

1 adequacy of the scientific evidence that will be
2 presented by Pfizer and the FDA today, to support a
3 determination whether the benefits of Pfizer BioNTech's
4 COVID-19 vaccine outweigh its risks to support
5 authorization of this product under an EUA. FDA very
6 much appreciates the Committee's input on this very
7 important topic, and I look forward to today's
8 discussion. Thank you.

9 **DR. PRABHAKARA ATREYA:** Great. Thank you, Dr.
10 Gruber. Now, I would like to acknowledge the presence
11 of Dr. Celia Witten, Deputy Director of CBER, and also
12 Dr. Phillip Krause, Deputy Director of Office of
13 Vaccines, who may join later making remarks. So I will
14 now proceed with the Conflict of Interest Statement.
15 Okay.

16 So the Food and Drug Administration is
17 convening virtually today, December 10, 2020, the 162nd
18 meeting of the Vaccines and Related Biological Products
19 Advisory Committee under the authority of the Federal
20 Advisory Committee Act of 1972. Dr. Arnold Monto is

1 serving as the acting voting chair for this meeting.
2 Today, on December 10, 2020, the Committee will meet in
3 open session to discuss the emergency use
4 authorization, EUA, of the Pfizer-BioNTech COVID-19
5 vaccine for the prevention of COVID-19 in individuals
6 16 years of age and older.

7 The topic is determined to be a particular
8 matter involving specific parties. With the exception
9 of industry representative member, all standing and
10 temporary voting members for the VRBPAC are appointed
11 special government employees or regular government
12 employees from other agencies, and they're subjected to
13 federal conflicts of interest laws and regulations.
14 The following information on the status of this
15 Committee's compliance with federal ethics and conflict
16 of interest laws, including but not limited to 18
17 United States Code Section 208, is being provided to
18 participants in today's meeting and to the public.

19 Related to the discussions at this meeting,
20 all members, regular government employees and special

1 government employee consultants of this committee have
2 been thoroughly screened for potential financial
3 conflicts of interest of their own, as well as those
4 imputed to them, including those of their spouse or
5 minor children and, for the purpose of 18 U.S. Code
6 208, their employer. These interests may include
7 investments, consulting, expert witness testimony,
8 contracts and grants, Corporate Research and
9 Development Agreements, or CRADAS, teaching, speaking,
10 writing, patents and royalties and primary employment.
11 These may include interests that are current or under
12 negotiation.

13 FDA has determined that all members of this
14 Advisory Committee are in compliance with federal
15 ethics and conflict of interest laws. Under 18 U.S.C.
16 Section 208, Congress has authorized the FDA to grant
17 waivers to special government employees and regular
18 government employees who have financial conflicts of
19 interest when it is determined that the Agency's need
20 for the special government employee's services

1 outweighs the potential for a conflict of interest
2 created by the financial interests involved or when the
3 interest of the regular government employee is not so
4 substantial as to be deemed likely to affect the
5 integrity of the services with which the government may
6 expect from the employee.

7 We have the following consultants serving as
8 temporary voting members today. They are Dr. Oveta
9 Fuller, Dr. Juan Gea-Banacloche, Dr. James Hildreth,
10 Captain David Kim, Jeanette Lee, Dr. Ofer Levy, Dr.
11 Pamela McInnes, Patrick Moore, Dr. Stanley Perlman,
12 Eric Rubin, Mark Sawyer, and Ralph Tripp and Melinda
13 Wharton.

14 Based on today's agenda and all financial
15 interests reported by Committee members and
16 consultants, there has been only one conflict of
17 interest waiver issued under 18 U.S. Code 208 in
18 connection with this meeting. Among these consultants,
19 Dr. James Hildreth, a special government employee, has
20 been issued a waiver for his participation in today's

1 meeting. The waiver was already posted on FDA's
2 website for public disclosure.

3 Dr. Paula Annunziato is currently serving as
4 the industry representative to this Committee. Dr.
5 Annunziato is employed by Merck. The industry
6 representatives are not appointed as special government
7 employees and serve as nonvoting members of the
8 Committee. Industry representatives on this Committee
9 is not screened for their financial interests.
10 Industry representatives act on behalf of all regulated
11 industry and bring general industry perspective to the
12 Committee.

13 Mr. Sheldon Toubman is serving as the consumer
14 representative for this Committee. Consumer
15 representatives are appointed special government
16 employees and are screened and cleared prior to their
17 participation in the meeting. They are voting members
18 of the Committee.

19 Today's meeting has multiple external
20 speakers. We have three speakers from the Centers for

1 Disease Control and Prevention. These are Dr. Nancy
2 Messonnier, Dr. Aron Hall, Dr. Anita Patel. Regular
3 government employees have all been screened for
4 conflicts of interest, and they have been cleared to
5 participate as speakers for today's meeting.

6 The guest speaker for this meeting is Dr.
7 Steven Goodman, a Professor of medicine and Associate
8 Dean for Clinical and Translational Research at
9 Stanford University. He has been asked to disclose any
10 financial interests he may have related to the product
11 before the meeting. Disclosure of conflicts of
12 interest for guest speakers follow all applicable
13 federal laws, regulations, and FDA guidance.

14 FDA encourages all meeting participants,
15 including open public hearing speakers to advise the
16 committee of any financial relationships that they may
17 have with any affected firm, its products and, if
18 known, it's direct competitors. We would like to
19 remind standing and temporary members today that if the
20 discussions involve any other products or firms not

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

6 This concludes my reading of the conflict of
7 interest statement for the public record. At this
8 time, I would like to hand over the meeting to our
9 chair, Dr. Monto. Thank you very much. Dr. Monto?

10 **DR. ARNOLD MONTO:** Thank you, Prabha. Here I
11 am. Technical issues, which are going to be one of our
12 biggest problems I predict during the day. Thank you
13 for getting the meeting kicked off. I'd like first --
14 we're actually running a little early -- to call on Dr.
15 Doran Fink of the FDA to talk about the situation that
16 we are facing and the presentation of a description of
17 the Emergency Use Authorization. Dr. Fink?

18

19 **FDA PRESENTATION ON EMERGENCY USE AUTHORIZATION**

20

1 **DR. DORAN FINK:** Good morning. I'm Doran
2 Fink. I'm the Deputy Director for Clinical Review in
3 the Division of Vaccines and Related Products
4 Applications within the Office of Vaccines Research and
5 Review, Center for Biologics Evaluation and Research at
6 FDA. The VRBPAC last convened on October 22 of this
7 year to discuss the development, licensure, and
8 emergency use authorization of COVID-19 preventative
9 vaccines. Since that meeting, COVID cases and
10 associated hospitalizations and deaths have increased
11 substantially in the U.S. and worldwide.

12 On November 20, Pfizer submitted an emergency
13 use authorization request for the Pfizer-BioNTech
14 COVID-19 vaccine, otherwise known as BNT162b2. This is
15 an mRNA and lipid nanoparticle vaccine administered as
16 a two-dose regimen 21 days apart. We'll be hearing
17 more about the vaccine and its proposed use in later
18 presentations.

19 The use being requested for emergency
20 authorization is for active immunization to prevent

1 COVID-19 caused by SARS-CoV-2 in individuals 16 years
2 of age and older. The information submitted with the
3 request includes safety and efficacy data from a large,
4 randomized, blinded, placebo-controlled phase 3 trial.
5 And these data will be discussed in detail in our
6 afternoon sessions.

7 Today, we will be considering whether to make
8 available to millions of Americans an as-yet
9 investigational vaccine that has been developed,
10 tested, and reviewed in record time, with additional
11 testing still underway in ongoing studies. The
12 American public demands and deserves a rigorous,
13 comprehensive, and independent review of the data. And
14 that's what FDA physicians and scientists -- all of us
15 career public health servants -- have been doing over
16 days, nights, weekends, and, yes, over the Thanksgiving
17 holiday. This is in addition to months of review work
18 already completed on information previously submitted
19 in preparation for an EUA request.

20 FDA has been conducting its comprehensive

1 review of the Pfizer-BioNTech COVID vaccine EUA
2 submission since its submission on November 20. Our
3 review has included verification of clinical data
4 integrity of Pfizer analyses and also our own
5 independent analyses using datasets that were provided
6 in the submission. We have continued an ongoing review
7 of chemistry, manufacturing, and control information,
8 non-clinical data, and review of clinical assays,
9 including information that was submitted shortly prior
10 to the EUA request.

11 We have been reviewing and revising along with
12 Pfizer, prescribing information and fact sheets for
13 vaccine recipients and healthcare providers. These
14 will be necessary to inform and instruct vaccine
15 recipients and healthcare providers during use of the
16 vaccine under EUA. And these materials are necessarily
17 informed by our review of the data.

18 We have sent and received back answers to
19 multiple information requests addressed to Pfizer to
20 clarify questions related to the data. And last but

1 certainly not least, we have been preparing for today's
2 VRBPAC meeting. Today's meeting in which the Committee
3 will advise FDA with its own independent assessment of
4 the data, continues FDA's commitment to an expedited
5 review process that is transparent, scientifically
6 sound and data driven.

7 The legal authority for Emergency Use
8 Authorization was established in section 564 of the
9 Federal Food, Drug and Cosmetic Act. This legal
10 authority allows for FDA authorization of unapproved
11 medical products, or unapproved uses of approved
12 medical products, to address public health emergencies
13 related to biological, chemical, radiological or
14 nuclear agents. Issuance of an Emergency Use
15 Authorization requires prior determination of a threat,
16 and declaration of circumstances justifying the need
17 for an EUA to address that threat, by the Secretary of
18 Homeland Security, Defense, or Health and Human
19 Services. To that end, Health and Human Services
20 Secretary Azar issued a declaration on March 27 of this

1 year justifying Emergency Use Authorization of drugs
2 and biological products to address the COVID-19
3 pandemic.

4 Once that declaration has been issued, there
5 are four criteria that must be met in order to issue an
6 EUA. First of all, the agent referred to in the EUA
7 declaration can cause a serious or life-threatening
8 disease or condition. We know this to be true for
9 SARS-coronavirus-2 and COVID-19. The second and third
10 criteria are closely linked. There must be a reason to
11 believe that the medical product may be effective to
12 prevent, diagnose or treat the serious or life-
13 threatening condition cause by the agent, and the known
14 and potential benefits of the product should outweigh
15 the known and potential risks of the product.

16 There are special considerations for a COVID-
17 19 vaccine anticipated for widespread deployment to
18 millions of individuals, and these will be discussed on
19 my next slides. The final criterion is that there
20 should be no adequate approved and available

1 alternative to the product for diagnosing, preventing,
2 or treating the disease or condition.

3 At this time, the only FDA approved product
4 for COVID-19 is remdesivir. This is an anti-viral
5 agent that is approved for treatment of COVID-19, not
6 prevention. Additional products have been issued under
7 emergency use authorization but have not been FDA
8 approved. And none of these products is authorized for
9 use to prevent COVID-19. Thus, at this time, there is
10 no adequate approved and available alternative to a
11 COVID-19 vaccine for preventing COVID-19 caused by
12 SARS-coronavirus-2.

13 In October of this year, FDA released guidance
14 outlining our expectations for submissions requesting
15 emergency use authorization of COVID-19 vaccines, and
16 these expectations were discussed at the VRBPAC meeting
17 in October. There are three main areas covered by our
18 expectation: first, data to demonstrate manufacturing
19 quality and consistency. FDA has reviewed the
20 manufacturing quality and consistency data for the

1 Pfizer-BioNTech vaccine and found it adequate to
2 support emergency use authorization of the vaccine.
3 This will not be discussed in detail further at this
4 meeting.

5 Second, we expect clear and compelling safety
6 and efficacy data to support a favorable benefit-risk
7 of the vaccine when rapidly deployed for administration
8 to millions of individuals, including healthy people.

9 And finally, we expect plans for further
10 evaluation of the vaccine safety and effectiveness,
11 including in ongoing clinical trials, active and
12 passive safety monitoring during their use under EUA as
13 well as observational studies.

14 In terms of clinical data expected to support
15 an EUA submission for a COVID-19 vaccine, we expect a
16 high bar for efficacy. Efficacy data from at least one
17 well-designed phase 3 trial to demonstrate protection
18 against SARS-CoV-2 infection or disease, with a point
19 estimate of at least 50 percent compared to a placebo.
20 Additionally, the appropriately alpha-adjusted

1 confidence interval lower bound around that point
2 estimate to be greater than 30 percent. This is to
3 ensure that a widely deployed COVID-19 vaccine will
4 have an appreciable impact.

5 In terms of safety data, we expect these data
6 from throughout clinical development to evaluate
7 reactogenicity, serious adverse events and adverse
8 events of special interest. And we expect that a high
9 proportion of phase 3 study subjects will have been
10 followed for at least one month after completion of the
11 full vaccination regime.

