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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

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Paula Annunziato, M.D.	Merck
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Archana Chatterjee, M.D., Ph.D.	Rosalind Franklin University
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Paul Offit, M.D.	The Children's Hospital of Philadelphia
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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
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Evan Anderson, M.D., FAAP	Emory University School of Medicine
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Dr. Ashley Serrano	
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Nicholas Giglia	
Lauren Dunnington	
Kathlyn Hinesley	
Melissa Braveman	
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Catharine Diehl	
Jessica Nehring	
Dr. Katarina Lindley	
Dr. Caroline Bishop	

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DAY 2

OPENING REMARKS: CALL TO ORDER AND WELCOME

MR. MICHAEL KAWCZYNSKI: Good morning and welcome to the day two of the 174th meeting of Vaccines and Related Biological Products Advisory Committee. I'm Mike Kawczynski, and I, along with the DFO Dr. Prabha Atreya and our Chair Arnold Monto -- we will be running today's meeting. We look forward to your participation as the public.

Please note this is a live public meeting, so we do have presenters and responders and all that from around the world joining us. If at any time we run into any technical difficulties, we may take a momentary break just to make sure that we can get everything squared away so that you don't miss any of the content in today's meeting.

So, with that being said, I'm going to hand it off to our Chair Dr. Monto. Dr. Monto, are you ready?

DR. ARNOLD MONTO: I'm ready. And it's my pleasure to open the second day of the 174th meeting of

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

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

ADMINISTRATIVE ANNOUNCEMENTS, ROLL CALL, INTRODUCTION OF COMMITTEE, CONFLICT OF INTEREST STATEMENT

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

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

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

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

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

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

Please direct any press and media questions for today's meeting to FDA's office of the media website, FDAOMA@FDA.hhs.gov. The transcriptionist for today's meeting is Ora Giles.

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

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

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

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

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

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

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

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

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

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

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

expertise in vaccine preventable diseases. Thanks.

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

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

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

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

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

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

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

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

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

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

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

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

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

immunologist, and I study viral pathogenesis. Thank you.

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

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

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

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

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

DR. WAYNE MARASCO: Good Morning. My name is

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

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

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

DR. PRABHAKARA ATREYA: Thank you. Dr. Meissner. Cody Meissner.

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

DR. PRABHAKARA ATREYA: Okay.

MR. MICHAEL KAWCZYNSKI: Go ahead, Dr. Meissner.

DR. PRABHAKARA ATREYA: We are getting a lot

of background, Mike.

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

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

MR. MICHAEL KAWCZYNSKI: I got it.

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

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

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

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

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

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

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

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

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

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

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

MR. MICHAEL KAWCZYNSKI: Prabha. Prabha, we have one more -- Prabha, we have one more member. Dr. Gans.

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

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

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

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

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

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

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

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

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

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

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

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

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

"Under 18 U.S.C. Section 208, Congress has authorized FDA to grant wavers to special government employees and regular government employees who have financial conflicts of interest when it is determined that the Agency's need for special government employees services outweighs the potential for a conflict of interest created by the financial interest involved or when the interest of the regular government employee is

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

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

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

Committee.

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

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

This concludes my reading of the Conflicts of Interest statement for the public record. At this time, I would like to hand over the meeting to our chair Dr. Monto. Thank you so much. Dr. Monto.

DR. ARNOLD MONTO: Thank you.

FDA INTRODUCTION

DR. ARNOLD MONTO: And now I'd like to call on Dr. Peter Marks, the director of the Center for Biologics Evaluation and Research of the FDA, to give us his welcome and tell us a little bit about what we are expected to do today.

DR. PETER MARKS: Thanks very much, Dr. Monto. First of all, welcome to people who are tuning in and thank you to both the advisory committee staff, the advisors, and to the FDA staff, and to the sponsors, as well as the open public speakers, for joining today. We appreciate everyone's participation. Today we will be considering applications for amending emergency use authorization for both the Moderna and Pfizer BioNTech

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

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

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

influenza in the past.

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

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

the youngest population.

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

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

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

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

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

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

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

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

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

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

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

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

the clinical package that supports this EUA request.

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

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

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

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

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

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

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

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

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

Pfizer submitted an EUA amendment request on

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

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

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

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

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

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

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

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

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

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

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

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

going ahead and jumping ahead to the presentations.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

In this slide we have maximum temperatures

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

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

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

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

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

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

approximately six weeks later.

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

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

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

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

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

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

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

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

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

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

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

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

when using the CDC definition.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Q&A SESSION

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

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

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

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

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

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

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

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

DR. JACQUELINE MILLER: Yes.

DR. HALEY GANS: Thank you.

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

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

DR. ARNOLD MONTO: That's right.

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

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

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

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

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

who had previously been infected?

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

DR. JAY PORTNOY: Great. Thank you.

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

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

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

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

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

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

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

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

DR. ARNOLD MONTO: A very quick one.

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

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

for influenza and a month for the other vaccinations.

DR. ARCHANA CHATTERJEE: Thank you.

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

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

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

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

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

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

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

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

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

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

DR. OFER LEVY: And the rash would be an

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

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

DR. OFER LEVY: Thank you.

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

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

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

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

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

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

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

DR. ARNOLD MONTO: Okay.

DR. JACQUELINE MILLER: Thank you.

DR. HENRY BERNSTEIN: Thank you.

DR. ARNOLD MONTO: We see it.

DR. JACQUELINE MILLER: Yup, thank you.

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

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

initiating immunization in these children.

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

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

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

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

age submitted under an emergency use authorization amendment.

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

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

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

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

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

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

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

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

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

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

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

the study as described yesterday.

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

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

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

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

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

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

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

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

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

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

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

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

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

This slide shows the coprimary endpoint of

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Events of abdominal pain occurred in less than

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

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

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

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

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

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

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

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

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

Additionally, the sponsor submits reports of

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

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

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

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

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

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

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

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

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

end of my presentation. Thank you.

Q&A SESSION

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

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

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

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

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

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

placebo recipients as compared to the vaccine recipients.

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

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

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

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

DR. ARNOLD MONTO: Dr. Fink.

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

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

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

DR. OFER LEVY: Thank you.

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

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

The disappearance of the disease may not have

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

DR. ARNOLD MONTO: Dr. Marasco, followed by Dr. Chatterjee.

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

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

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

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

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

DR. ROBIN WISCH: Thank you for that --

DR. JACQUELINE MILLER: Sorry, please go

ahead. I apologize.

DR. ROBIN WISCH: No, no, no. No, absolutely, go ahead.

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

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

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

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

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

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

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

you were as well.

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

DR. WAYNE MARASCO: I have it.

MR. MICHAEL KAWCZYNSKI: We can see it, Arnold.

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

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

DR. ARNOLD MONTO: Thank you.

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

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

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

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

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

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

DR. JACQUELINE MILLER: Yeah, so we --

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

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

DR. ARNOLD MONTO: Okay. Dr. Chatterjee,

followed by Dr. Kim.

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

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

DR. ARCHANA CHATTERJEE: Okay.

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

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

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

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

DR. ARCHANA CHATTERJEE: Thank you.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

comparison of Omicron and Delta to confirm that?

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

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

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

DR. ARNOLD MONTO: Okay. Let's do it quickly.

DR. JACQUELINE MILLER: Just real quick, I promise.

DR. ARNOLD MONTO: Okay.

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

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

DR. JAMES HILDRETH: Okay. Thank you.

DR. JACQUELINE MILLER: Thank you.

DR. ARNOLD MONTO: Thank you. Dr. Fuller, final question before the break.

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

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

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

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

DR. OVETA FULLER: Thank you.

DR. ROBIN WISCH: Sure.

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

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

[BREAK]

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

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

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

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

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

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

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

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

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

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

Given the high prevalence of omicron and the

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

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

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

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

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

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

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

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

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

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

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

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

shown.

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

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

higher dose levels.

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

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

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

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

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

considered related.

Further details are in the briefing document. There were no deaths reported in this age group. Adverse events occurring in 1 percent or more of participants by system organ class were comparable between vaccine and placebo recipients from dose 1 to cutoff whether for any adverse events or the subcategories shown. Lymphadenopathy in the BNT162b2 group at the 3-microgram dose was 0.1 percent. This was a lower frequency of lymphadenopathy than that reported in older children and adults.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

This was also true for the immunobridging

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Note that the large N in this table represents

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

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

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

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

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

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

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

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

Q&A SESSION

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

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

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

You may recall that while that's coming up

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

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

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

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

responses? It's just a clarification question.

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

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

DR. STEVEN PERGAM: Okay. Thanks.

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

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

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

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

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

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

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

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

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

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

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

DR. HAYLEY ALTMAN-GANS: I get that.

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

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

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

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

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

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

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

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

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

DR. JAY PORTNOY: Yeah.

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

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

DR. JAY PORTNOY: Okay. Thank you.

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

DR. ARNOLD MONTO: Very brief.

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

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

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

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

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

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

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

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

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

CAPT. AMANDA COHN: No?

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

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

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

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

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

DR. AMANDA COHN: Thanks.

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

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

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

DR. ARNOLD MONTO: We can.

DR. SUSAN WOLLERSHEIM: Thank you. Mike, if you could add my notes, that would be great. Fantastic. I see them now. Thank you so much.

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

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

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

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

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

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

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

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

slides are moving. Sorry.

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

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

Participants are randomized two to one to

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

for these age groups.

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

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

The number of baseline positive participants,

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

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

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

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

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

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

negative 10 percent.

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

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

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

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

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

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

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

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

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

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

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

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

This is based on two COVID cases in the

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

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

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

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

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

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

Interpretation of these vaccine efficacy

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

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

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

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

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

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

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

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

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

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

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

Celsius as noted in the briefing document.

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

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

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

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

The percentage of participants 2 through 4 years of age who reported e-diary data who are also baseline SARS-CoV-2 positive was 12.6 percent. Subgroup analyses of solicited adverse reactions in each age group by baseline SARS-CoV-2 status showed similar reactogenicity profile. The frequencies of unsolicited adverse events by age group were shown there. Let me see if I can go back.

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

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

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

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

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

recipients and 0.9 percent of placebo recipients reported SAEs.

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

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

areas the sponsor identified as missing information.

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

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

The sponsor will also conduct periodic

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

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

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

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

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

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

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

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

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

Q&A SESSION

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

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

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

CAPT. AMANDA COHN: Yes.

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

variant.

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

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

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

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

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

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

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

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

DR. AMANDA COHN: Thank you so much.

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

DR. HENRY BERNSTEIN: Thanks.

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

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

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

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

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

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

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

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

DR. ARNOLD MONTO: Okay. Final question --

DR. DORAN FINK: -- specific based on these titers.

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

DR. HENRY BERNSTEIN: Thank you.

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

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

they tracked as being similar.

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

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

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

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

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

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

[BREAK]

OPEN PUBLIC HEARING

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

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

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

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

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

Dr. Marks, please.

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

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

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

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

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

breastfeeding my one-year-old at this time.

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

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

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

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

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

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

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

DR. PRABHAKARA ATREYA: (Inaudible) is up.

DR. JASMINE KING: Excuse me?

MR. MICHAEL KAWCZYNSKI: Can you please wrap it up.

DR. PRABHAKARA ATREYA: Your time is up.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

it in the most timely fashion possible.

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

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

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

serious harm.

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

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

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

We received no funding from any individuals or

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

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

vaccine was available for their age group.

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

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

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

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

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

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

DR. PRABHAKARA ATREYA: Thank you. The next

speaker is Mr. Nicholas Giglia.

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

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

We have, through a combination of precautions,

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

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

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

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

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

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

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

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

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

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

My comment today is broadly in support of emergency use authorizations for both the Moderna and Pfizer vaccines for children under 5. Just last week, my kids had yet another COVID-19 exposure at daycare. The toddler came home with a fever, and I felt my stomach knot up. We had COVID in December and I kept asking, what's the impact going to be as a repeat COVID infection in my unvaccinated child. In May, my friend's four-year-old was hospitalized due to COVID-19. I ask that parent what she'd like me to say to the FDA on her behalf. Her response was, my daughter was

not yet eligible for a vaccine, and public health protections like masking had ended. A vaccine could have offered my daughter protection and prevented a four-night hospital stay.

I remain concerned about COVID-19 and its sequelae. And I want more tools in my toolbox to protect my kids, especially my toddler who cannot mask safely. We've seen increased incidents of diabetes, multi-systems inflammatory syndrome, myocarditis, brain fog and even potentially hepatitis in kids with a history of COVID-19 infection.

We know that these mRNA vaccines are safe and effective. Nine million kids over 5 have received an mRNA COVID vaccine in the United States. And in Germany, tens of thousands of under 5 have been safely vaccinated off label.

It's been a long anxious and frustrating wait, especially knowing now that the FDA has had Moderna's data to review since April. I cannot know the FDA's inner workings, but I can say that the lack of transparency, as to why the Moderna under 5 review has

taken longer than any other age cohort, has made me feel like vaccinating my kids was not a priority for the FDA.

But, I'm grateful that were finally here. And I have some important requests about how we move forward. First, please approve both vaccines. The data shows that we have two effective options for our kids. And families deserve a choice based on their circumstances. We know that boosters and a Moderna third dose are likely to come in the future. But as the parent of a child starting kindergarten at the end of summer, I would like the option of the 6-week Moderna series that show's superior immunobridging after two doses, to give my child the best protection as she begins the school year. This shorter series also reduces the burden on families who use public transit or have to take time off work to get kids vaccinated. The 13-week Pfizer series will leave incoming kindergarteners with less protection when school starts.

I also want to emphasize access. I'd like to

see emergency authorization for pharmacists to be able to vaccinate children under age 3. Enabling pharmacies to vaccinate our youngest would reduce the bottlenecks at pediatric clinics where providers will now have to accommodate vaccination on top of a regular patient workload.

And finally, I want to mention boosters. Looking ahead, our youngest kids must get on the same track as adults with access to updated boosters that protect against new COVID-19 variants. Delay with EUA, vaccine access, and boosters have real life consequences for our families. Every single day matters for our kids. Thank you and please approve these vaccines for under 5.

DR. PRABHAKARA ATREYA: Thank you. The next speaker is Kathlyn Hinesley.

