CoV-2 infection or with an  
2 unknown baseline status was similar to the efficacy  
3 results displayed on the slide.

4           These are the vaccine efficacy results for the  
5 first occurrence of COVID-19 starting 14 days after  
6 dose two based on the CDC and P301 case definitions for  
7 the preschool group. In this group there were also no  
8 severe COVID-19 cases reported during the study. Among  
9 the approximately nine percent of total study  
10 participants with evidence of prior SARS-CoV-2  
11 infection at baseline, one placebo participant and six  
12 vaccine participants developed COVID-19 starting 14  
13 days after dose two.

14           Analysis of vaccine efficacy including a  
15 population of participants with and without evidence of  
16 prior SARS-CoV-2 or with an unknown baseline status was  
17 similar to the efficacy results displayed here. I will  
18 now move on to the safety data.

19           Shown here are the frequencies of solicited  
20 local reactions in the infant/toddler group following  
21 each dose. Local adverse reactions generally occurred

1 more frequently and were more severe after dose two  
2 compared to after dose one, although Grade 3 events  
3 were uncommon. The most solicited local adverse  
4 reaction was injection site pain.

5           Solicited local adverse reactions persisting  
6 beyond seven days after any dose were reported more  
7 frequently in the vaccine group than the placebo group,  
8 and the majority events were mild. This table shows  
9 the frequency of solicited systemic reactions after  
10 each dose in the same age group. The frequencies of  
11 systemic reactions were generally comparable across  
12 doses and most events were mild to moderate in  
13 severity. The most common solicited systemic adverse  
14 reaction reported in the vaccine group was irritability  
15 and crying.

16           Grade 4 events were rare and only occurred  
17 with the adverse reaction fever. For all solicited  
18 reactions in this age group, local and systemic, the  
19 majority of events had onset within one to three days  
20 post vaccination and resolved within two to three days.  
21 Most events that persisted beyond the seven-day

1 reporting period were mild. Overall, the frequencies  
2 of solicited reactions were similar among participants  
3 with positive and negative baseline SARS-CoV-2 status,  
4 except for fever which was more common in those who  
5 were baseline seropositive.

6           Now we turn to solicited adverse reactions in  
7 the preschool group. In this age group solicited local  
8 adverse reactions generally occurred more frequently  
9 after dose two compared to after dose one. Adverse  
10 local reactions tended to be more severe after dose two  
11 but Grade 3 events, again, were uncommon. The most  
12 common solicited local adverse reaction was injection  
13 site pain in this age group as well. Solicited local  
14 adverse reactions persisting beyond seven days after  
15 any dose were reported more frequently in the vaccine  
16 group than in the placebo group. The majority of  
17 events were mild.

18           For the two to five years of age group the  
19 solicited systemic reactions terms differed for  
20 participants from 24 through 36 months of age and from  
21 37 months through 5 years of age, as shown in the

1 previous presentation. This slide shows the systemic  
2 reactions in the 24 through 36 months of age sub  
3 cohort. Overall, the frequency of solicited systemic  
4 adverse reactions were comparable across doses with the  
5 exception of fever which was reported more frequently  
6 after dose two.

7           The most common solicited systemic adverse  
8 reaction reported in the vaccine group was irritability  
9 and crying. Most events were mild to moderate in  
10 severity, and Grade 4 events were rate and only  
11 occurred with the adverse reaction fever.

12           The next two slides show the systemic  
13 reactions in the 37-month through 5 years of age sub  
14 cohort. Solicited systemic adverse reactions generally  
15 occurred more frequently and were more severe after  
16 dose two compared to after dose one although most  
17 events were mild to moderate in severity. The most  
18 common solicited systemic adverse reaction reported in  
19 the vaccine group was fatigue. And as with the other  
20 age groups, Grade 4 events were rare and only occurred  
21 with the adverse reaction fever.

1           This slide shows the remaining solicited  
2 systemic reactions in the 37-month through 5 years of  
3 age sub cohort. For the entire two through five years  
4 age group, most local and systemic adverse reactions  
5 had onset one to two days post vaccination and resolved  
6 within two days after onset. The majority of events  
7 that persisted beyond the seven-day reporting period  
8 were mild. As in the infant/toddler age group,  
9 overall, the frequencies of solicited reactions were  
10 similar among participants with positive and negative  
11 baseline SARS-CoV-2 status, except for fever, which was  
12 more common in those who were baseline seropositive.

13           This table presents the frequencies of  
14 unsolicited adverse events in the infant/toddler group.  
15 Overall, rates of unsolicited adverse reactions were  
16 similar across groups. Unsolicited events reported by  
17 at least one percent of participants in the vaccine  
18 group, and by a higher proportion of the vaccine group  
19 compared to the placebo group, included injection site  
20 reactions and some common childhood illness such as  
21 acute otitis media and croup.

1           The most commonly reported unsolicited AEs  
2 among vaccine recipients were upper respiratory  
3 infection, irritability, fever, and seizing. As  
4 discussed in yesterday's presentation, symptoms of  
5 myocarditis and pericarditis were solicited for the  
6 duration of the study through scripted safety calls  
7 conducted at seven days after each dose and every four  
8 weeks thereafter. This resulted in enhanced reporting  
9 frequency of associated symptoms in study P204 compared  
10 to those reported in earlier studies in adults and  
11 adolescents.

12           The same search strategy, as described  
13 yesterday, was also used for evaluation of the safety  
14 data set for participants six months through five years  
15 of age. In the infant/toddler group, neither the  
16 captured event dyspnea nor the events of irritability  
17 and vomiting shown on the slide were identified in the  
18 additional analyses met the CDC criteria for probable  
19 or confirmed myocarditis or pericarditis.

20           While some respiratory tract related  
21 infections were reported with greater frequency in the



1 infant/toddler vaccine group than in the placebo group,  
2 analyses including all respiratory tract related  
3 infections preferred terms with or without COVID-19  
4 showed generally comparable rates between the two  
5 groups.

6           As shown in the slide, events of croup, RSV,  
7 and pneumonia were reported with greater frequency in  
8 the vaccine group compared to the placebo group. But  
9 there was no pattern concerning time to onset or dose  
10 number for these events, and there is not a clear  
11 biological mechanism that would explain a causal  
12 association for certain respiratory infections but not  
13 others.

14           Overall, the frequency and clinical course for  
15 these events did not appear unusual given the age group  
16 of the study population and the season -- fall through  
17 winter -- during which the study took place. There was  
18 also an imbalance in lymphadenopathy-related events in  
19 the vaccine group compared to the placebo group, which  
20 were reported by 1.5 percent of vaccine recipients and  
21 0.2 percent of placebo recipients. This imbalance is

1 consistent with the imbalance observed for solicited  
2 events with axillary or groin swelling and tenderness.  
3 There were no reported events of anaphylaxis related to  
4 study vaccine.

5           This table presents the frequencies of  
6 unsolicited adverse events in the preschool group.  
7 Overall, rates of unsolicited adverse events were  
8 similar across groups. Unsolicited events reported by  
9 at least one percent of participants in the preschool  
10 vaccine group and by a higher proportion compared to  
11 the placebo group included injection site erythema.  
12 The most commonly reported unsolicited AEs among  
13 vaccine recipients were upper respiratory tract  
14 infection, rhinorrhea, and cough.

15           Regarding cardiac events in the preschool  
16 group, none of the events captured met CDC criteria for  
17 probable or confirmed myocarditis or pericarditis and  
18 no other events were identified in the additional  
19 analyses. One participant underwent evaluation by a  
20 cardiologist: a four-year-old male participant with  
21 chest pain five days after dose two that resolved

1 within 30 minutes. That evaluation included a physical  
2 exam, EKG, and troponin, which were all reported to be  
3 normal. The majority of events in this study were non-  
4 specific in nature, and many were associated with  
5 concurrent systems including respiratory tract  
6 infections or allergies.

7           In this age group, events of pneumonia and RSV  
8 infection were reported with greater frequency in the  
9 vaccine group than in the placebo group. Again, there  
10 was no pattern concerning time to onset or dose number  
11 for these events, and analyses including all  
12 respiratory tract related infection preferred terms  
13 with and without COVID-19 showed generally comparable  
14 rates between the two groups. Overall, the frequency  
15 and clinical course for these events did not appear  
16 unusual given the age group and the study population  
17 and the season during which the study took place, and,  
18 again, there's not a clear biological mechanism that  
19 would explain a causal association for certain  
20 respiratory infections but not others.

21           Events of abdominal pain occurred in less than

1 one percent of participants in each group but were  
2 reported more frequently in the vaccine group, 0.7  
3 percent of participants compared to the placebo group  
4 0.4 percent of participants. The three events assessed  
5 as related, two in the vaccine group and one in the  
6 placebo group, occurred within two days of vaccination  
7 and, as discussed yesterday, were likely to be  
8 manifestations of systemic reactogenicity.

9           There was also an imbalance in  
10 lymphadenopathy-related events which are reported by  
11 0.9 percent of vaccine recipients and less than 0.1  
12 percent of placebo recipients. This imbalance is  
13 consistent, again, with the balance of sero solicited  
14 events with axillary or groin swelling and tenderness.  
15 There were no reported events of anaphylaxis related to  
16 study vaccine.

17           In the infant/toddler group, there were no  
18 reported deaths and overall, there were few reported  
19 serious adverse events or SAEs: 0.9 percent in the  
20 vaccine group and 0.2 percent in the placebo group.  
21 FDA assessed all SAEs in this age cohort as unrelated

1 with the exception of the events previously discussed  
2 as pyrexia and febrile convulsion that occurred within  
3 two days of dose one in a one-year-old female  
4 participant, followed by the occurrence of a  
5 maculopapular rash that was considered possibly related  
6 to study vaccine with a possible alternate etiology of  
7 a viral illness.

8           For the two to five years of age group, there  
9 were also no deaths reported, and overall, there were  
10 few reported SAEs: 0.3 percent in the vaccine group and  
11 0.2 percent in the placebo group. Most SAEs were  
12 consistent with events typical in this age group and  
13 for the season during which the study took place. FDA  
14 agreed with the investigator assessments that none of  
15 the reported SAEs were considered related to study  
16 vaccine.

17           I'm now going to move on to pharmacovigilance.  
18 The sponsors submitted a pharmacovigilance plan to  
19 monitor safety concerns that could be associated with  
20 the Moderna COVID-19 vaccine. They identified  
21 anaphylaxis, myocarditis, and pericarditis as important

1 identified risks and vaccine associated enhanced  
2 disease including vaccine associated enhanced  
3 respiratory disease as important potential risk.

4 Areas the sponsor identified as missing  
5 information included use in pregnancy and lactation,  
6 vaccine effectiveness, long-term safety, interaction  
7 with other vaccines, use in immunocompromised or frail  
8 patients, or patients with autoimmune inflammatory  
9 disorders and use in pediatric individuals less than  
10 six months of age.

11 Pharmacovigilance activities under the EUA  
12 include adverse event reporting which may come from  
13 vaccine recipients, vaccination providers, the sponsor,  
14 or the CDC V-safe Program. So, the sponsor and vaccine  
15 providers administering Moderna COVID-19 vaccine must  
16 report the following information to VAERS: serious  
17 adverse events irrespective of attribution to  
18 vaccination, cases of multi-symptom inflammatory  
19 syndrome, and cases of COVID-19 that result in  
20 hospitalization or death.

21 Additionally, the sponsor submits reports of

1 myocarditis and pericarditis as 15-day reports to  
2 VAERS. The sponsor will also conduct periodic  
3 aggregate review of safety data, that I will discuss in  
4 an upcoming slide, and submit periodic safety reports  
5 at monthly intervals for FDA review. Furthermore, the  
6 sponsor has planned surveillance studies that are  
7 summarized on the next slide.

8           There are four post authorization safety  
9 studies of myocarditis and pericarditis shown here,  
10 including subclinical myocarditis, and one post  
11 authorization vaccine effectiveness study that includes  
12 individuals six months through 17 years of age. I've  
13 already presented adverse event reporting under EUA may  
14 come from vaccine recipients, vaccination providers, or  
15 the sponsor. Reports from vaccine recipients are  
16 voluntary, while adverse event reporting by vaccination  
17 providers and the sponsor is mandatory.

18           Periodic aggregate safety reports are required  
19 to contain a narrative summary and analysis of adverse  
20 events submitted during the reporting interval,  
21 including interval and cumulative counts by age groups,

1 special population, and adverse events of special  
2 interest, a narrative summary and analysis of vaccine  
3 administration errors, whether or not associated with  
4 an adverse event that were identified since the last  
5 interval, newly identified safety concerns in the  
6 interval, and actions taken since the last report due  
7 to adverse experiences.

8           Both FDA and CDC will take a collaborative and  
9 complimentary approach on reviewing adverse events. In  
10 the initial stage of post authorization surveillance,  
11 FDA will individually review all serious adverse events  
12 on a daily basis. FDA will also examine other sources  
13 for adverse events, such as the literature, and will  
14 perform data mining to determine if adverse events are  
15 disproportionately reported for the candidate vaccine  
16 compared to all other vaccines in VAERS. Any potential  
17 safety signals identified will be investigated.

18           And now for a summary of benefits and risks.  
19 This slide presents a summary of benefits and risks of  
20 the Moderna COVID-19 vaccine when administered as a  
21 two-dose series, 25 micrograms each dose, in children



1 six months through five years of age. Known and  
2 potential benefits include prevention of symptomatic  
3 COVID-19 based on immunobridging to young adults as  
4 well as supported evidence of vaccine efficacy against  
5 symptomatic COVID-19 with expected greater  
6 effectiveness against more severe disease.

7           Effectiveness against emerging variants and  
8 duration of protection are not yet known. Known and  
9 potential risks include symptoms of reactogenicity,  
10 potential myocarditis/pericarditis, and  
11 hypersensitivity reactions. Uncertainties remain  
12 regarding adverse reactions that are uncommon or  
13 require longer follow-up to be detected.

14           The voting question for today regarding the  
15 Moderna COVID-19 vaccine for use in children six months  
16 through five years of age is following: "Based on the  
17 totality of scientific evidence available, do the  
18 benefits of the Moderna COVID-19 vaccine when  
19 administered as a two-dose series, 25 micrograms each  
20 dose, outweigh its risks for use in children six months  
21 through five years of age?" And that brings me to the

1 end of my presentation. Thank you.

2

3

### Q&A SESSION

4

5 **DR. ARNOLD MONTO:** Thank you, Dr. Wisch, and  
6 you have given us a fair amount of time for you to be  
7 questioned because of your succinct presentation. Dr.  
8 Levy, is that you raising your hand?

9 **DR. OFER LEVY:** Hi. Thanks for the excellent  
10 presentation. I had a question about what appeared to  
11 be an imbalance with respect to RSV infections and  
12 pneumonia, and my question to you is -- I mean, a  
13 priori, we might not think that that's possible. On  
14 the other hand vaccines can have target effects,  
15 effects on innate memory, so who knows? But, just  
16 looking at the data is that a statistically significant  
17 higher RSV and pneumonia signal in the vaccine group?  
18 And then the list on the far right, if you could pull  
19 up that slide.

20 It was a little bit (audio skip) to me because  
21 at the same time it said an overall analysis of

1 respiratory infections did not show a difference. So,  
2 can you talk us through that and let us know what you  
3 think?

4 **DR. ROBIN WISCH:** Sure, let me go through my  
5 notes. I don't have the slides to pull up individually  
6 right this second. So, when we did the analysis  
7 looking at all respiratory tract infections, for third  
8 terms for the entire study, in the 6-to-23-month age  
9 group we saw basically the same number of events in  
10 each group, so, 21.5 percent in the vaccine group  
11 versus 21.4 percent in the placebo group.

12 In the two-to-five-year age group we saw a  
13 similar finding where the rate of all respiratory tract  
14 infection preferred terms were similar between the two  
15 groups around 17 percent. That's for the entire study  
16 period. When you look at individual preferred terms  
17 under different types of respiratory tract infections,  
18 there were some imbalances. The ones that were pointed  
19 out were imbalances where we saw more in the vaccine  
20 group compared to the placebo group, but there were  
21 also other events that were seen more frequently in the

1 placebo recipients as compared to the vaccine  
2 recipients.

3 I think, overall, our assessment was to think  
4 that these events were in a low enough percentage of  
5 participants and were common events in this age group  
6 and at the season that we did not consider any of these  
7 signals that were picked up. Don't know if any of my  
8 colleagues or Moderna would like to chime in and add to  
9 that.

10 **DR. ARNOLD MONTO:** Just your colleagues right  
11 now. Let's not confuse that.

12 **DR. JACQUELINE MILLER:** I'd be happy to add a  
13 bit to that. So, yes, respiratory infections are also  
14 something that we looked into as well with the  
15 imbalances that were noted/established. And you had a  
16 question about statistically significant, so I will say  
17 that because of the large number of comparisons of  
18 discreet (inaudible) terms, these analyses are  
19 descriptive. So, there's no adjustment made for  
20 multiplicity in all of the analyses in the two age  
21 groups.

1           The other thing I would point out is that  
2 there was an imbalance in the other direction for  
3 COVID-19 infections, and that really lead to the rates  
4 of upper respiratory tract infections actually being  
5 evenly distributed between the two groups. So, in  
6 children who were two to five years of age, the rate  
7 was 9.2 percent in the placebo group, 8.1 percent in  
8 the mRNA-1273 group. And in the 6- to 23-month-olds in  
9 the placebo group the rate was 12.2 percent. The rate  
10 with mRNA-1273 was 10.3 percent.

11           **DR. ARNOLD MONTO:** Dr. Fink.

12           **DR. DORAN FINK:** Thank you. I was going to  
13 make some of the same comments about the statistical  
14 considerations for these numerous for third term  
15 analyses but that being said, I do think that if the  
16 vaccine were to be authorized for use in this age  
17 group, clearly, we would want to continue looking at  
18 these types of events in post authorization  
19 surveillance. We're not highly concerned about a  
20 couple of imbalances in one direction in specific  
21 events of infections that are common in this age group.

1 We did not see increased severity of these types of  
2 infections in the vaccine group compared to the placebo  
3 group.

4 But it is something that I think bears keeping  
5 an eye on in the post authorization safety  
6 surveillance. Thank you.

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

8 **DR. ARNOLD MONTO:** Thank you all. Dr.  
9 Meissner, followed by Dr. Marasco.

10 **DR. CODY MEISSNER:** Thank you, Dr. Monto, and  
11 Ofer I guess got his hand up before I did because I had  
12 a question similar, that is both slide 37 and slide 40  
13 note that the listed diagnoses are higher in the mRNA-  
14 1273 group than they are in the placebo, but then the  
15 comment they seem to say the opposite. So, that's a  
16 little bit confusing. And I appreciate your  
17 explanation in clarifying that. And the reason that  
18 it's important, I think, is because the effect of  
19 COVID-19 or the SARS-CoV-2 pandemic on other  
20 respiratory viruses such as RSV is kind of interesting.

21 The disappearance of the disease may not have

1 all been due to non-pharmacologic intervention, so it  
2 may have been some viral interactions that reduced  
3 other viruses such as RSV and influenza. So, it is an  
4 interesting issue as to what's going on here but thank  
5 you for the clarification.

6 **DR. ARNOLD MONTO:** Dr. Marasco, followed by  
7 Dr. Chatterjee.

8 **DR. WAYNE MARASCO:** Hi, yeah, thank you very  
9 much, Dr. Monto, and I'd like to address a couple of  
10 questions to the Committee -- I mean, to the FDA, and  
11 I'm happy to have Moderna's input into this. So, the  
12 viral efficacy/vaccine efficacy against Omicron is  
13 lower than one would expect with Wuhan, and this is  
14 their first antigenic exposure. And I don't want to be  
15 an immunologist aficionado here, but it's pretty clear  
16 from influenza data, for example, that the first virus  
17 that you get exposed to is going to bias your immune  
18 response for the rest of your life. It's called immune  
19 imprinting.

20 So, when we're vaccinating with an ancestral  
21 strain or we're testing against a dosage strain,

1 there's an expected loss of efficacy, and this is  
2 because this is really antigenic shift, not drift, like  
3 we see in seasonal influenza. This is more like what  
4 happened in pandemic 2009.

5           So, the real question is are we gathering data  
6 on this? And my concern is if we just do this blindly  
7 -- and maybe this is to Moderna -- if we're just  
8 looking at titers, really are we going to understand  
9 the breadth of the repertoire that is being developed  
10 and whether we're biasing our protection against one  
11 lineage against another? And that's really the essence  
12 of my question. It's a matter of in 2022 the type of  
13 data that we're collecting for these studies. This is  
14 really more than just serologic to be able to get to  
15 the heart of the problem and the heart of what we're  
16 doing. Thank you.

17           **DR. ARNOLD MONTO:** Thank you. You've asked a  
18 very broad question that needs long-term follow-up in  
19 general, not just in terms of this product. Dr. Wisch.

20           **DR. ROBIN WISCH:** Thank you for that --

21           **DR. JACQUELINE MILLER:** Sorry, please go



1 ahead. I apologize.

2 **DR. ROBIN WISCH:** No, no, no. No, absolutely,  
3 go ahead.

4 **DR. JACQUELINE MILLER:** I was just going to  
5 comment that I think it's a really excellent question,  
6 and I think it's one that will be evaluated over time  
7 as Dr. Monto referred to. I wanted to mention that we  
8 will see the effectiveness or efficacy -- field  
9 efficacy of mRNA-1273 against Omicron in this study we  
10 are conducting actually in partnership with South  
11 African Research Council in South Africa. So really  
12 where the Omicron variant first emerged, and actually  
13 now we're boosting healthcare workers with mRNA-1273  
14 during the BA.4/BA.5 period.

15 And I think that those long-term effectiveness  
16 studies are really the best way to understand how a  
17 vaccine formulation is going to perform against  
18 emerging variants of concern. But given that at a  
19 certain moment in time what we're left with is being  
20 able to look at immune responses, I'd like to show, if  
21 I could, slide BF-12 which reflects some of the data

1 that we've been generating with respect to other  
2 variants in the youngest age group.

3           So, we've been looking actually throughout at  
4 neutralizing titers in our older subjects. At the  
5 moment, our Omicron neutralization is primarily being  
6 performed against the bivalent vaccines that this  
7 Committee will discuss in two weeks. But what we do  
8 have are some binding data with respect to the various  
9 variants, and I see the computer's thinking about it.  
10 There we go.

11           So, this this a complicated slide, but what  
12 you see in the four different rows are the MS (audio  
13 skip) -- Multiplex System binding antibody -- to the  
14 four key variants. So first starting with the  
15 ancestral strain (audio skip) in blue the Delta  
16 variant, and then in purple the Omicron variant. And  
17 then moving left to right what you see --

18           **DR. ARNOLD MONTTO:** Okay. Look, why don't you  
19 wait until we see it. We're not seeing it yet.

20           **DR. JACQUELINE MILLER:** Oh, I apologize. I  
21 apologize, I saw it. I'm able to see it so I thought

1 you were as well.

2 **DR. ARNOLD MONTO:** No, I'm -- we're not.

3 **DR. WAYNE MARASCO:** I have it.

4 **MR. MICHAEL KAWCZYNSKI:** We can see it,  
5 Arnold.

6 **DR. ARNOLD MONTO:** Oh, you see it? Go ahead.

7 **UNIDENTIFIED MALE 1:** Yeah, Arnold, some of us  
8 can see it.

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

10 **DR. JACQUELINE MILLER:** Okay, my -- not able.  
11 Okay. Good.

12 **DR. WAYNE MARASCO:** Dr. Miller, just to  
13 clarify, this is with the Omicron vaccine? Just to  
14 clarify.

15 **DR. JACQUELINE MILLER:** No, no. This is with  
16 mRNA-1273. These are samples of studies that you are  
17 viewing today. And so, we have tested children or sera  
18 from children for all of the different variants because  
19 as you mentioned while Omicron is our particular  
20 consideration today I think that it's likely that this  
21 virus continues to evolve over time.

1           So, you see different variants in different  
2 colors. The Omicron is in purple at the bottom of the  
3 slide. And the dotted line in each of the graphs  
4 represents the limit of detection of the assay. And  
5 so, in all cases, what we're seeing is an increase  
6 against the variants of concern.

7           I think the question around what is the right  
8 way to prime individuals is a very good one, and it's  
9 why we are going to start a primary vaccination study  
10 with the bivalent to see if the primary series looks  
11 different in terms of antibodies that are generated  
12 versus the original mRNA-1273 vaccine.

13           **DR. ARNOLD MONTO:** Thank you. And I assume  
14 you have some neutralization assays on some of them at  
15 least as well --

16           **DR. JACQUELINE MILLER:** Yeah, so we --

17           **DR. ARNOLD MONTO:** I don't want you to present  
18 them. I just -- you're following up. Okay, Dr. Wisch.  
19 Do you have anything in addition to add?

20           **DR. ROBIN WISCH:** Not beyond that. Thank you.

21           **DR. ARNOLD MONTO:** Okay. Dr. Chatterjee,

1 followed by Dr. Kim.

2           **DR. ARCHANA CHATTERJEE:** Thank you, Dr. Monto.  
3 I have two questions, and I have the suspicion that the  
4 sponsor might need to weigh in. But the first one is  
5 on slide 29 on Dr. Wisch's presentation, and this was  
6 with regard to the local reactions in the younger  
7 cohort. I was wondering how pain was determined in  
8 preverbal children. Was that inferred in some way, or  
9 how would they know if a six-month-old had pain?

10           **DR. ROBIN WISCH:** Well, the parents and  
11 caregivers of the children are provided e-diaries. I  
12 would have to, again, defer to the sponsor to see if  
13 they can give a more precise explanation of how parents  
14 assessed that.

15           **DR. ARCHANA CHATTERJEE:** Okay.

16           **DR. ROBIN WISCH:** I would think it would be,  
17 yeah, through --

18           **DR. JACQUELINE MILLER:** Yes, so, just to make  
19 sure I understood the question, the question is how we  
20 understand how pain is measured in six-month-old  
21 children?

1           **DR. ARCHANA CHATTERJEE:** In preverbal  
2 children, mm-hmm.

3           **DR. JACQUELINE MILLER:** Yeah, because you're  
4 absolutely right. Obviously, they can't complain about  
5 pain, but it has to do with the parent's assessment of  
6 the level of discomfort, for example, when the child's  
7 arm or leg is moved. Are they crying? So to maybe  
8 give you the different grades, Grade 1(audio skip) mild  
9 discomfort touch where maybe there's a reaction when  
10 things are touched. Moving to Grade 2, that they're  
11 crying when their limb is moved, and significant pain  
12 at rest presenting with just normally with what the  
13 child's doing is Grade 3.

14           **DR. ARCHANA CHATTERJEE:** Thank you.

15           **DR. ARNOLD MONTO:** Thank you. Dr. Kim,  
16 followed by Dr. Hildreth.

17           **DR. DAVID KIM:** Thank you very much, Dr.  
18 Monto, and that was a terrific presentation, Dr. Wisch.  
19 I have a question on your slide number 26 and 27. And  
20 I think this question would also apply to our Moderna  
21 colleagues. The efficacy study for the infants and

1 toddlers was 50 percent using the CDC definition, and  
2 using the study definition from Moderna 301 was 31  
3 percent. And on the following slide, 27, looking at  
4 these things for the preschool age group we're talking  
5 36 percent and 46 percent respectively for CDC and  
6 study 301.

7           Now, there's an overlap between these two  
8 efficacy results. But it's interesting that the CDC  
9 definition and the study 301 definition basically are  
10 inversely related between the infant/toddler group and  
11 the preschool group. And having looked at the data  
12 much more closely, to what, if any, attributes have you  
13 seen in the findings that might explain this opposite  
14 direction of vaccine efficacy findings between these  
15 two age groups? And perhaps our Moderna colleagues can  
16 add to that.

17           **DR. ARNOLD MONTO:** Other than small numbers  
18 and chance. Please, Dr. Wisch.

19           **DR. ROBIN WISCH:** Sure. Thank you for that.  
20 So, yes, if you look at the two (audio skip) Dr. Monto  
21 (audio skip) is where I'm thinking as well. You can

1 see the P301 definition is a more stringent definition  
2 of COVID-19 disease, and so the numbers are smaller for  
3 both age groups for those diagnosed with P301  
4 definition as compared to the CDC definition. If you  
5 look at the vaccine efficacy for the younger 6 to 23  
6 months that the confidence interval is much wider and  
7 crosses zero, so it's hard to interpret the reliability  
8 of that vaccine efficacy for that population with that  
9 definition.

10 But we do see the trends of that. Of course  
11 there were fewer cases with the P301 definition, and  
12 it's just it's difficult to tell because of the small  
13 case numbers using that more stringent definition in  
14 that population. But I defer to Moderna if they want  
15 to add to that. Thank you.

16 **DR. ARNOLD MONTO:** Let's go ahead so we can  
17 get to the bottom of our list of questioners. Dr.  
18 Hildreth, followed by Dr. Fuller, who will have the  
19 last question.

20 **DR. JAMES HILDRETH:** Thank you, Dr. Monto, and  
21 thank you, Dr. Wisch and Dr. Vinals, for your great



1 presentations. My question is related to just the  
2 prior question that was asked. The data shows that the  
3 efficacy for the toddlers and the infants have much  
4 lower efficacy than the 6- to 11-year-olds, but the  
5 data you've shown us show that they all have about the  
6 same geometric titers for neutralization. So, is there  
7 a disconnect there that you can help me understand?

8           The neutralizing antibody titers are clearly  
9 the same, but the efficacy is not. So, I just would  
10 like you to help me understand that.

11           **DR. ROBIN WISCH:** Thank you for that question.  
12 The one thing I can say is that in the time period when  
13 the infants and toddlers or the younger pediatric  
14 population were being evaluated was during Omicron,  
15 whereas I believe the 6- to 11-year-old age group was  
16 evaluated during the time of the Delta surge. So,  
17 there is that difference in time period as far as  
18 efficacy of the vaccine against the various variants.  
19 I don't know if anybody else--

20           **DR. JAMES HILDRETH:** During the prototype  
21 virus neutralization assay, did you do a side-by-side

1 comparison of Omicron and Delta to confirm that?

2 **DR. ROBIN WISCH:** I would have to defer to  
3 Moderna for that.

4 **DR. ARNOLD MONTTO:** A very quick response.  
5 We're going to have time to go into this in detail  
6 later on. So please quick response because I'd like to  
7 get to Dr. Fuller.

8 **DR. JACQUELINE MILLER:** Sure. Sure. So,  
9 great question and (audio skip) mentioned we're in the  
10 process of generating the neutralization data against  
11 Omicron and the other variants with respect to the  
12 youngest kids. We did review a slide yesterday, BF-11  
13 in the older children, just to show you how it looked  
14 across age groups versus the ancestral strains. So, I  
15 can have the slide up, please? BF-11.

16 **DR. ARNOLD MONTTO:** Okay. Let's do it quickly.

17 **DR. JACQUELINE MILLER:** Just real quick, I  
18 promise.

19 **DR. ARNOLD MONTTO:** Okay.

20 **DR. JACQUELINE MILLER:** Just to answer to Dr.  
21 Hildreth's question, which is are we looking into

1 Omicron. We continue to look at neutralization titers  
2 across age groups and also as new variants emerge.

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

4 **DR. JACQUELINE MILLER:** Thank you.

5 **DR. ARNOLD MONTA:** Thank you. Dr. Fuller,  
6 final question before the break.

7 **DR. OVETA FULLER:** Yes, so you mentioned that  
8 you looked at obesity as an underlying factor. Did you  
9 look at things between the two- and six-year-olds like  
10 sickle cell or asthma that might be underlying  
11 conditions and the results of the vaccine in both?

12 **DR. ROBIN WISCH:** Yes, there were. The  
13 underlying comorbidities that were looked at including  
14 obesity were also chronic respiratory conditions  
15 including asthma and cardiac conditions. The numbers  
16 of children in each of those subgroups were very small,  
17 so it was hard to come to conclusions about differences  
18 given the very small numbers.

19 **DR. OVETA FULLER:** But things like sickle cell  
20 or juvenile diabetes that can be diagnosed early, they  
21 did not look at?