12 We have an additional expectation for follow
13 up that I will explain on my next slide. We also
14 expect to be able to review sufficient cases of severe
15 COVID-19 that have occurred in clinical trial
16 participants to assess for signals of enhanced disease
17 and also, if possible, to assess for preliminary
18 evidence of protection against severe disease.

19 We recognize that a planned, case-driven
20 efficacy analysis, and associated safety analyses at

1 the same time, could provide data to support an
2 emergency use authorization. We have explained that we
3 expect these analyses to include a median follow up
4 duration of at least two months after completion of the
5 full vaccination regimen. The reasons for that
6 expectation are that, first of all, it allows time for
7 potential immune mediated adverse events to be
8 evaluated, understanding that uncommon but clinically
9 significant immune-mediated adverse events to
10 preventative vaccines generally have onset within the
11 first six weeks following vaccination. A median
12 follow-up of two months also ensures that vaccine
13 efficacy is assessed during the time when adaptive
14 and/or memory immune responses rather than innate
15 responses are mediating protection.

16 And finally, this follow-up period allows for
17 early assessment of waning protection and for
18 assessment of signals of enhanced disease.

19 Following issuance of an EUA for a COVID-19
20 vaccine, we understand and expect that further vaccine

1 evaluation would be needed for ongoing benefit-risk
2 assessment to support continuation of the EUA. But
3 equally important, further vaccine evaluation would be
4 needed to accrue additional data to support licensure
5 of the vaccine as soon as possible and/or to inform
6 labelling. This further vaccine evaluation following
7 issuance of an EUA would include longer term follow up
8 for safety, including in larger numbers of vaccine
9 recipients and in populations with lower representation
10 than in clinical trials.

11 Further evaluation would also allow for more
12 precise estimation of vaccine effectiveness, in
13 specific populations, and more robust assessment of
14 effectiveness against specific aspects of SARS-
15 coronavirus-2 infection or disease, for example,
16 asymptomatic infection. This further evaluation would
17 also characterize the duration of protection, could
18 investigate immune biomarkers that might predict
19 protection, and of course would be ongoing monitoring
20 for signals of enhanced disease.

1 Issuance of an EUA for a COVID-19 vaccine
2 would be contingent upon the ability to conduct further
3 vaccine evaluation, which would occur through a
4 combination of active follow up of vaccine recipients
5 under the EUA, passive monitoring for clinically
6 significant adverse reactions using established
7 reporting mechanisms -- for example, the vaccine
8 adverse events reporting system -- observational
9 studies including those that leverage healthcare claims
10 databases and, finally, continuation of blinded
11 placebo-controlled follow up in ongoing clinical trials
12 for as long as is feasible, and strategies to handle
13 loss of follow ups in those trials.

14 We acknowledge that placebo-controlled blinded
15 follow up cannot continue indefinitely as more
16 information about a vaccine's safety and effectiveness
17 becomes available. However, FDA does not consider
18 issuance of an EUA for a COVID-19 vaccine to
19 necessitate immediate unblinding of ongoing clinical
20 trials or offering vaccine to all placebo recipients.

1 Of course, trial participants may choose to
2 withdraw from follow up for any reason, including to
3 receive vaccine made available under EUA. And it may
4 be possible to offer vaccine to placebo recipients in
5 clinical trials in a reasonable timeframe that doesn't
6 compromise the integrity of the clinical trial. And
7 these considerations will be discussed further this
8 morning.

9 When an EUA is issued for a COVID-19 vaccine,
10 it will specify conditions of use for which benefit-
11 risk has been determined to be favorable based on
12 review of the totality of available data, including
13 those populations to be included or excluded from the
14 EUA, conditions for vaccine distribution and
15 administration and requirements for safety monitoring
16 and reporting of adverse events. Vaccine made
17 available under an EUA will also include provision of
18 information to vaccine recipients and healthcare
19 providers via prescribing information and fact sheets.
20 These materials will describe that the product remains

1 investigational, will inform about the known and
2 potential benefits and risks, and will also make clear
3 what are the available alternatives, and the option to
4 refuse vaccination.

5 Once issued, an EUA may be revised or revoked
6 for a number of reasons: first of all, if circumstances
7 justifying the EUA no longer exist; second, if criteria
8 for issuance are no longer met; and third, or any other
9 circumstances that arise that warrant changes necessary
10 to protect public health or safety. These other
11 circumstances may be based on new information
12 concerning vaccine safety or effectiveness, vaccine
13 manufacturing or quality, or COVID-19 epidemiology or
14 pathogenesis.

15 The agenda for today's VRBPAC meeting will
16 include, following the conclusion of my talk, first,
17 three presentations from the CDC providing an update on
18 COVID-19 epidemiology, plans for vaccine safety and
19 effectiveness monitoring under an EUA and operational
20 distribution plans for the vaccine under an EUA. We

1 will then hear about considerations for placebo-
2 controlled trial design if an unlicensed vaccine
3 becomes available. Following lunch, we will have an
4 open public hearing and then we'll dive into a
5 discussion of the data; first with a presentation by
6 Pfizer and then an FDA presentation.

7 At the end of the day, we will have a
8 Committee discussion and a vote. We have two questions
9 that we would like the Committee to consider for
10 discussion. These will not be voting questions.
11 First, Pfizer has proposed a plan for continuation of
12 blinded placebo-controlled follow up in ongoing trials
13 if the vaccine were made available under EUA. We would
14 like the Committee to discuss Pfizer's plan, including
15 how loss of blinded placebo-controlled follow-up in
16 ongoing trials should be addressed. Second, we would
17 like the Committee to discuss any gaps in plans
18 described today, and in the briefing documents, for
19 further evaluation of vaccine safety and effectiveness
20 in populations who receive the Pfizer-BioNTech vaccine

1 under an EUA.

2 Following discussion of these items, we will
3 have a single question for the Committee to vote on.
4 The question is: based on the totality of scientific
5 evidence available, do the benefits of the Pfizer-
6 BioNTech COVID-19 vaccine outweigh its risks for use in
7 individuals 16 years of age and older. This concludes
8 my presentation. Thank you very much.

9 **DR. ARNOLD MONTO:** Thank you, Dr. Fink, for a
10 very clear presentation. We have a fair amount of time
11 before the next scheduled presentation, which is very
12 good because I think there are some questions of
13 clarification that the committee may have about our
14 guidelines for discussion and for our eventual vote.

15 So committee members, please raise your hands
16 if you would like to ask Dr. Fink some specific
17 questions. We don't want to start our discussion of
18 the points raised by Dr. Fink, but just clarification
19 about the characteristics of an Emergency Use
20 Authorization and the other guidelines. So please

1 raise your hand. I may be having some technical
2 difficulties, so Mike, you may need to --

3 **MR. MICHAEL KAWCZYNSKI:** Yeah. I got it.

4 **DR. ARNOLD MONTO:** -- recognize the person.
5 Go ahead.

6 **MR. MICHAEL KAWCZYNSKI:** No problem. All
7 right. The first one we have is Dr. Sawyer. Would you
8 go ahead and turn your camera on?

9 **DR. MARK SAWYER:** Thanks very much, Dr. Fink.
10 You mentioned that issues related to manufacturing can
11 be one of the reasons to revise or revoke an EUA. What
12 is the monitoring process going forward, from this
13 point, with regard to manufacturing process?

14 **DR. DORAN FINK:** Thank you. So FDA continues
15 to engage with the vaccine manufacturer concerning
16 manufacturing quality and control issues to ensure that
17 these remain adequate to support use of the vaccine
18 under EUA. I'll invite any of my other FDA colleagues
19 to comment further.

20 **DR. MARION GRUBER:** Yeah. This is Marion.

1 Can you hear me, Mr. Chairman?

2 **MR. MICHAEL KAWCZYNSKI:** Yes, we can. We can
3 hear you.

4 **DR. MARION GRUBER:** Okay. Thank you very
5 much. So I think I wanted to second what Doran just
6 said. It is true that the monitoring of the CMC --
7 that is the Chemistry Manufacturing and Control
8 information -- that is currently available, and we, of
9 course, will get additional data from the different
10 manufacturing sites. We will review most of this
11 information, and we will work together with the vaccine
12 manufacturer to make sure that the product that is made
13 and generate is of adequate consistency and quality.
14 So this is work that's going to be ongoing over the
15 next month.

16 **DR. MARK SAWYER:** Thanks very much.

17 **MR. MICHAEL KAWCZYNSKI:** Okay. Arnold, are
18 you able to see the list?

19 **DR. ARNOLD MONTA:** No, that side of my screen
20 I see, but there's no activity there.

1 **MR. MICHAEL KAWCZYNSKI:** Okay. That's all
2 right.

3 **DR. ARNOLD MONTO:** Why don't you manage the
4 calling on?

5 **MR. MICHAEL KAWCZYNSKI:** We'll take care of
6 that. Dr. Kurilla?

7 **DR. MICHAEL KURILLA:** Thank you. I don't know
8 why my camera's not working, but it says it's on.
9 Doran, just trying to understand the question we're
10 being asked to vote on is what Pfizer has requested.
11 But if I understood your talk correctly, the FDA can
12 limit the actual -- can place limits on the target
13 populations through the specific indications regarding
14 the EUA. My question is, how do you view the
15 investigational status of the product under an EUA?

16 **DR. DORAN FINK:** Thank you for the question.
17 So a product that is made available under an EUA is an
18 unapproved product. It has not been FDA licensed.

19 **DR. MICHAEL KURILLA:** If I can just follow up
20 with that. So, if you limited the EUA to a specific

1 set of populations, even those populations that have
2 the EUA, placebo-controlled trials would still be
3 possible from that perspective?

4 **DR. DORAN FINK:** Well, we will have a
5 discussion on those considerations later this morning.
6 But in FDA's view, issuance of an EUA for a COVID-19
7 vaccine should not preclude the conduct of placebo-
8 controlled trials. In particular, in situations where
9 that vaccine made available under an EUA is available
10 only in limited quantity.

11 **DR. ARNOLD MONTO:** Okay. I think I can see
12 now. Thank you for fixing it. Dr. Lee?

13 **DR. JEANNETTE LEE:** So thank you. One of the
14 questions I have is a little bit more general. I
15 recognize we're considering the Pfizer product for an
16 EUA today. However, future EUA applications, if, for
17 example, there is a vaccine that is approved under a
18 BLA -- vaccine number one, let's just call it that --
19 will that make it more challenging for future products
20 to request an EUA?

1 **DR. DORAN FINK:** Right. I think what you're
2 getting at is the fourth criterion for issuance of an
3 EUA, which says that there must not be any adequate
4 approved and available alternative therapy.

5 **DR. JEANNETTE LEE:** Yes. Correct.

6 **DR. DORAN FINK:** So first of all, if a vaccine
7 is made available under an EUA, it is not approved, and
8 so therefore that would not preclude issuance of an EUA
9 for another vaccine. If a vaccine is approved by FDA,
10 that would also not necessarily preclude issuance of an
11 EUA for another investigational COVID-19 vaccine.

12 For example, if the approved vaccine is
13 available only in limited quantity, then it may not be
14 considered adequate to address the public health
15 emergency. Second of all, if the vaccine that is
16 approved is approved for use only in a limited
17 population, then that vaccine may not be considered
18 adequate to address the needs of the public health
19 emergency for other populations.

20 **DR. JEANNETTE LEE:** Thank you.

1 **DR. ARNOLD MONTO:** Mr. Toubman?

2 **MR. SHELDON TOUBMAN:** First of all, thank you.
3 Wonderful job.

4 **DR. ARNOLD MONTO:** Can you speak a little
5 louder, please? We're having problems hearing you.

6 **MR. SHELDON TOUBMAN:** Oh, yes. Sorry. Just
7 thanking Dr. Fink and everybody at the FDA for all the
8 work they've done independently reviewing the data.
9 Thank you. Two questions, one is you indicated that
10 since the submission came in from Pfizer you've had a
11 lot of ongoing discussions with them. And the first
12 question is does that include getting updated data?
13 Because the closing dates of data that's in their
14 submission is November 14, which is 26 days ago, which
15 is almost a month. It's about half of the entire
16 period for the two months minimum required for EUA. So
17 have you gotten more recent requests -- gotten more
18 recent data?

19 And the second question is a follow up to Dr.
20 Kurilla's. The question is, you've given us only one

1 question, and that is yes or no to recommending
2 approval for the entire amount, which is population,
3 which Pfizer's requesting which is the entire 16 and
4 over. But certainly the committee could view this as
5 something they'd like to grant EUA for, but given the
6 balancing of risk and benefit, it may be different for
7 different populations. So we might want to grant it or
8 recommend it for a smaller set than Pfizer's asking
9 for.

10 But your question doesn't seem to allow for
11 that. And I was wondering if you have a backup
12 question that might be used. I know that in the past
13 with the dengue review -- just a backup question. Just
14 ask if you could answer this.