MS. KATHLYN HINESLEY: I have no conflicts. Hello, everyone. I'm Kathlyn Hinesley, with Friends of the Constitution. Today I'll be presenting the facts for your consideration. But I want you to know that I fully understand how hard it is for you to be in your

position, and being literally inundated with facts. Everyone wants to do the right thing, but what is the right thing? That's a question that can be mindboggling at that. I'm hoping that what I say today will relieve some of the stress and fill you with the clear and peaceful understanding of the truth.

And now for the promised facts, the FDA is legally prohibited from approving any biological product for emergency use unless all of the following conditions are met. There must be an emergency that poses the risk of death to the target group. The product must be effective in preventing the disease. It must be safe, and finally the benefits must outweigh the risks.

With regard to the first point, children without comorbidities who acquire COVID-19 have a 99.98 percent survival rate; there is no emergency. Moving forward to effectiveness, a study by Carl A. Biddy (phonetic) which includes a data analysis of 145 countries found that COVID-19 vaccines were, in fact, associated with a 38 percent increase in COVID cases

and a 31 percent increase in deaths. Could these vaccines be negatively affecting immunity?

The number of severe adverse events, affecting children ages 5 to 17, reported to VAERS as of June 3rd was 8,811 including 114 deaths and 1,346 cases of myocarditis a condition that can be fatal. We can assume that if these vaccines are authorized, some babies will die. The benefits of these vaccines are questionable and the risks are clear.

Think about your personal priorities, your concerns for your reputation, your job, the approval of family and friends, and issues concerning the financial security of you and your loved ones as well as your private thoughts about some of the information you have reviewed. These concerns do matter, but there is something that matters more. If these vaccines are authorized, some babies will die.

If you were alone and saw a baby of six month old right in front of you, would you yourself take a (inaudible) and kill that child? My guess is the answer will be no. And yet, if you participate in

authorizing these dangerous injections for this age group, you in fact will be doing that. How would you feel about that at the end of your life when none of the other things matter? How would your soul feel? That's what you need to ask yourself in making the right decision. Thank you very much.

DR. PRABHAKARA ATREYA: Thank you. The next speaker is Melissa Braveman. You have three minutes.

MS. MELISSA BRAVEMAN: My name is Melissa Braveman. I'm a pediatrician and a mother. I have no conflicts. I implore you to recommend EUA of the Moderna vaccine presented today. Personal freedom arguments have led to removal of nearly all mitigation, effectively forcing parents to choose between safeguarding their children and participating in society. Under 2s can't mask. 2 to 4s don't mask well. We must provide parents the choice to vaccinate their children when benefits so clearly exceed risks.

(Inaudible) this vaccine offers the more efficacy against symptomatic Omicron in young children as is afford to adults. And this is so much better

than nothing. We can expect Moderna's booster will further improve protection in young children. And I'm thrill these studies are underway.

Crucially, Moderna's current mRNA vaccine continues to offer robust protection against severe Omicron disease in adults. And we have every reason to expect the same will hold true for young children. And, it will provide proven protection before the new school year begins.

This vaccine is also incredibly safe by the FDA usual rigorous standards, which is fantastic. Thank goodness we are finally here. But this day is bittersweet. The FDA must adapt its approach so that young children's access to updated vaccines and therapeutics doesn't continually lag 18 months behind adults. It's for this very purpose of strengthening the nation's public health protection during a public health emergency that EUA exists.

Yet there was no appearance of urgency with respect to our youngest. The long wait endured, through both the conventional pediatric trial design,

and the unanticipated delays, have been measured by families not in units of time, but rather by extended isolation and excruciating sacrifice, and tragically by vaccine preventable disease and disability, and in some cases death. It has been incredibly offensive to hear this wait trivialized as children died.

Evidence-based medicine, as I know it, entails making the best possible decisions based on the available information. Not being absolved with the responsibility to take any action at all while awaiting a perfect body of evidence that requires years to accumulate as lives hang in the balance. In this (inaudible) I ask first, why were age de-escalation conventions (inaudible) adhered to so strictly during the pandemic?

Second, when will the FDA (inaudible) the exaggerated concerns about fever and (inaudible) seizure that have impeded vaccine progress and resulted in Pfizer's vaccine being under-dose? The pathophysiology, that is the science, doesn't support fever phobia.

Third, why was the review of Moderna's data delayed? These decisions have profound implications for parents and children who are still waiting, suspended in time, 18 months after the members of this committee became vaccine eligible. In sum, how will the FDA evolve so that children lives are speared? Who among you will champion this change?

I am pleading with the FDA to prioritize actual children's lives over an unattainable unimpeachable abstraction, a perfect medicine. Please approve Moderna's lifesaving vaccine and please don't put children in this position again.

The FDA must adapt if it hopes to maintain the trust and respect of (inaudible) parents. We simply cannot let any more children die, or suffer unnecessarily, and still hold our heads high as physicians or as a nation. Thank you.

DR. PRABHAKARA ATREYA: The next speaker is Congressman Louis [sic] Gohmert. You have three minutes.

CONGRESSMAN LOUIE GOHMERT: Yes. Thank you

very much. There are many unanswered questions regarding the safety and efficacy of COVID vaccines, especially for babies and young children. I'm deeply concerned that the push to vaccinate these children is nothing more than a dystopian experiment with unknown consequences. Some of us have outlined these questions in a letter to VRBPAC, but have not received any answers. And I pose some of them here. The letter's at my website, gohmert.house.gov, and my Twitter account @replouiegohmert.

But number one, why has the FDA refused to release the hundreds of thousands of pages of data from preapproval manufacturers' studies, post-approval adverse events data, and other post-approval manufacturers' data?

Number two, what is the cardia risk factor in administering these COVID vaccines to children?

Number three, world renowned immunologists have raised concerns about potential antibody dependent enhancement, ADE, resulting from COVID vaccines. And since ADE was a problem in prior unrelated respiratory

vaccines trials, we need to know what (inaudible) studies, if any, the FDA has that is used regarding potential ADE from COVID vaccines in children 5 and under, or any age groups. Can the FDA affirm that there's no risk of ADE for vaccinated children?

Number four, if approved and widely used among children 5 and under, how many lives, if any, does the FDA estimate will be saved next year? Given the injuries reported in the FDA's VAERS system, how will FDA evaluate serious vaccine injuries versus serious COVID outcomes?

Number five, is it possible that the proposed COVID vaccines in young children would create increased risk from future novel COVID variants?

Number six, why has the FDA recently lowered the efficacy bar for COVID vaccines for youngest children? This change significantly lowers the expected benefits from any COVID vaccination for young children, and it's of particular concern given that over 70 percent of that age cohort are already seropositive.

These questions and others are critical and deserve thorough answers by FDA and VRBPAC, prior to any emergency use authorization with the accompanying protection from liability for all harm done. In conclusion, some of us have grave concerns that in balancing the risks to rewards here, all the risks are to the innocent children, and all the billions of dollars of rewards go to the government protected pharmaceuticals. Leaving me to wonder, if republicans get in majority may need to have a bill -- I'm working on it now -- to allow civil and criminal liability to vaccine providers and accessories, despite an EUA, which should force more sensitivity to vaccine harm to our young children. We got to care more about the children. And I appreciate the time to express this.

DR. PRABHAKARA ATREYA: Thank you. The next speaker is Dr. Heshie Klein. You have three minutes, sir.

DR. HARVEY (HESHIE) KLEIN: Thank you for allowing me to speak. I'm Heshie Klein. I have no conflicts. (Inaudible) of June 10th RFK said -- and

you have all the details so I'll just mention the main points. There is no COVID emergency for children. That's number one. Number two, the vaccines do not prevent transmission. They do not prevent infection. Number six, the Pfizer clinical trial for children, 2 through 4-year-old, failed to meet the FDA specified requirements of COVID vaccine EUAs. The proposing views of product on a schedule that failed FDA established criteria in its clinical trial.

On Page 117, of Moderna's submission, they hid their clinical data and instead used a computer model assimilation, where they adjusted the parameters to give them the results they wanted. Then on page 118, they say the risk of myocarditis was assessed using a 7-day risk window. A 7-day risk window, (inaudible) injection, how is that for long-term study?

Pfizer claims that they did a study of 4,526 participants, 6 months through 4-year-old. This of course is a lie. Like Moderna, Pfizer found ways to whittle down the numbers of participants, to force the data to fit a predetermined fictional narrative.

Pfizer has a unique problem, and this may be one reason why it has taken them so long to get to the application stage. After Pfizer thought that this clinical trial in kids was going to work, so they un-blinded it on September 28, 2021, and they started vaccinating the placebo group to destroy the control and eliminate any long-term safety data, on November 3rd, 2021.

Then in early December the data showed that the trial had failed. So Pfizer had to scramble to enroll even more kids in the attempt to save the clinical trial with a third dose. (Inaudible) becomes a complete muddle because Pfizer had to refer to the blinded period (inaudible) before September 28th, the un-blinded crossover period after September 28th. And then the post-protocol amending six period because they wanted data cutoff of April 29th.

I pray that you realize that if you choose to ignore the obvious that Moderna and Pfizer are lying, then you'll be doing a great disservice to humanity. You know that all it takes is for you to win is for good people to say nothing. If you remain silent and

do not call them on their lies, you're allowing Moderna and Pfizer to lie to the American public. And at what cost to human lives?

In the (inaudible) wanted to kill all the Jews, (inaudible). Do not think you'll be able to escape in the king's palace any more than the rest of the Jews. Or if you persist in keeping silent at a time like this, relief and deliverance will come to Jews from some other place and you and your (inaudible) will perish. And who knows if it was for just such a time as this that you obtained (inaudible) position.

We are at a cosmic turning point in the history of the world. We are in a war between good and evil. And who knows if it was for just such a time as this that you obtain you position under VRBPAC.

You have a once in a lifetime opportunity to do the right thing for humanity and for God. And all and you will be remembered in the history books for eternity. I pray for you that you look in your hearts and souls and find the courage to stand up to big pharma, like (inaudible) stood up to (inaudible) and

saved all the Jews. You have the opportunity to save humanity and the world.

DR. PRABHAKARA ATREYA: Your time has (inaudible). Please, wrap up.

DR. HARVEY (HESHIE) KLEIN: Pfizer and Moderna has not met requirements, and should not approve -- you know that. Stand up against them on the side of God, on the side of good, and may God smile on you always and in all ways.

DR. PRABHAKARA ATREYA: (Inaudible) your time is up. The next speaker is Kailey Soller. You have three minutes.

DR. KAILEY SOLLER: Hello. My name is Dr. Kailey Soller. I'm a Ph.D. chemist. And I have no conflicts at all today. Thank you so much for the opportunity to speak today. I'm a Ph.D. chemist, but even more importantly I'm a mom of an under 2-year-old. I spoke emotionally yesterday on all the reasons why parents are desperate to vaccinate their children under 5. Today I'm here to speak very scientifically and logically to ask you to make the only logical decision

available, which is to approve both the Pfizer and Moderna vaccines for this youngest age group, based on three points.

Number one, these vaccines, first and foremost, have been proven to be safe. Number two, these vaccines are effective. And number three, authorizing these vaccines gives all parents the ability to make the choice that they deem best for their family.

(Inaudible) points one and two. These vaccines are safe and effective. For all other age groups, when the vaccines have been proven to be safe and effective, we have approved after careful scientific review and without hesitation, we have authorized the vaccine.

I would like to thank the sponsors, as well as the FDA, CDC and the ad-hoc members for all of their dedication to a rigorous and complete scientific review and presentation of the data. It's very clear from the data that these vaccines are safe, and the benefit of vaccination helps decrease the risks associated with

COVID infection.

Beyond prevention of symptomatic infection, in addition, there's additional benefit of the cellular responses which helps prepares the immune system and the body to fight off future infection. This is harder to measure, but can be logically and scientifically inferred by the multitude of data that we have from older age cohorts and our knowledge of how vaccination and immunity work in general.

Regarding point three, and allowing parents a choice. Authorizing these vaccines gives all parents access to either choice that they desire to make for their children. For parents without access to the choice that we desire, which would be to (inaudible) their children, we're desperate for this choice. The pandemic has moved into a personal risk/benefit analysis stage where we are encouraging individuals to self-assess their risk and make decisions about their own house. Parents who assess that the risk/benefit of these vaccines versus COVID infections have two choices to consider, as it is clear that COVID infection will

likely become inevitable.

Number one, their child could get COVID without having been vaccinated, or number two, their child could get COVID with having been vaccinated. However, only one of these options today is available to parents under 5. However, my choice from these two options would be number two, to vaccinate my child, which is not available to me today.

However, today, we have the logical option, which is based on the scientific evidence that has been amassed indicating that both of these vaccines are safe and effective. And we need to allow access to both of these risk-based decisions options for parents. And authorize both of these vaccines. I will vaccine my daughter as soon as possible. I don't want a vaccine mandate. I don't want to force other parents to do the same, but I want the choice. And I'm asking for that choice that I desire to make.

For parent who choose option one, decisions made today of authorization would not have to change that choice. So for me and many others, the decision

without the authorization of these vaccines would be absolutely life-changing. I urge you to make the most logical and fact-based decision today, allow us the decision to vaccine our children and empower us as parents to protect our children. Thank you so much for your time today. And thank you so much for your dedication to the scientific process.

DR. PRABHAKARA ATREYA: Thank you. The next speaker is Shae Lynn. You have three minutes.

MS. SHAE LYNN: Good afternoon. I'm Shae, and I have no financial involvement in this discussion. I am a mother, former educator, director, and recently worked as a tech manager developing startups in the health space. I was never exposed to COVID-19. My children have also been enrolled in private schools with zero exposures. Please recall these products immediately. Do not harm our low-risk children. They do not need myocarditis from long (inaudible) COVID vaccines adverse reactions. We demand informed consent.

As a parent I wanted to do the right thing to

protect my children against COVID-19. So I received the first dose of Pfizer on April 3rd. Little did I know this would be the worst day of my life. After an hour I called 911, due to an anaphylactic reaction. I never experienced anything like this in my entire life. My heart was racing. I felt so weak, disoriented and vertigo, almost like I was going to faint. I had severe chest pains. I couldn't breathe due to throat closers (inaudible). I felt feverish, but I was fine just an hour ago.

