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

## OPEN PUBLIC MEETING

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

**June 14, 2022**

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

# ATTENDEES

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

| | |
|---|---|
| Cody Meissner, M.D. | Tufts University School of Medicine |
| 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 |
| **GUEST SPEAKERS** | |
| Ruth Link-Gelles, Ph.D., M.PH. | Centers for Disease Control and Prevention |
| CAPT. Tom Shimabukuro, M.D., M.P.H., M.B.A. | Centers for Disease Control and Prevention |
| Katherine Fleming-Dutra, M.D. | Centers for Disease Control and Prevention |
| Carla Vinals, Ph.D. | ModernaTX, Inc. |
| Evan Anderson, M.D., FAAP | Emory University School of Medicine |
| Jacqueline Miller, M.D., FAAP | ModernaTX, Inc. |
| Rituparna Das, M.D., Ph.D. | ModernaTX, Inc. |
| **FDA PARTICIPANTS/SPEAKERS** | |
| Sudhakar B. Agnihothram, Pharm., Ph.D. | Food and Drug Administration |
| Doran Fink, Ph.D. | Food and Drug Administration |
| Peter W. Marks, M.D., Ph.D. | Food and Drug Administration |
| Jerry Weir, Ph.D. | Food and Drug Administration |
| Ceila M. Witten, Ph.D., M.D. | Food and Drug Administration |
| Hui-Lee Wong, Ph.D. | Food and Drug Administration |
| Rachel Zhang, M.D. | Food and Drug Administration |

| FDA ADMINISTRATIVE STAFF | |
|---|---|
| Prabhakara Atreya, Ph.D. | Food and Drug Administration |
| Lisa Wheeler | Food and Drug Administration |
| Joanne Lipkind, M.S. | Food and Drug Administration |
| Sussan Paydar, Ph.D. | Food and Drug Administration |
| Karen Thomas | Food and Drug Administration |
| Christina Vert | Food and Drug Administration |
| Mr. Michael Kawczynski | Food and Drug Administration |
| **PUBLIC SPEAKERS** | |
| Dr. Ashley Serrano | |
| Corey C. | |
| Brucha Weisberger | |
| Dr. Jane Newburger | |
| Tamara Baker | |
| Aime Baker | |
| Carolina Bourque | |
| Robyn Handsman | |
| Ricard Erickson | |
| Dr. Caroline Bishop | |
| Dr. Kailey Soller | |
| Jennifer Dougherty | |

| | |
|---|---|
| Dr. Harvey (Heshie) Klein | |
| Donna Treubig | |
| Elle Pierce | |
| Kate Schenk | |
| Dr. Donald Middleton | |
| Michael Baker | |
| Justine Luzzi | |
| Tamara Thomson | |

# TABLE OF CONTENTS

DAY 1 ..... 7

OPENING REMARKS: CALL TO ORDER AND WELCOME ..... 7

ADMINISTRATIVE ANNOUNCEMENTS, ROLL CALL, INTRODUCTION OF COMMITTEE, CONFLICT OF INTEREST STATEMENT ..... 8

FDA INTRODUCTION ..... 25

INTRODUCTION TO TOPIC 1: MODERNA COVID-19 VACCINE: REQUEST FOR EMERGENCY USE AUTHORIZATION (EUA) AMENDMENT, USE OF A 2-DOSE PRIMARY SERIES IN CHILDREN AND ADOLESCENTS 6 YEARS THROUGH 17 YEARS OF AGE ..... 27

Q&A SESSION ..... 36

CDC PRESENTATIONS: COVID-19 EPIDEMIOLOGY AND DISEASE BURDEN IN INFANTS, CHILDREN, AND ADOLESCENTS ..... 40

CDC PRESENTATIONS: UPDATE ON MRNA COVID-19 VACCINE EFFECTIVENESS ..... 54

CDC PRESENTATIONS: UPDATE ON MRNA COVID-19 VACCINE POST-AUTHORIZATION SAFETY ASSESSMENT IN PEDIATRIC AGE GROUPS ..... 65

Q&A SESSION ..... 81

FDA PRESENTATION: SAFETY SURVEILLANCE OF COVID-19 VACCINES IN CHILDREN AND ADOLESCENTS ..... 98

SPONSOR PRESENTATION: mRNA-1273 (MODERNA COVID-VACCINE) -- REQUEST FOR EMERGENCY USE AUTHORIZATION IN INDIVIDUALS 6-17 YEARS OF AGE ..... 114

Q&A SESSION ..... 152

FDA PRESENTATION: FDA REVIEW OF EFFECTIVENESS AND SAFETY OF MODERNA COVID-19 VACCINE IN CHILDREN AND ADOLESCENTS 6 THROUGH 17 YEARS OF AGE ..... 161

Q&A SESSION ..... 191

OPEN PUBLIC HEARING ..... 197

ADDITIONAL Q & A FOR CDC, FDA AND SPONSOR PRESENTERS ..... 259

COMMITTEE DISCUSSION AND VOTING ..... 313

MEETING ADJOURNED ..... 360

**DAY 1**

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

**MR. MICHAEL KAWCZYNSKI:** Good morning, and welcome to the 174th meeting of Vaccines and Related Biological Products Advisory Committee meeting. I'm Mike Kawczynski. I'll be moderating today's meeting. Please note this is a two-day meeting. We have today and tomorrow, so, one, please note this is an international type of meeting. We have people from all around the world participating.

This is a 100 percent live meeting with sixty-some people from around the world participating. So, if at any time, we run into any technical glitches, we will take a momentary pause to assist that person and to make sure that the meeting continues. So with that being said, let's get this kicked off and started, and I'm going to hand it over to our chair, Dr. Arnold Monto. Arnold, are you ready?

**DR. ARNOLD MONTO:** I am.

**MR. MICHAEL KAWCZYNSKI:** All right, take it away.

**DR. ARNOLD MONTO:** I'd like to add my welcome to this, the 174th Meeting of the Vaccines and Related Biological Products Advisory Committee of the FDA. As Mike mentioned, this is a two-day meeting. Today our topic is the Committee will meet in open session to discuss amending the emergency use authorization of Moderna COVID vaccine to include the prevention of COVID-19 in children and adolescents 6 years through 17 years of age.

I would like to hand the meeting over to Prabha Atreya, who is the acting designated federal officer for this meeting who will go through further introductions and some of our housekeeping issues before we can get it back to the real discussion. 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 Dr. Prabha Atreya, and it is my great honor to serve as the designated federal officer for today's 174th Vaccines and Related Biological Products Advisory Committee meeting. On behalf of the FDA, the Center for Biologics Evaluation and Research, and also the Committee, I'm happy to welcome everyone to today's virtual meeting. Today the Committee will meet in open session to discuss amending the emergency use authorization of Moderna COVID-19 mRNA vaccine to include the administration of a primary series to children and adolescents 6 to 17 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 today. Ms. Christina

Vert is my backup DFO who will be conducting the voting process later today.

In addition to Sussan and Christina, the other staff who contributed significantly are Ms. Joanne Lipkind, Ms. Karen Thomas, Ms. Lisa Wheeler, and Ms. Viola Sampson (phonetic), who also provided excellent administrative support.

I would also like to express our sincere appreciation to Mr. Mike Kawczynski in facilitating the meeting today. Our sincere gratitude goes to many CBER and FDA staff working very hard behind the scenes trying to ensure that today's meeting will also be a really successful one, like all the previous VRBPAC meetings.

With regards to any press and media questions for today's meeting, please direct your inquiries to FDA's Office of Media Affairs at FDAOMA@fda.hss.gov. The transcriptionist for today's meeting is Ms. Ora Giles.

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

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

**DR. ARNOLD MONTO:** Yes, you can. I'm Arnold Monto. I'm at the University of Michigan School of Public Health where I have worked for many years in prevention and control of respiratory viral infections, particularly influenza and now coronaviruses. Thank you for your introduction and welcome to all.

**DR. PRABHAKARA ATREYA:** Thank you, Dr. Monto. Next, Dr. Hayley Gans.

**DR. HAYLEY ALTMAN-GANS:** -- specialist at Stanford University, and I do my research focus on the immunology of vaccines as well as viruses in children and other immunocompromised hosts, including adults with HIV and transplant recipients. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you, Dr. Gans.

Dr. Annunziato will be joining very shortly. And Dr. Adam Berger next.

**DR. ADAM BERGER:** Hi, Adam Berger. I'm a geneticist by training. I'm at the National Institutes of Health where I'm the director of the Division of Clinical and Healthcare Research policy where I oversee all of our clinical research and clinical trial policies for the Agency.

**DR. PRABHAKARA ATREYA:** Thank you, Dr. Berger. Next is Dr. Henry Bernstein.

**DR. HENRY BERNSTEIN:** Good morning. My name is Hank Bernstein. I'm a professor of pediatrics at the Zucker School of Medicine at Hofstra/Northwell. I have expertise in general pediatrics and a special interest in vaccines. Thank you.

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

**DR. ARCHANA CHATTERJEE:** Thank you, Prabha. Good morning. My name is Archana Chatterjee. I 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 an area of focus of vaccines. Thank you.

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

**CAPT. AMANDA COHN:** Good morning, everyone. This is Amanda Cohn. I'm a pediatrician at the Centers for Disease Control and Prevention with expertise in public health and vaccines.

**DR. PRABHAKARA ATREYA:** Thank you. Next, Dr. Captain David Kim.

**CAPT. DAVID KIM:** Good morning. This is David Kim with the National Vaccine Program in the Office of Infectious Disease and HIV/AIDS policy in the Office of the Assistant Secretary for Health where I serve as a director of the Division of Vaccines.

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

**DR. PAUL OFFIT:** Yes, good morning. My name is Paul Offit. I'm an attending physician in the

Division of Infectious Disease at the Children's Hospital of Philadelphia and a professor of pediatrics at the University of Pennsylvania School of Medicine. My published area of interest is in mucosal vaccines. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you, Dr. Offit. Next is Dr. Steven Pergam.

**DR. STEVEN PERGAM:** Thanks, Dr. Atreya. I'm Steve Pergam. I'm an adult infectious disease physician and a faculty member in the Vaccine and Infectious Disease Division at the Fred Hutchinson Cancer Center in Seattle, Washington.

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

**DR. ERIC RUBIN:** Good morning. I'm an infectious disease physician and a basic scientist at Harvard, the Brigham and Women's Hospital, and the *New England Journal of Medicine*.

**DR. PRABHAKARA ATREYA:** Thank you. Next, we will do a roll call of our temporary voting members, starting with Dr. Oveta Fuller. Dr. Fuller?

**DR. OVETA FULLER:** Yes, good morning. I'm Oveta Fuller. I'm the associate professor of microbiology/immunology. A virologist by training in the medical school of the University of Michigan. I studied viral entry and now I do community engagement and implementation.

**DR. PRABHAKARA ATREYA:** Thank you. Next, Dr. Randy Hawkins.

**DR. RANDY HAWKINS:** Good morning. I'm a physician in private practice in Inglewood, California. Internist and pulmonary care medicine in the Charles University of Medicine and Science. I'm an acting consumer representative.

**DR. PRABHAKARA ATREYA:** Thank you, Dr. Hawkins. Next is Dr. James Hildreth.

**DR. JAMES HILDRETH:** Good morning. Thank you, Dr. Atreya. I'm James Hildreth, president and CEO of Meharry Medical College and professor of internal medicine. I'm an immunologist by training, and I studied the viral pathogen of how viruses cause disease. Thank you.

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

**DR. JEANNETTE LEE:** Yes, good morning. My name is Jeannette Lee. I'm a professor of biostatistics and a member of the Winthrop 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:** Hello. My name is Dr. Ofer Levy, and I'm director of the Precision Vaccines Program at Boston Children's Hospital and a professor of pediatrics at Harvard Medical School.

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

**MR. MICHAEL KAWCZYNSKI:** Sir, you have your phone muted.

**DR. WAYNE MARASCO:** Can you hear me now?

**MR. MICHAEL KAWCZYNSKI:** Yes. Go ahead.

**DR. PRABHAKARA ATREYA:** Yes, go ahead.

**DR. WAYNE MARASCO:** Should I start again?

Yes, my name is Wayne Marasco. I'm a professor of medicine at Harvard Medical School and a professor in the Department of Cancer Immunology and Virology at Dana Farber Cancer Institute. I'm also a practicing infectious disease physician. My expertise is in anti-viral immunity with a focus on coronaviruses. Thank you.

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

**DR. PAMELA MCINNES:** Good morning. This is Pamela McInnes. I am a now retired deputy director of the National Center for Advancing Translational Sciences at the U.S. National Institutes of Health. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you. Next is Dr. Cody Meissner.

**DR. CODY MEISSNER:** Thank you, Dr. Atreya. Good morning, everyone. My name is Cody Meissner. I'm a professor of pediatrics at Tufts University School of Medicine. The Children's Hospital is going to close in a few weeks, so I will have a new professional address,

but I appreciate the opportunity to participate this morning in this VRBPAC Meeting. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you, Dr. Meissner. Dr. Nelson, Michael Nelson.

**DR. MICHAEL NELSON:** Hello. I'm Mike Nelson, I'm professor of medicine and chief of the Division of Asthma, Allergy, and Immunology at the University of Virginia. I'm also the president of the American Board of Allergy and Immunology. My interest is in vaccine immune responses and rare adverse events. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you. Next is Dr. Stanley Perlman.

**MR. MICHAEL KAWCZYNSKI:** Next is Art Reingold, Prabha.

**DR. PRABHAKARA ATREYA:** Okay. Thank you. Go ahead, Dr. Reingold.

**DR. ARTHUR REINGOLD:** Yeah, good morning, Prabha. Art Reingold. I'm a professor of epidemiology at the School of Public Health at the University of California, Berkeley. Nice to be with you.

**DR. PRABHAKARA ATREYA:** Thank you. Next, Dr.

Mark Sawyer.

**DR. MARK SAWYER:** Good morning. I am a professor of pediatric infectious disease at the University of California, San Diego. My expertise is in the public health implementation of vaccines.

**DR. PRABHAKARA ATREYA:** Thank you. Next is Dr. Melinda Wharton.

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

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

**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 14, 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 14, 2022, under Topic 1, the Committee will meet in open session to discuss amending the EUA of the Moderna COVID-19 mRNA vaccine to include administration of the primary series to children and adolescents 6 years to 17 years of age. This topic is determined to be a particular matter involving specific parties, PMISP. 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 Conflict of Interest law and regulations.

The following information on the status of this Committee's compliance with Federal Ethics and

Conflicts of Interest law 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 at this meeting all members, RGE and SGE consultants, of this Committee have been screened for potential financial conflict of interest of their own as well as those imputed to them, including those of their spouse or minor children and, for, the purposes of 18 U.S. Code 208, their employers.

These interests may include investments, 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 law.

Under 18 U.S.C. Section 208, Congress has authorized FDA to grant waivers to special government

employees and regular government employees who have financial conflicts of interest when it is determined that the Agency's need for a special government employee's service 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 Conflict of Interest waiver issued under 18 U.S. Code 208 in connection with today's meeting.

We have the following consultants serving as temporary voting members: Dr. Oveta Fuller, Dr. Randy Hawkins, Dr. James Hildreth, Dr. Jeannette Lee, Dr. Ofer Levy, Dr. Wayne Marasco, Dr. Cody Meissner, Dr. Pamela McInnes, 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 this participation in today's meeting. The waiver was posted on the FDA website for public disclosure. Dr. Pamela Annunziato of Merck will serve as the industry representative for today's meeting. Industry representatives are not appointed as a special government employee 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. Randy Hawkins is serving as the alternate 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.

The guest speakers for this meeting are the following: Dr. Katherine Fleming-Dutra, a medical officer in the COVID-19 Vaccine Policy Unit, National Center for Immunization and Respiratory Disease, CDC Atlanta, Georgia; Dr. Ruth Link-Gelles, primary program

lead for the COVID-19 Vaccine Effectiveness Epidemiology Task Force, also at CDC Atlanta, Georgia; Captain Tom Shimabukuro, M.D., director in the Immunization Safety Office, also at CDC Atlanta, Georgia.

Disclosure of conflicts of interest for speakers and guest speakers follows applicable federal law, regulations, and FDA guidance. FDA encourages all meeting participants, including open public hearing speakers, to advise the Committee of any financial relationships that they may have with any affected firms, its products, 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. Dr. Monto.

## FDA INTRODUCTION

**DR. ARNOLD MONTO:** Thank you for the introductions. It's my pleasure now to introduce the director of the Center for Biologics Evaluation and Research, Dr. Peter Marks, who will add his welcome and also help us in figuring out exactly what we are going to be discussing today. Dr. Marks.

**DR. PETER MARKS:** Thanks very much, Dr. Monto. First of all, thanks to Dr. Monto and to the other Advisory Committee members for their time today and for the time that they've put in preparing for this advisory committee. Also thanks to the Advisory Committee staff and the Center staff, who have prepared for this meeting.

Today's meeting and tomorrow's meeting will be going over pediatric indications for the Emergency Use

Authorization for COVID-19 vaccines. Today, we'll focus on the Moderna applications for ages 6 through 17. Tomorrow, we'll focus on Moderna for the 6-month through 5-year population. And then for Pfizer for the 6-month through 4-year population.

These vaccines will essentially extend down to the younger age ranges, as low as six months, coverage with vaccines. Obviously, the safety in this population is of paramount importance, and I think there will be a fair amount of discussion by the Committee on this particular area. Rather than say much more now, we'll look forward to the discussion.

Later on, we have excellent FDA presenters, CDC presenters, sponsors that will present, as well as an open public hearing in which a variety, a diverse number of opinions will be expressed, and we'll look forward to all of those.

So I will turn it back over to Dr. Monto. Thank you to all who have joined us today and our virtual audience as well.

**INTRODUCTION TO TOPIC 1: MODERNA COVID-19 VACCINE: REQUEST FOR EMERGENCY USE AUTHORIZATION (EUA) AMENDMENT, USE OF A 2-DOSE PRIMARY SERIES IN CHILDREN AND ADOLESCENTS 6 YEARS THROUGH 17 YEARS OF AGE**

**DR. ARNOLD MONTO:** Thank you, Dr. Marks. We will dive in now to the discussion topic for the day, and the topic will be introduced by Dr. Sudhakar Agnihothram, who is the primary reviewer in the Division of Vaccines and Related Products Applications at FDA. He will tell us about what we are to discuss today. And we'll introduce the vote that will occur later on today. Take it away.

**DR. SUDHAKAR AGNIHOTHRAM:** Thanks very much, Dr. Monto. Can you hear me well?

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

**DR. SUDHAKAR AGNIHOTHRAM:** Okay. Good morning, everyone. And then, welcome to the first day of Advisory Committee Meeting for discussing the pediatric EUAs.

Today, I'm going to provide an introduction on

the Moderna COVID-19 vaccine request for amending the Emergency Use Authorization for use of a two-dose primary series of Moderna COVID-19 vaccine in children and adolescents 6 through 17 years of age.

I'm Sudhakar Agnihothram, the primary reviewer in Division of Vaccines and Related Products Applications.

Here is the background of my talk. Initially, I will be providing the information on Moderna COVID-19 vaccine and Spikevax in the context of primary vaccination. Then I will provide an overview on the currently available COVID-19 vaccines for primary vaccination use in pediatric population.

This will be followed by the overview of the EUA request for amending the EUA for use of Moderna COVID-19 vaccine as a primary series in individuals 6 through 17 years of age, and the clinical package that supports this EUA request. Then I will be providing the literature on the statutory requirements for emergency use authorization followed by the presentation of today's agenda and presenting the

voting questions for the Committee.

Moderna COVID-19 vaccine is available under the emergency use authorization for use as a two-dose primary series given one month apart in individuals 18 years of age and older. Moderna COVID-19 vaccine is also available under the EUA for use as a third primary series dose given at least one month after the second dose in individuals 18 years of age and older who have been determined to have certain kinds of immunocompromise.

Spikevax is FDA approved for use as a two-dose primary series in individuals 18 years of age and older and can be used interchangeably with Moderna COVID-19 vaccine to provide doses for COVID-19 primary vaccination.

Currently available COVID-19 vaccines for primary vaccination 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.

And 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 vaccine to provide doses for COVID-19 primary vaccination.

Just to provide an overview of the EUA amendment request for amending the Moderna EUA for use of Moderna COVID-19 vaccine as a two-dose primary series in individuals 12 to 17 years of age. On June 9th, 2021, Moderna submitted their request for amending their EUA for use of a Moderna COVID-19 vaccine as a two-dose primary series in individuals 12 through 17 years of age.

That submission included blinded follow-up to the data cutoff of May 8, 2021. Because of the increased risk of myocarditis observed in younger males 18 to 24 years of age following administration of

Moderna COVID-19 vaccine and the limited follow-up of the data that were available in these myocarditis cases along with the totality of the evidence that was available at that time, FDA did not take regulatory action on amending the EUA for use of Moderna COVID-19 vaccine as a primary series in individuals 12 through 17 years of age.

In today's presentation, you will be hearing from our OBPV colleague on the additional data bar analysis that are available on the risk of myocarditis following the administration of Moderna COVID-19 vaccine that have led us to bring this EUA amendment request for VRBPAC discussion.

I would also like to state that on March 24th, 2022, Moderna submitted additional data that included blinded and open-label follow-up through the data cutoff date of January 31, 2022. The proposed dosing and regimen for 12 to 17 years of age include a primary series of two doses, 0.5 mL each, containing a hundred micrograms of mRNA given one month apart, administered intramuscularly in individuals 12 through 17 years of

age. The clinical package that supports this EUA request includes safety, immunogenicity, and efficacy data from approximately 2,500 vaccine recipients.

Now to give an overview on the request for amending the EUA for use of Moderna COVID-19 vaccine as a two-dose primary series in individuals 6 through 11 years of age. Moderna submitted a request for amending their EUA for use of Moderna COVID-19 vaccine as a two-dose primary series in individuals 6 through 11 years of age on March 8th, 2022. The proposed dosing and regimen includes a primary series of two doses, 0.5 mL each, containing 50 micrograms of mRNA given one month apart, administered intramuscularly in individuals 6 through 11 years of age. The clinical package that supports this EUA request includes safety, immunogenicity, and efficacy data from approximately 3,000 vaccine recipients.

I would like to state that we have presentations from FDA as well as the sponsors that will break down and then provide a detailed overview of the clinical data that supports this EUA package.

Those presentations will follow this morning.

To provide a refresher on the statutory requirements for the emergency use authorization. FDA may issue an emergency use authorization of an unapproved medical product following an EUA declaration 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 the serious or life-threatening condition caused by the agent. The known and potential benefit of the product outweighs the known and potential risks of the product and there are no adequate approved and available alternative to the product for diagnosing, preventing, or treating the disease or condition.

To provide an overview of today's agenda. Following my talk there will be a question and answer session for five minutes. This will be followed by three presentations from Centers for Disease Control and Prevention for approximately 55 minutes. The first presentation will be given by Dr. Katherine E. Fleming-

Dutra on COVID-19 epidemiology and disease burden in infants, children, and adolescents. That will go for 15 minutes.

Dr. Ruth Link-Gelles will provide us an update on mRNA COVID-19 vaccine effectiveness, which will go for approximately 15 minutes. This will be followed by an update from Dr. Tom Shimabukuro on mRNA COVID-19 vaccine post-authorization safety assessment in pediatric ages.

There will be a ten-minute question and answer session for presenters from CDC. This will be followed by an FDA presentation from Dr. Hui-Lee Wong, Office of Biostatistics and Pharmacovigilance, CBER, and the topic would safety surveillance of COVID-19 vaccine in children and adolescents. That will be for 15 minutes.

This would be followed by a Q&A session for five minutes and a break for about ten minutes. Then we will hear from Moderna for about 60 minutes from various presenters on mRNA-1273, which is Moderna COVID-19 vaccine request for emergency use authorization for use in children and adolescents 6

through 17 years of age. There will be a ten-minute Q&A for Moderna.

This will be followed by presentation from FDA given by Dr. Rachel Zhang on FDA review of effectiveness and safety of Moderna COVID-19 vaccine in children and adolescents 6 through 17 years of age. There will be a lunch break for 30 minutes followed by an open public hearing for 60 minutes. Then additional question and answer session for CDC, FDA, and sponsor presenters for about an hour. This will be followed by a break for ten minutes, and there will be Committee discussion and voting for about 110 minutes.

Now presenting the voting questions for the Committee. The first voting question is, based on the totality of scientific evidence available, do the benefits of the Moderna COVID-19 vaccine when administered as a two-dose series, a hundred micrograms each dose, outweigh its risk for use in adolescents 12 through 17 years of age?

The second voting question would be, based on the totality of scientific evidence available, do the

benefits of the Moderna COVID-19 vaccine when administered as a two-dose series, 50 micrograms each dose, outweigh its risks for use in children 6 through 11 years of age?

I would like to thank the Moderna COVID-19 vaccine review team, management, and the leadership for all of the work that went into the review of these pediatric EUAs. Thank you and I'm ready to take questions.

**Q&A SESSION**

**DR. ARNOLD MONTO:** We have a few minutes now for questions related to the process, what we're going to be doing today, including a little bit about the voting questions should there be any before we get into the substance of the meeting. Anyone wishing to talk right now? I see Dr. Gans.

**DR. HAYLEY ALTMAN-GANS:** Thank you very much. I did have a question about the process, and so I'm not sure if it belongs here or later. I'm wondering about

--

**DR. ARNOLD MONTO:** Well, we've seen that before so go ahead.

**DR. HAYLEY ALTMAN-GANS:** Thank you. I just wondered about two questions about sort of next steps that would actually relate to the decision today. When are the current EUAs going to move towards approval? So they've sort of been in use for a period of time that may allow for them to move towards approval.

And then, in context of what's being asked of us today for the use of EUA, why has the increased lapse of time not allowed this product to actually go instead of EUA towards an approval question?

**DR. SUDHAKAR AGNIHOTHRAM:** So typically for the approval of a licensing application, we would require six months of safety follow-up. And then a supplementary BLA application is submitted with the request for approving the use of an indication. We would definitely consider that. And we have not received a request from the sponsor yet. But I would like to invite Dr. Marks or Dr. Fink to add anything to

this question as well.

**DR. PETER MARKS:** I think that actually was an excellent response. Or I think it is a matter of having the appropriate amount of follow-up data on the population. And then, there are certain things that have to be: i's that have to be dotted; t's that have to be crossed; additional information that's required for a biologics license supplement, as opposed to an emergency use authorization. And so this is the first step.

At this point, we can't predict when there will be an end to the emergency declaration, so it's perfectly reasonable to have these under emergency use authorization, although I do expect that over the course of the next months, we will see these come through the process for supplemental biologics license applications.

**DR. HAYLEY ALTMAN-GANS:** I guess my question related more to we have that period of time, that extra time that we have for these coming forward, so I guess my real question is, what is missing in the eyes of the

FDA that would warrant these coming in the current form?

**DR. PETER MARKS:** I do know --

**DR. SUDHAKAR AGNIHOTHRAM:** I do not think there is -- go ahead, Dr. Marks.

**DR. PETER MARKS:** No, go ahead, please.

**DR. SUDHAKAR AGNIHOTHRAM:** No, I just wanted to say, like Dr. Marks mentioned, we still have the EUA in place because there is still emergency declaration that is in effect, that's number one. And then, as long as we have the prior data for approving a supplementary biological license application, which includes six months of safety follow-up, that is submitted by the sponsor with the request, we would definitely consider that. I don't think there is any hurdle in considering a supplementary BLA application for a request for approval.

**DR. PETER MARKS:** And it's possible that in some cases it may not be that long a period between the emergency use authorization being issued and us moving to approve a biologics license application.

**DR. HAYLEY ALTMAN-GANS:** Thank you.

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

**DR. SUDHAKAR AGNIHOTHRAM:** Thank you.

**DR. ARNOLD MONTO:** Next, as you heard, we are going to be moving to three presentations from CDC about the state of the epidemiology of vaccine effectiveness and safety determinations. And we are going to hear the presentations one after the other without a question period until the end. The first speaker is Dr. Katherine Fleming-Dutra.

Next, we will hear Ruth Link-Gelles and then Tom Shimabukuro, who will be presenting on their specific topics. After that, we'll have a few minutes for specific questions on the presentations. So over first to Dr. Fleming-Dutra.

## CDC PRESENTATIONS: COVID-19 EPIDEMIOLOGY AND DISEASE BURDEN IN INFANTS, CHILDREN, AND ADOLESCENTS

**DR. KATHERINE FLEMING-DUTRA:** Good morning. Here's an overview of what I will be covering today.

And I will be focusing on age groups divided by current COVID-19 vaccine eligibility. So we'll talk about children six months through four years of age who are currently not eligible for COVID-19 vaccination, and then children 5 through 11 years and adolescents 12 through 17 years who are currently eligible for COVID-19 vaccination.

So let's start with COVID-19 incidence and burdens. And here we see the trends in the number of COVID-19 cases in the U.S. among persons of all ages. As of June 8th, 2022, there were more than 85 million total reported cases of COVID-19 in the U.S. And the Omicron surge started in December 2021 and led to a large spike in COVID-19 cases through the winter of 2022. And as of June 8th, the seven-day moving average was greater than 100,000 cases.

Now, focusing in on the pediatric population, here we see the weekly rate of COVID-19 cases per 100,000 population by age group. COVID-19 case rates were much higher during the Omicron surge compared to any previous time during the pandemic with the highest

rates seen in adolescents ages 12 through 17 years, shown in dark blue; then older children 5 through 11 years, shown in light blue; followed by infants less than one, shown in gray; and children one through four years, shown in red.

Total during the pandemic, over 13.1 million COVID-19 cases have occurred in children and adolescents ages 0 through 17 years. But not all COVID-19 cases are captured using traditional disease surveillance methods because some cases are asymptomatic, not diagnosed or not reported. Tracking the proportion of the population with SARS-CoV-2 antibodies or the seroprevalence can improve understanding of population-level incidence of COVID-19.

This figure shows the seroprevalence of infection-induced SARS-CoV-2 antibodies from the National Commercial Labs Seroprevalence study from September 2021 to February 2022 by age groups. Seroprevalence in all ages increased substantially during the Omicron wave. And while children ages 5

through 11 years have had the highest seroprevalence since October 2021, you can see that children ages one through four years, who are not yet eligible for vaccination, have the largest increase in seroprevalence since December 2021.

So moving on to healthcare associated with COVID-19 and starting with emergency department or ED visits. Here is the weekly percent of ED visits with a COVID-19 diagnosis among all ED visits for children ages 1 through 17 years from CDC's National Syndromic Surveillance Program through May 2022. The dashed line marks December 19th, 2021, the first date when more than 50 percent of nationally sequenced SARS-CoV-2 specimens were Omicron variants which was followed by a surge in COVID-19 ED visits among children ages one year through four years, 5 through 11 years, and adolescents 12 through 17 years.

Moving on to COVID-19-associated hospitalizations, including burden and severity. Here we see COVID-19-associated hospitalizations for 100,000 population from CDC's COVID-NET surveillance system.

Hospitalization rates also increased during the Omicron surge to the highest rates yet seen during the pandemic. During 2022, among these age groups, hospitalization rates were highest among children ages six months through four years, shown in red; followed by adolescents 12 through 17, in dark blue; and then children 5 through 11, in light blue.

And to further illustrate this point, we can look at the cumulative COVID-19-associated hospitalization rates. You can see that during the Omicron surge among children six months through four years the slope of the cumulative hospitalization rate was steeper than among older children and adolescents. And by March 2022, the cumulative hospitalization rate was higher among children six months through four years who were not yet eligible for vaccination than among adolescents, who were.

And we know that vaccination prevents hospitalization. Here is a monthly COVID-19-associated hospitalization rate by vaccination status. Adolescents 12 through 17 years in dark blue, who were

vaccinated with at least a primary series, shown by the solid line, had a lower hospitalization rate than those who were unvaccinated in the dashed line. Although children ages 5 through 11 years, in light blue, have lower hospitalization rates overall than adolescents, the same pattern can be seen after they became eligible for vaccination in late 2021.

It's important to note that the benefits of vaccination are more pronounced when the disease burden is high, and we can predict that with future COVID-19 surges the unvaccinated will continue to bear the burden of disease.

Who is getting hospitalized for COVID-19? This figure shows the percent of children and adolescents ages 6 months through 17 years with COVID-19-associated hospitalization with at least one underlying health condition from two CDC surveillance platforms: COVID-NET and the new Vaccine Surveillance Network.

Just under half of children ages six months through four years with COVID-19-associated

hospitalization had one or more underlying health condition. Whereas about two-thirds of children 5 through 11 and adolescents 12 through 17 had underlying health conditions. This means that over half of children six months through four years and a third of those 5 through 11 and 12 through 17 had no underlying conditions.

Now let's look at markers of severity among COVID-19-associated hospitalization by age group in COVID-NET. Focusing on December 19th, 2021, to March 31st, 2022, or the Omicron period, children ages six months through four years, again in red, were more often admitted to the intensive care unit and more often placed on high-flow nasal cannula than older children and adolescents. Over six percent of children ages six months through four years were placed on mechanical ventilation versus about five percent of children 5 through 11 years, and four and a half percent of adolescents.

This indicates that during the Omicron predominance, COVID-19-associated hospitalization

severity among children six months through four years appeared to be higher than that in older children and in adolescents.

So now that we've examined burden and severity of COVID-19-associated hospitalizations among pediatric age groups, let's pivot and compare COVID-19 hospitalization in children to other key pediatric infectious diseases. And we'll start by comparing hospitalization for influenza and COVID-19.

This figure is from a recent paper, which used data from COVID-NET and FluSurv-NET, which conducts surveillance for influenza-associated hospitalizations from October 1st through April 30th each year -- the typical U.S. influenza season. The solid black line is the COVID-19-associated hospitalization rate during October '20 to September '21. And the solid red line is the preliminary COVID-19-associated hospitalization rate during October '21 to April '22.

Influenza-associated hospitalization rates from 2017 through 2022 are shown by flu season, in gray, and in the dashed red line for the preliminary

data from the most recent flu season.

Among children six months through four years, COVID-19 hospitalization rates from October ’20 through September ’21 were lower than influenza hospitalization rates during pre-pandemic influenza season. However, in this age group, preliminary COVID-19 hospitalization rates during October ’21 to April ’22, which includes the Omicron surge, were as high or higher than influenza hospitalization rates for all influenza seasons shown.

Among children 5 through 11 years, although the overall burden of hospitalization for both diseases is lower than among younger children, the pattern is the same. However, among adolescents 12 through 17 years, the cumulative rates of COVID-19 hospitalizations in both years are much higher than influenza hospitalization rates during all included flu seasons. And, as we all know, influenza vaccination is recommended every flu season for all children six months of age and older.

COVID-19-associated hospitalization burden

among children six months through four years was similar to, or exceeded, the pre-vaccine era of burden of other now vaccine-preventable diseases, including hepatitis A, varicella, and vaccine-type invasive pneumococcal disease.

And tragically, COVID-19 has become a leading cause of mortality in children. This figure shows the number of COVID-19 deaths in children by age through May 11, 2022. And, sadly, among children ages six months through four years, there have been 202 COVID-19-related deaths, accounting for 1.7 percent of all deaths in this age group.

Among children 5 through 11 years, there have been 189 COVID-19 deaths, accounting for 2.5 percent of deaths in this age group. And among adolescents, there have been 443 COVID-19 deaths, accounting for 2.4 percent of deaths in this age group. And COVID-19 was a leading cause of death among children and adolescents during the pandemic.