1           **DR. ROBIN WISCH:** No, I'm sorry. I apologize.  
2 Diabetes was included. I don't recall seeing sickle  
3 cell disease in those baseline comorbidities. I'm not  
4 sure of that. I can pull up -- I know in the briefing  
5 document I have -- there's a table of baseline  
6 comorbidities, and I will show you that. I can't  
7 recall -- if there were cases of diabetes, they were  
8 very, very small. They wouldn't be on these slides.  
9 It would be in the briefing document. I can find that  
10 information and get back to you.

11           **DR. OVETA FULLER:** Thank you.

12           **DR. ROBIN WISCH:** Sure.

13           **DR. ARNOLD MONTTO:** Okay. Thank you all. It's  
14 time for the break, and we will resume at 11:00  
15 Eastern, which is about 13 minutes from now. 11:00  
16 Eastern (inaudible).

17           **MR. MICHAEL KAWCZYNSKI:** All right. Thank  
18 you, Arnold. And yes, please take us to break.

19

20

[BREAK]

21

1 **SPONSOR PFIZER PRESENTATION: BNT162b2 (PFIZER-BIONTECH**  
2 **COVID-19 VACCINE) - REQUEST FOR EMERGENCY USE**  
3 **AUTHORIZATION FOR USE IN INFANTS AND CHILDREN 6 MONTHS**  
4 **THROUGH 4 YEARS OF AGE**

5  
6 **MR. MICHAEL KAWCZYNSKI:** All right. Welcome  
7 back from that break. We'll keep the ball rolling  
8 here, and I'm going to hand it back to our Chair, Dr.  
9 Monto.

10 **DR. ARNOLD MONTO:** Thank you, Mike. We are  
11 now switching to the BNT162B2 Pfizer-BioNTech COVID-19  
12 vaccine. The request is for emergency use  
13 authorization for use in infants and children 6 months  
14 to 4 years of age. We're going to hear from Dr.  
15 Gruber, the Senior Vice President at Pfizer. Take it  
16 away, Bill.

17 **DR. WILLIAM GRUBER:** Good morning. On behalf  
18 of Pfizer and BioNTech, it is my pleasure to share data  
19 supporting the BNT162b2 request for emergency use  
20 authorization in individuals 6 months through 4 years  
21 of age. My name is Bill Gruber, and I head the vaccine

1 clinical research and development group at Pfizer.  
2 Today's agenda covers the topics shown here with  
3 specific attention to coverage of the clinical safety,  
4 immunogenicity, and efficacy data along with the  
5 assessment of benefit/risk.

6           There is a clear unmet medical need in  
7 children 6 months to less than 5 years of age for a  
8 safe and effective COVID-19 vaccine. You've heard this  
9 discussed at length over the past two days. I'm going  
10 to summarize in a single slide. Less than 5-year-olds  
11 are currently the only pediatric group for whom vaccine  
12 is not available.

13           Severe COVID-19 occurs in children less than 5  
14 years of age, and as of May 2022, there were over  
15 45,000 hospitalizations with roughly half of these  
16 hospitalizations due to omicron with a high number of  
17 ICU admissions and deaths. The burden is comparable to  
18 influenza, as you heard from Mr. Marks, for which  
19 children are routinely immunized. Severe COVID-19  
20 outcomes are unpredictable and can occur in healthy  
21 children. Sixty-four percent of hospitalizations in

1 children less than 5 years of age occur in those  
2 without comorbidities.

3           COVID-19 can cause additional long-term  
4 sequelae in children. Three to 6 percent of children  
5 report continued symptoms for greater than 12 weeks.  
6 Importantly, the pandemic adversely impacts development  
7 and psychosocial well-being, whether or not a child is  
8 isolated because of COVID-19 infection, because of the  
9 social distancing and other requirements that limit in-  
10 person schooling and other social interactions. The  
11 need for three mRNA vaccine doses to protect against  
12 omicron related COVID-19 is clear.

13           Omicron is significantly more transmissible  
14 than prior variants. In adult populations, two doses  
15 of the current mRNA COVID-19 vaccines do not adequately  
16 neutralize omicron. A third dose increases breadth of  
17 coverage and can neutralize omicron more effectively.  
18 Real-world data showed that a third dose significantly  
19 improves protection against omicron related symptomatic  
20 disease and severe illness.

21           Given the high prevalence of omicron and the

1 emerging evidence that three doses of mRNA vaccine are  
2 needed against omicron, we studied three doses of  
3 BNT162b2 in children 6 months through less than 5 years  
4 of age. Pfizer-BioNTech is seeking emergency use  
5 authorization of the 3 microgram dose level of the  
6 vaccine in children 6 months through 4 years of age.  
7 The proposed indication is for active immunization to  
8 prevent COVID-19 caused by SARS Coronavirus 2 in  
9 individuals 6 months through 4 years of age.

10           The vaccine would be administered  
11 intramuscularly as three doses of 0.2 milliliters each.  
12 Two doses would be administered three weeks apart,  
13 followed by a third dose at least eight weeks after the  
14 second dose. The 3-microgram dose was chosen as it had  
15 the right balance between immune response and a  
16 satisfactory reactogenicity profile. I'm now going to  
17 share with you the clinical data that supports  
18 emergency use authorization.

19           Here is the study overview information, which  
20 should be familiar to you but now focuses on children 6  
21 months to less than 5 years of age. To select the



1 appropriate pediatric dose levels for infants,  
2 toddlers, and very young children, we carefully  
3 evaluated multiple dose levels in phase 1. We began in  
4 5- to 11-year-olds before progressing to 64  
5 participants in the 6-month through 4-year-old age  
6 group to achieve the right balance and safety profile  
7 and immune response.

8           These pediatric groups represent a more  
9 vulnerable population. So, it is particularly  
10 important to minimize reactions, including fever, while  
11 achieving an immune response likely to provide  
12 protection against COVID-19. We were, therefore, very  
13 deliberate in dose ranging. We found that nearly 19  
14 percent of 2 to less than 5-year-olds who received the  
15 10-microgram dose developed fevers after the first and  
16 second dose and one-third of those fevers were severe.

17           We were concerned that the frequency and  
18 severity of fevers seen after the 10-microgram dose  
19 would likely further increase in the infant and toddler  
20 group of 6 month to less than two years and could be  
21 poorly accepted by parents, reducing adherence to the

1 primary three-dose series. In contrast, the 3-  
2 microgram dose had a much better tolerability profile  
3 combined with comparable immune responses to the SARS  
4 Coronavirus 2 reference strain. Therefore, the 3-  
5 microgram dose level was advanced into phase 2/3 in the  
6 countries shown.

7           To infer efficacy in the pediatric population  
8 in the pivotal study, immunologic noninferiority to a  
9 16- to 25-year-old population for whom efficacy was  
10 established was assessed in addition to safety to  
11 satisfy emergency use authorization immune response  
12 criteria. Although not required for EUA approval,  
13 COVID-19 surveillance was conducted permitting an early  
14 evaluation of vaccine efficacy. This study schema  
15 should also be familiar to you.

16           Children were administered two doses, as shown  
17 at the top, 21 days apart. Then a third dose was  
18 administered at least 60 days later. Follow-up for  
19 reactions, adverse events, antibody response and  
20 surveillance are parallel to that described for older  
21 children. Current follow-up includes one-month post-

1 dose three serology and efficacy to the data cutoff of  
2 April the 29th. Safety data as of the April 29th  
3 cutoff date follows.

4 All safety data that I will present is in the  
5 blinded placebo-controlled follow-up period. I will  
6 first discuss the safety data in 2- to less than 5-  
7 year-olds and then the 6-month to less than 2-year-  
8 olds. Demographics in the 2- to less than 5-year-old  
9 age group are balanced between vaccine and placebo  
10 groups whether gender, race, or ethnicity. Note at the  
11 bottom of the table that 12.7 to 13.7 of participants  
12 had evidence of prior or current SARS Coronavirus 2  
13 infection at the time of the first dose.

14 Approximately 12 to 14 percent of participants  
15 had underlying comorbidities including obesity. Here  
16 are the tolerability data for 2- to less than 5 years  
17 age group. Care providers for participants with and  
18 without prior SARS Coronavirus 2 infection at baseline  
19 reported local reactions by maximum severity within  
20 seven days after each dose. These include redness,  
21 swelling, and pain at the injection site color-coded as

1 shown.

2           Local reactions were mostly mild to moderate  
3 in severity, somewhat higher in the vaccine recipients  
4 compared to placebo recipients, and did not show an  
5 increase from dose 2 to dose 3. Local reactions were  
6 higher or similar in frequency and severity and those  
7 with evidence of prior SARS Coronavirus 2 infection at  
8 baseline and all within a well-tolerated range. There  
9 were no grade 4 reactions. Care providers for  
10 participants 2 to less than 5 years of age with and  
11 without prior SARS Coronavirus 2 infection at baseline  
12 reported systemic events shown in this table.

13           Let me orient you to the slide. Dose 1, dose  
14 2, and dose 3 are shown in each of the rows with the  
15 color-coded rating scales as shown. Placebo recipients  
16 are paired up with the vaccine recipients for each of  
17 the symptoms shown. Systemic symptoms solicited by  
18 electronic diary were mostly mild to moderate. Fever,  
19 fatigue, or other symptoms rates were remarkably  
20 similar to those seen in placebo recipients and much  
21 lower than those in older age groups immunized with

1 higher dose levels.

2           Fever rates are comparable or lower than other  
3 childhood vaccines. The low incidence of fever  
4 observed after each vaccine dose generally peaked by  
5 day two and declined by day four. Only three or less  
6 than 0.2 percent of BNT162b2 participants reported  
7 fever greater than 40 degree centigrade after dose 1 or  
8 dose 2 starting on day two, day four, or day six with  
9 all returning to normal six to seven days after the  
10 dose. One of these had a presentation suggestive of a  
11 viral exanthem. None of these required hospitalization  
12 and all resolved quickly.

13           Systemic symptoms were higher or similar in  
14 frequency and severity and those with evidence of prior  
15 SARS Coronavirus 2 infection at baseline and all within  
16 a well-tolerated range. This highly favorable  
17 tolerability profile for the Pfizer BioNTech vaccine  
18 should be reassuring to parents and care providers. In  
19 the 2- to less than 5-year-old age group, blinded  
20 safety follow-up occurred from the time of dose 2 to  
21 dose 3 or cutoff date for a median of 4.3 months and

1 for dose 3 to the cutoff date for a median of 1.4  
2 months.

3           As a reminder, randomization was in a 2 to 1  
4 ratio. Unsolicited adverse events are shown here by  
5 proportion reporting at least one adverse event with  
6 vaccine recipients in blue and placebo recipients in  
7 red. Overall, unsolicited adverse events during the  
8 blinded part of the study to date of cutoff in 2 to  
9 less than 5-year-olds were comparable between vaccine  
10 and placebo recipients. An evaluation during the  
11 unblinded period did not change this assessment.

12           Related adverse events, serious adverse events  
13 and withdrawals were infrequent and comparable between  
14 vaccine and placebo groups. Most SAEs were  
15 gastrointestinal or respiratory infection illnesses  
16 with no imbalance between groups. Three subjects, or  
17 0.2 percent, in the BNT162b2 group withdrew from the  
18 study due to adverse events: pyrexia considered  
19 related, status epileptic as considered unrelated, and  
20 urticaria considered unrelated. One participant in the  
21 placebo group withdrew due to facial swelling and rash

1 considered related.

2 Further details are in the briefing document.

3 There were no deaths reported in this age group.

4 Adverse events occurring in 1 percent or more of  
5 participants by system organ class were comparable  
6 between vaccine and placebo recipients from dose 1 to  
7 cutoff whether for any adverse events or the  
8 subcategories shown. Lymphadenopathy in the BNT162b2  
9 group at the 3-microgram dose was 0.1 percent. This  
10 was a lower frequency of lymphadenopathy than that  
11 reported in older children and adults.

12 I'm now going to turn attention to the safety  
13 evaluation in 6 months to less than 2-year-olds. The  
14 demographics are shown here, again, with balance  
15 between the vaccine and placebo groups related to  
16 gender, race, or ethnicity. As shown at the bottom of  
17 the table between 7.6 and 7.4 percent of participants  
18 had evidence of prior or current SARS Coronavirus 2  
19 infection at the time of dose 1. Four percent to 6  
20 percent of individuals enrolled in the trial had  
21 underlying comorbidities.

1           Reports of local reactions by maximum severity  
2 are shown in this figure in the same way that they were  
3 shown for the older population. Local reactions in the  
4 6-month to less than 2-year-old group with and without  
5 prior SARS Coronavirus 2 infection were mild to  
6 moderate with incidence somewhat higher in vaccine  
7 recipients. Local reactions were somewhat higher or  
8 similar in frequency and severity in those with  
9 evidence of prior SARS Coronavirus 2 infection at  
10 baseline and all within a well-tolerated range.

11           There were no grade 4 events and frequency  
12 remained relatively the same after each dose, again,  
13 consistent with a very well-tolerated vaccine.  
14 Caregivers and participants reported e-diary systemic  
15 events by maximum severity within seven days in this  
16 age group with or without prior SARS Coronavirus 2  
17 infection. Note that the symptoms shown in this age  
18 group differ somewhat in terms of how they are captured  
19 because of age.

20           So shown here are fever, decreased appetite,  
21 drowsiness, and irritability, all of which were mostly



1 mild to moderate and similar to placebo rates. Fever  
2 rates were once again comparable or lower than those  
3 observed in older children and adults. Fever rates are  
4 comparable or lower than fever rates of other childhood  
5 vaccines. Fever usually occurred by day two and  
6 declined by at least day four or sooner after each  
7 dosing with vaccine.

8           Fever greater than 40 degree centigrade was  
9 reported by only three recipients, or less than 0.1  
10 percent, for each dose starting on day one, day two, or  
11 day three with all returning to normal by at least five  
12 to six days after the dose, two of whom had a  
13 concurrent viral infection. One fever greater than 40  
14 degrees centigrade was reported by a placebo recipient  
15 after the first dose. None of these required  
16 hospitalization and all resolved quickly.

17           Given the similarity in reactions, much of the  
18 febrile illness in both groups may reflect viral illness  
19 in both groups may reflect viral infections common in  
20 this age group. Systemic symptoms were somewhat higher  
21 or similar in frequency and severity in those with

1 evidence of prior SARS Coronavirus 2 infection at  
2 baseline and all within a well-tolerated range. Again,  
3 the overall incidence and low severity of systemic  
4 symptoms speaks to a favorable tolerability profile for  
5 the Pfizer BioNTech vaccine that should be reassuring  
6 to parents and care providers.

7           Safety follow-up including blinded follow-up  
8 from the time of dose 2 to dose 3 of a cutoff date was  
9 for a median of 6.3 months, and from dose 3 to the  
10 cutoff date was a median of 1.3 months. Unsolicited  
11 adverse events shown here are similar to the pattern  
12 I've described to you in the older age group. Overall,  
13 unsolicited adverse events were comparable between  
14 vaccine and placebo recipients. Related AEs, SAEs,  
15 withdrawals were infrequent and comparable between  
16 vaccine and placebo groups.

17           Most SAEs were gastrointestinal or respiratory  
18 infection illnesses. Three participants, or 0.3  
19 percent, in the BNT162b2 group withdrew from the study  
20 due to adverse events, all related -- two due to a  
21 fever greater than 40 degrees Celsius, one of which had

1 a viral exanthem and that was considered unrelated.  
2 One participant withdrew due to a generalized rash on  
3 the face and trunk. Further details of these events  
4 were included in your briefing document. There were no  
5 deaths reported in this age group.

6           Once again, adverse events rates in this group  
7 occurring in 1 percent or more of participants by  
8 system organ class were comparable between vaccine and  
9 placebo recipients from dose 1 to cutoff.  
10 Lymphadenopathy was reported in only two participants,  
11 or 0.2 percent, in the BNT162b2 group and none in the  
12 placebo group. The frequency of reported  
13 lymphadenopathy is lower than that reported in older  
14 children and adults.

15           Two adverse events of special interest were  
16 recorded and were of similar incidence to placebo. FDA  
17 adverse events of special interest are reported here  
18 for both age groups. Predominant categories were  
19 potential angioedema and hypersensitivity comprising  
20 mainly urticarias and rashes. For CDC defined adverse  
21 events of special interest, no vaccine related

1 anaphylaxis, no myocarditis, no pericarditis, no Bell's  
2 palsy, and no MIS-C was observed.

3           The carefully selected dose level of 3-  
4 micrograms for the BNT162b2 vaccine was shown to have  
5 an excellent safety profile and was well-tolerated in  
6 infants, toddlers, and very young children. Vaccine  
7 reactions were mostly mild to moderate and short-lived  
8 with systemic reactions comparable to placebo.  
9 Reactions were comparable after dose 1, 2, and 3. The  
10 unsolicited adverse event profile mostly reflected  
11 reactogenicity or common childhood illnesses.

12           The safe and well-tolerated vaccine profile of  
13 the carefully chosen 3-microgram dose should reassure  
14 parents and providers. Specifically, the vaccine  
15 provides high protection against omicron if all three  
16 doses are received, and I'll share that with you  
17 shortly. The low incidence of fever and systemic  
18 reactions similar to those of placebo recipients should  
19 encourage vaccine adherence for each of the three  
20 doses. I will now describe immune responses in  
21 children less than 5 years of age.

1            Demonstration of noninferior immune response  
2 in children less than 5 years of age after three doses  
3 compared to immune responses in 16- to 25-year-olds  
4 after two doses was judged by the FDA as sufficient to  
5 meet the immunologic success criteria for emergency use  
6 authorization. Immunobridging criteria in the 2 to  
7 less than 5-year-olds were met for both GMR and  
8 seroresponse, which infers vaccine effectiveness in  
9 this age group.

10            Shown here are the SARS Coronavirus 2  
11 neutralization assay titers to the reference strain  
12 post-dose 3 and children 2- to less than 5 years of age  
13 in the light blue after three doses compared to those  
14 16 to 25 years of age in the darker blue after two  
15 doses with the geometric mean ratio shown on the right-  
16 hand side. The median dosing time between dose 2 and  
17 dose 3 was 10.7 weeks. The geometric mean ratio  
18 observed was 1.30 and, importantly, had a lower bound  
19 of 1.13, thus, well above the 0.67 success criteria  
20 required by the FDA.

21            This was also true for the immunobridging

1 criterion relying on seroresponse. I draw your  
2 attention to the difference in percent responders on  
3 the right-hand side, which is 1.2 percent between the  
4 2-to-less-than-5-year-olds and the 16- to 25-year-olds  
5 with a lower bound of minus 1.5 percent, which is well  
6 above the minus 10 percent noninferiority success  
7 criterion. I now turn to the 6-month to less than 2-  
8 year-olds.

9           Immunobridging criteria were met for both GMR  
10 and seroresponse which infers vaccine effectiveness in  
11 this age group as well. The median dosing time between  
12 dose 2 and dose 3 was 12.9 weeks. The scheme is the  
13 same, and I draw your attention to the right-hand side  
14 of the slide where the geometric mean response was 1.19  
15 with the lower bound of 1 well above the 0.67 required  
16 success criteria. Immunobridging criteria were met for  
17 the seroresponse with 100 percent of children less than  
18 2 years of age responding and a difference in percent  
19 of responders of 1.2 percent with a lower bound of  
20 minus 3.4, again, well above the minus 10 percent  
21 required success criterion.

1           So for both younger children as well as the  
2 older children, immunobridging criteria were met.  
3 Given that most current COVID-19 cases are caused by  
4 Omicron, we also evaluated the ability of two and three  
5 dose immune sera from 6 months to less than 5-year-olds  
6 to neutralize Omicron compared to sera from adults.

7           In this graph, the older comparator group is a  
8 24- to 74-year-old adult sentinel cohort from the  
9 licensure trial that has been used throughout  
10 development to evaluate the antibody response to  
11 emerging variants. Immune responses to omicron shown  
12 in pink were compared to those of the reference vaccine  
13 strain shown in blue using a plaque reduction  
14 neutralization assay. GMTs are shown on the Y axis and  
15 age groups are shown left to right. As you can see, we  
16 see comparable immune responses across all three age  
17 groups to the reference strain and Omicron.

18           However, as reported by several groups,  
19 Omicron responses after only two doses are low and  
20 uniformly so across the pediatric and adult groups.  
21 Low Omicron neutralization titers after two doses

1 seemed to correlate with lower efficacy after two  
2 vaccine doses for Omicron. However, this picture  
3 changes when serum samples after three doses are being  
4 evaluated. In this dataset an adult comparator group  
5 was used that received a third dose at a similar time  
6 interval after the second dose as the pediatric group  
7 at about 11 to 13 weeks.

8           Neutralizing antibody responses were measured  
9 using a fluorescent focused neutralization assay. This  
10 data has been submitted to the FDA and is a supplement  
11 to the briefing document. Left to right, for 6 months  
12 to less than 2-year-olds and 2- to less than 5-year-  
13 olds, the Omicron specific neutralization titers after  
14 three doses are far higher than those on the prior  
15 slide after two doses. The Omicron specific titers are  
16 very similar across age groups.

17           Most importantly, the pediatric group titers  
18 are essentially the same as in the adult group  
19 predicting that similar efficacy as shown in adults  
20 could likely be observed for the 6 month to less than  
21 5-year-old age group. I will shortly share with you



1 descriptive data showing observed post-dose 3 efficacy  
2 matching this prediction. So, here are the  
3 immunogenicity conclusions in 6 months to less than 5-  
4 year-olds.

5 All immunobridging criteria post-dose 3 in  
6 young children required for an emergency use  
7 authorization were met for both age groups inferring  
8 effectiveness. Omicron neutralization titers were low  
9 after two doses for pediatric and adult cohorts but  
10 increased substantially after a third dose in the 6-  
11 month to less than 5-year-olds, with similar levels  
12 observed in adults. Thus, as it has been observed in  
13 other populations, a third dose is required also for  
14 the 6-month to less than 5 years of age group to ensure  
15 a more robust protection against COVID-19 due to  
16 Omicron.

17 So, what have we learned from the adult and  
18 pediatric experience about the potential for BNT162b2  
19 efficacy against COVID-19? Here is a summary of  
20 observed efficacy data in the blinded follow-period  
21 that while not required for an EUA supports the

1 importance of a third vaccine dose to protect children  
2 less than 5 years of age against Omicron just as a  
3 third dose is important to protect older children and  
4 adults against Omicron.

5           It's important to note that nucleic acid  
6 amplification testing was defined either based on  
7 central laboratory determination or an acceptable test  
8 in a local laboratory for all cases. In addition, it's  
9 important to remember that the follow-up for this  
10 population after the second dose was greater than four  
11 months for 2- to less than 5-year-olds and greater than  
12 six months for 6 months to less than 2-year-olds.

13           Details, including 95 percent confidence  
14 intervals are in your briefing document, and the 95  
15 percent confidence intervals for Omicron after the  
16 third dose are shown on the next slide. Efficacy is  
17 shown on the Y axis and by age, 6 months to less than 5  
18 years on the left with the age groups displayed  
19 progressively to the right.

20           Efficacy against the Delta variant is shown in  
21 blue and efficacy against the Omicron variant is shown

1 in pink. Please note that the Delta surge ended prior  
2 to the third dose. So, no children were exposed to  
3 Delta after the third dose, marked as N/A.

4           You can see efficacy against Delta post-dose 2  
5 in the evaluable population without evidence of  
6 infection prior to seven days post-dose 2 of 70.2  
7 percent was observed in 6 months to less than 5-year-  
8 olds shown on the left and, moving left to right, 56  
9 percent in 2-to-less-than-5-year-olds and 91.6 percent  
10 in 6 months to less than 2 year olds. This is  
11 consistent with the high level of efficacy against  
12 Delta after two doses of vaccine and comparable to that  
13 observed in older children and adults.

14           The emergence of Omicron presents a new  
15 challenge. Shown in pink on the left, you can see that  
16 for children 6 months to less than 5 years of age post-  
17 dose 2, efficacy was 21.8 percent in the 6-month to  
18 less than 5-year-old age group and correspondingly as  
19 shown for the other subgroups. This is consistent with  
20 the poor antibody response after the second dose that I  
21 shared with you and is consistent with lower efficacy

1 against Omicron in older children and adults after two  
2 doses compared to other variants like Delta.

3           Now, look what happens after the third dose.  
4 Cases post-dose 3 in this clinical study occurred after  
5 February 7th, 2022, and were confirmed to be Omicron.  
6 This confirmatory data is being submitted to the FDA.  
7 Efficacy in the all-available population against  
8 Omicron rises to 80.3 percent overall and  
9 correspondingly so for the respective age subgroups.  
10 This descriptive observed efficacy well exceeds the  
11 original FDA guidance for an efficacy point estimate of  
12 at least 50 percent.

13           This is consistent with the higher antibody  
14 response seen after the third dose against Omicron like  
15 that of older children and adults and consistent with  
16 corresponding higher efficacy in older children and  
17 adults after a third dose against Omicron. This table  
18 displays details of the high descriptive 80 percent  
19 efficacy observed after the third dose during a period  
20 when Omicron was predominant.

21           Note that the large N in this table represents

1 the population followed during the placebo controlled  
2 blinded period of the trial up to the data cutoff of  
3 April the 29th and note that the trial was randomized 2  
4 to 1 vaccine to placebo. Whether we're talking about  
5 the 6-month to less than 5-year-olds or for the  
6 subgroups, high efficacy was observed in the course of  
7 this trial with 80.3 percent efficacy shown in the  
8 overall age group with a 95 percent confidence interval  
9 lower bound of 13.9 percent.

10           82.3 and 75.5 percent efficacy were observed  
11 in the respective age subgroups with larger confidence  
12 intervals, of course, because these subgroups are  
13 smaller and individually have a smaller number of  
14 cases. So, what can we conclude about efficacy? As  
15 demonstrated in other pediatric and adult age groups,  
16 two doses of BNT162b2 are protective against variants  
17 of concern such as Delta but do not provide adequate  
18 protection against Omicron.

19           As demonstrated in other pediatric and adult  
20 age groups, a third dose is necessary to provide high  
21 protection against Omicron. In addition to six months

1 of follow-up as part of the current clinical trial  
2 ongoing and active pharmacovigilance and  
3 pharmacoepidemiology will continue with the focus on  
4 any expanded pediatric populations receiving vaccine.  
5 These include the pharmacoepidemiology studies for ages  
6 6 months and up, and you can see the five studies are  
7 noted here.

8           No myocarditis was noted in the clinical trial  
9 of children less than 5 years of age, and this rare  
10 event does appear to be less of a risk for 5- to 11-  
11 year-olds. However, evaluation for such a rare event  
12 will be expanded into this age group as part of routine  
13 pharmacovigilance. While active risk mitigation will  
14 continue including labeling educational material and  
15 bio differentiation with the maroon top and  
16 pharmacovigilance will continue as shown and be  
17 consistent with pharmacovigilance in older children and  
18 adults already underway.

19           The potential benefits of vaccinating children  
20 6 months to less than 5 years of age outweigh the known  
21 potential risk. This age group of 6 months to less

1 than 5 years of age is currently unprotected.  
2 Protection against COVID-19 is critical, particularly  
3 in light of the unpredictability of potential new waves  
4 and emergence of new variants of concern. Available  
5 safety, immunogenicity, and efficacy information  
6 support a highly favorable benefit/risk profile for  
7 administration of three doses of BNT162b2 at 3-  
8 micrograms to children less than 5 years of age.

9 Overall, given the favorable benefit/risk  
10 profile, Pfizer-BioNTech requests emergency use  
11 authorization of BNT162b2 for active immunization of  
12 individual 6 months through 4 years of age administered  
13 intramuscularly as a three-dose series. Pfizer and  
14 BioNTech wish to thank the clinical trial participants,  
15 sites, investigators, CRO, our partners and their  
16 staff, and the FDA guidance to assess this urgent  
17 medical need. I and my Pfizer colleagues will now be  
18 happy to take questions.

19

20

#### **Q&A SESSION**

21

1           **DR. ARNOLD MONTO:** Thank you, Dr. Gruber. Dr.  
2 Pergam is next, followed by Dr. Gans. Dr. Pergam?

3           **DR. STEVEN PERGAM:** Thanks, Dr. Gruber, for  
4 that presentation. I was curious. We haven't seen  
5 much of the data related to the dose finding in the  
6 initial phase 1 study. I'm curious if you can describe  
7 a little bit about whether there was a difference in  
8 immunogenicity between the 3-microgram versus 10-  
9 microgram? Is there a dose dependency in that  
10 particular comparison? I'm just curious based on  
11 differences in dosing of the vaccine.

12           **DR. WILLIAM GRUBER:** Thanks for that question.  
13 Obviously, as I said, we pay strict attention to  
14 defining just the right dose that gave us the  
15 appropriate immune response after three doses. There  
16 are really two lines of evidence that support the basis  
17 for the dosing decision. One is the reactogenicity  
18 that I already shared with you, but the second one is  
19 really -- if we can bring up the slide with the pink  
20 bars that speaks to the Omicron response.

21           You may recall that while that's coming up



1 that we made decisions at the time of phase 1 based on  
2 comparisons to an adult population that gave us  
3 reassurance that, for the reference strain, we were  
4 likely to meet noninferiority, right? Because that's  
5 the criteria for licensure.

6 But in addition to that -- so, if we can put  
7 slide 3 up -- this is really the most compelling  
8 information, that having chosen the 3-microgram dose  
9 and giving it as three successive doses, we now  
10 essentially nearly equal the sort of response that one  
11 sees in adults for which we know we have good  
12 protection against Omicron.

13 So, I think that confirms for us what the  
14 reactogenicity profile that I shared you and this  
15 finding that this is the right dose to provide  
16 protection, and again, although it's early, the 80  
17 percent efficacy that we're seeing essentially matches  
18 what you would expect based on this type of response.

19 **DR. STEVEN PERGAM:** Okay. Just as a piece of  
20 clarification, did you see a difference in the 3-  
21 microgram versus 10-microgram in terms of antibody

1 responses? It's just a clarification question.

2           **DR. WILLIAM GRUBER:** The nature of the  
3 antibody responses were both above the responses that  
4 we saw in adults, but combined with the reactogenicity  
5 profile and knowing that for the reference strain we  
6 would be in a position to potential meet  
7 noninferiority, we chose that strain because -- again,  
8 we chose that dose because we, again, want to be  
9 confident that the vaccine would be accepted.  
10 Obviously, we already know that in older individuals --  
11 30 percent of children are not getting the vaccine.

12           There could be a lot of reasons for that, but  
13 one of them is the reactogenicity. So, combined with  
14 that, and again the data that I'm showing you here, it  
15 seems pretty clear that the 3-microgram dose is the  
16 right dose and followed by, obviously, the phase 3 data  
17 that we have on reactions, which are very comparable to  
18 what we see in placebo recipients.

19           **DR. STEVEN PERGAM:** Okay. Thanks.

20           **DR. ARNOLD MONTO:** Thank you. Moving on, Dr.  
21 Gans, followed by Dr. Portnoy.

1           **DR. HAYLEY ALTMAN-GANS:** Thank you for that  
2 presentation. I had a follow-up question maybe to  
3 Steve's question regarding the dosing, and I was  
4 looking at the slightly lower immune responses in the  
5 2- to 5-year-old to the current dosing. I'm just  
6 wondering are there additional studies that actually  
7 may be looking at differing dosing and splitting these  
8 groups. As we know it's a very large immunologic,  
9 group, and there may be some nuances to how the  
10 toddlers or the preschool is different than the infant  
11 group. So that's one question.

12           I would also like you to talk a little bit  
13 about your breakthrough disease and see if there was  
14 any differences in the severity of disease in those who  
15 had received the vaccine versus those who were in the  
16 placebo group. I realize hospitalization wasn't  
17 something, so that's not really what I'm asking. I'm  
18 asking about the disease profiles in those two groups.

19           **DR. WILLIAM GRUBER:** Let me take your first  
20 question first about the nature of splitting the  
21 groups. I think the approach that we've taken is very

1 consistent with every other age group in terms of  
2 dealing with the pediatric population. So for 12- to  
3 17-year-olds, they get a 30-microgram dose. For the 5-  
4 to 11-year-olds, they get 10, and for now the 6 month  
5 to 5-year-olds, they receive 3 microgram.