My family was present, but they didn't know what to do. We just wanted to do the right thing. We were warned (inaudible) the vaccine would be safe, as our entire family and friends were all vaccinated. But I felt completely betrayed and lied to. I had no other choice but to call 911 for help after my Pfizer vaccine. I was asked to stay on the phone until paramedics arrived, to make sure I did not faint.

I honestly thought I was dying. And I wasn't sure if I was having a heart attack. I've always been incredibly healthy and in excellent shape. I felt like

my entire life flashed before my eyes. My vision was very blurry. And I couldn't stop shaking. I'm still shaking right now, 14 months later.

The paramedics finally arrived and advised me to take Benadryl, and I should be admitted into the ER right away. They assured me they would not let me die, but I realize they didn't know about adverse reactions. It seemed like no one was really prepared to deal with allergic reactions. It almost seemed like a drug overdose. I wouldn't really know since I never take medication nor do I drink alcohol.

At the ER I was only monitored and prescribed an EpiPen, then discharged immediately. My doctor didn't feel the need to do any further testing. I received no explanation other than I had an allergic reaction. I left feeling confused and I still didn't feel well. And now I had to prepare to deal with allergic reactions when I never had any severe allergies prior. I only had a minor rash as a child due to amoxicillin.

Prior to leaving the ER, I remember the ER

doctor being slightly confused and clearly stated only elderly people die from these issues. I was surprised he would even admit to that considering my elderly relatives were just vaccinated. I felt so alone, so lost, so confused with no answers. I felt dizzy. My vision was affected. I had to take Benadryl and Tylenol for a week straight. They wouldn't prescribe anything else for me. They didn't think this was going to be long term.

I contacted my doctor almost daily. My heart felt weird; it felt like flutters. I wrote emails for answers to my doctor. No one knew anything. I felt like I was being completely ignored and my symptoms were dismissed. My doctor denied referrals to cardiology, neurology, and denied me of an MRI. I kept calling and hoping to get new doctors on call for answers to urgent care and Zoom visits.

One doctor eventually prescribed me blood pressure medication for palpitations; it was for (inaudible). Did she realize I'm breastfeeding? I had the worst nightmares and ringing in my ears. I

couldn't sleep. I was afraid I would never wake up again. My doctor --

DR. PRABHAKARA ATREYA: Ms. Lynn? Your time is up; please could you wrap it up.

MS. SHAE LYNN: My doctor advised me to purchase blood pressure monitor and check my blood pressure daily. It was really high. I never experienced this issue prior. I also had internal tremors very similar to Parkinson. My legs were weak and felt numb. I kept thinking I'm too young to develop Parkinson or become paralyzed.

After two weeks of being on the heart monitor, I quit taking my medication as side effects stated it may cause heart failure. I was still breastfeeding and I'm worried that my child will experience long-term issues from these vaccines and adverse reactions, and affect his development. He's now under evaluation and may need to see (inaudible) --

MR. MICHAEL KAWCZYNSKI: Ma'am? Ma'am, you have to stop. We have to move on. My apologies. Next speaker.

DR. PRABHAKARA ATREYA: Kate Schenk. You have three minutes.

MS. KATE SCHENK: Good afternoon. Thank you for allowing me the opportunity to speak today. My name is Kate Schenk. I have no conflicts. I am the mother of three children, age 4 years, 2 years, and 7 months. Since the beginning of the pandemic, my husband and I have done everything we can to protect our children from COVID-19. Our children haven't been inside grocery stores or department stores, let alone typical childhood staples like indoor amusement parks, museums, malls and restaurants.

I am thankful that my children have remained healthy, but it's been a long two years. Last year I was pregnant with my third child, who was due in November 2021. After my husband and I received our COVID vaccines, as soon as they were available to us, it seemed hopeful that a pediatric vaccine would likely be coming in the fall, around the time the new baby was due.

I imagine we would still have to be careful

for the baby's first six months, until he was old enough to be vaccinated himself. But at least the risk could be somewhat mitigated since everyone else in the family would be vaccinated. As we all know that pediatric vaccine didn't come last fall or in February, or in April. That baby is now 7 months old and still none of my children are able to be vaccinated.

My oldest child will be 5 years old in mid-August. She is supposed to start kindergarten on September 1st. Because of the pandemic, she has stayed home with me instead of attending preschool. She is so very excited for kindergarten. She is eager to learn and play with kids her own age. Because of her late birthday, the only way she'll be fully vaccinated before kindergarten starts is if the under 5 vaccines is approved now, particularly Moderna since it's a shorter series.

Moderna would allow children starting preschool and kindergarten this fall, to reach the same protection antibody level in only two doses compared to Pfizer's 3-dose series, which instead produces similar

efficacy and immunobridging over a period of three months. Boosters for each have been considered in the future, making Moderna three doses and eventually Pfizer four. I urge you to please act now to authorize emergency use of both Moderna and Pfizer vaccines for children under age 5.

At this point in the pandemic, many people have seemingly moved on and are completely forgoing COVID precautions such as masking and social distancing. And our youngest children have been left behind unprotected. Those without children do not even recognize the toll this is taking on young families, since we have become invisible while they are living life as normal.

Please allow parents to give their children the layer of protection that vaccination allows. The data indicates that these vaccines are safe and have met immunobridging. They can protect against the most severe outcomes, the things that have kept parents awake at night since the beginning of the pandemic, death and hospitalization. And can potentially

decrease the risk of other complications, like long COVID, MIS-C, neurological effects, diabetes and hepatitis. We need to protect our children without further delay. Thank you for your time.

DR. PRABHAKARA ATREYA: Thank you. The next speaker is Tamara Thomson. You have three minutes.

MS. TAMARA THOMSON: Good afternoon, members of the committee, and thank you for allowing me to address you again today. I have no financial conflicts. My name is Tamara Thomson and I'm an attorney who represents children, as well as the mother of a 5 year old boy and 23-month-old girl.

Yesterday I urged you to recommend authorization of Moderna for the older pediatric cohort, and I'm thankful that you did. I also urged you yesterday to do the same for the youngest cohorts. I am here again today to request that you vote to authorize both Moderna and Pfizer for the youngest age groups so that our littlest Americans can have access to these lifesaving and necessary measures of protection against severe outcomes, disease and death

from COVID-19.

I spoke yesterday about how important this authorization is to me and my family, and how long we've waited to protect our sweet girl. She is actually one of the data points you saw in Moderna's presentation today, as we joined the trial in February.

Today I want to address how important it is that both vaccines are authorized for other families. In my social circle I have heard from many other parents that they are desperate to vaccinate their children under 5. They thank me for my advocacy and tell me how exhausted they are, and how very hard it has been to feel left behind and with no measures to protect their young children from the threat of COVID-19.

Referring both to the acute threat, and the possible long-term harm of infection after infection with SARS-CoV-2. Long COVID is a threat to children and adults alike. Like me, other parents have pulled kids from daycare during surges and worked their full-time jobs from home while trying to parent babies and

toddlers. They've also gone through interruptions after interruptions of care with illnesses, exposures, quarantine and isolation. Some parents are not able to work from home at all, and don't have the ability to pull kids during surges, but must take unpaid time off when exposures and quarantines occur.

I have heard over and over again that it is exhausting. And it's been even more difficult since the rest of the world has moved on, dropping all non-pharmaceutical interventions because they "have all the tools." We don't have the tools, not for our little ones, and therefore; not for our families.

It is essential to authorize both vaccines right now because there are advantages to each series that will help families in different positions. For example, we see greater efficacy and immunobridging in just two doses of Moderna versus two doses of Pfizer vaccine, which would allow rising kindergarteners to achieve more protection before starting school in September. At the same time, while Pfizer's end and calculating efficacy is low, and confidence interval

wide, it may be that it's 3-dose scheme provides greater efficacy in the long term.

In addition, having two vaccines for this age group available will help in insuring better access, a stronger supply chain and a choice for families who have waited so long for protection. We need options. We need access. And we need to make sure this group catches up to older cohort in terms of variant-specific boosters and up-to-date preventative (inaudible) treatment. As we heard Dr. Fauci saying April of this year, all of the stuff you hear about kids, let them get infected, is a bunch of nonsense. Please authorize both the Moderna and Pfizer vaccines for them today. Thank you for your time and dedication to the scientific process.

DR. PRABHAKARA ATREYA: Thank you. The next speaker is Mr. Sam Dodson. You have three minutes, please.

MR. SAM DODSON: Hello, my name is Sam Dodson. I run a podcast called To the Lifeboats, and I have no relationship with the pharmaceutical cartels. I'm

schooled in electrical engineering. And two years ago I'd never heard of mRNA. But let me tell you what I've learned since. It starts with the shot you told us stays at the injection site. We know it doesn't. You knew it didn't. Bio-distribution studies shows that it goes to every major organ, primarily the heart, liver and spleen, where thanks to the highly inflammatory lipid nanocomplex it transfect (inaudible) the cells. That complex contains a PEGylated lipid being mass injected into humans for the first time ever, while the animal studies showed heart attacks in pigs after the second injection.

You knew the lipid nanocomplex is collected in the ovaries, where they have the potential to cause devastating effects on reproductive health, yet you did nothing. When women started complaining of menstrual problems, you did nothing. Transfected cells in every organ pumped out the spiked protein that ends up in a nucleus where it interrupts p53, LINE-1, and BRCA, you didn't know this because you didn't care to ask the question. And when shown to you in a study, you did

nothing.

Every transfected cell expressing spike protein risks autoimmune disease, the most acute of which is myocarditis. When people started dying of myocarditis, you did nothing. The spike protein floats freely in the vasculature, finding its way into the brain, breastmilk, and the environment as the body sheds this protein in exosomes, making those around the vaccinated sick, despite protein directly affects toll-like (inaudible) receptors and CD4 T cells, which are essential to the immune defense against these very viruses.

When the vaccinated repeatedly caught COVID and suffered reactivation of herpes, shingles, papaloma virus in unprecedented numbers, you knew this was a massive problem yet you did nothing.

You knew that the mRNA stays around for months in lymph nodes germinal centers, causing P cell exhaustion, because the Stanford Group performed the study that you couldn't be bothered to do.

And then you ignored that massive safety

signal. You were warned about oncomiRs (inaudible) and the effect on p53, yet you did nothing. When you were warned about prion disease and amyloid as a result of the huge amounts of spiked protein produced by these therapies, you did worse than nothing; you silence those people who raised the alarms.

You were informed of fraud in the vaccine studies yet instead of investigating you colluded with the manufacturers to suppress trial data for 75 years.

Knowing all of these concerns you now want to inject the very young, who have zero clinical risk from COVID and for which not one single study has shown any clinical benefit. You have abjectly failed in your sole duty to ensure the safety of any drug given to Americans. The late Frances Oldham Kelsey would have been ashamed of how you've turned a once respected agency into a corrupted vessel for the very corporations you swore to protect the American public from.

If you have one shred of humanity left, you will recommend an immediate halt to all the shots and

pray that God has mercy on your souls. You might also want to figure out how we're going to diagnose myocarditis in very young babies who are unable to speak. Thank you.

DR. PRABHAKARA ATREYA: Thank you. The next speaker is Donna Treubig. You have three minutes.

MS. DONNA TREUBIG: Hi. Thank you. My name is Donna. I'm gramma to two-year-old Liam (phonetic), and a licensed-family daycare center owner-operator. I have no conflicts.

Please take a moment to picture your life right now if you weren't given access to even one COVID vaccine dose yet, two and a half years after this began. Now think about going into a small room with 20 other unmasked, unvaccinated people. Eating and napping, in close contact, spending up to ten hours there every weekday. This is the scenario parents are forced to put their unvaccinated children in every day, and is why I implore you to approve a vaccine for children under 5 today.

COVID seeks out those who are unvaccinated.

The convoluted task to approval these trials have taken have left the youngest of our society most vulnerable. The repeated reassurance that a vaccine would be available in the coming weeks or months has not brought hope to families, but rather frustration and despair when these claims did not come to fruition.

The truth is families have gone to extreme lengths to protect their babies because children are getting very sick and dying of COVID-19. The FDA should strive to be nimble and able to pivot quickly as the virus changes. If the rest of our country can choose a vaccination and subsequently drop any and all mitigation measures, before all vulnerable populations have protection, then parents deserve the right to vaccinate our children and to choose between Moderna and Pfizer.

We need a comprehensive plan to ensure this age group has access to up-to-date boosters and future variant-specific vaccine at the same pace as all other age groups. Our governmental bodies need to do what is necessary to ensure our children are not denied lifesaving vaccines for two and a half years during the

next pandemic.

When you cast your vote this afternoon please remember these small children and vote to approve both Moderna and Pfizer vaccines for children under 5 so that they have some protection with reduced risk of severe illness caused by COVID-19. Thank you for your hard work throughout this pandemic and for giving me the opportunity to share my views.

DR. PRABHAKARA ATREYA: Thank you. The next speaker is Catharine Diehl.

MS. CATHARINE DIEHL: Good afternoon. My name is Catharine Diehl. I'm a mother of two-year-old twins and a Ph.D. in philosophy with a focus in medical ethics. I have no financial conflicts. I'm here today to strongly urge the committee to recommend authorization for both vaccines.

The question before you for each vaccine is whether, based on the totality of medical information available, its benefits outweigh its risks. The data presented today, and real world information collected over the past two years, demonstrate that the answer to

this question a clear and resounding yes.

To evaluate the benefits we must follow the standard of probable improvement. Employing the tools of (inaudible) analysis, supported by the FDA's own guidelines, these vaccines very clearly meet the standard. We're better off with them than without them. This standard must guide our action, rather than any arbitrary statistical cutoff such as requirement of 50 percent efficacy against symptomatic illness. Such a standard would be additionally inappropriate in the context of current variants, when attention has shifted to protection against severe outcomes including hospitalization and death.

Evaluation of these vaccines does not occur in a vacuum; rather it occurs in a context in which these vaccines have proved to be safe and effective in adults, as well as in a slightly older age cohort. This background should inform our priors that is our starting point and our considerations here.

The success of both trials in meeting immunobridging, without any safety signals, allows us to

update these priors in light of positive evidence.

Following the standard of probable improvement let us infer from successful immunobridging, it's highly likely the vaccine will be similarly effective in the prevention of severe outcomes like hospitalization and death in children under 5.