During March 2020 through April 2022, COVID-19 ranked as the fourth and fifth causes of death among

children ages 1 through 19 years. COVID-19-associated deaths among children ages six months through four years exceed the pre-vaccine era of burden of other now vaccine-preventable diseases shown here.

Multisystem inflammatory syndrome in children, or MIS-C, is another important complication of COVID-19 in children. MIS-C is a severe illness in persons ages 0 through 20 years, characterized by fever, multisystem organ involvement, inflammation, and SARS-CoV-2 infection with no alternative diagnosis. It occurs two to six weeks after acute infection and 60 to 70 percent of patients are admitted to intensive care and one to two percent die.

Here are the daily MIS-C and COVID-19 cases reported to CDC. In total during the pandemic, more than 85,000 MIS-C cases and 69 deaths have occurred. Reports of MIS-C, shown by the blue line, typically follow increases in COVID-19 cases, shown by the dashed black line. However, following the Omicron surge, reports of MIS-C did not increase to the same level as occurred following prior waves of COVID-19 cases.

Now we can look at the weekly MIS-C case counts by age group through May 31st. Children six months through four years are shown in dark blue, 5 through 11 in orange, and adolescents 12 through 17 shown in the middle shade gray/blue.

Looking at our age groups of interest, during the pandemic a total of 1,990 cases of MIS-C have occurred among children ages six months through four years. More than 3,900 cases among children 5 through 11, and 1,900 cases among adolescents 12 through 17.

And, unfortunately, throughout the pandemic, MIS-C has disproportionally affected black children, which is shown here with the percent of MIS-C patients ages 6 months through 17 years during the pandemic by race and ethnicity and age group.

Moving on to post-COVID conditions, which include a wide range of physical and mental health consequences present for four or more weeks after SARS-CoV-2 infection. Post-COVID conditions occur in children, though it appears to be less common than in adults. A U.K. survey found seven to eight percent of

children with COVID-19 reported continued symptoms after 12 weeks. And post-COVID conditions can appear after mild to severe infections and after MIS-C.

The most common symptoms include fatigue, headache, insomnia, trouble concentrating, muscle and joint pain, and cough. And these conditions also have an impact on the quality of life in multiple ways.

And there are other impacts of the pandemic on children and families. One of the most important is disruption in in-person learning. This graph shows COVID-19-related K through 12 disruptions by week. Disruptions, which are defined as school moving away from regular in-person instruction caused by the pandemic, continue to occur through the 2021 to 2022 school year.

And childcare has been particularly challenging for families during the pandemic. This Kaiser Family Foundation graph shows the percent of parents during July and August 2021 who said that in the past year they or another adult in their household left a job or changed work schedules to take care of

their children.

And these data highlight the disparities of that impact. Parents of children under the age of five, younger parents, Black and Hispanic parents, and parents with lower household incomes were more likely to report that their household had a job disruption due to childcare needs. And job disruptions have negative impacts on both parents and families.

Other impacts of the pandemic on children include worsening of mental or emotional health, widening of education gaps, decreased physical activity and increased body mass index, decreased healthcare utilization and routine immunization, and increases in adverse childhood experiences.

So, in conclusion, COVID-19, as of June 7th, 2022, has caused more than 13.1 million cases among children and adolescents ages 0 through 17 years. And the Omicron surge led to the highest numbers of COVID-19 cases, emergency department visits, and hospitalization rates seen during the pandemic.

Children and adolescents are at risk of severe

illness from COVID-19. More than half of hospitalized children ages six months through four years had no underlying health conditions. During the Omicron predominance, COVID-19-associated hospitalizations among children ages six months through four years had similar or increased severity compared to older children and adolescents. And the burden of COVID-19 hospitalizations is similar to or exceeds that of other pediatric vaccine-preventable diseases.

And finally, the COVID-19 pandemic continues to have significant impacts on families and increases disparity.

This presentation is the work of many people that I would like to thank who are listed here. Thank you.

## CDC PRESENTATIONS: UPDATE ON MRNA COVID-19 VACCINE EFFECTIVENESS

**DR. RUTH LINK-GELLES:** Good morning. Today I'll be sharing updates on COVID-19 vaccine coverage in

the United States and vaccine effectiveness during Omicron for children and adolescents.

Starting with coverage. Here we see coverage of at least one dose, in the graph on the left, and fully vaccinated, on the graph on the right broken down by age group in the colored lines.

For both graphs, we see higher coverage in older groups and the lowest coverage, at 29 percent, for fully vaccinated among the 5- to 11-year-old group. This leaves approximately 18 million 5- to 11-year-olds currently unvaccinated compared to about 8.5 million 12- to 17-year-olds.

This graph shows coverage of at least one dose among 5- to 11-year-olds by race and ethnicity over time from CDC's National Immunization Survey. In the table, we've calculated the percent of children in this age group remaining unvaccinated by race and ethnicity. The highest coverages in individuals of other or multiple races who are non-Hispanic was 57 percent remaining unvaccinated. The lowest coverage rates are in Black, non-Hispanic individuals, with 72 percent

remaining unvaccinated.

This is the same graph, but now showing coverage of at least one dose among 12- to 17-year-olds by race and ethnicity over time. The highest coverage is in individuals of other or multiple races who are non-Hispanic and those of Hispanic ethnicity compared to lower coverage among black and white non-Hispanics.

Now I'll move on to vaccine effectiveness. I'll start first with CDC's PROTECT platform. This is a prospective cohort study in children aged 4 months to 17 years that includes weekly swabbing regardless of symptom status so should not be impacted by changes in testing practices due to the availability of home tests.

The study uses a Cox proportional hazards model with adjustment for propensity to be vaccinated, site, SARS-CoV-2 circulation, and community mask use. Results were separated by age group: 5 to 11 years and 12 to 17 years.

These results are updated from the Fowlkes et al., MMWR published in March and extend those findings

through April 23rd. Here we have VE against infection for 5- to 11-year-olds on the top and 12- to 17-year-olds on the bottom, further separated by time since last dose.

Note that for the 5- to 11-year-old group there was not enough power in the 60 plus days after the second dose. So the confidence interval was too wide to make meaningful conclusions, and so we did not include that estimate. Comparing the early post-second dose period, note that although the point estimates are different for the two age groups, the confidence interval for the adolescent group overlaps entirely with the confidence intervals for kids though the time intervals are a bit different.

In the adolescent group, a booster dose provides a significant increase in VE, bringing VE up to 83 percent, a median of 95 days or more than 3 months after the booster.

Moving on now to the increasing community access to testing, or ICATT, platform, which is a national community-based, drive-thru testing data from

pharmacies. This platform relies on self-reported vaccine history and uses a test-negative design where cases are persons with at least one COVID-like symptom and a positive NAAT test, and controls are symptomatic with a negative NAAT test. Models are adjusted for the variables shown here and not adjusted for prior infection.

We present data on adults first to show the differences between Delta and Omicron. Adults were tested from December 10th through January 1st with Omicron determined by s-gene target failure.

Testing kids were included between December 26th and February 21st when almost all circulating disease in the country was Omicron. These results have been previously shared with ASIP and VRBPAC, but we've included them here for completeness.

This is previously published adult data for Delta in orange and Omicron in blue by time since the second dose, shown on the x-axis with VE on the y-axis, the dotted line showing the 95 percent confidence intervals. You can see the lower starting VE for

Omicron and much quicker waning compared to Delta, including zero in the confidence interval by three months after the second dose.

And now we show the same adult data for Delta and Omicron and overlay data from adolescents 12 to 15 years of age in black and children 5 to 11 years of age in pink. Note the shorter follow-up time for the 5- to 11-year-olds due to the vaccine being recommended for them in November. Generally, we see a very similar pattern across the age groups with two doses of mRNA vaccines providing roughly 60 percent protection initially and quickly waning by a few months after the second dose, reaching zero by three to five months after the second dose.

Now concentrating on just the 12- to 15-year-old age group. In black, we have the same two-dose VE as shown on the previous slide, and here we've now overlaid the three- versus two-dose relative VE for the same age group in blue. We continue to see waning against symptomatic infection even after the third dose, though not quite as extreme as after the second

dose.

Moving on now from VE against infection to VE for emergency department and urgent care visits and hospitalization. The VISION network is a multi-state network based on electronic healthcare records. Like ICATT, it uses a test-negative design with cases having CLI and a positive PCR and controls having CLI with a negative PCR. VE is adjusted for propensity to be vaccinated weights, calendar time, region, local virus circulation, and age. And vaccination is determined via health records and state and city registries.

This is an update to data that was included in the Kline et al., MMWR in March showing VE against emergency department and urgent care for children 5 to 11 on the top and adolescents 12 to 15 on the bottom. For the 14 to 59 days after the second dose, we see almost identical VE point estimates in the two groups between 50 and 56 percent, with wider confidence intervals for the adolescents since it's been much longer since they were recommended to be vaccinated.

The adjusted VE drops substantially in the 60

days after vaccination for the 12- to 15-year-old age group, almost crossing zero. On the bottom of the slide, I've noted the case definition for an ED/UC visit, which highlights here the potential for inclusion of children visiting urgent cares and EDs with COVID instead of for COVID. Likely a larger concern for children than for adults as the case definition includes GI symptoms, which may have many frequent non-COVID causes in children and could potentially drive the VE estimates for ED and UC visits closer to those for infection in children.

As with infection, a booster dose provided a significant increase in VE among 12- to 15-year-olds, 73 percent, up to a median of 58 days after the booster.

Here we have VE of two doses against hospitalization for children 5 to 11, and adolescents 12 to 15 years of age during Delta and Omicron. This slide has been previously shared with ACIP and VRBPAC and published via MMWR. Updated data were not available due to the relatively few children

hospitalized since the initial Omicron wave subsided.

For the 5 to 11 group, you can see here that there were only two hospitalizations during the study period, which included two months after children in that age group could be fully vaccinated. While the point estimate for 5- to 11-year-olds, 74 percent, is lower than the point estimate for 12- to 15-year-olds, 92 percent, this is likely because the younger age group included 67 percent Omicron cases for which VE is lower compared to earlier variants. While the older age group included only 15 percent Omicron cases.

Finally, I'll show results from the Overcoming COVID platform. Overcoming COVID is a test-negative VE platform specifically aimed at children and adolescents hospitalized at 31 pediatric medical centers in 23 U.S. states. As with other platforms, cases have a CLI and a positive test, while controls have CLI and a negative test. Vaccination status is determined using a combination of documentation in the medical record and self-report models via logistic regression.

This is an update to a recent publication in

*The New England Journal of Medicine*. We see VE for 5- to 11-year-olds of 68 percent to a median of 37 days after the second dose, and VE for 12- to 18-year-olds of 51 percent. In the older kids, we can see VE split by time since vaccination, with some indication of waning at 23 for 45 weeks. Unfortunately, uptake of a booster dose in adolescents was not high enough to assess additional protection against hospitalization afforded by the booster dose.

Here we have updated data on VE against MIS-C for both age groups, with a VE of 78 percent for kids and 90 for hospitalizations. We do not see a signal here for waning in adolescent groups similar to hospitalization. And, also similar to hospitalization, we did not have power to assess additional protection due to a booster.

In summary, coverage remained lower among adolescents and children compared with adults and differs somewhat by race and ethnicity. For VE against infection, two doses declined quickly for children and adolescents during Omicron and followed a similar path

to that of adults.

A booster dose in adolescents substantially improved VE compared to two doses, though some waning appears evident. A similar pattern was noted for emergency department and urgent care visits, with similar VE after two doses in both age groups, with evidence of waning and substantial additional protection provided by the third dose among adolescents.

Finally, for severe disease, two doses provided protection for both children and adolescents with some waning evident for hospitalization in adolescents. There was not enough power to assess waning in children or the impact of boosters against hospitalization or MIS-C in adolescents.

I'd like to thank the individuals shown on this slide and with that, I conclude. Thank you.

**CDC PRESENTATIONS: UPDATE ON MRNA COVID-19 VACCINE POST-AUTHORIZATION SAFETY ASSESSMENT IN PEDIATRIC AGE GROUPS**

**DR. TOM SHIMABUKURO:** Good morning. Today I'm going to give you an update on myocarditis following mRNA COVID-19 vaccination. The topics will include a background on classic myocarditis and myocarditis associated with mRNA COVID-19 vaccination. These slides are nearly identical to the slides you saw last week, so I'm not going to cover these. They're included for reference, but I'm happy to come back to them at the Q&A session if there are questions.

And I'm going to give an update on myocarditis following mRNA COVID-19 vaccination with a focus on children ages 5 to 17 years, and that will include findings from the Vaccine Adverse Event Reporting System and the Vaccine Safety Datalink.

And then, finally, I'm going to provide some data, which has been previously presented, on comparative risk for myocarditis between the two

available mRNA COVID-19 vaccines, Moderna and Pfizer.

So I'll skip through these background slides and get right to the findings from the Vaccine Adverse Event Reporting System, or VAERS. VAERS is the national spontaneous reporting or passive surveillance system that's comanaged by CDC and FDA.

The key limitation for VAERS as a passive surveillance system is that generally, we cannot determine cause and effect from VAERS data alone.

This is a flow chart showing reports to VAERS of myocarditis after Pfizer vaccination among children ages 5 to 17 years.

There have been 972 preliminary reports of myocarditis detected through May 26, 2022. That's the surveillance period for this presentation for the VAERS data. Two hundred and fourteen remain under review, and 123 did not meet case definition. That leaves us with 635 reports that met the CDC case definition. To put that number into context, during the surveillance period, there have been roughly 54.8 million total Pfizer doses administered to children ages 5 to 17

years in the United States.

Here's a figure showing myocarditis reports after Pfizer in the age group by time to symptom onset and by dose number. The main takeaway from this figure is that reports of myocarditis occurring after mRNA COVID-19 vaccination tend to cluster several days. The onset tends to cluster several days after vaccination. You see that clustering on Days 1, 2, and 3, and to an extent, 4, after vaccination. And most of these cases occur within the first week of vaccination. I'll show you some additional data from our Vaccine Safety Datalink system later on in the presentation, which also confirms this finding.

So this is a table showing VAERS reporting rates of myocarditis per one million doses administered after mRNA COVID-19 vaccination in the Days 0 to 7 and 8 to 21 days post-vaccination. I've highlighted the pediatric age groups there, but I've also included the adult age groups for reference. The peach-shaded cells are where the reporting rate, or the observed, exceeds the background incidence or the expected. And that

background incidence is based on (audio skip).

**MR. MICHAEL KAWCZYNSKI:** Tom, we're not hearing you. Hold on a minute. We have you connected, make sure -- yep, let's reconnect your audio please. I'll give you the wizard. Just give us a moment while Tom reconnects his audio. I guess we'll have to blame the cellphone company on that one. All right. There you go. All right, I'm going to unmute you, Tom. You're back. How are you doing, sir?

**DR. TOM SHIMABUKURO:** All right. Where did you lose me? On this slide?

**MR. MICHAEL KAWCZYNSKI:** Yep, on this slide, you're good. Just on this slide.

**DR. TOM SHIMABUKURO:** Okay. This is a table showing the VAERS reporting rates of myocarditis per million doses administered after mRNA COVID-19 vaccination in Days 0 to 7 and 8 to 21 days post-vaccination. The peach-shaded cells are where the reporting rate exceeds the background incidence. And if you use that as a proxy for risk, you will see that both in males and in females, the risk is concentrated

in the Days 0 to 7 after vaccination. That's consistent with the figure that I showed you on the previous slide.

Also, the reporting rates are higher in males compared to females and higher after Dose 2 compared to Dose 1. In VAERS, the reporting rates for the booster doses tend to be somewhere in between Dose 1 and Dose 2.

So now I'm going to provide an update on some CDC-enhanced surveillance for myocarditis outcomes among children ages 5 to 17 years. This is actually in two cohorts, a 5- to 11-year-old cohort and a 12- to 29-year-old cohort. And I'm just basically combining these ages into a single cohort for the purpose of this presentation.

So the purpose of this activity was to assess the functional status and clinical outcomes among individuals reported to have developed myocarditis after COVID-19 mRNA vaccination. It's a two-component survey conducted at least 90 days after the onset of myocarditis. It includes a patient or patient survey

and a healthcare provider survey.

So, during the surveillance periods for these age groups, VAERS received 430 reports of myocarditis or myopericarditis in children ages 5 to 17 years that met the CDC case definition and that were at least 90 post-myocarditis diagnosis. We completed 190 patient or parent surveys and 226 cardiologists or other healthcare provider surveys.

The main finding from the cardiologist or healthcare provider assessment was that most patients appear to have fully or probably fully recovered from their myocarditis at 90 plus days after the onset of myocarditis. For the cardiologists, we were able to contact and get an assessment. 80.1 percent judge their patients as fully or probably fully recovered at at least 90 days after myocarditis diagnosis.

So the key findings from this enhanced surveillance project were that, at least 90 days after myocarditis diagnosis, most patients who were reached for the patient or parent survey reported no impact on their quality of life, and most did not report missing

school or work. As I previously stated, most -- just over 80 percent -- healthcare providers who completed the surveys indicated that the patient was fully recovered or probably fully recovered. There are substantial heterogeneity in initial and follow-up treatment and testing, and there did not appear to be a single test that was indicative of recovery.

For next steps, we are conducting additional follow-up with patients, who are not yet recovered at the time of the 90-plus day survey, and their healthcare providers to further assess recovery status at 12 plus months.

So now I'll move on to findings from the Vaccine Safety Datalink surveillance, and the VDS is CDC's electronic health record-based system for surveillance and research. It's a collaboration between CDC and nine integrated healthcare organizations.

CDC conducts rapid cycle analysis, which is weekly sequential monitoring. Its aims are to monitor the safety of COVID-19 vaccines weekly using

prespecified outcomes and to describe the uptake of COVID-19 vaccines over time among VSD members.

These are the VSD RCA prespecified surveillance outcomes and the settings in which they're monitored.

The methodology is a vaccinated concurrent comparator, so we're looking at cases in a risk interval in vaccinated individuals compared to cases in a comparison interval in vaccinated individuals matched on certain characteristics, such as time, site, age, and sex.

For the prespecified outcome myocarditis and pericarditis, cases were verified using the CDC case definition.

This is a figure showing Pfizer vaccine doses administered in VSD pediatric age groups, the 5 to 11, the 12 to 15, and the 16- to 17-year-old age groups. Of note, just over two million total Pfizer primary series doses were administered in children ages 5 to 17 years during the surveillance period. And this is a slide showing the Pfizer booster doses administered in

the pediatric age groups.

The main findings with respect to myocarditis and pericarditis is that in children ages 5 to 11 years for which right now we only have primary series vaccinations, no statistical signals to date for myocarditis and pericarditis. And for people ages 12 years and older, including adults, statistical signals were detected for myocarditis and pericarditis for Pfizer, and for both mRNA COVID-19 vaccines combined for primary series vaccination. Statistical signals were detected for myocarditis and pericarditis for both mRNA COVID-19 vaccines combined for the first booster dose. So, again, no statistical signals to date for children ages 5 to 11 years and statistical signals for the primary series and the booster dose series for myocarditis and pericarditis for the analytic group 12 years and older.

Here's a figure showing data of symptom onset of verified myocarditis and pericarditis cases among children 5 to 17 years after primary series. And you can see similar to the findings I showed for VAERS,

these cases tend to cluster within several days of vaccination. There's two statistically significant clusterings: Day 0 to 3 and Day 0 to 4 after vaccination.

This is a table showing verified myocarditis and pericarditis in the zero- to seven-day risk interval among male children 5 to 17 years by age group and by dose. You see, for 5 to 11 years, right now we have relatively small case counts and no statistical signals. When looking at the combined 12- to 17-year-old age group, we have elevated rate ratios after Dose 1, Dose 2, and first booster dose. Some of these rate ratios are highly elevated and highly statistically significant.

And then, when you split these into 12- to 15-year-old and 16- to 17-year-old subgroups, you'll see the statistically significant elevated rate ratios there after Dose 1 and Dose 2 for 12- to 15-year-old males and after Dose 2 and the booster dose for the 16- to 17-year-old males. Where we cannot estimate an adjusted rate ratio, that means that while there are

events in the risk interval, there are no events in the comparison interval. However, we can determine these are statistically significant by calculating a 95 percent confidence interval.

This is the same table, but for females. And you can see there are less elevated adjusted rate ratios. One statistically significant finding in 12- to 17-year-old female children after Dose 2 and also in the 12- to 15-year-old subgroup after Dose 2. If you look at the case counts, they're substantially lower than the case counts that we have observed in the males.

So this is a table showing VSD incidence rates of verified myocarditis and pericarditis in the zero to seven days following Pfizer vaccination. These are straight incidence rates, but it just shows the general trend here that the incidence rates following vaccination tend to be higher in males and tend to be highest after Dose 2.

If you look at the 16- to 17-year-old age group, you'll see that the incidence rates are actually

highest in males after first booster and after females after first booster. However, the case counts are fairly small, and the 95 percent confidence intervals are quite wide. So we really can't say that there's a difference between the Dose 2 incidences and the first booster incidence based on these data.

So this is a table showing level of care and status of myocarditis and pericarditis cases in the age group in the zero to seven days after both primary series and first booster dose of mRNA COVID-19 vaccine. See that most of these children regardless of primary series or booster dose are hospitalized.

A relatively small minority are treated in the emergency department. The length of stays tend to be fairly short: two days after primary series, one day after booster. And the overwhelming majority of these cases have stays of three days or less, a hundred percent in both primary series and booster dose were discharged home.

Now I'm going to move on to some findings of comparative risk for myocarditis between the two

available mRNA COVID-19 vaccines, Moderna and Pfizer. So I'm going to show you some data from a presentation that was given back at an October ACIP meeting looking at VAERS data.

These are reporting rates per million doses administered of myocarditis among males in the seven-day risk period. And if you look at the age groups 18 through 65, where you can actually do a direct comparison because Pfizer and Moderna were both authorized in that age group.

If you look at Moderna compared to Pfizer, you'll see that there's this general trend for slightly higher reporting rates following Moderna compared to Pfizer for either Dose 2 or Dose 1. Those differences tend to attenuate once you get to the older age groups.

This is a similar slide, but for females. You see a similar trend; however, the reporting rates are much lower than for males and the attenuation of the difference tends to occur at younger ages.

So this is not actually a direct comparison; this is really a side-by-side comparison of the two

products. In order to do a direct comparison, we looked at data from our Vaccine Safety Datalink system, and this is from a presentation that was given February 4th. We've recently run this data again, and the results have not changed. So these are current.

So this is a figure looking at both symptom onset and looking at incidence rates for Moderna for myocarditis after vaccination, for Moderna compared to Pfizer. And of note, you'll see this case clustering within the zero to seven days after vaccination. And you see slightly higher incidence from Moderna compared to Pfizer.

When we do statistical testing to look at that difference, we see that regardless of the analysis, whether it's either dose, Dose 1 or Dose 2, looking at males, looking at females, or looking at both sexes combined, the adjusted rate ratios are consistently above one, indicating that there's a higher risk from Moderna compared to Pfizer.

Although, most of these adjusted rate ratios are not statistically significant, and, in some cases,

the confidence intervals are quite wide. The statistically significant analysis was for either dose in both sexes where we had an adjusted rate ratio of 1.61, which was statistically significant, indicating in that analysis the risk for Moderna was greater than Pfizer and did reach statistical significance.

So this is a table looking at VSD incidence rates for myocarditis/pericarditis in the Day 0 to 7 following vaccination through March 31st. And I think the general trend here is if you look at the incidence rates for Moderna on the far right compared to Pfizer in the middle column, you see that generally the incidence rates for Moderna are consistently higher compared to Pfizer. There are some exceptions, especially in the 18- to 29-year-old age group and, for the most part, in the 30- to 39-year-old age group, you're seeing a general trend of slightly higher incidence rates for Moderna compared to Pfizer.

So, in summary, the current evidence supports a causal association between mRNA COVID-19 vaccines and myocarditis and pericarditis with cases clustering

within the first week of vaccination. Myocarditis is a rare event following mRNA COVID-19 vaccination.

CDC has verified 635 myocarditis case reports in children ages 5 to 17 years after 54.8 million Pfizer doses administered in this age group in the United States. The risk appears greatest in adolescents and in the age group 16 to 17 and 12 to 15 and is generally higher after Dose 2 compared to Dose 1 of the primary series and in males compared to females.

In VSD analysis, in a minority of age and sex strata, incidence is highest following the booster dose. The reporting rate in VAERS of myocarditis following Pfizer in male children ages 5 to 11 years after Dose 2 of the primary series is slightly elevated when compared to background incidence. Otherwise, reporting rates are within background incidence. And to date, myocarditis and pericarditis has not statistically signaled in VSD RCA surveillance in children ages 5 to 11 years.

The available information suggests that most persons with myocarditis after mRNA COVID-19

vaccination recover from their myocarditis by 90 plus days after diagnosis. In age groups where product comparisons can be made, some evidence suggests that myocarditis and pericarditis risk may be higher after Moderna than after Pfizer. However, the findings are not consistent in all U.S. monitoring systems, and you'll hear more about that in the following presentation from FDA.

I'd like to acknowledge the following groups for their contributions to this presentation. I have a couple more education slides, but, in the interest of time to get to discussion, this concludes my presentation, and I'm happy to address questions. Thank you.

**Q&A SESSION**

**DR. ARNOLD MONTO:** I'd like to thank all the CDC presenters for giving us a lot of data in a very succinct fashion.

What I'd like to do, we have only a few

minutes for questions here. We'll be able to handle more questions later on during the day. If we could try to ask questions first about impact, then about efficacy, and then about safety, it might order the questions a little bit. That may not be possible in the limited time we have, but I see Dr. Offit has his hand raised. Okay, Dr. Meissner, are you going to ask about impact? I'd like to try to do this, a couple questions about each.

**DR. CODY MEISSNER:** Arnold, I'll ask about impact.

**DR. ARNOLD MONTO:** Okay, you ask about impact. Good. Your hand went down, and I couldn't tell what that meant. Go ahead. But in any case, Dr. Offit, you're on.

**DR. PAUL OFFIT:** Thank you. This is for Dr. Fleming-Dutra. Thank you for that compelling presentation. You've made it clear that this can be a serious and occasionally fatal disease in young children. The data that you presented were primarily based, I guess, on Omicron, to a lesser extent on the

variants that circulated before Omicron. Those variants, including Omicron, are largely gone from the United States.

So my question to you is, do you have any information on the Omicron sub-variants like BA.2 or BA.2.12.1, or BA.4, BA.5 that are now more commonly (inaudible) in this country. How about in other countries where those viruses were circulating before here? Thank you.

**DR. KATHERINE FLEMING-DUTRA:** Thank you for that question. As you said, the data that I presented are based on U.S. epidemiology. I tried to focus on Omicron predominance, which was early, you know, BA.1 and then BA.2. But there are some data from prior in the pandemic. I do not have further information on the epidemiology from other countries that I can share at this point. But I can ask if there are others at CDC who can provide that information.

What we do know is that BA.4 and 5 now represent about 13 percent of the combined sequence specimens for new SARS-CoV-2 infection. It was posted

on the recent CDC COVID data tracker where they post the variants. But it's difficult to predict for what that's going to mean for the U.S. epidemiology.

**DR. PAUL OFFIT:** Thank you.

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

**DR. CODY MEISSNER:** Thank you, Dr. Monto. And I have a question that doesn't fall neatly into either of the categories you mentioned, but I think it overlaps all of them.

First of all, thanks very much to the CDC presenters. It's very valuable information.

I would like to ask you a question that some of the skeptical people in this country are asking and give you an opportunity to answer it. That is, if we look at today's data or the most recent data from CDC data tracker, it shows that 5- to 17-year-old children have a hospitalization rate of 0.7 per 100,000. So that's seven per million. And there's about 50 million adolescents and children in the age group that we're talking about. So that's 350 hospitalizations based on what's going on now. And if we say that half of those

hospitalizations are just associated and not caused by, then we're getting down around 200 hospitalizations among 50 million children and adolescents.

And if we pull out those children who have high-risk factors such as diabetes and certainly the vaccine is appropriate for them, you can understand why there's some question in people's minds about this risk of myocarditis that Dr. Shimabukuro presented relative to the risk of hospitalization. How does the CDC address that question? I think it would reassure a lot of people if you could give us your perspective.

**DR. KATHERINE FLEMING-DUTRA:** So thank you for that question. A couple of things that I want to address about that particular question.

So, first of all, among children ages 6 months through 17 years, the proportion -- so we have a couple of different surveillance systems that look at COVID-19-associated hospitalization. As you noted, COVID-NET looks at children who test positive for SARS-CoV-2 infection.

So there are some children in that

surveillance system who may have had incidental SARS-CoV-2 infection rather than hospitalized with COVID-19. However, in the published COVID-NET data, the majority of children are actually hospitalized with COVID-19. So they look at the medical chart, and they look at the reason for admissions. Most of those children, including about 87 percent of children ages six months through four years are actually primarily admitted for COVID now.

There are other CDC surveillance systems that use different methodologies, like the new Vaccine Surveillance Network. And that particular network enrolls children that have acute respiratory illness. And then (inaudible) testing on them, so (inaudible) SARS-CoV-2 positive in that particular network, all of them have COVID-19 disease. And what we see is that the severity of illness looks fairly similar in those surveillance systems.

I think that it's important to note that those children who are hospitalized with SARS-CoV-2 infection indeed have COVID-19 and that we see some severe

disease in all of those children.

The other thing is that we can't predict who will have severe disease. Certainly, children with underlying medical conditions are more at risk, but half of children ages six months through four years who are hospitalized with COVID-19 don't have underlying medical conditions.

So part of the concern is trying to decide what children are at risk, and, even though those with underlying conditions are more at risk, we still see children who don't have those conditions who end up with severe disease.

And maybe I'll stop there and defer to Dr. Link-Gelles and Dr. Shimabukuro if they have more to add.

**DR. ARNOLD MONTO:** Why don't we park the rest of that discussion which could go on for about 10 or 15 minutes for later on in the day. And I'd like to call on Dr. McInnes because we only have a few minutes here for targeted questions.

**DR. PAMELA MCINNES:** Thank you, Arnold. So

this is also again for Dr. Fleming-Dutra. I don't know, Arnold, if you want to put this in the parking lot too.

**DR. ARNOLD MONTO:** Well, let's just --

**DR. PAMELA MCINNES:** This specifically relates to Slide 16, which is your rates of monthly associated hospitalizations by vaccination status. I think you've got June 2022 through March 2022. I think you mean June '21 through March 2022. But if I look from February to March, I would like you to comment on this apparent very little difference between being immunized or non-immunized with regard to immunization by the time you get to March 2022.

**DR. ARNOLD MONTO:** And how much does Omicron have to do with that?

**DR. KATHERINE FLEMING-DUTRA:** Thank you for that question and thank you for pointing out that. I think it's really important that we look at the y-axis there. We see the most benefit for vaccination when the disease burden is high. It's most pronounced when the disease burden is high.

And so, it's very important that the unvaccinated children and adolescents are the ones who are bearing the burden of disease. And that they will continue to bear the burden of disease when we see future surges of COVID-19.

**DR. PAMELA MCINNES:** But could you comment specifically on March 2022? What are those data telling you?

**DR. KATHERINE FLEMING-DUTRA:** I think it's important that those are incidence, and the differences were a lot smaller when the incidences were lower. And I think that this is probably a better question for Dr. Link-Gelles because we're not calculating VE, or vaccine effectiveness, with those data. So maybe I'll defer to Dr. Link-Gelles about VE during that time.

**DR. ARNOLD MONTO:** Please, and comments about Omicron.

**DR. RUTH LINK-GELLES:** Sure, thanks so much, Katherine. I would just echo what Dr. Fleming-Dutra said, that really we see the biggest impact of vaccination during the surges. And so we saw a huge

impact of vaccination in January and February when Omicron was very high. And we expect, as data begin to come in on this more recent surge that we're going through now, that we will also pick up additional benefit of vaccination.

Certainly, vaccination remains highly effective when disease is less common, but just because the control group has less disease in March generally means that we'll see less of an impact of vaccination when disease is lower. But, as we know, given the current surge right now and the coming BA.4 and 5, as those pick up, it's extremely likely that we'll have additional surges in the coming months. And certainly, we expect surges in the fall and winter, and new variants are always on the horizon.

And so I think it's important to keep in mind that we are vaccinating children, or potentially vaccinating children, now with the expectation that that vaccination would protect them in the coming months when we expect additional surges.

**DR. ARNOLD MONTO:** Dr. Hildreth.

**MR. MICHAEL KAWCZYNSKI:** Dr. Hildreth, you have your own phone muted, sir. It's all right. Go ahead. Nope, we can't hear you, Dr. Hildreth. You have your own phone still muted. Dr. Hildreth, how about we come back to you. We'll reconnect your audio, and then we'll come back to you, okay?

**DR. ARNOLD MONTO:** And there's only going to be one more question other than Dr. Hildreth. Dr. Marasco.

**DR. WAYNE MARASCO:** Thank you, Dr. Monto and the CDC panel. This is a question for Dr. Ruth Link-Gelles. You show us vaccine effectiveness really dropping off in the population after about three months on your second dose. And even if you get a third dose, there's a drop off, waning immunity after perhaps maybe four months. So it looks like these vaccines are really only protecting, as we already know, for a period of three to six months.

So my question really is, how do you message that to the people if it's really not going to be protective for a full year? I mean, this is a CDC

messaging problem because I see the, why would I get the vaccine, or am I going to need to get it every six months? I mean, those kind of questions arise from this kind of data. Perhaps you can address that.

**DR. RUTH LINK-GELLES:** Sure. I think it goes to which outcome is under study. So most of the data that I showed, where we actually had information further out from vaccination for kids was looking at infection. And so we do know that vaccines wane fairly quickly against infection during Omicron. That was not the case with earlier variants. But because most of the data we have for children is during Omicron, we do see that waning against infection.

We know from the adult data that the vaccines wane much, much more slowly against more severe outcomes like hospitalizations. And so we would expect that since we see similar waning patterns for infection for adults and children, that we would see similar waning patterns for hospitalization for adults and children.

Because hospitalization is generally more rare

for children and just because of the timing of when the vaccines came out in conjunction with the Omicron surge ending, we don't have enough data to look at waning specifically against more severe disease, including hospitalization, in children.

But I would say to parents that are interested in getting their child vaccinated, it's true; you may have shorter protection against infection from these vaccines, but you will have sustained protection against hospitalization and severe disease, which is really what the vaccines are targeted for.

**DR. WAYNE MARASCO:** That's correct. That's a different messaging now I just want to bring up. And I think that's what's confusing the public because that messaging isn't always clear. That's my comment. Thank you.

**DR. ARNOLD MONTO:** Yeah, and don't you have problems telling the difference between waning and a new variant in terms of what you're seeing?

**DR. RUTH LINK-GELLES:** Well, at the moment, since most of the circulating disease has been BA.1 and

BA.2, most of our data is actually coming from the BA.1 era where there was a lot more disease circulating. And so, at this point, I would say that most of the information that we're looking at was confined to just the BA.1 and early BA.2 era of Omicron. We're really able to parse out waning specifically aside from a new variant. That's not always going to be the case, certainly. If we see new variants crop up more quickly, it'll be harder to parse that out.

**DR. ARNOLD MONTO:** Thank you. Dr. Hildreth, final question.

**DR. JAMES HILDRETH:** Thank you, Dr. Monto. Can you hear me?

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

**DR. JAMES HILDRETH:** Okay. Thank you. First, thanks to the three presenters for those very clear and informative presentations.