6           Again, based on what we saw in the older  
7 children, where we had 19 percent severe fevers in the  
8 phase 1 group, we really don't feel comfortable  
9 expanding on that dose, and we don't need to because we  
10 now see with the three-dose series, which I think most  
11 people now agree -- we heard from Paul Offit yesterday,  
12 the importance of a third dose in an Omicron era --  
13 that this is the right dose to immunize children to  
14 protect against Omicron.

15           For the second piece, the nature of severity  
16 of the illness we've actually included in your briefing  
17 document, and there was really no difference if we  
18 looked at all the cases. I'm talking about based on  
19 the number of symptoms that they had in terms of  
20 breakthrough compared to placebo whether it was one,  
21 two, three, or more symptoms. There really was not a

1 dimes worth of difference between the respective groups  
2 between those that breakthrough that have received  
3 vaccine versus placebo.

4 So that gave us confidence in that larger sort  
5 of population of cases that we have that that does not  
6 appear to be an issue.

7 **DR. HAYLEY ALTMAN-GANS:** It also doesn't seem  
8 to -- if the disease is the same in the placebo group,  
9 it didn't show a necessary advantage of the vaccine, I  
10 guess was what I was asking.

11 **DR. WILLIAM GRUBER:** Well, I guess the  
12 advantage of the vaccine is you're preventing the  
13 infection in the first place, right?

14 **DR. HAYLEY ALTMAN-GANS:** I get that.

15 **DR. WILLIAM GRUBER:** So that's the big  
16 advantage, right? The good news is it doesn't seem to  
17 make the disease worse if, in fact, you've received a  
18 vaccine. I think that's an important thing and why we  
19 looked at it.

20 **DR. ARNOLD MONTO:** Thank you. Dr. Portnoy,  
21 followed by Dr. Cohan.

1           **DR. JAY PORTNOY:** Thank you. I guess I'm a  
2 little bit confused about this dosing in terms of  
3 micrograms because your dosing is 3-micrograms. The  
4 Moderna dosing is 25 micrograms. Clearly, we're  
5 thinking in terms of micrograms the way we would think  
6 of proteins as the way of inducing an immune response.  
7 Yet, the purpose of the mRNA is to induce protein  
8 production.

9           So, is your mRNA just more efficient at making  
10 cells produce protein? Or how should we think of  
11 micrograms in terms of the amount of spike protein  
12 that's produced by the cells? Can you kind of clarify  
13 that?

14           **DR. WILLIAM GRUBER:** Yeah. I'll leave it to  
15 Moderna to describe the nature of how they address  
16 their vaccine dosage, but I think the -- obviously, we  
17 don't have a complete understanding of the nature of  
18 the way that the vaccine works in terms of producing  
19 immune response. So, you have to go by the results.  
20 The results are that in a setting of giving a 3-  
21 microgram dose we had low reactogenicity compared to

1 placebo, and after a third dose, just as in adults at  
2 higher doses, we're getting an immune response that's  
3 comparable.

4           It may well be that children we've seen  
5 certainly in -- that we are able to go down to a lower  
6 dose in children, and the expectation is perhaps they  
7 have a more robust response. That seems to be the case  
8 based on giving a 10-microgram dose to a 5 to 11s and  
9 3-micrograms to younger.

10           **DR. JAY PORTNOY:** Have you ever measured the  
11 amount of protein that's produced as a result of the  
12 mRNA and how many cells are producing it and how  
13 persistent that production is for a given microgram of  
14 mRNA?

15           **DR. ARNOLD MONTO:** That's a pretty broad  
16 question.

17           **DR. JAY PORTNOY:** Yeah.

18           **DR. WILLIAM GRUBER:** I think that that's  
19 obviously an interesting question to better understand  
20 the mechanism, and I would say it's somewhat academic  
21 in the setting of what we're trying to achieve here in

1 terms of getting an immune response and a safety  
2 profile that's satisfactory, but worthwhile for people  
3 to pursue.

4 **DR. JAY PORTNOY:** Okay. Thank you.

5 **DR. WILLIAM GRUBER:** Let me just -- Dr.  
6 Jansen, the head of vaccine research and development  
7 would like to make a comment about that last question.

8 **DR. ARNOLD MONTO:** Very brief.

9 **DR. KATHRIN JANSEN:** Thank you, Bill. I think  
10 one important consideration for the answer to the  
11 question that was just posed is that the two mRNA  
12 vaccines are not created equal. They're actually very  
13 different vaccines. They use the same platform. They  
14 have different formulations, and so I think that's  
15 important to recognize. The second piece is that we,  
16 of course, have optimized the vaccine for optimal  
17 expression of the antigens themselves. If you ask the  
18 question is there a logic number of protein molecules  
19 expressed in the cells, the answer is yes. Thank you.

20 **DR. ARNOLD MONTO:** Thank you both. Dr. Cohn,  
21 final question.



1           **CAPT. AMANDA COHN:** Thank you. Okay. So I  
2 have a -- this is maybe a multi-part question. I'm  
3 wondering how you can be so sure of both your  
4 immunogenicity and VE estimates in the setting of the  
5 requested interval that you requested between two and  
6 three doses is actually different than any of the -- is  
7 actually very different than the median in which your  
8 recipients received that third dose. So, how can you  
9 be sure that they would have a similar response eight  
10 weeks after the first dose?

11           That sort of goes back to this time period  
12 between the second dose where there appears to be very  
13 little to no effectiveness and the third dose would  
14 essentially mean that these kids would not be protected  
15 at all for an additional eight weeks. So I'm trying to  
16 sort through both you looked at effectiveness in kids  
17 who were vaccinated for a longer period after that  
18 second dose and if you have any kids or any data on  
19 immunogenicity after eight weeks.

20           **DR. WILLIAM GRUBER:** Thanks for the question.  
21 I think where we take a great deal of comfort is sort

1 of comparing like to like, so the nature of comparing  
2 this 11- to 13-week comparison in the older adult  
3 population to the immune response we're seeing in the  
4 younger sort of translates to the likelihood that  
5 you're going to get similar efficacy with that  
6 interval. Likewise, I think it's reasonable to assume  
7 that the -- if the interval were lower, you would  
8 compare to what we saw in adults as well.

9 I think there were a fair number of  
10 individuals that did actually get the vaccine in the 8-  
11 to 13-week period that are obviously being monitored as  
12 part of our ongoing assessment of efficacy, and perhaps  
13 we'll learn something from that, particularly as time  
14 goes on and we have longer follow-up.

15 **CAPT. AMANDA COHN:** But to clarify, we don't  
16 actually have -- do we have data on adults that are  
17 immunocompetent that were vaccinated eight weeks after  
18 their second dose?

19 **DR. WILLIAM GRUBER:** In terms of data, in  
20 terms of eight weeks, I'm not sure --

21 **CAPT. AMANDA COHN:** No?

1           **DR. WILLIAM GRUBER:** -- that we actually have  
2 data that we've analyzed at eight weeks.

3           **CAPT. AMANDA COHN:** Right. Essentially, what  
4 you're saying -- and I share your confidence which is  
5 great, but what you're asking for, this eight-week  
6 interval is not the same and can't be compared to  
7 adults or to many of the kids who are in your study.

8           **DR. WILLIAM GRUBER:** I guess what has to --  
9 and, Dr. Cohn, I appreciate the question. I think what  
10 has to be balanced here is a reasonable expectation  
11 that will have some level of efficacy, certainly seeing  
12 that we have 80 percent at 11 to 13 weeks -- and the  
13 need to get children vaccinated as quickly as possible  
14 to essentially achieve that efficacy. That was part of  
15 the reason, as you know, that for our primary series,  
16 we looked at 21 days.

17           We wanted to narrow that interval of what was  
18 reasonably possible to have enough maturation of immune  
19 response that you'd get a good response after the  
20 second dose. If we lengthen out now the period of time  
21 after the third dose -- and we're all hearing and what

1 the data supports that you need a third dose for  
2 Omicron -- you're essentially trading off a theoretical  
3 issue that maybe I'm not going to get quite as good  
4 efficacy for the notion of -- in a child having that  
5 period of exposure before they can get that third dose.  
6 So, I think that's the sort of thing that has be  
7 weighed.

8 **DR. AMANDA COHN:** Thanks.

9 **DR. ARNOLD MONTO:** Okay. Thank you, Dr.  
10 Gruber. We're moving on now to the FDA presentation on  
11 the efficacy and safety of the Pfizer-BioNTech vaccine.  
12 Dr. Susan Wollersheim in the clinical review branch FDA  
13 will be giving us the presentation. Dr. Wollersheim?

14

15 **FDA REVIEW OF EFFECTIVENESS AND SAFETY OF PFIZER-**  
16 **BIONTECH COVID-19 VACCINE IN INFANTS AND CHILDREN 6**  
17 **MONTHS THROUGH 4 YEARS OF AGE**

18

19 **DR. SUSAN WOLLERSHEIM:** Thank you so much, Dr.  
20 Monto. Can you hear me okay?

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

1           **DR. SUSAN WOLLERSHEIM:** Thank you. Mike, if  
2 you could add my notes, that would be great.

3 Fantastic. I see them now. Thank you so much.

4           I'm Susan Wollersheim, a medical officer in  
5 the Division of Vaccines and Related Products  
6 Applications at the FDA. I will be presenting the  
7 FDA's review of the effectiveness and safety of the  
8 Pfizer-BioNTech COVID-19 vaccine in children 6 months  
9 to 4 years of age submitted under an emergency use  
10 authorization amendment, or EUA. I'd like to start by  
11 acknowledging so many contributions from so many  
12 colleagues across the FDA. Thanks so much.

13           To outline my presentation for you, I will  
14 start by providing the regulatory background of the  
15 product and the study design, followed by a brief  
16 review of the phase 1 dose selection, then the phase  
17 2/3 immunogenicity, descriptive efficacy, and safety  
18 results, followed by the pharmacovigilance plan and a  
19 summary of the benefits and risks for this product.

20           To begin, the Pfizer-BioNTech COVID-19 vaccine  
21 is based on the SARS-CoV-2 spike glycoprotein S antigen

1 derived from the Wuhan strain encoded by RNA and  
2 formulated in lipid particles. This slide shows a  
3 summary of the various age groups, dose levels,  
4 regimens, and current authorizations and approvals for  
5 the primary series of this product. The EUA under  
6 discussion today is listed at the bottom of the slide  
7 and is intended to support use of a three-dose primary  
8 series of the Pfizer-BioNTech COVID-19 vaccine at the  
9 3-microgram mRNA dose level.

10           The FDA has issued related EUAs previously as  
11 listed at age-appropriate dose levels as a two-dose  
12 primary series and a third primary series dose for  
13 certain populations. In August of 2021, the Pfizer-  
14 BioNTech COVID-19 vaccine was approved under biologics  
15 licensed application under the proprietary name  
16 Comirnaty for use in individuals 16 years of age and  
17 older. This slide presents some key features of the  
18 two prior pediatric EUAs issued for the Pfizer-BioNTech  
19 COVID-19 vaccine in May of 2021, for adolescents 12  
20 through 15 years of age and October 2021 for children 5  
21 through 11 years of age.

1           The EUA issued for children 5 through 11 years  
2 of age is for the 10-microgram dose level while the 30-  
3 microgram dose levels authorized for use in adolescents  
4 12 through 15 years of age. Data from clinical studies  
5 submitted to support the EUAs for both age groups  
6 included similar safety endpoints, immunobridging  
7 approaches and descriptive efficacy analyses.

8           The safety database for vaccine recipients and  
9 percentage of participants with two months or more of  
10 follow-up at the time of each EUA data cutoff are  
11 shown. As you will see from the rest of the  
12 presentation, this EUA request for children 6 months  
13 through 4 years of age has similar features.

14           Now, we'll move on to the study design. Study  
15 C4591007 is an ongoing phase 1, 2, 3 randomized blinded  
16 placebo-controlled study to evaluate the safety and  
17 effectiveness of BNT162b2 in children 6 months through  
18 11 years of age and was the basis for the EUA issued  
19 for children 5 through 11 years of age. The focus of  
20 this EUA request is the remaining participants 6 months  
21 through 4 years of age, also enrolled in the study. My

1 slides are moving. Sorry.

2           Okay. So, for phase 1, a two-dose primary  
3 series of the vaccine was evaluated in U.S. children  
4 who are not at high risk for SARS-CoV-2 exposure, did  
5 not have medical conditions that represented risk  
6 factors for severe COVID-19 and did not have evidence  
7 of prior SARS-CoV-2 infection. Dose levels of 3 and 10  
8 micrograms were evaluated in an open-label manner for  
9 each age group, starting with the older age group and  
10 based upon safety evaluation and recommendation by the  
11 internal review committee.

12           Selection of the 3-microgram dose level for  
13 both age groups was driven by reactogenicity and  
14 supported by immunogenicity obtained at seven days  
15 post-dose 2. Phase 2/3 of study C4591007 is being  
16 conducted in the United States, Finland, Poland, and  
17 Spain. This portion of the study did not exclude  
18 children with a history of SARS-CoV-2 infection,  
19 children with known HIV, hepatitis B, hepatitis C, or  
20 stable preexisting chronic disease.

21           Participants are randomized two to one to



1 receive two doses of vaccine or saline placebo three  
2 weeks apart. Immunogenicity was assessed in a subset  
3 of participants at one-month post-dose two to infer  
4 effectiveness as the primary endpoint. Following  
5 analysis of the pose-dose 2 safety and effectiveness  
6 data, a third primary series dose was added for  
7 participants 6 months through 4 years of age at least  
8 eight weeks after dose 2 in protocol amendment 6.

9           Approximately 4,500 total participants have  
10 been enrolled at the time of this data cutoff, and  
11 enrollment is ongoing to expand the safety database.  
12 Immunogenicity at one-month post-dose 3 was assessed in  
13 the subset of participants, and efficacy data was  
14 obtained through continuous surveillance for potential  
15 cases of COVID-19. There were two circumstances for  
16 participants to be unblinded during the study, and the  
17 first was if they turned 5 years of age and became  
18 eligible to receive vaccine as available under the EUA  
19 from October of 2021.

20           The second was the planned unblinding at the  
21 6-month post-dose 2 visit in the original protocol

1 prior to the addition of the third dose to the primary  
2 series. The subjects randomized prior to protocol  
3 amendment 6 were unblinded six-month post-dose 2 and  
4 offered vaccine if they originally received placebo.  
5 The first placebo crossover occurred in November of  
6 2021. Subjects randomized after implementation of the  
7 protocol amendment 6 will be unblinded at their six-  
8 month post-dose 3 visit and offered vaccine if they  
9 originally received placebo.

10           The notable implications of unblinding during  
11 the study are that the descriptive efficacy analyses  
12 include only blinded participants. However, the safety  
13 analyses do include all participants who received any  
14 study intervention regardless of those who are blinded  
15 or unblinded.

16           This slide outlines the study objectives and  
17 endpoints. Immunogenicity was evaluated one-month  
18 post-dose 3, and analyses were conducted by age group  
19 with two primary endpoints of geometric mean titers and  
20 seroresponse rates tested sequentially. Efficacy was  
21 evaluated with continuous surveillance for potential

1 cases of COVID-19, and safety data was collected from  
2 all participants who received study intervention as  
3 follows.

4 Safety analyses included solicited local and  
5 systemic reactions or reactogenicity for seven days  
6 after each vaccination via e-diary. Unsolicited  
7 adverse events were collected within 30 minutes after  
8 each dose, which were considered immediate adverse  
9 events, and from dose 1 through one month after each  
10 dose. Serious adverse events will be collected from  
11 dose 1 through six months after dose 3 or the data  
12 cutoff.

13 The effectiveness of the Pfizer-BioNTech  
14 COVID-19 vaccine is being inferred by comparing  
15 neutralizing antibody responses against the Wuhan-like  
16 strain obtained one-month post-dose 3 in the pediatric  
17 age group separately compared to a subset of  
18 participants 16 through 25 years of age enrolled in a  
19 vaccine efficacy study C4591001 in which the overall  
20 vaccine efficacy was 91.2 percent in participants 16  
21 through 55 years of age.

1 Participants in each immunogenicity analysis  
2 population did not have evidence of prior SARS-CoV-2  
3 infections. Immunobridging endpoints and statistical  
4 success criteria will be discussed in the next two  
5 slides.

6 This slide shows the first immunobridging  
7 analysis based on geometric mean titer, or GMTs. A  
8 SARS-CoV-2 neutralizing antibody titers obtained one-  
9 month post primary series are being compared in  
10 participants without evidence of prior SARS-CoV-2  
11 infections. The GMT ratio compares each pediatric age  
12 group to the young adult age group from study C4591001  
13 with success criteria that the lower limit of the two-  
14 sided 95 percent confidence interval is greater than  
15 0.67 and the point estimate of the GMT ratio is greater  
16 than or equal to 1.

17 The second immunobridging analysis is based on  
18 seroresponse rate, which is defined as the percentage  
19 of participants with a greater than or equal to four-  
20 fold rise from baseline. The success criteria is a  
21 lower limit of the 95 percent confidence interval for

1 the difference in seroresponse rates being greater or  
2 equal to negative 10 percent. Both immunobridging  
3 analyses had to meet success criteria for overall  
4 success of the primary endpoints.

5 This slide provides the case definitions for  
6 protocol defined symptomatic COVID-19 and severe COVID-  
7 19 used for the vaccine efficacy analyses. Symptomatic  
8 COVID-19 was defined as the presence of at least one of  
9 the listed symptoms on the left side of this slide, as  
10 well as a confirmed SARS-CoV-2 PCR positive test during  
11 or within four days of the symptomatic period.

12 Severe COVID-19 includes the symptomatic  
13 COVID-19 case definition with at least one of the  
14 listed criteria on the right side of the slide, such as  
15 abnormal vital signs, various levels of respiratory and  
16 systemic illness, ICU admission, or death. Vaccine  
17 efficacy was the secondary objective planned after 21  
18 confirmed cases had been accrued across those age  
19 groups and conditional unsuccessful immunobridging.

20 This slide shows the various analysis  
21 populations for each age group for which you will see

1 results today. The numbers of vaccine and placebo  
2 recipients listed reflects the two to one  
3 randomization, and the first row shows the total  
4 numbers of participants who received any dose of study  
5 intervention. There are notably smaller numbers of  
6 participants in the dose 3 efficacy analysis population  
7 shown in the bottom row of this slide due to unblinding  
8 and attrition.

9           For the 6- through 23-month age group, a total  
10 of 715 original vaccine recipients and 377 original  
11 placebo recipients were unblinded during the study  
12 conduct. For the 2- to 4-year-age group, a total of  
13 842 original vaccine recipients and 424 original  
14 placebo recipients were unblinded. This slide presents  
15 the demographics and baseline characteristics of  
16 subjects 6 through 23 months of age. These  
17 demographics are also comparable to the immunogenicity  
18 and efficacy populations, which are subsets of this  
19 overall safety population.

20           The treatment groups are balanced in terms of  
21 demographics and baseline characteristics. The median

1 age was 16 months. Seven to 8 percent were positive at  
2 baseline for SARS-CoV-2 status. The majority of  
3 subjects were white, and 14 percent identified as  
4 Hispanic. Participants were enrolled in four  
5 countries: the U.S., Spain, Finland, and Poland, with  
6 the U.S. contributing most participants. Comorbidities  
7 were reported in 4 to 6 percent of participants,  
8 including asthma, cardiovascular disease, and  
9 congenital heart disease.

10           This slide shows the demographics of the  
11 safety population for the older age group which was  
12 generally comparable to the younger age group. As a  
13 reminder, the immunogenicity and efficacy populations  
14 are also subsets of this overall safety population.  
15 The treatment groups were balance in terms of  
16 demographics and baseline characteristics. The median  
17 age was 3 years. Comorbidities were reported in 12 to  
18 14 percent of participants including asthma, neurologic  
19 disorders, and congenital heart disease. Obesity was  
20 present in approximately 7 percent, and of note there  
21 were no HIV positive subjects enrolled into the study

1 for these age groups.

2           We will now move on to the immunogenicity  
3 data. Here, you see the results for the GMT primary  
4 endpoint in children 6 through 23 months of age. Among  
5 participants in the evaluable immunogenicity population  
6 without prior evidence of SARS-CoV-2 infection, the  
7 ratio of GMTs was 1.19, which met the success criteria  
8 for immunobridging as the lower bound of the two-sided  
9 95 percent confidence interval for the ratio was  
10 greater than 0.67 and the point estimate was greater  
11 than or equal to 1.

12           The results of a subgroup analysis of the GMTs  
13 in children 6 through 23 months of age by baseline  
14 SARS-CoV-2 status are displayed here. The definition  
15 of baseline SARS-CoV-2 status is based on results of N  
16 binding antibody in SARS-CoV-2 PCR tests obtained prior  
17 to dose 1. Participants with positive baseline SARS-  
18 CoV-2 status had numerically higher GMTs compared to  
19 those negative at baseline, which is consistent with  
20 immunogenicity results observed in the older age group.

21           The number of baseline positive participants,



1 though, was limited to six in the vaccine groups and  
2 eight in the placebo group. The baseline negative  
3 group may also include participants that became  
4 infected after dose 1 and before one-month post-dose 3  
5 of note. Results for the seroresponse rate  
6 immunobridging endpoint in children 6 through 23 months  
7 of age are displayed here.

8           Among participants in the evaluable  
9 immunogenicity population without evidence of SARS-CoV-  
10 2 infection, the percent difference in seroresponse  
11 rates was 1.2, which meant the success criteria as the  
12 lower bound of the two-sided 95 percent confidence  
13 interval was greater than negative 10 percent.

14           Here, we'll move on to the older age group.  
15 The results for the GMT immunogenicity endpoint for  
16 children 2 through 4 years of age are displayed here.  
17 Among participants in the evaluable immunogenicity  
18 population without evidence of SARS-CoV-2 infection,  
19 the ratio of GMTs was 1.3, which met the success  
20 criteria for immunobridging at the lower bound of the  
21 two-sided 95 percent confidence interval was greater

1 than 0.67 and the point estimate was greater than or  
2 equal to 1.

3 Results for subgroup analyses of the GMTs in  
4 children 2 through 4 years of age by baseline SARS-CoV-  
5 2 status are displayed here. Participants with  
6 positive baseline SARS-CoV-2 status had numerically  
7 higher GMTs compared to those negative at baseline,  
8 which is consistent with immunogenicity results  
9 observed in older age groups. There were small number  
10 at baseline positive participants as there were only 13  
11 in the vaccine groups and 8 in the placebo group.

12 Again, this does not account for participants  
13 that became infected after dose 1 but before one-month  
14 post-dose 3. Results for the seroresponse rate,  
15 immunogenicity endpoint for children 2 through 4 years  
16 of age are displayed here. Among participants in the  
17 evaluable immunogenicity population without prior  
18 evidence of SARS-CoV-2 infection, the percent  
19 difference in seroresponse rates with 1.2, which met  
20 the success criteria at the lower bound of the two-  
21 sided 95 percent confidence interval was greater than

1 negative 10 percent.

2           An additional exploratory immunogenicity  
3 analysis was performed in randomly selected subsets of  
4 participants from each age group without evidence of  
5 prior SARS-CoV-2 infection. Neutralization of the  
6 reference strain, Delta, and Omicron variants were  
7 evaluated using a non-validated assay measured before  
8 dose 3 and one month after dose 3. The neutralizing  
9 titers at one-month post-dose 3 are displayed here.  
10 The geometric fold rise from the baseline titer are  
11 also shown.

12           These results indicate that the third vaccine  
13 dose elicits neutralizing titers against all three  
14 SARS-CoV-2 viruses. Notable is that the Omicron  
15 neutralizing titers are approximately six-fold lower  
16 than neutralizing titers against the Delta variants and  
17 reference strain.

18           We'll now move on to the descriptive vaccine  
19 efficacy data. This slide provides the blinded follow-  
20 up time after dose 3 for each age group in the dose 3  
21 all available efficacy population. Just over 30

1 percent of participants had follow-up duration of two  
2 months or longer. The median efficacy follow-up time  
3 after dose 3 for the younger age group was 1.3 months  
4 or five weeks, and the older age group, the median  
5 follow-up time after dose 3 was 1.4 months or six  
6 weeks.

7           For participants 6 through 23 months of age,  
8 the median timing of dose 3 administration after dose 2  
9 of vaccine was 16 weeks with a range of 8 to 31.9  
10 weeks. For placebo, the median was 15.9 weeks with a  
11 range of 8 to 35 weeks. For participants 2 through 4  
12 years of age, the median timing of dose 3  
13 administration after dose 2 of vaccine was 11 weeks  
14 with a range of 8 to 34.1 weeks and, if placebo, was 11  
15 weeks with a range of 8 to 31.1 weeks.

16           Of note, the following vaccine efficacy  
17 estimates are preliminary as a total of 21 cases were  
18 not accrued and the analyses are not presented in the  
19 protocol specified efficacy analysis population. In  
20 participants 6 through 23 months of age with and  
21 without evidence of SARS-CoV-2 infection, prior to

1 seven days after dose 3, the observed vaccine efficacy  
2 against confirmed COVID-19 occurring at least seven  
3 days after dose 3 was 75.6 percent with a lower limit  
4 of the 95 percent confidence interval of negative 369.1  
5 based on one case in the vaccine group compared to two  
6 in the placebo group.

7           Again, vaccine efficacy post-dose 3 cannot be  
8 precisely estimated due to the limited number of cases  
9 accrued during blinded follow-up as reflected by the  
10 very wide confidence interval seen here. Vaccine  
11 efficacy in the dose 1 all available efficacy  
12 population for any confirmed COVID-19 case that  
13 occurred after dose 1 is displayed here. To show the  
14 progression of vaccine efficacy following dose 1 in the  
15 top row, which was approximately 14 percent, the  
16 vaccine efficacy estimates varied between dose 2 and 3,  
17 and following dose 3, the preliminary vaccine estimate  
18 appears improved but, again, has a very wide confidence  
19 interval and a lower limit of negative 370.1.

20           Here is the cumulative incidence curve for  
21 participants 6 through 23 months of age for confirmed

1 COVID-19 cases occurring at any time after dose 1.  
2 COVID-19 disease onset appears to occur similarly for  
3 both vaccine and placebo recipients until closer to the  
4 data cutoff at which point the curves begin to diverge.  
5 Dose 2 was administered three weeks after dose 1.

6           So, that's easy to track on this curve, near  
7 the 21-day mark on the bottom axis, but there's no  
8 clear -- and so you don't see a clear effect of dose 2  
9 on the incidence of cases between the treatment groups.  
10 What's a little more difficult to identify is the time  
11 point for dose 3 because there are highly variable  
12 dosing intervals between doses 2 and 3 with the median  
13 interval of 112 days at a range of 56 to 245 days.

14           We'll move on to the older age group here,  
15 participants 2 through 4 years of age with and without  
16 evidence of SARS-CoV-2 infection prior to dose 3. We  
17 observed vaccine efficacy against confirmed COVID-19  
18 occurring at least seven days after dose 3 was 82.4  
19 percent with a lower bound at the 95 percent confidence  
20 interval of negative 7.6.

21           This is based on two COVID cases in the

1 vaccine group compared to five in the placebo group.  
2 The vaccine efficacy post-dose 3 cannot be precisely  
3 estimated due to the limited number of cases accrued  
4 during blinded follow-up, as reflected by the wide  
5 confidence intervals associated with these estimates.

6           Here, you see the vaccine efficacy and the  
7 dose 1 all available efficacy population for any  
8 confirmed COVID-19 case that occurred after dose 1.  
9 This shows the progression of vaccine efficacy  
10 following dose 1 in the top row, which was 32.6  
11 percent, and then the vaccine efficacy estimates  
12 between dose 2 and 3 varied. Following dose 3, the  
13 preliminary vaccine efficacy estimate appears approved,  
14 again, with a very wide confidence interval and the  
15 lower limit of negative 8.

16           Here is the corresponding cumulative incidence  
17 curve for participants 2 through 4 years of age were  
18 confirmed COVID-19 cases occurring any time after dose  
19 1. COVID-19 disease onset appears to curve similarly  
20 for both vaccine and placebo groups until around the  
21 midway point of the curve where they begin to diverge

1 slowly. Dose 2 was administered about three weeks  
2 after dose 1.

3           So you can track that on the lower axis near  
4 the 21-day mark, and you don't see a clear benefit of  
5 dose 2 on the incidence of cases. What's more  
6 difficult, again, is the time point for dose 3 because  
7 there are highly variable dosing intervals between  
8 doses 2 and 3 with the median of 77 days and a range of  
9 42 to 239 days.

10           Additional consideration about the descriptive  
11 efficacy analyses are provided here. All cases  
12 occurred during a time period when Omicron was the  
13 predominant circulating variant. There is one  
14 hospitalization for severe COVID-19 disease in a two-  
15 year-old vaccine recipient which occurred 99 days after  
16 dose 2. The other seven severe cases that occurred any  
17 time after dose 1 met severe criteria because of one  
18 vital sign measurement, which was not considered  
19 clinically significant, and they were not hospitalized  
20 for COVID-19.

21           Interpretation of these vaccine efficacy



1 estimates is limited by the small number of confirmed  
2 cases and the short duration of follow-up after dose 3,  
3 which was only 35 days for the participants in the  
4 younger age group and 40 days in the participants in  
5 the older age group.

6           We will now move on to the phase 2/3 safety  
7 data. This slide provides the total follow-up time  
8 combining blinded and open-label follow-up after dose 3  
9 in the safety population. The blinded follow-up time  
10 durations are the same as the dose 3 efficacy  
11 population described earlier. The median total follow-  
12 up time after dose 3 for both age groups was 2.1  
13 months. Approximately 60 percent of participants 6  
14 through 23 months of age and 57 percent of participants  
15 2 through 4 years of age had more than two months of  
16 total follow-up time.

17           Here, we see the analyses for immediate  
18 adverse events, and there are very few immediate  
19 adverse events defined as an adverse event reported  
20 within 30 minutes of any vaccine dose. The events  
21 reported were consistent with local solicited adverse

1 events, and there were no anaphylaxis events reported  
2 within 30 minutes of vaccine.

3           Here, you can see the frequency of local  
4 reactions in children 6 through 23 months of age  
5 including injection site tenderness, redness, and  
6 swelling. Pain at the injection site was reported most  
7 commonly followed by redness and then swelling. Local  
8 reactions generally occurred at similar frequencies  
9 after any dose with slightly less frequency with  
10 subsequent doses.

11           Median day of onset and duration was one to  
12 two days for all doses and treatment arm. There were  
13 very few severe reactions with 0.1 percent reporting  
14 tenderness at the injection site post-dose 2 and 0.3  
15 percent reporting redness post-dose 3.

16           Here are the frequencies of local reactions in  
17 children 2 through 4 years of age. My slides are  
18 jumping. Let me go back to that slide. There we go.  
19 Local reactogenicity for the older age group included  
20 injection site pain, redness, and swelling. Pain at  
21 the injection site was reported most commonly followed

1 by redness and swelling. The local reactions generally  
2 occurred at similar frequencies after each dose.

3 Local reactions graded as severe were very  
4 uncommon, seen in only 0.1 percent of participants for  
5 redness at injection site followed by dose 1 and 2.  
6 The median day of onset and duration was one to two  
7 days for all doses and treatment arms.

8 Solicited systemic reactions in vaccine  
9 recipients occurred at similar frequencies after any  
10 dose with decreasing frequency with subsequent doses.  
11 The median day of onset and duration was two days for  
12 all doses and treatment arms. Severe systemic  
13 reactions were reported by 0.6 percent or less of  
14 participants following any dose. The percentage of  
15 participants 6 through 23 months of age who reported e-  
16 diary data and who are also baseline SARS-CoV-2  
17 positive was 7.5 percent.

18 Subgroup analyses of solicited adverse  
19 reactions by baseline SARS-CoV-2 status showed similar  
20 reactogenicity profiles. Of note, three vaccine  
21 recipients reported a fever greater than 40 degrees

1 Celsius as noted in the briefing document.

2           Here is the first part of the systemic  
3 solicited reactions for children 2 through 4 years of  
4 age. Of note, these are different than for the  
5 children in the younger age group based on age-  
6 appropriate reporting. Solicited systemic adverse  
7 reactions in the vaccine recipients generally occurred  
8 at similar frequencies after any dose or with  
9 decreasing frequency with subsequent doses.