The safety record in older cohorts, in absence of safety signal from the trial, also reassures us that new safety issues are not likely to crop up once vaccine distribution commences to the broader population. Using compelling evidence both companies' documentation that the benefit/risk analysis is favorable based on acute outcomes.

But there are additional factors that speak in favor of approval. COVID infection carries substantial long-term risks. Our understanding of these long-term implications is every evolving, (inaudible) that the methodology I have described is particularly helpful.

To ignore the growing evidence, lasting cardiovascular damage, new type 1 diabetes diagnoses, brain atrophy, vascular (inaudible) deposition,

hepatitis and so on, merely because we have yet to accumulate a decade worth of high-quality, double-bonded, randomized control trial, and met an analyses thereof, would be dangerous and irresponsible.

These vaccines are likely to reduce such effects in two ways. First, by preventing some portion of infection, they reduce the number of cases in which long-term damage can occur. Second, numerous studies have suggested that breakthrough infections are less likely to lead to long COVID. Again, this must be factored into our analysis.

As a philosopher and a parent, I urge you to approach your decision with these (inaudible) principles in mind, reach the conclusion that both vaccines should be approved. Thank you for your consideration. And thank you to the families in these trials who have made this possible.

DR. PRABHAKARA ATREYA: Thank you. The next speaker is Jessica Nehring. You have three minutes.

MS. JESSICA NEHRING: Good afternoon. I have no financial conflicts of interest. I am a mother of

two amazing children. My daughter is 6 and my son is 3. I'm speaking today to advocate for children under 5 years old, and their parents who wish to have the option of vaccinating these youngest children.

Since most masking mitigations have been lifted, children under 5 have been sitting ducks for COVID without protection while vaccination has been enthusiastically recommended to every other age group. We have been through six ways of COVID now, including the current surge, with no protection for our most vulnerable children.

The children 3 and over that can mast are obviously not wonderful at it, and the children under 3 have absolutely nothing at this point to protect them from severe and sometimes fatal outcomes. Based on real-world data in persons 5 and above it can be safely concluded that Moderna and Pfizer's vaccines for our youngest children offer excellent protection from hospitalization, severe illness and death.

I am frustrated that this process was stalled with Moderna since their studies were nearly complete in

December, when an expansion was requested by the FDA. Parents still long for a clear explanation regarding the reason for this expansion, which was requested during the largest COVID surge of the pandemic. One that resulted in thousands of children under 5 hospitalized. It is upsetting that a safe and effective vaccine has not been prioritized, especially with so many Americans getting back to their normal lives, resulting in our children being placed at even higher risk of infection.

In the past two years my husband has worked in nursing homes, schools, restaurants and churches as a union HVAC service tech. He has chronic asthma and has been wearing a mask for years at this point just to protect himself and our family until we can all be vaccinated. I have put off doctor's appointments these past two years for a pre-pandemic health issue, because of the fear of bringing the virus home to my son and daughter before they have been vaccinated.

Parents like me are frustrated that we are not being seen. We believe in science and the process of trials, evaluating data, and the health agencies

involved in managing all of these aspects. But moving forward, I would hope this age group doesn't get left behind again. I would like serious thought given to the possibility of running trials for future treatments and vaccines of all age groups at the same time so our youngest children are not forgotten.

Relevant agencies need to work with states and local government to facilitate a rollout that's truly fair and equitable for all kids under 5 and their parents. Parents like me just want the choice. Thank you for giving me the time to speak.

DR. PRABHAKARA ATREYA: Thank you. The next speaker is Katarina Lindley. You have three minutes.

DR. KATARINA LINDLEY: Thank you for this opportunity. My name is Dr. Katarina Lindley. I'm a member of the Steering Committee of the World Council for Health. I have no conflict of interest.

CDC data from February show that about 74.2 percent of children have had COVID already. Over 150 studies show that natural immunity is superior. The infection fatality rate under 5 years of age is 0.1 in a

hundred thousand or one in a million. The risk of the shot in the already immune is higher than one in a million.

Both Pfizer and Moderna expressly eliminated those that were naturally immune from their studies. They did this to avoid the high immune (inaudible) response and possibly death. Vaccinating the already immune puts them at serious risk for having a high immune response. That means you will be voting for some children to have a severe adverse reaction and possibly death if you vaccinate the already immune. This is bad medicine. There is zero reward, only risk.

These vaccines are not medically necessary or clinically indicated. VAERS shows children ages birth to 18, who have been vaccinated with Pfizer and Moderna vaccines, have had severe life-threatening adverse reactions such as myocarditis, (inaudible), seizures and most severe adverse reaction from death.

Article by (inaudible) that was published in May 22, of 2022, in American Academy Pediatrics, shows myocarditis 2.2 per million cases, seizures 7.6 per

million cases. I will share two cases seen by my colleagues.

Fourteen-year-old male, double vaccinated with Pfizer vaccine has recent history of chest pains on exertion. The initial echo and EKG were normal. (Inaudible) 22,000 increasing to 48,000 in six hours. Cardia MRI (inaudible) showed transmural and (inaudible) consistent with myocarditis.

Case number two, 13-year-old female, first Pfizer dose last August, had first seizure within 30 days. Got a second vaccine in December, had another seizure, then had a third booster and now has four to six seizures a day. She was an active soccer player and a good student, now unable to play sports or attend class in person.

We have no long-term safety data in any of these studies. The risks clearly outweigh the benefits. The VAERS reports 28,312 deaths so far in all age groups. When will we say this is enough? What is the magic number that will make a cutoff and stop pushing these vaccines? Will it be 50,000, 100,000, million?

When do we say that we cannot give this to our children?

Their recovery rate is over 99.9985 percent. These are healthy children and the risks do not outweigh the benefits. These vaccines are not medically necessary or clinically indicated.

DR. PRABHAKARA ATREYA: Your time is up.

DR. KATARINA LINDLEY: Thank you for your time.

DR. PRABHAKARA ATREYA: Thank you. The last speaker for the session is Caroline Bishop. You have three minutes.

DR. CAROLINE BISHOP: Hi. Thank you. My name is Dr. Caroline Bishop, and I'm an associate professor of classics at Texas Tech University. I have no financial conflicts of interest.

I'm here in my capacity not as a professor but as a mother to urge you to approve both the Moderna and Pfizer vaccines for children under 5. Today I wish to share with you the increasingly punishing lengths I've had to go to in order to keep myself and my 14-month-old daughter free from COVID as we've continued to wait for a vaccine. I could talk about the difficult decisions

we've been forced to make along the way. Cancelling our daycare during the Delta wave and keeping my daughter at home with me while I was technically on a Harvard-funded research sabbatical to write my second book, never having gotten to take her to a museum or to visit her cousins or to a playdate. Being able to count the times she's been in the grocery store on one hand.

But instead I'm going to focus on the fact that I've had to be a solo parent for the past month or so, watching my daughter full time, never leaving the house, while also feverously writing a conference paper that I have to deliver this Friday during naps and after bedtime, has been one of the most challenging experiences of my life. Why have I been doing this, because my husband, who's a trial attorney, can no longer wear a mask in court. Part and parcel of the countrywide removal of all mitigation at a time when we're seeing one of the worse COVID surges yet.

As cases began to grow in our area, he made the heartbreaking decision to move out to our guesthouse. At the time, we'd hope the committee might meet to

approve the Moderna vaccine on June 8th, and when the meeting got scheduled for today our hearts broke a little more. This past month I've been desperately holding on for my daughter to have the protection against severe outcomes that both the Moderna and Pfizer vaccines have been shown to provide.

I've been lonely and alone, devastated when my husband missed our daughter's first steps. I know he feels devastated too. He has to hear her call out, da, da, when she sees him in the yard, and know he can't cuddle and play with her. She's always so delighted to see him and doesn't understand why he won't horse around with her like he used to do. We didn't publicize this decision of our, only a few close friends know. That's because even among our highly educated friend group, almost everyone is acting like the pandemic is over.

I spoke to you yesterday about the special kind of heartbreak you feel when you see people you love, like and respect, start to act with absolutely no concern about the fact that you're child has no protection against COVID. Today I just add that it's

both disorienting and maddening to see almost everyone living like it's 2019 again, when you're still stuck in March 2020.

However, I can now say with certainty that my husband and I made the right decision hard as it might've been. How do I know? Because this past Friday he came home from work with a sore throat, and as I'm speaking to you he's sick with COVID. Fortunately, he's vaccinated and boosted with Moderna and his case has been mild.

My daughter deserves that same protection. You have the ability to give it to her and to reunite our family. For myself and for the many parents who didn't have the privilege to isolate like I've done, I'm begging you to approve these vaccines. Thank you very much.

DR. PRABHAKARA ATREYA: Thank you. That completes the Open Public Hearing session. And I would like to hand over the meeting back to our chair, Dr. Monto; take it away for the next item on the agenda.

ADDITIONAL Q&A FOR FDA AND SPONSOR PRESENTERS – MODERNA COVID-19 VACCINE

DR. ARNOLD MONTO: Thank you, Prabha. And I thank all the participants in the open public hearing. We really do listen to what you have to say us. We now return to the question and answer sessions. We will first deal with the question and answer about the Moderna vaccine. And these questions can be for the FDA presenters or the sponsor presenters. We have a relatively short period for the question and answer sessions, 25 minutes, after which we have our own internal discussion.

So remember there's that session as well -- and following that, the vote, completing the action on the Moderna vaccine. So we're completing the action on the Moderna vaccine. Okay. Let me see if I've got the full list in front of me here. Dr. Berger followed by Dr. Pergam.

DR. ADAM BERGER: Hi, thank you all for the earlier presentations. I had a question based on FDA's

briefing document that was supplied, and specifically it was the two tables that looked at the subpopulation analysis, specifically looking at the vaccine efficacy in children who are obese. I noticed that the vaccine efficacy rates for the 6 to 23 month olds were negative 5.6 and two to five year olds were listed as negative 15.4 -- and totally recognizing that the confidence intervals in these were huge.

Just wanted to get a sense of whether, I didn't see this listed in any of the post-approval examinations. What kind of data are you currently collecting on children who are obese to understand the efficacy there or to at least dive into this signal a little bit more?

DR. JACQUELINE MILLER: So I believe that was a question for me, but if I'm wrong, please correct me. So I think the question is about Moderna and how we follow-up on the efficacy rates in children who are obese. So, as you mentioned, we have some efficacy data from the original clinical trial. However, those data right now are a relatively small subgroup of the

overall (audio skip).

And so the way in which we will be moving forward to follow vaccine effectiveness would be actually in the long-term effectiveness study that we have ongoing in Southern California. So in that study we are able to enroll hundreds of thousands of individuals, and we actually are parsing those analyses by specific risk groups. I can show you the immunogenicity in the young children. So if you can please put up slide IM23 for me?

MR. MICHAEL KAWCZYNSKI: Oh, give me a second, I gave it to the wrong share. So Moderna, give me one second.

DR. JACQUELINE MILLER: No problem.

MR. MICHAEL KAWCZYNSKI: Actually, Moderna, no you should have the right share right now. Oh, you moved it. Hold on, one second. Take it away. You got it.

DR. JACQUELINE MILLER: Okay. There we go. And then I'm just going to say that I'll want the slide in a moment for the 6 month to 23 month olds. So what

you see here are the geometric mean titers and associated 95 percent confidence intervals for the children who are two to five that received mRNA-1273, and you also see the respective GMT ratios. And this is again versus the adult population.

I need to note again that the sample size of the children who are obese is relatively small (Audio skip) will require further follow-up. And then, if we can put up the next slide, which is IM24, we'll see the infants and toddlers. And so here we see GMT ratios of 0.9 to 1.4. Again, sample size is relatively small, so wider 95 percent confidence intervals in those who are obese but, overall, greater than 1500.

DR. ADAM BERGER: Thank you.

DR. ARNOLD MONTO: Thank you. Dr. Pergam followed by Dr. Sawyer.

DR. STEVEN PERGAM: Thanks. I had a question for the sponsor. I didn't get to ask this question initially when you presented your data. You had a fairly large study population in the Phase 1 trial that got the higher dose of the vaccine, similar to what I

asked Pfizer. I'm curious, did you see a dose dependent response in that higher dose compared to the lower dose that you ended up choosing?

And then, as a second question to that that's somewhat relevant is, in your post-marketing studies that are planned, there's no discussion of the immunosuppressed population. And as we have seen in post-marketing immunosuppressed populations have received an extra or a third dose as the primary series. And I'm curious if there are studies planned for Moderna for immunosuppressed children to specifically address this question?

DR. JACQUELINE MILLER: Yep. Thank you for that. So what I would like to do is address your first question first, which is the comparison of the 25 microgram and 50 microgram, which are the doses that we investigated in this trial. And so could you please project AA8, sorry that's alliteration, but 2 As and an 8. There you go. Thank you.

What you see in this slide is the young children, and you had asked about a dose response. So

we do see a dose response with a higher dose. And we saw GMT ratios in the initial part one population of 0.8 and 1.4, respectively. We were also looking at the safety profile at the time, made our recommendation to a data and safety monitoring board. And they in fact confirmed that they agreed with our selection of the 25 microgram dose in the children two to five.

And because we selected the 25 microgram dose, then we did not go up to 50 micrograms in the youngest babies. And then your second question for me is with respect to immunocompromised children. And so we have already committed to doing in Europe an immunocompromised trial, and in fact we were waiting until we had selected the dose and had confirmation that that dose was safe and effective in healthy children before moving to the immunocompromised population. And of course we'll be studying a three-dose schedule as we're administering to adults with the selected dose.

DR. STEVEN PERGAM: Thank you very much. Appreciate that.

DR. ARNOLD MONTO: Dr. Sawyer followed by Dr. Kim. Or are we up to -- yeah, Dr. Sawyer.

DR. MARK SAWYER: Thank you, Dr. Monto. So it appears that fever is occurring at a significant rate, which is something we see with other routine childhood vaccinations. But the pediatricians in the group have certainly lived through the experience of seeing enhanced fever and even febrile fevers with coadministration of other vaccines together that all cause fever.

Dr. Chatterjee brought up this question earlier, and the sponsor replied that they are planning some coadministration studies. My question is for FDA. Are such coadministration studies required for a full BLA, or is it up to the sponsor to just decide how much to study that question and/or do we need to wait for post-marketing or post-authorization studies to really get a handle on that question?