15 **DR. ARNOLD MONTO:** Okay. So could I say that
16 your last question, we can bring that up during the
17 discussion later on. So I'm going to excuse Dr. Fink
18 from having to answer that part of the question.

19 **DR. DORAN FINK:** Thank you. To answer your
20 first question, no, we have not received additional

1 datasets beyond the datasets that were submitted to us
2 comprising a cutoff date of November 14. As you can
3 imagine, there is tremendous amount of work that goes
4 into preparing a dataset for submissions, and so it
5 really is infeasible for the sponsor and for FDA to be
6 chasing our tails trying to get datasets that encompass
7 more and more data as time goes on. That being said,
8 if the sponsor becomes aware of, or if we become aware
9 of, any data that would potentially impact our benefit-
10 risk assessment, we do have discussions with the
11 sponsor regarding those data.

12 **DR. ARNOLD MONTO:** And we will be able, Mr.
13 Toubman, to ask questions of the sponsor after their
14 presentation later on. So we can revisit this issue.
15 Next, Dr. Perlman.

16 **DR. STANLEY PERLMAN:** So I just had a question
17 about the last part of what you were talking about when
18 you talked about how Pfizer was going to deal with the
19 issue of placebos going off the vaccine trial. And you
20 asked for advice from the committee. Is that part of

1 the EUA vote, or is that a separate issue?

2 **DR. DORAN FINK:** No, that is not a question
3 for a vote. It's just an item for discussion. We'd
4 like to hear the committee's thoughts on the plan that
5 is being proposed by Pfizer, which you will hear about
6 in greater detail later today.

7 **DR. ARNOLD MONTO:** Dr. McInnes?

8 **DR. PAMELA MCINNES:** I have a question that's
9 sort of a follow up from Mike Kurilla originally
10 started. Given that this is considered an
11 investigational product under an EUA, I'm assuming that
12 any manufacturer cannot actually market such an
13 investigational vaccine. Is that correct?

14 **DR. DORAN FINK:** So Emergency Use
15 Authorization does not allow for commercial
16 distribution of the vaccine via the usual marketing
17 that would be available to a licensed vaccine. I hope
18 that clarifies things. If anyone else from FDA wants
19 to chime in, I'd welcome the additional remarks.

20 **DR. PAMELA MCINNES:** So Doran, thank you. I'm

1 happy to get the comments. I'm just trying to
2 understand. So it's not marketed traditionally, but
3 compensation for an investigational vaccine is possible
4 under an EUA, like for a government entity?

5 **DR. DORAN FINK:** So again, this is not my area
6 of expertise.

7 **DR. PAMELA MCINNES:** I understand.

8 **DR. DORAN FINK:** The Emergency Use
9 Authorization may include conditions related to
10 advertising and other similar issues. In terms of
11 transfer of money between vaccine recipients and
12 providers, or between the U.S. government and the
13 manufacturer, I can't speak to those.

14 **DR. ARNOLD MONTO:** Dr. Meissner?

15 **DR. CODY MEISSNER:** Thank you, Dr. Monto, and
16 I would like to thank Dr. Marks and Dr. Fink and Dr.
17 Gruber, and everyone else at the FDA, because the
18 amount of work that you have done is just
19 extraordinary. And the briefing packets that have been
20 circulated are clear and extremely helpful, so thank

1 you very much for your ongoing work.

2 The question I have for you is it will be
3 advantageous, for a number of reasons, to have one of
4 the COVID-19 vaccines available under a biologic
5 license application instead of an EUA. And I realize
6 it's a difficult question, but can you offer any
7 comments about the route or the pathway forward for the
8 FDA to begin to think about when you've reached a point
9 that you would consider a BLA?

10 **DR. DORAN FINK:** Yes. So first of all, we do
11 want any vaccine that is made available under an EUA to
12 continue its testing to allow for its licensure as soon
13 as possible after issuance of the EUA. So this
14 continued evaluation, as I explained in my
15 presentation, I think first and foremost would include
16 some longer term follow up of participants enrolled in
17 ongoing studies, as well as safety and effectiveness
18 data coming out of use of the vaccine under the EUA.

19 This additional evaluation would then meet our
20 usual expectations for clinical data to be included in

1 a licensure application. There are some other sources
2 of information that involve manufacturing and
3 facilities, and potentially nonclinical studies as
4 well, that we would typically require to support a
5 licensure application but are not absolutely necessary
6 to support issuance of an EUA.

7 **DR. CODY MEISSNER:** Is it possible to predict
8 or estimate when conditions of safety and efficacy
9 might be satisfied for BLA?

10 **DR. DORAN FINK:** In terms of the time it would
11 take? Yeah. I couldn't predict, but I will say that
12 we typically ask for at least six months of follow up
13 in a substantial number of clinical trial participants
14 to constitute a safety database that would support
15 licensure.

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

17 **DR. ARNOLD MONTTO:** And finally, Dr. Fuller?

18 **DR. OVETA FULLER:** My question -- did I
19 understand you to say that the FDA in the October 22
20 meeting looked at the manufacturing quality of the

1 Pfizer vaccine and that was satisfactory? And if so,
2 how will that be valued in the actual distribution of
3 the vaccine, and will we talk about that later?

4 **DR. DORAN FINK:** Right. So to clarify what I
5 said earlier, as part of the EUA submission and in
6 information submitted prior to the EUA, FDA's been
7 conducting an ongoing review of manufacturing quality,
8 consistency, and control. And we have found this
9 information to be adequate to support emergency use
10 authorization of the vaccine.

11 We are not intending to discuss details of the
12 manufacturing process, many of which are proprietary,
13 during today's meeting. But as Dr. Gruber and I
14 discussed in response to a previous question, our
15 review of the manufacturing information is an ongoing
16 process and will continue even after the vaccine is
17 authorized, if that is the decision that we make.

18 **DR. OVETA FULLER:** Okay. Thank you.

19 **DR. ARNOLD MONTA:** Thank you, Dr. Fink.
20 You've kicked us off with a lot of information, which

1 we're going to be coming back to later on this
2 afternoon. I'd like next to call on Dr. Aron Hall from
3 CDC who's the co-lead in the epidemiology taskforce,
4 and he is going to give us an update about the current
5 situation.

6

7

UPDATE ON EPIDEMIOLOGY

8

9 **DR. ARON HALL:** All right. Thank you very
10 much. Good morning. Can you hear me okay?

11 **DR. ARNOLD MONTO:** Yes, we can.

12 **DR. ARON HALL:** Wonderful. So good morning.
13 I'm Dr. Aron Hall, co-lead of the epidemiology
14 taskforce in CDC's COVID-19 response and chief of the
15 Respiratory Viruses Branch. To help further subsequent
16 discussions today about COVID-19 vaccines, I would like
17 to provide a brief update on the current epidemiology
18 of COVID-19 in the United States. As of December 8,
19 over 4.8 million COVID-19 cases and over 280,000
20 associated deaths have been reported in the United

1 States.

2 The initial peak in early April was driven
3 largely by elevated activity in the New York Metro
4 area, followed by a second larger peak, in late July,
5 primarily due to increase activity across much of the
6 southern U.S. Since mid-September, daily counts of new
7 cases have again been on the rise, with even sharper
8 increases since mid-October. Since submission of these
9 slides in advance of this meeting, we have now
10 surpassed 15 million cases and 285,000 deaths
11 nationally, with over 200,000 new cases and over 2,500
12 new deaths reported yesterday.

13 In addition to reported cases, CDC uses
14 several other systems to track the pandemic, which are
15 compiled in the weekly surveillance summary called
16 COVIDView. This weekly report includes the percent
17 positivity of molecular tests for SARS-CoV-2, the virus
18 that causes COVID-19, shown in blue, as well as
19 syndromic surveillance for COVID-19-like illness, or
20 CLI, among ambulatory patients, shown in red.

1 Both of these leading indicators have been
2 increasing since September. Also included in COVIDView
3 are weekly hospitalization rates, shown in grey, which
4 are currently at the highest point since the beginning
5 of the pandemic. And also the percent of deaths due to
6 COVID-19, influenza, or pneumonia based on death
7 certificates, shown in green, both of which are lagging
8 indicators that have been increasing since October.

9 One component of the weekly COVIDView report
10 is an assessment of COVID-19 hospitalizations through
11 COVID-NET. COVID-NET conducts hospitalization
12 surveillance in 14 states, representing about 10
13 percent of the U.S. population. Patients must be a
14 resident of the surveillance area and have a positive
15 SARS-CoV-2 test within 14 days prior to or during
16 hospitalization. Medical chart reviews are conducted
17 by trained surveillance officers and data are updated
18 weekly on an interactive website.

19 While focused on the more severe end of the
20 illness spectrum, COVID-NET provides active population-

1 based surveillance, thus overcoming some of the biases
2 with passive surveillance and providing robust data on
3 the epidemiology of COVID-19. Looking at weekly
4 hospitalization rates by age, we see that each of the
5 peaks in April, late July and currently have been most
6 pronounced among adults age 65 years and older.
7 Hospitalization rates in children have been
8 considerably lower than those among adults but have
9 remained stable or increasing since the spring. Note
10 that the last few data points are subject to reporting
11 lag and may increase subsequently.

12 Looking at the cumulative hospitalization
13 rates through late November from COVID-NET and
14 stratifying by age group, we see a strong increasing
15 trend with increasing age. As of November 28, adults
16 age 65 years and older had a cumulative rate of 756 per
17 100,000, which is roughly equivalent to one in every
18 130 people in this age group being hospitalized with
19 COVID-19. This rate is approximately four and a half
20 times greater than that of adults age 18 to 49.

1 COVID-NET surveillance has also helped to
2 identify significant racial and ethnic disparities in
3 the rates of COVID-19. Shown here are age-adjusted
4 cumulative hospitalization rates by race and ethnicity.
5 Demonstrating rates are three to four times greater
6 among persons that are Hispanic or Latino, non-Hispanic
7 American Indian or Alaska Native, or non-Hispanic Black
8 or African-American, compared with those that are non-
9 Hispanic white. These disparities are likely
10 multifactorial, potentially influenced by differential
11 exposure rates, prevalence of underlying medical
12 conditions, access to care, and other socioeconomic
13 factors.

14 To help further tease apart these issues and
15 identify risk factors for severe COVID-19, CDC and
16 public health partners analyzed the relative rates of
17 in-hospital mortality from COVID-NET using models that
18 adjust for age, sex, race, and ethnicity, smoking and
19 several underlying medical conditions. As shown in the
20 red box, older age was the strongest independent risk

1 factor for in-hospital death, and the risk increased
2 with increasing age. Other characteristics
3 significantly associated with in-hospital mortality
4 include male sex, immunosuppression, renal disease,
5 chronic lung disease, cardiovascular disease,
6 neurologic disorder, and diabetes.

7 Combining data with COVID-NET with population-
8 based data from the Behavioral Risk Factor Surveillance
9 System, or BRFSS, we likewise developed models to
10 assess risk for COVID-19 hospitalization among adults
11 with specific underlying conditions. Again, after
12 adjusting for age, sex, and race and ethnicity, the
13 risks for COVID-19 associated hospitalization was
14 greatest for adults with severe obesity, chronic kidney
15 disease and diabetes, as shown in the red box.
16 Compared with adults without these conditions, those
17 that have them were three to five times more likely to
18 be hospitalized for COVID-19.

19 Furthermore, the risk of COVID-19
20 hospitalization increased with the number of underlying

1 medical conditions, as shown in the red box on this
2 table. While specific risks varied depending on the
3 specific underlying medical condition, adults with
4 three or more conditions had five times the risk of
5 COVID-19 hospitalization compared to adults with no
6 conditions. Due to increased age, underlying medical
7 conditions, and their congregate living situation,
8 residents of long-term care facilities have been
9 disproportionately impacted by COVID-19.

10 As shown here, residents of these facilities
11 comprise nearly 50 percent of COVID-19 hospitalizations
12 among adults age 75 to 84 years, and nearly two-thirds
13 of COVID-19 hospitalizations among adults age 85 years
14 and older. As such, the Advisory Committee for
15 Immunization Practices, or ACIP, recently recommended
16 long-term care facility residents as a priority group
17 to receive initial doses of COVID-19 vaccines once
18 approved. Similarly, healthcare personnel have been
19 prioritized for vaccination to preserve capacity to
20 care for patients with COVID-19 and other illnesses.

1 Again, based on COVID-NET data, 6 percent of
2 adults hospitalized with COVID-19 were healthcare
3 personnel, with nursing related occupations being the
4 most frequent. Healthcare personnel hospitalized with
5 COVID-19 had similar prevalence of underlying medical
6 conditions, most notably obesity, as that observed
7 among adults hospitalized with COVID-19 -- all adults.
8 Likewise, a similar proportion of severe clinical
9 outcomes, including ICU admission, mechanical
10 ventilation, and death, occurred among healthcare
11 personnel as that across all adult COVID-19
12 hospitalizations.