10           The median day of onset was one to two days,  
11 and the median duration was also one to two days for  
12 all doses and treatment arms. Of note, vaccine  
13 recipients 2 through 4 years of age reported a fever of  
14 greater than 40 degrees Celsius, as noted in the  
15 briefing document as well.

16           Here's a continuation of the solicited  
17 systemic reactions for participants 2 through 4 years  
18 of age. Solicited systemic adverse reactions in the  
19 vaccine recipients generally occurred at similar  
20 frequencies after any dose or with decreasing frequency  
21 with subsequent doses. The percentages of participants

1 who used antipyretic or pain medication within seven  
2 days of each study intervention are shown as well.

3           The percentage of participants 2 through 4  
4 years of age who reported e-diary data who are also  
5 baseline SARS-CoV-2 positive was 12.6 percent.

6 Subgroup analyses of solicited adverse reactions in  
7 each age group by baseline SARS-CoV-2 status showed  
8 similar reactogenicity profile. The frequencies of  
9 unsolicited adverse events by age group were shown  
10 there. Let me see if I can go back.

11           The most commonly reported adverse events were  
12 consistent with solicited adverse reactions or events  
13 which commonly occur in this age group, such as  
14 infections and injuries considered not related to the  
15 study intervention. The events that were considered  
16 related to vaccine included lymphadenopathy and  
17 hypersensitivity as has been previously described.

18           Analyses for the adverse events of clinical  
19 interest are displayed for both age groups here. The  
20 FDA conducted standardized MedDRA queries or SMQs to  
21 evaluate for constellations of unsolicited adverse

1 events. No new or unexpected adverse reactions were  
2 identified based on SMQ results for either age group.  
3 Lymphadenopathy and hypersensitivity events were noted  
4 in both age groups and were previously seen in older  
5 age groups.

6           For lymphadenopathy, there were three events  
7 reported from both age groups, all from vaccine  
8 recipients and for hypersensitivity -- the incidence  
9 for hypersensitivity events was actually similar  
10 between treatment groups. Most were skin and  
11 subcutaneous tissue disorders commonly seen in this age  
12 group, such as rash, eczema, atopic dermatitis, and  
13 contact dermatitis. There were no vaccine related  
14 events of anaphylaxis reported.

15           Here are the serious adverse events, or SAEs,  
16 for each age group. For the younger age group, 3.1  
17 percent of vaccine recipients and 2.3 percent of  
18 placebo recipients reported SAEs. Most were common GI  
19 or respiratory illnesses or infections that occur in  
20 this age group. None were considered related to the  
21 vaccine. For the older age group, 0.7 percent vaccine

1 recipients and 0.9 percent of placebo recipients  
2 reported SAEs.

3           One participant reported two SAEs of fever and  
4 calf pain, which were considered possibly related to  
5 the vaccine by the investigator. However, the FDA  
6 considered the events to be potentially consistent with  
7 symptoms of viral myositis. There were no notable  
8 differences found in the type, frequency, or severity  
9 of unsolicited AE or serious AEs in either group in  
10 seropositive subjects relative to zero negative  
11 subjects. There are no deaths reported in this study.

12           Now we will review the pharmacovigilance plan  
13 for the Pfizer-BioNTech COVID-19 vaccine. The sponsor  
14 submitted a pharmacovigilance plan to monitor safety  
15 concerns that could be associated with the Pfizer-  
16 BioNTech COVID-19 vaccine. The sponsor identified  
17 anaphylaxis, myocarditis, and pericarditis as important  
18 identified risks and vaccine associated enhanced  
19 disease as an important potential risk. Use in  
20 pregnancy and lactation, vaccine effectiveness and use  
21 in pediatric individuals under 6 months of age are

1 areas the sponsor identified as missing information.

2           The pharmacovigilance plan is for all  
3 indications as it lists the use in pregnancy and  
4 lactation which is not applicable for individuals 6  
5 months through 4 years of age receiving the vaccine.  
6 The pharmacovigilance activities under the EUA include  
7 adverse events reporting, which may come from vaccine  
8 recipients, vaccination providers, the sponsor, or  
9 through the CDC Be Safe program. Reports from vaccine  
10 recipients are voluntary.

11           Both the sponsor and vaccine providers  
12 administering the Pfizer-BioNTech COVID-19 vaccine must  
13 report to VAERS the following information: serious  
14 adverse events irrespective of attribution to  
15 vaccination, any cases of multisystem inflammatory  
16 syndrome, cases of COVID-19 that result in  
17 hospitalization or death. Additionally, following the  
18 approval of Comirnaty, the sponsor was also asked to  
19 submit reports of myocarditis and pericarditis as 15-  
20 day reports to VAERS.

21           The sponsor will also conduct periodic



1 aggregate review of safety data and submit periodic  
2 safety reports at monthly intervals for FDA review.  
3 Furthermore, the sponsor's plans surveillance studies  
4 that are summarized on the next slide.

5           The sponsor's pharmacovigilance activities  
6 also include post-authorization surveillance studies  
7 which covers all indications for use, not just this  
8 pediatric age group. There were four post-  
9 authorization safety studies and one post-authorization  
10 vaccine effectiveness study that include individuals 6  
11 months through 4 years of age. Study C4591009 will  
12 assess the occurrence of safety events of interest,  
13 including myocarditis and pericarditis in the general  
14 U.S. population of all ages in the U.S. Sentinel  
15 system.

16           Study C4591021 is being conducted in Europe  
17 and will assess whether an increased risk of pre-  
18 specified adverse events of special interest, including  
19 myocarditis and pericarditis, exists following the  
20 administration of the Pfizer-BioNTech COVID-19 vaccine.  
21 A sub study of this study is being conducted in Europe

1 and will describe the clinical course of myocarditis  
2 and pericarditis following administration of Pfizer-  
3 BioNTech COVID-19 vaccine.

4           Study C4591036 is being conducted in  
5 collaboration with the National Heart, Lung, and Blood  
6 Institute, Pediatric Heart Network and will  
7 characterize the clinical course, risk factors,  
8 resolution, long-term sequelae, and quality of life in  
9 children and young adults under 21 years of age with  
10 acute post-vaccine myocarditis and pericarditis. Study  
11 C4591014 is a vaccine effectiveness study being  
12 conducted at Kaiser Permanente Southern California that  
13 will include individuals 6 months through 4 years of  
14 age.

15           So next, I'll go ahead and summarize the  
16 benefits and the risks for this age group. The known  
17 and potential benefits include the prevention of  
18 symptomatic COVID-19 based on successful immunobridging  
19 analyses to allow for inference of effectiveness for  
20 individuals 6 months through 4 years of age,  
21 preliminary evidence of vaccine efficacy against COVID-

1 19 and descriptive analyses and the expectation of  
2 greater effectiveness against more severe COVID-19.

3           Uncertainties in the benefits include vaccine  
4 efficacy against emerging SARS-CoV-2 variants, the  
5 long-term effects of COVID-19, the effectiveness in  
6 certain populations, and the duration of protection.  
7 The known and potential risks include reactogenicity,  
8 myocarditis, lymphadenopathy, anaphylaxis, and  
9 hypersensitivity reactions. The uncertainties and  
10 risks include the safety in certain populations and  
11 adverse events that are uncommon or that require longer  
12 follow-up to be detected.

13           Here, I'll end with our voting question for  
14 our Committee members today. "Based on the totality of  
15 scientific evidence available, do the benefits of the  
16 Pfizer-BioNTech COVID-19 vaccine, when administered as  
17 a three-dose series (3 micrograms each dose), outweigh  
18 its risks for use in infants and children 6 months  
19 through 4 years of age?" Thanks so much.

20

**Q&A SESSION**

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**DR. ARNOLD MONTO:** Thank you, Dr. Wollersheim.

Very succinct and careful presentation. Dr. Cohn, you've got your hand raised, followed by Dr. Bernstein.

**CAPT. AMANDA COHN:** Thanks, Dr. Wollersheim.

That was really an incredible presentation. I really appreciate the transparency and clarity. Two questions. One is is it possible for FDA or did you tease out reactogenicity in the population of infants and young children who got vaccinated with that third dose between 8 and 12 weeks? Is it similar to the kids who got vaccinated more towards the median third dose interval that was done in the study?

Then my second question is when you -- is the FDA assessment that the three-dose primary series of Pfizer is based on immunobridging studies meets the criteria compared to two doses of adult vaccine, or are you able to also feel confident that it would be similar to three doses in the adult vaccine?

**DR. SUSAN WOLLERSHEIM:** Thanks, Dr. Cohn, for

1 great questions as always. Your first question is  
2 related to reactogenicity based on the dose interval  
3 between dose 2 and dose 3 if I understand the question.  
4 We did try to do that analysis.

5           From what I recall from that -- I'm sorry I  
6 don't have a slide to show you with those numbers.  
7 There was no significant difference in the  
8 reactogenicity based on dose intervals. Your second  
9 question, I think, is related to comparisons of vaccine  
10 effectiveness following two doses in adults or three  
11 doses of adults; is that correct?

12           **CAPT. AMANDA COHN:** Yes.

13           **DR. SUSAN WOLLERSHEIM:** Okay. Thank you. I  
14 think that's a difficult question to address based on  
15 the data that we have here because our immunogenicity  
16 comparisons are to adults who received the two-dose  
17 primary series. There's further discussion in some of  
18 the benefit/risk profile and within our briefing  
19 document with the benefit of a third dose for adults.  
20 So, I think that that benefit is really reflected by  
21 the variant that's circulating currently, the Omicron

1 variant.

2 I don't know that the data would be available  
3 from the appropriate time periods to make that  
4 comparison at this point, if that makes sense, because  
5 we don't have data pre-Omicron for these younger age  
6 groups.

7 **CAPT. AMANDA COHN:** So, is FDA's assessment,  
8 though, that there would also need to be an additional  
9 dose, a booster dose, in this population?

10 **DR. SUSAN WOLLERSHEIM:** That's a great  
11 question. Thank you. I might defer to Dr. Fink if he  
12 wants to weigh in here because it's a bit beyond the  
13 scope of the data that I presented from the study here.  
14 Thank you.

15 **DR. DORAN FINK:** Yes. Thanks, Susan. Happy  
16 to weigh in. I think we have a situation here where,  
17 as you've seen from the Pfizer presentation and FDA's  
18 independent analysis of the data, we have some very  
19 preliminary vaccine efficacy results after dose 3 that  
20 are limited by a small number of cases and limited  
21 follow-up time, that appeared to suggest that an

1 improvement in protection following dose 3, as compared  
2 to following dose 2. We do consider this estimate to  
3 be preliminary. We consider it to be imprecise and  
4 potentially unstable.

5           So, exactly what the vaccine efficacy is after  
6 dose 3 I think needs further data to inform. We would  
7 expect to get some of these data, hopefully, from  
8 updated analyses from the clinical trial if more cases  
9 are accrued, recognizing, of course, that if the  
10 vaccine is authorized, that will result in unblinding  
11 of placebo recipients so that they can get their three-  
12 dose series -- and also, from real-world effectiveness  
13 data once the vaccine is used.

14           I do want to make it very clear that based on  
15 the totality of evidence that we presented, including  
16 primarily the immunobridging data to the two-dose adult  
17 primary series, as well as a number of pieces of  
18 supportive data including preliminary descriptive  
19 efficacy analyses and other inferential lines of data  
20 that you've seen from Pfizer, we do feel very confident  
21 that the evidentiary standard for benefit for EUA has

1 been met here. I think in terms of what the efficacy  
2 is after a third dose and whether an additional dose  
3 beyond that would be needed is going to require a  
4 little bit more data to sort out. Thank you.

5 **DR. AMANDA COHN:** Thank you so much.

6 **DR. ARNOLD MONTO:** Thank you, Dr. Fink. We're  
7 moving on -- two more questions. We have a hard stop -  
8 - or one more question from Dr. Offit. Dr. Bernstein,  
9 you're next.

10 **DR. HENRY BERNSTEIN:** Thanks.

11 **DR. ARNOLD MONTO:** I'm juggling things here.

12 **DR. HENRY BERNSTEIN:** Great presentation, Dr.  
13 Wollersheim. I just had a question. Could you go to  
14 slide 27, please?

15 **DR. SUSAN WOLLERSHEIM:** Which slide, I'm  
16 sorry?

17 **DR. HENRY BERNSTEIN:** With the Omicron  
18 neutralization analysis that was done, they used a  
19 fluorescent focused reduction neutralization test, and  
20 on slide 27, it shows -- I think it's a slide before  
21 that. Yeah. On that slide, it shows that the post-



1 dose 3 GMTs against Omicron were lower as compared to  
2 the ancestral strain and the Delta variant. What's the  
3 clinical significance of that?

4 **DR. SUSAN WOLLERSHEIM:** Thank you for the  
5 question, and I think that is a great question because  
6 we're not sure. We don't have a correlative  
7 protection. Additionally, this is a non-validated  
8 assay that's been used just to have this information so  
9 that we can see that there's neutralization of these  
10 various viruses. The clinical interpretation, though,  
11 I think is limited at this point in terms of what my  
12 understanding of what this assay shows. I welcome Dr.  
13 Fink if he has additional insights to interpretation of  
14 these numbers as well.

15 **DR. DORAN FINK:** Thank you. I think what we  
16 can say is that the data you see on the slide here  
17 tracks with what we've seen in real-world effectiveness  
18 studies and immunogenicity studies of this vaccine and  
19 other vaccines in older age groups, that the  
20 neutralizing antibody titers are lower for Omicron  
21 compared to Delta and the ancestral strain. And that

1 does correlate with a lower level of effectiveness  
2 against at least more mild disease and in some cases  
3 more severe disease due to Omicron than the Delta  
4 variant and ancestral strain. I don't think we can  
5 conclude anything --

6 **DR. ARNOLD MONTO:** Okay. Final question --

7 **DR. DORAN FINK:** -- specific based on these  
8 titers.

9 **DR. ARNOLD MONTO:** Okay. Dr. Offit --

10 **DR. HENRY BERNSTEIN:** Thank you.

11 **DR. ARNOLD MONTO:** I'm trying to get our  
12 organizers the time to prepare for the OPH. So Dr.  
13 Offit, please.

14 **DR. PAUL OFFIT:** Okay. So, Dr. Wollersheim,  
15 again, thank you for that clear presentation. What I'm  
16 trying to understand, if you look back in December 2020  
17 when we considered the Pfizer/Moderna vaccine as two-  
18 dose vaccines, they were potentially equivalent in  
19 terms of efficacy. Similarly, if you look at the  
20 efficacy for two doses of Pfizer versus Moderna for the  
21 12- to 17-year-old or the 6- to 11-year-old, again,

1 they tracked as being similar.

2           This is the first time you've really seen a  
3 difference in the less than 5-year-old where two doses  
4 of Moderna does offer some level of protection whereas,  
5 that wasn't true at all for the Pfizer vaccine. The  
6 (inaudible) strength were essentially identical, which  
7 is the Omicron (inaudible).

8           I realize these weren't side to side  
9 comparisons, but do you have any sense of why that  
10 would be true, why there was for the first time a clear  
11 difference where Pfizer's didn't present that it would  
12 protect after two doses where Moderna had where they  
13 had perhaps tracked so similarly previously?

14           **DR. SUSAN WOLLERSHEIM:** Thanks, Dr. Offit.  
15 Great question, of course, and it's I don't want to say  
16 impossible. But it's difficult, really, to make the  
17 comparisons between these two vaccines. So, I don't  
18 think we can really move there with the data that we  
19 have. Thank you for the question.

20           **DR. ARNOLD MONTO:** Okay. We can revisit that  
21 question later on because I'm sure it's going to come

1 up again. Thank you to all our presenters. It's now  
2 time for a half-hour break. We will resume at 1:00  
3 p.m. Eastern for the oral public hearing, the OPH.

4 **MR. MICHAEL KAWCZYNSKI:** All right. Thank  
5 you, Arnold. Yes, let's take us to break. Please hold  
6 off, members, for a moment before we go to break.  
7 Studio, please put us on break.

8

9 **[BREAK]**

10

11

#### OPEN PUBLIC HEARING

12

13 **MR. MICHAEL KAWCZYNSKI:** Good afternoon and  
14 welcome back from our lunch break to the 174th Vaccine  
15 Related Biological Product Advisory Committee (VRBPAC)  
16 meeting, day two. I'd now like to hand this meeting  
17 over to our chair, Dr. Monto, as well as Peter Marks.  
18 Take it away, Arnold.

19 **DR. ARNOLD MONTO:** I'd like to welcome you  
20 back and to the Open Public Hearing session. Please  
21 note that both the Food and Drug Administration, and

1 the public, believe in the transparent process for  
2 information gathering and decision making. To ensure  
3 such transparency, at the Open Public Hearing session  
4 of the Advisory Committee meeting, FDA believes that it  
5 is important to understand the context of an  
6 individual's presentation. For this reason FDA  
7 encourages you, the Open Public Hearing speaker, at the  
8 beginning of your written or oral statement to advise  
9 the committee of any financial relationship that you  
10 may have with the sponsor, its product, and if known,  
11 it's direct competitors.

12 For example, this financial information may  
13 include the sponsor's payment of expenses in connection  
14 with your participation in this meeting. Likewise, FDA  
15 encourages you at the beginning of your statement to  
16 advise the committee if you do not have any financial  
17 relationships.

18 If you choose not to address this issue of  
19 financial relationships, at the beginning of your  
20 statement, it will not preclude you from speaking.

21 Dr. Marks, please.

1           **DR. PETER MARKS:** Thanks very much, Dr. Monto,  
2 and thank you to the Open Public Hearing speakers. As  
3 noted, FDA welcomes comments from interested members of  
4 the public during the Open Public Hearing portion of  
5 the Advisory Committee meeting. We welcome and respect  
6 the input about the topics being discussed at today's  
7 meeting. But we don't in any way accept or condone  
8 comments that include offensive remarks or hate speech;  
9 particularly any such remarks directed at a member of  
10 the Advisory Committee or FDA staff. Thanks very much.

11           **DR. PRABHAKARA ATREYA:** Thank you. This is  
12 Prabha Atreya. Before I begin calling the registered  
13 speakers I would like to add the following additional  
14 guidance. FDA encourages participation from all public  
15 stakeholders into decision making processes. Every  
16 Advisory Committee meeting includes an Open Public  
17 Hearing session during which interested persons may  
18 present relevant information or views.

19           Participants during the Open Public Hearing  
20 session are not FDA employees or members of the  
21 Advisory Committee. FDA reminds us that the speaker

1 may present a range of viewpoints. These statements  
2 made during this Open Public Hearing session reflect  
3 the viewpoints of the individual speakers or their  
4 organizations and are not meant to indicate agency  
5 agreement with the statements made. With this  
6 additional guidance I would like to now call upon the  
7 first speaker, Dr. Jasmine King. You have three  
8 minutes to speak.

9           **DR. JASMINE KING:** Hello. I'd ask my first  
10 and only slide be presented. My name is Jasmine King.  
11 My health and life has been completely altered since  
12 July of 2021, when I received (inaudible) during a  
13 vaccination. I was 38 at the time. It does take an  
14 awful lot of courage to open up to a group of strangers  
15 about such personal matters. Then again, the life-  
16 threatening health issues I'm facing have evoked a  
17 level of courage and bravery I could never before have  
18 fathom. Before this vaccination I was active,  
19 energetic, upbeat and my husband and I run an organic  
20 farm, I as the grant writer attorney. I ran, taught  
21 yoga. I very recently had two natural births and was

1 breastfeeding my one-year-old at this time.

2           I ignore the initial hit the vaccine took on  
3 me regarding this is "to be expected" but the  
4 compromise on my immune system started showing within  
5 days. I had previously been able to avoid the dozen of  
6 annual colds my two children get, but after vaccination  
7 I quickly caught their cold and it happened again and  
8 again. Then a topical fungal infection, and a few  
9 weeks in I began experiencing several muscle spasms and  
10 sensory issues. I constantly felt unusually hot burnt  
11 on my skin, or as if something invisible was crawling  
12 on me. How odd, I thought.

13           I had no idea my (inaudible) (audio distorted)  
14 my back, arms, face burned as if scorched by fire. The  
15 pain went deep into my muscles. Zaps and booms were  
16 sounding in my head. My glands all swelled up. My  
17 sweating became abnormal making me intolerant to heat  
18 and my heartrate doubled. Electric pins and needles,  
19 twitches and muscle spasms that were strong enough to  
20 jolt me in my sleep (inaudible). It was all so bad so  
21 that I could not sleep for six weeks.



1           Then in late December, I (inaudible) again, and  
2 it began in a painful manner. What I'm told that  
3 Moderna's trial is (inaudible) zero neurological adverse  
4 effects. There are thousands of individuals like me. I  
5 found this out after testing positive, eventually that  
6 is, for antibody related to sensory (inaudible). I  
7 initially joined a male patient support forum then found  
8 other (inaudible) forums where these actual injured  
9 individuals are congregating for peer assistance.

10           I also learned this upon trying to get into  
11 several (inaudible) neurology clinics -- and they're all  
12 backed up -- many of those injured experienced these  
13 side effects long before I was vaccinated. Yet I wasn't  
14 afforded this knowledge, no disclosures, no PSA, no  
15 federal health agencies and no media coverage about this  
16 whatsoever. Apparent from where I stand it's a missed  
17 opportunity to collect and act on neurological  
18 vaccination risks in the non-child population, to inform  
19 the public and disseminate the trends to medical  
20 providers, particularly neurologists. This lack of  
21 dissemination hurt my ability to be quickly treated.

1 And I want everyone to understand that; it affects at  
2 the patient level.

3 Now I also see some (inaudible) that it is  
4 (inaudible) self-supporting when persons like myself  
5 are going through crises that compares to nothing I've  
6 ever been through in my entire life.

7 (Inaudible) of the non-child population for  
8 years (inaudible). I believe this is the approach  
9 right now that explains why there's so little  
10 discussion of this. I understand from a statistical  
11 standpoint but given what is at stake I do not  
12 understand.

13 **DR. PRABHAKARA ATREYA:** (Inaudible) is up.

14 **DR. JASMINE KING:** Excuse me?

15 **MR. MICHAEL KAWCZYNSKI:** Can you please wrap  
16 it up.

17 **DR. PRABHAKARA ATREYA:** Your time is up.

18 **DR. JASMINE KING:** Absolutely, yes. As you  
19 contemplate the decision to had, please keep in mind  
20 that there are mandates and immense pressured involved  
21 here. I believe there's more room for (inaudible)

1 comparison. For example looking at my age group and  
2 health profile, I had minimum risks in the virus  
3 itself. How do this apply to young children?  
4 Likewise, just because the vaccination -- I'm sorry but  
5 there's a lot of looking at the hospitalization rate of  
6 virus versus vaccine, but you take a case like mine, I  
7 haven't been hospitalized.

8 **MR. MICHAEL KAWCZYNSKI:** Ma'am, you have to  
9 end it here, please.

10 **DR. JASMINE KING:** Okay, well, thank you all.

11 **DR. PRABHAKARA ATREYA:** The next speaker is  
12 Dr. Ashley Serrano. You have three minutes.

13 **DR. ASHLEY SERRANO:** Hi. I have no conflicts.  
14 My name is Ashley and I'm a mother of a three-year-old,  
15 as well as a clinic psychologist who focuses my work on  
16 evaluating and treating youths.

17 I am here again today to strongly urge the  
18 committee to recommend emergency use authorization for  
19 both the Pfizer's and Moderna's vaccines in children  
20 under 5 years. As I mentioned yesterday, when I was  
21 referring to children under 5, Moderna easily met

1 immunobridging endpoints after just two doses for the 5  
2 and younger age group. This will give our children  
3 full protection more quickly when compared to Pfizer's  
4 vaccine, which means we would start the school year  
5 vaccinated. And that's really great news for my  
6 daughter.

7           For children 6 months to 5 years of age,  
8 Moderna's 2-dose series also showed improved efficacy  
9 when comparing it to Pfizer's data against Omicron  
10 after two doses. We know both these vaccines would  
11 eventually require what we now call boosters doses,  
12 implying a third dose for Moderna and perhaps a fourth  
13 for Pfizer.

14           Next slide, please. It took me a long while  
15 to conceive my daughter, but it wasn't without the help  
16 of amazing scientists within the infertility world to  
17 help me. These are just a few of the supplies I used  
18 throughout the many months of infertility treatment.  
19 Many others of these supplies would have been in  
20 various airports and hotel as we are a family who love  
21 to travel. This is also me the night before I was

1 rushed to the hospital via ambulance, and little did I  
2 know that I would be meeting my daughter just a couple  
3 of days later.

4           Who could have known that after my daughter's  
5 first Christmas, would be her last time visiting most  
6 of her family members for over two years? She was just  
7 an infant the last time she saw them in person or at  
8 all. You should see her face when she gets to see her  
9 family members via video. And I can only imagine what  
10 it will be like when she gets to see them in person  
11 once she is fully vaccinated.

12           Slide 4, please. When I had my daughter, I  
13 had so many dreams for her and couldn't wait to share  
14 all of the experiences with her. It was already sad  
15 that we didn't have Toys "R" Us, but once March 2020  
16 came we lost so many other opportunities to visit  
17 family in other countries and states, swim lessons,  
18 birthday parties, and the list goes on.

19           I never would have thought I'd have to take  
20 more than normal precautions at a lake or a playground  
21 to protect us from potentially fatal illnesses. It has

1 always been my goal to protect her, ranging from  
2 (inaudible) prenatal care, to wearing sunscreen, to  
3 receiving all the vaccines to protect against  
4 potentially fatal diseases. As a three-year-old, she  
5 is now asking to go inside stores, restaurants and  
6 people's houses. All things that were completely  
7 normal for us at three years old. But I often have to  
8 say no because my job is to protect her. All she wants  
9 to do when she is vaccinated is to go into a restaurant  
10 and have an indoor (inaudible) birthday party.

11           As a clinical psychologist I evaluate zero to  
12 5-year-olds for autism. When COVID-19 came, I  
13 collaborated with colleagues to create a virtual  
14 evaluation to allow these children to obtain  
15 appropriate treatment. We continue offering these  
16 virtual evaluations because this age group can't be  
17 vaccinated yet. Many families don't feel comfortable  
18 taking their unvaccinated children to playgrounds to  
19 strengthen their skills. We continue offering  
20 telehealth, but what happens when telehealth is no  
21 longer covered by insurance? Or when the public health

1 emergency expires next month? Now is the time to  
2 approve these vaccines for this age group.

3           Finally, while many people resume life as  
4 normal, there are many kids and teenagers who have not.  
5 My family has not since my three-year-old continues to  
6 be ineligible for the vaccine, 399 day since our  
7 teenagers became eligible to be vaccinated. Let's help  
8 our future generation start living now and allow them  
9 to be protected against the harms of COVID-19. Thank  
10 you.

11           **DR. PRABHAKARA ATREYA:** Thank you. The next  
12 speaker is Mr. Michael Baker.

13           **MR. MICHAEL BAKER:** Good afternoon members of  
14 the committee. Thank you for listening to my  
15 statement. I have no financial conflicts of interest.  
16 I'm a father of two wonderful children, age one and  
17 three. And I would like to take a moment to talk about  
18 how the past two years have impacted our lives. This  
19 slide is a non-exhaustive list of some of the things  
20 that we have missed out on. And although what I've  
21 shared here is specific to my family, our experiences

1 are in no way unique. Our children have all to one  
2 degree or another been subject to the largest social  
3 experiment in history. And it will be many years  
4 before we fully understand the developmental impact  
5 that this pandemic has caused.

6           My wife and I have had to continuously weigh  
7 the risk of disease against the risk of stunned  
8 development for our children. And every single day I  
9 fear for them. I want to make the best choices for my  
10 children as I possibly can. And I ask myself  
11 constantly, have we made the right choice.

12           And yet, for all that burden, I am endlessly  
13 grateful. We have been incredibly privileged to have  
14 had the option to make these choices. Not all parent  
15 in our position have had the choice to do what they  
16 thought was best. This problem has only become worse.  
17 Pediatric infections have skyrocketed as the rest of  
18 the country has in many ways completely moved on. All  
19 I'm asking is now that the rest of the country can  
20 choose not to care about COVID, that I have the choice  
21 to vaccinate my children. And I have the choice to do



1 it in the most timely fashion possible.

2           We have utterly failed as a society to protect  
3 those among us who cannot protect themselves. There  
4 have been as you know nearly 1600 pediatric deaths due  
5 to COVID-19 as of June 12th, thousands more  
6 hospitalization, and an unknown number of future  
7 potential complications. As we can no longer rely on  
8 any sort of layered medication to control the spread,  
9 vaccination is our last remaining hope. It must be  
10 offered as an option with all due haste.

11           And this committee should consider the  
12 differences between each vaccine through a lens of  
13 equity. There is a vast difference for working  
14 families between making it to two appointments versus  
15 three. And there is a vast difference in waiting an  
16 additional seven weeks to be fully vaccinated.

17           I have been listening to today's meeting and I  
18 want to reiterate that I understand a booster dose will  
19 likely be needed at some point. My primary concern as  
20 a parent is not to avoid symptomatic illness; it is to  
21 keep my children out of the hospital and safe from

1 serious harm.

2           My wife and I have succeeded in keeping COVID  
3 out of our household thus far. But now we are calling  
4 on you to help us take one small step back into  
5 normalcy. We are asking for options. For us, the  
6 superior option will be vaccination with Moderna. For  
7 other it may be Pfizer. We ask that you afford us, and  
8 all parents who wish to protect their children, the  
9 possibility to make that choice now. Thank you for  
10 your time.

11           **DR. PRABHAKARA ATREYA:** (AUDIO/VIDEO BLANK -  
12 TECHNICAL DIFFICULTIES).

13           **MS. FATIMA KHAN:** Thank you for allowing me to  
14 speak today. I have no conflicts. My name is Fatima  
15 Khan, and I'm a mother to a six and four-year-old. I'm  
16 also a cofounder of Protect Their Future, and entirely  
17 volunteer grassroots group of physicians, parents and  
18 activists, advocating for health leader to prioritize  
19 children including allowing our youngest equitable  
20 access to safe COVID vaccines.

21           We received no funding from any individuals or

1 corporation. Our group is composed of thousands of  
2 families who accept that COVID can cause significant  
3 harm to children, and that vaccines offer a strong  
4 layer of protection against not only infections but  
5 also long-term complications like MIS-C, long COVID,  
6 neurological effects, and in worse cases death. Based  
7 on all available data, we support emergency use  
8 authorization for both Moderna and Pfizer COVID  
9 vaccines.

10           Our public health leaders have left families  
11 of children under 5 behind, making any semblance of a  
12 balance life difficult to achieve. As a cofounder of  
13 Protect Their Future, I hear from families across the  
14 country struggling to keep their children safe, while  
15 also balancing real life necessities such as work,  
16 school and other obligations. Not a day goes by that I  
17 don't hear of a parent lamenting that their child  
18 either contracted COVID, or was exposed, despite taking  
19 all reasonable precautions. Each parent feels an  
20 overwhelming sense of failure and defeat because they  
21 weren't able to keep their child protected until a

1 vaccine was available for their age group.

2           We know that families of color and low-income  
3 families have greatly suffered. These are often the  
4 families who don't have the choice to keep their  
5 children home. And who must make impossible decisions  
6 between protecting their loved ones and bringing food  
7 to their tables. Delaying vaccines to our youngest  
8 only exacerbates these disparities.

9           Almost eight months out from when children 5  
10 and older could access vaccines, millions of children  
11 under 5 have been infected. Moreover, the majority of  
12 hospitalization and deaths recorded in children under 5  
13 occurred during the Omicron surge, a time when trials  
14 were meant to have already been completed in this age  
15 group. Anymore death and illness for our youngest, and  
16 most vulnerable, is unacceptable. Every day of  
17 inaction leads to more suffering and damage.

18           As others stated yesterday, Moderna was shown  
19 to not only meet trial criteria for the 2-dose  
20 regiment, but also had a higher efficacy rate against  
21 Omicron when compared to Pfizer's 2-dose series. It

1 seems to be the case that Pfizer's efficacy improves  
2 significantly after a third dose. And it can be  
3 inferred that a third dose of Moderna, like boosters  
4 for other age groups, will yield even better results  
5 than the 2-dose regiment.

6 Moderna also showed higher antibody levels  
7 after just two doses than Pfizer's 3-dose series. Trial  
8 and real world data are proving Moderna may be offering  
9 superior protection. This is why it is critical to  
10 approve both vaccines today, so that parents have  
11 options and so that our children can be fully  
12 vaccinated before school. If they need additional  
13 dosage later that can be evaluated as needed.