DR. ROBIN WISCH: Thank you for that question. Thank you, Dr. Fink. I think you're about to -- ready to handle that.

DR. DORAN FINK: Thank you. I'll answer that. So we have routinely requested coadministration studies in licensure applications of vaccines that are intended for the very young infants, those who are younger than six months of age, because the immunization schedule is so compressed, and it is difficult to avoid coadministration.

We have not routinely requested or required coadministration studies for older children, but we have always encouraged vaccine manufacturers to study safety and evaluate for immune interference of coadministration when introducing a new vaccine into the pediatric schedule. And we do expect that studies will be done going forward looking at this.

DR. MARK SAWYER: Thank you.

DR. ARNOLD MONTO: Thank you. Dr. Kim followed by Dr. Gans.

DR. DAVID KIM: Thank you very much. On the topic of primary series and booster dose, I think the Committee has discussed this on several occasions. But on that topic for Moderna vaccine, the definition of

primary series is two dose, and you're currently working on a study to evaluate the impact of the third dose.

And it's on that third dose that I'd like to ask you if you have any preliminary information or actually, if you can share with us some of the characteristics of the study design and the possible impact and then perhaps your hypothesis on how that might influence your definition of primary series versus booster dose?

DR. JACQUELINE MILLER: Yeah, so I'll speak a little bit about the boosting that we're planning in each age cohort. We don't have hypotheses to define two versus three dose series, but as I mentioned we've heard your feedback about that. But in terms of the third dose booster, in adolescents we (audio skip) once we saw the incidence rates climbing after Omicron, as we discussed yesterday. And those data actually we are anticipating momentarily and will be sharing them with the FDA once we have them compiled. That will be the first group.

Then in July, we will be getting the data from the 6 to 11 year olds. So the 6 to 11 year olds were followed primarily through Delta. There the longer-term follow-up cohort is now mostly the mRNA-1273 cohort because of the authorization of another vaccine and people going to get vaccinated. So we'll really see just primarily what that third dose booster looks like in that cohort that will come in July, and of course we'll share those data when available.

And then, the youngest children actually, based on other feedback we've received from this Committee, we tried to keep the blinding in place as long as possible to have as long of double blinded efficacy follow-up as we could. I think once a decision is made and one or more vaccines, hopefully, will be authorized we will be unblinding and then offering that third dose at least three months after the second dose.

And that three month interval is really defined by an interval that we've seen from DMID, so DMID assessed heterologous boosting with that three

month interval afterwards. And, as you mentioned, there may be some safety and immunogenicity benefits to that interval. So we will share those data when available. And then, we have mRNA-1273, and we have some clinical supply with an Omicron-containing variant.

And so there will be some of the cohort in the youngest kids receiving the Omicron-containing variant. And that really is to bracket the booster responses, so we'll see the Omicron data that we'll share with you in two weeks in the adults. And then, in these youngest kids, the Omicron-containing variant and we believe that will really help give the cumulative picture of the capabilities of the vaccine.

DR. ARNOLD MONTO: Thank you very much. Very broad response to a broad question. Dr. Gans followed by Dr. Reingold.

DR. HAYLEY ALTMAN-GANS: Thank you so much, and I really appreciate all the thought that you've put into what you will be doing moving forward. And so my question really for the FDA -- and I don't know if

Doran Fink is available, but I'm impressed with how much there is after already predicted to be available to the FDA. And my question is, before moving onto licensure, will there be availability of the data to be reviewed by the Committee? And maybe even some recommendations moving forward of whether (audio skip).

DR. ARNOLD MONTO: Dr. Fink.

DR. DORAN FINK: Thank you. FDA always makes a case-by-case decision on seeking input from the VRBPAC depending on whether we consider there to be important questions about benefits and risks that would benefit from or require input from the VRBPAC. And, as you know, we have taken certain actions without a VRBPAC meeting when we felt that those actions needed to be done expediently or when we felt that the most pertinent issues regarding benefits and risks had already been discussed and there was nothing new to discuss. And so we will consider those factors before we take any future action on a case-by-case basis.

DR. HAYLEY ALTMAN-GANS: Thank you. And then just --

DR. ARNOLD MONTO: Thank you very much.

DR. HAYLEY ALTMAN-GANS: My question for Moderna is are you going to be looking at immune correlates in any of your studies moving forward? Because we seem to be stuck on looking at neutralizing antibodies, which we all know for viruses, while show you some correlates that is there in the immune system, it's not necessarily the correlate of protection for these respiratory viruses.

DR. JACQUELINE MILLER: Yeah. So this absolutely is an area of interest for us. We have published our work from the ancestral strain, which Dr. Das discussed a bit with you yesterday. And we're now speaking with our collaborators at the CoVPN and then also at the NIH about now how we might take those results as we're getting the Omicron neutralization titers and Omicron cases and work on an Omicron correlate of protection.

I think our feeling is that probably Omicron is the next most important variant to investigate, so we're discussing how we might do that now that we're so

distant from the original blinded efficacy trial. But it's definitely an area of interest.

DR. HAYLEY ALTMAN-GANS: Okay.

DR. ARNOLD MONTO: Thank you very much. Moving on to Dr. Reingold followed by Dr. Nelson. And there will be one question after that. We're falling behind schedule. Dr. Reingold.

DR. ARTHUR REINGOLD: Thanks very much. I'll try and make it quick. So first, Mark Sawyer asked my questions about coadministration, but the other question I have, you know, for a lot of routine childhood immunizations there's much circulation of the agent in the population. So we're not typically faced with the problem of administering the vaccine to a child who's recently been infected or already has antibodies.

And clearly, with COVID-19, that's not the case. And you may have shown these data, but in terms of reactogenicity, either with a preexisting antibody or recent documented COVID-19 is there any reason that the safety profile would be considered different? This

presumably will be an issue for CDC if vaccine is given EUA, what kind of clinical guidance they give about either delaying vaccination or proceeding with vaccination under different circumstances. Thank you.

DR. JACQUELINE MILLER: Yes, we actually do have the safety data by seropositive and seronegative adverse events. So if you can put the slide up, please, it's SY23. Thank you. So what you see on this slide are the children who are two to five years of age in (audio skip) are children that were SARS-CoV-2 positive at the start of the study. In black, the ones that were SARS-CoV-2 negative. The rates were relatively comparable between those two subgroups.

If there was a trend that we noticed it was that systemic rates of reaction tended to be higher after post-dose-2 in the initially seronegative children as opposed to post-dose-1, which was more frequently observed in the seropositive children. And then, let's also put up the data for the infants and toddlers. Oh, sorry, Dr. Monto.

DR. ARNOLD MONTO: Go ahead, please.

DR. JACQUELINE MILLER: No, I just wanted to show you for the other age group what the data looked like post-dose-2 and post-dose-1 for the seropositive and seronegative children. Thank you.

DR. ARNOLD MONTO: Okay. Thank you. Dr. Nelson. Followed by Dr. Fuller, who will be the last questioner in this session.

DR. MICHAEL NELSON: Yeah, so I just had a couple of quick questions. I know we're falling behind. One has to deal with the subpopulations of Blacks who were enrolled in your current study. So I did note the overall low enrollment at 3.2 percent and 4.7 percent. I'm sure that there were many challenges in getting a higher percentage. But I also noted with interest the higher immunogenicity or hemo-immune response.

One was consistent with the older age groups you did with the data you presented yesterday. And in particularly the 6 to 23 month, it was almost two-fold higher than the white population or other populations. So one question I have for you is this a real distance,

or are we victims of small numbers? Is there some significance to the trend of a higher immune response that you're seeing with the Black participants?

And then a second question, just to prime you, is with respect to the immunogenicity dataset as a whole is there any evidence of possible over-representation from individuals with higher titers, either of Black race or perhaps even post-baseline infections?

DR. JACQUELINE MILLER: Yeah, thank you for those questions. So let me first put up the slide looking at the immunogenicity by race. So those slides are -- if you guys can find SY31. There we go. Put the slide up, please. I just saw it, Michael. I don't know.

DR. ARNOLD MONTO: Why don't you discuss it --

DR. JACQUELINE MILLER: There we go.

DR. ARNOLD MONTO: Okay.

DR. JACQUELINE MILLER: Yep, there we go. So these are the children, two to five. The pattern is similar in the youngest infants. In the interest of

time I'm happy to show it, but I understand we're short of time. So as you mentioned the immunogenicity cohort, which is of course a subset of the total cohort, there were 20 African-American children, and their titers were higher. But the 95 confidence intervals overlapped.

And, in terms of representation in the trial, I think we didn't see over-representation of groups that might have had reason to think that there were higher titers. So you see the proportion of the groups that had the highest titer in terms of race. And certainly, in terms of seropositives, they were much less frequent than seronegatives. And I can show you in the toddlers as well if you want to see, or if you want to move on, it's up to you.

DR. ARNOLD MONTO: I think we can move on.

DR. MICHAEL NELSON: That's okay.

DR. ARNOLD MONTO: Dr. Fuller, final question.

DR. OVETA FULLER: I just wanted to follow-up on the earlier question. I suspect that you're going to be looking at those things in the future, but my

concern is that the one child that had the seizure, was there any underlying thing like sickle cell or asthma or anything that could be detected? Because even though there only may be one, if that's someone's child that can identify that they have a risk factor that would be very useful to know.

DR. JACQUELINE MILLER: Yes, Dr. Fuller. So we don't really have other medical history on that child. They were previously well. I will say and I'll just add maybe for reference as a pediatrician febrile seizures often happen in children who are healthy with no underlying conditions. So they occur at a rate of about three percent between the peak ages of one to five. It didn't necessarily surprise us that this was a child who had no otherwise underlying conditions.

DR. ARNOLD MONTO: Thank you.

DR. OVETA FULLER: So did you look at things or will you look at things like sickle cell or that sort of thing in the future? I heard you mention immunocompromised earlier.

DR. JACQUELINE MILLER: Yeah, no, so the trial

in the immunocompromised is going to be specific and standalone. The power of our large effectiveness study in a diverse database like Kaiser Southern California, really allows us to look at events by different underlying conditions, allows us to look at different age groups and so forth. And so certainly hear the interest in seeing what the effectiveness looks like in children with sickle cell. So we will look into that.

DR. OVETA FULLER: Great. Thank you.

COMMITTEE DISCUSSION AND VOTING – MODERNA COVID-19 VACCINE

DR. ARNOLD MONTO: Thank you. And thank you to the sponsor and to FDA for their answering our questions. We now move on to the discussion of the voting question and the vote. And what we're going to be doing as usual is having the Committee discussion over the voting question. We will then vote, and then we will have explanation of votes for those who wish to explain their votes. Do we have the voting question

we're going to be discussing?

"Based on the totality of scientific evidence, do the benefits of Moderna's COVID-19 vaccine administered as a 2-dose series outweigh its risks for use in infants and children 6 months through 5 years of age?" Discussion. Dr. Meissner. Followed by Dr. Portnoy.

DR. CODY MEISSNER: Thank you, Dr. Monto. I'd like to make a couple of comments in regard to this. I don't think anyone could listen to the public -- the open public hearing session without being troubled by the diversity and the emotional commitment that's been put into this issue of immunizing children between six months and five years. It was quite moving.

My personal feeling is that it would be hard not to include six months to five years of age in an amendment to the EUA in view of the strength of the data that we have seen today. But I would like to make this comment. And I think it's very important, as Dr. Cohn said yesterday, that the communication or the messaging be made as clear as possible for parents to

understand the relative risk and the relative benefit. I think we -- for example, we've heard several times that there were approximately 442 deaths so far in the pandemic among children less than five.

So that means about 220 deaths a year, approximately. Now if you look at the number of people who are struck by lightning in the United States on a year, it's 270. So we're talking about a very rare event. If we talk about hospitalizations among children between six months and five years of age, the hospitalization rate on the CDC website, the latest study, is 2.3 per 100,000 or 23 per million. And there are about 20 million children in this age group.

So 20 times 23 is 460 hospitalizations associated with COVID in this age group that we're considering today. And probably only a fraction of those are because of COVID-19 infection rather than a coincidental association. So really we'd be talking about vaccinating close to 20 million children in order to prevent two or three hundred deaths. And it's a matter of how an individual weighs the risk and

benefit. I think the vaccine should be available for certainly high risk children and for families that are so concerned they are troubled by that risk ratio, and they should have access to the vaccine.

But I, again, feel very strongly that parents should understand how small these numbers are. The very low risk from the vaccine, but it's also a very low risk from the infection itself. And I think that has to be communicated clearly to parents so that they can participate in the decision about vaccinating a child in this age group. Thank you.

DR. ARNOLD MONTO: Thank you. Dr. Portnoy followed by Dr. Berger.

DR. JAY PORTNOY: Great. Thank you. I've really enjoyed this conversation, and I have to say I was extremely moved by the public comments as well. Nobody cannot be moved by it. But I work at a children's hospital, and I remember earlier this year walking by the emergency room and looking in and seeing that the place was completely filled. I asked one of the security guards what's going on, and he said, well,

it's COVID. And the emergency room was filled. Our hospital was loaded up with children who had COVID.

Now, I know that the death rate from COVID and young children may not be extremely high, but it's absolutely terrifying to parents to have their child be sick, have to go to the hospital or even go to the emergency room or their primary care doctor because they're sick and having trouble breathing.

So this is it's not just doubts. We have to understand how distressing this is for parents whose children are affected by this disease. Every pediatrician that I know at our hospital has been waiting eagerly for this vote to occur because they can't wait to start giving this vaccine.

So our question today is does the benefit outweigh the risk of this vaccine? And I think that the evidence is pretty clear for preventing severe disease, hospitalization, emergency visits. This vaccine is very effective. It's also very safe to use. I'm a little bit disappointed that it doesn't prevent infection by COVID as effectively as it could because

that's what spreads it around, but even in adults we can't prevent infection. But at least we can stop people from being terribly sick.

So this is a long-awaited vaccine. I feel the pain of those who are opposed to it, who have had bad experiences with it. They can choose simply to not get the vaccine. But there are so many parents who are absolutely desperate to get this vaccine, and I think we owe it to them to give them a choice to have the vaccine if they want to. Thank you.

DR. ARNOLD MONTO: Thank you. Dr. Berger followed by Dr. Fuller.