13 As we prepare for COVID-19 vaccines, it's
14 important to establish baselines to assess their future
15 impact and maintain ongoing assessment of the total
16 burden of SARS-CoV-2 infections in the U.S. To that
17 end, CDC has implemented a nationwide seroprevalence
18 survey to help track the number of people with evidence
19 of previous SARS-CoV-2 infection, including milder
20 infections that do not result in care seeking or

1 testing for acute infection. These involve biweekly
2 testing of approximately 50,000 residual specimens from
3 commercial laboratories for antibodies against SARS-
4 CoV-2.

5 Through the first few rounds of this survey,
6 estimated seroprevalence has ranged from 0.4 to 23
7 percent across U.S. jurisdictions. However, as of late
8 September, less than 10 percent of specimens from most
9 jurisdictions had evidence of previous SARS-CoV-2
10 infection. In general, the highest seroprevalence was
11 observed among children and adults aged less than 50
12 years, and lowest among older adults age 65 and older.

13 Using a different multiplier modelling
14 approach, which uses reported cases and other data
15 sources to then account for under detection and under
16 reporting, CDC recently released estimates of the total
17 number of hospitalizations, illnesses, and infections
18 with SARS-CoV-2 in the U.S. This analysis estimated
19 that one of every 2.5 hospitalized cases, and one of
20 every 7.1 non-hospitalized cases, may have been

1 nationally reported.

2 Applying these multipliers to reported cases
3 through the end of September yielded a national
4 estimate of 2.4 million hospitalizations, 44.8 million
5 illnesses, and 52.9 million total infections. As the
6 figure to the right shows, most estimated
7 hospitalizations occurred among older adults, while
8 most illnesses and infections were among younger
9 adults.

10 So in summary, now, as of December 9, over 15
11 million cases and over 285,000 deaths associated with
12 COVID-19 have been reported in the United States.
13 However, based on seroprevalence surveys and models,
14 the total estimated number of infections is likely two
15 to seven times greater than reported cases. Though,
16 less than 10 percent of the population in most states
17 had evidence of previous infection through September.

18 Factors associated with increased risk for
19 severe COVID-19 included older age, racial and ethnic
20 minority group membership, and several specific

1 underlying medical conditions. Ongoing surveillance
2 and epidemiologic studies will help inform further
3 development and implementation of candidate vaccines,
4 including assessment of their impacts, safety, and
5 effectiveness.

6 Lastly, even with the promising advent of
7 COVID-19 vaccines, there's continued need for non-
8 pharmaceutical interventions, including mask use,
9 physical distancing, hand hygiene, and environmental
10 disinfection to help bring an end to this devastating
11 pandemic. Finally, I would like to acknowledge the
12 thousands of public health professionals that have
13 worked tirelessly over the last 11 months on the CDC
14 COVID-19 response, including the dedicated staff from
15 the Respiratory Viruses Branch. Thank you.

16 **DR. ARNOLD MONTO:** I think I wasn't on at
17 first. Thank you so much for being clear about the
18 differential impact of COVID-19 in the U.S. population.
19 We have time for relatively few questions. I see, Dr.
20 Meissner, you have your hand raised.

1 **DR. CODY MEISSNER:** Yes, sir. Thank you very
2 much for that presentation, doctor. I would like to
3 ask you about the severity of disease particularly in
4 older adolescents, that is individuals who are 16 and
5 17 years of age, because they have been included in the
6 company's request for an EUA. I assume it's unlikely
7 that hospitalizations and disease are broken down by
8 age, but is it safe to assume that adolescents who are
9 16 and 17 years of age are similar in the five- through
10 17-year-old age group?

11 **DR. ARON HALL:** Yeah. Thank you for that
12 question. So of course as we refine to smaller and
13 smaller age brackets, the numbers get smaller,
14 particularly in children where overall we see lower
15 rates, particularly of severe disease -- of
16 hospitalization. In general, we do see higher rates of
17 hospitalization among children aged zero to five
18 relative to those age five to 17. Of course, this is
19 potentially confounded by differential rates of care
20 seeking.

1 As you might imagine, there are certainly
2 lower thresholds for care seeking for the very youngest
3 and most vulnerable children. However, as we start to
4 look at the more mild end of the illness spectrum and
5 look at rates of detection of SARS-CoV-2 virus using
6 molecular assays, we do see indication of higher rates
7 of infection among older children, among adolescents,
8 particularly, then, as we move into kind of older
9 teenagers and people in their young 20s. Much of this
10 may have been driven in part by outbreaks in the fall
11 among institutes of higher education.

12 But the broader impacts in children perhaps
13 are not entirely clear until the full resumption of
14 normal activities ensues in the United States,
15 including in person education across all schools in the
16 United States. So we'll continue to monitor closely,
17 but thus far the indication is the highest rates of
18 severe illness in young children but higher rates of
19 infection in older children.

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

1 **DR. ARNOLD MONTO:** Dr. Rubin?

2 **DR. ERIC RUBIN:** Thanks, Dr. Hall. I was
3 interested in the multiplier that you described that
4 applies to the diagnosis of infection. Do you think
5 that applies to deaths as well?

6 **DR. ARON HALL:** Yeah. So we have used, at
7 CDC, the same multiplier model previously for tracking
8 influenza and generating in-season estimates of the
9 disease burden. And that same approach has been used
10 previously to estimate deaths in the same manner that
11 are presented today for hospitalizations and milder
12 illness. There're, of course, differential multipliers
13 that would have to be considered for deaths as the
14 rates of underreporting of death are different than
15 those for milder infection.

16 In general, we have better capture of deaths.
17 We have lower rates of underreporting and under-
18 ascertainment for deaths. But as folks are aware, the
19 dynamics of the pandemic itself have greatly changed
20 those multipliers, and so there's also a considerable

1 time component that needs to be factored in when using
2 these multiplier models. So the underreporting of
3 deaths, for example, has changed over time, and the
4 attribution of deaths to COVID-19 has changed overtime,
5 which complicates interpretation. But we do have
6 several efforts underway using these models and other
7 approaches to generate estimates of death. And we do
8 feel, as with hospitalizations and illnesses, that the
9 reported number of deaths is likely an underestimate of
10 the true number of deaths.

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

12 **DR. ARNOLD MONTA:** Thank you. Dr. Gans, we're
13 going to go over a little bit. Please keep your
14 question short.

15 **DR. HAYLEY GANS:** Thank you very much. Thank
16 you for that, and I agree, heroic effort to all of the
17 people who are working on this. I had two quick
18 questions. The data concerning the immunocompromised
19 or immunosuppressed individuals is not really granular
20 enough to make it something that we can use in terms of

1 how we're thinking about high-risk populations. There
2 are registries looking at this, but it would be nice if
3 there was some national information that you could
4 provide to us. As well as I didn't see any information
5 from pregnant women, which is a population which we're
6 all concerned about. And which we've definitely seen
7 post-natal transmission to very young infants who end
8 up being hospitalized. So if you would just take those
9 up.

10 **DR. ARON HALL:** Yeah. Thank you for those
11 comments. Absolutely, there are numerous surveillance
12 efforts currently underway to assess the impacts of
13 COVID-19 in pregnant women. In the interest of time,
14 unfortunately, today I didn't have a chance to present
15 those. But through COVID-NET, as described today, as
16 well as another surveillance system called SET-NET,
17 which was established during the zika epidemic, we have
18 been very closely monitoring the impacts of COVID-19 in
19 both pregnant women and subsequently following up with
20 their infants.

1 Thankfully, the rates overall have been
2 relatively low thus far. But as we continue to
3 accumulate a critical mass of data in this demographic,
4 we indeed do hope to have more specific estimates of
5 the risks that are imposed to pregnant women and their
6 infants. The early indication is that there may be a
7 higher risk of pre-term delivery among pregnant women
8 infected with COVID-19 relative to women without COVID-
9 19. But there's ongoing efforts to assess those and
10 other potential pregnancy-related risks and fetal
11 outcomes.

12 **DR. ARNOLD MONTO:** Thank you very much, Dr.
13 Hall, and it's now time for our morning break. We've
14 eaten into the time a little bit, but I do want to
15 start again at 10:30 Eastern so we can hear from Dr.
16 Messonnier from CDC. See you later.

17

18 **[BREAK]**

19

20 **MR. MICHAEL KAWCZYNSKI:** All right. Welcome

1 back from break. We'll now enter our second half of
2 our next group of speakers. Arnold?

3 **DR. ARNOLD MONTO:** We're next going to hear
4 from -- again from the Centers for Disease Control.
5 We're going to have a few presentations and questions
6 afterwards. First, we're going to hear a presentation
7 from Dr. Nancy Messonnier, the Director of the Center
8 for Immunization and Respiratory Diseases, on vaccine
9 safety and effectiveness monitoring, and then from
10 Anita Patel, the Deputy of the Vaccine Task Force on
11 operational distribution plans. Dr. Messonnier?

12

13 **VACCINE SAFETY AND EFFECTIVENESS MONITORING**

14

15 **DR. NANCY MESSONNIER:** Thank you, Dr. Monto,
16 and thank you for the opportunity to speak today on
17 this really auspicious day. Despite the completely
18 appropriate size and scope of the clinical trials, it's
19 always important to continue to monitor vaccines post-
20 licensure or post-authorization. And that is certainly

1 especially true with COVID vaccines.

2 I'm going to talk about the U.S. government
3 plans for monitoring of safety and effectiveness.

4 First, safety. The rapid implementation of safety
5 monitoring under an EUA requires a whole of U.S.
6 government approach with an initial focus on the early
7 populations targeted for vaccination, voluntary active
8 surveillance of adverse events focused on healthcare
9 worker vaccination, and rapid follow-up of reported
10 serious adverse events. As the program continues and
11 more vaccine is given, active surveillance systems will
12 provide increasingly useful information on safety in
13 different populations. Close collaboration of safety
14 experts across the USG will facilitate data sharing and
15 rapid recognition of responses to safety signals.

16 Now, there is a quite extensive plan for
17 safety monitoring, but I'm just going to summarize a
18 few high points. On day one of the COVID-19 vaccine
19 programs, systems will be in place to monitor the
20 safety of vaccine recipients. These include the

1 traditional systems that we use -- VAERS, which is the
2 national spontaneous reporting system monitored and
3 implemented by CDC and FDA, but also similar programs
4 at DOD and the VA as well as the National Healthcare
5 Safety Network, or NHSN, which is an acute care and
6 long-term care facility monitoring system. CDC's CISA
7 system is stood up, that provides individual case
8 consultation.

9 But in addition to really enhance this period,
10 CDC has stood up a new system called V-safe. It's an
11 active surveillance tool that uses text messaging and
12 web-based surveys to monitor vaccine recipients for
13 adverse events. Recipients complete brief surveys up
14 to intermittent surveys to 12 months following
15 vaccination. But then as part of the program,
16 recipients that report a significant health event that
17 impacts their daily activities, or leads them to seek
18 medical attention, will be called for more information
19 and a report will be generated. This is an opt-in
20 system, so we're going to have heavily enhanced

1 engagement around implementation of the program. We
2 really need people to sign on to this system to give us
3 the best data possible.

4 Large, linked database monitoring systems will
5 provide safety data when vaccine becomes more widely
6 available in the priority groups and the general
7 public. This includes, again, existing systems like
8 VSD, the FDA's extensive system, and systems from DOD
9 and VA. We're enhancing this by Genesis, which is a
10 new collaboration with NIH and Brown University, to
11 monitor safety in long-term care facility residents.
12 This system operates nationally and has near real time
13 data for 250 facilities.

14 To look at this another way, this is a table
15 that showcases the systems that we'll be using to
16 monitor safety in the populations that, based on ACIP
17 recommendations, will be vaccinated first, specifically
18 healthcare workers and long-term care facility
19 residents. So you'll see that early on we have a
20 series of systems to monitor healthcare workers and

1 long-term care facility residents through VAERS. VAERS
2 will be enhanced in this time period, especially around
3 long-term care facility residents, to ensure that we're
4 getting those reports. And then V-safe which will
5 specifically target healthcare workers.

6 And then you'll see all the systems that are
7 going to be in place for later monitoring in all of
8 those populations. I think the team has done a really
9 good job of thinking through what systems we have, how
10 to enhance those systems and looking for any weaknesses
11 and attempting to fill them in. And I'm giving it
12 short shrift by going through it so quickly, but
13 hopefully you'll understand how robust these systems
14 are.

15 In addition, the ACIP COVID Vaccine Safety
16 Technical Sub-Group was established to provide expert
17 consultation on COVID-19 vaccine safety issues. This
18 group, which we call VaST, was built off lessons
19 learned during H1N1 safety monitoring. The terms of
20 reference and composition have been finalized, and VaST

1 is ready to begin reviewing data once implementation
2 commences. The group is co-chaired by a member of ACIP
3 and a member of the National Vaccine Advisory Committee
4 or NVAC. There are 10 independent expert consultants
5 that make up the group, as well as ex officio members
6 from NIH, FDA, OIDP, CMS, HRSA, and IHS. And we also
7 have representatives from the VA and the DOD.