14 Children like my daughter, who will proudly  
15 join the ranks of junior kindergarten this fall, must  
16 have the same access the rest of their school-age peers  
17 has. We have waited too long and too many families  
18 have suffered already. Please ensure that our children  
19 are protected with these highly safe and effective  
20 vaccines. Thank you.

21 **DR. PRABHAKARA ATREYA:** Thank you. The next

1 speaker is Mr. Nicholas Giglia.

2           **MR. NICHOLAS GIGLIA:** Thank you for the  
3 opportunity to speak. I have no conflicts. I am  
4 Nicholas Giglia, father of two great kids, a  
5 supernaturally empathetic son, and an energetic and  
6 curious daughter who participated in the Pfizer trial.  
7 I'm so grateful we could contribute in a small way to  
8 this wonderful scientific achievement. And I look  
9 forward to one day telling my little girl how she  
10 helped saved the world.

11           It is vital to approve both these vaccines.  
12 The 3-dose regiment for Pfizer and the 2-dose regiment  
13 for Moderna have both met immunobridging, the primary  
14 goal of the study, without any major safety concerns.  
15 Moderna's 2-dose regiment would allow kids, like my  
16 son, to start preschool or kindergarten fully  
17 vaccinated. And the Pfizer vaccine provides  
18 protections spread out over three doses. Parents and  
19 children deserve a choice, especially since our only  
20 choice up to now has been hope and pray.

21           We have, through a combination of precautions,

1 remote work and luck, kept COVID at bay so far. This  
2 has come at a high price of my mental health, my  
3 waistline, sleepless nights, deferred dreams, and the  
4 (inaudible) that I wish I could've given my kids.  
5 Every decision requires detailed and exhausting risk  
6 calculation. And I wonder at every daycare drop off if  
7 today is the day our luck runs out.

8           When exposed, the kids are home for seven to  
9 ten days, where we have to be full-time employees and  
10 full-time parents while feeling like we're failing at  
11 both. We have navigated a world without protection or  
12 empathy, while those with the luxury have moved on from  
13 COVID. We have heard constantly that we have the tools  
14 to end the pandemic while we were prohibited from using  
15 these tools to protect our children.

16           We must grant children under 5 access to these  
17 two safe and effective vaccines, especially during  
18 surge. These applications are welcome, but this  
19 meeting should not be considered a victory. Our  
20 governments have abandoned the youngest children,  
21 allowing millions to be infected with a novel virus of

1 unknown long-term effects, without the protection  
2 vaccines offers.

3           Process is important and necessary. But  
4 (inaudible) route we've taken to get here, including  
5 unexplained trial expansions, cancelled meetings,  
6 deferred applications, and almost a year of promises of  
7 release in the coming weeks, has rob this day of the  
8 joy I expected to feel. Real families have been  
9 impacted by every twist and turn in this process. In  
10 my line of work it is vital to take an honest look at  
11 issues to prevent recurrence. And it must happen here  
12 as well.

13           We must receive for approval, two detailed  
14 transparent (inaudible) reviews to understand how to  
15 streamline the approval process, for the Omicron  
16 specific booster, that I'm sure is coming, and  
17 unfortunately the next pandemic, without sacrificing  
18 the rigor I saw firsthand in the Pfizer's trial.

19           There has been much sacrifice to get here,  
20 from health workers, trial families, the hundreds of  
21 children who have died from COVID, and the countless



1 children and families that may never be the same. We  
2 must honor these sacrifices by approving both  
3 applications while acknowledging we can never leave our  
4 children behind again. Thank you.

5 **DR. PRABHAKARA ATREYA:** Thank you. The next  
6 speaker is Lauren Dunnington. You have three minutes.

7 **MS. LAUREN DUNNINGTON:** Good afternoon. My  
8 name is Lauren Dunnington. I work in global public  
9 health, and I'm the parent of two children under 5, in  
10 w=Washington State. I have no conflict.

11 My comment today is broadly in support of  
12 emergency use authorizations for both the Moderna and  
13 Pfizer vaccines for children under 5. Just last week,  
14 my kids had yet another COVID-19 exposure at daycare.  
15 The toddler came home with a fever, and I felt my  
16 stomach knot up. We had COVID in December and I kept  
17 asking, what's the impact going to be as a repeat COVID  
18 infection in my unvaccinated child. In May, my  
19 friend's four-year-old was hospitalized due to COVID-  
20 19. I ask that parent what she'd like me to say to the  
21 FDA on her behalf. Her response was, my daughter was

1 not yet eligible for a vaccine, and public health  
2 protections like masking had ended. A vaccine could  
3 have offered my daughter protection and prevented a  
4 four-night hospital stay.

5 I remain concerned about COVID-19 and its  
6 sequelae. And I want more tools in my toolbox to  
7 protect my kids, especially my toddler who cannot mask  
8 safely. We've seen increased incidents of diabetes,  
9 multi-systems inflammatory syndrome, myocarditis, brain  
10 fog and even potentially hepatitis in kids with a  
11 history of COVID-19 infection.

12 We know that these mRNA vaccines are safe and  
13 effective. Nine million kids over 5 have received an  
14 mRNA COVID vaccine in the United States. And in  
15 Germany, tens of thousands of under 5 have been safely  
16 vaccinated off label.

17 It's been a long anxious and frustrating wait,  
18 especially knowing now that the FDA has had Moderna's  
19 data to review since April. I cannot know the FDA's  
20 inner workings, but I can say that the lack of  
21 transparency, as to why the Moderna under 5 review has

1 taken longer than any other age cohort, has made me  
2 feel like vaccinating my kids was not a priority for  
3 the FDA.

4           But, I'm grateful that were finally here. And  
5 I have some important requests about how we move  
6 forward. First, please approve both vaccines. The  
7 data shows that we have two effective options for our  
8 kids. And families deserve a choice based on their  
9 circumstances. We know that boosters and a Moderna  
10 third dose are likely to come in the future. But as  
11 the parent of a child starting kindergarten at the end  
12 of summer, I would like the option of the 6-week  
13 Moderna series that show's superior immunobridging  
14 after two doses, to give my child the best protection  
15 as she begins the school year. This shorter series  
16 also reduces the burden on families who use public  
17 transit or have to take time off work to get kids  
18 vaccinated. The 13-week Pfizer series will leave  
19 incoming kindergarteners with less protection when  
20 school starts.

21           I also want to emphasize access. I'd like to

1 see emergency authorization for pharmacists to be able  
2 to vaccinate children under age 3. Enabling pharmacies  
3 to vaccinate our youngest would reduce the bottlenecks  
4 at pediatric clinics where providers will now have to  
5 accommodate vaccination on top of a regular patient  
6 workload.

7           And finally, I want to mention boosters.  
8 Looking ahead, our youngest kids must get on the same  
9 track as adults with access to updated boosters that  
10 protect against new COVID-19 variants. Delay with EUA,  
11 vaccine access, and boosters have real life  
12 consequences for our families. Every single day  
13 matters for our kids. Thank you and please approve  
14 these vaccines for under 5.

15           **DR. PRABHAKARA ATREYA:** Thank you. The next  
16 speaker is Kathlyn Hinesley.

17           **MS. KATHLYN HINESLEY:** I have no conflicts.  
18 Hello, everyone. I'm Kathlyn Hinesley, with Friends of  
19 the Constitution. Today I'll be presenting the facts  
20 for your consideration. But I want you to know that I  
21 fully understand how hard it is for you to be in your

1 position, and being literally inundated with facts.  
2 Everyone wants to do the right thing, but what is the  
3 right thing? That's a question that can be  
4 mindboggling at that. I'm hoping that what I say today  
5 will relieve some of the stress and fill you with the  
6 clear and peaceful understanding of the truth.

7           And now for the promised facts, the FDA is  
8 legally prohibited from approving any biological  
9 product for emergency use unless all of the following  
10 conditions are met. There must be an emergency that  
11 poses the risk of death to the target group. The  
12 product must be effective in preventing the disease.  
13 It must be safe, and finally the benefits must outweigh  
14 the risks.

15           With regard to the first point, children  
16 without comorbidities who acquire COVID-19 have a 99.98  
17 percent survival rate; there is no emergency. Moving  
18 forward to effectiveness, a study by Carl A. Bidy  
19 (phonetic) which includes a data analysis of 145  
20 countries found that COVID-19 vaccines were, in fact,  
21 associated with a 38 percent increase in COVID cases

1 and a 31 percent increase in deaths. Could these  
2 vaccines be negatively affecting immunity?

3           The number of severe adverse events, affecting  
4 children ages 5 to 17, reported to VAERS as of June 3rd  
5 was 8,811 including 114 deaths and 1,346 cases of  
6 myocarditis a condition that can be fatal. We can  
7 assume that if these vaccines are authorized, some  
8 babies will die. The benefits of these vaccines are  
9 questionable and the risks are clear.

10           Think about your personal priorities, your  
11 concerns for your reputation, your job, the approval of  
12 family and friends, and issues concerning the financial  
13 security of you and your loved ones as well as your  
14 private thoughts about some of the information you have  
15 reviewed. These concerns do matter, but there is  
16 something that matters more. If these vaccines are  
17 authorized, some babies will die.

18           If you were alone and saw a baby of six month  
19 old right in front of you, would you yourself take a  
20 (inaudible) and kill that child? My guess is the  
21 answer will be no. And yet, if you participate in

1 authorizing these dangerous injections for this age  
2 group, you in fact will be doing that. How would you  
3 feel about that at the end of your life when none of  
4 the other things matter? How would your soul feel?  
5 That's what you need to ask yourself in making the  
6 right decision. Thank you very much.

7 **DR. PRABHAKARA ATREYA:** Thank you. The next  
8 speaker is Melissa Braveman. You have three minutes.

9 **MS. MELISSA BRAVEMAN:** My name is Melissa  
10 Braveman. I'm a pediatrician and a mother. I have no  
11 conflicts. I implore you to recommend EUA of the  
12 Moderna vaccine presented today. Personal freedom  
13 arguments have led to removal of nearly all mitigation,  
14 effectively forcing parents to choose between  
15 safeguarding their children and participating in  
16 society. Under 2s can't mask. 2 to 4s don't mask  
17 well. We must provide parents the choice to vaccinate  
18 their children when benefits so clearly exceed risks.

19 (Inaudible) this vaccine offers the more  
20 efficacy against symptomatic Omicron in young children  
21 as is afford to adults. And this is so much better

1 than nothing. We can expect Moderna's booster will  
2 further improve protection in young children. And I'm  
3 thrilled these studies are underway.

4           Crucially, Moderna's current mRNA vaccine  
5 continues to offer robust protection against severe  
6 Omicron disease in adults. And we have every reason to  
7 expect the same will hold true for young children.  
8 And, it will provide proven protection before the new  
9 school year begins.

10           This vaccine is also incredibly safe by the  
11 FDA usual rigorous standards, which is fantastic.  
12 Thank goodness we are finally here. But this day is  
13 bittersweet. The FDA must adapt its approach so that  
14 young children's access to updated vaccines and  
15 therapeutics doesn't continually lag 18 months behind  
16 adults. It's for this very purpose of strengthening  
17 the nation's public health protection during a public  
18 health emergency that EUA exists.

19           Yet there was no appearance of urgency with  
20 respect to our youngest. The long wait endured,  
21 through both the conventional pediatric trial design,



1 and the unanticipated delays, have been measured by  
2 families not in units of time, but rather by extended  
3 isolation and excruciating sacrifice, and tragically by  
4 vaccine preventable disease and disability, and in some  
5 cases death. It has been incredibly offensive to hear  
6 this wait trivialized as children died.

7           Evidence-based medicine, as I know it, entails  
8 making the best possible decisions based on the  
9 available information. Not being absolved with the  
10 responsibility to take any action at all while awaiting  
11 a perfect body of evidence that requires years to  
12 accumulate as lives hang in the balance. In this  
13 (inaudible) I ask first, why were age de-escalation  
14 conventions (inaudible) adhered to so strictly during  
15 the pandemic?

16           Second, when will the FDA (inaudible) the  
17 exaggerated concerns about fever and (inaudible)  
18 seizure that have impeded vaccine progress and resulted  
19 in Pfizer's vaccine being under-dose? The  
20 pathophysiology, that is the science, doesn't support  
21 fever phobia.

1           Third, why was the review of Moderna's data  
2 delayed? These decisions have profound implications  
3 for parents and children who are still waiting,  
4 suspended in time, 18 months after the members of this  
5 committee became vaccine eligible. In sum, how will  
6 the FDA evolve so that children lives are speared? Who  
7 among you will champion this change?

8           I am pleading with the FDA to prioritize  
9 actual children's lives over an unattainable  
10 unimpeachable abstraction, a perfect medicine. Please  
11 approve Moderna's lifesaving vaccine and please don't  
12 put children in this position again.

13           The FDA must adapt if it hopes to maintain the  
14 trust and respect of (inaudible) parents. We simply  
15 cannot let any more children die, or suffer  
16 unnecessarily, and still hold our heads high as  
17 physicians or as a nation. Thank you.

18           **DR. PRABHAKARA ATREYA:** The next speaker is  
19 Congressman Louis [sic] Gohmert. You have three  
20 minutes.

21           **CONGRESSMAN LOUIE GOHMERT:** Yes. Thank you

1 very much. There are many unanswered questions  
2 regarding the safety and efficacy of COVID vaccines,  
3 especially for babies and young children. I'm deeply  
4 concerned that the push to vaccinate these children is  
5 nothing more than a dystopian experiment with unknown  
6 consequences. Some of us have outlined these questions  
7 in a letter to VRBPAC, but have not received any  
8 answers. And I pose some of them here. The letter's  
9 at my website, gohmert.house.gov, and my Twitter  
10 account @replouiegohmert.

11 But number one, why has the FDA refused to  
12 release the hundreds of thousands of pages of data from  
13 preapproval manufacturers' studies, post-approval  
14 adverse events data, and other post-approval  
15 manufacturers' data?

16 Number two, what is the cardiac risk factor in  
17 administering these COVID vaccines to children?

18 Number three, world renowned immunologists  
19 have raised concerns about potential antibody dependent  
20 enhancement, ADE, resulting from COVID vaccines. And  
21 since ADE was a problem in prior unrelated respiratory

1 vaccines trials, we need to know what (inaudible)  
2 studies, if any, the FDA has that is used regarding  
3 potential ADE from COVID vaccines in children 5 and  
4 under, or any age groups. Can the FDA affirm that  
5 there's no risk of ADE for vaccinated children?

6           Number four, if approved and widely used among  
7 children 5 and under, how many lives, if any, does the  
8 FDA estimate will be saved next year? Given the  
9 injuries reported in the FDA's VAERS system, how will  
10 FDA evaluate serious vaccine injuries versus serious  
11 COVID outcomes?

12           Number five, is it possible that the proposed  
13 COVID vaccines in young children would create increased  
14 risk from future novel COVID variants?

15           Number six, why has the FDA recently lowered  
16 the efficacy bar for COVID vaccines for youngest  
17 children? This change significantly lowers the  
18 expected benefits from any COVID vaccination for young  
19 children, and it's of particular concern given that  
20 over 70 percent of that age cohort are already  
21 seropositive.

1           These questions and others are critical and  
2   deserve thorough answers by FDA and VRBPAC, prior to  
3   any emergency use authorization with the accompanying  
4   protection from liability for all harm done. In  
5   conclusion, some of us have grave concerns that in  
6   balancing the risks to rewards here, all the risks are  
7   to the innocent children, and all the billions of  
8   dollars of rewards go to the government protected  
9   pharmaceuticals. Leaving me to wonder, if republicans  
10  get in majority may need to have a bill -- I'm working  
11  on it now -- to allow civil and criminal liability to  
12  vaccine providers and accessories, despite an EUA,  
13  which should force more sensitivity to vaccine harm to  
14  our young children. We got to care more about the  
15  children. And I appreciate the time to express this.

16           **DR. PRABHAKARA ATREYA:** Thank you. The next  
17  speaker is Dr. Heshie Klein. You have three minutes,  
18  sir.

19           **DR. HARVEY (HESHIE) KLEIN:** Thank you for  
20  allowing me to speak. I'm Heshie Klein. I have no  
21  conflicts. (Inaudible) of June 10th RFK said -- and

1 you have all the details so I'll just mention the main  
2 points. There is no COVID emergency for children.  
3 That's number one. Number two, the vaccines do not  
4 prevent transmission. They do not prevent infection.  
5 Number six, the Pfizer clinical trial for children, 2  
6 through 4-year-old, failed to meet the FDA specified  
7 requirements of COVID vaccine EUAs. The proposing  
8 views of product on a schedule that failed FDA  
9 established criteria in its clinical trial.

10 On Page 117, of Moderna's submission, they hid  
11 their clinical data and instead used a computer model  
12 assimilation, where they adjusted the parameters to  
13 give them the results they wanted. Then on page 118,  
14 they say the risk of myocarditis was assessed using a  
15 7-day risk window. A 7-day risk window, (inaudible)  
16 injection, how is that for long-term study?

17 Pfizer claims that they did a study of 4,526  
18 participants, 6 months through 4-year-old. This of  
19 course is a lie. Like Moderna, Pfizer found ways to  
20 whittle down the numbers of participants, to force the  
21 data to fit a predetermined fictional narrative.

1 Pfizer has a unique problem, and this may be one reason  
2 why it has taken them so long to get to the application  
3 stage. After Pfizer thought that this clinical trial  
4 in kids was going to work, so they un-blinded it on  
5 September 28, 2021, and they started vaccinating the  
6 placebo group to destroy the control and eliminate any  
7 long-term safety data, on November 3rd, 2021.

8           Then in early December the data showed that  
9 the trial had failed. So Pfizer had to scramble to  
10 enroll even more kids in the attempt to save the  
11 clinical trial with a third dose. (Inaudible) becomes  
12 a complete muddle because Pfizer had to refer to the  
13 blinded period (inaudible) before September 28th, the  
14 un-blinded crossover period after September 28th. And  
15 then the post-protocol amending six period because they  
16 wanted data cutoff of April 29th.

17           I pray that you realize that if you choose to  
18 ignore the obvious that Moderna and Pfizer are lying,  
19 then you'll be doing a great disservice to humanity.  
20 You know that all it takes is for you to win is for  
21 good people to say nothing. If you remain silent and

1 do not call them on their lies, you're allowing Moderna  
2 and Pfizer to lie to the American public. And at what  
3 cost to human lives?

4 In the (inaudible) wanted to kill all the  
5 Jews, (inaudible). Do not think you'll be able to  
6 escape in the king's palace any more than the rest of  
7 the Jews. Or if you persist in keeping silent at a  
8 time like this, relief and deliverance will come to  
9 Jews from some other place and you and your (inaudible)  
10 will perish. And who knows if it was for just such a  
11 time as this that you obtained (inaudible) position.

12 We are at a cosmic turning point in the  
13 history of the world. We are in a war between good and  
14 evil. And who knows if it was for just such a time as  
15 this that you obtain you position under VRBPAC.

16 You have a once in a lifetime opportunity to  
17 do the right thing for humanity and for God. And all  
18 and you will be remembered in the history books for  
19 eternity. I pray for you that you look in your hearts  
20 and souls and find the courage to stand up to big  
21 pharma, like (inaudible) stood up to (inaudible) and



1 saved all the Jews. You have the opportunity to save  
2 humanity and the world.

3 **DR. PRABHAKARA ATREYA:** Your time has  
4 (inaudible). Please, wrap up.

5 **DR. HARVEY (HESHIE) KLEIN:** Pfizer and Moderna  
6 has not met requirements, and should not approve -- you  
7 know that. Stand up against them on the side of God,  
8 on the side of good, and may God smile on you always  
9 and in all ways.

10 **DR. PRABHAKARA ATREYA:** (Inaudible) your time  
11 is up. The next speaker is Kailey Soller. You have  
12 three minutes.

13 **DR. KAILEY SOLLER:** Hello. My name is Dr.  
14 Kailey Soller. I'm a Ph.D. chemist. And I have no  
15 conflicts at all today. Thank you so much for the  
16 opportunity to speak today. I'm a Ph.D. chemist, but  
17 even more importantly I'm a mom of an under 2-year-old.  
18 I spoke emotionally yesterday on all the reasons why  
19 parents are desperate to vaccinate their children under  
20 5. Today I'm here to speak very scientifically and  
21 logically to ask you to make the only logical decision

1 available, which is to approve both the Pfizer and  
2 Moderna vaccines for this youngest age group, based on  
3 three points.

4           Number one, these vaccines, first and  
5 foremost, have been proven to be safe. Number two,  
6 these vaccines are effective. And number three,  
7 authorizing these vaccines gives all parents the  
8 ability to make the choice that they deem best for  
9 their family.

10           (Inaudible) points one and two. These  
11 vaccines are safe and effective. For all other age  
12 groups, when the vaccines have been proven to be safe  
13 and effective, we have approved after careful  
14 scientific review and without hesitation, we have  
15 authorized the vaccine.

16           I would like to thank the sponsors, as well as  
17 the FDA, CDC and the ad-hoc members for all of their  
18 dedication to a rigorous and complete scientific review  
19 and presentation of the data. It's very clear from the  
20 data that these vaccines are safe, and the benefit of  
21 vaccination helps decrease the risks associated with

1 COVID infection.

2           Beyond prevention of symptomatic infection, in  
3 addition, there's additional benefit of the cellular  
4 responses which helps prepares the immune system and  
5 the body to fight off future infection. This is harder  
6 to measure, but can be logically and scientifically  
7 inferred by the multitude of data that we have from  
8 older age cohorts and our knowledge of how vaccination  
9 and immunity work in general.

10           Regarding point three, and allowing parents a  
11 choice. Authorizing these vaccines gives all parents  
12 access to either choice that they desire to make for  
13 their children. For parents without access to the  
14 choice that we desire, which would be to (inaudible)  
15 their children, we're desperate for this choice. The  
16 pandemic has moved into a personal risk/benefit  
17 analysis stage where we are encouraging individuals to  
18 self-assess their risk and make decisions about their  
19 own house. Parents who assess that the risk/benefit of  
20 these vaccines versus COVID infections have two choices  
21 to consider, as it is clear that COVID infection will

1 likely become inevitable.

2           Number one, their child could get COVID  
3 without having been vaccinated, or number two, their  
4 child could get COVID with having been vaccinated.  
5 However, only one of these options today is available  
6 to parents under 5. However, my choice from these two  
7 options would be number two, to vaccinate my child,  
8 which is not available to me today.

9           However, today, we have the logical option,  
10 which is based on the scientific evidence that has been  
11 amassed indicating that both of these vaccines are safe  
12 and effective. And we need to allow access to both of  
13 these risk-based decisions options for parents. And  
14 authorize both of these vaccines. I will vaccinate my  
15 daughter as soon as possible. I don't want a vaccine  
16 mandate. I don't want to force other parents to do the  
17 same, but I want the choice. And I'm asking for that  
18 choice that I desire to make.

19           For parent who choose option one, decisions  
20 made today of authorization would not have to change  
21 that choice. So for me and many others, the decision

1 without the authorization of these vaccines would be  
2 absolutely life-changing. I urge you to make the most  
3 logical and fact-based decision today, allow us the  
4 decision to vaccinate our children and empower us as  
5 parents to protect our children. Thank you so much for  
6 your time today. And thank you so much for your  
7 dedication to the scientific process.

8 **DR. PRABHAKARA ATREYA:** Thank you. The next  
9 speaker is Shae Lynn. You have three minutes.

10 **MS. SHAE LYNN:** Good afternoon. I'm Shae, and  
11 I have no financial involvement in this discussion. I  
12 am a mother, former educator, director, and recently  
13 worked as a tech manager developing startups in the  
14 health space. I was never exposed to COVID-19. My  
15 children have also been enrolled in private schools  
16 with zero exposures. Please recall these products  
17 immediately. Do not harm our low-risk children. They  
18 do not need myocarditis from long (inaudible) COVID  
19 vaccines adverse reactions. We demand informed  
20 consent.

21 As a parent I wanted to do the right thing to

1 protect my children against COVID-19. So I received  
2 the first dose of Pfizer on April 3rd. Little did I  
3 know this would be the worst day of my life. After an  
4 hour I called 911, due to an anaphylactic reaction. I  
5 never experienced anything like this in my entire life.  
6 My heart was racing. I felt so weak, disoriented and  
7 vertigo, almost like I was going to faint. I had  
8 severe chest pains. I couldn't breathe due to throat  
9 closers (inaudible). I felt feverish, but I was fine  
10 just an hour ago.

11 My family was present, but they didn't know  
12 what to do. We just wanted to do the right thing. We  
13 were warned (inaudible) the vaccine would be safe, as  
14 our entire family and friends were all vaccinated. But  
15 I felt completely betrayed and lied to. I had no other  
16 choice but to call 911 for help after my Pfizer  
17 vaccine. I was asked to stay on the phone until  
18 paramedics arrived, to make sure I did not faint.

19 I honestly thought I was dying. And I wasn't  
20 sure if I was having a heart attack. I've always been  
21 incredibly healthy and in excellent shape. I felt like

1 my entire life flashed before my eyes. My vision was  
2 very blurry. And I couldn't stop shaking. I'm still  
3 shaking right now, 14 months later.

4           The paramedics finally arrived and advised me  
5 to take Benadryl, and I should be admitted into the ER  
6 right away. They assured me they would not let me die,  
7 but I realize they didn't know about adverse reactions.  
8 It seemed like no one was really prepared to deal with  
9 allergic reactions. It almost seemed like a drug  
10 overdose. I wouldn't really know since I never take  
11 medication nor do I drink alcohol.

12           At the ER I was only monitored and prescribed  
13 an EpiPen, then discharged immediately. My doctor  
14 didn't feel the need to do any further testing. I  
15 received no explanation other than I had an allergic  
16 reaction. I left feeling confused and I still didn't  
17 feel well. And now I had to prepare to deal with  
18 allergic reactions when I never had any severe  
19 allergies prior. I only had a minor rash as a child  
20 due to amoxicillin.

21           Prior to leaving the ER, I remember the ER

1 doctor being slightly confused and clearly stated only  
2 elderly people die from these issues. I was surprised  
3 he would even admit to that considering my elderly  
4 relatives were just vaccinated. I felt so alone, so  
5 lost, so confused with no answers. I felt dizzy. My  
6 vision was affected. I had to take Benadryl and  
7 Tylenol for a week straight. They wouldn't prescribe  
8 anything else for me. They didn't think this was going  
9 to be long term.

10 I contacted my doctor almost daily. My heart  
11 felt weird; it felt like flutters. I wrote emails for  
12 answers to my doctor. No one knew anything. I felt  
13 like I was being completely ignored and my symptoms  
14 were dismissed. My doctor denied referrals to  
15 cardiology, neurology, and denied me of an MRI. I kept  
16 calling and hoping to get new doctors on call for  
17 answers to urgent care and Zoom visits.

18 One doctor eventually prescribed me blood  
19 pressure medication for palpitations; it was for  
20 (inaudible). Did she realize I'm breastfeeding? I had  
21 the worst nightmares and ringing in my ears. I



1 couldn't sleep. I was afraid I would never wake up  
2 again. My doctor --

3 **DR. PRABHAKARA ATREYA:** Ms. Lynn? Your time  
4 is up; please could you wrap it up.

5 **MS. SHAE LYNN:** My doctor advised me to  
6 purchase blood pressure monitor and check my blood  
7 pressure daily. It was really high. I never  
8 experienced this issue prior. I also had internal  
9 tremors very similar to Parkinson. My legs were weak  
10 and felt numb. I kept thinking I'm too young to  
11 develop Parkinson or become paralyzed.

12 After two weeks of being on the heart monitor,  
13 I quit taking my medication as side effects stated it  
14 may cause heart failure. I was still breastfeeding and  
15 I'm worried that my child will experience long-term  
16 issues from these vaccines and adverse reactions, and  
17 affect his development. He's now under evaluation and  
18 may need to see (inaudible) --

19 **MR. MICHAEL KAWCZYNSKI:** Ma'am? Ma'am, you  
20 have to stop. We have to move on. My apologies. Next  
21 speaker.

1           **DR. PRABHAKARA ATREYA:** Kate Schenk. You have  
2 three minutes.

3           **MS. KATE SCHENK:** Good afternoon. Thank you  
4 for allowing me the opportunity to speak today. My  
5 name is Kate Schenk. I have no conflicts. I am the  
6 mother of three children, age 4 years, 2 years, and 7  
7 months. Since the beginning of the pandemic, my  
8 husband and I have done everything we can to protect  
9 our children from COVID-19. Our children haven't been  
10 inside grocery stores or department stores, let alone  
11 typical childhood staples like indoor amusement parks,  
12 museums, malls and restaurants.

13           I am thankful that my children have remained  
14 healthy, but it's been a long two years. Last year I  
15 was pregnant with my third child, who was due in  
16 November 2021. After my husband and I received our  
17 COVID vaccines, as soon as they were available to us,  
18 it seemed hopeful that a pediatric vaccine would likely  
19 be coming in the fall, around the time the new baby was  
20 due.

21           I imagine we would still have to be careful

1 for the baby's first six months, until he was old  
2 enough to be vaccinated himself. But at least the risk  
3 could be somewhat mitigated since everyone else in the  
4 family would be vaccinated. As we all know that  
5 pediatric vaccine didn't come last fall or in February,  
6 or in April. That baby is now 7 months old and still  
7 none of my children are able to be vaccinated.

8           My oldest child will be 5 years old in mid-  
9 August. She is supposed to start kindergarten on  
10 September 1st. Because of the pandemic, she has stayed  
11 home with me instead of attending preschool. She is so  
12 very excited for kindergarten. She is eager to learn  
13 and play with kids her own age. Because of her late  
14 birthday, the only way she'll be fully vaccinated  
15 before kindergarten starts is if the under 5 vaccines  
16 is approved now, particularly Moderna since it's a  
17 shorter series.

18           Moderna would allow children starting  
19 preschool and kindergarten this fall, to reach the same  
20 protection antibody level in only two doses compared to  
21 Pfizer's 3-dose series, which instead produces similar

1 efficacy and immunobridging over a period of three  
2 months. Boosters for each have been considered in the  
3 future, making Moderna three doses and eventually  
4 Pfizer four. I urge you to please act now to authorize  
5 emergency use of both Moderna and Pfizer vaccines for  
6 children under age 5.

7           At this point in the pandemic, many people  
8 have seemingly moved on and are completely forgoing  
9 COVID precautions such as masking and social  
10 distancing. And our youngest children have been left  
11 behind unprotected. Those without children do not even  
12 recognize the toll this is taking on young families,  
13 since we have become invisible while they are living  
14 life as normal.

15           Please allow parents to give their children  
16 the layer of protection that vaccination allows. The  
17 data indicates that these vaccines are safe and have  
18 met immunobridging. They can protect against the most  
19 severe outcomes, the things that have kept parents  
20 awake at night since the beginning of the pandemic,  
21 death and hospitalization. And can potentially

1 decrease the risk of other complications, like long  
2 COVID, MIS-C, neurological effects, diabetes and  
3 hepatitis. We need to protect our children without  
4 further delay. Thank you for your time.

5 **DR. PRABHAKARA ATREYA:** Thank you. The next  
6 speaker is Tamara Thomson. You have three minutes.

7 **MS. TAMARA THOMSON:** Good afternoon, members  
8 of the committee, and thank you for allowing me to  
9 address you again today. I have no financial  
10 conflicts. My name is Tamara Thomson and I'm an  
11 attorney who represents children, as well as the mother  
12 of a 5 year old boy and 23-month-old girl.

13 Yesterday I urged you to recommend  
14 authorization of Moderna for the older pediatric  
15 cohort, and I'm thankful that you did. I also urged  
16 you yesterday to do the same for the youngest cohorts.  
17 I am here again today to request that you vote to  
18 authorize both Moderna and Pfizer for the youngest age  
19 groups so that our littlest Americans can have access  
20 to these lifesaving and necessary measures of  
21 protection against severe outcomes, disease and death

1 from COVID-19.

2 I spoke yesterday about how important this  
3 authorization is to me and my family, and how long  
4 we've waited to protect our sweet girl. She is  
5 actually one of the data points you saw in Moderna's  
6 presentation today, as we joined the trial in February.