I have a question for Dr. Fleming-Dutra. In your slide about seroprevalence, it went by too quickly for me to actually see the numbers. What is the current seroprevalence in the children from 1 year old

to 11 years old? Is it more than 70 percent?

**DR. KATHERINE FLEMING-DUTRA:** Yes. I don't know if we can get the slide back. Thank you. So just to point out these data, it should be Slide number 10. So these data are from September 2021 to February 2022 for these most recent estimates shown in this particular slide went from February 2022.

Among children 5 through 11 years of age, the seroprevalence in February 2022 was 77 percent. Among children 12 to 17, it was 74 percent. There we go, thank you so much. And among children one to four years old, it was 58.

**DR. JAMES HILDRETH:** So the reason I asked the question, if that's true that 70 percent of the children have been infected with SARS-CoV-2, the true rate of hospitalizations and deaths is vanishingly small if we take that into consideration. Is that a true interpretation of the data? We have a different perspective?

**DR. KATHERINE FLEMING-DUTRA:** I'm not sure if I fully understand the statement. Go ahead.

**DR. JAMES HILDRETH:** What I'm saying is that if 70 percent of children have in fact been infected by SARS-CoV-2 and many of those do not come into care or get diagnosed, it means the true rate of severe disease, hospitalizations, and deaths is much smaller than what it appears to be from the other data. Is that not correct?

**DR. KATHERINE FLEMING-DUTRA:** The other data is per population. So the rates that I showed for hospitalization and severe were population-based rates rather than based on the number infected or who tested positive. So that's one point.

And the other thing to note is that the data that I showed with the hospitalization rate were from the Omicron predominant period. And so those are rates of hospitalization that occur during a period of high seroprevalence amongst (audio skip).

**DR. JAMES HILDRETH:** Okay.

**DR. KATHERINE FLEMING-DUTRA:** Does that (inaudible)?

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

**DR. ARNOLD MONTO:** I just wanted to make the point, since we've got some surveillance going and I know there's surveillance going in Seattle looking at seroprevalence, there are certainly other populations in which the seroprevalence is not nearly as high in younger children. Would you agree with that in terms of the population that you're studying?

**DR. KATHERINE FLEMING-DUTRA:** Those graphs that I showed was a national estimate, so it is not. It may (inaudible).

**DR. ARNOLD MONTO:** Based on which specimens?

**DR. KATHERINE FLEMING-DUTRA:** The national commercial laboratory. They're based on blood samples that are taken from commercial laboratories for children who are having blood tested for reasons other than COVID-19.

**DR. ARNOLD MONTO:** Okay, so it is children that do go to hospitals to be tested for other things because what we're looking at also is households in which the children have not had conditions requiring blood collection. So there is some difference of

opinion about the seroprevalence that we're seeing right now.

Let's move on. We've got the FDA presentations coming up on safety surveillance of COVID-19 vaccines in children and adolescents. Dr. Hui-Lee Wong will speak to us for 15 minutes and then another very short question and answer. Dr. Wong.

## FDA PRESENTATION: SAFETY SURVEILLANCE OF COVID-19 VACCINES IN CHILDREN AND ADOLESCENTS

**DR. HUI-LEE WONG:** Thank you, Dr. Monto. My name is Hui-Lee Wong, and I present on the safety surveillance of COVID-19 vaccines in children and adolescents.

I'll first present a summary of evidence of comparative risk between the post-vaccination risk of myocarditis and pericarditis between the two available mRNA vaccine brands, followed up with our own FDA BEST study of this direct comparison of this risk. And I'll end with safety surveillance in vaccine recipients aged

5 to 17 years.

First, the overview of the available evidence of the comparative risk between Moderna and Pfizer-BioNTech vaccines.

As of last fall, majority of the available data received this year, on the right-hand corner of that, suggests that risk after receipt of Moderna COVID-19 vaccines were around two-fold to seven-fold higher than Pfizer-BioNTech vaccines. This is where they make the conclusions of increased risk and mostly qualitative statements.

Most of this data you see on the right-hand corner up here actually were mostly in direct comparison in international passive surveillance. And there's one actually (inaudible) after similar study that didn't have formal physical testing of these estimates of increased risk. So, in terms of addressing some of these possible mutations of indirect comparisons and also in passive surveillance, one can actually look into direct comparisons of active surveillance.

We see in the right column once again there is the CDC's active surveillance vaccine safety datalink here where they found actually a two-fold difference higher. In contrast at the time, on the left column here, you see that the VAERS, the U.S. passive surveillance and the other active surveillance direct comparisons in U.S. active surveillance study that the U.S. updated that did not actually find a (inaudible) significant risk here.

What we did also, to let you know, that on the right-hand column here is that in terms of the higher or lower risk down here, we actually did a simple division of these indirect comparisons of the point estimates of Moderna and Pfizer. There is no position estimates around this here. (Inaudible) limitations in these results generated by these comparisons at the time, the reported differences in myocarditis and pericarditis risk between these two mRNA vaccines across these multiple data sources were concerning.

So therefore, based on the FDA assessment at the time, the totality of evidence available on those

data available at time, there was limited information of the follow-up cases. And availability of Pfizer-BioNTech for youth adolescents, FDA did not take regulatory action on the emergency use amendment for use of Moderna COVID-19 vaccine in adolescents. However, FDA still continues to monitor that as data accrues and as we get actually more robust data to try to verify the signals in there.

So here, as of late last month, what we see here now is that on the right-hand corner here, there is no additional active surveillance information here. These are all still indirect comparisons. There is one now direct comparison in the right-hand corner here that appear to be actually enhanced passive surveillance for Canada and Ontario.

And once again, they point to around a two-fold to seven-fold high interest here. So, at the same time, we also have the addition follow-up in clinical conversation (phonetic) of the mRNA vaccine-associated myocarditis. This includes in the pediatric age groups as presented by Dr. Shimabukuro in the preceding

presentation.

On the right column now we see that all the international data was (inaudible) is indirect comparisons, except for direct comparisons with Canadian and Ontario. What we do like to suggest here is that interpretation of these indirect comparisons of these mRNA vaccines without formal testing would actually benefit from the consideration of the lack of precision around the estimates and the possible differences in the proportion of risk factors for myocarditis and pericarditis among the vaccine recipients.

For example, maybe we have to consider that based on these different brands that were actually available at different kind of time in some countries and to take to account then the differential proportion of risk factors in these different brands. For example, younger age groups or risk factors that vary by kind of time, SARS-CoV-2 circulation, for example.

In contrast, now we see on the left-hand column, recent analysis of the U.S. data sources here

do not support such a difference of myocarditis and pericarditis risk for Moderna vaccines as compared to Pfizer-BioNTech vaccines. Either that or they actually suggest a small difference. This is due to uncertainties and broad confidence intervals.

So, as of last month, there still remains only two direct comparisons in active surveillance studies. These are in the U.S. That's the CDC's Vaccine Safety Datalink and the FDA BEST. Dr. Shimabukuro presented the more recent VSD results, and I will present the more recent FDA results right after this.

Both CDC VSD and FDA BEST reported a non-statistically significant increase of around 50 percent and 25 percent, respectively.

In summary, by fall of 2021, FDA reviewed results from eight surveillance systems, which suggested an estimated two- to seven-fold increase of risk of myocarditis and pericarditis following Moderna vaccination as compared to Pfizer-BioNTech in international passive and active surveillance systems as well as a two-fold increase in the U.S. active

surveillance system, which is the Vaccine Safety Datalink.

Based on the totality of evidence available previously outdated and also due to the limited lack of follow-up of these cases, FDA did not take regulatory action on the EUA amendment for the use of Moderna's COVID-19 vaccines in adolescents. Now we have more recent evidence from the U.S. surveillance systems, and we do not observe a significantly higher myocarditis risk in the Moderna COVID-19 vaccine recipients compared to the Pfizer-BioNTech COVID-19 vaccine recipients. What we've shown you is mostly around males 18 to 25 years of age after Dose 2.

We'd like to note however that these results may be limited by, among other things, small case counts, lack of adjustments and confounders, self-reported data. And comparisons between U.S. and international data sources would benefit from considerations that's actually heterogenous (inaudible). So they may be different. They are actually different intervals between doses, case

definitions, and availability of vaccines.

At present time, FDA is considering the totality of surveillance information from myocarditis and pericarditis risk, along with other information in determining the potential benefit of the Moderna vaccines outweigh the potential risk of COVID-19 in use for adolescents.

So now I move on to actually provide more details on the FDA study of indirect comparisons as mentioned. And particularly, this will be in males 18 to 25 years of age because this is the youngest age group that's available for comparisons between these two vaccines and is seen as the highest risk among adults.

So we conducted a study in the FDA active surveillance program for biologics. The BEST system leverages multiple partners and data sources, and this includes especially electronic health records, linked claims to electronic health records, and claims databases. Vaccine safety will be used to distribute network of large administrative claims databases that

collectively covers every state in the United States.

So last October at VRBPAC, we provided preliminary results that compared the risk for myocarditis and pericarditis risk of Pfizer-BioNTech and Moderna COVID-19 vaccines among 18 to 64. And because these rates were highest among males aged 18 to 25 years, we focused on this highest risk group for comparative risk analysis.

Now this time, for today, we're going to present an updated analysis where we actually added an increase around 68 percent this case counts. So in this case, what you see on here is around -- these cases going to be a total of 25 million doses of mRNA vaccine among 50 million persons aged 18 to 64.

We saw 411 myocarditis and pericarditis events. Of which, 114 cases were in the highest risk group and is 18 to 25 years males. And I'm going to present results for this next in this slide here.

So on the x-axis here, you see the incidence rate ratio here. And what we did was that we imported regression models. We compared incidence rates of

myocarditis and pericarditis risk following Moderna COVID-19 vaccination compared to, as a reference, to Pfizer-BioNTech COVID-19 vaccines here.

So the circles here is the rate ratio, and the whiskers here is the 95 percent confidence interval. And the circles here -- that's to the right here -- represent the Moderna vaccine risk is higher, and then to the left here, depicts that the Pfizer-BioNTech risk will be higher. And then, on the y-axis here, that's actually by dose.

So as you can see, our conclusions here didn't change with this additional case count. We did not observe a statistically significant risk difference here. However, this risk may range from 20 percent lower to 94 percent higher in Moderna recipients compared to Pfizer-BioNTech recipients for 18 to 25 years after Dose 2.

In addition, based on the other surveillance systems that we saw -- so to compare with these other direct studies, we also conducted scientific analysis. We expanded the age group 18 to 35 years and also

restricted this to the more severe care setting. This is in-patient and emergency. And once again, our conclusions did not change. If anything, the incident rate ratios actually were attenuated.

Additionally, also since then, we've also performed medical chart review here to actually verify that the cases that we see here that we've identified in our claims here and participative value that is the probability of what we identify or what we call the case here is truly verified. But is actually verified as a true case in medical chart review. That's our 83 percent. And when you actually restrict that to the more severe care setting -- that's in-patient and emergency department -- that's 100 percent.

There are a number of limitations. I only list a few down here. As mentioned, the events chart review events are ongoing. We have estimated PPVs. We also have done a clinical (inaudible) which is somewhat consistent with what CDC had just presented also. We only partially adjusted for some potential confounders, so we cannot rule out biased estimates. And there

remains a large uncertainty in incidence rate ratios due to the rarity of these outcomes in this vaccinated population.

In summary, the FDA BEST study did not identify significantly higher myocarditis and pericarditis risk following vaccination with Dose 2 of Moderna COVID-19 vaccines compared to Pfizer-BioNTech COVID-19 vaccines among males 18 to 25 years of age.

Our results were compatible with a 20 percent lower to 94 percent higher myocarditis and pericarditis rates in Moderna COVID-19 vaccine recipients compared to Pfizer-BioNTech COVID-19 vaccine recipients.

And finally now, I would like to provide updates on the safety surveillance that we are currently performing for those aged 5 to 17 years of age in FDA BEST system. We used three claims' databases. These are international claims databases. And they are also linked to a few, around 23, immunization information systems to capture vaccine exposures.

The total enrollee for 5 to 17 years of age is

9.4. Today, I present data based on the current data cutoff, and that is based on 5.4 million vaccine doses.

So for 5 to 17 years of age, we've monitored descriptively the post-vaccination rates of adverse events of interest, AESI, and we stratified that separately in 5 to 11, 12 to 15, 16 to 17, by sex, by region, by (inaudible), and in each data source for the AESI listed here.

In addition to the descriptive monitoring on the right column here, we also conduct a type of rapid safety signal detection. It's also known as near-real time surveillance or rapid cycle analysis. This aims to rapidly screen for potential safety signals that will be further verified and evaluated in robust studies to assess if that's indeed a true association. So as the vaccine data accrues, we run sequential hypothesis testing every month by testing for increased risk following vaccination and compare that to a historical pre-vaccine comparator calculated in each database while adjusting for multiple tests.

Every month we tested in 5 to 11, 12 to 15, 16

to 17 separately for primary series and booster actually by dose and treated as the vaccine data here accumulates.

So next going to show you here, then the current updates and the results that we have here. So this table shows that there are no signals that were identified for the listed AESI in any of the three (inaudible), except for what is seen here in red. That is for myocarditis and pericarditis after Dose 1 and Dose 2 for ages 12 to 17 years of age.

At the current data accrual stage similar to CDC, no signals were observed for myocarditis or for any of the AESIs for those aged 5 to 11 years old. This is among two million doses, nor for any of the third or booster doses. However, we only 320,000 doses for third or booster doses. So in that case, we'll continue to monitor as the data accrues.

This is additional information about the myocarditis signal in the 12 to 17 years of age where we calculated the rate ratio. And this is the observed versus expected rate ratio.

What we did here is on the x-axis here is that we compared the observed post-vaccination rate here with a proxy of rates in what we consider to be the unvaccinated group. That's historical rates in 2019 prior to availability of vaccines. Because I've actually talked about comparative first for 18 to 25 years of age here, I provide that on the y-axis at bottom. And here we see 12 to 15 and 16 to 17 that we see the (inaudible) that was expected, which is actually measure of the magnitude of risk.

But once again, this is interim results and because of that we did not actually compare between 12 to 15 years of age and 16 to 17 years of age. We also not presenting here 5 to 11 years because we actually have fewer than five cases for those two million doses that we've observed here.

In summary, myocarditis and pericarditis was identified as a safety signal in vaccine recipients 12 to 15 years of age and 16 to 17 years of age following Dose 1 and Dose 2. This did not signal for 5 to 11 years of age, nor in any of the booster analysis, nor

were any other safety signals identified.

In conclusion, FDA BEST study results could not identify a statistically significant high myocarditis and pericarditis risk in the recipients of Moderna COVID-19 vaccine compared to Pfizer-BioNTech COVID-19 vaccine among males 18 to 25 years of age. Myocarditis and pericarditis did signal for vaccine recipients aged 12 to 17 years post-Dose 1/Dose 2. No other signals were identified.

FDA continues to monitor myocarditis and pericarditis risk, and the state of COVID-19 vaccines in the pediatric population.

I would like to thank all of our FDA BEST partners and all of our FDA colleagues who were involved in this work. Thank you.

**DR. ARNOLD MONTO:** Thank you very much, Dr. Wong. We can have just a few questions specifically on Dr. Wong's presentation before our break. Seeing no questions right now, thank you, Dr. Wong. And we're going to take a break for ten minutes, returning at 10:45 Eastern. So a ten-minute break.

**MR. MICHAEL KAWCZYNSKI:** All right, thank you, Arnold, and let me put that up on the screen. So, studio, if you could take us to break, please?

**[BREAK]**

**SPONSOR PRESENTATION: mRNA-1273 (MODERNA COVID-VACCINE) -- REQUEST FOR EMERGENCY USE AUTHORIZATION IN INDIVIDUALS 6-17 YEARS OF AGE**

**MR. MICHAEL KAWCZYNSKI:** Okay. Welcome back after that break, and I'm going to hand this back over to our chair, Dr. Monto. Arnold, take it away.

**DR. ARNOLD MONTO:** Thank you. We next have the sponsor presentation of Moderna. The Moderna group will speak about the request for emergency use authorization in individuals 6 to 17 years of age. We have four presenters from Moderna. Dr. Carla Vinals will be the first speaker, and I hope you will be the traffic cop to introduce the other speakers for the whole presentation. Over to you.

**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 to the FDA and VRBPAC for the opportunity to present our safety immunogenicity and efficacy data for mRNA-1273, the Moderna COVID-19 vaccine in children and adolescents. I'll begin with a brief regulatory update.

In January of this year, our hundred microgram two-dose primary series was approved in the U.S. for those 18 years of age and older after being authorized under emergency use since December of 2020. Additionally, a third dose of a hundred micrograms primary series for immunocompromised individuals and first and second 50 microgram booster doses have also been authorized in the U.S.

mRNA-1273 is also authorized or approved for use in adults as a primary series in 86 countries worldwide and for boosters in 48 countries.

To date, more than 633 million doses of the Moderna COVID-19 vaccine mRNA-1273 have been

administered globally and more than 220 million individuals have been fully vaccinated with more than 120 million individuals who have received a booster dose.

Furthermore, our vaccine has now been authorized or approved for use in children and adolescents from 6 to 17 years of age outside of the U.S. For adolescents, the hundred microgram two-dose primary series is available in 42 countries, and we've recently received approval of the 50 microgram two-dose primary series for children 6 to 11 years of age in 40 countries. To date, more than 6.4 million adolescents and 300,000 children have been fully vaccinated with a primary course of mRNA-1273 outside of the U.S.

As the pandemic persists, a new highly transmissible variant of concern, like Omicron, emerged. Today, I continue to demonstrate that COVID-19 vaccines provide protection against severe disease and reduce COVID-19-associated hospitalizations.

This figure shows the rate of COVID-19-associated hospitalizations among fully vaccinated and

unvaccinated adults in the U.S. As shown by the red line, unvaccinated adults continue to be challenged by high burden of disease. In contrast, vaccinated adults, are shown by the blue line, continue to benefit from clinically meaningful levels of protection against COVID-19-associated hospitalizations.

Unfortunately, with the emergence of variants of concern like Omicron, we have also seen a substantial increase in the number of COVID-19 infections and hospitalizations among children and adolescents. This figure shows the rate of COVID-19-associated hospitalizations in the U.S. in this population.

While event rates are lower than those in adults, there remains a significant risk of COVID-19-associated morbidity in those children. In fact, recently, they have shown that approximately 25 percent or one in every four children and adolescents hospitalized due to COVID-19 require ICU intervention. Children and adolescents who remain unprotected need safe and effective vaccines that can reduce COVID-19-

associated morbidity and mortality.

Today, we will share the data supporting our request for emergency use authorization of mRNA-1273 as a two-dose primary series for the prevention of COVID-19 caused by SARS-CoV-2 in adolescents 12 to 17 years of age and children 6 to 11 years of age. The proposed two-dose primary series of a hundred microgram per dose for adolescents and a 50 microgram per dose for children 6 to 11 years of age are to be administered one month apart.

The totality of safety immunogenicity and efficacy data from our clinical development program and our pharmacovigilance data supports that the benefits of mRNA-1273 in children and adolescents outweigh the known and potential risks. mRNA-1273 was generally well-tolerated, and the safety profile is consistent with that observed in young adults. No new safety concerns have been identified.

Pediatric studies met 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 those age groups, the prespecified co-primary immunogenicity endpoints were met. In addition, there was evidence of efficacy against COVID-19 conferred by mRNA-1273 ranging from 88 to a hundred percent.

Our clinical trials enrolled more than 8,000 participants across the two age groups and more than 5,800 have received at least one injection of mRNA-1273. The median duration of follow-up in each study cohort is greater than 5.6 months, meeting the recommendations outlined in the EUA guidance. In both age groups, the co-primary immunogenicity objectives were met, 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 children and adolescents outweigh the potential risks.

Here's now the agenda for today's presentation. I will now turn the presentation over to Dr. Anderson, who will review the unmet medical need for safe and effective COVID-19 vaccines for children and adolescents in the U.S.

**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 the burden of COVID-19 in children and the need for vaccines.

This slide lists my conflicts of interest. I've been intricately involved with the Moderna Phase 1 and Phase 3 COVID vaccine clinical trials in adults, and I am an investigator in the Moderna study of children less than 12 years of age. I'm also the father of four children. So I have a vested personal interest in seeing children protected against COVID-19.

Early in the pandemic, there were several common misperceptions about COVID-19 in children and

adolescents as well as the potential need for a vaccine. The early understanding was that children don't, or at least infrequently, get symptomatic infections with SARS-CoV-2. Second, that children don't get hospitalized with COVID-19. Third, that children don't die with COVID-19. Finally, that COVID-19 is mostly just an inconvenience for children.

Data now demonstrates that these were clearly misperceptions. Let's look at the first misperception. We now clearly know that children do get infected with SARS-CoV-2. These data from CDC show the incidence of SARS-CoV-2 infections per 100,000 population over time. Children between 5 and 11 years are represented with a yellow dashed line and adolescents between 12 and 17 years with a yellow solid line.

Also, seniors are shown with gray dashed and solid lines, respectively. While very few cases of SARS-CoV-2 infections were observed in children early in the pandemic beginning with the delta wave and now during the Omicron wave, children are being infected at similar rates to those observed in adults.

Since the start of the pandemic, more than 10 million children 5 to 17 years of age have been diagnosed with SARV-CoV-2 representing about 14 percent of all U.S. cases.

Turning to the next misperception, we now know that children do get hospitalized with COVID-19. The benchmark for the burden of COVID is influenza. Care data from the CDC-sponsored network that I'm involved with performed population-based surveillance of influenza hospitalizations for about two decades and for COVID-19 since March of 2020. These data evaluate the burden of COVID-related hospitalizations in comparison to influenza in the 2017 through 2021 seasons.

The rate of COVID hospitalizations in children 5 to 11 years of age from October of 2020 through September 2021 is similar to that from influenza in the three seasons prior to the pandemic. When we compare COVID to influenza observed during the 2020 to 2021 seasons shown in the bottom line in light yellow, we see that the rate of influenza-related hospitalizations

was very low with only a few identified cases.

That's important because although the social interventions that were implemented were successful in preventing influenza-related hospitalizations, we still saw high rates of COVID-related hospitalizations in our children.

This figure shows the same data for adolescents 12 to 17 years of age. The number of COVID-19-associated hospitalizations was significantly greater than that of all recent individual influenza seasons.

These are data then from our network that show the relative burden of COVID compared to influenza in children of all ages. This bar graph shows COVID-19 hospitalizations in yellow and influenza in blue. You can see that influenza essentially disappeared in March of 2020 when COVID-related hospitalization began. The black circles here highlight the almost imperceptible influenza cases during the 2020 to 2021 season. In comparison, COVID was associated with large numbers of hospitalizations.

Hospitalizations have continued throughout the pandemic as different variants have emerged. Importantly, we have served a substantial increase in hospitalizations during the Omicron surge.

We often hear that it is uncommon for healthy children to be hospitalized with COVID. While this is correct, comparing those hospitalized with COVID-19 to those with influenza is helpful. These data show different underlying conditions in children and adolescents hospitalized with COVID in yellow on the left and influenza in blue on the right.

It's important to note that approximately 35 percent of children and adolescents hospitalized with COVID and flu have no underlying medical conditions. While obesity is a significant risk factor for COVID in comparison to influenza, asthma is less commonly observed in children hospitalized with COVID in comparison to influenza.

Looking further into these hospitalizations, this slide compares outcomes between COVID and influenza-related hospitalizations. Importantly, the

duration of hospitalization is longer, and the percentage requiring ICU admission is similar or more frequent with COVID. Mechanical ventilation is reported with a similar frequency. So we see that hospitalizations, in fact, are associated with similar or more severe outcomes when directly compared with influenza.

Another complication that we are concerned about with COVID is MIS-C, a potentially life-threatening complication of SARS-CoV-2 infections, which can occur in previously healthy children. More than 8,500 hospitalizations and 69 documented deaths have now occurred in the U.S. due to MIS-C.

Although it is, thankfully, not common, children can and do die with COVID-19. As of June 2nd, more than 600 children ages 5 to 17 have died with COVID as documented by CDC. This is a tremendous burden of disease with more than a hundred deaths in 2020, more than 350 in 2021, and more than 160 through the beginning of June.

This table evaluates the leading causes of

death in children in the U.S. using the CDC Wonder database. Young adults 15 to 24 years of age are on the top row, and children 5 to 14 years of age are on the bottom row. It plots COVID-19 mortality on a month-to-month basis, extrapolating the burden observed each month and then annualizing that mortality to the entire year to identify where COVID falls in terms of all caused mortality in that age range.

You can see spikes in COVID-related mortality occur with the Delta wave, and now with the Omicron wave. COVID is among the leading causes of death in children and young adults 5 to 24 years of age. It is now vaccine-preventable.

In placing this 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 occurred in children with these pathogens before implementation of routine vaccination were all less than about 60 per year.

Flu, in the years immediately before the

pandemic, ranged up to about 112 deaths per year in children 5 to 17 years of age. Even during the 2009 H1N1 influenza pandemic, 246 deaths were observed in this age cohort. For COVID-19 since the beginning of the pandemic, we've observed 117 to 364 deaths in children 5 to 17 years of age each year here in the U.S.

What we saw with COVID last year exceeded the deaths in the same age range associated with the 2009 H1N1 influenza pandemic in the first year. This is a tremendous burden in our children. Having cared for many children that have been in the ICU on ventilators with COVID-19 and MIS-C and having cared for several children that have died with COVID, we need to be able to prevent COVID.

Although I have focused on the morbidity and mortality associated with COVID, COVID-19 has dramatically impacted children in many other ways. We know that, for so many of us, families and children are not just inconvenienced by COVID. In fact, the quality of life has significantly worsened for our children.

One study documented that 40 percent of children have a low health-related quality of life in comparison to 15 percent pre-pandemic. Nearly 70 percent of children have experienced mental health deterioration and claimed depression during the pandemic. Two-thirds have found it difficult to complete their schoolwork, including actually most of my poor children.

National test scores have shown that progress and learning has slowed, and the gap has widened in math and reading for millions of U.S. students. The American Academy of Pediatrics, American Academy of Child and Adolescent Psychiatry, and the Children's Hospital Association have all joined together to declare a national emergency in children's mental health fighting the serious toll of the COVID pandemic.

So, in summary, children do get infected with SARS-CoV-2. We've had more than 10 million cases diagnosed in the U.S. in those 5 to 17 years of age, comprising 14 percent of all U.S. cases. Children do get hospitalized with COVID-19. This has been similar

to or greater than pre-pandemic burden of seasonal influenza despite substantial social interventions and tended to mitigate transmission. Children do die with COVID-19, and the number of deaths far exceeds that of many other pathogens for which vaccines are now available.

This is not just an inconvenience to our children and for our families. There has been a profound impact upon their developmental and mental health as well as their educational and extracurricular opportunities. All of this, taken together, is why a safe and effective vaccine for COVID-19 is needed specifically for our children.

Thank you very much for the opportunity to present to you today. I will now turn the presentation over to Dr. Miller.

**DR. JACQUELINE MILLER:** Thank you, Dr. Anderson. Good morning. My name is Jacqueline Miller, and I'm the therapeutic area head for infectious diseases at Moderna. I'm also a pediatrician. So, it gives me great pleasure to speak to you about the

clinical data generated as part of our pediatric clinical development program for mRNA-1273. Our pediatric development program includes two clinical studies, which incorporated feedback from the FDA and this vaccine's advisory committee.

Study 203 evaluated adolescents 12 to 17 years of age at the 100-microgram dose. It enrolled more than 3,700 participants, nearly 2,500 of whom received mRNA-1273. Study 204 enrolled children 6 months to 11 years of age, and we will only discuss the children 6 years to 11 years of age today. More than 3,300 children received the selected 50 microgram dose. It enrolled more than 5,800 children 6 to 17 years of age, who received 1273 establishing a substantial prelicensure safety database.

The median safety follow-up times in each age stratum met the FDA recommendations for at least two months after the final dose in at least 1,000 vaccinated individuals. In the 203 study, 100 micrograms was the only dose evaluated, and the entire study was conducted as a double-blinded placebo-

controlled trial. The participants in this trial had a median safety follow-up time of 11.1 months.

In study 204, lower doses of mRNA-1273 were investigated in an open-label dose-escalation design. The second part of the study then evaluated the selected dose as compared to placebo control in a double-blinded fashion. The median follow-up was nearly 8 months for the dose-ranging portion and 5.6 months for the larger study cohort.

Both studies, 203 and 204, included a primary safety objective. Specific safety endpoints included solicited local and systemic adverse events which were collected for seven days post-vaccination. Unsolicited adverse events were captured for 28 days, and serious medically attended and adverse events of special interest were followed throughout the entire study.

Let's talk about the follow-up for myo- and pericarditis in more detail. Myocarditis first emerged as a post-authorization safety signal when both clinical studies were still ongoing. We updated our fact sheets, investigator brochures, and informed

consent forms to increase awareness amongst investigators, study participants, and their parents. These conditions were also specified as adverse events of special interest to ensure that they would be reported rapidly.

To further increase the sensitivity of detection, a script was developed to ask about the symptoms of myocarditis during safety follow-up calls on Day 8 and Day 36 post-vaccination. The clinical database was also actively reviewed for symptoms, which may have reflected myocarditis. Events were submitted to an independent Cardiac Event Adjudication Committee or CEAC, composed of expert cardiologists.

Two overlapping approaches were used to evaluate all unsolicited AEs for potential cases of myo- and pericarditis. First, we used the standard MedDRA queries, and second, we developed an algorithm that was generated using MedDRA terms included in the CDC case definitions. Our ongoing post-authorization safety studies continue to capture myo- and pericarditis as adverse events of special interest.

Vaccine effectiveness was a primary objective in both studies, and it was successfully inferred by meeting pre-defined immunogenicity criteria, which were agreed with the FDA. In each age group, immune responses were compared to a subset of adults 18 to 25 years of age from the 301 study, which demonstrated the efficacy of mRNA-1273 against SARS-CoV-2. The younger adult subset was chosen to ensure a sufficiently high bar for the inference of vaccine effectiveness given that immune responses in the younger adults have been observed to be higher than those in older adults.

There were two noninferiority criteria. First, the lower bound for the GMT 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 GMT ratio be at least 1.0. Second, the lower bound of the group difference in seroresponse rates, which were defined as a four-fold rise from baseline titers, had to be greater than minus ren percent with a point estimate greater than minus five percent.

Evaluation of efficacy was a pre-specified secondary objective. As in the 301 study, there were two case definitions applied: the CDC case definition, which requires one systemic or respiratory symptom; and the 301 case definition, which required two systemic or one respiratory symptom. Both case definitions 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-19 than adults.

As these studies were conducted, an efficacy follow-up was performed. The predominant SARS-CoV-2 strain changed over time, and the efficacy results must be interpreted in this context. During Study 301, the original strain was almost exclusively circulating. The efficacy follow-up for adolescents was conducted when the original strain and Alpha variant were dominant, and the 6 to 11 year of age cohort was followed when the Delta variant was dominant.

Now, I would like to review the clinical data from Study 203 in adolescents. A total of 3,732

adolescent participants were randomly assigned 2:1 to receive either 100 micrograms of mRNA-1273 or placebo. The dose level and schedule were identical to that administered in Study 301 with each treatment group receiving two doses administered one month apart. Participants have now received a booster and are being followed for an additional 12 months.

This slide shows the demography in the mRNA-1273 and placebo groups. Overall, the two groups were well-balanced.

Now, let's discuss the safety profile in adolescents. This slide presents the percentage of participants reporting solicited local reactions, which include injection site pain, erythema, swelling, and axillary swelling or tenderness after Dose 1 and 2. The light blue depicts the mRNA-1273 group as compared to the placebo group in gray. The lower row presents the results from 301 young adults with the mRNA-1273 group in dark blue.

Injection site pain was the most commonly reported solicited local adverse reaction after either

injection. The majority of reported events were Grade 1 to 2 in severity and lasted for a median of three days. Reactions were reported at approximately the same frequency after Doses 1 and 2 and were reported more frequently in the mRNA-1273, than in the placebo group. These reactions were also reported more frequently in adolescents than in young adults. This slide shows the solicited systemic reactions.

Headache and fatigue were the most commonly reported adverse reactions followed by myalgia and chills. The majority is systemic reactions were Grade 1 to 2 in severity with a median duration of two days. Consistent with the established safety profile of mRNA-1273, systemic reactions were reported more frequently after Dose 2 than Dose 1. These reactions tended to be reported at a similar or a lower rate in adolescents than in young adults. This suggests that the reactogenicity profile of the 100-microgram dose in adolescents is acceptable and generally comparable to that observed in young adults.

This slide details the percentages of

unsolicited adverse events reported up to 28 days after vaccination. Twenty-one percent of participants in the mRNA-1273 and 16 percent in the placebo group reported unsolicited AEs, and 13 percent and 6 percent respectively were considered by the investigator to be potentially vaccine-related.

This imbalance was primarily driven by reports of lymphadenopathy and injection site reactions. The percentage of medically attended events is similar between the two groups. There were very few SAEs, severe AEs, or AEs leading to discontinuation, and no vaccine-related SAEs or deaths were reported. Long-term safety data were also collected with a median follow-up of 11.1 months after Dose 2. The adverse event profile was typical for this age group, and no new safety concerns were identified.

The most commonly reported medically attended event was COVID-19, although, importantly, there were no serious adverse events of COVID-19. This increased rate of COVID-19 likely reflected the Omicron surge and the fact that these study participants were nearly one

year after their second vaccination. There were no confirmed cases of myo- or pericarditis in the long-term follow-up period. Given the importance of these events, I'd also like to discuss our ongoing post-authorization surveillance, as mRNA-1273 is authorized for adolescents in 42 countries worldwide.

So let's look at the rates of myocarditis post-vaccination reported per million doses administered. These data come from our global safety database analyzed by age cohort, dose number, and gender with males depicted in blue and females depicted in pink. Consistent with other reports in the published literature, we see a higher reporting rate after Dose 2 and in males. The highest rates were in males 18 to 24 years of age after Dose 2 with approximately 43 cases per million doses, and there were 13.3 cases per million doses in adolescents.

Before comparison, Block, et al., recently reported the incidence of myocarditis after SARS-CoV-2 infection. The incidence of myocarditis in adolescents and young adult males diagnosed with SARS-CoV-2 is over

500 cases per million, suggesting that the rate is substantially higher than after Dose 2 of mRNA-1273.

Now, we will review the primary effectiveness objective. The co-primary hypothesis was to demonstrate that the immune response in adolescents was non-inferior to the young adult cohort of the 301 study in which efficacy against COVID-19 was demonstrated.

The first criterion was the GMT ratio of the adolescents over the young adult group. The observed GMT ratio was 1.1 with a lower limit of 0.9. The second criterion was the group difference in seroresponse rates. The rate was 98.8 percent in the adolescent group and 98.6 percent in the adult group with a difference of 0.2 percentage points and a lower limit of 1.8 percent. Therefore, the primary effectiveness hypothesis was met.

Now, we will discuss vaccine efficacy, which was evaluated as a secondary objective. In terms of the case definition used by the CDC, there were seven cases reported in the placebo group and one case reported in the mRNA-1273 group with an observed

efficacy of 93.3 percent. If the more stringent case definition from Study 301 is used, there were four cases reported in the placebo group and zero cases reported in the mRNA-1273 group. We observed vaccine efficacy as 100 percent.

In summary, the mRNA-1273 vaccine was well tolerated in adolescents with a reactogenicity profile similar to that in the younger adult cohort of Study 301. Solicited adverse reactions were mostly Grade 1 to 2 in severity with a median duration of two to three days. No SAEs reported within 28 days of vaccination were considered vaccine-related, and there have been no deaths or cases of myocarditis in the mRNA-1273 group through 11 months median follow-up.