8 Now to briefly summarize our efforts around
9 post-authorization vaccine effectiveness. Post-
10 authorization or post-licensure VE estimates are needed
11 to address important evidence gaps from phase 3
12 clinical trials, particularly for secondary endpoints
13 that may not be adequately addressed. For example, the
14 trials may be limited in their ability to address a VE
15 against secondary endpoints like infection transmission
16 or in subpopulations. And we won't have great data
17 early on the duration of protection. We also believe
18 it's important to evaluate the real-world performance
19 of vaccines as protection may differ from efficacy
20 under trial conditions.

1 So this table attempts to lay out the VE
2 policy priorities that were determined based on
3 consultants with policy experts and internal and
4 external experts. The most immediate priority is to
5 determine whether the vaccine protects against
6 symptomatic disease as expected based on the phase 3
7 trial data but understanding that implementation for
8 these vaccines might be slightly complicated by folks
9 who don't exactly get the second dose exactly on
10 schedule ,and by the necessity to keep the vaccine in
11 cold chain. So that's going to be the focus, but then
12 there are a variety of subsequent and late stage
13 studies that are being planned or implemented.

14 A number of strategies are used to plan for
15 the assessment of VE, but to facilitate a rapid launch,
16 we've leveraged existing platforms. And for early-
17 stage vaccination, we focused on populations likely to
18 be vaccinated first. We're harmonizing and
19 coordinating across the U.S. government on a variety of
20 platforms, for example, using common case definitions,

1 data elements, and methods to improve comparability of
2 results. And we've been working to combine similar
3 platforms to improve geographic representation,
4 increase statistical power and generate more timely and
5 robust VE estimates. And we do have a diversity of
6 methods as we understand that all observation methods
7 have limitations.

8 Here's a summary of the studies that are being
9 planned, and, again, I don't have time to go through
10 all of them. But I would just point you to the top
11 row. The most immediate question is whether vaccines
12 work as expected. We're planning a prospective study
13 among healthcare workers. There is no large existing
14 databased rich for this group, and so we're doing a
15 test negative design case control study among
16 healthcare workers, which should help us relatively
17 quickly assess this outcome.

18 So in summary, planned VE studies will provide
19 a robust assessment of COVID-19 vaccine performance in
20 real-world settings. We believe we will have early VE

1 estimates in groups prioritized for vaccination, VE
2 against key outcomes and in important sub-groups, and
3 data from these studies will address critical gaps and
4 help guide future use of vaccine.

5 Systems are in place to monitor the safety of
6 COVID-19 vaccination in healthcare workers and long-
7 term care facility residents. V-safe, VAERS, and NMSN
8 will detect adverse event signals for further follow up
9 and evaluation. CMS, Genesis, and other claims based
10 and EHR systems will be used for both signal detection
11 and evaluation. Vaccine effectiveness in healthcare
12 workers is the immediate priority and will address the
13 question of does the vaccine work as expected? We
14 expect those studies to start immediately.

15 Vaccine effectiveness evaluations in older
16 adults, including those in long-term care facilities,
17 are planned and include both test negative design and
18 cohort evaluations. I hope that that does justice to
19 all the systems that we're planning and that are in
20 place. Understand that vaccine safety and effective

1 monitoring is a top priority for the U.S. government.
2 And we're committed to ensuring that all these systems
3 are in place and ready to go as soon as the vaccine
4 program is implemented. Thank you.

5 **DR. ARNOLD MONTO:** Thank you, Dr. Messonnier.
6 We're going to go directly on to Dr. Patel's
7 presentation, and then we'll have questions afterwards
8 so we have plenty of time. Dr. Patel?

9

10 **OPERATIONAL DISTRIBUTION PLANS**

11

12 **DR. ANITA PATEL:** Great. Thank you so much.
13 So thank you for having me today, and we'll be walking
14 through today at a high level what the USG's
15 distribution strategy is for a COVID vaccine,
16 specifically focusing around this Pfizer vaccine
17 product. The USG plan for COVID vaccine distribution
18 will adjust as volume of vaccine doses increases.
19 Early on, we do anticipate that we'll have a
20 constrained supply where vaccine administration is

1 really targeted towards select population groups, and
2 distribution will facilitate that. As sufficient
3 supply becomes available and the populations that we're
4 trying to reach expand, our distribution network will
5 also further expand.

6 This schematic here outlines what our concept
7 is for distribution at a very high level. All vaccines
8 will be ordered through CDC's COVID vaccine ordering
9 systems. For the Pfizer vaccine, we will be providing
10 those vaccine orders directly to the manufacturer for
11 distribution to administration sites. We've been
12 working very closely with our state and local partners
13 to make sure that they have plans in place to identify
14 providers that are able to receive, store, and use the
15 vaccine for the specific populations that they're
16 trying to reach. These administration sites will be
17 receiving the Pfizer vaccine product, and they should
18 expand, as well, over time as the targeted populations
19 we're trying to reach expand.

20 In addition to the hospitals, the vaccination

1 clinics that have been set up to support early
2 distribution and use of Pfizer vaccine, we have also
3 set up a program called the Long-Term Care Facility
4 Pharmacy Program. This federal program is a
5 partnership that allows for jurisdictions to be able to
6 opt-in to the program, allowing for onsite vaccination
7 support to occur to long-term care facilities. Our
8 pharmacy partners would be providing the onsite
9 vaccination support for those facilities that actually
10 sign up for the program.

11 I'd also like to draw your attention to the
12 Operation Warp-Speed Coordination cell at the bottom of
13 this slide. The idea is for us to be able to have a
14 clear understanding of what is happening in terms of
15 supply of vaccine as well as administration and uptake
16 information throughout the vaccination program.

17 Focusing a little bit more on the long-term
18 care facility plan, in order for us to be able to reach
19 skilled nursing facilities we have been working to
20 bring skilled nursing facilities on board to the

1 program and opt-in. Once a state determines that
2 they're ready to expand vaccination to reach staff and
3 residents within skilled nursing facilities and other
4 assisted living facilities, the program would be turned
5 on. Right now, we do have a very high percentage of
6 the skilled nursing facilities within the United States
7 that have opted in to receive services from the federal
8 program.

9 The vaccine characteristics of the Pfizer
10 program have actually -- are very different and unique
11 compared to other vaccines that we've seen before, and
12 they do impact distribution, site storage, as well as
13 administration requirements. The details depicted on
14 this slide are very specific to the Pfizer program and
15 outline some of the challenging requirements of the
16 vaccine that have to be implemented in terms of vaccine
17 distribution and storage sites. The additional
18 planning that is needed for distribution, storage,
19 handling, and use has been underway for the last few
20 months based on the information we know for the Pfizer

1 products.

2 There is a dedicate cold chain given that the
3 products have to be managed at ultra-low temperature
4 requirements. In addition, the timing of the vaccine,
5 ancillary supplies, which include the diluents, as well
6 as dry ice replenishment has also been a challenge. We
7 have built the distribution system in a way that all
8 three of these elements will arrive within a 36-hour
9 period of time. So once the vaccine is there, these
10 additional pieces will also be delivered to the
11 vaccination site.

12 Another major challenge that we've had with
13 the product is the actual minimal order requirement.
14 975 doses is the smallest volume of product that can be
15 ordered for the Pfizer vaccine. This has posed
16 challenges especially in rural areas of the country
17 where that volume of product is more difficult to
18 manage. And it's also been a planning factor that, at
19 the local level, has been used to determine where
20 exactly the product should be received.

1 There's also a new element of the thermal
2 shipping container that has been introduced with this
3 product. The container allows for the movement and
4 shipment of the vaccine from one site to another and
5 allows it to be managed in the ultra-low temp
6 conditions. There is training required with using this
7 thermal shipping container and staff being able to be
8 trained on the monitoring, the dry ice replenishment
9 requirements, as well as understanding how to manage
10 the product over time, how many times to open the
11 container. And the details have also been part of the
12 training and what we're getting vaccination sites ready
13 for.

14 There're also complexities with mixing and
15 using the product. It is a little bit different than
16 other vaccines that we've seen as far as the diluent
17 being required, how the product is drawn up, and also
18 how quickly the product needs to be used. Once
19 diluted, we do have a six-hour period in time in which
20 the vaccine needs to be administered, and that has also

1 been factored in and built into the planning at the
2 administration site level.

3 Lastly, we do have inventory planning that is
4 underway to ensure that there's sufficient supply
5 available for administration. This includes ensuring
6 that administration sites have actual clinic planning
7 times, that they're able to have enough people to come
8 manage the 975 doses for each of the trays, and the
9 planning for the actual clinics, as well as the
10 planning for the second dose. Since the second doses
11 are required, the timing's 21 days and any cushion that
12 we have beginning or ending from the 19 to 23 days that
13 we saw in the clinical trials.

14 What exactly that looks like and how that gets
15 operationalized and implemented is also part of the
16 planning factor. Second dose reminders are part of
17 insuring that people come back for that second dose,
18 and additional strategies are also underway. So with
19 that, I'd like to pause and turn it back over to the
20 moderator.

1 **DR. ARNOLD MONTO:** Thank you, Dr. Patel.
2 We're going to have time for just a couple of questions
3 at this point. Dr. Levy?

4 **DR. OFER LEVY:** Hello. I have a brief
5 question for Dr. Messonnier. First of all, thank you
6 so much for your presentation. It was very helpful.
7 You needed to move very quickly through some very
8 important information about the safety surveillance
9 systems that are in place to monitor the progress of
10 coronavirus vaccine.

11 I did have a question. You described a number
12 of interlocking national systems that would monitor
13 vaccine safety. I wanted to know if there's any
14 consideration or plans for also integrating these
15 systems with international efforts monitoring
16 coronavirus vaccine safety, for example, World Health
17 Organization, WHO. There's also an international
18 network of special immunization services and others.
19 So that's my first question.

20 My second question has to do with vaccine

1 effectiveness. You mentioned some key subgroups that
2 you'll be monitoring vaccine effectiveness in. Those
3 all made good sense. It went by quickly, but I didn't
4 see teens or maybe even eventually younger children
5 listed among those special populations. But I would
6 imagine they would be of interest as well, and I'd
7 value your comments on that. Thank you.

8 **DR. NANCY MESSONNIER:** Thank you for easy
9 questions. The answers to both questions is yes.
10 There's actually a WHO coordinated group looking at
11 sharing data for both safety and effectiveness and
12 coordinating across the globe on that. In addition, we
13 are working directly with collaborators in the UK and
14 in Canada to make sure that we're sharing information
15 as quickly as possible, and we're already gearing up to
16 help a number of countries for immunization campaigns.

17 The answer to the second is definitely yes. I
18 didn't put it on the slide because authorization for
19 those groups was not really up for discussion today,
20 but certainly it will be really important to be able to

1 monitor both safety and effectiveness in an enhanced
2 way in those groups, period.

3 **DR. ARNOLD MONTTO:** And the final question from
4 Dr. Kurilla. After that, we'll have to move on.

5 **DR. MICHAEL KURILLA:** Thank you. This is for
6 Dr. Messonnier. You described a very comprehensive
7 assessment, aggregation, collation of a lot of safety
8 signals, and I'm wondering the intention for that group
9 -- is that to provide ongoing advice to the people who
10 would be distributing the vaccine, potentially
11 administering it, public health officials, or is that
12 primarily to be focused towards the FDA in terms of
13 refinement of the EUA itself? What's the real focus of
14 all of that safety assessment? Where's it going?

15 **DR. NANCY MESSONNIER:** I mean, I think it
16 could be for multiple uses. However, our standing up
17 of an ACIP work group is to be a part of our ACIP
18 recommendations, that is the recommendations for use of
19 the vaccine. CDC and FDA and all the USG partners
20 coordinate, collaborate, work together in the safety

1 landscape every day on all our routine vaccines. And
2 as you look at our systems, you'll see how intertwined
3 they are. Any information, for example, that we get
4 will be shared quickly with FDA, as well as putting
5 these systems in place so that our Advisory Committee
6 can review it.

7 I also might say that CDC and FDA are also
8 discussing a contract with NASM -- the National Academy
9 so that we also have them to provide expert independent
10 review of vaccine safety issues that may arise in the
11 COVID-19 vaccination program. So in addition to
12 everything we've set up, we're also setting up that
13 collaboration contract with NASM so that we also have
14 them ready if we need to help adjudicate a safety
15 signal. Thank you.

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

17 **DR. ARNOLD MONTTO:** Well, thank you to both of
18 our CDC presenters. I'd like now to move on to the
19 presentation from Dr. Steven Goodman, who is Associate
20 Dean of Clinical and Translational Research at Stanford

1 University School of Medicine. And he is going to be
2 talking about considerations for placebo-controlled
3 trial designs if an unlicensed vaccine becomes
4 available under EUA. Dr. Goodman?