DR. ADAM BERGER: Thank you as well. And I was going to say something similar to what Dr. Portnoy was pointing out, is it's not just about deaths; it's about preventing hospitalization. And I think some of the really distressing information that we've heard is that a quarter of those children that are going to the hospital are ending up in the ICU. And 63 percent of them have no underlying comorbidity to actually be directing this. So you have to ask yourself like what

other -- those that do have comorbidities might be at a higher risk.

And so it really is about giving a choice. But yeah, I actually had a question about the question we're being asked. And part of this is just the framing. All the data we've been given and specifically the way it was collected was dividing up the 6 month to 23 month olds from the two to five year olds. And yet the question is putting them altogether. Now this may not change the outcome, but just it occurs to me that it's sort of an oddity in terms of the voting questions itself that we're being presented with because the data isn't exactly aligned 100 percent across both of those groups.

There are slight differences in vaccine efficacy and some of the side effects that we've seen. It may not be significant, but I did have a question for FDA as to why it was combined in the voting question as opposed to having it be separated into those two different age groups for voting.

DR. ARNOLD MONTO: Do we have an answer from

FDA, Dr. Fink?

DR. DORAN FINK: The EUA request from Moderna was for Emergency Use Authorization of the 25 microgram dose level for use in the age group of six months through five years. That is why the voting question is constructed accordingly. We yesterday dealt with two separate EUA amendment requests: one for adolescents, one for ages 6 through 11. And that's why those questions were constructed accordingly.

I do recognize that the data was presented according to the two smaller age groups within six months through five years, and for Pfizer it was done the same. But I would hope that the Committee would really focus on similarities and then consider the age group as a whole. And if they feel compelled -- if any Committee members feels compelled to have a different opinion for one smaller age group versus another, then of course you can raise that concern.

DR. ARNOLD MONTO: Thank you. And I am reminded that this is a discussion right now. We will have a second session after the vote in which you can

explain your vote. So technically you're not supposed to say how you are voting at the moment. But you can say whether you support or not the approval. Dr. Fuller followed by Dr. Reingold.

DR. OVETA FULLER: Yes. That is what I was going to say, that the need for clear messaging to parents and guardians about the choice for having the vaccine or not is very important and that the follow-up studies that are planned are very important. The benefits seem to clearly outweigh the risk, particularly for those with young children who may be in kindergarten or in collective childcare so that those who want to do this will have that option.

But I would ask should this pass, or should this be recommended by FDA and by the Committee and passed by FDA and CDC, that parents really consult their pediatrician for their children. My question earlier wasn't just for sickle cell but any other unknown underlying condition that might impact the outcome. So this is a decision that parents and grandparents and guardians will have to carefully weigh

should this actually go through.

DR. ARNOLD MONTO: Thank you. Dr. Reingold followed by Dr. Sawyer.

DR. ARTHUR REINGOLD: So, thanks. One of the speakers in the public session urged us multiple times to think of the children. Now I think he and I may think of the children in slightly different ways. But my way of thinking about the children is that if we have a vaccine that's benefits outweigh the risks, that making it available to people is a reasonable choice. I would point out that we as a country continue to give a large number of vaccines to children where the risk of the child dying or being hospitalized of those diseases is pretty close to zero.

Those include polio. Those include measles. We vaccinate large numbers of people against HPV even though very few of them would ever develop cancer related to HPV. So we, with our vaccines, are trying to minimize serious illness and death or perhaps reintroduction of something like polio into the United States. But we generally know that many of the

infections that we are vaccinating against, that the serious outcomes are quite rare actually.

And we nevertheless try and vaccinate a large part of the population, if not everyone. So I think we do need to focus on the serious outcomes and even if they're relatively infrequent and even if a vaccine is less than 100 percent effective. Flu is another good example. We continue to recommend flu vaccines for people even though it only may be 30 to 40 percent effective. And so if we have a prevention opportunity, I believe we should take it.

But just one last caveat. My personal preferred wording is not to tell the people that something is safe. I think that's the wrong messaging. I think nothing in life is perfectly safe. No drug, no vaccine, no personal choice to get on a plane or get into a car is, quote, safe. I think what we need to emphasize is that the benefits outweigh the risks. Thank you.

DR. ARNOLD MONTO: Thank you. Dr. Sawyer followed by Dr. Levy.

DR. MARK SAWYER: First of all, I'm generally in support of approval for many of the reasons that have been outlined. To follow-up Dr. Reingold's comment I would like to add to the benefit column the fact that as we heard in the public comment some parents are so concerned about the risk of exposure that they're still completely isolating their children socially, perhaps above and beyond what the current CDC and AAP guidelines suggest.

And the potential adverse impact of that isolation was brought up also in the public comment session. So the availability of these vaccines will liberate those children to some extent whose parents will find relief and feel a little more comfortable to let their children start to socialize in the appropriate environment.

The other potential benefit that's been touched on is the impact on long COVID, which has further potential challenges for development as we learn more about long COVID does and what the implications are for school performance. So I think

there's a lot in favor of the benefit column in the risk/benefit equation.

DR. ARNOLD MONTO: Thank you, Dr. Sawyer. Dr. Levy last question so far.

DR. OFER LEVY: Thank you. I am generally supportive of this direction, and I also want to emphasize the importance of knowledge and that we keep building on our knowledge. We saw a lot of good information today, including some immunogenicity information. But as I mentioned yesterday, we have a ways to go to understand the correlates of protection against coronavirus. Antibodies are likely very important but not the whole story. We'd like to see T cell data; we'd like a recognition that correlates may be age specific. You might get a similar antibody response at a given age.

But antibodies act in a context together with a compliment system, with phagocytes, and those systems might be distinct by age due to immune ontogeny. So I encourage FDA and the sponsors to continue to develop more sophisticated and nuanced information about

correlates of protection. The other key here will be safety surveillance. The possibility of febrile seizures, particularly in those unusual cases where there's a high fever after the vaccine in the young age groups, it's possible we'll see febrile seizures as this gets pushed out, if indeed that's the determination by FDA.

So we have to keep an eye on that, and also potential impact on other -- balance of other respiratory infections is what was alluded to by FDA by Dr. Doran Fink. So those are areas that I think where knowledge -- it needs to continue to evolve. But overall, I'm supportive. It's a bioethical concept of a presumption of inclusion.

We have reasonable safety data, and this vulnerable population should be included. And there's a broader context. This platform, this mRNA vaccine platform may be useful not just against this current coronavirus and its current variants but the next ones as well as future pandemics. Thank you.

DR. ARNOLD MONTO: Thank you, Dr. Levy. That

concludes the questioning -- I mean, the comments concerning the voting question. We will now have the vote, and then we will have explanations from those who wish to explain their vote further.

MS. CHRISTINA VERT: Thank you, Dr. Monto. Only our 10 regular members and 11 temporary voting members, a total of 21, will be voting in today's meeting. With regards to the voting process, Dr. Monto will read the final voting question for the record, and afterwards all regular voting members and temporary voting members will cast their vote by selecting one of the voting options, which include yes, no, or abstain.

You have two minutes to cast your vote after the question is read, and please note that once you have cast your vote you may change your vote within the two minute timeframe. However, once the poll has closed, all votes will be considered final. Once all the votes have been placed, we will broadcast the vote results and read the individual votes aloud for the public record. Does anyone have any questions related to the voting process before we begin? Okay. Okay,

Dr. Monto, if you could please read the voting question?

DR. ARNOLD MONTO: For the record: Based on the totality of scientific evidence available, do the benefits of the Moderna COVID-19 vaccine when administered as a 2-dose series, 25 micrograms each dose, outweigh its risks for use in infants and children 6 months through 5 years of age?

MS. CHRISTINA VERT: Okay. Please pull up the voting pod. At this time you may start to vote. Okay, it looks like all the votes are in. We can go ahead and close the poll. Thank you. Okay. There are a total of 21 voting members for today's meeting, and the vote is unanimous. We have 21 out of 21 yes votes, zero no votes, and zero abstain votes. Okay. I will now read the specific votes for the record. Okay.

Dr. Berger, yes; Dr. Nelson, yes; Dr. Fuller, yes; Dr. Levy, yes; Dr. Monto, yes; Dr. Sawyer, yes; Dr. Offit, yes; Dr. Reingold, yes; Dr. Bernstein, yes; Dr. McInnes, yes; Dr. Wharton, yes; Dr. Pergam, yes; Dr. Chatterjee, yes; Dr. Portnoy, yes; Dr. Lee, yes;

Dr. Kim, yes; Dr. Cohn, yes; Dr. Marasco, yes; Dr. Meissner, yes; Dr. Hildreth, yes; Dr. Gans, yes. And that completes my reading of the votes. And I will hand the meeting back over to Dr. Monto.

DR. ARNOLD MONTO: Now we will proceed to explanations of the vote from anybody who wishes to speak. Dr. Hildreth.

DR. JAMES HILDRETH: Thank you, Dr. Monto. I think the evidence that we had in front of us justified a vote of yes. I did want to make a point that I made yesterday, that Dr. Meissner made a few minutes ago. We got to be transparent about the real risk of COVID-19 for children.

Tens of millions of children in this age group have been infected and have done just fine, but I think we need to make parents aware of what the real risks are and let them make decisions. But for those parents who choose to do so, especially those parents of kids with underlying conditions, this is a choice they should have and I'm pleased that they'll have it. Thank you.

DR. ARNOLD MONTO: Thank you. Dr. Portnoy.

DR. JAY PORTNOY: Thank you. As the designated consumer representative member of the Committee I can speak on behalf of the patients that I take care of. I know that there were a lot of very relieved parents, almost certainly who are listening to this right now. They've been waiting for a very long time. I again want to emphasize how terrified parents get when their children get sick, even if they don't die from it.

I take care of patients who have food allergy. The number of deaths from food allergy is extremely low and yet the parents are terribly anxious and worried about this disease. COVID actually causes a lot more deaths. I understand why parents are very nervous and fearful of doing normal activities and especially if their child actually catches COVID. But even the fear that they could catch COVID -- this will certainly alleviate a lot of their concerns, and so I'm really happy that the vote went the way it is. And I think it was the right vote. Thank you.

DR. ARNOLD MONTO: Thank you. And Dr. Nelson.

DR. MICHAEL NELSON: Than you, Dr. Monto. I do believe the benefits far outweigh the risks that were involved. And personally I really do believe this recommendation does fill a significant unmet need for a really ignored younger population in need of options. Families will now have choice that they did not have before.

And I fully believe in the intelligence of families to make the right choice for their family and children, particularly when we provide clear recommendations with respect to the information we have on hand regarding the risk and benefits. It's my personal hope that every child in the U.S. seeks and gets vaccinated in the near future. Thank you, Dr. Monto.

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

DR. HENRY BERNSTEIN: Thanks, Dr. Monto. I want to express my agreement with everyone else. With over 600 million COVID vaccine doses that have been already administered in the U.S. we really -- the

overall safety profiles are quite reassuring. And I think having a COVID vaccine available for this younger population is critically important given that pediatric cases can be, have been, and may be problematic in the future. I also think that there's a huge safety -- vaccine safety monitoring system in the United States that's historic.

And so that should be reassuring to many, and I do think that there are advances in science -- in the COVID-19 science. They'll continue on for many years, not just vaccines, but treatments and testing and social distancing, masks, et cetera. I also think that hybrid immunity will provide more protection against future infections and will be helpful as well, even for those who have already experienced COVID because I think overall those who are vaccinated tend to do better in all outcomes than those that are unvaccinated.

And I think that the ultimate aim of COVID-19 vaccine is to prevent severe disease, hospitalization, and death more than preventing transmission and

infection. I think the messages I want to emphasize what others have said -- the messaging must be communicated very clearly to the public. And I still feel that there are tens of millions of people who are unvaccinated, and we must also encourage them to get vaccinated. Thanks.

DR. ARNOLD MONTO: Thank you. Dr. Levy followed by Dr. Gans.

DR. OFER LEVY: Yeah, I just wanted to take a moment to acknowledge the public commentary that shows the wide diversity of opinions in the U.S. public about this whole vaccine enterprise. And I think it becomes important that we continue that tradition of being open to all the public commentary, provided it's not hate speech, provided it's respectful -- but to cast a big tent here. And I think what we've heard from a lot of the Committee members -- they'll each speak for themselves, but what I've heard is the emphasis on a choice, a choice for families.

They can partner with their pediatrician, make the decision. If they're in a situation in a community

where there's a lot of spread of COVID, if they have children that may be at higher risk, if they have family members who are particularly vulnerable, we encourage them, if this moves forward, to avail themselves of this option. So it's a concept of making it available. And the ongoing safety surveillance, the U.S. public should hear that that's a serious enterprise. It's not a rubber stamp.

We've seen entire vaccine programs put on hold for rare cases of thrombosis. And I was interviewed in the media saying Dr. Levy, isn't it a mistake? Doesn't it shake public confidence when they stop a program? I said to the contrary. It should show the public that the safety surveillance works. That's its serious and that if we do detect further signals that are concerning, something will be done about it. So I think this is the right path forward, and I'm very honored to be part of this Committee. Thank you.

DR. ARNOLD MONTO: Thank you, Dr. Levy. Dr. Gans followed by Dr. Marasco.

DR. HAYLEY ALTMAN-GANS: Thank you very much.

I just wanted to add a voice to the significance of this as a pediatric disease. I think as you weigh it in terms of being the fourth and fifth most risk factor for death is really important. So I think we really do need to not underplay the importance of this as a pediatric disease. And therefore, prevention is really the way to go. It's also of note and was brought up earlier that there are just all these treatments now that we have for COVID.

That's not the case for our youngest individuals. We actually have very restricted and limited ability to help anyone who is infected, and they are actually not the most efficacious. And so I think it's very important. The other point I wanted to bring up for the individuals who will be considering this for their families is that infection -- that the immune response that you can get from vaccine versus infection is different.

When you have an infection and you have viral replication and also tissue invasion and damage, it's different. You do get immune response, but getting

immune response without that is also, should be an option for individuals so that they don't have to suffer from the actual viral disease. So I think that's a really important point that hasn't been raised. I'm trying not to be repetitive for my colleagues who I know have raised some really great points.