The co-primary immunogenicity objectives were met. Immune responses in terms of GMT ratio and seroresponse rates were non-inferior to the young adults from Study 301. Therefore, vaccine effectiveness was successfully inferred based on immunobridging. The vaccine efficacy in adolescents was 93.3 percent according to the CDC case definition

and 100 percent according to the case definition from Study 301.

I would now like to hand this presentation over to Dr. Rita Das to review the clinical data in children 6 to 11 years of age.

**DR. RITUPARNA DAS:** Good morning. My name is Rota Das, and I'm the vice president of COVID-19 vaccines at Moderna. I'm also a pediatrician. I'm pleased to be here today to present to you the safety, immunogenicity, and efficacy data from Study 204 in children 6 through 11 years of age. Study 204 was conducted in two parts: first to identify the correct dose of mRNA-1273 in children 6 to 11 years and then to evaluate that dose in a randomized placebo-controlled study.

In Part 1, two doses of mRNA-1273 were evaluated in an open-label design. The lower 50 microgram dose was selected as it showed an acceptable tolerability profile and demonstrated a high likelihood of meeting the pre-specified immunogenicity success criteria. After Part 1 was completed, a DSMB meeting

occurred to ensure the committee's concurrence with the selected dose. Part 2 was designed to randomize children in a three-to-one ratio to receive either mRNA-1273 or saline placebo.

The data we will present today focused on the randomized phase of Study 204, which evaluated the two-dose 50-microgram primary series in children 6 to 11. All study participants will be followed for 12 months after their last dose of mRNA-1273.

Here are the demographics for children ages 6 to 11. The groups were well-matched in the vaccine and placebo recipients. The mean age in both groups was 8.5, and there was a good balance of males and females.

Next, I'll review the safety findings. This slide shows the solicited local reactions in children 6 to 11 years. The mRNA-1273 group is shown in blue, and the placebo is in gray. Pain was the most common effect with similar rates in severity following Dose 1 and Dose 2. Most local AEs including pain were Grade 1 or Grade 2 with few Grade 3 reactions. The median duration of local adverse reactions for this age group

was two to three days.

Turning now to the systemic reactions. Fatigue and headache were the most commonly reported systemic adverse reactions. Reporting rates for headache and fatigue were similar to those seen in adolescents and young adults. The rest of the systemic adverse reactions were reported at lower rates compared to the young adults.

Rates of systemic adverse reactions post-Dose 1 were often similar to placebo. Among vaccine recipients, systemic adverse reactions were reported more frequently post-Dose 2 than post-Dose 1. Again, events were mostly Grade 1 and Grade 2 in severity with a median duration of two to three days.

Next, I will discuss the unsolicited adverse events. Presented here are the unsolicited adverse events reported up to 28 days after any injection in children 6 to 11 years. Thirty percent of participants in the vaccine group compared to 25 percent of participants in the placebo group reported any AE. The imbalance in AEs was primarily driven by local AEs and

axillary swelling or tenderness similar to what was seen in the adolescents.

Medically attended adverse events were similar among the two groups at 13 and 14 percent. There were no SAEs considered by the investigator to be related to vaccination, and there were no fatal AEs, events of MIS-C, or myocarditis or pericarditis reported.

We have data now for long-term safety follow-up for a median duration of 5.6 months among the original vaccine recipients. This table has the accumulative incidence of the unsolicited AEs through this time. No new safety signals were observed, and there were no death-related SAEs or adverse events of MIS-C or myocarditis in the original vaccine group.

We also collected safety on the original placebo recipients who got vaccine in the crossover phase. There was one related SAE after vaccination of ileus reported in a participant with a complex GI medical history from the placebo crossover group.

Next, we will turn our attention to the immunogenicity data. Immunogenicity was the primary

objective of this study. After the two-dose 50-microgram series among the 6- to 11-year-old group, the GMT was 1,600 in the older children compared to 1,300 in young adults. This resulted in a GMT ratio of 1.2 meeting the prespecified noninferiority criteria. The seroresponse rate was 99.1 percent, also meeting the noninferiority seroresponse criteria.

On to the efficacy assessment, which were a secondary objective of the study. Assessment of placebo-controlled vaccine efficacy in the 6- to 11-year-old group was limited due to the authorization of another COVID-19 vaccine. Per the study protocol, participants were unblinded then to offer them access to mRNA-1273. Only seven cases were captured in the per-protocol population which was the post-Dose 2 population and had a 1.8-month blinded median follow-up time. The point estimate of efficacy there was 76.8 percent with a wider confidence interval.

I'm going to talk to you about the assessment that was conducted in the mITT population, which was based on a higher number of cases, 25 cases. The mITT

calculation is specifically a more conservative calculation because it counts cases starting 14 days post-Dose 1. This provided an additional month for case accrual. The overwhelming majority of study participants did, however, receive the second dose of vaccine.

Here are the efficacy results for the mITT cohort. Efficacy was high at 88 percent using the broad CDC definition, and at 92 percent using the more stringent 301 case definition. Additionally, as Dr. Miller showed, this trial was conducted during the Delta period in the U.S. So, this data represents direct efficacy against the Delta variant.

In summary, for the 6- to 11-year-old group, mRNA-1273 was well-tolerated. Solicited adverse reactions were mostly Grade 1 to 2 with a median duration of two to three days. There were no related SAEs within 28 days of any vaccination in the original vaccinated group. No death, myocarditis, pericarditis, or MIS-C have been reported among vaccine recipients through 5.6 months of follow-up.

The pre-specified co-primary immunogenicity objectives were met. GMTs and seroresponse rates in the children 6 to 11 years were non-inferior to young adults 18 to 25. Therefore, vaccine effectiveness was successfully inferred based on immunobridging.

Finally, vaccine efficacy of mRNA-1273 against COVID-19 assessed during the Delta wave ranged from 88 to 92 percent. I will now turn the presentation back over to Dr. Miller.

**DR. JACQUELINE MILLER:** Thank you, Dr. Das. I'll now summarize our presentation. The slide depicts the immune responses ranging from young adults 18 to 25 to adolescents and children in Studies 203 and 204. The GMT ratios compared to young adults were 1.1 and 1.2 successfully meeting all primary effectiveness objectives. The immune responses to mRNA-1273 have been remarkably consistent across age groups despite administering lower doses to children 6 to 11 years of age.

Additional support is provided from the efficacy analysis. Vaccine efficacy utilizing the CDC

case definition was 88 to 93.3 percent and using the Study 301 case definition was 92 to 100 percent. As a reminder, vaccine efficacy in adults from Study 301 was 93 percent against symptomatic COVID-19 and 98 percent against severe disease.

Although we did not observe any severe cases in either age group at the time of the data cutoff, this consistency with the efficacy in adults leads us to believe that protection against severe disease will also be similar.

Let's review the benefit-risk profile of mRNA-1273 in these age groups. This slide shows the estimated number of hospitalizations and ICU stays prevented by one million second doses of mRNA-1273 at current levels of SARS-CoV-2 circulation. This model, which is based on reported COVID-19 hospitalization rates from the CDC predicts 95 hospitalizations would be prevented per million doses of mRNA-1273 administered to children 5 to 11 years. In adolescents, the model predicts that 200 hospitalizations would be prevented.

Now, looking at the risk of myocarditis, which is based on a post-authorization safety study, the expected number of myocarditis cases per million doses of mRNA-1273 would be 46 in adolescents. The risk for 6- to 11-year-olds could not be estimated because no cases of myocarditis have been reported in our post-authorization safety study. These data support that the benefit-risk profile of mRNA-1273 in these cohorts is strongly favorable.

We continue to evaluate the safety and effectiveness of mRNA-1273 in adolescents and school-aged children. The booster phases of Studies 203 and 204 are ongoing where children 12 to 17 years of age are receiving a 50-microgram booster dose, and children 6 to 11 years of age are receiving a 25-microgram booster dose administered at least four months after the second dose.

We will continue to follow these participants for 12 months after the booster dose. Four of our ongoing post-authorization safety studies are evaluating myocarditis. Two of these studies are also

evaluating other safety endpoints in both the U.S. and the European Union. We will also extend these studies and the Kaiser Permanente vaccine effectiveness study to younger age groups.

The totality of clinical and post-authorization data from our development program support that the benefits of mRNA-1273 in school-aged children and adolescents outweigh the known potential risks.

mRNA-1273 was generally well-tolerated with a safety profile consistent with that observed in young adults, and no new safety concerns have been identified. Our pediatric studies were designed to meet FDA criteria for the inference of vaccine effectiveness compared to young adults as the vaccine efficacy and a diverse population of adults have already been demonstrated. In both age groups, the co-primary immunogenicity hypotheses were met. In addition, there was evidence of efficacy against COVID-19 conferred by mRNA-1273 ranging from 88 to 100 percent.

Our pediatric development plan has met all FDA

recommendations for authorization in adolescents and children 6 to 11 years of age. We have enrolled more than 8,000 children with more than 5,800 receiving at least one dose of mRNA-1273 and a median duration of at least 5.6 months in each age stratum. Vaccine effectiveness was successfully inferred in both age strata and vaccine efficacy estimates are similar to adults.

We have established a robust plan to continue to evaluate safety and effectiveness post-authorization, and the benefit-risk profile in both age groups is strongly favorable.

We are requesting emergency use authorization of mRNA-1273 as a two-dose primary series for the prevention of COVID-19 caused by SARS-CoV-2 in adolescents 12 to 17 years at the 100-microgram dose level and children 6 to 11 years at the 50-microgram dose level. The proposed two-dose primary series will be administered one month apart consistent with our approved dosing schedule in adults.

I'd like to conclude this presentation with an

enormous and heartfelt thank you to the entire community that made these studies possible. Without the support and sacrifice of our study investigators, their personnel, our colleagues at BARDA, NIH, and the COV-PN, and most importantly, the children and their families, this submission package would not have been possible. Thank you.

I'll now hand over to Dr. Das to take any questions you might have.

**Q&A SESSION**

**DR. ARNOLD MONTO:** Thanks to all of the presenters for being very succinct and getting us almost back on schedule. My question is about the immunobridging and what the target was. This was the ancestral Wuhan strain, correct?

**DR. RITUPARNA DAS:** Yes. It was the neutralization antibody for the ancestral Wuhan strain.

**DR. ARNOLD MONTO:** Right. You are currently also looking at boosters in terms of any variants that

might be coming along?

**DR. RITUPARNA DAS:** Yes. Yes. We have already -- yes. We have -- we do already have one --

**DR. ARNOLD MONTO:** I'm thinking of Omicron.

**DR. RITUPARNA DAS:** Yes, I know. We do have boosters already completed in the adolescents and the 6- to 11-year-old group. We are starting a study in the under 6 group, which will evaluate both the original vaccine booster as well as our Omicron-containing vaccine booster.

**DR. ARNOLD MONTO:** Thank you. We're not going to be able to handle all the questions now because the key in our timing is to get to the open public hearing at exactly 1:00. We will have more time to ask the sponsors questions, so I will go as long as we have some time available. First to Dr. Gans.

**DR. HAYLEY ALTMAN-GANS:** Hi. Thank you for those wonderful presentations. I appreciate it. Given that the questions before us could be helped with the data from all of your international groups that you've already vaccinated in multiple countries with 6.4

million doses given to the 12- to 17-year-old and 300 in children, and I'm sure also booster doses, so it would be helpful to see that data provided to us and so we could understand on a greater level other than the 2,000 that were done within the studies.

That's question 1. Question 2 relates to data related to a 50-microgram dosing that maybe was done in the 12- to 17-year-olds in some preliminary in the adult studies. The immunogenicity of that dose appears to be fairly equivalent to the 100. So, I'm curious about that data, if there -- certainly, it elicited a T cell immunity.

**DR. RITUPARNA DAS:** Yes. So, Dr. Gans, I'll take your second question first. So, the second question, you asked about the 50-microgram dose that was evaluated in adults. So, this was in our Study 201 Part A. We did see a difference in immunogenicity between the 50 and the hundred micrograms with the hundred-microgram dose being more immunogenic than the 50-microgram dose, kind of confirming our dose selection going forward. We have started a study for a

50-microgram dose in adolescents.

That's arm in enrolling incredibly slowly, and, you know, we are still setting up to meet the same FDA immunobridging criteria, the bridging for 18 to 25 from our CoV study with the point estimate of 1. So, we've built in a rescue dose in that 50-microgram dosing study in adolescents in case that bridging is not successful, but I don't have an estimate of when that will read out because it is enrolling slowly.

So, next, your second question, was that about effectiveness in our pediatric and adolescent vaccinees internationally? Is that what you were asking about?

**DR. HAYLEY ALTMAN-GANS:** Yeah. Because it's relevant to the variants that are circulating at this point.

**DR. RITUPARNA DAS:** Yes. Yes. Absolutely. So our primary effectiveness work is with the Kaiser Permanente health system, which is in the U.S. We have been looking in the U.K. and in Spain who have done a lot of really nice effectiveness work for adolescents. The data from Spain is just coming out. There was just

recently a publication about it.

It's extremely positive during the Omicron wave, very consistent with the adult data that we saw in the Kaiser system. Some more work needs to be done to break that out by the age groups. There's promising data from the U.K., and then we are looking for more collaborators for the 5 to 12 group.

**DR. HAYLEY ALTMAN-GANS:** Thank you.

**DR. ARNOLD MONTO:** Dr. Reingold.

**DR. ARTHUR REINGOLD:** Hello, can you hear me?

**DR. ARNOLD MONTO:** Yes.

**DR. ARTHUR REINGOLD:** So, very nice presentation. My question relates to the slide showing the substantial better benefits compared to risks and hospitalizations averted and things like that. It went by kind of quickly, and I'm not sure what assumptions are made there about VE and duration of protection and protection against Omicron.

But it would be nice to see those sorts of calculations with conservative estimates of how long the protection lasts, how high the efficacy will be

against Omicron. I don't know how robust. I assume you would still see pretty good benefits compared to risks, but it would be good to see across a range of estimates of VE and duration of protection of VE against Omicron. Thank you.

**DR. RITUPARNA DAS:** Okay. So can I get that slide back up? So, this slide does show the benefit-risk during the relatively current transmission period. So, this is data as of April 2nd. So, the estimate for vaccine effectiveness against hospitalization in this model is consistent with what we've seen in adults. It estimates a 72 percent vaccine effectiveness against Omicron.

Now, you were asking about the durability of protection for the vaccine particularly against Omicron. Was that the specific of your question? I apologize for a little bit of time to get the slide up. While we're waiting for that, did I capture your question properly?

**DR. ARNOLD MONTO:** Yeah. We're going to have to move on. We're really tight on time here. Oh,

there it is.

**DR. RITUPARNA DAS:** Yes. So, here, we have the slide up. Again, as I mentioned, this estimates a vaccine effectiveness against Omicron hospitalization of 72 percent, and the data is of the circulation as of April 2nd.

**DR. ARNOLD MONTO:** Okay. I guess we've settled this one. We're going to have to move on to Dr. Berger's question. Dr. Berger?

**DR. ADAM BERGER:** Hi. Just checking if you can hear me first.

**DR. ARNOLD MONTO:** Yes.

**DR. RITUPARNA DAS:** Yes.

**DR. ADAM BERGER:** Great. Thank you. This is a clarification question on the immunogenicity data for 12- to 17-year-olds. I noticed that you presented the demographic information for the safety set, but you didn't present the demographic information for the immunogenicity subset. I noticed in the data that FDA provided in their brief that for Black or African Americans, it looked like it was only 1.2 percent of

the population that was involved in that subset.

So, I'm just wondering if you might comment on the applicability of the immunogenicity, immunobridging data specifically for Black adolescents. Part of the reason is because if you go back to Dr. Ruth Gelles's data, 70 percent of this population is unvaccinated at the moment. So, I really want to understand the applicability and the effectiveness there. Thanks.

**DR. RITUPARNA DAS:** Yes. Absolutely. So, enrolling a diverse population is very important to us at Moderna. For our adult population, our CoV study, we had a very nice representation of all races and ethnicities that were consistent with the U.S. population. For our adolescents, as you mentioned, we did set specific targets, and I'll show you our 6 to 11, it was actually -- there was better representation as we kind of moved forward in our pediatric program.

Can I get the slide up for immunogenicity by race and ethnicity for adolescents? Oh, here we go. Yeah. So, here's the immunogenicity by race and ethnicity for adolescents. It's very consistent with

what we saw in the CoV study. In our CoV study population, we saw no differences by race or ethnicity for immune responses.

Here, as you say, in the immuno subset, there's not a large representation of Black or African American. The immunogenicity there is very consistent as it was in our adult. Then I'll show you 6 to 11 as well, and -- can I get that slide up, too, please? So, in 6 to 11, again, it's also very consistent across the board by race and ethnicity.

**DR. ADAM BERGER:** Okay. Just a quick follow-up. Is there additional data from the international subsets that might substantiate some of the 12- to 17-year-old data a little bit further?

**DR. RITUPARNA DAS:** So, we don't have -- so, these two trials were conducted exclusively in the U.S. The international (inaudible) outside of our trials, and we have not done any immunogenicity in our validated neutralization assays.

**DR. ADAM BERGER:** Thank you.

**DR. ARNOLD MONTO:** I'm sorry. But we're going

to have to go on because of this hard stop we've got for the oral hearings. I want to point out that the questions of the FDA presentation that we're going to hear right now are all in the afternoon. So, we're not discriminating in any way about where we have the questions.

Next, we hear from Dr. Rachel Zhang who will give us the FDA presentation on the effectiveness and safety of Moderna COVID-19 vaccine in children and adolescents 6 through 17 years of age. Dr. Zhang?

**FDA PRESENTATION: FDA REVIEW OF EFFECTIVENESS AND SAFETY OF MODERNA COVID-19 VACCINE IN CHILDREN AND ADOLESCENTS 6 THROUGH 17 YEARS OF AGE**

**DR. RACHEL ZHANG:** Thank you, Dr. Monto. Good morning, everyone. I'm Rachel Zhang. I'm a medical officer in the Division of Vaccines of Related Products and Complications at the FDA. Today, I'll be presenting the FDA review of effectiveness and safety of the Moderna COVID-19 vaccine in children 6 through

17 years of age under EUA.

To start off with, I want to acknowledge the work of everyone at the FDA that contributed to this review and the presentation.

So, this is an outline of the presentation today. I will first start with a brief background and then take you through the data in adolescents followed by data in 6 to 11 years. I will then provide a summary of the planned pharmacovigilance activities before concluding with an overall summary of the benefit and risks for the 6 through 17 years age group.

So, starting with the background, the Moderna COVID-19 vaccine is an mRNA vaccine encoding the SARS-CoV-2 spike glycoprotein formulated in lipid particles. The vaccine was licensed as Spikevax on January 31st, 2022, for individuals 18 years of age and older.

The EUA requests for ages 6 through 17 years, included data from two studies. P203 was a Phase 2/3 randomized, placebo-controlled study to evaluate the safety and effectiveness of mRNA-1273 in healthy adolescents ages 12 to 17 years. Data submitted from

this study included blinded safety and efficacy data through a cutoff date of May 8th, 2021, with the subsequent data cutoff for safety of January 31st, 2022.

Study P204 was a phase 2/3 multipart study including an open-label, dose-escalation, and age de-escalation phase, and a randomized, observer-blind, placebo-controlled phase to evaluate the safety and effectiveness of mRNA-1273 in healthy children 6 months through 11 years.

For today's presentation, I will only focus on the 6 through 11 years age group included in the study. Data submitted for this age group from Study P204 included blinded safety and efficacy data through a cutoff date of November 10th, 2021, with a subsequent data cutoff for safety of February 21st, 2022.

Displayed on this slide are all the age groups evaluated in Studies P204 and P203 and the associated dose levels, study sample size, and study endpoints. Again, for today's presentation, I will only focus on adolescents 12 through 17 years and children six years

through 11 years as shown in the right-most columns.

These are the study objectives and endpoints from the two pediatric studies. In both studies, solicited local and systemic reactions were followed for seven days after each dose. Unsolicited adverse events were followed for 28 days after each dose. A medically attended adverse event, serious adverse events, and adverse events of special interest will be followed through the end of the study.

Starting with Study P204, active monitoring for myocarditis and pericarditis was included in the protocol. Scripted safety calls were conducted at seven days after each vaccination and at every four weeks thereafter to specifically solicit for symptoms which may be associated with myocarditis and pericarditis. In addition, an independent Cardiac Event Adjudication Committee was established to assess all suspected cases of myocarditis and pericarditis.

The primary endpoint for both studies was comparison of immune response as measured by GMT ratio and seroresponse rate difference between the pediatric

age groups and young adults from P301. Clinical efficacy was analyzed descriptively as secondary endpoints.

As mentioned previously, the primary endpoints of the study was comparison of neutralizing antibody responses at one-month post-Dose 2 between a subset of adolescent participants or a subset of participants 6 to 11 years compared to those in a similarly sized subset of young adults 18 through 25 from Study P301 and whom vaccine efficacy was demonstrated.

Neutralizing antibody response is measured using a validated pseudovirus neutralization assay against Washington 1/2020 Wuhan strain with D614G mutation, which I will refer to from now on as the ancestral strain. Immunobridging endpoints and statistical success criteria will be discussed in the next two slides.

So, the first co-primary immunogenicity endpoint for the two studies is the GMT ratio of SARS-CoV-2 neutralizing titers in the pediatric age group at one-month post-Dose 2 compared to those in young adults

18 to 25 years.

The success criteria for this endpoint is considered to be met if the lower limits of the two-sided 95 percent confidence interval for GMT ratio is greater than 0.67 and the point estimate is greater than 0.8.

The second immunobridging endpoint was seroresponse difference between the -- I apologize. This slide keeps skipping ahead. There we go. Yes. So the seroresponse rate difference between the pediatric age group and the young adult comparator group.

For Study P203, the protocol-defined seroresponse definition with a change from below the lower limit of quantification to greater than or equal to LLOQ or at least 3.3-fold rise in participants with titers equal to or above LLOQ at baseline.

For Study P204, the seroresponse definition was the more conventional definition of four-fold rise from baseline where baseline titers below LLOQ was set to LLOQ for this analysis. The success criteria is

considered met for this endpoint if the lower limits of the 95 percent confidence interval for the difference in seroresponse rate is greater than negative ten percent with a point estimate greater than negative five percent.

So, for your reference, this slide provides the two definitions of COVID-19 used for the descriptive analysis of vaccine efficacy.

To meet the CDC definition, the participant needs to have one of the following systemic symptoms listed and a positive RT-PCR for SARS-CoV-2.

For a P301 case definition in addition to positive RT-PCR, at least two systemic symptoms or at least one of the listed respiratory signs or symptoms must be present. The P301 definition was the same definition used in the primary efficacy endpoint for the adult efficacy studies.

This slide shows the most pertinent analysis populations used in the two studies. I promise I'm only clicking once with each slide. I don't know why it's skipping ahead, but hopefully -- so, the per-

protocol immunogenicity subset was used for the primary immunogenicity endpoints from immunobridging.

The per-protocol set for efficacy was used for the evaluation of the descriptive efficacy endpoint. The solicited safety sets contributed to the evaluation of solicited adverse events after each dose, and the safety set was used for evaluation of all remaining safety analysis, including unsolicited adverse events, medically attended adverse events, serious adverse events, and adverse events of clinical interest.

So, going into the P203 study design. In Study P203, approximately 3,700 participants, 12 through 17 years were randomized 2 to 1 to receive 2 doses of 100 micrograms of mRNA-1273 or saline placebo given one month apart. This slide provides a follow-up time for study participants. Based on the data cutoff date --

**MR. MICHAEL KAWCZYNSKI:** Dr. Zhang, if you'd like, I can move your slides for you, just say next slide.

**DR. RACHEL ZHANG:** Okay. Sure. Thank you so

much. I don't know why it's doing that. So, based on this data cutoff of May 8th, 2021, the median duration of blinded follow-up for safety and efficacy was 53 days post-Dose 2. Around the time of this data cut, an alternate COVID-19 vaccine was authorized for use in this age group, and the study protocol was subsequently revised to allow study participants to be unblinded to seek available vaccine under EUA and later for placebo recipients to cross over to receive mRNA-1273, thus effectively ending the blinded, placebo-controlled phase of the study.

A later data cut on January 31st, 2022, was done to allow for review of additional safety data with longer follow-up time.

Based on the January data cut, the median duration of follow-up including both blinded and open-label follow-up was 312 days post-Dose 2 among vaccine recipients. Follow-up duration for the placebo group is not shown as the majority of these participants discontinued from the study to receive an alternate COVID-19 vaccine under EUA or crossed over to receive

mRNA-1273. Next slide, please.

Demographics of adolescent participants in Study P203 are displayed on this slide. Demographic characteristics were comparable between the vaccine and placebo groups. The majority of study participants were white and non-Hispanic. All participants in the study were enrolled in the U.S. Approximately seven percent of study participants were obese, and approximately six percent of study participants had evidence of prior SARS-CoV-2 infection at baseline. Next slide.

I will go on to the immunogenicity data for this study. Next slide.

Shown here, the co-primary endpoint of ratio of neutralizing antibody GMTs in the adolescent group compared to young adults at one-month post-Dose 2. The study met the prespecified success criterion of lower bound of GMT ratio greater than 0.67 and a point estimate greater than 0.8. Next slide.

This slide shows the co-primary endpoint of differences in seroresponse rates in the adolescent

group to young adults at one-month post-Dose 2. The study met the prespecified success criterion of lower bound greater than negative ten percent and a point estimate greater than negative five percent. The results are the same based on the pre-specified seroresponse definition of 3.3-fold rise from baseline and the post-hoc seroresponse definition of four-fold rise in baseline.

The GMTs in seroresponse rate differences at Day 57 were generally similar across demographic subgroups although the small number of participants in some subgroups limit the interpretation of the results. Next slide.

Results for the subgroup analyses of GMTs by baseline SARS-CoV-2 status are displayed here. In the small number of participants who had evidence of prior SARS-CoV-2 infection at baseline in the immunogenicity subsets, there was a higher immune response observed on Day 57 compared to participants without evidence of prior SARS-CoV-2 infection. Next slide.

In a study published by the sponsor,

immunogenicity against Omicron was in a subset of 20 adult participants from P301 and 20 adolescent participants from P203 using a non-validated pseudovirus neutralization assay and compared to the immune response against the ancestral strain. As you can see in this figure, at four weeks post-Dose 2, GMTs against Omicron were 28-fold lower compared to the ancestral strain in adults 18 years and older compared to 11-fold lower in adolescents 12 through 17 years.

It is unknown whether these results translate to differences in clinical efficacy against Omicron between adults and the adolescent population after two doses of mRNA-1273. Of note, these data have not been independently verified by the FDA. Next slide.

Next, I will go on to the efficacy data. Next slide.

Vaccine efficacy was descriptively analyzed at the secondary endpoint in the study with the data cutoff date of May 8th, 2021, entering a period when the ancestral strain and then the Alpha variant was the predominant circulating strain in the U.S.

It shows here vaccine efficacy results for the first occurrence COVID-19 starting 14 days after Dose 2 based on the P301 and CDC case definitions. These results appear to be consistent with the vaccine efficacy observed from adults in the adult efficacy study. However, the small number of COVID-19 cases, especially using the P301 definition, resulted in large confidence intervals. A final efficacy analysis of the blinded phase of the study was based on the data cutoff of May 31st, 2021, and was comparable to the results obtained based on the original data cut.

No severe COVID-19 cases were reported during the study. Among the approximately six percent of total participants with evidence of prior SARS-CoV-2 infection at baseline, no participants developed COVID-19 starting 14 days after Dose 2. Next slide.

Next, I will go on to the safety data. Next slide.

Shown here are the frequencies of solicited local reactions following each dose. The majority of these events occurred within the first one to two days

after each dose and persistence for a median of three days. Next slide.

This table shows some of the systemic adverse reactions following each dose. Systemic reactions occurred more frequently after Dose 2 compared to Dose 1. Headache and fatigue were the most frequently reported solicited systemic adverse reactions in vaccine recipients after any dose. Systemic reactions following any dose were mostly mild to moderate, and Grade 3 or 4 events were rare. Next slide.

Additional systemic adverse reactions are shown here. In general, solicited systemic reactions had a median onset of one to two days after vaccination and a median duration of two days. Next slide.

This table shows the frequency -- was there a slide before this? Yes, here. After Dose 1, among vaccine recipients solicited, systemic adverse reactions were commonly reported in participants who had evidence of prior SARS-CoV-2 infection at baseline compared to participants who did not have prior infection. Shown here are the average reactions with

the most notable difference after Dose 1 between the two groups.

Rates of solicited local reactions were similar after Dose 1 between the two groups except for axillary swelling or tenderness, which was also higher in the baseline SARS-CoV-2 positive group compared to baseline negative. Rates of solicited local and systemic reactions after Dose 2 were similar regardless of baseline SARS-CoV-2 status. Next slide.

This table shows the frequencies of unsolicited adverse events reported by adolescent participants in the study. There was a slightly higher rate of unsolicited AEs within 20 days of vaccination in the vaccine group compared to placebo. The observed difference was mostly driven by events consistent with injection site reactions and systemic reactogenicity. Frequencies have medically attended adverse events collected through the data calls were similar between the vaccine and placebo groups. Next slide.

FDA conducted standard MedDRA queries using FDA-developed software to evaluate for constellations

of unsolicited adverse event preferred terms that could represent some cardiomyopathy events. In addition to these standard MedDRA queries, the database was also queried using additional potentially cardiac-related preferred terms including symptoms listed in the CDC working case definition for myocarditis and pericarditis.

Events identified through this search included chest pains, dyspnea, palpitations, and syncope. A majority of these events reported in the study were not specific in nature, and very few participants who reported these events underwent cardiac workups for their symptoms. No events of myocarditis or pericarditis were identified in the study through the data cutoff of January 31st, 2022. Next slide.

Within 28 days after each dose, an imbalance in lymphadenopathy-related events was observed which were reported by 5 percent of vaccine recipients compared to 0.5 percent of placebo recipients. These events are plausibly related and consistent with a solicited adverse reaction of axillary swelling and

tenderness. There were no events of anaphylaxis reported in the study related to study vaccine. Next slide.

Next, we will move on to Study 204 in participants 6 through 11 years. Next slide.

Study P204 in children 6 to 11 years started with a Part 1, open-label, dose-escalation phase. Participants in this part of the study were dosed with either 50 micrograms or a hundred-microgram dose level of mRNA-1273. Because immunogenicity results from the 50-microgram dose group suggested that the prespecified noninferiority immunobridging criteria could be met in Part 2 with this dose level, and the safety profile was tolerable but also less reactogenic compared to the hundred-microgram dose. The 50-microgram dose level was chosen for evaluation in Part 2. Next slide.

In Part 2, the randomized, placebo-controlled, blinded portion of the study, approximately 4,000 participants 6 through 11 years were randomized 3 to 1 to receive two doses of 50 micrograms of mRNA-1273 or a placebo given one month apart. Next slide.

This slide provides a follow-up time for study participants in this study. Based on the data cutoff of November 10th, 2021, the median duration of blinded follow-up for safety and efficacy was 51 days post-Dose 2. Around the time of this data cut, an alternate COVID-19 vaccine was authorized for use in this age group, and a study protocol was revised to allow study participants to be unblinded and, for placebo recipients, the crossover to receive mRNA-1273, thus, effectively ending the blinded placebo-controlled phase of the study.

A later data cut on January 21st, 2022, was done to allow for review of additional safety data with a longer follow-up time. Based on the February data cut, the median duration of follow-up including both blinded and open-label follow-up was 158 days post-Dose 2 among vaccine recipients. Follow-up duration for placebo recipients was not shown as a majority of these participants crossed over to receive active vaccine. Next slide.

Demographics of children 6 to 11 years in

Study P204 are displayed on this slide. Demographic characteristics were comparable between the vaccine and placebo groups. The majority of study participants were white and non-Hispanic. Almost all study participants were enrolled in studies inside the U.S. Approximately 20 percent of study participants were obese, and approximately 9 percent of study participants had evidence of prior SARS-CoV-2 infection at baseline. Next slide.

Shown here is the co-primary endpoint of ratio of neutralizing antibody GMTs in the 6 to 11 years age group compared to young adults at four weeks pose-Dose 2. The study met the prespecified success criteria of lower bound for GMT ratio greater than 0.67 and a point estimate of GMT ratio greater than 0.8. Next slide.

This slide shows the co-primary endpoint and difference in seroresponse rate in the pediatric age group compared to young adults. The study met the prespecified success criteria of lower bound greater than negative ten percent and a point estimate greater than negative five percent. The GMT ratio and

difference in seroresponse rates across demographic subgroups were consistent with the results obtained based on the general study population, although some of these analyses were limited by small subgroup size. Next slide.

Results for the subgroup analyses of GMT site baseline SARS-CoV-2 status are displayed here. In the small number of participants who had evidence of prior SARS-CoV-2 infection at baseline in the immunogenicity subset, there was a higher immune response observed on Day 57 compared to participants without evidence of prior SARS-CoV-2 infections. Next slide.

Exploratory assessment of the immune response against the Delta variant using a qualified non-validated pseudovirus neutralization assay was conducted in a subset of participants 6 to 11 years in the open-label, Part 1 portion of the study. As shown in this table, GMT observed at four weeks post-Dose 2 against Delta was approximately 2.5-fold lower compared to those against the ancestral strain. This was consistent with the result observed in adults from

Study P301. Next slide.

In the same study showing the adolescent portion of this presentation, immunogenicity against Omicron and the ancestral strain was also assessed in a subset of 20 participants 6 through 11 years from P204. As you can see in this figure, at four weeks post-Dose 2, GMTs against Omicron were 22-fold lower compared to the ancestral strain in children 6 through 11, which was only slightly less compared to the 28-fold reduction observed in adults. Again, these data have not been independently verified by the FDA. Next slide.

Next slide will go on to the efficacy data. Next slide.

Vaccine efficacy was descriptively analyzed as a secondary endpoint in the study with the data cutoff date of November 10th, 2021, and during a period when the Delta variant was the predominant circulating strain in the U.S. Shown here are the vaccine efficacy results for the first occurrence COVID19 starting 14 days after Dose 2, based on the P301 and CDC case

definitions.

As a result of the authorization of an alternate COVID-19 vaccine for this age group and subsequent unblinding and crossover vaccination for placebo recipients, the median duration of blinded follow-up for efficacy was limited and vaccine efficacy cannot be reliably determined due to the small number of COVID-19 cases accrued, resulting in a wide 95 percent confidence interval.

No severe COVID-19 cases were 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 no mRNA-1273 participants developed COVID-19 starting 14 days after Dose 2. Analysis of vaccine efficacy including a population of participants with and without evidence of prior SARS-CoV-2 infection was similar to the vaccine efficacy results displayed above. Next slide.

Additional analysis of the efficacy endpoint were conducted to evaluate VE against COVID-19 based on

the CDC definition by time period, including starting any time after Dose 1, any time between Dose 1 and Dose 2, and any time after Dose 2. Given the longer time period and a broader population used for these analyses, a larger number of COVID-19 cases were accrued resulting in titer confidence intervals around the VE point estimate with a lower bound of 95 percent confidence interval both of zero. Next slide.

Next, I will go on to discuss the safety data. Next slide.

Shown here are the frequencies of solicited local reactions following each dose. Local adverse reactions were reported slightly more frequently following Dose 2 compared to Dose 1. The majority of these events occurred within the first one to two days after each dose and resolved within one to three days after onset. Next slide.