5

6 **CONSIDERATIONS FOR PLACEBO-CONTROLLED TRIAL DESIGN IF**
7 **AN UNLICENSED VACCINE BECOMES AVAILABLE**

8

9 **DR. STEVEN GOODMAN:** Thank you very much. I
10 want to thank the FDA for inviting me to speak to this
11 Advisory Committee today on one of its most important
12 decisions. And the title on this slide says exactly
13 what I'll be speaking to. Let's see. There we go.

14 So what are these considerations? Well, there
15 are two, and they're intertwined. First are the
16 ethical considerations, which concern the questions
17 about what is the right thing to do with the placebo
18 group in this case. The second class of considerations
19 are epistemic, concerning what we know or what we
20 believe, which is determined by the strength and

1 totality of the evidence. That's what's generated by
2 the designs we are already using and the ones we'll use
3 going forward, which might be the most consequential
4 thing that we discuss today. Let's see.

5 Now, I will be speaking about ethical issues,
6 but I am not a card-carrying or PhD carrying
7 bioethicist. But I've enjoyed working with many, and I
8 want to acknowledge before I talk the contribution
9 several have made to my remarks today, although the
10 views and ethical lapses are my own. They are
11 Professors Nancy Kass and Ruth Faden from Johns Hopkins
12 and David Magnus from Stanford.

13 Now, there are a lot of questions embedded in
14 what should happen with the designs and particularly
15 the control groups in studies going forward. This
16 slide outlines a lot of sub-questions, but I think the
17 title of the presentation pretty much captures it. If
18 an EUA for this and other vaccines are granted, what do
19 we do with the placebo control groups in this trial and
20 potentially in ongoing and in upcoming trials for the

1 next vaccine?

2 Now, I want to start with a set of ethical
3 preliminaries. I'll start with something that seems
4 very basic, but I can't tell you how many committees
5 I've been a part of and that I've watched whose
6 conversations have founded on this simple issue. We're
7 going to be dealing with ethical dilemmas here, but
8 it's worth thinking about what an ethical dilemma is.

9 So an ethical dilemma is not a choice between
10 right and wrong. That's what we write to advice
11 columnists for. And ethical dilemma is a choice
12 between two actions that are both ethically justifiable
13 under different moral frameworks or principles. In
14 that sense, it's a competition between two rights --
15 two right actions, which of course is exactly what
16 makes it a dilemma.

17 We face this is in every clinical trial, but
18 particularly on data monitoring committees there's
19 tension between actions that are good for an
20 individual, which in the current setting might mean

1 giving them a vaccine immediately, and what's best for
2 society, which might mean holding off on that vaccine
3 so placebo-controlled randomized trials can continue.
4 Resolution of ethical dilemmas always requires
5 compromise to balance the competing dictates and
6 minimizes physical harms or ethical wrongs which are
7 caused by unfairness, violations of autonomy, or actual
8 personal or societal harm.

9 Now, to continue, our ability to conduct
10 clinical trials, which is to experiment on each other,
11 is something that society gives us permission to do.
12 We don't need that permission to do chemistry or
13 biology experiments. And because the procedures and
14 oversites for RCTs are so structured and standardized,
15 it's easy to forget how fragile that permission to
16 conduct RCTs is. But anybody who's worked as an
17 institution whose research enterprise has been
18 completely shut down because of a single ethical lapse
19 knows that this trust can never be taken for granted,
20 and it's continually earned and re-earned through fair

1 and transparent processes to determine what's
2 acceptable. And that's what we're doing today and why
3 it's so important that we're doing it in public.

4 Now, final preliminaries which is ethical
5 acceptability depends often on context or background
6 conditions. Offering a placebo subject the vaccine can
7 be judged quite differently depending on whether the
8 evidence -- depending on the evidence we have about
9 efficacy and safety and whether or not that participant
10 can actually get the vaccine outside of the trial. And
11 both of those are part of the context today.

12 Now, epistemic preliminaries, I'll start by
13 saying something that shouldn't be too controversial,
14 which is that RCTs, or randomized controlled trials,
15 provide the most reliable knowledge about the relative
16 efficacy and safety of intervention, at least as
17 permitted by the sample size, and follow up time.
18 Obviously, we can't detect safety issues that come up
19 after the RCT closes. A second principle is that
20 reliable knowledge can come from non-randomized

1 designs.

2 And Dr. Messonnier just introduced us to some
3 of those. This includes exactly the kinds of things
4 she described: vaccine safety surveillance, all of
5 epidemiology, quasi-randomized design, natural
6 experiment, and understanding of biologic mechanism.
7 These can play a critical role. And finally, there are
8 many things to learn about these vaccines. We've
9 talked about them already. Some of them are best
10 learned through an RCT but not all of them, and there
11 are many things we can learn from these other designs
12 that do not require RCTs.

13 Now, finally, in the stage setting, there
14 should be no bright line. That is bright lines are
15 almost always unjustified, and they are the enemy of
16 ethical and epistemic compromise. In ethics, this
17 means we can't allow one moral framework or principle
18 to trump another.

19 We can argue about how one principle takes
20 precedence over another, but it's not helpful to hear

1 assertions like "It's unethical to deny an effective
2 vaccine to a placebo recipient." Asserting that
3 anything is unethical effectively shuts down the debate
4 and also demonizes people on the other side. And I
5 found it extremely healthy for committees not to use
6 that word at all. There's a corollary epistemology
7 where we can have reasonable discussion about what we
8 can learn and what we can't learn from randomized and
9 non-randomized studies but saying things like "You
10 can't learn anything from a study without
11 randomization," is both obviously not true and inimical
12 to a balanced solution.

13 Now, what do RCT participants know? Let's get
14 into the issue of ethical obligation. All consent
15 forms and consent processes are required to tell the
16 patient or the participant in the study that the
17 purpose is to produce scientific knowledge that
18 benefits society, not necessarily them directly.
19 They're also told or they trust that they won't be
20 exposed to known serious harm not listed in the consent

1 and that they can withdraw at any time for any reason
2 and that they'll be given information arising during
3 the trial that's highly relevant to their decision to
4 continue.

5 This is exactly what is in the Pfizer consent
6 in quite plain language. I've put it up here. I won't
7 take the time to read through it, but it's quite
8 explicit. And we have no reason to believe that the
9 study was misrepresented in any way.

10 Here in the highlighted area you can see
11 "you're free to stop participating at any time, and the
12 study team will tell you in a timely manner if new
13 information is learned that would change your mind
14 about continuing in this study." And that certainly
15 would be an EUA.

16 Now, let's talk about -- I'm sorry. I skipped
17 a slide there -- whether there's special obligations to
18 placebo recipients. Obviously, they have exactly the
19 same -- we have the same obligation to them that we
20 have overall to the trial. They're free to withdraw.

1 And because of that, the trial structure and
2 investigator shouldn't actively deny them vaccine in
3 any way if it became otherwise available to them
4 through a social prioritization and local
5 circumstances. And this is consistent with the FDA
6 position stated earlier. We'll come back to this.

7 I would also argue that the investigators are
8 not obligated to provide immediate vaccination in the
9 trial before their turn -- of the participant is called
10 out by the trial. First, this is not what they signed
11 up for, and there are many prioritization criteria out
12 there by very, very good groups. And I haven't seen
13 one that includes trial participation as a basis for
14 jumping the queue. It is not considered a reason to
15 get it before somebody else who might deserve it or
16 need to because of higher risk or other consideration.

17 But it should be reasonable. When a trial
18 participant becomes eligible through societal priority
19 and local ability, that they are then -- can be
20 provided vaccine in the trial context. So in a sense,

1 they jump to the front of their own line, and that also
2 binds them to the trial. It's a form of reciprocity,
3 and it facilitates further follow up.

4 Now, what are some issues related to the
5 COVID-19 context that will have relevance to these
6 decisions? The first is the most obvious. We're in a
7 pandemic. It's a public health emergency, which
8 magnifies potential consequences, both positive and
9 negative, and the consequences of knowledge or
10 ignorance and of action or inaction.

11 I would say that some rules that apply in
12 peace time might have to be modified in war, and we're
13 in a bit of a war right now. But I want to focus
14 specifically on the health risks to an individual.
15 Given the recent numbers -- not yesterday's, which are
16 particularly terrible with over 3,000 reported dying --
17 but those in the last few weeks, a randomly chosen U.S.
18 citizen has an average risk of dying from COVID in the
19 next six months -- that is by the end of May -- of
20 roughly one in 1,000 and the risk of hospitalization of

1 roughly about one in 200. These numbers obviously vary
2 widely by individual, and they don't include the harms
3 from non-fatal COVID. But they're highly ethically
4 relevant, and let's start to talk about that.

5 So if the risk of death in the U.S. in the
6 next six months is around one in 1,000, that means the
7 maximum benefit of the vaccine for an individual, at
8 least with respect to mortality, is also one in 1,000
9 or 0.1 percent. So imagine if we had a drug that
10 purportedly raised cancer survival from 40 percent to
11 40.1 percent. If there was more to learn -- and we do
12 have that here -- that's a setting where we would
13 typically allow many placebo-controlled trials. We see
14 this in meta analyses all the time with multiple trials
15 -- placebo-controlled trials of agents with therapeutic
16 benefit orders of magnitude larger than this.

17 So while this risk obviously has huge
18 population impact, in terms of trial ethics, it's not
19 the kind of risk that incurs a great ethical debt to
20 the placebo group or a prohibition on further placebo-

1 controlled trial. Also, unlike a therapeutic drug for
2 patients with a disease who can't change their own
3 prognosis, many but not all individuals can take
4 actions that reduce their own risk of death from COVID,
5 like masks and social distancing. So as long as
6 there's still important things to learn about the
7 vaccine, placebo-controlled trials should not be
8 regarded as unethical. However -- a big however --
9 they might be infeasible, and that is a big issue
10 because people may not be willing to either remain in
11 the study or to enroll. But it's very important to not
12 conflate the feasibility with the ethics.

13 Now, in terms of the vaccine context on what
14 we know, I'm actually not going to spend my time on
15 this. You're going to hear -- you've already heard a
16 lot about the Pfizer vaccine. The only one I want to
17 highlight is that if a participant wants to unblind
18 themselves in a trial they can. If they have the
19 resources and knowledge about which antibody --
20 commercial antibody test would unblind them, some of

1 them are to the spiked protein which would unblind
2 them. Others it's a nucleic acid, which might not.

3 Now, in terms of the vaccine context or
4 background position, what we don't know -- well, this
5 has actually already been covered. There's a whole
6 raft of things that we don't know yet and that we want
7 to learn, both from continued RCTs and also from
8 observational studies. Now, I want to outline a
9 possible adverse scenario. If placebo participants who
10 want vaccine when otherwise available and eligible are
11 not given access within the trial in the name of
12 scientific rigor, there may be many who respond to
13 appeals by investigators not to seek vaccine even if
14 available to them.

15 And to them, this argument doesn't apply. And
16 we've seen that willingness to hang in in studies with
17 placebo controls in many other trials of even greater
18 personal consequence. So it's not at all unlikely that
19 there would be a sizeable number of people who wouldn't
20 do that on appeal. But some participants at higher

1 risk will want the vaccine as soon as it becomes
2 available to them.

3 And if they can't get it through trial
4 mechanisms, many will lose trust in the investigator
5 and the trial itself and may leave the trial without
6 further follow up. They may seek vaccine outside the
7 trial, and as more vaccines come on the market, perhaps
8 they'll get another one that's available recently with
9 very uncertain effect. This will get a lot of
10 publicity, meaning that recruitment to future vaccine
11 trials will be that much more difficult because of a
12 collective loss of trust.

13 So some might appeal to the experimental
14 status of the vaccine under the EUA as justification --
15 as ethical justification for maintaining a placebo
16 control. I understand why this has salience within the
17 FDA, but I suspect that this distinction will not get
18 much traction among future or current -- current or
19 future trial participants when literally millions of
20 people are being urged to get vaccinated as quickly as

1 possible. The point is that once the vaccine's widely
2 available or any vaccine is widely available and
3 encouraged, the ability to maintain double blinded
4 placebo control groups voluntarily for more than a
5 nominal period, by which I might mean perhaps a few
6 months, will likely not be under the control of the
7 sponsor or the FDA. And some efforts to do so could
8 undermine future trials as people don't trust that
9 their interests will be watched out for.

10 Now, I want to mention an important
11 countervailing view, which is that many people out
12 there, as we well know, are very wary about an
13 expedited approval process and will refuse a vaccine
14 that they believe to be under-tested. They want to see
15 those trials going through their planned end, but
16 unless these people can be found and are willing to
17 enroll in placebo-controlled trial, the argument about
18 the feasibility of the trial still hold.