7 Today I want to address how important it is  
8 that both vaccines are authorized for other families.  
9 In my social circle I have heard from many other  
10 parents that they are desperate to vaccinate their  
11 children under 5. They thank me for my advocacy and  
12 tell me how exhausted they are, and how very hard it  
13 has been to feel left behind and with no measures to  
14 protect their young children from the threat of COVID-  
15 19.

16 Referring both to the acute threat, and the  
17 possible long-term harm of infection after infection  
18 with SARS-CoV-2. Long COVID is a threat to children  
19 and adults alike. Like me, other parents have pulled  
20 kids from daycare during surges and worked their full-  
21 time jobs from home while trying to parent babies and

1 toddlers. They've also gone through interruptions  
2 after interruptions of care with illnesses, exposures,  
3 quarantine and isolation. Some parents are not able to  
4 work from home at all, and don't have the ability to  
5 pull kids during surges, but must take unpaid time off  
6 when exposures and quarantines occur.

7           I have heard over and over again that it is  
8 exhausting. And it's been even more difficult since  
9 the rest of the world has moved on, dropping all non-  
10 pharmaceutical interventions because they "have all the  
11 tools." We don't have the tools, not for our little  
12 ones, and therefore; not for our families.

13           It is essential to authorize both vaccines  
14 right now because there are advantages to each series  
15 that will help families in different positions. For  
16 example, we see greater efficacy and immunobridging in  
17 just two doses of Moderna versus two doses of Pfizer  
18 vaccine, which would allow rising kindergarteners to  
19 achieve more protection before starting school in  
20 September. At the same time, while Pfizer's end and  
21 calculating efficacy is low, and confidence interval

1 wide, it may be that it's 3-dose scheme provides  
2 greater efficacy in the long term.

3           In addition, having two vaccines for this age  
4 group available will help in insuring better access, a  
5 stronger supply chain and a choice for families who  
6 have waited so long for protection. We need options.  
7 We need access. And we need to make sure this group  
8 catches up to older cohort in terms of variant-specific  
9 boosters and up-to-date preventative (inaudible)  
10 treatment. As we heard Dr. Fauci saying April of this  
11 year, all of the stuff you hear about kids, let them  
12 get infected, is a bunch of nonsense. Please authorize  
13 both the Moderna and Pfizer vaccines for them today.  
14 Thank you for your time and dedication to the  
15 scientific process.

16           **DR. PRABHAKARA ATREYA:** Thank you. The next  
17 speaker is Mr. Sam Dodson. You have three minutes,  
18 please.

19           **MR. SAM DODSON:** Hello, my name is Sam Dodson.  
20 I run a podcast called To the Lifeboats, and I have no  
21 relationship with the pharmaceutical cartels. I'm



1 schooled in electrical engineering. And two years ago  
2 I'd never heard of mRNA. But let me tell you what I've  
3 learned since. It starts with the shot you told us  
4 stays at the injection site. We know it doesn't. You  
5 knew it didn't. Bio-distribution studies shows that it  
6 goes to every major organ, primarily the heart, liver  
7 and spleen, where thanks to the highly inflammatory  
8 lipid nanocomplex it transfect (inaudible) the cells.  
9 That complex contains a PEGylated lipid being mass  
10 injected into humans for the first time ever, while the  
11 animal studies showed heart attacks in pigs after the  
12 second injection.

13           You knew the lipid nanocomplex is collected in  
14 the ovaries, where they have the potential to cause  
15 devastating effects on reproductive health, yet you did  
16 nothing. When women started complaining of menstrual  
17 problems, you did nothing. Transfected cells in every  
18 organ pumped out the spiked protein that ends up in a  
19 nucleus where it interrupts p53, LINE-1, and BRCA, you  
20 didn't know this because you didn't care to ask the  
21 question. And when shown to you in a study, you did

1 nothing.

2           Every transfected cell expressing spike  
3 protein risks autoimmune disease, the most acute of  
4 which is myocarditis. When people started dying of  
5 myocarditis, you did nothing. The spike protein floats  
6 freely in the vasculature, finding its way into the  
7 brain, breastmilk, and the environment as the body  
8 sheds this protein in exosomes, making those around the  
9 vaccinated sick, despite protein directly affects toll-  
10 like (inaudible) receptors and CD4 T cells, which are  
11 essential to the immune defense against these very  
12 viruses.

13           When the vaccinated repeatedly caught COVID  
14 and suffered reactivation of herpes, shingles, papaloma  
15 virus in unprecedented numbers, you knew this was a  
16 massive problem yet you did nothing.

17           You knew that the mRNA stays around for months  
18 in lymph nodes germinal centers, causing P cell  
19 exhaustion, because the Stanford Group performed the  
20 study that you couldn't be bothered to do.

21           And then you ignored that massive safety

1 signal. You were warned about oncomiRs (inaudible) and  
2 the effect on p53, yet you did nothing. When you were  
3 warned about prion disease and amyloid as a result of  
4 the huge amounts of spiked protein produced by these  
5 therapies, you did worse than nothing; you silence  
6 those people who raised the alarms.

7           You were informed of fraud in the vaccine  
8 studies yet instead of investigating you colluded with  
9 the manufacturers to suppress trial data for 75 years.

10           Knowing all of these concerns you now want to  
11 inject the very young, who have zero clinical risk from  
12 COVID and for which not one single study has shown any  
13 clinical benefit. You have abjectly failed in your  
14 sole duty to ensure the safety of any drug given to  
15 Americans. The late Frances Oldham Kelsey would have  
16 been ashamed of how you've turned a once respected  
17 agency into a corrupted vessel for the very  
18 corporations you swore to protect the American public  
19 from.

20           If you have one shred of humanity left, you  
21 will recommend an immediate halt to all the shots and

1 pray that God has mercy on your souls. You might also  
2 want to figure out how we're going to diagnose  
3 myocarditis in very young babies who are unable to  
4 speak. Thank you.

5 **DR. PRABHAKARA ATREYA:** Thank you. The next  
6 speaker is Donna Treubig. You have three minutes.

7 **MS. DONNA TREUBIG:** Hi. Thank you. My name  
8 is Donna. I'm grandma to two-year-old Liam (phonetic),  
9 and a licensed-family daycare center owner-operator. I  
10 have no conflicts.

11 Please take a moment to picture your life  
12 right now if you weren't given access to even one COVID  
13 vaccine dose yet, two and a half years after this  
14 began. Now think about going into a small room with 20  
15 other unmasked, unvaccinated people. Eating and  
16 napping, in close contact, spending up to ten hours  
17 there every weekday. This is the scenario parents are  
18 forced to put their unvaccinated children in every day,  
19 and is why I implore you to approve a vaccine for  
20 children under 5 today.

21 COVID seeks out those who are unvaccinated.

1 The convoluted task to approval these trials have taken  
2 have left the youngest of our society most vulnerable.  
3 The repeated reassurance that a vaccine would be  
4 available in the coming weeks or months has not brought  
5 hope to families, but rather frustration and despair  
6 when these claims did not come to fruition.

7           The truth is families have gone to extreme  
8 lengths to protect their babies because children are  
9 getting very sick and dying of COVID-19. The FDA should  
10 strive to be nimble and able to pivot quickly as the  
11 virus changes. If the rest of our country can choose a  
12 vaccination and subsequently drop any and all mitigation  
13 measures, before all vulnerable populations have  
14 protection, then parents deserve the right to vaccinate  
15 our children and to choose between Moderna and Pfizer.

16           We need a comprehensive plan to ensure this age  
17 group has access to up-to-date boosters and future  
18 variant-specific vaccine at the same pace as all other  
19 age groups. Our governmental bodies need to do what is  
20 necessary to ensure our children are not denied  
21 lifesaving vaccines for two and a half years during the

1 next pandemic.

2           When you cast your vote this afternoon please  
3 remember these small children and vote to approve both  
4 Moderna and Pfizer vaccines for children under 5 so that  
5 they have some protection with reduced risk of severe  
6 illness caused by COVID-19. Thank you for your hard  
7 work throughout this pandemic and for giving me the  
8 opportunity to share my views.

9           **DR. PRABHAKARA ATREYA:** Thank you. The next  
10 speaker is Catharine Diehl.

11           **MS. CATHARINE DIEHL:** Good afternoon. My name  
12 is Catharine Diehl. I'm a mother of two-year-old twins  
13 and a Ph.D. in philosophy with a focus in medical  
14 ethics. I have no financial conflicts. I'm here today  
15 to strongly urge the committee to recommend  
16 authorization for both vaccines.

17           The question before you for each vaccine is  
18 whether, based on the totality of medical information  
19 available, its benefits outweigh its risks. The data  
20 presented today, and real world information collected  
21 over the past two years, demonstrate that the answer to

1 this question a clear and resounding yes.

2           To evaluate the benefits we must follow the  
3 standard of probable improvement. Employing the tools  
4 of (inaudible) analysis, supported by the FDA's own  
5 guidelines, these vaccines very clearly meet the  
6 standard. We're better off with them than without them.  
7 This standard must guide our action, rather than any  
8 arbitrary statistical cutoff such as requirement of 50  
9 percent efficacy against symptomatic illness. Such a  
10 standard would be additionally inappropriate in the  
11 context of current variants, when attention has shifted  
12 to protection against severe outcomes including  
13 hospitalization and death.

14           Evaluation of these vaccines does not occur in  
15 a vacuum; rather it occurs in a context in which these  
16 vaccines have proved to be safe and effective in adults,  
17 as well as in a slightly older age cohort. This  
18 background should inform our priors that is our starting  
19 point and our considerations here.

20           The success of both trials in meeting  
21 immunobridging, without any safety signals, allows us to

1 update these priors in light of positive evidence.

2           Following the standard of probable improvement  
3 let us infer from successful immunobridging, it's highly  
4 likely the vaccine will be similarly effective in the  
5 prevention of severe outcomes like hospitalization and  
6 death in children under 5.

7           The safety record in older cohorts, in absence  
8 of safety signal from the trial, also reassures us that  
9 new safety issues are not likely to crop up once vaccine  
10 distribution commences to the broader population. Using  
11 compelling evidence both companies' documentation that  
12 the benefit/risk analysis is favorable based on acute  
13 outcomes.

14           But there are additional factors that speak in  
15 favor of approval. COVID infection carries substantial  
16 long-term risks. Our understanding of these long-term  
17 implications is every evolving, (inaudible) that the  
18 methodology I have described is particularly helpful.

19           To ignore the growing evidence, lasting  
20 cardiovascular damage, new type 1 diabetes diagnoses,  
21 brain atrophy, vascular (inaudible) deposition,



1 hepatitis and so on, merely because we have yet to  
2 accumulate a decade worth of high-quality, double-  
3 bonded, randomized control trial, and met an analyses  
4 thereof, would be dangerous and irresponsible.

5           These vaccines are likely to reduce such  
6 effects in two ways. First, by preventing some portion  
7 of infection, they reduce the number of cases in which  
8 long-term damage can occur. Second, numerous studies  
9 have suggested that breakthrough infections are less  
10 likely to lead to long COVID. Again, this must be  
11 factored into our analysis.

12           As a philosopher and a parent, I urge you to  
13 approach your decision with these (inaudible) principles  
14 in mind, reach the conclusion that both vaccines should  
15 be approved. Thank you for your consideration. And  
16 thank you to the families in these trials who have made  
17 this possible.

18           **DR. PRABHAKARA ATREYA:** Thank you. The next  
19 speaker is Jessica Nehring. You have three minutes.

20           **MS. JESSICA NEHRING:** Good afternoon. I have  
21 no financial conflicts of interest. I am a mother of

1 two amazing children. My daughter is 6 and my son is 3.  
2 I'm speaking today to advocate for children under 5  
3 years old, and their parents who wish to have the option  
4 of vaccinating these youngest children.

5           Since most masking mitigations have been  
6 lifted, children under 5 have been sitting ducks for  
7 COVID without protection while vaccination has been  
8 enthusiastically recommended to every other age group.  
9 We have been through six waves of COVID now, including  
10 the current surge, with no protection for our most  
11 vulnerable children.

12           The children 3 and over that can mask are  
13 obviously not wonderful at it, and the children under 3  
14 have absolutely nothing at this point to protect them  
15 from severe and sometimes fatal outcomes. Based on  
16 real-world data in persons 5 and above it can be safely  
17 concluded that Moderna and Pfizer's vaccines for our  
18 youngest children offer excellent protection from  
19 hospitalization, severe illness and death.

20           I am frustrated that this process was stalled  
21 with Moderna since their studies were nearly complete in

1 December, when an expansion was requested by the FDA.  
2 Parents still long for a clear explanation regarding the  
3 reason for this expansion, which was requested during  
4 the largest COVID surge of the pandemic. One that  
5 resulted in thousands of children under 5 hospitalized.  
6 It is upsetting that a safe and effective vaccine has  
7 not been prioritized, especially with so many Americans  
8 getting back to their normal lives, resulting in our  
9 children being placed at even higher risk of infection.

10           In the past two years my husband has worked in  
11 nursing homes, schools, restaurants and churches as a  
12 union HVAC service tech. He has chronic asthma and has  
13 been wearing a mask for years at this point just to  
14 protect himself and our family until we can all be  
15 vaccinated. I have put off doctor's appointments these  
16 past two years for a pre-pandemic health issue, because  
17 of the fear of bringing the virus home to my son and  
18 daughter before they have been vaccinated.

19           Parents like me are frustrated that we are not  
20 being seen. We believe in science and the process of  
21 trials, evaluating data, and the health agencies

1 involved in managing all of these aspects. But moving  
2 forward, I would hope this age group doesn't get left  
3 behind again. I would like serious thought given to the  
4 possibility of running trials for future treatments and  
5 vaccines of all age groups at the same time so our  
6 youngest children are not forgotten.

7           Relevant agencies need to work with states and  
8 local government to facilitate a rollout that's truly  
9 fair and equitable for all kids under 5 and their  
10 parents. Parents like me just want the choice. Thank  
11 you for giving me the time to speak.

12           **DR. PRABHAKARA ATREYA:** Thank you. The next  
13 speaker is Katarina Lindley. You have three minutes.

14           **DR. KATARINA LINDLEY:** Thank you for this  
15 opportunity. My name is Dr. Katarina Lindley. I'm a  
16 member of the Steering Committee of the World Council  
17 for Health. I have no conflict of interest.

18           CDC data from February show that about 74.2  
19 percent of children have had COVID already. Over 150  
20 studies show that natural immunity is superior. The  
21 infection fatality rate under 5 years of age is 0.1 in a

1 hundred thousand or one in a million. The risk of the  
2 shot in the already immune is higher than one in a  
3 million.

4 Both Pfizer and Moderna expressly eliminated  
5 those that were naturally immune from their studies.  
6 They did this to avoid the high immune (inaudible)  
7 response and possibly death. Vaccinating the already  
8 immune puts them at serious risk for having a high  
9 immune response. That means you will be voting for some  
10 children to have a severe adverse reaction and possibly  
11 death if you vaccinate the already immune. This is bad  
12 medicine. There is zero reward, only risk.

13 These vaccines are not medically necessary or  
14 clinically indicated. VAERS shows children ages birth  
15 to 18, who have been vaccinated with Pfizer and Moderna  
16 vaccines, have had severe life-threatening adverse  
17 reactions such as myocarditis, (inaudible), seizures and  
18 most severe adverse reaction from death.

19 Article by (inaudible) that was published in  
20 May 22, of 2022, in American Academy Pediatrics, shows  
21 myocarditis 2.2 per million cases, seizures 7.6 per

1 million cases. I will share two cases seen by my  
2 colleagues.

3 Fourteen-year-old male, double vaccinated with  
4 Pfizer vaccine has recent history of chest pains on  
5 exertion. The initial echo and EKG were normal.

6 (Inaudible) 22,000 increasing to 48,000 in six hours.

7 Cardia MRI (inaudible) showed transmural and (inaudible)  
8 consistent with myocarditis.

9 Case number two, 13-year-old female, first  
10 Pfizer dose last August, had first seizure within 30  
11 days. Got a second vaccine in December, had another  
12 seizure, then had a third booster and now has four to  
13 six seizures a day. She was an active soccer player and  
14 a good student, now unable to play sports or attend  
15 class in person.

16 We have no long-term safety data in any of  
17 these studies. The risks clearly outweigh the benefits.  
18 The VAERS reports 28,312 deaths so far in all age  
19 groups. When will we say this is enough? What is the  
20 magic number that will make a cutoff and stop pushing  
21 these vaccines? Will it be 50,000, 100,000, million?

1 When do we say that we cannot give this to our children?

2           Their recovery rate is over 99.9985 percent.

3 These are healthy children and the risks do not outweigh  
4 the benefits. These vaccines are not medically  
5 necessary or clinically indicated.

6           **DR. PRABHAKARA ATREYA:** Your time is up.

7           **DR. KATARINA LINDLEY:** Thank you for your time.

8           **DR. PRABHAKARA ATREYA:** Thank you. The last  
9 speaker for the session is Caroline Bishop. You have  
10 three minutes.

11           **DR. CAROLINE BISHOP:** Hi. Thank you. My name  
12 is Dr. Caroline Bishop, and I'm an associate professor  
13 of classics at Texas Tech University. I have no  
14 financial conflicts of interest.

15           I'm here in my capacity not as a professor but  
16 as a mother to urge you to approve both the Moderna and  
17 Pfizer vaccines for children under 5. Today I wish to  
18 share with you the increasingly punishing lengths I've  
19 had to go to in order to keep myself and my 14-month-old  
20 daughter free from COVID as we've continued to wait for  
21 a vaccine. I could talk about the difficult decisions

1 we've been forced to make along the way. Cancelling our  
2 daycare during the Delta wave and keeping my daughter at  
3 home with me while I was technically on a Harvard-funded  
4 research sabbatical to write my second book, never  
5 having gotten to take her to a museum or to visit her  
6 cousins or to a playdate. Being able to count the times  
7 she's been in the grocery store on one hand.

8           But instead I'm going to focus on the fact that  
9 I've had to be a solo parent for the past month or so,  
10 watching my daughter full time, never leaving the house,  
11 while also feverously writing a conference paper that I  
12 have to deliver this Friday during naps and after  
13 bedtime, has been one of the most challenging  
14 experiences of my life. Why have I been doing this,  
15 because my husband, who's a trial attorney, can no  
16 longer wear a mask in court. Part and parcel of the  
17 countrywide removal of all mitigation at a time when  
18 we're seeing one of the worse COVID surges yet.

19           As cases began to grow in our area, he made the  
20 heartbreaking decision to move out to our guesthouse.  
21 At the time, we'd hope the committee might meet to



1 approve the Moderna vaccine on June 8th, and when the  
2 meeting got scheduled for today our hearts broke a  
3 little more. This past month I've been desperately  
4 holding on for my daughter to have the protection  
5 against severe outcomes that both the Moderna and Pfizer  
6 vaccines have been shown to provide.

7 I've been lonely and alone, devastated when my  
8 husband missed our daughter's first steps. I know he  
9 feels devastated too. He has to hear her call out, da,  
10 da, when she sees him in the yard, and know he can't  
11 cuddle and play with her. She's always so delighted to  
12 see him and doesn't understand why he won't horse around  
13 with her like he used to do. We didn't publicize this  
14 decision of our, only a few close friends know. That's  
15 because even among our highly educated friend group,  
16 almost everyone is acting like the pandemic is over.

17 I spoke to you yesterday about the special kind  
18 of heartbreak you feel when you see people you love,  
19 like and respect, start to act with absolutely no  
20 concern about the fact that you're child has no  
21 protection against COVID. Today I just add that it's

1 both disorienting and maddening to see almost everyone  
2 living like it's 2019 again, when you're still stuck in  
3 March 2020.

4           However, I can now say with certainty that my  
5 husband and I made the right decision hard as it  
6 might've been. How do I know? Because this past Friday  
7 he came home from work with a sore throat, and as I'm  
8 speaking to you he's sick with COVID. Fortunately, he's  
9 vaccinated and boosted with Moderna and his case has  
10 been mild.

11           My daughter deserves that same protection. You  
12 have the ability to give it to her and to reunite our  
13 family. For myself and for the many parents who didn't  
14 have the privilege to isolate like I've done, I'm  
15 begging you to approve these vaccines. Thank you very  
16 much.

17           **DR. PRABHAKARA ATREYA:** Thank you. That  
18 completes the Open Public Hearing session. And I would  
19 like to hand over the meeting back to our chair, Dr.  
20 Monto; take it away for the next item on the agenda.

21

1 **ADDITIONAL Q&A FOR FDA AND SPONSOR PRESENTERS - MODERNA**  
2 **COVID-19 VACCINE**

3  
4 **DR. ARNOLD MONTO:** Thank you, Prabha. And I  
5 thank all the participants in the open public hearing.  
6 We really do listen to what you have to say us. We now  
7 return to the question and answer sessions. We will  
8 first deal with the question and answer about the  
9 Moderna vaccine. And these questions can be for the  
10 FDA presenters or the sponsor presenters. We have a  
11 relatively short period for the question and answer  
12 sessions, 25 minutes, after which we have our own  
13 internal discussion.

14 So remember there's that session as well --  
15 and following that, the vote, completing the action on  
16 the Moderna vaccine. So we're completing the action on  
17 the Moderna vaccine. Okay. Let me see if I've got the  
18 full list in front of me here. Dr. Berger followed by  
19 Dr. Pergam.

20 **DR. ADAM BERGER:** Hi, thank you all for the  
21 earlier presentations. I had a question based on FDA's

1 briefing document that was supplied, and specifically  
2 it was the two tables that looked at the subpopulation  
3 analysis, specifically looking at the vaccine efficacy  
4 in children who are obese. I noticed that the vaccine  
5 efficacy rates for the 6 to 23 month olds were negative  
6 5.6 and two to five year olds were listed as negative  
7 15.4 -- and totally recognizing that the confidence  
8 intervals in these were huge.

9           Just wanted to get a sense of whether, I  
10 didn't see this listed in any of the post-approval  
11 examinations. What kind of data are you currently  
12 collecting on children who are obese to understand the  
13 efficacy there or to at least dive into this signal a  
14 little bit more?

15           **DR. JACQUELINE MILLER:** So I believe that was  
16 a question for me, but if I'm wrong, please correct me.  
17 So I think the question is about Moderna and how we  
18 follow-up on the efficacy rates in children who are  
19 obese. So, as you mentioned, we have some efficacy  
20 data from the original clinical trial. However, those  
21 data right now are a relatively small subgroup of the

1 overall (audio skip).

2           And so the way in which we will be moving  
3 forward to follow vaccine effectiveness would be  
4 actually in the long-term effectiveness study that we  
5 have ongoing in Southern California. So in that study  
6 we are able to enroll hundreds of thousands of  
7 individuals, and we actually are parsing those analyses  
8 by specific risk groups. I can show you the  
9 immunogenicity in the young children. So if you can  
10 please put up slide IM23 for me?

11           **MR. MICHAEL KAWCZYNSKI:** Oh, give me a second,  
12 I gave it to the wrong share. So Moderna, give me one  
13 second.

14           **DR. JACQUELINE MILLER:** No problem.

15           **MR. MICHAEL KAWCZYNSKI:** Actually, Moderna, no  
16 you should have the right share right now. Oh, you  
17 moved it. Hold on, one second. Take it away. You got  
18 it.

19           **DR. JACQUELINE MILLER:** Okay. There we go.  
20 And then I'm just going to say that I'll want the slide  
21 in a moment for the 6 month to 23 month olds. So what

1 you see here are the geometric mean titers and  
2 associated 95 percent confidence intervals for the  
3 children who are two to five that received mRNA-1273,  
4 and you also see the respective GMT ratios. And this  
5 is again versus the adult population.

6 I need to note again that the sample size of  
7 the children who are obese is relatively small (Audio  
8 skip) will require further follow-up. And then, if we  
9 can put up the next slide, which is IM24, we'll see the  
10 infants and toddlers. And so here we see GMT ratios of  
11 0.9 to 1.4. Again, sample size is relatively small, so  
12 wider 95 percent confidence intervals in those who are  
13 obese but, overall, greater than 1500.

14 **DR. ADAM BERGER:** Thank you.

15 **DR. ARNOLD MONTO:** Thank you. Dr. Pergam  
16 followed by Dr. Sawyer.

17 **DR. STEVEN PERGAM:** Thanks. I had a question  
18 for the sponsor. I didn't get to ask this question  
19 initially when you presented your data. You had a  
20 fairly large study population in the Phase 1 trial that  
21 got the higher dose of the vaccine, similar to what I

1 asked Pfizer. I'm curious, did you see a dose  
2 dependent response in that higher dose compared to the  
3 lower dose that you ended up choosing?

4           And then, as a second question to that that's  
5 somewhat relevant is, in your post-marketing studies  
6 that are planned, there's no discussion of the  
7 immunosuppressed population. And as we have seen in  
8 post-marketing immunosuppressed populations have  
9 received an extra or a third dose as the primary  
10 series. And I'm curious if there are studies planned  
11 for Moderna for immunosuppressed children to  
12 specifically address this question?

13           **DR. JACQUELINE MILLER:** Yep. Thank you for  
14 that. So what I would like to do is address your first  
15 question first, which is the comparison of the 25  
16 microgram and 50 microgram, which are the doses that we  
17 investigated in this trial. And so could you please  
18 project AA8, sorry that's alliteration, but 2 As and an  
19 8. There you go. Thank you.

20           What you see in this slide is the young  
21 children, and you had asked about a dose response. So

1 we do see a dose response with a higher dose. And we  
2 saw GMT ratios in the initial part one population of  
3 0.8 and 1.4, respectively. We were also looking at the  
4 safety profile at the time, made our recommendation to  
5 a data and safety monitoring board. And they in fact  
6 confirmed that they agreed with our selection of the 25  
7 microgram dose in the children two to five.

8           And because we selected the 25 microgram dose,  
9 then we did not go up to 50 micrograms in the youngest  
10 babies. And then your second question for me is with  
11 respect to immunocompromised children. And so we have  
12 already committed to doing in Europe an  
13 immunocompromised trial, and in fact we were waiting  
14 until we had selected the dose and had confirmation  
15 that that dose was safe and effective in healthy  
16 children before moving to the immunocompromised  
17 population. And of course we'll be studying a three-  
18 dose schedule as we're administering to adults with the  
19 selected dose.

20           **DR. STEVEN PERGAM:** Thank you very much.  
21 Appreciate that.



1           **DR. ARNOLD MONTO:** Dr. Sawyer followed by Dr.  
2 Kim. Or are we up to -- yeah, Dr. Sawyer.

3           **DR. MARK SAWYER:** Thank you, Dr. Monto. So it  
4 appears that fever is occurring at a significant rate,  
5 which is something we see with other routine childhood  
6 vaccinations. But the pediatricians in the group have  
7 certainly lived through the experience of seeing  
8 enhanced fever and even febrile fevers with  
9 coadministration of other vaccines together that all  
10 cause fever.

11           Dr. Chatterjee brought up this question  
12 earlier, and the sponsor replied that they are planning  
13 some coadministration studies. My question is for FDA.  
14 Are such coadministration studies required for a full  
15 BLA, or is it up to the sponsor to just decide how much  
16 to study that question and/or do we need to wait for  
17 post-marketing or post-authorization studies to really  
18 get a handle on that question?

19           **DR. ROBIN WISCH:** Thank you for that question.  
20 Thank you, Dr. Fink. I think you're about to -- ready  
21 to handle that.

1           **DR. DORAN FINK:** Thank you. I'll answer that.  
2 So we have routinely requested coadministration studies  
3 in licensure applications of vaccines that are intended  
4 for the very young infants, those who are younger than  
5 six months of age, because the immunization schedule is  
6 so compressed, and it is difficult to avoid  
7 coadministration.

8           We have not routinely requested or required  
9 coadministration studies for older children, but we  
10 have always encouraged vaccine manufacturers to study  
11 safety and evaluate for immune interference of  
12 coadministration when introducing a new vaccine into  
13 the pediatric schedule. And we do expect that studies  
14 will be done going forward looking at this.

15           **DR. MARK SAWYER:** Thank you.

16           **DR. ARNOLD MONTO:** Thank you. Dr. Kim  
17 followed by Dr. Gans.

18           **DR. DAVID KIM:** Thank you very much. On the  
19 topic of primary series and booster dose, I think the  
20 Committee has discussed this on several occasions. But  
21 on that topic for Moderna vaccine, the definition of

1 primary series is two dose, and you're currently  
2 working on a study to evaluate the impact of the third  
3 dose.

4           And it's on that third dose that I'd like to  
5 ask you if you have any preliminary information or  
6 actually, if you can share with us some of the  
7 characteristics of the study design and the possible  
8 impact and then perhaps your hypothesis on how that  
9 might influence your definition of primary series  
10 versus booster dose?

11           **DR. JACQUELINE MILLER:** Yeah, so I'll speak a  
12 little bit about the boosting that we're planning in  
13 each age cohort. We don't have hypotheses to define  
14 two versus three dose series, but as I mentioned we've  
15 heard your feedback about that. But in terms of the  
16 third dose booster, in adolescents we (audio skip) once  
17 we saw the incidence rates climbing after Omicron, as  
18 we discussed yesterday. And those data actually we are  
19 anticipating momentarily and will be sharing them with  
20 the FDA once we have them compiled. That will be the  
21 first group.

1           Then in July, we will be getting the data from  
2 the 6 to 11 year olds. So the 6 to 11 year olds were  
3 followed primarily through Delta. There the longer-  
4 term follow-up cohort is now mostly the mRNA-1273  
5 cohort because of the authorization of another vaccine  
6 and people going to get vaccinated. So we'll really  
7 see just primarily what that third dose booster looks  
8 like in that cohort that will come in July, and of  
9 course we'll share those data when available.

10           And then, the youngest children actually,  
11 based on other feedback we've received from this  
12 Committee, we tried to keep the blinding in place as  
13 long as possible to have as long of double blinded  
14 efficacy follow-up as we could. I think once a  
15 decision is made and one or more vaccines, hopefully,  
16 will be authorized we will be unblinding and then  
17 offering that third dose at least three months after  
18 the second dose.

19           And that three month interval is really  
20 defined by an interval that we've seen from DMID, so  
21 DMID assessed heterologous boosting with that three

1 month interval afterwards. And, as you mentioned,  
2 there may be some safety and immunogenicity benefits to  
3 that interval. So we will share those data when  
4 available. And then, we have mRNA-1273, and we have  
5 some clinical supply with an Omicron-containing  
6 variant.

7           And so there will be some of the cohort in the  
8 youngest kids receiving the Omicron-containing variant.  
9 And that really is to bracket the booster responses, so  
10 we'll see the Omicron data that we'll share with you in  
11 two weeks in the adults. And then, in these youngest  
12 kids, the Omicron-containing variant and we believe  
13 that will really help give the cumulative picture of  
14 the capabilities of the vaccine.

15           **DR. ARNOLD MONTO:** Thank you very much. Very  
16 broad response to a broad question. Dr. Gans followed  
17 by Dr. Reingold.

18           **DR. HAYLEY ALTMAN-GANS:** Thank you so much,  
19 and I really appreciate all the thought that you've put  
20 into what you will be doing moving forward. And so my  
21 question really for the FDA -- and I don't know if

1 Doran Fink is available, but I'm impressed with how  
2 much there is after already predicted to be available  
3 to the FDA. And my question is, before moving onto  
4 licensure, will there be availability of the data to be  
5 reviewed by the Committee? And maybe even some  
6 recommendations moving forward of whether (audio skip).

7 **DR. ARNOLD MONTO:** Dr. Fink.

8 **DR. DORAN FINK:** Thank you. FDA always makes  
9 a case-by-case decision on seeking input from the  
10 VRBPAC depending on whether we consider there to be  
11 important questions about benefits and risks that would  
12 benefit from or require input from the VRBPAC. And, as  
13 you know, we have taken certain actions without a  
14 VRBPAC meeting when we felt that those actions needed  
15 to be done expediently or when we felt that the most  
16 pertinent issues regarding benefits and risks had  
17 already been discussed and there was nothing new to  
18 discuss. And so we will consider those factors before  
19 we take any future action on a case-by-case basis.

20 **DR. HAYLEY ALTMAN-GANS:** Thank you. And then  
21 just --

1           **DR. ARNOLD MONTO:** Thank you very much.