This table shows the systemic adverse reactions following each dose. The systemic reactions occurred more frequently and were more severe after Dose 2 compared to Dose 1. Headache and fatigue were

the most frequently reported solicited systemic adverse reactions in vaccine recipients after any dose. Reported events were mostly mild to moderate. There were no Grade 4 reactions reported. And in general, solicited reactions had onset one to two days after vaccination and a duration of one to three days. Next slide.

After Dose 1 among vaccine recipients, solicited systemic adverse reactions were more commonly reported in participants who had evidence of prior SARS-CoV-2 infection at baseline compared to participants who did not have prior infections. Shown here are adverse reactions with the most notable difference after Dose 1 between the two groups.

Rates associated with local reactions after Dose 1 was similar between the two groups, again, except for axillary swelling or tenderness, which was higher in the baseline positive group compared to baseline negative. Rates of solicited local and systemic reactions after Dose 2 were similar regardless of baseline SARS-CoV-2 status. Next slide.

This table shows the frequencies of unsolicited adverse events reported by participants in the study. There's a slightly higher rate of unsolicited AEs within 28 days after vaccination in a vaccine group compared to placebo.

Events reported by greater than one percent of participants in the vaccine group and by a higher proportion compared to the sequel where events consistent with the injection site reactions and upper respiratory tract infections. Frequencies of medically attended adverse events collected through the data cutoff were similar between the vaccine and placebo groups. Next slide.

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 intense 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

previously for the adolescent studies was also used for evaluation of the safety data set for participants 6 through 11 years. The events identified through the search included chest pain or discomfort, dyspnea, palpitations, angina pectoris, and cardiac flutter. Few participants underwent workups for their symptoms. Among the small number of participants who have cardiac evaluations for their symptoms, all were reported to be normal.

A majority of the events were not specific in nature, and many were associated with concurrent upper respiratory tract symptoms. None of the events identified met the CDC criteria for probable or confirmed myocarditis or pericarditis. Next slide.

Additional adverse events (inaudible) include lymphadenopathy-related events, which was reported by 1.9 percent of vaccine recipients and 0.6 percent of placebo recipients within 28 days of vaccination. This imbalance is consistent with the imbalance observed for solicited axillary swelling and tenderness in the injected arm. Abdominal pain including events under

the (inaudible) of abdominal pain, abdominal pain upper, and abdominal pain lower were reported by 1.1 percent of vaccine recipients and 0.6 percent of placebo recipients. All were mild to moderate in severity.

Related abdominal pain events all occurred within seven days of vaccination and were likely to be manifestations of systemic reactogenicity. There were no events of anaphylaxis reported in the study related to the study vaccine. Next slide.

In the blinded phase of the study, with a median duration of blinded follow-up of 51 days after Dose 2, serious adverse events were reported by 0.2 percent of participants in both the vaccine and placebo groups.

No SAE was assessed as related. Additional SAEs accrued during the open-label phase which represented a median duration of follow-up of 158 days post-Dose 2 revealed no concern in safety events. But one SAE of ileus with onset one day after Dose 2 in a medically complex participant with a history of

imperforate anus cecostomy, the vaccine contributions of onset cannot be excluded and was considered possibly related by the investigator and FDA. Next slide.

Next, I will go on to the pharmacovigilance. The sponsor submitted a pharmacovigilance plan to monitor safety concerns that could be associated with the Moderna 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 certain populations not included in the clinical study, long-term vaccinated effectiveness, and safety and interactions with other vaccines are areas the sponsor identified as missing information. From co-vigilance activities under the UA will be presented in more detail in the next few slides. Next slide.

The sponsor's pharmacovigilance activities include post-authorization surveillance studies. There are five post-authorization safety studies of myocarditis and pericarditis including subclinical myocarditis and one post-authorization vaccine

effectiveness study that included individuals 6 through 17 years of age. Next slide.

Pharmacovigilance activities include adverse events reporting. AE reporting under EUA may come from vaccine recipients, vaccination providers, or the sponsor. In addition, the sponsor will also conduct periodic aggregate review of safety data and submit periodic safety reports at month-three intervals for FDA review. Both FDA and CDC will take a collaborative and complementary approach on reviewing AEs.

In addition to review all serious adverse events, FDA will also examine other sources for adverse events such as the literature and will perform data mining to determine if AEs are disproportionately reported for the authorized vaccine compared to all other vaccines under VAERS. Any potential safety signals identified will be investigated. Next slide.

I will conclude with a summary of benefit/risk. Though this slide presents a summary of the benefits and risks of the Moderna COVID-19 vaccine in individuals 6 years through 17 years, known and

potential benefits include prevention of symptomatic COVID-19 based on immunobridging for young adults as well as supportive 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. Next slide.

So just to remind everyone again, here are the voting questions for today. One, based on the totality of scientific evidence available, do the benefits of the Moderna COVID-19 vaccine when administered as a two-dose series (100 micrograms each dose) outweigh its risks for use in adolescents 12 through 17 years of age?

Two, based on the totality of scientific evidence available, do the benefits of the Moderna

COVID-19 vaccine when administered as a two-dose series (50 micrograms each dose) outweigh its risks for use in children 6 to 11 years of age?

That concludes my presentation. Thank you.

## Q&A SESSION

**DR. ARNOLD MONTO:** Thank you very much, Dr. Zhang, for getting us even more back on time. We actually have some time to ask you questions. So, you've given us a great gift here. So, Dr. Levy, your hand is up. Was that from before, or is that now? From before. All right. Thank you. Questions of the FDA presentation?

**DR. OFER LEVY:** Yes. Hi.

**DR. ARNOLD MONTO:** Oh, it is you. They lowered your hand. Go ahead, Dr. Levy.

**DR. OFER LEVY:** Yes. Hi. Thank you. My question, though -- is it okay to ask question of --

**DR. ARNOLD MONTO:** Please.

**DR. OFER LEVY:** I'm sorry?

**DR. ARNOLD MONTO:** I'd rather not from the sponsor right now. We'll get back to them later on.

**DR. OFER LEVY:** Okay. Well, my question was to the sponsor. So, then, I'm going to wait.

**DR. ARNOLD MONTO:** Yeah. You're right. I'm sorry I had to cut you off because I didn't think --

**DR. OFER LEVY:** Yeah. Yeah.

**DR. ARNOLD MONTO:** -- we were going to be done a little bit earlier here.

**DR. OFER LEVY:** Okay.

**DR. ARNOLD MONTO:** Questions of Dr. Zhang. Dr. Marasco?

**DR. WAYNE MARASCO:** Yes. Thank you very much, Rachel. So, my question really is at the start of the pandemic, it's pretty clear that the bar was somewhat lower in terms of vaccine efficacy because we were trying to get vaccines out the door and get the population protected. But, in the data that saw in P203, unless I'm mistaken, the follow-up in terms of efficacy was basically 60 days after the second dose.

So, I mean, we know that -- I know I keep

harping on this, but it seems to be an important point. These vaccines are of limited duration, and while they are protective, it's of limited duration and even more so with immunobridging.

My question is, are we really capturing viral efficacy as a function of time because what these vaccines need is really to be able to try to get more durability out of them and immunobridging, not just immunobridging. So, I'd just like, if possible, is a representative from CBER to address that if it's possible.

**DR. RACHEL ZHANG:** Well, I will start. I'm not quite sure I'll be able to address your question, but I guess the Study P203, as I mentioned, because of the availability of an alternate COVID-19 vaccine, after a certain period of time, after basically end of May, we have lost the placebo group. So we cannot really say anything about the duration of vaccine efficacy. After that, there's no more efficacy data basically after that time point.

So, unfortunately, all we are limited to in

this study would be the results that we have shown in this slide with the data cutoff. The latest one would be the May 31st one. And that is still unfortunately very few cases. So, there is nothing that we have from the clinical studies that will give us more information about the durability of the vaccine efficacy. I guess it will have to come from real-world effectiveness.

**DR. ARNOLD MONTO:** Dr. Fink? Dr. Fink, I see you trying to get on.

**DR. DORAN FINK:** Thank you. I'll jump in and mention that immunobridging is a regulatory approach that we've used to infer effectiveness and prevented vaccines for a long time now. This is based on an understanding that the mechanism of protection conferred by the vaccine is similar across age groups and that we have an immune marker that, while it may not be scientifically established to predict protection at a given threshold, is clinically relevant, and we do have that understanding for neutralizing antibody response for COVID-19 vaccines.

Certainly, when efficacy data are available,

we are not going to rely on the immunobridging data in and of itself in a vacuum. We'll also look at the efficacy data and make sure that it supports the conclusions that we would draw from the immunobridging analysis.

We don't have efficacy data specific for Omicron for either of these age groups, although you'll see tomorrow that we do have Omicron-specific data for the younger age groups that tracks with the real-world effectiveness data that we're seeing in adults.

So, I do think that all of the data that we're seeing is pointing in the same direction in terms of conclusions about efficacy against Omicron, both for less severe disease and also for more severe disease. So, that's how we make those inferences about effectiveness. Thank you.

**DR. ARNOLD MONTO:** Thank you. While you're still there, since you mentioned Omicron, we know that to get better efficacy against Omicron, a third dose is required. We're being asked to prove a two-dose regimen. So, the process of getting a third dose

approved after somebody has received the primary outcome, that will be a separate process; is that correct?

**DR. DORAN FINK:** Right. That will be a separate process. We are well aware that individuals who choose to receive the Moderna vaccine primary series will be also interested in a booster dose to improve their protection. And once we have data in from the vaccine manufacturer, at least some safety and immunogenicity data for a booster dose, we will move expediently toward making the booster dose available.

**DR. ARNOLD MONTO:** Thank you. I see no hands raised. So, we are going to break for lunch. We're going to have the oral public hearing starting at 1:00, and the question-and-answer session will be continued after that. So, lunch break. We'll see you for the oral public hearing at 1:00.

**[LUNCH BREAK]**

**OPEN PUBLIC HEARING**

**MR. MICHAEL KAWCZYNSKI:** Welcome back to the 174th VRBPAC meeting. I'm going to hand it off to our colleague and DFO, Dr. Prabhakara Atreya, and Dr. Arnold Monto. Take it away.

**DR. ARNOLD MONTO:** I'd like to welcome you to the Open Public Hearing session. Please note that both the Food and Drug Administration, and the public, believe in a transparent process for information gathering and decision making. To ensure such transparency, in the Open Public Hearing session of the Advisory Committee, FDA believes that it is important to understand the context of an individual's presentation.

For that 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 have with the sponsor, the 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 the 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. Over to you, Prabha.

**DR. PRABHAKARA ATREYA:** Thank you, Dr. Monto. Before I begin calling the registered speakers, I would like to add the following additional guidance. FDA encourages participation from all public stakeholders in decision making process, every Advisory Committee meeting, including 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. The statements made

during this Open Public Hearing session reflect the viewpoints of the individual speakers or their respective organizations, but are not meant to indicate agency agreement with the statements made. With this guidance I would like to first call upon the registered speaker, Dr. Ashley S. Thank you.

**DR. ASHLEY SERRANO:** Thank you. And thank you for accepting my request to speak today. I have no financial conflicts. I would like to strongly urge the committee to recommend the Emergency Use Authorization for both Pfizer and Moderna vaccines, for school age children and teens. My name is Dr. Ashley Serrano, and I am a mother of a three-year-old, and a clinical psychologist who focuses my work on evaluating and treating children and adolescents.

Over the last two years Moderna's vaccine has proven to be superior in protecting against variants. And studies have shown that Moderna's vaccine creates higher level of IgA antibodies, when compared to Pfizer's vaccine. The safety of Moderna's vaccine has be rigorously monitored in the 40 other countries that

have already approved its use in children aged 6 through 17.

For the youngest age group, Moderna easily met immunobridging endpoints after just two doses. This will be the youngest age group our children would be given more protection more quickly. For children 6 months to 5 years of age, Moderna's 2-dose series have showed improved efficacy, when comparing it to Pfizer's data, against Omicron after two dosages.

Unfortunately, the BA.4 and BA.5 strains in South Africa are resulting in more hospitalizations in young kids compared to the previous variants. Delaying an approval to see the additional harm and death (inaudible - audio distorted) bring upon our children, is unethical. We do not have a full and clear picture of the harm that COVID-19 has on these developing bodies and brains, what we do know is that long COVID exists and it's not rare; it's not a rare phenomenon.

MIS-C has hospitalized thousands of children and it is now being recognized that severe hepatitis cases in children are likely linked to those with

previous COVID infections. We know that COVID can cause inflammation in many organ systems, so this is not in any way surprising. Families need options when it comes to choosing which vaccine they prefer. Now is our chance as the committee to give families that option.

Older children and adolescents deserve the ability to choose as well, as having more than one option for boosting and mix and matching will likely improve efficacy even further. Additionally, these vaccines need to be easily and readily accessible to all children. It shouldn't have to be pointed out, but all sites offering vaccinations, especially to young children and babies, need to have a strict mask mandate in place in order to allow parents to feel safe taking their vulnerable children to their vaccination appointments.

As you can imagine, I gained many new patients in my therapy practice during the height of the pandemic. I continue seeing these, and many new patients, due to continued anxiety, trauma and grief.

Thankfully, we have been able to see many patients through telemedicine, but I do fear that when our public health emergency is no longer extended, many of these kids will no longer receive the therapy or have access to therapy that they need.

I believe there will be continued anxiety, trauma and grief for those who are missing out on their childhood, if we do not get a vaccine to protect our youngest against COVID. Thank you for giving me time to speak today.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Ms. Corey C.

**MS. COREY C:** Hi. Thank you for giving me the time today. I have no financial conflict. I'm here to urge the committee to approve Moderna and Pfizer vaccines for children under 5. Giving parents the option of both vaccines is imperative to allow for individual consideration, due to the massive differences in the time to full protection. It would be unconscionable to deny access to Moderna, when it's easily met immunobridging endpoints with half the time.

The comic you see displayed perfectly captures the last one and a half years it felt like to a parent with a child under 5. Trusting our government -- you -- to finally allow us to protect our children as we hang on, white knuckled, only to be continually left behind. In the 227 days since children over 5 had access to a vaccine, millions of vulnerable younger children have been infected. Thousands have been hospitalized. And hundreds have died. Not to mention the thousands struggling with long COVID and MIS-C.

The comic is obviously meant to figuratively depict the danger our children are in, in this mitigation-free world without vaccines. But I want to remind you that there are children that actually look like the boy in the comic. Literally gasping for breath and terrified due to the country's failure to prioritize them. I know what that's like as a parent. As a mom to an 11 month, NICU stay (inaudible) graduate, who went home with a trac and a ventilator, I have seen my beautiful daughter turn blue multiple times.

I have watched a team of our medical heroes resuscitate her. There is nothing in this world that can equal the abject terror and anguish as watching your child fight for their life and not be able to help. I kindly ask you to imagine that now. Imagine your beautiful child, lifeless and gray as you shake uncontrollably and feel that the world is crumbling beneath your feet. Now imagine that you knew that the shattering of your world was likely preventable.

Unlike on an airplane we can't take our mask and give them to our children. Instead, your inaction has necessitated our sacrifice in quitting jobs, going years without adequate sleep and support, decreases in physical health, and a mental health nightmare.

When making the argument for kids under 5, I'm frequently told, eh, they don’t die that often. Sidestepping the tragedy of even one child dying needlessly, I feel I need to point out that just because a child doesn’t die, doesn’t mean it’s acceptable. Coming from a community of children with frequent hospitalizations, I can unequivocally say that

they bring potential trauma, new infections, developmental regression, chronic illness and monetary issues for families.

High-risk children need to be prioritized alongside high-risk adults. As they suffer the most due to the need for medical appointments and therapies, contracting COVID during hospitalizations, lack of socialization, and the risk of developmental regression or stagnation.

We aren't asking for perfection. We're asking for a chance to avoid serious outcomes, and an opportunity for our children to experience the world for the first time. These children deserve protection. They deserve more from us. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Brucha W. You have three minutes, please.

**MS. BRUCHA WEISBERGER:** Hello, my name is Brucha Weisberger. I have no financial conflicts of interest. I want to start by reminding all that God is listening to every word said here, knows the thoughts of every being. And as the all powerful, he will repay

each (inaudible). He is the only power. (Inaudible).

God has entrusted you, the FDA, with enormous responsibility to safeguard the lives of Americans. We trusted you implicitly for decades. But now you broke the trust. As tens of thousands die from the COVID injections, you've taken no action. Murder by poison shot is the same as murder by gunshot. God and the world will judge you. So I urge you to have the courage to stand for the truth that you know as well as I do and not allow pressure, financial incentives, or threats to influence you.

Perhaps it is for your lifesaving vote today that you were born. You're being asked to vote on whether millions of babies and children will be receiving the COVID shots. But before injecting anything into a human being, a rational person will ask three questions. Is it necessary? Does it work? And is it totally safe? The first (inaudible) do no harm.

Let us examine these three questions. First, do children need these shots to prevent dangerous illness? Definitely not, children's very active thymus

gland and lack of H2 receptors results in a very low virial load. Children rarely get very ill with COVID, and they simply do not die of COVID. You are aware that the CDC drastically exaggerated COVID morbidity and mortality, especially in the pediatric population, to hype up the fear, which is what we just heard in the comments of the two parents now.

Also, there is treatment for COVID that is effective, but it has been suppressed in order to hype up the fear. Actual data show that hospitalizations are usually for other reasons than the child just happened to test positive.

Slide 3, please. The fatality rate for the 5 to 11-year-old kids could not even be calculated due to an absence of cases. Slide 4, please. It turns out that 100 percent of so called COVID deaths in children are in kids with a preexisting condition. The truth here is that these children died of their preexisting condition and not of COVID.

Most children have already been exposed and developed immunity, making a vaccine even more

redundant and even more dangerous to them. Will you explain to the world then, what is your rational for giving this shot to kids?

Second question, do the shots even work. Slide 5, please. Fraudulent claims of efficacy are being made based on antibody levels. That's immunobridging that was being referred to. It' is not a true marker of immunity. Pfizer's initial trial failed to show any benefit to children. And efficacy for kids plummeted to 12 percent within a month.

Slide 8, please. Here is (inaudible) where COVID death grew from four a day to 51 a day, within five weeks of starting their vaccination campaign. Similar scenarios repeated worldwide. The shots have a negative efficacy as they weaken the immune system.

Slide 9, please. Question 3, are the COVID shots safe? Pfizer (inaudible) briefing document predicted more excess hospitalization due to myocarditis (inaudible) the shots, then the number they might present.

Slide 10, please. U.K. data shows that COVID

shots increase children's risk of death by 8,100 percent or more. U.S. data shows we're killing 117 kids for every 12 we might save. Hospitals across America are overflowing with young patients with rare cancers, strokes, heart attacks, and unusual diseases as never before. Doctors and Nurses are starting to speak up.

Slide 17, please. How can you live with yourself, if we ignore 29,000 deaths, after COVID injections, on the CDC website? And 49,000 reports of injuries or death to children, after COVID injection, and keep saying safe and effective when you know they're not.

Slide 19, please. I urge the members of the FDA to seize the moment and do what is right in God's eyes. And what history will judge you favorably for. And not only reject the authorization of both Moderna and Pfizer for young children. But also, revoke authorizations for all the COVID shots, which have killed and disabled so many Americans and human beings worldwide. I and millions of others pray to God that

you will do what is morally right. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Dr. Jane N.

**DR. JANE NEWBURGER:** The ACC has no relevant conflicts. I'm please to represent the American College of Cardiology's position in favor of support of COVID vaccination in children. The most common cause of cardiovascular injury in youth, exposed to SARS-CoV-2, is a rare but serious post-infectious condition called multisystem inflammatory syndrome in children, or MIS-C.

MIS-C is defined by fever, severe inflammation, and involvement of multiple organs of the body. Approximately 80 percent, or four in every five children with MIS-C, have cardiovascular involvement. Proponent levels indicating injuries to heart muscle cells are elevated in more than half of MIS-C patients in whom they are measured. About one third, or 34 percent, have depressed or low left ventricular function and 13 percent develop coronary aneurysm. Approximately 0.8 percent of children, teens and young

adults with MIS-C have died.

The occurrence of MIS-C is prevented by COVID vaccination. In a research letter in JAMA, (inaudible) first showed the protective effect of COVID-19 vaccination on the development of MIS-C. In the U.S., CDC investigators showed that among 102 MIS-C case patients, and 181 hospitalized controls, the estimated effectiveness of two dosages of Pfizer-BioNTech vaccine against MIS-C was 91 percent. All 38 MIS-C patients requiring life support were unvaccinated.

Cardiac complications, particularly myocarditis or pericarditis, can very rarely be associated with COVID vaccines. Boys, age 12 to 17 years, are in the highest risk group for vaccine myocarditis. A recent study, using the electronic health record, (inaudible), compared heart complications after SARS-CoV-2 infections versus mRNA COVID-19 vaccination. Even among boys in that high-risk age range of 12 to 17 years, the risk of cardiac complications was significantly higher after infection than after vaccination.

In summary, the American College of Cardiology supports COVID vaccination in children and young adults, because cardiovascular complications are higher after infection than after vaccination. Thank you very much.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Tamara T.

**MS. TAMARA THOMSON:** Good afternoon. Thank you for allowing me the opportunity to address you today. I have no conflict. My name is Tamara Thomson. I'm an attorney who represents children. I have two beautiful children of my own, a 5-year-old boy, and my pandemic baby a 23-month-old girl. I'm here to urge this body and the FDA to recommend and authorize Moderna pediatric vaccine for all ages. Even more crucially, I am requesting authorization for both the Pfizer and Moderna vaccines for the youngest children, to protect from severe disease, poor outcomes and deaths in this group.

My son was vaccinated with the Pfizer vaccine on his 5th birthday in February of this year. The same

day his little sister was scheduled to get her own Pfizer vaccine. We celebrated his bravery, and the ability to protect him. But we were devastated when our daughter's appointment that same day was cancelled after Pfizer pulled its submission for her age group.

Nearly every day since then my son asks me when his baby will be able to get her vaccine, so we can visit museums, see friends, and protect our sweet girl. We have taken significant precautions to try to avoid infection with this virus. We have also gone to great length to be a part of Moderna's pediatric trials, so one of the data points you will see tomorrow will be my daughter.

Here are some things we know about COVID in young children that I'd like you to keep in mind as you consider allowing them access to their first vaccines. First, children under 5 are still at risk for death. Nearly 500 children in this age group have died from this disease. These kids are still at risk for MIS-C and long COVID. Their risk of hospitalization, during the Omicron wave, was the same as the 18 to 49-year-old

age group. And four times higher than the older pediatric cohort, for whom this body has enthusiastically recommended vaccine.

Meanwhile, non-pharmaceutical interventions to try and protect them have dwindled to nearly zero in the midst of a surge nearly equivalent to the January wave. But with much less data for people to understand how great the risk is right now. Every day of delay in authorization causes additional harm to children and families.

We know that these vaccines are safe, with a better safety profile than some pediatric vaccines we routinely give young children. We know that both have met their primary endpoints of immunobridging and that they are effective. Sever, acute outcomes are preventable, and worthy of prevention. Additionally, many next generation vaccines are piggybacking on the primary first generation authorization. And we can't let our children be left behind yet again. Thank you so much.

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

comments. The next speaker is Aime Baker.

**MS. AIME BAKER:** No conflicts, thank you for giving me the chance to speak today. I can go through the facts, such as it's been 872 days since the first COVID case was reported in my state. And, 481 children under 5 in the U.S. have died from COVID. But I'll stop there because I hope you know these facts given your position.

Instead I'll help you personalize this by having you imagine a few scenarios. Imagine working a job from home, while your spouse works their job from home, and caring for your toddler, (inaudible) also a newborn, without any help because daycare is not safe. Imagine after doing that for a year and a half, your spouse being required to go back into the workplace and you still don't have a COVID-safe and affordable daycare option, so you become yet another woman forced to leave the workplace to protect her kids, also knowing that some parents don't have this option to keep their kid safe.

Imagine preparing to give birth and

anticipating it not only with excitement and anxiety of giving birth, but with an immense fear of who will be watching your almost two-year-old, since vaccines at the time are only available to high-risk populations, but not yet pregnant women, and you are relying on asking someone to quarantine for two weeks. Fingers crossed, you don't go into labor early, since social distancing has been dropped for a long time, and if you end up testing positive prior to delivery, your spouse will be able to join you if you need a C-section. To make matter worse, since you've been keeping your child safe from COVID this past year by staying home, anybody who comes to watch her has only seen her over FaceTime. And she knows Daniel Tiger (phonetic) better than them.

Imagine a month after giving birth, you end up in a hospital for an emergency appendectomy, forced to leave your newborn at home (inaudible) every two to three hours and you have about one bottle worth of just pumped milk, hoping that he'll catch on real or otherwise it'll be two days until he can eat again.

I don't have to imagine. That was all my life

last year alone. Add on the family that has never met my son, the typical toddler socialization my daughter has missed out on, the (inaudible) lack of support we've have these last 27 months, my mental health has been through the wringer. And I can only imagine the long term impact this has had on my children. We've taught our daughter that we need to give space and wear our mask to keep our friends safe. But I'm not sure how to answer if and when she asks why others don't keep her safe.

So what I'm asking of you, give us the choice to protect our kids. We've waited far too long. The fact that this meeting is prioritizing an age group that already has access to a vaccine, prior to the under 5, is unacceptable. The fact that the meeting tomorrow was not scheduled until Pfizer submitted, when another option has been ready for weeks is unacceptable. Due to the need for three dosages, vaccination with Pfizer will take seven more weeks for a child to be fully vaccinated compared to Moderna. Too late for kids to start preschool safely this fall.

And another seven weeks (inaudible) jumping hurtles to protect our kids in a society that has dropped all precaution.

Finally, when the updated boosters come up to protect against Omicron, and new variants we've yet to face, approve them for children of all ages simultaneously. Stop leaving these kids behind like they don't matter. Thank you.

**DR. PRABHAKARA ATREYA:** The next speaker is Carolina Bourque.

**MS. CAROLINA BOURQUE:** Thank you for the opportunity. I have no conflict. I'm a 43-year-old researcher biologist and a mother. I'm here sharing my personal nightmare story with after my Moderna injections. I was in very good health before my Moderna injection. But I did suffer from seasonal allergies. I lived a normal active life and happy life. I worked full-time, took care of my family, my farm, rescued dogs, and enjoyed multiple physical activities.

I took my first Moderna injection early in

March 2021. I took the injection because I believe it was needed to protect myself, my family and others in my community. I believe it was safe, effective, and the right thing to do. After my first injection, I had and anaphylactic reaction, rash, tachycardia (inaudible), dizziness, shortness of breath, intense gastro pains that lasted months.

My doctors ignored my reactions, from the first injection, and unbelievably recommended a second shot. They said it was needed to be safe. I took the second Moderna injection in June of 2021. I got dizzy right away. Two days after the injection I could not get out of bed for a couple days. My right leg and my arms were weak. I developed social paralysis and migraines. My eyesight became fuzzy. I was dizzy and confused. I had no choice but to stay down.

It has been about 12 and 15 months post reaction to the injections. I still deal with daily fatigue, dizziness, memory problems, nerve and joint pains, burning of the skin, numbness, ringing of the ears, headaches, tingling sensations up my body. My

face (inaudible) and my right hand tremors.

These injections have badly harmed my life, my family, my work, and my health. They have taken me away from everything that made my life happy and fulfilling. So far, there is no effective treatments that can help me. I have seen numerous specialists, tried special diets, supplements. I have found no answers or guidance. There's no pathway of improvement. No one knows if I will ever get better. This makes me feel really helpless and hopeless sometimes.

Since the injections, I have been diagnosed with dysautonomia (inaudible), small fiber neuropathy, (inaudible). I'm unable to do most basic tasks including driving. The effects of the shots are so extreme and never ending. As soon as I mention that the symptoms are vaccine related, I feel completely ignored. Most doctors do not want to talk about the possibility of vaccine injury. How is that going to effect the little kids that cannot communicate or explain what's going on with their bodies? Side

effects need to be acknowledged correctly. Long term research needs to be done before we can push this into our kids. Knowing the level of (inaudible) before injecting those into our kids should be accounted for. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Robyn Handsman.

**MS. ROBYN HANDSMAN:** Hi, everyone. I have no conflict. I do not want approval of this vaccine. I'm going to tell you my own story. I got the first injection on September 15th, 2021. Sorry -- sorry, emotional for me. I got the first dose and everything was fine until Friday morning at eight o'clock. I woke up and my hands and my arms were completely numb and tingly.

I called 911, but instead of going to the hospital I went to my doctor's and did a urine sample and an EKG and I was sent home. By Sunday night I was just watching TV. I got up to go to the bathroom. And I said out loud that I was really dizzy. My husband said we need to take your blood pressure. He took my

blood pressure and he immediately called 911; it was 211 over 105.

I took one of my husband's blood pressure pills because I was not on anything because I was a completely healthy person. And I also took 325 milligrams of aspirin. The paramedics confirmed my extremely high blood pressure. But since I took the pill I decided to stay home. At 11:30 my husband said let's take it one more time before going to sleep. And my blood pressure was even higher, so 911 was called again. I took another aspirin and a second pill from my husband. The ambulance came, they did an EKG and they said my heart looked good, and COVID was rampant in the hospital so I stayed home.

The next morning I woke up, it was 198 over 98, so I went to the ER. I took a third pill of my husband's blood pressure medication. I was in and out of the ERs and urgent cares Monday and Tuesday. By Wednesday I went back to my doctor's and did another urine sample. He gave me a second blood pressure pill to take, so now I was on two.

By Thursday, my left arm had pain and numbness, and was admitted into the ER. By Friday in the hospital I got an email from my doctor that I had protein in my urine. In five days it went from zero to 433. And I now have permanent kidney damage.

I released all my medical records to Moderna. Moderna called my doctor, because I had 100 percent proof it was vaccine related from the urine samples. They said that they're seeing many cases like mines. I also had all my bloodwork taken three months earlier. My glucose was 82. I had no A1c problems. My blood pressure ten days earlier in the doctor's office was 100 over 70. After the vaccine, my liver enzymes glucose is now 125. I have high A1c. My Epstein-Barr virus (inaudible) activated. My hands are still tingly and numb. And the worse part about it is I'm allergic to foods that I've never been allergic to. And, I eat them and my blood pressure goes to 200 over 100. And I would say that's crazy, except I don't know that I ate something that I was allergic to.

Why on earth would you give this to kids and

young people when the risk of dying from COVID is practically zero? How many people have to go to sleep and never wake up? It is not a coincident. Kids are dying on the fields from heart conditions like never before. Me and thousands and thousands of lives are forever changed. We have no recourse. We can't go after the vaccine injury program. Moderna has complete immunity. And we're censored on our support groups. We have to talk in code. And I'm very concerned that, you know, this is all about money. And, I really don't know how people sleep at night knowing this is injuring and killing people all over the place.

And I really want answers. I'll give you my Moderna's case numbers. It's Mod21145534 on 9/20. The second one was Mod21158661 on 10/29. My third one is Mod-2021-369784 on 11/18. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Richard Erickson.

**MR. RICHARD ERICKSON:** Hi, thank you for allowing me to speak. I have no financial conflicts. My name is Richard Erickson. I'm a technology

executive co-business leader, entrepreneur, a coach, a husband, a father of four amazing children 20 down to 11 years of age.

I work my career as a creator (inaudible) leader, and supporter of a number of our large enterprises, coming up with visionary ideas and technology and help thousands of companies innovate and become more competitive and grow. I started and launched many companies, employed thousands of people, and helped grow our U.S. economy over the last 30 years. I've also been a competitive athlete, mountain biker, youth coach and supporter of local community, giving back when I can.

I was supportive of a vaccine mandate to help save lives and to get our economy back running again. In April of 2021 I received my second Moderna vaccine. And within about two weeks I immediately had temperature intolerance, tinnitus, and exercise intolerance with a disruption in my sleep schedule. Prior to this, by the way, I've had absolutely no underlining issues or conditions. I assumed all this

was due to stress, and tried to kind of move on with my life last year, continuing to work and sitting on board seats as I had done previously.

In late December of 2021, I received my third shot, my booster. And at that point I became seriously ill. I had an eruption of new symptoms that included bazaar nerve vibration in my head, neck, body, debilitating headaches, chronic fatigue, sensitivity to light and sound, the sever exercise intolerance, muscle spasms, and sever insomnia.

I don't remember much in January and February of this year. I live in Minnesota. I was brought down to Mayo, had to take a leave of absence from my position and my executive board seats. In March I went down to Mayo and had an extensive set of testing, with a variety of findings but no clear understanding of how to treat for an adverse event or even long COVID for that matter. I spent most of my time in March reaching out to research institutions, attempting to understand what had happened to me and determine how I could treat my symptoms.

I, unlike maybe some of the others that have had adverse reactions, I have not had any conversation or discussion with Moderna. You know, or any institutions regarding the adverse reaction. I would love to do that if they're able to help. I've met hundreds of people dealing with similar symptoms, who are disabled, unable to work and contribute. Many of us have the same story or have no or limited support from our local medical systems, and are searching for research that might help.

My ask is, quite simply, we need help to coordinate access to resources, directions for treatment, acknowledgement and hope that we can recover. I've gone from a highly active person and contributor to our economy, to someone who is now dealing with a chronic illness with no clear treatment path. My challenges every day are just simply doing the basics of life. Not being able to go out and see my kids play soccer or join in the events that are remote. I'm struggling with just figuring out how to get my life back in order and get back to working on

the economy, which is one of the things that I love to do.

In conclusion, I really think we need a public private partnership with those that are financially benefiting, and should be contributing, to help those who have adverse reactions. Despite my reaction to the vaccine, I still have support for the vaccine mandate. My ask is, again, we need help that provides direction and support for those who have been affected and turn their lives around. (Inaudible) have had their lives turn upside down by Moderna and other vaccines. I also would ask for help for those that are being affected by long COVID. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Caroline Bishop.

**DR. CAROLINE BISHOP:** Thank you very much for giving me the opportunity to speak with you today. My name is Dr. Caroline Bishop. And I have no financial conflicts of interest. I'm here to urge the committee to approve both the Pfizer and Moderna vaccines for children under 5, as well as the Moderna vaccine for

older kids. While I'll mostly speak to the urgent need for these safe and effective vaccines for children under 5, I also wanted to say that my two COVID-conscience high school babysitters, who being STEM students, were very excited that I was speaking to the FDA, asked me to mentioned how much they would like to get a Moderna booster, given the studies that show increased protection from mixing and matching vaccines.

I'm the mother of a so called pandemic baby, who was born in March 2021. Becoming a new parent is always tough, but it's hard to imagine a more heartbreaking time to have entered parenthood. As I was experiencing for the first time the all-consuming love and obsessive desire to keep this vulnerable little human being alive, I was also forced to learn just how little people in this country care about keeping our baby safe.

This has been made abundantly clear from our country's gleeful abandonment of all mitigations to curb the spread of COVID months, and in some places years, before there was even the possibility of

children under 5 being vaccinated. The most heartbreaking part of this realization has been that people that I love and respect has embraced the idea that COVID is over.

I had to beg my parents to wear masks on the plane before they saw my daughter. My brother and sister-in-law refused to be vaccinated. So we've had to keep her away from her aunt, uncle and cousins. Even medical experts that I respect decided this spring that it was more convenient to cater to the whims of those who have decided to move on, then to protect these little lives.