19 Now, what's the Pfizer proposal for
20 continuation? Now, it implicitly recognizes this

1 reality, and it's consistent with everything I've
2 discussed so far, except in one important regard.
3 First, they propose urging as many people in the trial
4 to stay as long as possible, which I think is the right
5 thing to do. But for placebo participants who become
6 eligible according to local or national recommendations
7 -- that's an important condition -- and who ask for the
8 vaccine, they propose unblinding them and vaccinating.

9 For those who stay in the trial blinded, it's
10 proposed that everyone be vaccinated after six months
11 and followed for an additional 18 months to the trial's
12 planned end. This is coupled with a robust
13 observational pharmacovigilance plan for long-term
14 safety monitoring that augments what the FDA and CDC
15 are doing. While not unreasonable, I think that we
16 have to remember that this design will not only unblind
17 placebo recipients. It will also unblind vaccinated
18 participants who make the same request because, of
19 course, they won't know. And once unblinded, risk
20 behavior can change. Many of the benefits of

1 randomization within the trial are lost.

2 So is there an alternative? And I would say
3 there is and should be considered. There are two
4 alternative designs that achieve the same ethical goals
5 without compromising far less -- without compromising
6 on the epistemic ones. That is we can give people
7 vaccine who are eligible and who want it but maintain
8 the blinding, thereby preserving trust that the
9 investigators and regulators care both about the
10 science and the participants.

11 And let's talk about those designs. One is
12 called deferred immunization. It's been presented in a
13 variety of settings and gotten coverage, also a blinded
14 crossover design. And the second are active control
15 designs, which are really not the issue for today, but
16 I'll discuss them briefly.

17 The first of these was developed by a
18 biostatistician at the NIAIB, the NIH, named Dean
19 Follmann. It involved blinded crossover designs, and
20 the idea here is that the placebo -- when either a

1 placebo or vaccine recipient becomes eligible for a
2 vaccine or requests it -- exactly the situation that
3 the Pfizer proposal describes -- that the placebo
4 recipient gets a vaccine, and the vaccine recipient
5 gets a placebo without being told what they were
6 originally. So the blind is maintained. And then they
7 are followed forward. So they stay within the trial
8 confines and to some extent also protected by the
9 randomization.

10 As I mentioned, the second design is active
11 control. At some point in the evolution of vaccine
12 testing, we may no longer be able to conduct placebo-
13 controlled trials of any type in settings where
14 vaccines were available. Although it's not a question
15 for today, at that time, when there are a lot out
16 there, a comparison vaccine with reasonably well-
17 established properties may have to be used in one arm
18 in those areas where they're a variable. But we're not
19 at that stage yet, but we may be within the next year
20 in some countries.

1 Now, in countries or regions where vaccine has
2 seen poor distribution it may still be possible to
3 conduct placebo randomized trials, but that has ethical
4 complications of its own. And I'm not going to get
5 into that here. I want to talk just a little bit more
6 about the deferred randomization scheme, and you see
7 that in this picture. The idea is that we'd start with
8 a vaccine and placebo arm, as we already have. And
9 then at the point when people are eligible and ask for
10 the vaccine -- you have to have both conditions --
11 that's the point where a blinded crossover occurs.

12 Because every participant is ultimately
13 assigned to the vaccine arm at some point, this design
14 actually in some situations -- in very plausible
15 situations -- can have greater or equal power to detect
16 the duration -- the sustenance of immunity more than a
17 standard 50/50 RCT. And you can sort of see that in
18 the figure where you see the contrast between the
19 vaccine efficacy in the width of the bar -- in the
20 delayed vaccine arm compared to the waning efficacy in

1 the original arm. And this increases over time, and
2 these can be compared statistically. So you can see
3 how this can work for vaccine efficacy.

4 But, of course, it decreases power to detect
5 some other things like long-term safety issues and some
6 other important parameters, but it doesn't lose them as
7 completely as designs where subjects are unblinded and
8 effective randomization is lost. So if the standard
9 50/50 RCT is not reasonable or feasible, which I
10 believe it very quickly won't be, this design is far
11 better than any that would break the blind and break
12 the randomization. We can, of course, also reduce some
13 of the ethical tension in any placebo-controlled trial
14 by increasing the allocation ratio to the vaccine arm,
15 but that may not be enough to solve the enrollment
16 problem.

17 The next slide shows another picture of this
18 deferred vaccination schema, and it shows that it's
19 possible -- you see the crossover on the right. On the
20 left-hand side, we have the trials as they've been

1 designed so far. On the righthand side you see what
2 they look like after the crossover, which is that
3 everybody's been immunized. But it's possible
4 statistically to impute an unvaccinated control group
5 to help estimate secular trend.

6 So to finish up, I want to summarize that
7 these alternative designs require compromises, the kind
8 of compromises I talked about before on both the
9 ethical side and the epistemic side -- that is the
10 evidence. Ethically, placebo recipients don't get a
11 vaccine as quickly as some might want, and this will
12 become more of an issue going forward as new vaccines
13 need to be tested with multiple ones already available
14 through EUAs. But of course, those subjects are not
15 being forced to enroll, but the ones who do enroll can
16 expect to get immunized at a certain number of months
17 going forward. As noted, placebo-controlled trials may
18 continue to be possible in areas or populations for
19 whom vaccines are not available, but that is
20 complicated for other reasons.

1 Finally, on the epistemic side with this
2 crossover designs we don't learn as reliably or as
3 quickly about long-term safety and infectiousness and
4 other factors. Although, we still might learn as much
5 or more about durability when compared with a trial
6 that continues with the placebo arm. But as I said,
7 that trial may not be doable. We might not have the
8 perfect design going forward and continued blinded
9 observation of the deferred vaccination group can still
10 be tremendously informative and potentially more
11 informative than one with broken randomization,
12 particularly in combination with observational studies
13 of the population that we've heard about today.

14 By reducing the ethical tension within the
15 trial and by retaining the trust in trial testing
16 system, it provides a way further for future studies of
17 other vaccines. So none of these are the last words on
18 this very difficult and complicated subject, but for
19 today, these will be my last words. So I hope this
20 will be helpful to you, and I welcome your questions

1 and comments. Thank you.

2 **DR. ARNOLD MONTA:** Thank you, Dr. Goodman.
3 You've given us a lot to think about and to discuss. I
4 just wanted to start by raising one question. With the
5 blinded crossover design, when would that take place?
6 When an individual becomes -- reaches the priority
7 listing for their group, or would that be at the time
8 of issuance of the EUA?

9 **DR. STEVEN GOODMAN:** So this is a subject of
10 tremendous controversy and discussion. For the reasons
11 I've already outlined, I don't think it should be --
12 and this is my opinion -- at the moment of the EUA
13 because otherwise they are jumping the queue, and I
14 discussed that earlier. I believe it should be when
15 the -- for those subjects, they come up on the social -
16 - you know, they come up as they would come up in terms
17 of priorities for the vaccine and it's available to
18 them in their area -- that is they can get it outside
19 the trial.

20 As soon as they can get it outside the trial,

1 then this would kick in because we want to keep them in
2 the trial. If it's given at another time, we're
3 basically giving them priority over other populations
4 that have been deemed to be at greater risk or greater
5 need. And the price I think we have to pay by
6 compromising the trial I believe would be too high, and
7 we don't have -- again, I made this argument earlier.
8 I don't think we have that special obligation to give
9 them the vaccine immediately. Those are my views.

10 **DR. ARNOLD MONTA:** Okay. Thank you. I think
11 we'll defer questions about how feasible this is to the
12 sponsor after the sponsor's presentation. Next is Dr.
13 Levy. And please unmute and show yourself if you'd
14 like.

15 **DR. OFER LEVY:** Sorry. That was an error. I
16 don't have a question.

17 **DR. ARNOLD MONTA:** Okay. Dr. Meissner?

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

20 **DR. STEVEN GOODMAN:** I guess I answered all

1 questions.

2 **MR. MICHAEL KAWCZYNSKI:** Should we go to the
3 next one?

4 **DR. ARNOLD MONTA:** Yeah. Dr. Chatterjee?

5 **DR. ARCHANA CHATTERJEE:** Yes, thank you, Dr.
6 Goodman, for your presentation. It was certainly
7 thought-provoking. I have a question with regard to
8 the current study participants. By reviewing the
9 briefing documents, it appears that there's a
10 difference between participants who received the active
11 vaccine versus placebo recipients in terms of adverse
12 events that they experienced. And so there's a
13 potential that people who are participating in the
14 trial can actually guess which arm they were surmised
15 to.

16 **DR. STEVEN GOODMAN:** Yes, absolutely. Yes.

17 **DR. ARCHANA CHATTERJEE:** Yeah. So is there
18 then a possibility that those who believe that they
19 were placebo recipients might wish to withdraw in
20 greater numbers and that that would then compromise the

1 study as well?

2 **DR. STEVEN GOODMAN:** Again, if they are -- it
3 absolutely could, so even going forward it could. And
4 that would be an issue for the statisticians and for
5 the FDA. The point of this particular proposal is this
6 would give them an avenue not to withdraw, that is stay
7 within the trial under these conditions. Now, if they
8 didn't want to wait for their allocation to become
9 available or eligibility locally, withdrawing wouldn't
10 do them anything. It wouldn't get them the vaccine any
11 earlier, so there would be no motivation to withdraw.

12 And also, I do think that the majority of
13 people who signed up for these trials did so in good
14 faith and with altruistic motive. I do believe the
15 vast majority want their contribution to produce a
16 valid scientific result. So I don't think self-
17 interest completely in any way dominates. And again,
18 yes, I do believe that there's a fair amount of
19 unblinding just due to reactogenicity of the vaccine
20 and obviously non-reactogenicity of the placebo. But

1 this -- again, at the time when they might be able to
2 get the vaccine outside the trial, this would give them
3 a way to still contribute to the science of the trial
4 without leaving. I don't know if that answers your
5 question.

6 **DR. ARCHANA CHATTERJEE:** No, that did, and I
7 was thinking about the people who would meet the
8 priority criteria obviously. They would be the ones
9 who would want to withdraw if they thought they were in
10 the placebo arm.

11 **DR. STEVEN GOODMAN:** Correct. And I do
12 believe -- that's what I said. I do believe that could
13 happen.

14 **DR. ARNOLD MONTO:** We've got a lot of
15 questions. I think we -- and what we're going to do is
16 I'm going to ask all the speakers to please be
17 available during our discussion because we may have
18 additional questions that come up at that point. I'd
19 like to move on to Dr. Kurilla, please. We've got a
20 lot of hands raised and no time.

1 **DR. MICHAEL KURILLA:** Thank you, Arnold.
2 Great presentation. So the blinded crossover design
3 looks quite feasible. However, the caveat is that it
4 will take -- it does take longer to get to the answer.
5 Did I hear that correctly? That's number one. But
6 would we also be facing a first mover effect where this
7 would basically dictate future trial designs short of
8 any vaccine having the full BLA going forward? So
9 everyone else would have considered this option as the
10 de facto approach.

11 **DR. STEVEN GOODMAN:** Yeah. That's a really
12 good question. That's why I emphasized that -- I'm
13 sorry. I see you talking, but I don't hear you. I'll
14 just answer what I heard.

15 I can't judge exactly what will happen in the
16 future because fact patterns are going to change, so I
17 hesitate to predict too much. It is possible that this
18 might represent, as we go forward, a default design
19 that reduces the ethical tension of these trials as
20 vaccines, as I mentioned, become available in the area

1 of potential enrollees in the trial. And what we'd
2 then be asking them to do is not completely deny
3 themselves a vaccine which they could just go out and
4 get if they themselves are eligible but just defer it
5 for a few months. It might be two months, three
6 months, four months. And that might be less of an ask.
7 I can't say whether it will become the default.

8 Again, it's going to be a while before enough
9 vaccines of any type, no less just this one, are rolled
10 out even in the U.S. Remember also that these trials
11 are going on all over the world, so the U.S. places
12 where -- they will not always be occurring in places
13 where vaccines are otherwise available for quite a
14 while. So it is possible we might evolve.

15 I do see that there's going to be a staging
16 where there's going to be a point or places where we
17 cannot any longer do the placebo-controlled randomized
18 trial. We might move to this. And then ultimately, as
19 I said -- and it might be a year or two from now --
20 have to move to active control. That's the evolution I

1 see.

2 Whether you're committing to this design going
3 forward harder to say. That's very complicated, and,
4 again, it's going to depend a lot on vaccine
5 distribution and what we learn about these vaccines.
6 If we learn -- if there start to be safety signals that
7 we're not seeing right now, that could change the
8 dynamic dramatically.

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

10 **DR. ARNOLD MONTO:** I'm just going to allow one
11 more question because we have to start at noon Eastern
12 for the public comment, which is difficult to control
13 otherwise. So Mr. Toubman, you'll be the last
14 question, and we're going to come back to this
15 discussion as part of the afternoon. And I think we
16 will really want to pick up where we've left off on
17 some of these issues at that point. So Mr. Toubman?