2           **DR. HAYLEY ALTMAN-GANS:** My question for  
3 Moderna is are you going to be looking at immune  
4 correlates in any of your studies moving forward?  
5 Because we seem to be stuck on looking at neutralizing  
6 antibodies, which we all know for viruses, while show  
7 you some correlates that is there in the immune system,  
8 it's not necessarily the correlate of protection for  
9 these respiratory viruses.

10           **DR. JACQUELINE MILLER:** Yeah. So this  
11 absolutely is an area of interest for us. We have  
12 published our work from the ancestral strain, which Dr.  
13 Das discussed a bit with you yesterday. And we're now  
14 speaking with our collaborators at the CoVPN and then  
15 also at the NIH about now how we might take those  
16 results as we're getting the Omicron neutralization  
17 titers and Omicron cases and work on an Omicron  
18 correlate of protection.

19           I think our feeling is that probably Omicron  
20 is the next most important variant to investigate, so  
21 we're discussing how we might do that now that we're so

1 distant from the original blinded efficacy trial. But  
2 it's definitely an area of interest.

3 **DR. HAYLEY ALTMAN-GANS:** Okay.

4 **DR. ARNOLD MONTO:** Thank you very much.

5 Moving on to Dr. Reingold followed by Dr. Nelson. And  
6 there will be one question after that. We're falling  
7 behind schedule. Dr. Reingold.

8 **DR. ARTHUR REINGOLD:** Thanks very much. I'll  
9 try and make it quick. So first, Mark Sawyer asked my  
10 questions about coadministration, but the other  
11 question I have, you know, for a lot of routine  
12 childhood immunizations there's much circulation of the  
13 agent in the population. So we're not typically faced  
14 with the problem of administering the vaccine to a  
15 child who's recently been infected or already has  
16 antibodies.

17 And clearly, with COVID-19, that's not the  
18 case. And you may have shown these data, but in terms  
19 of reactogenicity, either with a preexisting antibody  
20 or recent documented COVID-19 is there any reason that  
21 the safety profile would be considered different? This



1 presumably will be an issue for CDC if vaccine is given  
2 EUA, what kind of clinical guidance they give about  
3 either delaying vaccination or proceeding with  
4 vaccination under different circumstances. Thank you.

5 **DR. JACQUELINE MILLER:** Yes, we actually do  
6 have the safety data by seropositive and seronegative  
7 adverse events. So if you can put the slide up,  
8 please, it's SY23. Thank you. So what you see on this  
9 slide are the children who are two to five years of age  
10 in (audio skip) are children that were SARS-CoV-2  
11 positive at the start of the study. In black, the ones  
12 that were SARS-CoV-2 negative. The rates were  
13 relatively comparable between those two subgroups.

14 If there was a trend that we noticed it was  
15 that systemic rates of reaction tended to be higher  
16 after post-dose-2 in the initially seronegative  
17 children as opposed to post-dose-1, which was more  
18 frequently observed in the seropositive children. And  
19 then, let's also put up the data for the infants and  
20 toddlers. Oh, sorry, Dr. Monto.

21 **DR. ARNOLD MONTTO:** Go ahead, please.

1           **DR. JACQUELINE MILLER:** No, I just wanted to  
2 show you for the other age group what the data looked  
3 like post-dose-2 and post-dose-1 for the seropositive  
4 and seronegative children. Thank you.

5           **DR. ARNOLD MONTO:** Okay. Thank you. Dr.  
6 Nelson. Followed by Dr. Fuller, who will be the last  
7 questioner in this session.

8           **DR. MICHAEL NELSON:** Yeah, so I just had a  
9 couple of quick questions. I know we're falling  
10 behind. One has to deal with the subpopulations of  
11 Blacks who were enrolled in your current study. So I  
12 did note the overall low enrollment at 3.2 percent and  
13 4.7 percent. I'm sure that there were many challenges  
14 in getting a higher percentage. But I also noted with  
15 interest the higher immunogenicity or hemo-immune  
16 response.

17           One was consistent with the older age groups  
18 you did with the data you presented yesterday. And in  
19 particularly the 6 to 23 month, it was almost two-fold  
20 higher than the white population or other populations.  
21 So one question I have for you is this a real distance,

1 or are we victims of small numbers? Is there some  
2 significance to the trend of a higher immune response  
3 that you're seeing with the Black participants?

4 And then a second question, just to prime you,  
5 is with respect to the immunogenicity dataset as a  
6 whole is there any evidence of possible over-  
7 representation from individuals with higher titers,  
8 either of Black race or perhaps even post-baseline  
9 infections?

10 **DR. JACQUELINE MILLER:** Yeah, thank you for  
11 those questions. So let me first put up the slide  
12 looking at the immunogenicity by race. So those slides  
13 are -- if you guys can find SY31. There we go. Put  
14 the slide up, please. I just saw it, Michael. I don't  
15 know.

16 **DR. ARNOLD MONTO:** Why don't you discuss it --

17 **DR. JACQUELINE MILLER:** There we go.

18 **DR. ARNOLD MONTO:** Okay.

19 **DR. JACQUELINE MILLER:** Yep, there we go. So  
20 these are the children, two to five. The pattern is  
21 similar in the youngest infants. In the interest of

1 time I'm happy to show it, but I understand we're short  
2 of time. So as you mentioned the immunogenicity  
3 cohort, which is of course a subset of the total  
4 cohort, there were 20 African-American children, and  
5 their titers were higher. But the 95 confidence  
6 intervals overlapped.

7           And, in terms of representation in the trial,  
8 I think we didn't see over-representation of groups  
9 that might have had reason to think that there were  
10 higher titers. So you see the proportion of the groups  
11 that had the highest titer in terms of race. And  
12 certainly, in terms of seropositives, they were much  
13 less frequent than seronegatives. And I can show you  
14 in the toddlers as well if you want to see, or if you  
15 want to move on, it's up to you.

16           **DR. ARNOLD MONTO:** I think we can move on.

17           **DR. MICHAEL NELSON:** That's okay.

18           **DR. ARNOLD MONTO:** Dr. Fuller, final question.

19           **DR. OVETA FULLER:** I just wanted to follow-up  
20 on the earlier question. I suspect that you're going  
21 to be looking at those things in the future, but my

1 concern is that the one child that had the seizure, was  
2 there any underlying thing like sickle cell or asthma  
3 or anything that could be detected? Because even  
4 though there only may be one, if that's someone's child  
5 that can identify that they have a risk factor that  
6 would be very useful to know.

7 **DR. JACQUELINE MILLER:** Yes, Dr. Fuller. So  
8 we don't really have other medical history on that  
9 child. They were previously well. I will say and I'll  
10 just add maybe for reference as a pediatrician febrile  
11 seizures often happen in children who are healthy with  
12 no underlying conditions. So they occur at a rate of  
13 about three percent between the peak ages of one to  
14 five. It didn't necessarily surprise us that this was  
15 a child who had no otherwise underlying conditions.

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

17 **DR. OVETA FULLER:** So did you look at things  
18 or will you look at things like sickle cell or that  
19 sort of thing in the future? I heard you mention  
20 immunocompromised earlier.

21 **DR. JACQUELINE MILLER:** Yeah, no, so the trial

1 in the immunocompromised is going to be specific and  
2 standalone. The power of our large effectiveness study  
3 in a diverse database like Kaiser Southern California,  
4 really allows us to look at events by different  
5 underlying conditions, allows us to look at different  
6 age groups and so forth. And so certainly hear the  
7 interest in seeing what the effectiveness looks like in  
8 children with sickle cell. So we will look into that.

9 **DR. OVETA FULLER:** Great. Thank you.

10

11 **COMMITTEE DISCUSSION AND VOTING - MODERNA COVID-19**

12 **VACCINE**

13

14 **DR. ARNOLD MONTO:** Thank you. And thank you  
15 to the sponsor and to FDA for their answering our  
16 questions. We now move on to the discussion of the  
17 voting question and the vote. And what we're going to  
18 be doing as usual is having the Committee discussion  
19 over the voting question. We will then vote, and then  
20 we will have explanation of votes for those who wish to  
21 explain their votes. Do we have the voting question

1 we're going to be discussing?

2 "Based on the totality of scientific evidence,  
3 do the benefits of Moderna's COVID-19 vaccine  
4 administered as a 2-dose series outweigh its risks for  
5 use in infants and children 6 months through 5 years of  
6 age?" Discussion. Dr. Meissner. Followed by Dr.  
7 Portnoy.

8 **DR. CODY MEISSNER:** Thank you, Dr. Monto. I'd  
9 like to make a couple of comments in regard to this. I  
10 don't think anyone could listen to the public -- the  
11 open public hearing session without being troubled by  
12 the diversity and the emotional commitment that's been  
13 put into this issue of immunizing children between six  
14 months and five years. It was quite moving.

15 My personal feeling is that it would be hard  
16 not to include six months to five years of age in an  
17 amendment to the EUA in view of the strength of the  
18 data that we have seen today. But I would like to make  
19 this comment. And I think it's very important, as Dr.  
20 Cohn said yesterday, that the communication or the  
21 messaging be made as clear as possible for parents to

1 understand the relative risk and the relative benefit.  
2 I think we -- for example, we've heard several times  
3 that there were approximately 442 deaths so far in the  
4 pandemic among children less than five.

5           So that means about 220 deaths a year,  
6 approximately. Now if you look at the number of people  
7 who are struck by lightning in the United States on a  
8 year, it's 270. So we're talking about a very rare  
9 event. If we talk about hospitalizations among  
10 children between six months and five years of age, the  
11 hospitalization rate on the CDC website, the latest  
12 study, is 2.3 per 100,000 or 23 per million. And there  
13 are about 20 million children in this age group.

14           So 20 times 23 is 460 hospitalizations  
15 associated with COVID in this age group that we're  
16 considering today. And probably only a fraction of  
17 those are because of COVID-19 infection rather than a  
18 coincidental association. So really we'd be talking  
19 about vaccinating close to 20 million children in order  
20 to prevent two or three hundred deaths. And it's a  
21 matter of how an individual weighs the risk and



1 benefit. I think the vaccine should be available for  
2 certainly high risk children and for families that are  
3 so concerned they are troubled by that risk ratio, and  
4 they should have access to the vaccine.

5 But I, again, feel very strongly that parents  
6 should understand how small these numbers are. The  
7 very low risk from the vaccine, but it's also a very  
8 low risk from the infection itself. And I think that  
9 has to be communicated clearly to parents so that they  
10 can participate in the decision about vaccinating a  
11 child in this age group. Thank you.

12 **DR. ARNOLD MONTO:** Thank you. Dr. Portnoy  
13 followed by Dr. Berger.

14 **DR. JAY PORTNOY:** Great. Thank you. I've  
15 really enjoyed this conversation, and I have to say I  
16 was extremely moved by the public comments as well.  
17 Nobody cannot be moved by it. But I work at a  
18 children's hospital, and I remember earlier this year  
19 walking by the emergency room and looking in and seeing  
20 that the place was completely filled. I asked one of  
21 the security guards what's going on, and he said, well,

1 it's COVID. And the emergency room was filled. Our  
2 hospital was loaded up with children who had COVID.

3 Now, I know that the death rate from COVID and  
4 young children may not be extremely high, but it's  
5 absolutely terrifying to parents to have their child be  
6 sick, have to go to the hospital or even go to the  
7 emergency room or their primary care doctor because  
8 they're sick and having trouble breathing.

9 So this is it's not just doubts. We have to  
10 understand how distressing this is for parents whose  
11 children are affected by this disease. Every  
12 pediatrician that I know at our hospital has been  
13 waiting eagerly for this vote to occur because they  
14 can't wait to start giving this vaccine.

15 So our question today is does the benefit  
16 outweigh the risk of this vaccine? And I think that  
17 the evidence is pretty clear for preventing severe  
18 disease, hospitalization, emergency visits. This  
19 vaccine is very effective. It's also very safe to use.  
20 I'm a little bit disappointed that it doesn't prevent  
21 infection by COVID as effectively as it could because

1 that's what spreads it around, but even in adults we  
2 can't prevent infection. But at least we can stop  
3 people from being terribly sick.

4           So this is a long-awaited vaccine. I feel the  
5 pain of those who are opposed to it, who have had bad  
6 experiences with it. They can choose simply to not get  
7 the vaccine. But there are so many parents who are  
8 absolutely desperate to get this vaccine, and I think  
9 we owe it to them to give them a choice to have the  
10 vaccine if they want to. Thank you.

11           **DR. ARNOLD MONTO:** Thank you. Dr. Berger  
12 followed by Dr. Fuller.

13           **DR. ADAM BERGER:** Thank you as well. And I  
14 was going to say something similar to what Dr. Portnoy  
15 was pointing out, is it's not just about deaths; it's  
16 about preventing hospitalization. And I think some of  
17 the really distressing information that we've heard is  
18 that a quarter of those children that are going to the  
19 hospital are ending up in the ICU. And 63 percent of  
20 them have no underlying comorbidity to actually be  
21 directing this. So you have to ask yourself like what

1 other -- those that do have comorbidities might be at a  
2 higher risk.

3           And so it really is about giving a choice.  
4 But yeah, I actually had a question about the question  
5 we're being asked. And part of this is just the  
6 framing. All the data we've been given and  
7 specifically the way it was collected was dividing up  
8 the 6 month to 23 month olds from the two to five year  
9 olds. And yet the question is putting them altogether.  
10 Now this may not change the outcome, but just it occurs  
11 to me that it's sort of an oddity in terms of the  
12 voting questions itself that we're being presented with  
13 because the data isn't exactly aligned 100 percent  
14 across both of those groups.

15           There are slight differences in vaccine  
16 efficacy and some of the side effects that we've seen.  
17 It may not be significant, but I did have a question  
18 for FDA as to why it was combined in the voting  
19 question as opposed to having it be separated into  
20 those two different age groups for voting.

21           **DR. ARNOLD MONTO:** Do we have an answer from

1 FDA, Dr. Fink?

2 **DR. DORAN FINK:** The EUA request from Moderna  
3 was for Emergency Use Authorization of the 25 microgram  
4 dose level for use in the age group of six months  
5 through five years. That is why the voting question is  
6 constructed accordingly. We yesterday dealt with two  
7 separate EUA amendment requests: one for adolescents,  
8 one for ages 6 through 11. And that's why those  
9 questions were constructed accordingly.

10 I do recognize that the data was presented  
11 according to the two smaller age groups within six  
12 months through five years, and for Pfizer it was done  
13 the same. But I would hope that the Committee would  
14 really focus on similarities and then consider the age  
15 group as a whole. And if they feel compelled -- if any  
16 Committee members feels compelled to have a different  
17 opinion for one smaller age group versus another, then  
18 of course you can raise that concern.

19 **DR. ARNOLD MONTTO:** Thank you. And I am  
20 reminded that this is a discussion right now. We will  
21 have a second session after the vote in which you can

1 explain your vote. So technically you're not supposed  
2 to say how you are voting at the moment. But you can  
3 say whether you support or not the approval. Dr.  
4 Fuller followed by Dr. Reingold.

5 **DR. OVETA FULLER:** Yes. That is what I was  
6 going to say, that the need for clear messaging to  
7 parents and guardians about the choice for having the  
8 vaccine or not is very important and that the follow-up  
9 studies that are planned are very important. The  
10 benefits seem to clearly outweigh the risk,  
11 particularly for those with young children who may be  
12 in kindergarten or in collective childcare so that  
13 those who want to do this will have that option.

14 But I would ask should this pass, or should  
15 this be recommended by FDA and by the Committee and  
16 passed by FDA and CDC, that parents really consult  
17 their pediatrician for their children. My question  
18 earlier wasn't just for sickle cell but any other  
19 unknown underlying condition that might impact the  
20 outcome. So this is a decision that parents and  
21 grandparents and guardians will have to carefully weigh

1 should this actually go through.

2           **DR. ARNOLD MONTO:** Thank you. Dr. Reingold  
3 followed by Dr. Sawyer.

4           **DR. ARTHUR REINGOLD:** So, thanks. One of the  
5 speakers in the public session urged us multiple times  
6 to think of the children. Now I think he and I may  
7 think of the children in slightly different ways. But  
8 my way of thinking about the children is that if we  
9 have a vaccine that's benefits outweigh the risks, that  
10 making it available to people is a reasonable choice.  
11 I would point out that we as a country continue to give  
12 a large number of vaccines to children where the risk  
13 of the child dying or being hospitalized of those  
14 diseases is pretty close to zero.

15           Those include polio. Those include measles.  
16 We vaccinate large numbers of people against HPV even  
17 though very few of them would ever develop cancer  
18 related to HPV. So we, with our vaccines, are trying  
19 to minimize serious illness and death or perhaps  
20 reintroduction of something like polio into the United  
21 States. But we generally know that many of the

1 infections that we are vaccinating against, that the  
2 serious outcomes are quite rare actually.

3           And we nevertheless try and vaccinate a large  
4 part of the population, if not everyone. So I think we  
5 do need to focus on the serious outcomes and even if  
6 they're relatively infrequent and even if a vaccine is  
7 less than 100 percent effective. Flu is another good  
8 example. We continue to recommend flu vaccines for  
9 people even though it only may be 30 to 40 percent  
10 effective. And so if we have a prevention opportunity,  
11 I believe we should take it.

12           But just one last caveat. My personal  
13 preferred wording is not to tell the people that  
14 something is safe. I think that's the wrong messaging.  
15 I think nothing in life is perfectly safe. No drug, no  
16 vaccine, no personal choice to get on a plane or get  
17 into a car is, quote, safe. I think what we need to  
18 emphasize is that the benefits outweigh the risks.  
19 Thank you.

20           **DR. ARNOLD MONTO:** Thank you. Dr. Sawyer  
21 followed by Dr. Levy.



1           **DR. MARK SAWYER:** First of all, I'm generally  
2 in support of approval for many of the reasons that  
3 have been outlined. To follow-up Dr. Reingold's  
4 comment I would like to add to the benefit column the  
5 fact that as we heard in the public comment some  
6 parents are so concerned about the risk of exposure  
7 that they're still completely isolating their children  
8 socially, perhaps above and beyond what the current CDC  
9 and AAP guidelines suggest.

10           And the potential adverse impact of that  
11 isolation was brought up also in the public comment  
12 session. So the availability of these vaccines will  
13 liberate those children to some extent whose parents  
14 will find relief and feel a little more comfortable to  
15 let their children start to socialize in the  
16 appropriate environment.

17           The other potential benefit that's been  
18 touched on is the impact on long COVID, which has  
19 further potential challenges for development as we  
20 learn more about long COVID does and what the  
21 implications are for school performance. So I think

1 there's a lot in favor of the benefit column in the  
2 risk/benefit equation.

3 **DR. ARNOLD MONTO:** Thank you, Dr. Sawyer. Dr.  
4 Levy last question so far.

5 **DR. OFER LEVY:** Thank you. I am generally  
6 supportive of this direction, and I also want to  
7 emphasize the importance of knowledge and that we keep  
8 building on our knowledge. We saw a lot of good  
9 information today, including some immunogenicity  
10 information. But as I mentioned yesterday, we have a  
11 ways to go to understand the correlates of protection  
12 against coronavirus. Antibodies are likely very  
13 important but not the whole story. We'd like to see T  
14 cell data; we'd like a recognition that correlates may  
15 be age specific. You might get a similar antibody  
16 response at a given age.

17 But antibodies act in a context together with  
18 a compliment system, with phagocytes, and those systems  
19 might be distinct by age due to immune ontogeny. So I  
20 encourage FDA and the sponsors to continue to develop  
21 more sophisticated and nuanced information about

1 correlates of protection. The other key here will be  
2 safety surveillance. The possibility of febrile  
3 seizures, particularly in those unusual cases where  
4 there's a high fever after the vaccine in the young age  
5 groups, it's possible we'll see febrile seizures as  
6 this gets pushed out, if indeed that's the  
7 determination by FDA.

8           So we have to keep an eye on that, and also  
9 potential impact on other -- balance of other  
10 respiratory infections is what was alluded to by FDA by  
11 Dr. Doran Fink. So those are areas that I think where  
12 knowledge -- it needs to continue to evolve. But  
13 overall, I'm supportive. It's a bioethical concept of  
14 a presumption of inclusion.

15           We have reasonable safety data, and this  
16 vulnerable population should be included. And there's  
17 a broader context. This platform, this mRNA vaccine  
18 platform may be useful not just against this current  
19 coronavirus and its current variants but the next ones  
20 as well as future pandemics. Thank you.

21           **DR. ARNOLD MONTO:** Thank you, Dr. Levy. That

1 concludes the questioning -- I mean, the comments  
2 concerning the voting question. We will now have the  
3 vote, and then we will have explanations from those who  
4 wish to explain their vote further.

5 **MS. CHRISTINA VERT:** Thank you, Dr. Monto.  
6 Only our 10 regular members and 11 temporary voting  
7 members, a total of 21, will be voting in today's  
8 meeting. With regards to the voting process, Dr. Monto  
9 will read the final voting question for the record, and  
10 afterwards all regular voting members and temporary  
11 voting members will cast their vote by selecting one of  
12 the voting options, which include yes, no, or abstain.

13 You have two minutes to cast your vote after  
14 the question is read, and please note that once you  
15 have cast your vote you may change your vote within the  
16 two minute timeframe. However, once the poll has  
17 closed, all votes will be considered final. Once all  
18 the votes have been placed, we will broadcast the vote  
19 results and read the individual votes aloud for the  
20 public record. Does anyone have any questions related  
21 to the voting process before we begin? Okay. Okay,

1 Dr. Monto, if you could please read the voting  
2 question?

3 **DR. ARNOLD MONTO:** For the record: Based on  
4 the totality of scientific evidence available, do the  
5 benefits of the Moderna COVID-19 vaccine when  
6 administered as a 2-dose series, 25 micrograms each  
7 dose, outweigh its risks for use in infants and  
8 children 6 months through 5 years of age?

9 **MS. CHRISTINA VERT:** Okay. Please pull up the  
10 voting pod. At this time you may start to vote. Okay,  
11 it looks like all the votes are in. We can go ahead  
12 and close the poll. Thank you. Okay. There are a  
13 total of 21 voting members for today's meeting, and the  
14 vote is unanimous. We have 21 out of 21 yes votes,  
15 zero no votes, and zero abstain votes. Okay. I will  
16 now read the specific votes for the record. Okay.

17 Dr. Berger, yes; Dr. Nelson, yes; Dr. Fuller,  
18 yes; Dr. Levy, yes; Dr. Monto, yes; Dr. Sawyer, yes;  
19 Dr. Offit, yes; Dr. Reingold, yes; Dr. Bernstein, yes;  
20 Dr. McInnes, yes; Dr. Wharton, yes; Dr. Pergam, yes;  
21 Dr. Chatterjee, yes; Dr. Portnoy, yes; Dr. Lee, yes;

1 Dr. Kim, yes; Dr. Cohn, yes; Dr. Marasco, yes; Dr.  
2 Meissner, yes; Dr. Hildreth, yes; Dr. Gans, yes. And  
3 that completes my reading of the votes. And I will  
4 hand the meeting back over to Dr. Monto.

5 **DR. ARNOLD MONTO:** Now we will proceed to  
6 explanations of the vote from anybody who wishes to  
7 speak. Dr. Hildreth.

8 **DR. JAMES HILDRETH:** Thank you, Dr. Monto. I  
9 think the evidence that we had in front of us justified  
10 a vote of yes. I did want to make a point that I made  
11 yesterday, that Dr. Meissner made a few minutes ago.  
12 We got to be transparent about the real risk of COVID-  
13 19 for children.

14 Tens of millions of children in this age group  
15 have been infected and have done just fine, but I think  
16 we need to make parents aware of what the real risks  
17 are and let them make decisions. But for those parents  
18 who choose to do so, especially those parents of kids  
19 with underlying conditions, this is a choice they  
20 should have and I'm pleased that they'll have it.  
21 Thank you.

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

2           **DR. JAY PORTNOY:** Thank you. As the  
3 designated consumer representative member of the  
4 Committee I can speak on behalf of the patients that I  
5 take care of. I know that there were a lot of very  
6 relieved parents, almost certainly who are listening to  
7 this right now. They've been waiting for a very long  
8 time. I again want to emphasize how terrified parents  
9 get when their children get sick, even if they don't  
10 die from it.

11           I take care of patients who have food allergy.  
12 The number of deaths from food allergy is extremely low  
13 and yet the parents are terribly anxious and worried  
14 about this disease. COVID actually causes a lot more  
15 deaths. I understand why parents are very nervous and  
16 fearful of doing normal activities and especially if  
17 their child actually catches COVID. But even the fear  
18 that they could catch COVID -- this will certainly  
19 alleviate a lot of their concerns, and so I'm really  
20 happy that the vote went the way it is. And I think it  
21 was the right vote. Thank you.

1           **DR. ARNOLD MONTO:** Thank you. And Dr. Nelson.

2           **DR. MICHAEL NELSON:** Than you, Dr. Monto. I  
3 do believe the benefits far outweigh the risks that  
4 were involved. And personally I really do believe this  
5 recommendation does fill a significant unmet need for a  
6 really ignored younger population in need of options.  
7 Families will now have choice that they did not have  
8 before.

9           And I fully believe in the intelligence of  
10 families to make the right choice for their family and  
11 children, particularly when we provide clear  
12 recommendations with respect to the information we have  
13 on hand regarding the risk and benefits. It's my  
14 personal hope that every child in the U.S. seeks and  
15 gets vaccinated in the near future. Thank you, Dr.  
16 Monto.

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

18           **DR. HENRY BERNSTEIN:** Thanks, Dr. Monto. I  
19 want to express my agreement with everyone else. With  
20 over 600 million COVID vaccine doses that have been  
21 already administered in the U.S. we really -- the



1 overall safety profiles are quite reassuring. And I  
2 think having a COVID vaccine available for this younger  
3 population is critically important given that pediatric  
4 cases can be, have been, and may be problematic in the  
5 future. I also think that there's a huge safety --  
6 vaccine safety monitoring system in the United States  
7 that's historic.

8           And so that should be reassuring to many, and  
9 I do think that there are advances in science -- in the  
10 COVID-19 science. They'll continue on for many years,  
11 not just vaccines, but treatments and testing and  
12 social distancing, masks, et cetera. I also think that  
13 hybrid immunity will provide more protection against  
14 future infections and will be helpful as well, even for  
15 those who have already experienced COVID because I  
16 think overall those who are vaccinated tend to do  
17 better in all outcomes than those that are  
18 unvaccinated.

19           And I think that the ultimate aim of COVID-19  
20 vaccine is to prevent severe disease, hospitalization,  
21 and death more than preventing transmission and

1 infection. I think the messages I want to emphasize  
2 what others have said -- the messaging must be  
3 communicated very clearly to the public. And I still  
4 feel that there are tens of millions of people who are  
5 unvaccinated, and we must also encourage them to get  
6 vaccinated. Thanks.

7 **DR. ARNOLD MONTTO:** Thank you. Dr. Levy  
8 followed by Dr. Gans.

9 **DR. OFER LEVY:** Yeah, I just wanted to take a  
10 moment to acknowledge the public commentary that shows  
11 the wide diversity of opinions in the U.S. public about  
12 this whole vaccine enterprise. And I think it becomes  
13 important that we continue that tradition of being open  
14 to all the public commentary, provided it's not hate  
15 speech, provided it's respectful -- but to cast a big  
16 tent here. And I think what we've heard from a lot of  
17 the Committee members -- they'll each speak for  
18 themselves, but what I've heard is the emphasis on a  
19 choice, a choice for families.

20 They can partner with their pediatrician, make  
21 the decision. If they're in a situation in a community

1 where there's a lot of spread of COVID, if they have  
2 children that may be at higher risk, if they have  
3 family members who are particularly vulnerable, we  
4 encourage them, if this moves forward, to avail  
5 themselves of this option. So it's a concept of making  
6 it available. And the ongoing safety surveillance, the  
7 U.S. public should hear that that's a serious  
8 enterprise. It's not a rubber stamp.

9           We've seen entire vaccine programs put on hold  
10 for rare cases of thrombosis. And I was interviewed in  
11 the media saying Dr. Levy, isn't it a mistake? Doesn't  
12 it shake public confidence when they stop a program? I  
13 said to the contrary. It should show the public that  
14 the safety surveillance works. That's its serious and  
15 that if we do detect further signals that are  
16 concerning, something will be done about it. So I  
17 think this is the right path forward, and I'm very  
18 honored to be part of this Committee. Thank you.

19           **DR. ARNOLD MONTTO:** Thank you, Dr. Levy. Dr.  
20 Gans followed by Dr. Marasco.

21           **DR. HAYLEY ALTMAN-GANS:** Thank you very much.

1 I just wanted to add a voice to the significance of  
2 this as a pediatric disease. I think as you weigh it  
3 in terms of being the fourth and fifth most risk factor  
4 for death is really important. So I think we really do  
5 need to not underplay the importance of this as a  
6 pediatric disease. And therefore, prevention is really  
7 the way to go. It's also of note and was brought up  
8 earlier that there are just all these treatments now  
9 that we have for COVID.

10           That's not the case for our youngest  
11 individuals. We actually have very restricted and  
12 limited ability to help anyone who is infected, and  
13 they are actually not the most efficacious. And so I  
14 think it's very important. The other point I wanted to  
15 bring up for the individuals who will be considering  
16 this for their families is that infection -- that the  
17 immune response that you can get from vaccine versus  
18 infection is different.

19           When you have an infection and you have viral  
20 replication and also tissue invasion and damage, it's  
21 different. You do get immune response, but getting

1 immune response without that is also, should be an  
2 option for individuals so that they don't have to  
3 suffer from the actual viral disease. So I think  
4 that's a really important point that hasn't been  
5 raised. I'm trying not to be repetitive for my  
6 colleagues who I know have raised some really great  
7 points.

8           The other aspect I would like to just add to  
9 Dr. Levy's point and others on this Committee is that  
10 we do take the science very seriously. And I hope that  
11 really has come through to those who maybe are doubting  
12 the fact that we're listening. We are considering all  
13 of the different science. And I just want to applaud  
14 the scientific community.

15           This is really a breakthrough that has allowed  
16 us to move through the pandemic in a way that has  
17 allowed less suffering and disease. I'm very glad for  
18 this option for people in the scientific community who  
19 care for children as well as families. Thank you.

20           **DR. ARNOLD MONTO:** Thank you, Dr. Gans. Dr.  
21 Marasco followed by Dr. Lee.

1           **DR. WAYNE MARASCO:** Hi. Thank you, Dr. Monto.  
2 So I've been impressed, as everybody has, with the  
3 comments by the public. They're very important. I  
4 take them seriously; I think we all do. It has not  
5 escaped me or other members of the Committee that we've  
6 received thousands upon thousands of emails from people  
7 on both sides of this issue.

8           I think it's really been largely a matter of  
9 misinformation or disinformation, people thinking that  
10 children weren't as susceptible as they were earlier in  
11 the pandemic. I don't think many people understand the  
12 increase in infection with Omicron. But I think it's  
13 all about people making their own decisions for  
14 themselves and their family.

15           Dr. Meissner and everybody else has really  
16 said it right. It's a matter of choice. I just want  
17 to make sure the messaging from the CDC and the FDA is  
18 coordinated in such a way that the healthcare providers  
19 -- the local healthcare providers can also provide that  
20 information to help families and parents make this  
21 decisions. So I'm proud to be part of this Committee,

1 and I agree with the decision that's been made.

2 **DR. ARNOLD MONTO:** Dr. Lee.

3 **DR. JEANNETTE LEE:** Yes, I just wanted to also  
4 add my support for this decision. I think as we heard  
5 in the public comments the lack of the vaccines for  
6 these young children has been a gap for many and has  
7 really had an impact on their lives. So I think this  
8 is really, really very positive. I will say I think  
9 it's clear the story isn't over.

10 The pandemic has taken some different twists  
11 and turns. And there may be more options for these  
12 children in the future, and I think we will consider  
13 that as well. And I'd also like to say I'm very proud  
14 to be part of this Committee and very, very pleased  
15 with all the science we've been able to see from the  
16 investigators and the companies. Thank you.

17 **DR. ARNOLD MONTO:** Thank you, Dr. Lee. That  
18 concludes our action on the Moderna vaccine. We're  
19 going to take a break until 3:25 Eastern. That gives  
20 us about 15 minutes; is that right?