In a twitter thread urging the removal of the mask mandate on public transit, Dr. Bob Wachter (phonetic), whose opinion on COVID I have otherwise appreciate, wrote, "Yes, I worry about the babies. Until vaccines are approved for them, parents will have to accept a higher risk for an infant who can't wear a mask on a plane. If I had an infant, this would give me pause before flying, which is hard. But it seems like a lot to ask every person on every plane to mask

to protect a small number of babies that may or may not be onboard."

Is this really a lot to ask that people care about the vulnerable amongst them, when we know that COVID has killed far more children this year than the average flu? When there are 483 parents of children under 5 who have lost their baby to this virus. Well, apparently the answer is yes. Mitigations are now gone and they clearly aren't coming back. So for the sake of my daughter, and for the other children who are too young to mask, I beg you to approve these safe and effective vaccines without delay.

In a country where even friends and family have proven themselves to selfish to do the absolute minimum to protect my baby, she urgently needs the protection these vaccines would provide. Thank you very much.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Dr. Kailey Soller.

**DR. KAILEY SOLLER:** Hello, everyone, and thank you so much for letting me speak today. My name is Dr.

Kailey Soller. I have my Ph.D. in chemistry. And even more importantly, I'm a mom to a child under two years old. I'm here today to advocate for the approval of all the vaccines under consideration today and tomorrow, the Moderna 6 to 11, and even more importantly the age cohort that does not have a vaccine available at all to them today, the children under 5. I urge you to approve both the Moderna and Pfizer vaccines under consideration today and tomorrow.

There are so many reasons for these vaccines to be approved. First, and most importantly, the reasons are scientific. As you all know so well, and that I considered very strongly, being a scientist myself. Most importantly, and undoubtedly, these vaccines have met all of the predetermined endpoints for safety and efficacy and they should be approved.

But as a Ph.D. and a scientist, I could talk about forever the scientific benefits of these vaccines. But we all know the benefits and we've all read the data and the submissions, to know that these vaccines have not only met our safety and scientific

requirements, but we also know that immunity is not simply an on/off switch. But that we garner many additional benefits beyond just the immunobridging endpoint and vaccine efficacy endpoints that we see through this data.

I also want to talk today as a parent. Because what has become extremely apparent over the last two years, but especially since the vaccine for 5 to 11-year-old children has become approved, is that we need to allow parents access to a vaccine so that they can choose to protect their children in the way that they desire.

There have been some people today speaking about their desire to not vaccinate their children, or not vaccinate themselves. However, I don't have that same option as a parent. I don't want a vaccine mandate. I just want the option to do what I have deemed best for my child, which is give her access and vaccinate her against this horrible deadly disease. There's an ethical obligation for this committee to allow parents access to that lifesaving vaccine that

will allow them to protect their children when no one else is protecting their children.

As my daughter is under two, she's even unable to mask to protect herself. And I realize that she may likely become infected with COVID at some point in her lifetime, but all I want is for her immune system to have been primed with vaccinations so that she can have a better outcome. I know that vaccinations provide her that best possible path to the best outcome. It will allow her immune system to develop T and B cell memory responses, prior to being infected with COVID. That will help prevent severe COVID infection and long COVID effects that many people on the call have listed today.

These past few years have been some of the hardest of my and my family life. Having a child during the pandemic meant wearing a mask during labor. And then having a child in the NICU, during a pandemic, meant that we had no visitors allowed and we had no support. Our child was not able to meet her grandparents the first ten days of her life, which was incredibly hard. And on top of this we have had

constant risk-based decisions since the day that she was born. Should we allow her grandparents and other family to visit? Should we allow them to visit without mask after they were vaccinated?

**MR. MICHAEL KAWCZYNSKI:** Please wrap up.

**DR. KAILEY SOLLER:** Is the benefit of seeing their faces greater than the risk of contracting the most deadly virus in American history? All I want to do is protect my child in the way that I know is best. Please allow me to do so and approve these lifesaving vaccines. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Jennifer Dougherty.

**MS. JENNIFER DOUGHERTY:** Hello. Thank you for the opportunity to speak to you today. I do not have any conflict. I'm the mother of four-year-old twins. My kids have been living with the pandemic since they were one year old. From the age of 23 months to three and a half years old, when we finally found a safe, masked, small outdoor playgroup, they knew zero other children. We live in a densely populated area, and we

don't feel safe having them do indoor activities since they're not vaccinated. They've had to stop swimming lessons, music classes, and art classes. We don't see any friends and only see very close family after quarantine and tests and always masked. Since we have to avoid public transportation and don't own a car, our world has become extremely limited.

We've been feeling isolated and anxious for so long. We are more than ready for our kids to get back to living a more normal childhood. So many experiences have been taken away from them already. Most importantly our kids will start Pre-K in the fall, and we are extremely concerned that they may not be fully vaccinated before they start school. Particularly as mask mandates for school have ended, leaving them completely unprotected.

Omicron has hit children particularly hard. More than three and a half million kids were diagnosed with COVID in January alone. And each new variant is even more contagious. Nearly 1500 children have died of COVID, and many more have suffered medical

complication such as MIS-C, long COVID, neurological effects including brain inflammation, and an increased risk for type 1 diabetes. It is now becoming increasingly clear that the hepatitis cases, in children currently under investigation, are likely related to effects of a prior COVID infection. And unfortunately there are likely further (inaudible) (audio distorted) of a childhood COVID infection that we've yet to discover.

We have the data and science to show that mRNA vaccines are safe. Both Moderna and Pfizer met immunobridging and safety standards and have shown similar efficacy against Omicron when compared to other age groups. At this late date, the Moderna 2-dose will give kids better protection where school starts in September. Given this information, both Moderna and Pfizer should be approved immediately.

Many families haven't has the privilege my family has had to keep our kids home during these unprecedented time. And those in underserved communities, and those with medically high-risk family

members, have been forced into impossible decisions. No one should have to choose between the health of their family and their financial security, especially when safe vaccines are available. I urge you to approve both Moderna and Pfizer's EUAs and to make sure that any future boosters or variant-specific vaccines are available to all ages immediately. Our kids have waited long enough. Thank you for your time.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Dr. Harvey Klein. You have three minutes.

**DR. HARVEY KLEIN:** Thank you for having me on today. I have no conflict of interest. My only interest is in saving children's lives. I pray that the Advisory Committee members will open your hearts to God's truth about protecting his children, which includes your children and grandchildren. I'm an MD, graduate of Tufts (inaudible) Medical School, one of the top ten in the country. I am trained as an orthopedic surgeon.

Before I went to medical school I was a mechanical engineer, a system and electrical engineer

for Brooklyn Poly Tech, and a rocket scientist. In the late 60's I had a machine shop and we made parts for Grumman, who has a contract for the lens of lunar excursion module that landed on the moon in 1969 with Neil Armstrong and Buzz Aldrin. I myself machined the parts for the lens that I held in my hand that are still sitting on the moon as we speak. So when I look up at the moon, it's a totally different experience than for most people.

I am appalled at the arrogance that you, meaning the FDA, has in even thinking about vaccinating healthy children with outdated highly toxic COVID vaccines. Children have a 99.998 percent survival rate, with (inaudible) if they get COVID. Vast statistics show that over 100,000 children, ages birth to 18 that have been vaccinated with Pfizer-BioNTech and Moderna's so called vaccines, has had severe life-threatening adverse reactions such as myocarditis, (inaudible), and many more severe adverse reactions and even death.

We know that (inaudible) is under reported by

a factor of 100. The data cries out loudly to stop this insanity immediately before you kill or maim one more innocent child. These vaccines are not experimental, they are bioweapons designed to maim and kill. In a risk/benefit analysis, since children up to age 18 have a survival rate of 99.9 (inaudible) reactions and virtually no deaths, why in the world would you want to try to improve on perfection by exposing them to significant chances of being permanently severely injured or dead? The risk is infinite, and the benefits are nonexistent, and the efficacy is extremely negative. Why do you want to mess with God's given perfect system?

The best treatment you can do is to leave these children alone under God's care. And failing to do that, then your only purpose is to maim and kill. That clearly being the case, the FDA should change its name to the JMI, the Josef Mengele Institute. It is not too late to repent and return to God and his (inaudible). If you want to experiment, do it on yourselves. Don't think that for one second that God

is not aware of your very nefarious and murderous plans and actions. If you, heaven forbid, go through with mandating vaccines for innocently healthy children, you will burn in hell for eternity. Thank you for your time and for listening with open hearts.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Donna Treubig:

**MS. DONNA TREUBIG:** Hello. Thank you for the opportunity to speak today. I have no conflicts. I would like to tell you about my grandson, Liam (phonetic). He is a smart, fun, almost three-year-old that has never stepped foot into a public building other than the occasional doctor's office. Has never had a birthday party with friends. Never been to a grocery store and never met most of his extended family. We adults, while vaccinated, have lived the same life for over two years to protect him. Some might think that this is extreme, but there is even more at stake because Liam's type 1 diabetic mother is in her third trimester with Liam's baby sister.

COVID seeks out those who are unvaccinated.

The FDA refusal to act has left the youngest of our society most vulnerable. Children are getting very sick, and dying of COVID-19, as we have heard from the professional presentations earlier today. Today I plea that you approve the vaccine, for children under 5, so that they have some protection with reduce risk of severe illness and long term effects caused by COVID-19.

You must immediately develop 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. Do not leave them behind again. The FDA needs to be nimble and able to pivot as the vaccine changes. We do not want to be forced to wait while the FDA and the virus changes the rules of the game halfway through the next trial. You can make up for the vaccine rollout mismanagement with your promise to remember Liam when you vote to approve both the Moderna and the Pfizer vaccines for children under 5.

Parents deserve the right to choose if we vaccinate our children with a vaccine that offers any

efficacy rate, rather than having no option at all. We also deserve the right to choose between Moderna or Pfizer based on the needs of our children. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Elle Pierce. You have three minutes.

**MS. ELLE PIERCE:** Hello, my name is Elle Pierce. I'm mom to two amazing toddlers, a wife and a certified pediatric registered nurse. I'm speaking in advance of tomorrow's review, and in support of Moderna's and Pfizer's EUA applications for COVID vaccines for the under 5 cohorts. The repeated messaging that we all have the tools to move forward is patently untrue. And the protracted wait for this age group have been unprecedented and excruciating. Although the "E" in EUA stands for emergency, nothing about this process seems to have been done with urgency in mind. What you've all have asked, and continued to ask, a family and their under 5 children, going on our third year now, is truly incomprehensible with the promise of vaccines in the coming days, weeks, months, playing on a loop.

Our public health agencies have taken an enormous risk with the health of our children, and allowing our children to be serially infected with the novel coronavirus is neither a sustainable nor ethical solution. The narrative being pushed that COVID is not a threat to children, does real harm and is demonstrably false. We know COVID infection and reinfection comes with consequences. We know COVID causes inflammation and auto-immunities that affect multiple organ systems, and is the underline cause of diagnoses such as encephalitis, type 1 diabetes, MIS-C, and likely plays a role in the emerging hepatitis cases. We know COVID can kill children. This is just a preview of what COVID has in store, and it will take many years before we can fully appreciate its long term damage.

Unfortunately, the virus evolved during the period of lengthy regulatory delay and as the result our children will not be afforded the same level of protection other groups appreciated. But parents deserve the opportunity to protect their children from severe illness and death should they wish to do so. The

vaccines are safe, and any chance to reduce the likelihood of infection and negative outcomes is welcomed by those eager to vaccinate.

Trailblazer, Dr. Mark Kline, Chief Medical Officer of Children's Hospital New Orleans, and Tulane professor of pediatrics, put it best when he wrote, not vaccinating our children against COVID is like throwing them into the deep end of the pool without a life vest or adult supervision. It won't end badly every time, but that doesn't make it any less irresponsible. Nothing is more tragic than the preventable death of a child.

Additional, while these mRNA vaccines are incredible, they're only one layer of a comprehensive approach. In the future, trials need to be run concurrently across all age groups so our children aren't perpetually abandoned. We need to ensure they have timely access to updated vaccines, as well as vaccines that use different platforms, and safe effective therapeutics including monoclonal antibodies and prophylactics. The moral compass of a society is

how it treats its children. While they can't participate in the political process by voting, paying taxes, or making contributions to political campaigns, the failure to prioritize their lives will haunt us as a society for generations.

Finally, I would be remised not to thank the children and the families that have selflessly volunteered as trial participants. Now I ask you to please expeditiously and without delay authorize both vaccines up for review. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Kate Schenk.

**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'm speaking today to advocate for the approval of vaccines for children under age 5. I believe the communication regarding children and COVID, since the beginning of the pandemic, has unfortunately caused confusion and ultimately has resulted in our youngest children being left behind unprotected.

At the beginning of the pandemic, when COVID deaths were primarily among older individuals, the thought was that children were overall unaffected by COVID. While many were optimistic that would be the case, it has proven over time to not be quite so simple. As more and more children have been infected, thousands have been hospitalized and nearly 1500 children have died. Some people have continued to minimize the impact by saying it's not that many children, or, inaccurately, it's only children with preexisting conditions. I cannot even begin to understand this line of thinking. How many children is the right number to lose? Are children with preexisting condition somehow expendable? No. All childhood deaths are tragic. Children with preexisting conditions didn't ask for or caused those conditions.

In April it's estimated that 3 out of 4 children had had COVID. Millions of children have been infected. Four times more children have been hospitalized this year with the Omicron variant then with Delta last year. And the large increases were in

children too young to be vaccinated. Even if COVID was truly mild for all children, it would still be problematic. Sick children miss school and daycare. Parents of sick children miss work. And no one likes to see their child feeling miserable. These are the best case scenarios though for systematic infections. Having a child sick enough to be hospitalized is far more traumatic for parents and children alike.

Furthermore, this is a novel virus. We are still learning the long term ramifications that so many children may face in the future. What does long COVID look like if it starts when you're less than a decade old? How does an infant or young child convey that they're experiencing (inaudible)? We are now realizing that children who have previously had COVID are at an increased risk of being diagnosed with diabetes. And more recently, the pediatric hepatitis cases has a link to prior COVID infections. It is clear that children are indeed affected by COVID-19.

Unfortunately, perhaps due to confusing communication or pandemic fatigue, COVID mitigation

efforts like masking have ceased in most places. The messaging has now become, everyone who wants to be vaccinated can be. That is why today and tomorrow are so important. Not everyone wants to be vaccinated can be vaccinated today. Our youngest children have waited and waited for a vaccine, despite the fact that some of the data submitted several weeks ago is just now being reviewed.

Vaccination is the best way to protect our children. Priming their immune systems with a safe and effective vaccine will give them a best chance of avoiding severe outcomes like death and hospitalization, and will hopefully decrease the potential for long term effects. Please act now to authorize Moderna and Pfizer vaccines for children under 5. Please make them easy to access so parents can promptly protect their children. Please give pediatric boosters, and vaccines for future pandemic, greater priority and more expeditious review. Our children are our future, and we need to give them the best future possible. Thank you for your time.

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

speaker is Dr. Donald Middleton. You have three minutes.

**DR. DONALD MIDDLETON:** I'm Don Middleton, a professor of family medicine at the University of Pittsburg. Although I serve on a Moderna vaccine advisory board, I am speaking unofficially to support the Moderna COVID-19 mRNA vaccine request for EUA use in children.

The 2-dose vaccine has superior immunogenicity, at least non-inferior, and significant clinical effectiveness. The Moderna COVID vaccine offers both medical evidence and emotional justification supporting an EUA approval.

COVID infection is extraordinary common in children. 75 percent of children have elevated COVID antibody levels, outpacing all other age groups. Because of transmission to others, on a societal level, reduction of childhood disease is critical. Adults with COVID are sequestered. No one does that to their child, so disease is spread. Although COVID is often a-symptomatic in children, some require hospitalization,

the outcome of which may sadly be prolonged disability or death. Treatment is supportive. Clearly prevention is a cure for a disease with inadequate treatment. Vaccine given to children, regardless of prior COVID infection, produces higher antibody levels so is likely to provide at least temporary protection.

Studies have proven that the Moderna COVID vaccine for children reduces infection. Hospitalization, prolong illness and death are by inference also likely to be reduced. Moderna vaccine side-effects are generally tolerable and transient. ]

The addition of a second childhood vaccine to control COVID has obvious advantages. The supply of vaccine will be reassured. Use of a single vaccine product line in an office reduces the risk for error. A 2-dose series is advantageous for its completion. Additionally, the public always approves of having a choice of vaccine.

Many consider COVID to be under control, which it is not, so have become much less cautious. The infection rate may rise again and lead to disruption in

family existence. Children have missed school, church, birthday parties, playgroups and movies. Masking has led to reduction in interpersonal contact. Hospitalization is traumatic, frightening. Thousands of children have lost beloved parents, grandparents, uncles and aunts to COVID. CDC data states that 1252 children have died from COVID, 44 per month. Can you imagine the impact of the death of your child from COVID, knowing that vaccine could've protected against severe disease?

The Moderna vaccine for children offers additional hope that this pandemic can be kept at bay. Please advise the FDA to give this vaccine EUA status for children. Thank you.

**DR. PRABHAKARA ATREYA:** Thank you. The next speaker is Mr. Michael Baker. You have three minutes, please.

**MR. MICHAEL BAKER:** Good afternoon. I have no financial conflict of interest. I'm a father of two incredible children, age one and three. If the past two years has felt like a decade to us adults, please recognize that they have been a literal lifetime to our

children.

So much of a child's development happens before the age of three. In the past two years, my daughter has weaned off of breast milk and purees, and started to learn how to cook with me. She started walking, gone from speaking about five words to talking literally all of the time. She's learned how to use the potty on her own, learned how to recognize and write a few letters, learned to dress herself, feed herself, and advocate for her own needs. Although I will say they are usually more like wants. She's learned to recognize colors and shapes. She's learning to ride a bike, learning how to keep her eye close when I wash her hair. She's trying to learn, albeit slowly, how to not steal toys from her little brother. She's learned to play pretend. She's learned how to keep herself busy on her own because after being out of daycare for so long, and with two busy parents, she often has no other choice.

This period of development is known to be critical in a child's social and emotional development. I pray every day that we have done enough for her to

keep her development on tract, despite the enormous challenges of near complete isolation that we have at time faced.

According to the FDA documentation, Moderna submitted their data, for children aged 6 month to 5 years, on April 18th. Furthermore, it was possible to allow children to begin the first two dosages of Pfizer 3-dose series after safety and some immunogenicity had been proven. It has been 277 days since children aged 5 and older have had access to a vaccine. The wave of pediatric hospitalization seen in January of 2022 should dispel any notion that our youngest children are not at risk. But it also shows us that vaccination works. During that time period, the rate of hospitalization for children under 5 was higher than other older children who have had vaccines available.

We know that despite Omicron mutations, vaccination gives the immune system a crucial head start in recognizing and fighting this illness, which will keep children out of the hospital and lower the risk of other complications such as hepatitis, MIS-C, and long

COVID. Any further delay in vaccination leaves our children vulnerable to another such wave. And going forward, we need to make sure that children have access to the appropriate boosters without delay. Every day that goes by without protection is a day that we continue to risk their health, development and future.

The safety and immunobridging profiles of these vaccines clearly demonstrate that the benefit of their approval outweighs their risk. Thank you for your time.

**DR. PRABHAKARA ATREYA:** Thank you. The last speaker for the Open Public Hearing session is Ms. Justine Luzzi. Thank you.

**MS. JUSTINE LUZZI:** Hi. I do not have (inaudible) (audio distorted) conflicts. On April 7th, 2021, I was excited to get my Moderna vaccine. Like many people I wanted to do my part to end the pandemic and keep people safe. Five weeks later I had my second dose, on May 5th, 2021. I had flu-like symptoms for three days and then was fine, so I thought. On Saturday morning, June 5th, 2021, exactly one month later, I started to develop vertigo. By Monday afternoon I had

lost my vision in my one eye, developed slurred speech, lost motor skills, and developed immense brain fog.

I went to the emergency room immediately. When I got there everyone was sure I was having a stroke. But after five hours of testing, they found out this wasn't the case. I was released and referred to a neurologist. After many weeks of test the neurologist believes it was from the vaccine, that it is not the neuro inflammation, but doesn't know how to treat me. The only thing she offered me was good luck. Throughout the course of the next year I saw a PCP, an ophthalmologist, a cardiologist, an endocrinologist, and a natural path, all hypothesizing the same thing. I've been completely on my own without any proper medical care for over a year now. No one really knows what's going on with me and my brain.

Last summer, at a (inaudible), I had experienced Alzheimer-like symptoms, losing pockets of time, forgetting who I was and where I was. I'm 36 years old. Other issues that still exist today include heart palpitations, constant migraine headaches, hand

numbness and extreme memory loss. (Inaudible) it's been hard to do the most basic of task.

Before the vaccine I was completely healthy. Since my injury I've had to quit my full time job, and instead work part-time spending all my additional time researching science articles, natural remedies, and how to heal myself so I can function every day. All while accruing five-figure medical debt. I am not the collateral damage in the war against disease. I'm a human being who deserves proper medical care, proper compensation, and empathy.

In the court of public opinion I've been called a murder, an anti-vaxxer, and delusional. And, ironically, you are the ones that lie to the American people that vaccines are completely safe for the average person. You are offensive to actual science and medicine, lacking any type of curiosity of adverse events. I have met other vaccine injured along the way that are losing their homes, their lifesavings, in addition to their health. How do you sleep at night? You're a disgrace to humanity. You're a narcissist

cloaked in healers clothing.

The vaccine injured deserves proper medical care and financial compensation that is the least of what you can do. One thing I know for sure is that there are only three things that are guaranteed to never fully stay hidden; the sun always rises, the moon comes out every night, and then there's the truth. And when the truth comes out, I pray God have mercy on your souls. Myself and million others will never stop fighting and telling the truth. Our resilience is bigger than your cowardice. Only cowards would avoid accountability as innocent people suffer. Approving this for children without fully researching the adverse effect is nothing short of criminal, extremely wicked, and shockingly evil. Thank you for your time.

**DR. PRABHAKARA ATREYA:** Thank you. This concludes the Open Public Hearing session, and thank you all for making your comments known to us. Dr. Monto, take it away for the next session of the meeting.

**DR. PETER MARKS:** Dr. Monto, this is Peter Marks. I'd like to just take a moment before we move

off of the Open Public Hearing, if that's okay?

**DR. ARNOLD MONTO:** That's fine.

**DR. PRABHAKARA ATREYA:** Yes, go ahead.

**DR. PETER MARKS:** Thank you very much. I want to thank the Open Public Hearing speakers. But I do need to just make a comment here that the statements were those of the speakers, and the last comment back from the FDA does not imply that we agree with what was said or that we find any potentially offensive statement acceptable. Thank you.

**ADDITIONAL Q & A FOR CDC, FDA AND SPONSOR PRESENTERS**

**DR. ARNOLD MONTO:** Thank you, Dr. Marks. Next we are moving on to the additional question and answer session. We had a very short time for questions and answers, and to avoid a free-for-all I think it would be prudent for us to compartmentalize our questions as our agenda states with the (inaudible), first for CDC, next for the sponsor presentations, and then for any additional questions for the FDA presentations. So, let

have the discussion on the presentation of CDC right now. And then move on to the actual vaccine questions next. Hands raised, please.

**DR. PAMELA MCINNES:** Arnold?

**DR. ARNOLD MONTO:** Yes.

**DR. PAMELA MCINNES:** This is Pamela.

**DR. ARNOLD MONTO:** Yes, Pamela?

**DR. PAMELA MCINNES:** I'm very sorry and apologetic to interrupt. But I am so incensed about the comment that was made in the public session, I cannot remain silent.

**DR. ARNOLD MONTO:** All right, Pamela, you've got the floor.

**DR. PAMELA MCINNES:** I have worked for the Federal Government for almost 30 years. I'm retired now. I have not always agreed with the FDA. But never in my life have I heard them acquainted with the Josef Mengele Institute, and I'm sorry I take very -- actually, I'm not sorry. But I take very deep offense at that comment. And by association, those who are on the committee and those who are consultants are

associated with that committee. So, I will not accept that attribution. And I demand that the gentleman who made that comment disassociate himself from that comment. It is outrageous. Thank you.

**DR. ARNOLD MONTO:** Thank you, Pamela. And, I think there are other comments that were made which also have very little foundation. Given the fact that we are all screened for lack of conflict of interest (inaudible) -- and I'll stop right there. Dr. Reingold.

**DR. ARTHUR REINGOLD:** I have two quick questions for my CDC colleagues. The one for Katherine or Ruth relates to the fact that when the FDA listed possible but unknown benefits of the vaccines, we haven't heard anything about prevention of transmission. Right now there are household transmission (inaudible) in the U.K. that suggest that there is an effect on transmission at least for a period of time. And I'm curious if you think that that is in fact the case as is true for some other viral vaccines. Whether there's reduced infection and transmission for any period of time.

And for Tom, just a quick question, obviously with increasing seroprevalence in kids, the question could be asked whether the risk of myocarditis changes depending on whether you had prior infection. And there could be studies of that. It's also plausible that the risk of myocarditis is changing over time with changing seroprevalence. And I wonder if we have any information about that. Thanks very much to both of you.

**DR. RUTH LINK-GELLES:** Hi, this is Ruth Link-Gelles. Apologies I don't have video as I'm in transit. But I can respond to the first question. I think there's a little bit of evidence that vaccine prevent against transmission, from other countries. I think it's been a little mixed, and maybe not as up to date with current variants as we'd like.

I will say I think there's pretty good evidence that the third dose especially, at least for the first couple of months, does give some protection against infection which would certainly protect against transmission. That protection does of course wane quickly, and so we would expect it to be less effective

a couple of months after your last dose against infection and; therefore, again transmission as well.

**DR. TOM SHIMABUKURO:** Dr. Reingold, to address your question about prior infection and vaccination and subsequent risk of myocarditis, I think we have evidence that prior infection prior to getting vaccinated does increase the risk for reactogenicity, systemic reactogenicity. But we really don't have evidence that that translates into an increased risk for more clinically serious adverse events.

I think it would be difficult to evaluate risk of infection, or infection as a risk factor, for vaccine associated myocarditis, because so many children have been infected and probably many of those children infected but not having that documented in the medical record. But that is certainly an avenue for research in the future.

**DR. ARTHUR REINGOLD:** Thank you both.

**DR. ARNOLD MONTO:** Thank you. Dr. Pergam.

**DR. STEVEN PERGAM:** Thanks. I had a question for Dr. Shimabukuro. It's a question about long COVID

in children. You had a slide that talks about some U.K. data, but I'm curious, does the CDC have any information about COVID-related long term complications in children that are available for the committee to sort of think about as the discussions on vaccine (inaudible).

And I think it's particularly important if there's data that would look at whether vaccine is protected. There's very little data (inaudible). If that data doesn't exist, what work is being done to sort of (inaudible) it could be quite beneficial for helping (inaudible).

**DR. KATHERINE FLEMING-DUTRA:** Thank you for that question. Just note that I am not the long (inaudible) expert, there are other CDC that are more expert on that. And I apologize for the brevity of that section of the presentation due to time limits and we weren't able to include more information. There is some data available about post-COVID conditions in children, but it's admittedly more limited than the data that are available among adults. And there is some ongoing work regarding post-COVID conditions in children.

Specifically regarding the benefits, you know, whether or not vaccination can prevent post-COVID conditions, that's more of a vaccine effectiveness question and I'm not sure if Dr. Link-Gelles wants to weigh in a little bit more on that question.

**DR. RUTH LINK-GELLES:** Sure, happy to. I'm aware of a couple of studies that included adolescents and look at vaccine effectiveness against post-COVID conditions and found that there was some effectiveness. I think it was about 78 percent effectiveness in one of the studies. I will say across the board vaccine effectiveness studies have very different definitions, post-COVID conditions, and that often affects the findings. I think post-COVID conditions, in particular, have been very difficult to study because of the sort of nebulous symptoms involved, and the difficulties with coming up with a standardize case definition.

I'm not aware at this point of any studies that have been published in 5 to 11-year-olds looking at vaccine effectiveness against post-COVID conditions. It is something that we are looking at in a number of

different platforms at CDC. And I think it'll just be kind of dependent on sample size and, again, coming back to this issue of the case definition moving forward. But it is certainly something that's part of our research agenda.

**DR. STEVEN PERGAM:** Thank you very much, both of you.

**DR. ARNOLD MONTO:** Dr. Sawyer, and then, Dr. McInnes.

**DR. MARK SAWYER:** Thank you. Dr. Fleming-Dutra addressed a question of hospitalization with COVID as opposed to hospitalization due to COVID, with some information about the vast majority of hospitalized children actually being hospitalized because of their COVID. And I believe that she may be referring to data that were shown at the recent HDIP (phonetic) meeting on that topic. Could you remind me whether that data was collected during the Omicron era, or not? Because presumably more children with asymptomatic infection are occurring during Omicron and thus the rate of hospitalization from COVID may be reduced compared to

the previous era.

**DR. KATHERINE FLEMING-DUTRA:** Thank you for that question. Again, I briefly during the last Q&A period talked about data from COVID-NET and then also the new vaccine survey launched network. The data that I quoted earlier were from all the entire pandemic. But I do have -- our COVID-NET colleague did provide percentages, which I'm sorry did not make it into the main presentations due to time limits. Children ages 6 months to 4 years, with COVID-19 and associated hospitalization who were primarily admitted for COVID-19. And, again, that's based on a medical chart review looking for symptoms of COVID-19.

During the Omicron predominant period from December 19th, 2021, to March 31st, 2022, is the data that they were able to provide. 86.1 percent children in that age group, 6 months to 4 years, were primarily admitted for COVID-19. And when they looked at that compared to a pre-Omicron period, from March 1st, 2020, to December 18th, 2021, it was 87.3 percent. So, effectively in the youngest children it's about equal

with the percent that were primarily admitted for COVID during Omicron and pre-Omicron periods.

**DR. MARK SAWYER:** Thank you.

**DR. ARNOLD MONTO:** Thank you. Dr. McInnes, did you have your hand raised? I wasn't sure.

**DR. PAMELA MCINNES:** Dr. Sawyer asked my question. Thank you.

**DR. ARNOLD MONTO:** Dr. Fuller.

**DR. OVETA FULLER:** Thank you. Thank you for these presentations. My question is concerning I believe a lot of parents are concerned, or some parents are concerned about the side effects of the vaccine. The data show that they're not great. But for adults there are some side effects or some people who are sharing that the vaccine is what makes them ill. We know that there're side effects or long term effects from COVID. I'm wondering what CDC is doing to look at the side effects of the vaccine. Because I think that's one of the concerns of many parents. And, I believe in giving people a choice, so could someone address that for us, please?

**DR. TOM SHIMABUKURO:** Is your question more generally how we monitor vaccine safety and communicate that information, or something else?

**DR. OVETA FULLER:** No, I think that's pretty clear how you monitor it. The question is there are people reporting that they are having effects of the vaccine. And so I want to know if there's research going on in understanding that. Because, if we know that's the case, then the people who want to give their children the vaccine should have that choice. Those who don't want to should know what's happening with the vaccine so that eventually they can make that choice based on knowing what happens with the vaccine or at least some idea.

So, just if you have any idea of why there're different effects from the vaccine, or claimed effects, maybe these are people who have been exposed to COVID and these are COVID symptoms and not vaccine symptoms. But I know that's a concern of some parents.

**DR. TOM SHIMABUKURO:** I can't really speculate on individual cases of individuals claiming certain

adverse events as maybe like what was heard in public comment or maybe heard elsewhere. What I can tell you is that CDC and FDA are conducting the most rigorous monitoring in the history of vaccine safety for these COVID vaccines. Systemic and local reactions are common. In some cases more common after dose two compared to dose one. Those are expected reactions. They tend to be transient, relatively mild and go away quickly on their own.

With respect to more clinically serious adverse events, I can say that we have detected cases of severe allergic reactions, or anaphylaxis, after vaccination, and that can occur with any vaccination or any medical product.

And, I think we have a sufficient body of evidence to conclude that there's a causal relationship between mRNA vaccination and myocarditis. As I presented previously, it's most commonly in adolescents and young adult males, more common after dose two compared to dose one. We're continuing monitoring in younger age groups, the 5 to 11-year-old children. And

we will monitor very closely in the youngest, the 6 months to 4 or 5-year-olds. Myocarditis is an adverse event of special interest, so we follow up on every case that is reported to the vaccine adverse event reporting system. But really when it comes to clinically serious adverse events, those are the adverse events that we have identified for these vaccine, anaphylaxis and myocarditis.

I think what you may be getting at is more of a public health communications issue. And, our office, the Immunization Safety Office, mostly focuses on monitoring risk, quantifying risk, and communicating risk. And, we would defer to the folks in the immunization program for benefit/risk assessment and communication in the context of benefit and risk.

**DR. OVETA FULLER:** I just would like to offer one explanation. It's not a science explanation, but a numbers explanation. And Dr. Monto might be able to comment on this. I'm understanding that even with influenza now there's some understandings that there's some longer term effects both of getting influenza, as

well as for some people who can't get the vaccine. So, because we're having so many vaccine vaccinations with COVID, perhaps that's showing up effects of long term disease as well as long term vaccination. In general, but clearly the benefits of preventing disease outweigh the risk of those very rare events. So, I'm thinking we're learning a lot from COVID that we never knew before. And that's whether you have a statement or not, Dr. Monto. I just want to bring out that point.

**DR. ARNOLD MONTO:** Thank you, Dr. Fuller. I think we're gradually relearning that there are multiple benefits in preventing disease. And our job here is to look at risk/benefit. And that is something which we really need to consider in examining the whole picture. Thank you. I call now on Dr. Bernstein.

**DR. HENRY BERNSTEIN:** Thank you, great presentations by the CDC as always. My question relates to, and this may be a better question for the sponsor, but with concern to myocarditis, particularly in the males after dose number two, are data available or being collected using a lengthened interval between doses one

and two in the primary series for those males 12 to 17 and those 18 to 25 young adults?

**MR. MICHAEL KAWCZYNSKI:** Katherine, I think Tom lost sound there for a second, so we're going to get Tom's audio back on. Do you want to take that momentarily?

**DR. KATHERINE FLEMING-DUTRA:** That's really a better question for Dr. Shimabukuro, so it'd be best if we can wait until he's reconnected.

**DR. HENRY BERNSTEIN:** All right. And the sponsor may have comments.

**DR. RITUPARNA DAS:** Sure, thank you for the question, Dr. Bernstein. In our studies our study populations were incredibly compliant, so we don't have any clinical data at more than a four weeks duration. But we are looking at kind of observational studies to help inform that.

**DR. HENRY BERNSTEIN:** So you're looking at a longer interval between the primary series, with two dosages of primary series in older teenagers and young adults?

**DR. RITUPARNA DAS:** We are actually not looking at it. I mean, I know there are other observational studies such as those in Canada that have explored the longer interval. We are clinically not exploring the longer interval for adolescents. We're looking at infants and whether a longer interval would be beneficial there.

**DR. HENRY BERNSTEIN:** The longer intervals in Canada were with Moderna, or they were only with Pfizer?

**DR. RITUPARNA DAS:** No, there is data from Canada with eight weeks or so with Moderna as well.

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

**DR. ARNOLD MONTO:** I saw Dr. Shimabukuro appear and disappear. Do you have a comment, Tom?

**MR. MICHAEL KAWCZYNSKI:** He's connecting his audio right now, so you're going to have to give him a moment.

**CAPT AMANDA COHN:** Dr. Monto, this is Amanda. I can actually help respond to that as well if you'd like?

**DR. ARNOLD MONTO:** Okay, go ahead.

**CAPT AMANDA COHN:** I just want to let everybody know that it's actually in the CDC clinical guidelines to allow for a --

**DR. TOM SHIMABUKURO:** This is Dr. Shimabukuro. If you can hear me I'm having a lot of -- can you hear me?

**MR. MICHAEL KAWCZYNSKI:** Yes, we got you now Tom.

**DR. ARNOLD MONTO:** Dr. Cohn was weighing in.

**CAPT AMANDA COHN:** In the CDC clinical guidelines, interim clinical considerations, we do allow for an extension of the interval between the first and second dose to that eight weeks as discussed and based off of the data from Canada and from a couple of other countries.