The other aspect I would like to just add to Dr. Levy's point and others on this Committee is that we do take the science very seriously. And I hope that really has come through to those who maybe are doubting the fact that we're listening. We are considering all of the different science. And I just want to applaud the scientific community.

This is really a breakthrough that has allowed us to move through the pandemic in a way that has allowed less suffering and disease. I'm very glad for this option for people in the scientific community who care for children as well as families. Thank you.

DR. ARNOLD MONTO: Thank you, Dr. Gans. Dr. Marasco followed by Dr. Lee.

DR. WAYNE MARASCO: Hi. Thank you, Dr. Monto. So I've been impressed, as everybody has, with the comments by the public. They're very important. I take them seriously; I think we all do. It has not escaped me or other members of the Committee that we've received thousands upon thousands of emails from people on both sides of this issue.

I think it's really been largely a matter of misinformation or disinformation, people thinking that children weren't as susceptible as they were earlier in the pandemic. I don't think many people understand the increase in infection with Omicron. But I think it's all about people making their own decisions for themselves and their family.

Dr. Meissner and everybody else has really said it right. It's a matter of choice. I just want to make sure the messaging from the CDC and the FDA is coordinated in such a way that the healthcare providers -- the local healthcare providers can also provide that information to help families and parents make this decisions. So I'm proud to be part of this Committee,

and I agree with the decision that's been made.

DR. ARNOLD MONTO: Dr. Lee.

DR. JEANNETTE LEE: Yes, I just wanted to also add my support for this decision. I think as we heard in the public comments the lack of the vaccines for these young children has been a gap for many and has really had an impact on their lives. So I think this is really, really very positive. I will say I think it's clear the story isn't over.

The pandemic has taken some different twists and turns. And there may be more options for these children in the future, and I think we will consider that as well. And I'd also like to say I'm very proud to be part of this Committee and very, very pleased with all the science we've been able to see from the investigators and the companies. Thank you.

DR. ARNOLD MONTO: Thank you, Dr. Lee. That concludes our action on the Moderna vaccine. We're going to take a break until 3:25 Eastern. That gives us about 15 minutes; is that right?

MR. MICHAEL KAWCZYNSKI: Nope, 10 minutes.

Oh, 3:25 -- yeah, 15 minutes. Yes, you are right.

DR. ARNOLD MONTO: Yeah. Yep. A reward for getting done. We'll start when we should have been taking the break, 15 minutes. And then we will repeat what we've just done: questions, discussion, and vote for Pfizer.

MR. MICHAEL KAWCZYNSKI: All right. And with that we will now take our 15 minute break. Studio.

[BREAK]

ADDITIONAL Q&A FOR FDA AND SPONSOR PRESENTERS – PFIZER-BIONTECH COVID-19 VACCINE

MR. MICHAEL KAWCZYNSKI: Okay. Good afternoon and welcome to the closing session of the 174th Vaccines and Related Biological Products Advisory Committee Meeting. Dr. Arnold Monto, our chair, take it away.

DR. ARNOLD MONTO: Thank you very much. We will now repeat the process of questions to both the

sponsors and to FDA and then discussion and votes and explanation of votes. So hands raised for questions for either the sponsor or FDA. Dr. Marasco followed by Dr. Gans.

DR. WAYNE MARASCO: Thank you, Dr. Monto. Dr. Gruber, this is a question for you. It's a question that was touched on by Dr. Pergam, Portnoy, and Offit, and it really has to do with your 3 microgram dose. So there's a pretty impressive step-up in protection from your second to third dose for Omicron and a pretty low dose of mRNA, and I heard from your associate that you've got good protein production.

But the question I really am asking is, is there a fundamental difference that has occurred with your vaccine? In other words, because of the low dose that you have given, are you getting any different quantitative or qualitative response in terms of, for example, higher affinity antibodies? So when you do your titering and you get your main geometric titer, you get a number.

Is that because of higher titer antibodies --

I mean, higher titers or more higher affinity to the Omicron? And those kind of studies can be done quite simply serologically, and I'm wondering if you're pursuing that to find out if there's something qualitatively and quantitatively different about the effect you see in your third dose?

DR. WILLIAM GRUBER: Thanks for the question. I may ask Kena Swanson to actually come up to provide maybe a little bit more detail, but to this point we haven't actually specifically looked in detail, certainly in the pediatric population, about the nature of antibody affinity. I come back to the fundamental observation that, as best as we can determine, the level of neutralizing antibody that we see against Omicron seems to reliably predict the likelihood that you're gonna have protection.

When that antibody is low, regardless of whether it's related to affinity or related to the actual quantity of antibody that's there that has neutralizing potential, it predicts the likelihood that you're gonna be successful. Low antibody, less

efficacy. Higher antibody, higher efficacy.

And again, we've shown that antibody that we induce in these young children matches that in older adults or in older children and adults after three doses and provides protection. But maybe I can ask Dr. Swanson just to comment on any other sort of work that we're doing related to characterizing antibody.

DR. KENA SWANSON: Hi, Kena Swanson from Pfizer Viral Vaccines. And just to add briefly to what Dr. Gruber mentioned, I think the key to what we're seeing in the development of the immune response is between the second and the third dose. There is not only an increase in the neutralizing titer but the activity and binding affinity of those antibodies, particularly that you can notice against Omicron. And that's been seen in the data in the adults.

And we're seeing indications that the trend is similar as well in children less than five years of age. And there are other publications and preprints out there that have done similar analysis in other populations.

DR. WAYNE MARASCO: Thank you.

DR. WILLIAM GRUBER: Yeah, maybe if I can just enlarge on that on a point because I want to clarify something that was being said this morning that this really interdigitates with. And that is that both in the briefing document as well as in the information that the FDA shared with you in their slide presentation, you've seen Kaplan Meier curves.

And for the two to four year olds it's pretty clear that, whether we're talking about Delta or we're talking about Omicron, even after the second dose you do see a spreading of those curves. And if you think about it, the amount of Delta that we saw is actually dwarfed by the amount of Omicron. So much of that efficacy that you're seeing even after the second dose is due to efficacy against Omicron.

For the six months to less than two year olds, it's less clear about when that efficacy may start to occur, but you can see as you go farther out that the curve begins to spread a little bit. And the goal really is with the third dose to move everything to the

left, to maximize the potential that we can have for protection against Omicron by giving that third dose.

DR. ARNOLD MONTO: Thank you. Dr. Gans.

DR. HAYLEY ALTMAN-GANS: Thank you. And I think I would love to hear some of the vision of what Pfizer is going to do. We heard quite a bit from Moderna about some of the studies that they're going to be doing forthcoming. And thank you for providing the ones that we heard about earlier today. We don't have to repeat those. The ones that I was really considering is it's not unusual to need a prime-prime-boost strategy. So the three doses here doesn't surprise many people.

And I think that's all within keeping. My question for you, particularly because these were developed during a time when there's obviously disease progression, variants coming into being, what will be your follow-up studies? How likely is it that -- and probably pretty likely because we're seeing that in the adult population -- but what are you doing to prepare for future doses, and are you looking at any other

dosing in terms of how much you're giving and the intervals?

DR. WILLIAM GRUBER: Yeah, so thanks for that question. We're obviously all looking forward to the end of this month when at the VRBPAC further decisions on the nature of what future vaccines should look like will be informed, both by information that we're providing based on our bivalent vaccine experience and our Omicron experience in adults. We are actually working then based on the information that comes out of that meeting to best tailor what we do to investigate young children.

It's no surprise to you, Dr. Gans, we have sort of two groups we have to contend with here, those that are naïve, what's going to be best for them moving forward as well as those that we put in good position, we hope, based on hopefully today's recommendation from the VRBPAC Committee to have them fully primed, ready for whatever else we might bring in the future.

DR. HAYLEY ALTMAN-GANS: Thank you.

COMMITTEE DISCUSSION AND VOTING – PFIZER-BIONTECH COVID-19 VACCINE

DR. ARNOLD MONTO: Thank you. And thanks both to the sponsor and to the FDA group. We have no more questions from the panel. And therefore we will move to discussion of the voting question. And could we have the voting question put up?

Based on totality of evidence, do the benefits of the Pfizer-BioNTech COVID Vaccine when administered as a 3-dose series outweigh its risks for use in infants and children 6 months through 4 years of age? That is going to be our voting question. Now discussion, we don't want to say how you're voting, but you can say whether you support approval. So, Dr. Offit.

DR. PAUL OFFIT: Thanks, Arnold. I think that the way that this question is written, do the benefits outweigh the risks, is something I could support. But I do have some concerns about this vaccine, and I just want to sort of air them. It does worry me actually

that there was no protection after dose two. I thought that was surprising. I think it was probably surprising to the company. And I fear that they may have under-dosed.

We were supposed to meet on February 15th to discuss this. We didn't, I think, in part because those data probably were surprising. And with Moderna, you have, for example, low levels of protective efficacy after dose two, but you can assume that probably is predictive of better protection against severe disease. I'm not so sure you can predict that with Pfizer's vaccine.

Now, on the other hand, with the third dose, you get the kind of immune briefing data that is reassuring. The neutralizing antibodies against Omicron is reassuring. But that's dose three. So for people who've gotten that vaccine, who've gotten, say, two doses of that vaccine, they have to know they're not protected. And they're going to have to wait a few months till they are protected. And I just wonder whether parents will understand that. So I do worry

about this because I think it was a surprisingly negative result.

Although the protective efficacy that was listed with 75 percent for the six month old to two year old and 80 percent for the older group, those were based on very small numbers. I mean it was seven cases in one instance, three cases in another. It's a little hard to feel comfortable about that since the numbers were so low. But so, I do support this, but I do worry that parents aren't necessarily going to know that after two doses they may not be protected at all and would engage in the kind of activity that would put their child at risk. So, thank you.

DR. ARNOLD MONTO: Dr. Offit, would you be more comfortable if in the post-approval period careful surveillance be given about protection after two doses given the relatively small numbers? Is this something that can't be fixed?

DR. PAUL OFFIT: Yes, exactly. No, I think that's a really good point. And as more and more children are vaccinated we'll learn more. And it may

be that what Dr. Cohn said earlier is true, that this may end up being a four-dose vaccine. But I do think we should certainly learn as much as we can when it gets out there. I think it's safe. I think it will certainly offer something, but I do worry that those two dose data were surprisingly poor but thank you.

DR. ARNOLD MONTO: Okay. Dr. Chatterjee followed by Dr. Lee.

DR. ARCHANA CHATTERJEE: Thank you, Dr. Monto. I was actually going to make a very similar comment to what Dr. Offit did, with regard to the two doses not providing sufficient protection. I think with two vaccines that have different dosing regiments it's going to be even more important than ever that the public education, the education of providers is done very, very carefully so that people understand what the ramifications of the choices that was discussed earlier this afternoon are, that we are making choices between two different vaccines that have a little bit different profiles.

And that's going to be important for people to

take into consideration. Having said that, I would say that I was pleased to see the three dose data showing that it brings it up to par basically, like we see in older children and adults, the level of protection, recognizing of course that this virus is continually changing and that those numbers are maybe true today and may not be true down the road.

But with all of those caveats, I am in support of the authorization of this vaccine as well, making sure, again, that the education around this is done very, very carefully so that people are not mislead by what the vaccines actually provide.

DR. ARNOLD MONTO: Yes, and I think we should not underestimate the problems of rolling out various approaches to vaccination which have different intervals and different doses and the rest. This is going to be quite challenging. Dr. Lee followed by Dr. Cohn.

DR. JEANNETTE LEE: Yes, thank you. So I share the concerns of the last two speakers about the two-dose data. I was also actually quite surprised. I

guess my concern is I do recognize that the three doses, they're certainly of benefit. I have a lot of concern that many of these kids will not get the third dose. As we know, it's a struggle to get people in for two. We've already seen with the boosters for adults, lots of people don't take them. And so my concern is that you have to get the three doses to really get what you need. I'm just concerned that some won't. Having said that, I will say that I am supportive of this though. Thank you.

DR. ARNOLD MONTO: Dr. Cohn and then Dr. Marks is going to be making some comment.

CAPT. AMANDA COHN: Thank you. I'm also very supportive and agree that the benefits do outweigh the risk of this vaccine. Just to add to what the previous commentors have said, I think it is imperative that we do post-licensure surveillance for effectiveness for both vaccines. But in particular, I'm also concerned about people comparing the VE estimates or point estimates between these two, which I think is a real problem given the few number of cases.

And I would really hope in our communications that we not use that 80 percent effectiveness because my level of confidence in that number, I believe the vaccine is effective. I do not have any idea what that number will actually end up being. And additionally, I think it's really important for people to understand not -- that this was effectiveness after 30 days. Other vaccines have looked at effectiveness after longer periods of time of follow-up. So 30 days after vaccination, this could fall off very quickly, and we just want to monitor it closely.

DR. ARNOLD MONTO: Yeah, Dr. Cohn, you noticed the confidence intervals around some of these estimates, correct? We really can't go with the point estimates because the confidence intervals for a lot of them were pretty wide until you grouped together. Dr. Marks, you had some comments.

DR. PETER MARKS: I just thought it might be helpful. I apologize if I missed this, but I didn't hear the sponsor reply to this. But it may be helpful. There does seem to be a lot mystery around the second

dose effectiveness with Pfizer. And it might be helpful for both the public and for the Committee if they commented on that two-dose effectiveness.

DR. ARNOLD MONTO: Okay. That's fine. I remember their saying that the Kaplan Meier plots did separate. Dr. Gruber, would you supplement the information we've got?

DR. WILLIAM GRUBER: Yeah, so again, there are really two lines of evidence. We've already spent time showing the slides in terms of the Delta response, right? And for both age groups after a second dose we had high levels of efficacy, both in the six month to less than two year olds. In the individuals that were two to five we also demonstrated efficacy after Delta. The real question obviously in an Omicron environment is what we're seeing after Omicron.

And if my slide pullers can pull it up, or people can likely remember it or you may see it in your briefing document -- again, if you looked at the two to less than five year olds you see separate of the curve. Yeah, let's bring slide one to screen, please. So keep

in mind again that we have a total of 10 cases in terms of post-dose three. So most of the cases that you're seeing here represent cases after dose two. And you can see based on the X-axis, the number of days, and sort of calculate then, well, if it's 21 days between the first dose and the second dose -- because this is a Kaplan Meier based on the time from the first dose, you can see spreading of the curve that starts fairly early and then continues to spread in the two to four year olds.