21 **MR. MICHAEL KAWCZYNSKI:** Nope, 10 minutes.

1 Oh, 3:25 -- yeah, 15 minutes. Yes, you are right.

2 **DR. ARNOLD MONTO:** Yeah. Yep. A reward for  
3 getting done. We'll start when we should have been  
4 taking the break, 15 minutes. And then we will repeat  
5 what we've just done: questions, discussion, and vote  
6 for Pfizer.

7 **MR. MICHAEL KAWCZYNSKI:** All right. And with  
8 that we will now take our 15 minute break. Studio.

9

10 **[BREAK]**

11

12 **ADDITIONAL Q&A FOR FDA AND SPONSOR PRESENTERS - PFIZER-**  
13 **BIONTECH COVID-19 VACCINE**

14

15 **MR. MICHAEL KAWCZYNSKI:** Okay. Good afternoon  
16 and welcome to the closing session of the 174th  
17 Vaccines and Related Biological Products Advisory  
18 Committee Meeting. Dr. Arnold Monto, our chair, take  
19 it away.

20 **DR. ARNOLD MONTO:** Thank you very much. We  
21 will now repeat the process of questions to both the



1 sponsors and to FDA and then discussion and votes and  
2 explanation of votes. So hands raised for questions  
3 for either the sponsor or FDA. Dr. Marasco followed by  
4 Dr. Gans.

5 **DR. WAYNE MARASCO:** Thank you, Dr. Monto. Dr.  
6 Gruber, this is a question for you. It's a question  
7 that was touched on by Dr. Pergam, Portnoy, and Offit,  
8 and it really has to do with your 3 microgram dose. So  
9 there's a pretty impressive step-up in protection from  
10 your second to third dose for Omicron and a pretty low  
11 dose of mRNA, and I heard from your associate that  
12 you've got good protein production.

13 But the question I really am asking is, is  
14 there a fundamental difference that has occurred with  
15 your vaccine? In other words, because of the low dose  
16 that you have given, are you getting any different  
17 quantitative or qualitative response in terms of, for  
18 example, higher affinity antibodies? So when you do  
19 your titering and you get your main geometric titer,  
20 you get a number.

21 Is that because of higher titer antibodies --

1 I mean, higher titers or more higher affinity to the  
2 Omicron? And those kind of studies can be done quite  
3 simply serologically, and I'm wondering if you're  
4 pursuing that to find out if there's something  
5 qualitatively and quantitatively different about the  
6 effect you see in your third dose?

7 **DR. WILLIAM GRUBER:** Thanks for the question.  
8 I may ask Kena Swanson to actually come up to provide  
9 maybe a little bit more detail, but to this point we  
10 haven't actually specifically looked in detail,  
11 certainly in the pediatric population, about the nature  
12 of antibody affinity. I come back to the fundamental  
13 observation that, as best as we can determine, the  
14 level of neutralizing antibody that we see against  
15 Omicron seems to reliably predict the likelihood that  
16 you're gonna have protection.

17 When that antibody is low, regardless of  
18 whether it's related to affinity or related to the  
19 actual quantity of antibody that's there that has  
20 neutralizing potential, it predicts the likelihood that  
21 you're gonna be successful. Low antibody, less

1 efficacy. Higher antibody, higher efficacy.

2           And again, we've shown that antibody that we  
3 induce in these young children matches that in older  
4 adults or in older children and adults after three  
5 doses and provides protection. But maybe I can ask Dr.  
6 Swanson just to comment on any other sort of work that  
7 we're doing related to characterizing antibody.

8           **DR. KENA SWANSON:** Hi, Kena Swanson from  
9 Pfizer Viral Vaccines. And just to add briefly to what  
10 Dr. Gruber mentioned, I think the key to what we're  
11 seeing in the development of the immune response is  
12 between the second and the third dose. There is not  
13 only an increase in the neutralizing titer but the  
14 activity and binding affinity of those antibodies,  
15 particularly that you can notice against Omicron. And  
16 that's been seen in the data in the adults.

17           And we're seeing indications that the trend is  
18 similar as well in children less than five years of  
19 age. And there are other publications and preprints  
20 out there that have done similar analysis in other  
21 populations.

1           **DR. WAYNE MARASCO:** Thank you.

2           **DR. WILLIAM GRUBER:** Yeah, maybe if I can just  
3 enlarge on that on a point because I want to clarify  
4 something that was being said this morning that this  
5 really interdigitates with. And that is that both in  
6 the briefing document as well as in the information  
7 that the FDA shared with you in their slide  
8 presentation, you've seen Kaplan Meier curves.

9           And for the two to four year olds it's pretty  
10 clear that, whether we're talking about Delta or we're  
11 talking about Omicron, even after the second dose you  
12 do see a spreading of those curves. And if you think  
13 about it, the amount of Delta that we saw is actually  
14 dwarfed by the amount of Omicron. So much of that  
15 efficacy that you're seeing even after the second dose  
16 is due to efficacy against Omicron.

17           For the six months to less than two year olds,  
18 it's less clear about when that efficacy may start to  
19 occur, but you can see as you go farther out that the  
20 curve begins to spread a little bit. And the goal  
21 really is with the third dose to move everything to the

1 left, to maximize the potential that we can have for  
2 protection against Omicron by giving that third dose.

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

4 **DR. HAYLEY ALTMAN-GANS:** Thank you. And I  
5 think I would love to hear some of the vision of what  
6 Pfizer is going to do. We heard quite a bit from  
7 Moderna about some of the studies that they're going to  
8 be doing forthcoming. And thank you for providing the  
9 ones that we heard about earlier today. We don't have  
10 to repeat those. The ones that I was really  
11 considering is it's not unusual to need a prime-prime-  
12 boost strategy. So the three doses here doesn't  
13 surprise many people.

14 And I think that's all within keeping. My  
15 question for you, particularly because these were  
16 developed during a time when there's obviously disease  
17 progression, variants coming into being, what will be  
18 your follow-up studies? How likely is it that -- and  
19 probably pretty likely because we're seeing that in the  
20 adult population -- but what are you doing to prepare  
21 for future doses, and are you looking at any other

1 dosing in terms of how much you're giving and the  
2 intervals?

3 **DR. WILLIAM GRUBER:** Yeah, so thanks for that  
4 question. We're obviously all looking forward to the  
5 end of this month when at the VRBPAC further decisions  
6 on the nature of what future vaccines should look like  
7 will be informed, both by information that we're  
8 providing based on our bivalent vaccine experience and  
9 our Omicron experience in adults. We are actually  
10 working then based on the information that comes out of  
11 that meeting to best tailor what we do to investigate  
12 young children.

13 It's no surprise to you, Dr. Gans, we have  
14 sort of two groups we have to contend with here, those  
15 that are naïve, what's going to be best for them moving  
16 forward as well as those that we put in good position,  
17 we hope, based on hopefully today's recommendation from  
18 the VRBPAC Committee to have them fully primed, ready  
19 for whatever else we might bring in the future.

20 **DR. HAYLEY ALTMAN-GANS:** Thank you.

21

1           **COMMITTEE DISCUSSION AND VOTING - PFIZER-BIONTECH**

2                           **COVID-19 VACCINE**

3

4           **DR. ARNOLD MONTO:** Thank you. And thanks both  
5 to the sponsor and to the FDA group. We have no more  
6 questions from the panel. And therefore we will move  
7 to discussion of the voting question. And could we  
8 have the voting question put up?

9                   Based on totality of evidence, do the benefits  
10 of the Pfizer-BioNTech COVID Vaccine when administered  
11 as a 3-dose series outweigh its risks for use in  
12 infants and children 6 months through 4 years of age?  
13 That is going to be our voting question. Now  
14 discussion, we don't want to say how you're voting, but  
15 you can say whether you support approval. So, Dr.  
16 Offit.

17           **DR. PAUL OFFIT:** Thanks, Arnold. I think that  
18 the way that this question is written, do the benefits  
19 outweigh the risks, is something I could support. But  
20 I do have some concerns about this vaccine, and I just  
21 want to sort of air them. It does worry me actually

1 that there was no protection after dose two. I thought  
2 that was surprising. I think it was probably  
3 surprising to the company. And I fear that they may  
4 have under-dosed.

5           We were supposed to meet on February 15th to  
6 discuss this. We didn't, I think, in part because  
7 those data probably were surprising. And with Moderna,  
8 you have, for example, low levels of protective  
9 efficacy after dose two, but you can assume that  
10 probably is predictive of better protection against  
11 severe disease. I'm not so sure you can predict that  
12 with Pfizer's vaccine.

13           Now, on the other hand, with the third dose,  
14 you get the kind of immune briefing data that is  
15 reassuring. The neutralizing antibodies against  
16 Omicron is reassuring. But that's dose three. So for  
17 people who've gotten that vaccine, who've gotten, say,  
18 two doses of that vaccine, they have to know they're  
19 not protected. And they're going to have to wait a few  
20 months till they are protected. And I just wonder  
21 whether parents will understand that. So I do worry



1 about this because I think it was a surprisingly  
2 negative result.

3           Although the protective efficacy that was  
4 listed with 75 percent for the six month old to two  
5 year old and 80 percent for the older group, those were  
6 based on very small numbers. I mean it was seven cases  
7 in one instance, three cases in another. It's a little  
8 hard to feel comfortable about that since the numbers  
9 were so low. But so, I do support this, but I do worry  
10 that parents aren't necessarily going to know that  
11 after two doses they may not be protected at all and  
12 would engage in the kind of activity that would put  
13 their child at risk. So, thank you.

14           **DR. ARNOLD MONTO:** Dr. Offit, would you be  
15 more comfortable if in the post-approval period careful  
16 surveillance be given about protection after two doses  
17 given the relatively small numbers? Is this something  
18 that can't be fixed?

19           **DR. PAUL OFFIT:** Yes, exactly. No, I think  
20 that's a really good point. And as more and more  
21 children are vaccinated we'll learn more. And it may

1 be that what Dr. Cohn said earlier is true, that this  
2 may end up being a four-dose vaccine. But I do think  
3 we should certainly learn as much as we can when it  
4 gets out there. I think it's safe. I think it will  
5 certainly offer something, but I do worry that those  
6 two dose data were surprisingly poor but thank you.

7 **DR. ARNOLD MONTO:** Okay. Dr. Chatterjee  
8 followed by Dr. Lee.

9 **DR. ARCHANA CHATTERJEE:** Thank you, Dr. Monto.  
10 I was actually going to make a very similar comment to  
11 what Dr. Offit did, with regard to the two doses not  
12 providing sufficient protection. I think with two  
13 vaccines that have different dosing regimens it's  
14 going to be even more important than ever that the  
15 public education, the education of providers is done  
16 very, very carefully so that people understand what the  
17 ramifications of the choices that was discussed earlier  
18 this afternoon are, that we are making choices between  
19 two different vaccines that have a little bit different  
20 profiles.

21 And that's going to be important for people to

1 take into consideration. Having said that, I would say  
2 that I was pleased to see the three dose data showing  
3 that it brings it up to par basically, like we see in  
4 older children and adults, the level of protection,  
5 recognizing of course that this virus is continually  
6 changing and that those numbers are maybe true today  
7 and may not be true down the road.

8           But with all of those caveats, I am in support  
9 of the authorization of this vaccine as well, making  
10 sure, again, that the education around this is done  
11 very, very carefully so that people are not misled by  
12 what the vaccines actually provide.

13           **DR. ARNOLD MONTO:** Yes, and I think we should  
14 not underestimate the problems of rolling out various  
15 approaches to vaccination which have different  
16 intervals and different doses and the rest. This is  
17 going to be quite challenging. Dr. Lee followed by Dr.  
18 Cohn.

19           **DR. JEANNETTE LEE:** Yes, thank you. So I  
20 share the concerns of the last two speakers about the  
21 two-dose data. I was also actually quite surprised. I

1 guess my concern is I do recognize that the three  
2 doses, they're certainly of benefit. I have a lot of  
3 concern that many of these kids will not get the third  
4 dose. As we know, it's a struggle to get people in for  
5 two. We've already seen with the boosters for adults,  
6 lots of people don't take them. And so my concern is  
7 that you have to get the three doses to really get what  
8 you need. I'm just concerned that some won't. Having  
9 said that, I will say that I am supportive of this  
10 though. Thank you.

11 **DR. ARNOLD MONTO:** Dr. Cohn and then Dr. Marks  
12 is going to be making some comment.

13 **CAPT. AMANDA COHN:** Thank you. I'm also very  
14 supportive and agree that the benefits do outweigh the  
15 risk of this vaccine. Just to add to what the previous  
16 commentators have said, I think it is imperative that we  
17 do post-licensure surveillance for effectiveness for  
18 both vaccines. But in particular, I'm also concerned  
19 about people comparing the VE estimates or point  
20 estimates between these two, which I think is a real  
21 problem given the few number of cases.

1           And I would really hope in our communications  
2 that we not use that 80 percent effectiveness because  
3 my level of confidence in that number, I believe the  
4 vaccine is effective. I do not have any idea what that  
5 number will actually end up being. And additionally, I  
6 think it's really important for people to understand  
7 not -- that this was effectiveness after 30 days.  
8 Other vaccines have looked at effectiveness after  
9 longer periods of time of follow-up. So 30 days after  
10 vaccination, this could fall off very quickly, and we  
11 just want to monitor it closely.

12           **DR. ARNOLD MONTO:** Yeah, Dr. Cohn, you noticed  
13 the confidence intervals around some of these  
14 estimates, correct? We really can't go with the point  
15 estimates because the confidence intervals for a lot of  
16 them were pretty wide until you grouped together. Dr.  
17 Marks, you had some comments.

18           **DR. PETER MARKS:** I just thought it might be  
19 helpful. I apologize if I missed this, but I didn't  
20 hear the sponsor reply to this. But it may be helpful.  
21 There does seem to be a lot mystery around the second

1 dose effectiveness with Pfizer. And it might be  
2 helpful for both the public and for the Committee if  
3 they commented on that two-dose effectiveness.

4 **DR. ARNOLD MONTO:** Okay. That's fine. I  
5 remember their saying that the Kaplan Meier plots did  
6 separate. Dr. Gruber, would you supplement the  
7 information we've got?

8 **DR. WILLIAM GRUBER:** Yeah, so again, there are  
9 really two lines of evidence. We've already spent time  
10 showing the slides in terms of the Delta response,  
11 right? And for both age groups after a second dose we  
12 had high levels of efficacy, both in the six month to  
13 less than two year olds. In the individuals that were  
14 two to five we also demonstrated efficacy after Delta.  
15 The real question obviously in an Omicron environment  
16 is what we're seeing after Omicron.

17 And if my slide pullers can pull it up, or  
18 people can likely remember it or you may see it in your  
19 briefing document -- again, if you looked at the two to  
20 less than five year olds you see separate of the curve.  
21 Yeah, let's bring slide one to screen, please. So keep

1 in mind again that we have a total of 10 cases in terms  
2 of post-dose three. So most of the cases that you're  
3 seeing here represent cases after dose two. And you  
4 can see based on the X-axis, the number of days, and  
5 sort of calculate then, well, if it's 21 days between  
6 the first dose and the second dose -- because this is a  
7 Kaplan Meier based on the time from the first dose, you  
8 can see spreading of the curve that starts fairly early  
9 and then continues to spread in the two to four year  
10 olds.

11 So it's not as if there's no efficacy at all.  
12 The notion is we're building on a level of efficacy  
13 that, in every other population, we regard as  
14 insufficient for Omicron. And the goal here, based on  
15 what we're showing you with the third dose, is to  
16 improve upon that efficacy.

17 If we then show, if you put slide -- well,  
18 let's see. Yeah, slide one up, please. So slide one,  
19 in this case we're talking about the six month to two  
20 year olds, and it's true that if you walk through most  
21 of the period of time here you're not seeing a

1 separation of the curves. But given that they're a  
2 total of three cases, some of that separation at the  
3 end may well be due to maturation of immune response  
4 and the fact that those children now are beginning to  
5 show some evidence of efficacy.

6 But the goal with the third dose in this  
7 circumstance is to shift that to the left where we  
8 essentially can build upon the ability to provide some  
9 protection against disease by moving that separation of  
10 the curve to the left. And keep in mind again, as with  
11 every other circumstance, there's some expectation that  
12 protection against severe disease is likely to be  
13 higher than what we're seeing against just symptomatic  
14 infection. So hopefully, Dr. Marks, that helps  
15 clarify.

16 **DR. PETER MARKS:** I appreciate it. Thank you.

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

18 Thanks, Dr. Marks. Thanks, Dr. Gruber. And Dr. Gans,  
19 it looks like you are going to have the final word in  
20 our discussion.

21 **DR. HAYLEY ALTMAN-GANS:** Thank you. I just



1 wanted to point out that a lot of people have pointed  
2 out particularly that there's three doses needed here  
3 to provide protection. But in terms of what the public  
4 and parents should expect, it's likely that Moderna's  
5 also going to be a three-dose schedule.

6           So I just wanted to put that into context of  
7 what we understand. And that doesn't take away from  
8 the comments that my colleagues have already provided  
9 or the feelings that we have about these different  
10 vaccines. Thank you.

11           **DR. ARNOLD MONTO:** Thank you, Dr. Gans. No  
12 more hands raised, so we move to the vote. Christina.

13           **MS. CHRISTINA VERT:** Thank you, Dr. Monto.  
14 Okay. Can you please -- let's go down to the next  
15 slide.

16           **DR. ARNOLD MONTO:** Let's get the right  
17 question up.

18           **MS. CHRISTINA VERT:** Okay. As you can see  
19 before us on the slide, here are the members and  
20 temporary voting members that will be voting. And  
21 then, Dr. Monto, if you could please read the voting

1 question?

2           **DR. ARNOLD MONTO:** Okay. Based on the  
3 totality of scientific evidence available, do the  
4 benefits of the Pfizer-BioNTech COVID-19 vaccine when  
5 administered as a 3-dose series, 3 micrograms each  
6 dose, outweigh its risks for use in infants and  
7 children 6 months through 4 years of age?

8           **MS. CHRISTINA VERT:** Okay. At this time you  
9 can go ahead and vote. You have two minutes to vote.  
10 Okay. It looks like all the votes are in. You can go  
11 ahead and close the poll and broadcast the results.  
12 Okay. There are 21 total voting members, and we have  
13 here 21 yes votes. This is a unanimous vote. And  
14 there are zero no votes and zero abstain.

15           And now I will go ahead and read the specific  
16 voting responses for the record. Dr. Berger, yes; Dr.  
17 Nelson, yes; Dr. Fuller, yes; Dr. Levy, yes; Dr. Monto,  
18 yes; Dr. Sawyer, yes; Dr. Offit, yes; Dr. Reingold,  
19 yes; Dr. Bernstein, yes; Dr. McInnes, yes; Dr. Wharton,  
20 yes; Dr. Pergam, yes; Dr. Chatterjee, yes; Dr. Portnoy,  
21 yes; Dr. Lee, yes; Dr. Kim, yes; Dr. Cohn, yes; Dr.

1 Marasco, yes; Dr. Meissner, yes; Dr. Gans, yes; Dr.  
2 Hildreth, yes. And that concludes my reading of the  
3 specific votes. And I will now hand the meeting back  
4 over to Dr. Monto.

5 **DR. ARNOLD MONTO:** Thank you. And before I  
6 hand -- oh, we have an explanation of votes. Dr. Levy.

7 **DR. OFER LEVY:** Yeah, I just wanted to offer  
8 some thoughts here. I'm really pleased that we've  
9 reached this kind of milestone. I recall our first  
10 vote a year ago or more on the first Pfizer  
11 authorization. I was one of the 17 votes in favor. I  
12 remember those early discussions even then should the  
13 16 and 17 year olds be included. At that point that  
14 was a controversial topic that was being discussed.  
15 And here we are now as a Committee unanimously  
16 recommending authorization down to six months of age.  
17 So we've come a long way.

18 The warp speed of vaccine initiative more or  
19 less worked. It got us safe and effective vaccines in  
20 record time. But I just want to make the point that  
21 there's a lot of work to do ahead in vaccinology. We

1 have inequities globally in access to the vaccine.  
2 I'll point out that the majority of the vaccine  
3 infrastructure in the world is pediatric. And  
4 pediatric vaccines achieve higher population  
5 penetration for that reason.

6           So that's something interesting to contemplate  
7 as we think about global inequities in immunization  
8 against this pandemic. The other point I'll point out,  
9 and it was evident in the discussion, is the number of  
10 doses required -- two, three, maybe four in  
11 immunocompromised individuals, maybe five. So we're  
12 very fortunate to have safe and effective vaccines in  
13 record time, and yet still we can't all go home now.  
14 There's a lot of work, a lot of research still to be  
15 done.

16           Can we design vaccines that give single-shot  
17 protection, that cover all of the different variants,  
18 that are pan-coronavirus vaccines, are vaccine  
19 adjuvants a potential approach to get better efficacy  
20 with one or two doses, instead of needing three, four,  
21 or five doses? So this is a public plea to keep

1 supporting around the globe vaccine research so that we  
2 can have even better vaccines in the future. Thank  
3 you.

4 **DR. ARNOLD MONTO:** Dr. Nelson.

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

6 Just a couple of quick comments clearly in favor of the  
7 voted question as voted. Having options at every age  
8 group is important. And certainly this second vote  
9 contributes to that and does contribute to options and  
10 choice for families throughout the United States. Two  
11 quick comments/caveats. I do think there is certainly  
12 needed data to look specifically at the stratification  
13 of both the immune response and the reactogenicity  
14 based on the interval between that second and third  
15 dose.

16 We saw discordance today with the  
17 immunogenicity data generated early, but the safety  
18 data with the larger groups spread out throughout that  
19 entire period. And with the numbers involved I'm not  
20 sure we have the full signal of where that benefit/risk  
21 ratio is for that third dose. To me it probably looks

1 closer to a vaccine like hepatitis B, where there is  
2 evidence that that third dose actually given later  
3 might work.

4           But in this case, with the gap in efficacy  
5 apparently having it closer to that second dose may be  
6 advantageous and would certainly, if families are  
7 listening, err towards that direction. And then  
8 finally, the coadministration issue that has come up  
9 over and over today is something that I too have been  
10 concerned about going into today's discussion. I'm  
11 glad to hear that our sponsors are going to look into  
12 the question.

13           I will tell you that if we don't get a quick  
14 answer to the coadministration question, it will serve  
15 as a barrier to completion of these three dose series  
16 for this vaccine and likely the Moderna vaccine.  
17 Having to get it in isolation is going to be a great  
18 challenge for families and children here in the U.S.  
19 Thank you, Dr. Monto.

20           **DR. ARNOLD MONTO:** Thank you, Dr. Nelson. Dr.  
21 Fuller followed by Dr. Chatterjee.

1           **DR. OVETA FULLER:** Yes, thank you, Dr. Monto.  
2 I just want to say that the idea of having Pfizer and  
3 Moderna is very for good families and also that we  
4 should not forget that the mitigations of masking and  
5 these things that work, that we know work, should not  
6 be forgotten, even with those who are vaccinated,  
7 because we don't understand the reinfections or the new  
8 infections with new strains.

9           So people need to be reminded in the messaging  
10 the importance of the things that we do know that  
11 works, such as distancing and just being careful and  
12 using what we know. And so I'm very pleased that we  
13 have two opportunities to help those with younger  
14 families, and there's a lot of work still ahead to be  
15 done.

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

17           **DR. ARCHANA CHATTERJEE:** Yes, thank you, Dr.  
18 Monto. As a pediatrician, today is a red letter day  
19 for me. To be able to vote for authorization of two  
20 vaccines that will protect children down to six months  
21 of age against this deadly virus is a very, very

1 important thing. And I am also thinking back, like Dr.  
2 Levy, to December 10, 2020, which is the day that we  
3 authorized the very first vaccine for use in people who  
4 are 16 years of age and older.

5           And I was actually one of the no votes, which  
6 got me into a lot of trouble. But the reasoning behind  
7 that, and we were able to explain that later, was that  
8 the four of us who voted no that day all had  
9 essentially the same reasoning, I believe. And that  
10 was that we insufficient data in the 16 and 17 year  
11 olds. We had data only on 150 participants when the  
12 ongoing had 2,000 in it. If we had just waited a  
13 little longer, we would have had those data.

14           It's interesting to think back to that time,  
15 but it's also important to look forward as Dr. Levy has  
16 pointed out. There is much work still to be done  
17 against this virus and against other infectious disease  
18 threats that face our population. And so I am just  
19 very, very grateful to have been part of this effort,  
20 and I'm delighted that we have been able to recommend  
21 authorization for these two vaccines for our very



1 youngest children. Thank you.

2 **DR. ARNOLD MONTO:** Thank you. Dr. Cohn and  
3 then Dr. Pergam.

4 **CAPT. AMANDA COHN:** Thanks. I just wanted to  
5 say quickly I am obviously, as a pediatrician, super  
6 happy that we can now vaccinate down to six months of  
7 age. But really I just want to express my deep  
8 gratitude and admiration for the staff at FDA who have  
9 made this happen because my confidence in this vote  
10 today is entirely related to the just clearly  
11 incredible amount of work that many, many staff at FDA  
12 have been put in.

13 The number of people who have presented and  
14 put this all together is incredible. And I know we  
15 have another meeting in two weeks, and the work is not  
16 done. But I just think taking a moment and thanking  
17 the staff that put all this effort into this, I just  
18 wanted to do that.

19 **DR. ARNOLD MONTO:** Dr. Cohn, you're stealing  
20 my closing remarks, but I'm still going to say it when  
21 we get to the close. Dr. Pergam.

1           **DR. STEVEN PERGAM:** I just laughed because  
2 Amanda always says such great comments, and they're  
3 always appreciated by other members of the Committee.  
4 I can say that. I do think it is important as we have  
5 this discussion about the importance of having two  
6 vaccines available for children that, as the FDA thinks  
7 about this and the CDC in terms of providing vaccine  
8 across the country -- that when the primary vaccine  
9 doses were given, Moderna and Pfizer were not  
10 adequately distributed in different parts of the  
11 country.

12           And so I think it's really important that both  
13 of these options are available throughout. And we're  
14 in a different situation with vaccine availability than  
15 we were in the past, but I think it's going to be  
16 really contingent upon both -- to provide both of these  
17 options throughout the U.S. and not have specific  
18 locations where one or the other as offered.

19           I think it's really important since these are  
20 different. There are different caveats that parents  
21 may look at when they're offering these to children or

1 making decisions that I think it's critical that  
2 they're made available across the country.

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

4 **DR. CODY MEISSNER:** Thank you, Dr. Monto. One  
5 very brief comment. Similar to my comment regarding  
6 Moderna, I think it's the right decision today to make  
7 these vaccines available for this age group. But I  
8 also think it's important that people understand it's a  
9 small number of children who have received these  
10 vaccines. And the safety is not as well-established as  
11 it is in adolescents and adults. So it's so important  
12 to continue to follow the safety profile of these  
13 vaccines. Again, I don't think they should be required  
14 for any specific situation. Thank you.

15 **DR. ARNOLD MONTO:** Thank you, Dr. Meissner.  
16 Dr. Marks, do you want to make any closing comments?  
17 And after that, I'd like to make some closing comments.

18 **DR. PETER MARKS:** Yeah, no, thanks, Dr. Monto.  
19 I'm going to -- I think Amanda started it very nicely,  
20 but I just want to summarize that the past two days we  
21 heard excellent presentations from sponsors, from FDA.

1 We heard open public hearing speakers, and I think it  
2 is a bit of a milestone to bring down the age range for  
3 these vaccines as we work through this. I also think  
4 we heard -- we have to be aware of the fact that we  
5 care tremendously at FDA about the safety and  
6 effectiveness of these vaccines.

7           And we will continue to monitor these vaccines  
8 as they are deployed. I would just remind the public  
9 that VAERS is a method that captures all adverse events  
10 and causality. And VAERS is not -- it's not  
11 established. There seems to be a lot of  
12 misinformation, and I'm saying it right now in real  
13 time because I'm watching Twitter storms in front of me  
14 about misunderstanding VAERS. VAERS, anyone is able to  
15 submit an adverse event to VAERS.

16           We actually require that certain things be  
17 submitted to VAERS. And so it can, from casual  
18 inspection of VAERS, look like there are things that  
19 are associated with the vaccines. But until one sorts  
20 through that, one does not know what is truly  
21 associated with the vaccines. And indeed we have

1 experts that spend a lot of time and that pride  
2 themselves -- they work day and night to ensure that  
3 they understand the safety profile of these vaccines.

4           That has been done and will continue to be  
5 done diligently. And as we have findings, as we did  
6 with myocarditis, thrombosis-thrombocytopenia syndrome,  
7 Guillain Barré syndrome, for rare adverse events, we  
8 will make sure the public knows about them. So I just  
9 want to say that -- want to just remind people of that  
10 and just take a final moment to thank the Committee  
11 members for an incredible amount of time and thank our  
12 FDA staff, who have really worked beyond anything that  
13 could have ever been expected of them.

14           From the Advisory Committee staff to those  
15 helping to run today's meeting technically, to those  
16 reviewers and management in the Office of Vaccines and  
17 the Office of Biostatistics and Pharmacovigilance and  
18 Biologics Quality who have relentlessly worked on this,  
19 very grateful for all their work. Thank you and thank  
20 you, Dr. Monto, for chairing this meeting. I'll turn  
21 it back over to you.

1           **DR. ARNOLD MONTTO:** And I wanted to thank you,  
2 Dr. Marks, and your staff for an enormous amount of  
3 work that's gone into this. I was glad to hear our  
4 Committee members remember back to December 10, 2020,  
5 when we first approved a vaccine for SARS-CoV-2 virus  
6 and the fact that there were negative votes and we've  
7 now, a year and a half later, almost to the day,  
8 approved a vaccine down to age six months of age, so  
9 essentially all of the American population can now  
10 choose or be chosen to get vaccine.

11           And we had some negative votes there, and I  
12 remember that we didn't even have time because we were  
13 running over and all sorts of things going on because  
14 of the pressure to get vaccines approved at that point.  
15 And we didn't have the time to have individuals like  
16 Dr. Chatterjee explain their vote, which wasn't against  
17 the vaccine but the fact that we didn't have sufficient  
18 data.

19           What's happened since that time is that we  
20 have had observational studies which have guided us in  
21 terms of the parade of variants that we've had since

1 that time, the need for booster doses, and now a year  
2 and a half later we've got pediatric vaccines approved  
3 down to age six months. Why a year and a half?  
4 Because of a lot of things that have happened over that  
5 time. It has not been easy. And to say that there  
6 have been delays, unnecessary delays, is not  
7 representing the true situation, which involved not  
8 working with adults but with a vulnerable younger  
9 population for whom special care is necessary.

10           So, in closing, I would like to let the public  
11 know how hard Dr. Marks and the entire staff at FDA  
12 have worked to reach this milestone. When we organize  
13 these meetings, emails come in at 11 o'clock at night  
14 over the weekend. People are working overtime to get  
15 the public availability of these nearly miraculous  
16 vaccines.

17           I work in flu, where if we have 50-60 percent  
18 effectiveness. That's pretty good. And here we have  
19 vaccines which are highly effective in preventing  
20 severe disease. I'm very delighted to have had the  
21 privilege of sharing these sessions and getting us

1 these very critically important vaccines. I just wish  
2 everybody would realize how well they work in  
3 preventing severe disease.

4 I would like to close this meeting and hand  
5 this over for the official closing to Dr. Atreya. And  
6 thank you, Dr. Atreya, and I hope you get some rest so  
7 you don't have to send me emails at 11 o'clock at night  
8 when I can't read things through my regular email  
9 assistant. Thank you.

10

11

**MEETING ADJOURNED**

12

13 **DR. PRABHAKARA ATREYA:** No problem. Thank you  
14 all with those closing comments. I really thank the  
15 whole Committee and the staff. We've all been working  
16 really hard in making these meetings successful. I  
17 greatly appreciate it. So, with that, I officially  
18 adjourn the meeting for today. Thank you all and  
19 namaste.

20 **MR. MICHAEL KAWCZYNSKI:** All right. And with  
21 that, this meeting has been officially adjourned. Any



1 questions or comments, please send them to our email  
2 address and have a great day. Studio, please end the  
3 meeting.

4 **[MEETING ADJOURNED]**