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

**DR. ARNOLD MONTO:** Dr. Chatterjee, please.

**DR. ARCHANA CHATTERJEE:** Thank you, Dr. Monto. My question is I believe for either the sponsor or our CDC colleagues to answer. I'm trying to verify something that I think I read. It might've been

presented today as well in some of the data. And that is the risk of myocarditis, pericarditis from the vaccines, relative to the risk of myocarditis, pericarditis from COVID. As I understood it, it was about five times as high, with COVID mostly related to MIS-C. But I just wanted to verify whether that was correct or not.

**DR. KATHERINE FLEMING-DUTRA:** Do we still have Dr. Oster (phonetic) on the (inaudible) (audio distorted)?

**DR. OSTER:** Yes, I'm here.

**DR. KATHERINE FLEMING-DUTRA:** (Inaudible) (audio distorted), would you like to take this question?

**DR. OSTER:** Yes, that's correct. Just recently at (inaudible) that we have an increased risk after COVID of having myocarditis or cardiac complications anywhere from about two times in the teenage (inaudible) (audio fades) males to -- yeah, six or eight times even in some of the others. And that includes not just myocarditis, but other cardiac complications including MIS-C, which can be quite severe in (inaudible).

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

**DR. ARNOLD MONTO:** Thank you. Dr. Meissner. And then after Dr. Meissner we're going to have to move to questions directed more to the vaccine presentations.

**DR. CODY MEISSNER:** Listening to the public comments, it's very disturbing. And I realize there is clearly a lot of misinformation that people are carrying with them, and I think it's unfortunate. I just feel a responsibility, I have no relationship with the FDA but I don't think anyone works harder than the folks at the FDA. And to imply that there would be a deliberate delay in a vaccine, I think is pretty outrageous. There's absolutely no evidence that I or anyone else that I know of on the committee has witness that.

But the question that I have is -- two questions. First, on post-COVID or long COVID, there was an interesting study in Nature in the last couple of weeks looking at a very large subset of people in the VA system. And they found that there was only some protection, relatively mild protection, against long COVID among people who had received the vaccine. So we

may not be able to say that immunization prevents long COVID. And, so that's the first question. And then I'm interested in what the folks at the CDC think about that.

And then the second question goes to the one that Dr. Oster was just commenting on. That is the issue of myocarditis from the vaccine versus from infection. My concern is there are probably many, many COVID infections than we know about. So the denominator, I mean, if 75 percent of the population or even 95 percent of the adult population has been infected, we don't really know what the denominator is when we're addressing this issue of myocarditis. We know very precisely what it is following immunization, but it's hard to compare that with an infection itself. So, I'll stop at that point. Thank you.

**DR. ARNOLD MONTO:** Appreciate your responses.

**DR. KATHERINE FLEMING-DUTRA:** (Inaudible) (audio distorted) is on the line, I'll have her address the question regarding vaccine (inaudible) (audio distorted). (Inaudible) and, Tom, feel free to go ahead

on this question.

**DR. TOM SHIMABUKURO:** Dr. Monto, I just got back online right now, so I probably missed the question. Sorry about that. Dr. Meissner, could you repeat the question?

**DR. ARNOLD MONTO:** Cody, can you do it succinctly?

**DR. CODY MEISSNER:** The question I have is the relative risk of myocarditis following infection versus following the vaccine. And, we know what the denominator is pretty clearly in terms of vaccine associated myocarditis. I mean, you've done terrific work to clarify that. But we don't know what the denominator is for myocarditis following infection, because so many infections are asymptomatic. So, can we make that statement fairly, saying that myocarditis is more common after the vaccine than it is after infection?

**DR. ARNOLD MONTO:** Thank you, Cody.

**DR. TOM SHIMABUKURO:** I'm not sure I have an answer to that question. But I think you're getting at

a benefit/risk assessment of adverse cardiac outcomes after COVID disease compared to myocarditis and pericarditis after vaccination. And I think probably the best data we have on that comes from the PCORnet (phonetic) study, which was led by Harvard and also included CDC authors, where they looked at adverse cardiac outcomes after disease versus myocarditis and pericarditis after vaccination. And I will say that many of these adverse cardiac outcomes are associated with MIS-C. And their conclusion was that the risk was greater after disease than after vaccination. So I think that's the best answer I can give you right now. But, I agree with you that that probably is an area of research which deserve some additional attention.

**DR. ARNOLD MONTO:** Thank you. We're going to be moving now into questions specifically directed to both the sponsor and might as well include the FDA representatives in this discussion so we'll broaden the discussion. You've had your hand raised for a while, Dr. Gans, have I changed the subject on you?

**DR. HAYLEY ALTMAN-GANS:** No, this is perfect.

I actually would love an opportunity to speak with our colleagues at Moderna. So, thank you. I have questioned we know that there's availability for what the CDC has provided obviously for interval differences in individuals who wish to have those. And I'm also curious about the choice and what data you have. I understand that the way you set up the studies is the way you set up the studies, but I'm interested in any R&D using the 50 micrograms as the second dose for individuals who are within a high-risk age group.

And/or are there (inaudible) (audio distorted) at a lower dose moving forward. And any data you can give us (inaudible) given that you've (inaudible) (audio distorted) multiple country.

**DR. ARNOLD MONTO:** We've got backtalk.

**DR. RITUPARNA DAS:** Dr. Gans, you're asking about whether we have data about 100 microgram first dose and 50 micrograms second dose for primary series? We do not have those data. I think as Dr. Cohn said, the Canadian data are probably right now the best data about the increased interval. We don't have a mixed

dose 150 for adolescents. I don't believe their kind of mixed dose work in our preclinical data either.

**DR. HAYLEY ALTMAN-GANS:** And what about studies moving forward? Because that would be something that I think would be of interest.

**DR. RITUPARNA DAS:** Yes, as you know, our booster is half of the primary series dose for all of the age groups. So, for adolescents that's 50 micrograms, for 6 to 12 that's 25 micrograms, and for under 6 that's 10 micrograms. And so, we are following the model and as we've seen (inaudible) CDC present the data on the Moderna booster, the reactogenicity is lower and the myocarditis post the booster dose is lower as well. So we are using that half-dose model for boosters across our clinical program.

**DR. HAYLEY ALTMAN-GANS:** Yes, it's the second dose that is the highest range. All right, thank you.

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

**DR. RITUPARNA DAS:** Would it be possible to prepare a slide about the durability of the vaccine response? I believe there was a question at the first

session about how long the vaccine responses lasted.

**DR. ARNOLD MONTO:** Why don't we park that and wait until that comes up again, which I'm sure it will. Dr. Offit followed by Dr. Levy.

**DR. PAUL OFFIT:** Thank you. This gets to a question actually you asked earlier, Arnold. I think it's clear from the adult data that a third dose of vaccine (inaudible) at 4 to 6 months of mRNA vaccine there's a value in terms of action against serious illness (inaudible) Omicron or the Omicron subvariant.

Near as I can tell, we're being ask to approve two doses of this vaccine. Is there an understanding, and I guess this is a question for Moderna and for the FDA, is there an understanding that since you're in the midst of doing booster dosing four months later, that those data would be available five months from now when those children who got two doses would then be getting a third dose? Is that the way this is going to work? Because right now there's a 3-dose vaccine that's now available from Pfizer, which is the better choice, as compared to two doses from Moderna.

**DR. ARNOLD MONTO:** And I will add -- excuse me, before you answer. We heard comments in the Open Public Hearing about it's better to get a 2-dose vaccine than a 3-dose vaccine. I think there is really misunderstanding out there about the value of the third dose when we are putting a 2-dose vaccine next to a 3-dose vaccine in terms of our approvals tomorrow. I've interrupted, please answer the question.

**DR. RITUPARNA DAS:** Sure, I think the adult data show us that the booster doses are necessary particularly for variant. And we have data from our pediatric studies -- and if somebody will bring the incident rates from the adolescents slide up, please, and then we can show it -- that the incident rates for the adolescents stayed very low actually through the Delta wave in the U.S. And can I have Preview B up, please.

The incident rates in the adolescents, so this is no longer a placebo controlled study. This is just our incident rates from the original vaccinated group. And they stayed extremely low through the Delta wave.

And it was the Omicron wave where we started to have the breakthrough.

We started boosting our adolescents in December and those data are being compiled and will be ready shortly. Our booster data, with the prototype, is also being compiled for 6 to 12 and those will be available shortly as well. I think we'll have to look at the pediatric data in more detail tomorrow. Tomorrow we have the 2-dose data that meets the non-inferiority immunogenicity criteria.

And we're working with the FDA on what to do about that third dose. Is that going to be the 1273 booster? Or is that going to be an updated Omicron booster that will be offered to those children.

**DR. PAUL OFFIT:** Maybe just to follow up and maybe this is a question for Doran Fink or for Peter Marks. Is it your understanding that this would be a 3-dose vaccine and that we would have the third dose available within five months of this vaccine launching, because that's really what we're talking about? I don't think we should have to wait for an Omicron boost,

because first of all that may not happen. And so I think we should just have it very clearly that this is a 3-dose vaccine but you're launching it as a 2-dose vaccine. Which is it?

**DR. ARNOLD MONTO:** Dr. Fink, or Dr. Marks, would you weigh in here, please?

**DR. PETER MARKS:** The sponsor has asked for this as a 2-dose regiment. I think right now we're evaluating it as a 2-dose regiment. But the question is would we potentially assume that a booster will be forthcoming at some point for this. I think that's been the natural state of events. I think Doran's on now as well, if he wants to comment. That was the question here, correct?

**DR. PAUL OFFIT:** Correct. Yes.

**DR. DORAN FINK:** I'll add that for these age groups, 6 through 17, for the other mRNA vaccine that has been authorized, we have also authorized a booster dose once we've had the data that has supported doing so. And so we would anticipate taking the same course for this vaccine, understanding that the data to support

the effectiveness of this vaccine is tracking alongside with the other mRNA vaccines.

I don't want to make a promise about a specific date by which we would authorize a booster dose, but I will say that you've heard from Moderna that they intend to provide us data very soon. And we will evaluate it and take regulatory action expediently.

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

**DR. PAUL OFFIT:** Great, thank you, appreciate it.

**DR. ARNOLD MONTO:** I think the problem here is also a messaging problem. Because we should be careful not to have people predict that there will not be a third dose required to handle the variants. (Inaudible) (audio distorted) that we should not have people predict that this is a 2-dose vaccine versus a 3-dose vaccine, which was the comment we heard from a couple of people during the Open Public Hearing. Next is, Dr. Levy, followed by, Dr. Wharton.

**DR. OFER LEVY:** My question is to the sponsor, Moderna. All, thank you for the presentations. Queries

around safety, first of all there were some increased incidents of abdominal pain, I believe in children 2 to 11 years of age in the vaccine group. Can you tell us a little bit more about that? Was it statistically significant? What were associated symptoms or findings? And what was it ascribed to in cases. And then, more generally, what your understanding is to the mechanism for that abdominal pain?

The other question from Moderna is around the correlate of protection. Based on the totality of data that Moderna has, what is Moderna's view of what is the correlate of protection in general and versus Omicron. (Inaudible).

**DR. RITUPARNA DAS:** Okay. I'll take your question about the abdominal pain. As we have in our briefing book and the FDA has in the briefing book as well, if you aggregate terms of abdominal pain, upper abdominal pain, lower abdominal pain, you do see a small imbalance. It is about one percent versus .6/.4 (inaudible) percent in vaccine versus placebo.

These all do occur early after vaccination.

There's not a cause that we're seeing. To us, right now, it seems like it may be part of the reactogenicity of the vaccine. And maybe as you said in the 2 to 11 age group. Did the FDA want to comment any further on that?

**DR. RACHEL ZHANG:** Yes, we took a close look at those cases as well. They were mostly very nonspecific, you know, a child complained of abdominal pain without -- sometimes it was early on with the nausea the vomiting that is also part of the solicited systemic reaction. But very few of those participants sought medical care, so there's nothing else sort of documented with that and it seemed to resolve. So they were all pretty much mild or moderate in intensity.

**DR. OFER LEVY:** Okay, thank you. And the second part of the question (inaudible) (audio fades) correlate of protection and your view of that.

**DR. RITUPARNA DAS:** Yes. So the correlate of protection work that's been done so far has been with the original strain, noting with Delta or Omicron yet. And has been done kind of as a correlate of risks rather

than a correlate of protection, that's the work from our collaborators at the CoVPN, where they've seen that both binding antibodies and neutralizing antibodies are correlated with protection.

We haven't identified a threshold, but higher binding antibodies and neutralizing antibodies seem to correlate with protection. We have not done the work, and we are collaborating with our CoVPN colleagues to see how we should do that work for the Omicron variant. But, we have not done that work yet.

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

**DR. OFER LEVY:** And, (inaudible) this question of durability. Does the correlate predict durability? And my comment is to FDA, this is an ongoing issue, VRBPAC is being convened and repeatedly being asked to consider immunologic dates of antibody (inaudible), neutralizing antibodies and the rest with a very little understanding or discussion of what the correlate of protection are. This is an ongoing issue in the field that's limiting progress and I really call this to FDA's attention. I believe there needs to be a larger federal

effort to understand systematically to help advance coronavirus vaccine now and in the future. Thank you.

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

**DR. RITUPARNA DAS:** Dr. Levy, I did want to share this slide that I shared earlier about the durability of the protection. And as I showed previously the incident rate stay very low. So as long as the variant stayed the same, and even when the variant changed to a more closely related variant like Delta, the incident rates stayed very low. It was only with that step change with the Omicron that the incident rates went up. And so, I mean, the antibodies --

**DR. ARNOLD MONTO:** And what was the overall incidents in the population during that period of durability in the unvaccinated?

**DR. RITUPARNA DAS:** That's the problem with the data here. This is only the vaccinated group. There's not a comparison placebo group, but if you look at kind of the U.S. incidents compared to this, there was certainly a spike during the Delta wave and we did not see that spike in our vaccinated participants.

**DR. ARNOLD MONTO:** Thank you. Dr. Wharton, did you have your hand raised? I don't see it now.

**DR. MELINDA WHARTON:** Thank you, Dr. Monto. I did have my hand raised. I lowered it because of the previous discussion about booster which was what I wanted to ask about.

**DR. ARNOLD MONTO:** Okay, thanks.

**DR. MELINDA WHARTON:** But can I just ask a follow up question on the booster issue.

**DR. ARNOLD MONTO:** Please.

**DR. MELINDA WHARTON:** Clearly the work is ongoing to look at a third dose in the populations of 6 to 11 and 12 to 17-year-olds. Can you tell us when there will be results from that work you're currently doing to look at a third dose?

**DR. RITUPARNA DAS:** Yes. The adolescents and the adults correlate very well. We saw that GMR being 1.01. And so we feel like the adolescents data could certainly be extrapolated from the adults if we so desire. We will have the clinical data in our hand for the immunogenicity and the safety by the end of the

month. But the adolescents, just as a reminder, are getting the same dose as the adults and would get the same booster dose as the adults. For our 6 to 11 population it should be by the middle of July that we have the data, and we'll submit it subsequently.

**DR. MELINDA WHARTON:** Thank you.

**DR. ARNOLD MONTO:** Thank you. Dr. Rubin, followed by, Dr. Nelson.

**DR. ERIC RUBIN:** Thank you. Thanks for those great presentations. And I have a question for our FDA colleagues. I realize this is an apple to oranges comparison, but what would help members of the public a lot is to kind of set the risk/benefit analysis as far as you would know it right now, with the limited data we have, in the context of other childhood vaccines.

And a lot of our childhood vaccines don't prevent deaths, or are not intended for diseases that are commonly fatal, like COVID-19. And how do you think about this vaccine as compared to the usual things that kids are getting?

**DR. RACHEL ZHANG:** Thank you for that question.

I'll try to attempt to answer that and if anyone at the FDA want to chime in. I guess, for safety-wise, we sort of consider other childhood vaccines and (inaudible) reactogenicity profile is not outside the norm of other routine childhood vaccines. Again, there are adverse events that would require larger population or a longer follow up, so those unknown risks will have to be defined once this vaccine go into more of the larger population.

In terms of the benefits, each disease that the vaccine is preventing is very specific to that indication for that vaccine, so sort of considered on a case-by-case bases. I'm not sure if there's a general statement that I can make about how this vaccine will compare against childhood vaccines, in general, in terms of efficacy data that we have and effectiveness data.

**DR. RITUPARNA DAS:** We did have a benefit/risk model at the end of our presentation. I can ask my colleague, Dr. Martin (phonetic) to go through the benefit/risk model some more.

**DR. ARNOLD MONTO:** Would that be helpful, Dr.

Rubin?

**DR. ERIC RUBIN:** It would be helpful if it puts it in context of other vaccines. Just by itself it's hard for other people to (inaudible).

**DR. ARNOLD MONTO:** I don't think it did, but --

**DR. ERIC RUBIN:** Yeah, and I'm not sure if that --

**DR. ARNOLD MONTO:** (Inaudible) vaccine (inaudible)?

**DR. RITUPARNA DAS:** No, our benefit/risk model is not (inaudible).

**DR. ARNOLD MONTO:** Okay, because that's really what's being asked for.

**DR. RITUPARNA DAS:** Okay.

**DR. ARNOLD MONTO:** Thank you. Moving on to Dr. Nelson.

**DR. DORAN FINK:** I sorry, Dr. Monto, maybe I can jump in and try to respond to Dr. Rubin's question a little bit more.

**DR. ARNOLD MONTO:** Yes, go ahead.

**DR. DORAN FINK:** First I want to say that for

preventive vaccines, including and especially for those that are used in pediatric populations, we expect a very favorable benefit to risk balance, precisely because vaccines are being used in large numbers of individuals including healthy individuals.

So that has been the typical benefit/risk profile for vaccines the FDA has approved. And we think that the COVID vaccines that we have authorized, and in some cases approved, do have a very favorable benefit/risk profile. You've heard that the most common adverse reactions that we have evaluated in both preauthorization clinical trials as well as through post-authorization safety surveillance has been mainly mild and self-limited common vaccine reactogenicity that is similar to the reactogenicity associated with other preventive vaccines.

We do have the risk of anaphylaxis, which is not unique to COVID vaccines. Any vaccine can rarely cause anaphylaxis in a susceptible individual. And then we have the risk of myocarditis, which is the other more serious risk that has been more (inaudible) identified

and characterized mainly through post-authorization surveillance. That is more unique to the COVID-19 vaccines. And I think you've heard a lot of discussion that puts that risk into the proper context in considering the serious outcomes of COVID that the vaccine is able to prevent. And so we still would consider the benefit/risk balance to be favorable even taking into account the established risk of myocarditis as well as events.

**DR. ARNOLD MONTO:** Thank you, Dr. Fink. Dr. Nelson, followed by, Dr. Lee.

**DR. MICHAEL NELSON:** Thank you, Dr. Monto, and, I to want to thank the CDC, the sponsor and the FDA for some very clear and objective presentations today. My two related questions center on how best to interpret the data in the setting of natural infection from the circulating variant, especial Omicron. I share a similar interest in piecing out the impact of prior infection on both the immunogenicity and reactogenicity. And you've heard this from some of my colleagues in some of the earlier questions.

We're faced today with making some recommendations largely on immunobridging data more so than vaccine efficacy data, due to the low prevalent of cases throughout the clinical trials. And I do want to thank you for providing at least some data on solicited systemic adverse events following baseline seropositivity where it demonstrated somewhere between six to eight percent, post-dose one, that then evened out after dose two. That was great.

It is clear that those with baseline seropositivity were definitely excluded from the immunogenicity studies. What's not clear to me is whether participants post-dose one or post-two were studied for nucleocapsid seropositivity. Whether their data was excluded from immunogenicity? And what are the possibility of asymptomatic infection actions might interpret, or impact the interpretation of immunogenicity and reactogenicity?

So my two specific questions are as follows. The first one was post-baseline seropositivity participant data excluded from the immunogenicity data?

And if not, was the rate low enough that it was negligible and really wouldn't impact the overall findings from immunogenicity data? This is probably most relevant for Study 204, which was done during the peak Omicron wave.

**DR. RITUPARNA DAS:** So we did a careful characterization of our immunogenicity cohort, and while the -- can I get 56 up, please -- while they were excluded from the per-protocol immunogenicity analysis that I showed you, here's the immunogenicity analysis for the seropositive as well.

And I'm saying seropositive, but seropositive is the nucleoprotein, plus anybody who had positive nasal PCR. So, the immediate and the more remote was included in this seropositive analysis. And the numbers are small, and the number will get bigger as we go farther down the COVID wave. But this is for the adolescents, and as you can see these seropositives do have a much higher kind of immune response after vaccination.

I have that for the 6 to 11 as well. And can I

get Preview B up? And so, you see similarly that you get to a much higher place (inaudible) immunologically. That combined with the safety data that you saw the FDA present, and that we have talked about as well, that after dose one there is a bit more fever and a bit more systemic reactogenicity. And after dose two that evens out. So that's the immunogenicity and the safety and seropositive.

**DR. MICHAEL NELSON:** Yes, and thank you for confirming that those numbers were indeed fairly small and probably would not impact the overall per-protocol data you showed use. Thank you.

The second question deals specifically with myocarditis. So given that adolescents and young males are at the highest risk for vaccine-induced myocarditis, and there were no cases in studies 203 and 204, is there any reactogenicity data from the 18 to 25 group, (inaudible) also at higher risk, that would suggest (inaudible) that vaccine disproportionately increases the risk of myocarditis in those with serologic or clinical evidence of prior infection?

**DR. RITUPARNA DAS:** In our Study 301 that occurred before the myocarditis signal, but there were no cases, when we went back and looked at it, there're no cases of myocarditis in Study 301 either. And, so, I don't think that our clinical data will allow us to get any type of a handle on that. We do have the data from the post-marketing that is continuing to be refined with analyses like the FDA BEST analysis where we're understanding the risk and the clinical course of vaccine-associated myocarditis much more.

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

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

**DR. JEANNETTE YEN LEE:** Thank you for the opportunity to ask these questions. I know for the pediatric group the decision was made to make the criteria be immunobridging and immune response. So my question to the FDA, as there're two parts to this, one is given that especially in the 6 to 11-year-olds we see that the vaccine efficacy itself, the estimates are not very robust, especially since the confidence intervals

goes pretty much from minus to 97 percent, would it be fair to say that if we were in fact to approve the vaccine, we probably would never have the opportunity to ever assess that what the true vaccine efficacy is, because there won't be an opportunity to do that? So that's question number one.

And then question number two is, and this is really more a speculative one. Because we've used these immune response and immunobridging criteria, as the one we're using to approve this, do you think that maybe impeding the adoption of these vaccines in these younger age groups? Because I think as you know for the under 11 the uptake is 35 to 39 percent. Thanks.

**DR. RACHEL ZHANG:** Okay, I will address your first one first. Thank you for the question. Yes, as we have heard in the presentations, because of the authorization of another COVID-19 vaccine, most of the placebo persons (inaudible) crossed over. So there's no more placebo control group. So, unfortunately, after the data (inaudible) there's not going to be any efficacy data that we'll have available.

We did present and we sort of discuss in more detail in our briefing document that if you look at a longer interval, not just the 14 days after dose two, but starting even after dose two, there were few more cases accumulated. And that does allow you to tighten the (inaudible) interval a little bit. So that does give you some more confidence in that number as well. But unfortunately in terms of clinical efficacy results, we will not have any more after this point in time.

**DR. RITUPARNA DAS:** Yes, and if we show our MITT analysis, just as a reminder there were only seven cases, as was mentioned in the per-protocol population. But in the MITT, which is usually the more conservative way to assess efficacy, because it doesn't allow the full two doses and the 14 days waiting period, there we had 25 cases. and the efficacy was directionally similar, and the confidence intervals tighten up.

**DR. JEANNETTE YEN LEE:** And the question about whether the approval based on these immune response and so forth may in fact might not be a powerful persuasion for getting adoption of the vaccine, any comments on

that?

**DR. RITUPARNA DAS:** We always do post-marketing surveillance of effectiveness as well. And so, we have done that from the Kaiser study. And our effectiveness from the Kaiser study has looked very consistent with our clinical trial efficacy data. And, with the authorization, we will lower the age ranges in the Kaiser study. So, we will also, along with other in the community, be doing post-marketing effectiveness work for these younger age groups as well.

**DR. ARNOLD MONTO:** Dr. Marks, your comments.

**DR. PETER MARKS:** Just as a technical comment here. What will come from today is not an approval; it is an authorization. That authorization, under emergency use, will be followed as of actually said earlier today, by additional post-authorization surveillance, close surveillance, of safety events, as well as real-world effectiveness studies as has been done.

And those real-world effectiveness studies may be something, I'm not saying that this sponsor has to

use them, but sponsors use such real-world evidence studies to help show effectiveness in the field in the setting where a randomized trial is no longer possible. So, there are ways that vaccine effectiveness could be looked at in the post-authorization setting.

**DR. ARNOLD MONTO:** And I will say as somebody who does observational studies that they have been the ones that have given us all the data on what happens with the variants and durations and all the rest. So these studies are critical and will continue. Final question for this session from Dr. Hildreth.

**DR. JAMES HILDRETH:** Thank you, Dr. Monto. My question, I think, is to the FDA and to the sponsor and relates to boosters. In the briefing materials that you provided, and also in your comments today, you made reference to using booster vaccines that contain the sequence from Omicron. So by definition that's a new chemical entity, and my question is, what is the process to determine the safety of the new chemical entity? Because it has not been fully evaluated as have the original vaccines. So is there a plan to make sure that

there are no up target, consequences, autoimmune antibodies or anything like that when you change the vaccine without extensive evaluation? That's my question. Do you understand my question?

**DR. ARNOLD MONTO:** We really are not talking about an Omicron containing vaccine at this point.

**DR. JAMES HILDRETH:** So, Arnold, a couple of times today, and also in the briefing materials, reference was made to using a Omicron booster vaccine. And I'm asking what is the process.

**DR. ARNOLD MONTO:** I'll defer to FDA.

**DR. PETER MARKS:** Thanks, Dr. Hildreth. I think the answer to your question is that various sponsors have already started studies with Omicron boosters. They're not large scale studies, but they are immunogenicity studies of the kind that have been done for essentially changing strains. So we will have some safety data with these.

We'll now actually have data from several different immunogenicity studies with different manufacturers. Different manufacturers have now made

and studied various variants, I can think of at least three Greek letters plus the original prototype. So, it's our hope that at our meeting on the 28th, when we review these various data, we will be able to make some comments about how comfortable we are with the level of information we have about changing a variant strain. But it's a very good question, it's just beyond, I think, the scope of today.

**DR. JAMES HILDRETH:** Thank you. Thank you so much.

**DR. PETER MARKS:** Thank you.

**DR. ARNOLD MONTO:** Thank you. I think that ends the current question session. A hand just went up.

**DR. PAMELA MCINNES:** I just want to kind of put this in context. An EUA doesn't certify that a vaccine is safe and effective -- we've learned that since 2020, and I presume that applies also to an addition to an EUA -- but rather that the benefits and risks outweigh the known risks. So that's what our question looks like.

What I'm struggling with is if that's true that the manufacture doesn't have to demonstrate necessarily

safety and effectiveness, but has to do a benefit/risk (inaudible) on the one side to outweigh the other. I'm still struggling with understanding the numbers that are available in each of these bridges.

So, from Moderna -- and I read all 189 pages of the briefing document plus all the accessory information -- so, for P203 and P204 I would like to see a simple table created by Moderna, please, when we're going to take a break. What is really available in terms of N?

We need to see what is available in terms of 12 to 17 in terms of N that receives the dose for which they are seeking an EUA amendment, and the same for P204. Not for six months versus 11 years, but for the actual age indication that they're looking for, so for 6 to 11.

This is actually quite difficult to figure out from the briefing document. So, I've made my own tables and I know what they should look like in terms of N that give us immunogenicity data, safety data, and maybe observed efficacy data? But, I wonder why this can't be in one table.

**DR. ARNOLD MONTO:** Well, what are your numbers, Pamela? Maybe if you mention the numbers, we can see whether there's agreement.

**DR. PAMELA MCINNES:** Well, I can give them all to you. But I'm wondering why the manufacture can't produce them.

**DR. ARNOLD MONTO:** Okay. Let's hear it.

**DR. RITUPARNA DAS:** Yes, we have them. Can we have Preview B up, please? Yes. So this is the total N by age group for the doses that were selected. So, as you see, for 12 to 17 -- and this is the safety set and typically the safety set received at least one dose -- so that's 2486 adolescents, and 3726 were total in the trial. For 6 to 11 it's 3387 vaccinated, 995 placebo, so that's 4382 for the whole dataset.

Our immuno groups are smaller, as you know, because we spare the children some blood draws. And we have used smaller immuno subsets. And the immuno criteria are to meet the non-inferiority, and so the subsets are calculated based on the variability of the --

**DR. PAMELA MCINNES:** Yes, I would like to see a table for 203 that shows me the numbers that you have who received the dose for which you are seeking approval, or an amendment to EUA, for both the safety and data you have on the immunogenicity and what you have on the observed efficacy. Tomorrow we talk about 204, so could we just look at 203? And, can you break that down?

**DR. RITUPARNA DAS:** Okay. So this is the safety set. The efficacy set is very similar to the safety set, but the per-protocol efficacy just remove the people who didn't receive two doses. (Inaudible) --

**DR. PAMELA MCINNES:** Yes, I would like to see a table with the N, the number against what you're measuring, safety, immunogenicity, and observed efficacy.

**DR. RITUPARNA DAS:** Okay, can we bring that back after the break? We'll compile it all into one.

**DR. PAMELA MCINNES:** Fine by me. It's up to Arnold.

**DR. ARNOLD MONTO:** We do have a ten minute

break. Let's take that ten minute break right now, and we'll start with the answers to your question, Pamela.

**DR. PAMELA MCINNES:** Thank you very much, I appreciate it.

**DR. RITUPARNA DAS:** Thank you.

**MR. MICHAEL KAWCZYNSKI:** Welcome back to the 174th VRBPAC meeting. Let's get started and I'll hand it back to our chair, Dr. Monto.

**DR. ARNOLD MONTO:** We were in the middle of a discussion about the total numbers of individual children that participated in the studies. Dr. McInnes, would you again repeat what you are looking for? And then the response. And then we go into the discussion.

**DR. PAMELA MCINNES:** Thank you so much. So, I'm repeating my statement, followed by a question. So, given that an EUA doesn't requires certification that a vaccine is safe and effective -- and I believe that's a correct statement -- but rather that the benefits and risks outweigh the current known risks for all or a subset of the (inaudible) group, which, I think, relates back to the question. So I was asking the manufacturer,

given that I have to do a risk/benefit ratio assessment, and given that there's a lot of work that they put in to preparing their material, I was kind of making my own tables, but I thought maybe that was a little bit risky and that I should just ask them to put in the table.

So, we have two questions that are based on 12 to 17, 6 to 11. And I'd like to know -- this is perfect -- what contributed to the safety, the observed efficacy, and then the immunogenicity set. And this is exactly the table that I was looking for.

**DR. RITUPARNA DAS:** Thank you.

**DR. ARNOLD MONTO:** So you've had instant -- not instant gratification, but at least we got the numbers available that you are requesting.

**DR. PAMELA MCINNES:** So may I ask one clarification?

**DR. ARNOLD MONTO:** You may indeed.

**DR. PAMELA MCINNES:** For 12 to 17, you're actually seeking for 100 micrograms? Is that correct?

**DR. RITUPARNA DAS:** Yes, that's correct.

**DR. PAMELA MCINNES:** Okay. So we should just

look at the top lines?

**DR. RITUPARNA DAS:** Yes.

**DR. ARNOLD MONTO:** And that's why we're having two votes, because there are two different quantities in the vaccines.

**DR. PAMELA MCINNES:** Right, so that's what you're looking for, and then we go to the 6 to 11 and you're asking for 50 micrograms. Correct?

**DR. RITUPARNA DAS:** Yes.

**DR. PAMELA MCINNES:** So, we've got those two. So those are the data underpinning the questions that we're facing today.

**DR. RITUPARNA DAS:** Yes, that's correct.

**DR. PAMELA MCINNES:** Thank you, I appreciate it.

## COMMITTEE DISCUSSION AND VOTING

**DR. ARNOLD MONTO:** Okay. We're now moving on to the general discussion. And we have a reasonable amount of time to go over these questions among ourselves. And, the time allotted includes two votes,

one for the 100 micrograms dose, and another for the 50.

And these are the voting questions, just to focus our attention. Voting Question One, and since I have to read it for the record later on I'm not going to read it for the record right now. We can all read what is up in terms of Voting Question One, which is approval of the EUA, 12 to 17 years of age. And it's based, as Dr. McInnes pointed out, on the totality of scientific evidence available that the benefits outweigh the risks. That's question number one that we'll be considering.

Question number two is the exact same question, different age group, 6 to 11 years of age and 50 micrograms as the dose. So the reason we have two questions is because the dose is different for the younger children that we are considering today compared to the older children. To open the discussion, we have Dr. Meissner.

**DR. CODY MEISSNER:** Thank you, Dr. Monto. Are our sponsor still with us on this discussion?

**DR. ARNOLD MONTO:** They can be if we need them to be. I thought we were done with the sponsors.

**DR. CODY MEISSNER:** Well, I had one question and maybe others from the FDA can answer it.

**DR. ARNOLD MONTO:** Well, why don't you ask the question and let's see if anybody from Moderna is still on? Okay, Dr. Meissner has a question.

**DR. CODY MEISSNER:** Thank you for coming back. So, this will be a situation where we have two vaccines that are available for pretty much the same indication. And they will both have pretty similar platforms. There are small differences (inaudible) --

**DR. ARNOLD MONTO:** Excuse me. What two vaccines are you talking about?

**DR. CODY MEISSNER:** Pfizer and Moderna.

**DR. ARNOLD MONTO:** Okay.

**DR. CODY MEISSNER:** And, I think most people would agree it's helpful to have more than one manufacturer because there could be production problems. There are inventory problems. One may be two, and one may be three doses. But the uptake as we have discussed, particularly in the 6 to 11-year-old is about 30 percent, or somewhere around there. Do you think

your vaccines can improve the uptake? What do you expect will happen when your vaccine becomes available?

**DR. ARNOLD MONTO:** Dr. Meissner, as we answer the question I think we need to straighten out the 2-dose versus 3-dose issue. We have been skirting around that all day in terms of whether this is a 2-dose vaccine with a booster to follow, or a 3-dose eventual vaccine. So, having interjected that could you please answer for the company?

**DR. RITUPARNA DAS:** Sure. I don't think we can speculate about the uptake in the 6 to 11. We are doing outreach with the pediatricians and with other vaccinators to ensure they are aware of the new product that's coming, and to answer any questions. We are doing outreach with groups of doctors. We are doing outreach with teachers and families. And so, I mean, I think the goal would be for all of us together to increase vaccine uptake, but I can't speculate on what the authorization specifically would do.