So it's not as if there's no efficacy at all. The notion is we're building on a level of efficacy that, in every other population, we regard as insufficient for Omicron. And the goal here, based on what we're showing you with the third dose, is to improve upon that efficacy.

If we then show, if you put slide -- well, let's see. Yeah, slide one up, please. So slide one, in this case we're talking about the six month to two year olds, and it's true that if you walk through most of the period of time here you're not seeing a

separation of the curves. But given that they're a total of three cases, some of that separation at the end may well be due to maturation of immune response and the fact that those children now are beginning to show some evidence of efficacy.

But the goal with the third dose in this circumstance is to shift that to the left where we essentially can build upon the ability to provide some protection against disease by moving that separation of the curve to the left. And keep in mind again, as with every other circumstance, there's some expectation that protection against severe disease is likely to be higher than what we're seeing against just symptomatic infection. So hopefully, Dr. Marks, that helps clarify.

DR. PETER MARKS: I appreciate it. Thank you.

DR. ARNOLD MONTO: Thank you. Thank you. Thanks, Dr. Marks. Thanks, Dr. Gruber. And Dr. Gans, it looks like you are going to have the final word in our discussion.

DR. HAYLEY ALTMAN-GANS: Thank you. I just

wanted to point out that a lot of people have pointed out particularly that there's three doses needed here to provide protection. But in terms of what the public and parents should expect, it's likely that Moderna's also going to be a three-dose schedule.

So I just wanted to put that into context of what we understand. And that doesn't take away from the comments that my colleagues have already provided or the feelings that we have about these different vaccines. Thank you.

DR. ARNOLD MONTO: Thank you, Dr. Gans. No more hands raised, so we move to the vote. Christina.

MS. CHRISTINA VERT: Thank you, Dr. Monto. Okay. Can you please -- let's go down to the next slide.

DR. ARNOLD MONTO: Let's get the right question up.

MS. CHRISTINA VERT: Okay. As you can see before us on the slide, here are the members and temporary voting members that will be voting. And then, Dr. Monto, if you could please read the voting

question?

DR. ARNOLD MONTO: Okay. Based on the totality of scientific evidence available, do the benefits of the Pfizer-BioNTech COVID-19 vaccine when administered as a 3-dose series, 3 micrograms each dose, outweigh its risks for use in infants and children 6 months through 4 years of age?

MS. CHRISTINA VERT: Okay. At this time you can go ahead and vote. You have two minutes to vote. Okay. It looks like all the votes are in. You can go ahead and close the poll and broadcast the results. Okay. There are 21 total voting members, and we have here 21 yes votes. This is a unanimous vote. And there are zero no votes and zero abstain.

And now I will go ahead and read the specific voting responses for the record. Dr. Berger, yes; Dr. Nelson, yes; Dr. Fuller, yes; Dr. Levy, yes; Dr. Monto, yes; Dr. Sawyer, yes; Dr. Offit, yes; Dr. Reingold, yes; Dr. Bernstein, yes; Dr. McInnes, yes; Dr. Wharton, yes; Dr. Pergam, yes; Dr. Chatterjee, yes; Dr. Portnoy, yes; Dr. Lee, yes; Dr. Kim, yes; Dr. Cohn, yes; Dr.

Marasco, yes; Dr. Meissner, yes; Dr. Gans, yes; Dr. Hildreth, yes. And that concludes my reading of the specific votes. And I will now hand the meeting back over to Dr. Monto.

DR. ARNOLD MONTO: Thank you. And before I hand -- oh, we have an explanation of votes. Dr. Levy.

DR. OFER LEVY: Yeah, I just wanted to offer some thoughts here. I'm really pleased that we've reached this kind of milestone. I recall our first vote a year ago or more on the first Pfizer authorization. I was one of the 17 votes in favor. I remember those early discussions even then should the 16 and 17 year olds be included. At that point that was a controversial topic that was being discussed. And here we are now as a Committee unanimously recommending authorization down to six months of age. So we've come a long way.

The warp speed of vaccine initiative more or less worked. It got us safe and effective vaccines in record time. But I just want to make the point that there's a lot of work to do ahead in vaccinology. We

have inequities globally in access to the vaccine. I'll point out that the majority of the vaccine infrastructure in the world is pediatric. And pediatric vaccines achieve higher population penetration for that reason.

So that's something interesting to contemplate as we think about global inequities in immunization against this pandemic. The other point I'll point out, and it was evident in the discussion, is the number of doses required -- two, three, maybe four in immunocompromised individuals, maybe five. So we're very fortunate to have safe and effective vaccines in record time, and yet still we can't all go home now. There's a lot of work, a lot of research still to be done.

Can we design vaccines that give single-shot protection, that cover all of the different variants, that are pan-coronavirus vaccines, are vaccine adjuvants a potential approach to get better efficacy with one or two doses, instead of needing three, four, or five doses? So this is a public plea to keep

supporting around the globe vaccine research so that we can have even better vaccines in the future. Thank you.

DR. ARNOLD MONTO: Dr. Nelson.

DR. MICHAEL NELSON: Thank you, Dr. Monto. Just a couple of quick comments clearly in favor of the voted question as voted. Having options at every age group is important. And certainly this second vote contributes to that and does contribute to options and choice for families throughout the United States. Two quick comments/caveats. I do think there is certainly needed data to look specifically at the stratification of both the immune response and the reactogenicity based on the interval between that second and third dose.

We saw discordance today with the immunogenicity data generated early, but the safety data with the larger groups spread out throughout that entire period. And with the numbers involved I'm not sure we have the full signal of where that benefit/risk ratio is for that third dose. To me it probably looks

closer to a vaccine like hepatitis B, where there is evidence that that third dose actually given later might work.

But in this case, with the gap in efficacy apparently having it closer to that second dose may be advantageous and would certainly, if families are listening, err towards that direction. And then finally, the coadministration issue that has come up over and over today is something that I too have been concerned about going into today's discussion. I'm glad to hear that our sponsors are going to look into the question.

I will tell you that if we don't get a quick answer to the coadministration question, it will serve as a barrier to completion of these three dose series for this vaccine and likely the Moderna vaccine. Having to get it in isolation is going to be a great challenge for families and children here in the U.S. Thank you, Dr. Monto.

DR. ARNOLD MONTO: Thank you, Dr. Nelson. Dr. Fuller followed by Dr. Chatterjee.

DR. OVETA FULLER: Yes, thank you, Dr. Monto. I just want to say that the idea of having Pfizer and Moderna is very for good families and also that we should not forget that the mitigations of masking and these things that work, that we know work, should not be forgotten, even with those who are vaccinated, because we don't understand the reinfections or the new infections with new strains.

So people need to be reminded in the messaging the importance of the things that we do know that works, such as distancing and just being careful and using what we know. And so I'm very pleased that we have two opportunities to help those with younger families, and there's a lot of work still ahead to be done.

DR. ARNOLD MONTO: Thank you. Dr. Chatterjee.

DR. ARCHANA CHATTERJEE: Yes, thank you, Dr. Monto. As a pediatrician, today is a red letter day for me. To be able to vote for authorization of two vaccines that will protect children down to six months of age against this deadly virus is a very, very

important thing. And I am also thinking back, like Dr. Levy, to December 10, 2020, which is the day that we authorized the very first vaccine for use in people who are 16 years of age and older.

And I was actually one of the no votes, which got me into a lot of trouble. But the reasoning behind that, and we were able to explain that later, was that the four of us who voted no that day all had essentially the same reasoning, I believe. And that was that we insufficient data in the 16 and 17 year olds. We had data only on 150 participants when the ongoing had 2,000 in it. If we had just waited a little longer, we would have had those data.

It's interesting to think back to that time, but it's also important to look forward as Dr. Levy has pointed out. There is much work still to be done against this virus and against other infectious disease threats that face our population. And so I am just very, very grateful to have been part of this effort, and I'm delighted that we have been able to recommend authorization for these two vaccines for our very

youngest children. Thank you.

DR. ARNOLD MONTO: Thank you. Dr. Cohn and then Dr. Pergam.

CAPT. AMANDA COHN: Thanks. I just wanted to say quickly I am obviously, as a pediatrician, super happy that we can now vaccinate down to six months of age. But really I just want to express my deep gratitude and admiration for the staff at FDA who have made this happen because my confidence in this vote today is entirely related to the just clearly incredible amount of work that many, many staff at FDA have been put in.

The number of people who have presented and put this all together is incredible. And I know we have another meeting in two weeks, and the work is not done. But I just think taking a moment and thanking the staff that put all this effort into this, I just wanted to do that.

DR. ARNOLD MONTO: Dr. Cohn, you're stealing my closing remarks, but I'm still going to say it when we get to the close. Dr. Pergam.

DR. STEVEN PERGAM: I just laughed because Amanda always says such great comments, and they're always appreciated by other members of the Committee. I can say that. I do think it is important as we have this discussion about the importance of having two vaccines available for children that, as the FDA thinks about this and the CDC in terms of providing vaccine across the country -- that when the primary vaccine doses were given, Moderna and Pfizer were not adequately distributed in different parts of the country.

And so I think it's really important that both of these options are available throughout. And we're in a different situation with vaccine availability than we were in the past, but I think it's going to be really contingent upon both -- to provide both of these options throughout the U.S. and not have specific locations where one or the other as offered.

I think it's really important since these are different. There are different caveats that parents may look at when they're offering these to children or

making decisions that I think it's critical that they're made available across the country.

DR. ARNOLD MONTO: Dr. Meissner.

DR. CODY MEISSNER: Thank you, Dr. Monto. One very brief comment. Similar to my comment regarding Moderna, I think it's the right decision today to make these vaccines available for this age group. But I also think it's important that people understand it's a small number of children who have received these vaccines. And the safety is not as well-established as it is in adolescents and adults. So it's so important to continue to follow the safety profile of these vaccines. Again, I don't think they should be required for any specific situation. Thank you.

DR. ARNOLD MONTO: Thank you, Dr. Meissner. Dr. Marks, do you want to make any closing comments? And after that, I'd like to make some closing comments.

DR. PETER MARKS: Yeah, no, thanks, Dr. Monto. I'm going to -- I think Amanda started it very nicely, but I just want to summarize that the past two days we heard excellent presentations from sponsors, from FDA.

We heard open public hearing speakers, and I think it is a bit of a milestone to bring down the age range for these vaccines as we work through this. I also think we heard -- we have to be aware of the fact that we care tremendously at FDA about the safety and effectiveness of these vaccines.

And we will continue to monitor these vaccines as they are deployed. I would just remind the public that VAERS is a method that captures all adverse events and causality. And VAERS is not -- it's not established. There seems to be a lot of misinformation, and I'm saying it right now in real time because I'm watching Twitter storms in front of me about misunderstanding VAERS. VAERS, anyone is able to submit an adverse event to VAERS.

We actually require that certain things be submitted to VAERS. And so it can, from casual inspection of VAERS, look like there are things that are associated with the vaccines. But until one sorts through that, one does not know what is truly associated with the vaccines. And indeed we have

experts that spend a lot of time and that pride themselves -- they work day and night to ensure that they understand the safety profile of these vaccines.

That has been done and will continue to be done diligently. And as we have findings, as we did with myocarditis, thrombosis-thrombocytopenia syndrome, Guillain Barré syndrome, for rare adverse events, we will make sure the public knows about them. So I just want to say that -- want to just remind people of that and just take a final moment to thank the Committee members for an incredible amount of time and thank our FDA staff, who have really worked beyond anything that could have ever been expected of them.

From the Advisory Committee staff to those helping to run today's meeting technically, to those reviewers and management in the Office of Vaccines and the Office of Biostatistics and Pharmacovigilance and Biologics Quality who have relentlessly worked on this, very grateful for all their work. Thank you and thank you, Dr. Monto, for chairing this meeting. I'll turn it back over to you.

DR. ARNOLD MONTO: And I wanted to thank you, Dr. Marks, and your staff for an enormous amount of work that's gone into this. I was glad to hear our Committee members remember back to December 10, 2020, when we first approved a vaccine for SARS-CoV-2 virus and the fact that there were negative votes and we've now, a year and a half later, almost to the day, approved a vaccine down to age six months of age, so essentially all of the American population can now choose or be chosen to get vaccine.

And we had some negative votes there, and I remember that we didn't even have time because we were running over and all sorts of things going on because of the pressure to get vaccines approved at that point. And we didn't have the time to have individuals like Dr. Chatterjee explain their vote, which wasn't against the vaccine but the fact that we didn't have sufficient data.

What's happened since that time is that we have had observational studies which have guided us in terms of the parade of variants that we've had since

that time, the need for booster doses, and now a year and a half later we've got pediatric vaccines approved down to age six months. Why a year and a half? Because of a lot of things that have happened over that time. It has not been easy. And to say that there have been delays, unnecessary delays, is not representing the true situation, which involved not working with adults but with a vulnerable younger population for whom special care is necessary.

So, in closing, I would like to let the public know how hard Dr. Marks and the entire staff at FDA have worked to reach this milestone. When we organize these meetings, emails come in at 11 o'clock at night over the weekend. People are working overtime to get the public availability of these nearly miraculous vaccines.

I work in flu, where if we have 50-60 percent effectiveness. That's pretty good. And here we have vaccines which are highly effective in preventing severe disease. I'm very delighted to have had the privilege of sharing these sessions and getting us

these very critically important vaccines. I just wish everybody would realize how well they work in preventing severe disease.

I would like to close this meeting and hand this over for the official closing to Dr. Atreya. And thank you, Dr. Atreya, and I hope you get some rest so you don't have to send me emails at 11 o'clock at night when I can't read things through my regular email assistant. Thank you.

MEETING ADJOURNED

DR. PRABHAKARA ATREYA: No problem. Thank you all with those closing comments. I really thank the whole Committee and the staff. We've all been working really hard in making these meetings successful. I greatly appreciate it. So, with that, I officially adjourn the meeting for today. Thank you all and namaste.

MR. MICHAEL KAWCZYNSKI: All right. And with that, this meeting has been officially adjourned. Any

questions or comments, please send them to our email address and have a great day. Studio, please end the meeting.

[MEETING ADJOURNED]