In terms of the dosing schedule, we are here talking about a 2-dose primary series schedule. And, to

be followed -- I think we all agree -- to be followed with a booster. And the primary series schedule is 100 micrograms, two doses one month apart for adolescents. And 50 micrograms, two doses one month apart for 6 to 11. And then the boosters, which we are studying at half dose of the primary series, those will be brought forward afterward.

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

**DR. ARNOLD MONTO:** So in other words, no claim is being made versus a -- 2-dose being better than a 3-dose, which is what -- okay, I want to get that very clear because we've had several references to that issue. Dr. Cohn.

**CAPT AMANDA COHN:** Thank you. Dr. Monto, first of all I just want to respond to the question that you posed in the discussion, which is that I do believe that the benefits of this vaccine, in the way that it's being presented, two doses one month apart 100 micrograms for the adolescents and 50 micrograms for the 6 to 11-year-olds, the benefits do outweigh the risks. I think that this vaccine has met the exact same level of criteria

that we voted for FDA to authorize for the Pfizer vaccine. And so, I am fully in support of this.

I do also want to commend both the sponsor and FDA. I think that the briefing documents were incredible. They were incredibly long, but very clear. And I think in particular FDA did a really nice job outlining the timeline of Moderna's submission on these products. And they were very clear that the FDA continued to assess the myocarditis issue while considering this product. And I appreciate that time and effort that FDA made. And I concur with the FDA's conclusion that the 100 micrograms of the Moderna is unlikely to have a clear increased risk compared to the Pfizer.

I also want to remind the committee that we now have millions of doses of the Pfizer vaccine in arms of 6 to 11-year-olds and we're not seeing myocarditis to nearly the same level of incidents as we see in young adult males.

I do want to say that I disagree with the 2-dose and 3-dose discussion that's happening here. I

think that Moderna is requesting to be authorized for the 2-dose primary series. That is the same as Pfizer has for these two age groups. I think tomorrow's discussion and the comments that have been confused are related to this younger than 6-year-old discussion for tomorrow. And I also think that both of those products are requesting a two or three dose primary series. So, I don't think that the issue of having booster dose available at this moment is a problem, from my perspective, around authorizing the Moderna vaccine as a primary series. Because, as you know, we do allow heterologous boosting in older age groups, and Moderna is working on the booster dose. And these adolescents and younger children won't be eligible for that booster dose for several months. And so it sounds like the data will be available prior to that time. But it is a booster dose. It's not a three -- even though many members have said that it maybe should've been a 3-dose primary series, we're calling it -- the Pfizer vaccine and this vaccine a 2-dose primary series.

And then, finally, I just want to say that I

agree we've had lots of discussions about the low uptake of the vaccine especially in the elementary school age group. And, I think, as the sponsor has said it's going to take all of us, CDC will work on communication around this new product as we have continued to try to instill confidence in the product that has been available for this age group for several months with very low uptake. But it really is going to require lots of one-on-one single conversations, and educating providers and parents about the benefits that have been demonstrated in these presentations today. Thank you.

**DR. ARNOLD MONTO:** Thank you. I just want to reiterate what you said about the approval of the Pfizer's vaccine originally was a 2-dose series. The reason I was mentioning the 2-doses versus 3-doses, is that in the Open Public Hearing we had three people who referred to -- it's better to have a 2-dose vaccine than a 3-dose vaccine. And I think that we don't want to have that kind of confusion that just because this is being offered as a 2-dose vaccine, when the other mRNA vaccine has been by many people a 3-dose -- two primary

series plus booster -- is that there'd be any confusion about the two products.

**CAPT AMANDA COHN:** Yes, but to clarify. I think that those public commenters were speaking about the younger than 6-year-olds. And, from what I --

**DR. ARNOLD MONTO:** I don't think they were. They were talking about preference for a two-dose vaccine.

**CAPT AMANDA COHN:** Yes, in the younger age group. And I think that tomorrow those 3-dose --

**DR. ARNOLD MONTO:** They were not talking about -- let's park that, but we don't want to further confuse the world by having an unnecessary discussion about this. Dr. Rubin.

**DR. ERIC RUBIN:** I am going to say exactly what Dr. Cohn said. Very briefly, for both of the questions that we're voting on, the evidence that's been presented is very (inaudible) (audio distorted) and it suggested there's protection from two doses. There might be increased protection from a third dose. If so, great, but that's not the question before us. And I think that

the question passes on the bases of the data that we have.

**DR. ARNOLD MONTO:** I agree. Dr. Gans.

**DR. HAYLEY ALTMAN-GANS:** Thank you. Yes, I just wanted to weigh in because I largely agree with everything that's been said. And I think just for our colleagues I completely agree also that we need more choices. And certainly, what we've seen from the safety data we feel comfortable with that second choice. And it also will hopefully allow within these age groups to do what we've done effectively in the older age groups where there are mix and match abilities particularly for that third dose.

And then, certainly on the horizon hopefully we will see some even further consideration of the makeup of these vaccines, which I think it would be very important for us all moving forward. And I would just encourage, given what we've seen in terms of our ability to bring this to market later than the other ones which was necessary in terms of the figuring out the dosing and doing this as a staged way in which we do it. But I

hope that we can move quickly, and then hopefully ensure individuals, if a third dose is needed when they need it -- which will be months off -- is available to them. And so that's something I would like to see.

I would also like us to see, since we can learn a lot more from the way in which these companies have been doing studies and the millions of doses that have been available to individuals. We really should be getting the data from those, because these are their studies and they should know about them. There should also be some flexibility to how we think about this moving forward in terms of scheduling and dosing, and thinking about different strategies.

Clearly the question before us is actually a little bit straightforward, but I wanted to put out some of the ways in which I hope that our colleagues are thinking about presenting even for the data tomorrow. So that's all I wanted to say.

**DR. ARNOLD MONTO:** Thank you. Dr. Sawyer, followed by, Dr. Wharton.

**DR. MARK SAWYER:** I agree with the previous

speakers that the data presented and the overall benefit outweighs the risks for both questions that we're being asked.

I am a little bit sobered by the myocarditis data and the frequency with which that is occurring. So that clearly needs to be watched closely going forward as we expand the use of the vaccine.

We've recently seen from HDIP (inaudible) an extension of the interval between dose one and dose two, from three or four weeks, depending on which product we're talking about, up to as long as eight weeks. Because of data, I think primarily from Israel, that the incidents of myocarditis are reduced with a longer dosing interval, and that the efficacy or at least the antibody levels may be higher.

So, given what we've heard today about myocarditis incidents with this vaccine in the age groups we've discussed, it's going to be very important that somebody gather data on an extended interval. And I don't know whether that's something the FDA can ask the company to do, or whether we have to rely on data

from other sources. So I'd be interested in any comments on that question.

**DR. ARNOLD MONTO:** I think we need to park that question for the moment. Dr. Wharton, followed by, Dr. Offit.

**DR. MELINDA WHARTON:** Thank you. So, based on the totality of the evidence available, I'm supportive on both of the questions. I think that the data do support that the benefits will outweigh the risks for both of these doses and both of these age groups.

I did want to comment on what a good job I thought that the sponsor and FDA did on the briefing materials; they were really well-written. And, I really thought that those were just awfully well put together.

And I also wanted to express my appreciation to the sponsor for so clearly presenting the reactogenicity data in the group of participants who were positive for COVID, prior COVID infection at baseline, I think those were really helpful data and it was great to see those so clearly presented.

And I think that the clarity of both the

written presentations as well as the verbal presentations today have made this, at least from my perspective, a pretty straightforward decision, so thank you.

**DR. ARNOLD MONTO:** Dr. Offit, followed by, Dr. Reingold.

**DR. PAUL OFFIT:** I'm going to take a somewhat contrary position, I think, to Dr. Rubin and Cohn. We're at a different part in this pandemic. I mean, when we say that they did as Pfizer did show protection, what they showed was for the 12 to 17-year-olds there were eight cases of illness when Alfa and D614g were predominant.

With regard to the 6 to 11-year-old, they looked at 25 cases of illness when Delta was predominant. We're not there anymore. Where we are right now, is we are now dominant (inaudible) (audio fades) on subvariant. So the question is will two doses of this vaccine offer adequate protection against Omicron subvariant? And I think the answer is certainly regarding mild illness, no. And I think regarding

severe illness, yes, as long as there's a third dose.

So I feel uncomfortable saying that this is the same place where Pfizer was when they were submitted, because it's not. So, I'm comfortable, and I agree with you that I'm comfortable saying that I think the benefits clearly outweigh the risks. But I say that with the comfort being provided that there will be a third dose. Because I think if that was not true, I wouldn't feel the same way. We're not in at the same part of this pandemic anymore. It's a different time. Thank you.

**DR. ARNOLD MONTO:** Yes, I think, Dr. Offit, what we have to do is do what we need to do because this is the question that's put in front of us. But message exactly what you said otherwise we undermine our own efforts to get people to get boosters down the road. Dr. Reingold.

**DR. ARTHUR REINGOLD:** Thanks. I basically agree with what Paul just said and I fundamentally agree that the benefits outweigh the risks. I did want to make three other points if I might very quickly.

Since I have family members in prior generations who either did or did not escape the holocaust, which may be true of others on this call, I'm not used to having either my morals or my place in the afterlife put together with that of Josef Mengele. So I do want to explain my thinking about this issue. And, by the way, that's a common theme with the emails that flood my inbox at the moment and I suspect the inboxes of others.

First, I agree, I'd like to give parents as many choices as possible. And let them make the decisions about this for their children. Secondly, I want to remind people, we've heard quite a bit about how common SARS-CoV-2 infection is and that 99. whatever percent of infections are asymptomatic or mild. I want to remind those who are too young to remember that that was true of polio as well. I'm probably one of the few people on this call who has seen acute paralytic polio and many of the people who survived polio through my work in West Africa. And the estimate at the time was something like 1 in 200 polio virus infections produced

paralysis. But it was the picture of those kids in wheelchairs or with crutches or in iron lungs, that made us decide we should try and do something about polio to prevent these very, very severe but rare outcome. And I think the same is true for COVID-19.

And, last, I just want to say something about this issue that's been raised by some in the public about needing long-term safety data, implying that we don't know what the effects of these vaccines might be on reproduction or cancer or other thing 20 or 30 years from now. I just want to say that as an epidemiologist that a) those are fundamentally unanswerable questions; and b) that we have never had "long-term safety data" on any vaccine or drug that we currently use today. Thank you.

**DR. ARNOLD MONTO:** Thank you. Dr. Marasco, followed by, Dr. Rubin.

**DR. WAYNE MARASCO:** Thank you, Arnold. I just wanted to follow up on a point that was made by, Dr. Fuller, and Dr. Sawyer. And this really gets to adverse effect of events and perception by the public. If we

just use the case of myocarditis as an example. We're monitoring it closely to find out who gets it and what the incident is. But is the FDA and the CDC doing anything proactively to really in real time collect what might be valuable biologically specimens to interrogate this more?

The sense I think of everybody on the committee that this is immune or inflammatory mediated, and if we don't sort of have a system in place to be able to try to get relevant samples, we might miss our ability to sort of further -- no, because there could be risk factors; it's not just monitoring. Thank you.

**DR. ARNOLD MONTO:** Dr. Rubin, followed by, Dr. Chatterjee.

**DR. ERIC RUBIN:** Thanks, Dr. Monto. I want to respond to Dr. Offit's comment, because, absolutely agree. But at the same time, we're always going to be behind the 8-ball. We're always going to be looking at the last variant or the variant before that because that's how long it takes to produce these data. And I think we have to make decisions based on the best data

we have, which is always going to be old data in an outbreak that's constantly moving.

Dr. Offit said (inaudible)(audio distorted) children against severe disease. Very difficult to tell from the data, but by extrapolation that's very likely to be true. It probably don't do very much for protecting them against the current strain that's circulating. We very likely won't do a great job against the next strain that's circulating.

However, I think that the ability to protect against severe disease is quite compelling. So, I don't think we want to pass up the opportunity to offer something to these kids.

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

**DR. ARCHANA CHATTERJEE:** Thank you, Dr. Monto. I basically agree with the viewpoints that both, Dr. Rubin, and Dr. Offit has expressed. Which is we don't have perfect data; we never will really with these vaccine. It's going to be very difficult to get those. And, so, we do the best with what we have. We have the

questions before us. The questions are whether the data supports voting for an emergency use authorization. And I would say that that is probably true.

Having said that, the importance of additional doses, as the pandemic progresses, cannot be minimized, and so it won't necessarily be in the language that we recommend. But it is something for our FDA colleagues to maybe take note of. Is that they could certainly put language in the authorization document to suggest that additional doses might be needed in these children that will be receiving only two doses to start with.

**DR. ARNOLD MONTO:** Couldn't agree more, it's a question of how you message. Dr. Cohn.

**CAPT AMANDA COHN:** Thanks. I was also going to talk about communication and messaging. And I think what Dr. Chatterjee just mentioned is a good start. I think the way that CDC is messaging vaccination right now is, if you haven't gotten a dose in the last five months, you need to get a dose.

I think in general we're speaking about this group that may not be eligible based on the EUA

authorization for a booster, but in our general communication to the public we will be and we do talk about booster doses. But, the people who we need to target with this product, and continue to target with the Pfizer product, are those groups that haven't gotten their primary series yet. And so, I think sometimes in our communications we're focusing so much on the booster dose that we're sort of getting lost in there that we still need a large group of Americans to get their primary series.

And so, I think focusing on those who haven't been vaccinated at all, with these two options for a primary series, continues to be something we have to communicate just as much as booster doses for those who become eligible for them.

**DR. ARNOLD MONTO:** I believe we are all in agreement, but speaking from slightly different perspectives. But we all agree vaccination needs to be given especially to those who've not been vaccinated before. Dr. Hildreth

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

First, I want to thank the FDA team and the sponsor's team for the great briefing documents we were provided. I found them to be much better honestly than the ones we've received before. And I also believe that the data that we received today justify an answer of yes to the two questions.

But, one thing I think we owe the public is to make them aware of the true risk of COVID-19 in children. According to the seroprevalence data that 70 percent of kids have been exposed to SARS-CoV-2, means that as many as 35 million children have been infected. And with 637 deaths in kids zero to 11 years old that means the risk is relatively small.

Now, to the families that have lost their kids of course, it's tragic and important, but I think in discussing this with the public let's be honest about the true risk of this. And empower those families who want to protect their children to do so but to certainly make it optional because clearly some kids get infected and do just fine. But I think the answer to the two questions, my vote will be yes. Thank you.

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

**DR. OFER LEVY:** Yes, I wanted to say a few comments about the bioethics of this. I mean, there is the concept of vulnerable population. Typically includes the very young, the very old, people who are disadvantaged in various ways. And medical ethics is an important concept, the concept of presumption of inclusion. And this mRNA vaccine form is a relatively new platform. It came out of the Warp Speed initiative. But it has been successful. Not perfect, but successful.

Of course safety comes first, and that's why the safety data need to be so carefully scrutinized. But in addition to serving as a tool to help protect younger populations, against this virus, another potential benefit of an authorization, provided the committee agrees and FDA agrees that it outweighs the risks, which is my opinion. Another benefit of this direction would be to position the platform to be able to more rapidly protect these vulnerable populations in

the case of additional variants emerging.

We don't know what this fall will look like as the weather cools off and kids go back to school. We also don't know what other pandemics lies in the future. So, in many ways the presumption of inclusion from a bioethical perspective is another way to frame what we're talking about today. Thank you.

**DR. ARNOLD MONTO:** Thank you. Dr. Berger, followed by, Dr. Offit.

**DR. ADAM BERGER:** Thanks, and thanks to the FDA and CDC and the sponsor. I do think everything was really nicely laid out. It was really much easier to follow along with where the data was going and what the outcomes were looking at. With that I'll just state upfront I do think the benefits outweigh the risks here for both questions.

But I agree with Dr. Hildreth in making sure that people understand the limitations of what the data is telling us right now. I think one of the pieces -- and I asked this question earlier about some of the minority populations representation and immunogenicity

data, I really do wish that it was more robust than just having four individuals from a 12 to 17-year-old population that were black or African American. I do think this is an important population that we need to make sure that we're able to offer vaccines to. And according to the earlier data, you're looking at 40 percent of these individuals haven't had a primary series yet. So I do think we need to make sure that we are making everyone aware of what the limitations are. Making sure we're addressing what those limitations speak to, and that we're getting robust answers to this.

I also just want to take the opportunity to say I think one thing we definitely need to make sure that we're looking at is durability of the response. I think we're looking at a timeframe where we're saying everyone between three and five months is when your immunity is going to wane. At what level are we going to get that information out of the immunogenicity data if we're going to be using that going forward? So I do think we want to make sure that we have a better understanding of durability as we move forward. Thanks.

**DR. ARNOLD MONTO:** Thank you. Dr. Marks, did you have a comment?

**DR. PETER MARKS:** Thanks very much. Just to try to reassure the committee from knowing and stepping back and looking at all of the different vaccine applications in adults. And that we've seen today in adults and children. For COVID-19 vaccines we have -- and this is not an excuse not to have data on different ethnics or racial groups, but we have to date seen any differences in the immune response in different groups of individuals. And that's despite the fact that in the adult clinical trials, they were some of the most diverse and well-diversely enrolled trials that we have seen for vaccines.

And just to try to reassure people a little here, again, not taking the onerous off of sponsors to try to enroll the most diverse clinical trials that they can, but just to try to reassure people that we have not seen differences in adults and older children.

**DR. ARNOLD MONTO:** Thank you, Dr. Marks. Dr. Offit, followed by, Dr. Hawkins.

**DR. PAUL OFFIT:** Thank you, Arnold. So, getting back to points made by both Dr. Chatterjee and Cohn in terms of messaging. Here's what I would say. You've probably have seen the paper that was published in Clinical Infectious Diseases by Mark Penfold (phonetic) and co-workers at the CDC. What they found was if they looked at March to December of last year, with two doses of vaccine you had excellent protection against serious disease that was relatively long lasting for everybody over 18, including people over 65, including people with at least one co-morbidity. But that was Delta. The minute that Omicron came into this country, and now the Omicron subvariant, we crossed the line.

So, now you had a new (inaudible) strain. So two doses you were not going to get good protection at all against mild illnesses. The good news is that with a third dose you get the kind of affinity maturation that allows you to be protected against serious illnesses. That's the good news about Omicron and these Omicron subvariants.

So I guess I disagree with the term "booster dose." The third dose is not a booster dose for the Omicron subvariant. It is part of the primary series. And that's what worries me here. This is a 3-dose primary series whether it's a Pfizer vaccine or a Moderna vaccine. And I think if we message it as something else, then we're going to get a less amount of immunization than we need. It's a 3-dose primary series for these Omicron subvariants. Thanks.

**DR. ARNOLD MONTO:** Dr. Hawkins, followed -- last comment -- by, Dr. Kim.

**DR. RANDY HAWKINS:** Thank you very much. This is not to make the comments, because it's been stated multiple times. Notwithstanding Moderna's and FDA's attempts, I really wanted to see a greater inclusion of African American adolescents' participation. (Inaudible) discuss or (inaudible) African American patients, mothers, parents, fathers about the vaccine. And I agree with the conclusion of those who've spoken already. Thank you very much.

**DR. ARNOLD MONTO:** Thank you. Dr. Kim, final

comments. And just to remind people, you will have a further chance to explain your vote.

**DR. DAVID KIM:** Well, thank you very much. I to would like to thank FDA, CDC and Moderna for their hard work in getting us to this point. The standards for vaccine safety and efficacy have been set through past VRBPAC meetings and FDA authorizations and approvals. The safety and efficacy of Moderna vaccine, for kids 6 to 11 and 12 to 17, is consistent with what this committee has already recommended. So my response to the question posed is really not hard to make.

I appreciate the earlier discussion on comparing the disease burden, and benefits of the COVID vaccine to those of the flu for children. And, we can further contextualize COVID in comparison with other diseases. A disease that's been around a long time and perhaps known to many for which an effective vaccine is currently available. And several were mentioned earlier today, but measles and many (inaudible) diseases come to mind.

So, as Dr. Cohn mentioned earlier, clear and

effective communication with the public and healthcare providers is continually needed. We certainly have a challenge ahead of us. And there's a lot of work that needs to be done on this front to promote the confidence in COVID vaccine and reduce hesitancy (inaudible). So thanks again to the FDA for leading this discussion and for today's vote.

**DR. ARNOLD MONTO:** Okay. I see a hand raised. Dr. Bernstein, you have a burning comment before we go into a vote?

**DR. HENRY BERNSTEIN:** I don't know how burning it is, but I just wanted to suggest that I am supportive of these two voting questions. And, although I believe as some others have said a third dose will likely be indicated, due to evolving variants that are going to continue since so many people continue to be unvaccinated even with the primary series. I think adding this vaccine, making it more available to families, is good because families like more choice.

And I'd like to say that I think we need to do whatever we can to allay parental concern regarding

myocarditis, because I do think that that's a major concern for the public. And I think one of the things that we can do, which is why I had brought it up earlier, is we need to emphasis the longer interval between doses one and two for a lot of most people except for certain high-risk groups. I think that that's quite important.

And, I'll end with thanking the FDA and Moderna, because I do think the briefing documents were incredibly comprehensive and detailed and it was very important and helpful in our discussion. Thanks.

**DR. ARNOLD MONTO:** We seem to have some late additions to our speaker's list. Dr. Marasco.

**DR. WAYNE MARASCO:** Well, that was left over, I'm good.

**DR. ARNOLD MONTO:** That was left over. Dr. McInnes, do you want to have the last word?

**DR. PAMELA MCINNES:** Oh, wow, that's dangerous. I have a question about the choice, so from the practicing pediatricians and internists. My experience where I live is that a facility only keeps one

particular vaccine. And that's sort of governed by where you can go and what your insurance is and if you're an HMO etcetera. So, in reality, if you're going to an HMO, do you have HMOs that keep both vaccines, giving parents a choice of which one? Or, if you don't belong to an HMO and you're like in a PPO situation, is that depending on where the parents want to go? Could you explain this choice concept a little bit more?

**DR. ARNOLD MONTO:** I'm not sure who you're directing your question to.

**DR. PAMELA MCINNES:** To the practicing pediatricians and to people who has talked about choice of vaccines.

**DR. ARNOLD MONTO:** Okay, Dr. Bernstein wants to answer. You'll have the final word.

**DR. HENRY BERNSTEIN:** I don't want to have the final word. I like it when Pamela was doing the final word. But, you're absolutely right that offices, health centers, don't stock each and every product that's available. But, fortunately, as far as COVID vaccines are concerned, if they're interested in one and not the

other they oftentimes can find it in their local community even if it's not in their primary care practice. So, having that choice if somebody feels that it's available, our health system is supplying only a single product, and that's above my pay grade on why we have that product. But, it's the same thing that happens with combination vaccines. For the longest time we have VAXELIS (phonetic) for our government-insured patients, but not commercially. And so it really makes it a little bit difficult when you're trying to offer vaccines to improve vaccination rates. I hope that answers what you're saying. Now take the last word.

**DR. ARNOLD MONTO:** Okay, Dr. Pamela, I can tell you in our own community that the same pharmaceutical chain, some of their stores offer one of the vaccines and some of the stores offer another one of the vaccines. So if you want to choose, you can figure out where to go. Dr. Fuller. I'm going to have to call an end at some point. Dr. Fuller, do you wish to make a comment?

**DR. OVETA FULLER:** I just want to answer

Pamela. So Dr. Monto just told you the situation where we are that you can go to your pediatrician or you can find a place that offers a different one. But the other thing I was addressing is, if this is not EUA approved, then the people who want to get it from their pediatrician or any place can't get it.

So a choice would be to have your child vaccinated, which in my opinion is a wise thing to do, or not. If we don't approve it then those who want it who are really waiting for it won't have that opportunity. So that's what I meant by the point.

**DR. ARNOLD MONTO:** Thank you, and I'm glad to give you the final word that we should all get vaccinated.

**DR. OVETA FULLER:** And we should.

**DR. ARNOLD MONTO:** Okay. We are ready for the voting question. What I propose is that we have the two votes and then we have the committee members explain their votes if they wish to do so. We will do the votes in order. And then we'll go around for explanations of votes. First voting question, please.

**MS. CHRISTINA VERT:** Dr. Monto, first I want to give a little explanation of the process. Only our ten regular members and 12 temporary voting members, a total of 22, will be voting in today's meeting. And with regards to the voting process, Dr. Monto will read the final voting question for the record. And afterward, all regular voting members and temporary voting members will cast their vote by selecting one of the voting options, which includes yes, no, or abstain.

You'll have two minutes to cast your vote after the question is read. Please note that once you have casted your vote, you may change your vote within the two-minute timeframe. However, once the poll has close, all votes will be considered final. And once all the votes have been placed, we will broadcast the results and read the individual votes out loud for the public record. Do anyone have any questions related to the voting process before we begin? Okay, Dr. Monto, if you could please read the voting question.

**DR. ARNOLD MONTO:** Okay. Voting Question One, Based on the totality of scientific evidence available,

do the benefits of the Moderna COVID-19 Vaccine when administered as a 2-dose series, 100 micrograms each dose, outweigh its risks for use in adolescents 12 through 17 years of age?

**MS. CHRISTINA VERT:** Thank you. And, Michael, can you please pull up the voting pod. At this time you may select your choice. Okay. I'm just going to check the votes. Okay, great, time's almost up. Does anyone needs any more time? Or I can close the poll early if the votes are all in. Okay, no one is raising their hand or needs more time. We can go ahead and close the poll and broadcast the results.

Again, there are 22 voting members for today's meeting. And, we had a unanimous vote of 22 out of 22 yes votes. And so we have a favorable result. And I will now read the voting responses of each voting member.

Dr. Levy, yes. Dr. Hildreth, yes. Dr. Rubin, yes. Dr. Wharton, yes. Dr. Monto, yes. Dr. Chatterjee, yes. Dr. Nelson, yes. Dr. Sawyer, yes. Dr. Fuller, yes. Dr. Reingold, yes. Dr. Berger, yes.

Dr. Lee, yes. Dr. Bernstein, yes. Dr. Marasco, yes. Dr. Kim, yes. Dr. Cohn, yes. Dr. Offit, yes. Dr. Meissner, yes. Dr. Hawkins, yes. Dr. McInnes, yes. Dr. Hayley Gans, yes. Dr. Pergam, yes.

Okay, that concludes my reading of the votes. And it concludes the vote for Question One. Now move on to Question Two Dr. Monto if you could please read the second voting question.

**DR. ARNOLD MONTO:** Based on the totality of scientific evidence available, do the benefits of the Moderna COVID-19 Vaccine when administered as a 2-dose series, 50 micrograms each dose, outweigh its risks for use in children 6 through 11 years of age?

**MS. CHRISTINA VERT:** Okay, you can go ahead and start voting. Thank you. Okay, it looks like all the votes are in. Does anyone need more time? Okay, we can go ahead and end the poll. Again, we have 22 out of 22 yes votes, zero no votes and zero abstain votes. So we have a unanimous vote in favor. And I will go ahead and read the specific votes for the record.

Dr. Levy, yes. Dr. Hildreth, yes. Dr. Rubin,

yes. Dr. Wharton, yes. Dr. Monto, yes. Dr. Chatterjee, yes. Dr. Nelson, yes. Dr. Sawyer, yes. Dr. Fuller, yes. Dr. Reingold, yes. Dr. Berger, yes. Dr. Lee, yes. Dr. Bernstein, yes. Dr. Marasco, yes. Dr. Kim, yes. Dr. Cohn, yes. Dr. Offit, yes. Dr. Meissner, yes. Dr. Hawkins, yes. Dr. McInnes, yes. Dr. Hayley Gans, yes. Dr. Pergam, yes.

And that concludes my reading of the votes out loud for the record. And I will now hand the meeting back over to you, Dr. Monto.

**DR. ARNOLD MONTO:** Okay, those who wish to explain their votes, please raise your hand. Dr. Levy, followed by, Dr. Offit.

**DR. OFER LEVY:** I wanted to say that I believe this vote. And I'm happy to see that it was unanimous. It's standing up for vulnerable populations that merit consideration in terms of protection against this virus. I believe that this will provide families an important option. And, again, we don't know what this fall will bring, but even under current conditions this can be a valuable tool. And, having this available to families

particularly in areas where there's rising of viral spread and particularly parents of children who may have comorbidities or be at higher risk, to make that determination with their pediatrician. I know this is not our purview, but as a personal matter, I'm not pushing for mandates but I believe this vaccine should be made available because the data we saw today, and review carefully and discussed, indicated that the benefits outweigh the risks in these age groups. Thank you.

**DR. ARNOLD MONTO:** Dr. Offit, followed by, Dr. McInnes.

**DR. PAUL OFFIT:** I voted yes because I think the way that the question is worded is clear that the benefits outweigh the risks. But I just would make this plea, and I guess I'm making the plea to Amanda Cohn and Melinda Wharton to use your considerable influence at the CDC to please make sure that this 2-dose series is not described as being fully vaccinated, and that the third dose is simply described as being up to date or a booster. This is a 3-dose series if it is to be

effective against preventing serious disease against these Omicron subvariants.

And I believe that the company is within -- as they said by July going to have a third dose available, great. I felt better when Dr. Cohn said that worst case scenario you can have a heterologous boost, that's good. But you do need the affinity maturation that comes with the third dose to get protection against Omicron or Omicron subvariant. So, that's my plea. Thank you.

**DR. ARNOLD MONTO:** Thank you. Dr. McInnes, followed by, Dr. Meissner.

**DR. PAMELA MCINNES:** Ditto to Paul's comments. And, in addition, I really would like to see this as a clinical (inaudible) supplement to the BLA, in order to sustain strain changes as we move down the road. I don't believe we can live in this EUA structure the entire road here. So, I would like to urge companies to move in that direction. I'm sure they're doing it; I would like to see the data for it put before us. It would be a pleasure.

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

followed by, Dr. Nelson.

**DR. CODY MEISSNER:** Thank you, Dr. Monto. I agree that it's important to have this vaccine available, because it makes it easier in terms of maintaining inventory for a site where the vaccines are being administered, if they want to stock both vaccines. It's awkward if one vaccine is for older adolescents and another one for children -- or not available for children. So, I think that makes good sense.

I also want to make two other points. One, I think the numbers that I heard from Moderna, there were 10,884 recipients of mRNA 1273, between 6 months and 17 years of age. And so that does not really address the myocarditis issue. Remember, myocarditis, I think is between one and ten cases per 100,000. So we haven't addressed that. I think the evidence as has been pointed out is that it's much less commonly a problem in young children than it is in adolescent males. And hopefully, that continues to be the case going forward.

And, the last point I want to say is I think this vaccine should be available for children who have

what are pretty well recognized risk factors. I agree with what I think Dr. Ofer Levy was saying, it should not be mandated, I don't think that would be the appropriate way to proceed, but I think that for those families that really want to vaccinate their children, and for those children who do fall into high-risk categories, the vaccine should be available.

**DR. ARNOLD MONTO:** Thank you, Dr. Meissner. Dr. Nelson, followed by, Dr. Hildreth.

**DR. MICHAEL NELSON:** Thank you, Dr. Monto. With respect to the benefits outweighing the risks I believe the answer is clear and certainly very supportive. I did want to make a couple of points and/or caveats.

My question earlier had to deal with the influence of prior infection on the data that was presented. And it was in the context that I believe the great majority or at least a significant piece of the population feels that if they were previously infected they don't need a vaccine. Well, I think there is an opportunity and really a mandate for us to communicate

the benefits of vaccination, even if you had prior infection. So, certainly that should be taken up as part of our communication messaging strategy.

I would also like to pay a little bit of attention to our highest risk populations. As an allergist and clinical immunologist, dealing with primary immune deficiencies affecting one percent of the population, and the vast majority of it being in children, we didn't hear a lot of data about those with immune deficiencies or immune dysregulation or comorbidities with respect to the data. Some was in the briefing material, but I think it's important to address these high-risk populations early up front. And it has significant impact with respect to dosing, not only between the first and second dose, but as has been stated, the very likely need of early third does. Thank you, Dr. Monto.

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

**DR. JAMES HILDRETH:** Thank you, Dr. Monto. I want to repeat that I think the data provided to us clearly showed that the benefits outweigh the risks for

this vaccine and the age groups under consideration.

But I have to go back again to making sure we're honest with parents about the true risk of COVID-19 in children. Again, 35 million children have probably been infected by this virus, and many of them are doing just fine. Most of those with underlining conditions, especially minority children, we need to make sure we're protecting them. So, I would just urge us to be completely honest and forthright in discussing the risks with parents so they can make the appropriate decision.

But I think that the data we have before us calls for a vote of yes, and so I did so. Thank you.

**DR. ARNOLD MONTO:** Thank you, Dr. Hildreth. Dr. Marks, would you like to make some final comments?

**DR. PETER MARKS:** Thanks. I want to thank the committee for a very vibrant discussion. I think it was very helpful to hear that. I think we as well as our CDC colleagues certainly heard the concern about making sure that there is follow up booster vaccination. We'll take that up moving forward. I think there is the

concern about we were talking about the primary series today, but we do take the point of making sure that there is adequate immunity overall with additional doses, particularly given the shift in variants that we're seeing. So, really appreciate that.

And, we'll look forward to a further discussion tomorrow as we move into younger populations. But in the meantime, I do want to thank -- I very much appreciate the comments about the briefing books. I do think the FDA staff spends a tremendous amount of time trying to put together comprehensive briefing books with a tremendous amount of data, and want to thank them for that.

I want to thank the Advisory Committee meeting staff and also the technical staff that ran the meeting today. Because, we had a relatively -- despite my mess-ups with my phone occasionally, they were not the mess-ups on the part of the technical staff. So I want to thank them for a relatively flawless meeting.

And, want to thank everyone for a very honest discussion here. I think this is the kind of

transparent discussion that we need. I think it's very important for people to understand that there's nothing being hidden here, that this is really important that people understand that there are vaccines -- are associated with some adverse effects, short term, and we monitor them closely for long term. And for that reason we have large safety surveillance systems like the Sentinel BEST system. And, we are very concerned to make sure that we detect adverse event. And when we detect them, we're transparent with them.

But really the hope here is that by making available vaccine, we will protect the population. And I think it's then a matter of individuals here understanding and making choice about what degree of risk they are willing to take here, especially as we move into this children's vaccine area where I think you heard, from even among our members, there are different levels of risks that people are willing to take and different considerations that they might take.

But that I think is why we provide the information, and why, ultimately, CDC will consider this

and whatever we come out with as a decision, and then make their recommendation. But I think this really appreciate the open dialogue. And very much appreciate the committee members.

I also need to acknowledge that the committee members and many of the staff have received a number of very troubling email messages across the spectrum. And I really appreciate your tolerance with these. We recognize it's people's right to exert their free speech, but sometimes these have been very troubling messages. And we appreciate your hanging in there with them. So, with that I'll wish everyone a good evening. And we'll see everyone tomorrow. I'll turn it back to you, Dr. Monto.

**DR. ARNOLD MONTO:** And I want to thank you, Dr. Marks, and the staff for putting this meeting agenda together so that we could have a very robust, and I won't say relaxed discussion, but certainly one in which we did not feel that we had to shorten anything so that we could really look into the whole situation in detail. Thanks to everybody, and see you tomorrow morning. Over

to you, Prabha, for the formal close.

**MEETING ADJOURNED**

**DR. PRABHAKARA ATREYA:** With that, I also thank everybody for participating in today's meeting. And I appreciate everybody's support. And this meeting is adjourned now. Thank you very much, see you tomorrow.

**[MEETING ADJOURNED FOR THE DAY]**