18 **MR. SHELDON TOUBMAN:** Thank you. I really
19 appreciate the presentation. On the blinded crossover
20 design, if I understand this, basically you solve the

1 problem of maintaining blindness. You don't have to
2 unblind, but you do lose the placebo. That group
3 that's been put into that blinded crossover system,
4 they won't have a placebo group (audio skip) for
5 purposes of (audio skip).

6 **DR. STEVEN GOODMAN:** That's right. You lose
7 the contemporaneous placebo. That's right. You retain
8 the value of having had a placebo at the beginning,
9 though, because of deferral. And if there's a waning -
10 - particularly on the issue of waning immunity,
11 obviously that difference might continue over time. So
12 you retain some of the value of having a placebo at the
13 beginning but not all of the value because things like,
14 particularly, safety and other issues which might not
15 be contingent just on the specific timing of when you
16 got the vaccine. You will probably lose that or
17 diminish that.

18 You don't completely lose it. It depends on
19 the characteristics of what it is you're measuring.
20 There are many things we can look at still with this

1 design, but that's why it has to be these designs
2 coupled with the observational designs outside, which
3 is obviously both what Pfizer's proposed but also what
4 the CDC and the FDA are also doing.

5 So there's many things that can be learned
6 outside the trial that we might have been looking to
7 the trial to provide. Now, we'll be depending more on
8 observational designs if we move more to these trials.
9 So we don't lose all the benefits of placebo group, but
10 we do lose some of them. But that may not be a
11 practical option, which was my point.

12 **MR. SHELDON TOUBMAN:** All right. Your
13 position's that we should not move people into the
14 blinded crossover design until they're eligible in
15 their particular societal group for getting it anyway.
16 I will say that we have gotten a lot of comments from
17 folks who are in trials -- like, dozens of them -- and
18 their line seems to be "Well, if EUA is granted, I
19 should be (audio distortion)." I'm not asking you to
20 opine on that. But my question is your view is you

1 should wait until it's readily -- their group comes up.
2 But if EUA didn't cover them at all -- that's one of
3 the possibilities we'll talk about later -- would that
4 help in the ethical determination that, yes, they
5 should definitely wait because, after all, EUA has not
6 been granted for their group yet anyway?

7 **DR. STEVEN GOODMAN:** I haven't thought through
8 that whole chain. All I will say is that they don't --
9 again, I mentioned this previously. I don't think that
10 they're -- it wasn't part of the initial contract.
11 They understood that they could do without the vaccine
12 for much longer, in fact, then they probably will have
13 under a deferred policy. And they still get priority
14 under this plan. It's just they get it first within
15 their own priority group, so it's not that they are not
16 owed anything.

17 There is a reciprocity here in that when
18 their, in a sense, turn comes up they get it first
19 through the trial mechanism. And so they're not
20 completely -- they're not disadvantaged by being in the

1 trial. In fact, they're advantaged, just maybe not as
2 much as they might want by demanding it today. But as
3 I said, I don't think the ethical calculus is such, and
4 other groups have not thought it such, that they are
5 necessarily owed that just by virtue of being in the
6 trial. But they do get a benefit.

7 **DR. ARNOLD MONTO:** Okay. Thank you very much.
8 I know these are very difficult situations and
9 scenarios that we will need to be talking about again
10 during the first part of our discussion. I apologize
11 also to those people who I haven't been able to call
12 on. You'll have your chance during the discussion
13 because there's going to be a lot that we're going to
14 have to talk about in the first part of our two-hour
15 period that we have assigned this afternoon. I am not
16 sure -- Prabha, when should he come back because I know
17 some of the public presenters are ready to go at noon
18 Eastern? Prabha or Kathleen?

19 **MR. MICHAEL KAWCZYNSKI:** So we're scheduled to
20 come back at -- we're originally scheduled to come back

1 around 12:00, but we still have to call in all the
2 public speakers. So let's just schedule it for right
3 now, as long as -- Prabha, are you there?

4 **DR. PRABHAKARA ATREYA:** Yes, I am here.

5 **MR. MICHAEL KAWCZYNSKI:** Okay. Go ahead.

6 **DR. PRABHAKARA ATREYA:** So we are scheduled to
7 start at noon time, so are they all lined up now to go
8 at noon or do we have five minutes extra to give them?

9 **MR. MICHAEL KAWCZYNSKI:** No, I need to call
10 them in all now. So we will project to be scheduled
11 for a 25-to 30-minute break, but we have to confirm all
12 the OP speakers come in. So let's at this time --
13 Prabha, if you agree, we'll do a 25-minute break, but
14 we may have to extend it a little to make sure we have
15 time to get everybody in. Okay?

16 **DR. PRABHAKARA ATREYA:** Yes, okay.

17 **DR. ARNOLD MONTTO:** Okay. That's the guidance
18 I needed. Thank you. So we're going to try to resume
19 around noon Eastern.

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

1 **MR. MICHAEL KAWCZYNSKI:** Thank you. So with
2 that, we are going to take a break.

3

4 **[LUNCH BREAK]**

5

6 **OPEN PUBLIC HEARING**

7

8 **MR. MICHAEL KAWCZYNSKI:** Hold on, Arnold.
9 Alright. And welcome back to the 162nd meeting of the
10 Vaccines and Related Biological Products Advisory
11 Committee break. I'd like to now hand it back over to
12 Arnold. Arnold, are you ready?

13 **DR. ARNOLD MONTO:** I am. I'd like to welcome
14 everybody to the open public hearing session. Please
15 note that both the Food and Drug Administration and the
16 public believe in a transparent process for information
17 gathering and decision making. To ensure such
18 transparency, at the open public hearing session of the
19 Advisory Committee, FDA believes that it is important
20 to understand the context of an individual's

1 presentation.

2 For this reason FDA encourages you, the open
3 public hearing speaker, at the beginning of your
4 written or oral statement to advise the committee of
5 any financial relationship that you may have with a
6 sponsor, it's products, and if known, it's direct
7 competitors. For example, this financial information
8 may include the sponsor's payment of your travel,
9 lodgings, or other expenses in connection with your
10 attendance at the meeting.

11 Likewise, FDA encourages you, at the beginning
12 of your statement, to advise the committee if you do
13 not have any such financial relationships. If you
14 choose not to address this issue of financial
15 relationships, at the beginning of your statement, it
16 will not preclude you from speaking. Prabha.

17 **DR. PRABHAKARA ATREYA:** Good afternoon
18 everyone. This is Dr. Prabhakara Atreya. I am going
19 to conduct the open public hearing session and I will
20 read your names in order. And then, when I call your

1 name please unmute your phone and then start speaking.

2 And you have three minutes to complete your remarks.

3 Thank you. The first name is Dr. Kermit Kubitz.

4 **DR. KERMIT KUBITZ:** Hello. These are my
5 comments to the Vaccine Advisory Committee on the
6 BNT162b2 Coronavirus vaccine. Cover efficacy,
7 structured benefit-risk and follow up. I have no
8 conflicts except for a lot of elderly relatives. Next
9 slide.

10 The Pfizer vaccine appears efficacious based
11 on 95 percent relative reduction in infections and T
12 Cell responses comparable to human convalescent sera,
13 see Figure 2 page 22 and Figure 4 page 24. Some
14 uncertainty is introduced by the possibility of mild
15 asymptomatic infections, including among placebo
16 patients, feelings of pain or injection site effects
17 that may have caused more vaccinated participants to be
18 tested than placebo recipients. Next slide.

19 Benefit-risk. I have reviewed the available
20 evidence. And as a Caltech graduate, despite the

1 uncertainties, the structured benefit-risk of Pfizer
2 BNT162b2 is very positive. The Coronavirus, as we have
3 heard, is a serious medical condition with 3,000 daily
4 deaths. While there are therapeutics, there are no
5 prophylactics against COVID-19.

6 Even in the event of approval of the Pfizer
7 vaccine, limited supplies will require EUA of other
8 efficacious vaccines when available, such as Moderna or
9 others. Benefits of the vaccine include prevention of
10 COVID-19 after the second dose, prevention of severe
11 COVID-19, and preventing COVID-19 after the first dose.
12 Risks appear to be mild injection site pain, fever, or
13 fatigue.

14 Increased reactogenicity for recipients over
15 55 is more than offset by the benefits of preventing
16 COVID-19 cases in older adults with weaker immune
17 systems. I note that allergy-susceptible persons
18 should be informed of any issues in the EUA vaccine
19 following approval. The net benefit is highly
20 positive. I would recommend the vaccine to my siblings

1 over 80 and my relative in an assisted living facility
2 where there are have been three cases for staff and
3 three cases among residents.

4 There is a need for follow up of vaccination
5 effect including how long after immunization patients
6 are protected, whether the vaccine prevents infections
7 which cause further transmission, and how any
8 violations of cold-chain supply, dilutions, shaking, or
9 administration affect efficacy. Thank you, Dr. Fink,
10 Dr. Gruber, Secretary Azar, Dr. Gans, and Dr.
11 Messonnier. They need this vaccine yesterday.

12 **DR. PRABHAKARA ATREYA:** Okay. Great. Thank
13 you. The next speaker is Diana Zuckerman.

14 **DR. DIANA ZUCKERMAN:** Yes. Hi. Can you hear
15 me?

16 **DR. PRABHAKARA ATREYA:** Yes.

17 **DR. DIANA ZUCKERMAN:** Thank you. I'm Dr.
18 Diana Zuckerman, president of the National Center for
19 Health Research. Next slide. Our center scrutinizes
20 the safety and effectiveness of medical products and we

1 don't accept funding from companies that make those
2 products. My expertise is based on my post-doctoral
3 training in epidemiology, and as a faculty member and
4 researcher at Vassar, Yale, and Harvard, and also
5 previously a Fellow in Bioethics at Penn. I've also
6 previously worked at HHS and the U.S. Congress. Next
7 slide.

8 Today I'm going to focus on two major concerns
9 on how we can improve the data that are already
10 available. Number one, the two-month median follow up
11 is just too short to have long term safety information
12 and long-term efficacy information. So it's essential
13 that the randomized control trial be continued.

14 Number two, there's a lack of diversity in
15 COVID cases. There were zero black cases in the
16 vaccine group and only seven black cases in the placebo
17 group. And there were zero cases that were ages 75 and
18 up in the vaccine group and five in the placebo group.

19 And it was very disturbing, Wall Street
20 Journal did a chart saying it was 100 percent effective

1 for Black patients, for example. So that's one of the
2 reasons why we need more people, so we have reasonable
3 data. Next slide.

4 There are also too few severe cases to draw
5 any conclusions. There were only four severe cases
6 after the second dose. That's just too few to conclude
7 anything. Next slide. Long term care patients were
8 not in the study. There were about 800 people, ages 75
9 and over in the study, but only five were cases.

10 So we want to save their lives but how can we
11 ensure informed consent to nursing home patients when
12 we have no data to provide? And how many frail,
13 elderly or their family members can make an informed
14 decision based on so little information? Next slide.

15 We need long term data to fully understand if
16 the benefits outweigh the risks for frail patients, and
17 for all races and ethnicities, and for all patients.
18 And that's why continuing the randomized control trial
19 is so important. Next slide.

20 In conclusion, the EUA is not approval and it

1 should have more restrictions than you'd have for
2 approval. So FDA should require continuation of the
3 RCT while targeting EUA to priority populations,
4 especially healthcare workers. I agree, don't let
5 anyone in the placebo group jump the queue.

6 Second, EUA should not allow off-label use for
7 non-priority groups whether they're celebrities or
8 anybody else. Off-label use could potentially occur
9 under FDA's expanded access program. And last, FDA
10 should delay access to vaccines by the placebo group
11 unless they are in the priority populations.

12 And I am concerned that the blinded crossover
13 would be informative if the vaccine is not long term
14 efficacious. But if it was efficacious long term, we
15 would lose that information in a blinded crossover.
16 Thank you very much for the opportunity to speak today.

17 **DR. PRABHAKARA ATREYA:** Great. Next speaker
18 is Peter Doshi.

19 **DR. PETER DOSHI:** Hi. This is Peter Doshi.
20 Hopefully, you can hear me. Thanks for the chance to

1 speak. For identification purposes, I'm on the faculty
2 of University of Maryland and a medical journal editor
3 with the BMJ. I have no relevant conflicts of interest
4 and no one has paid for my attendance. Slide two,
5 please.

6 My experience has been that careful review of
7 a large trial takes considerable time and effort. As
8 FDA has already reviewed the data, I'd like to know
9 whether FDA's confident in the data collection for the
10 primary endpoint. Specifically, that any unofficial
11 unblinding did not affect the result. And that fever
12 and pain medications did not mask symptoms, thus
13 preventing case detection. I didn't find answers to
14 these questions in the FDA's briefing documents. Slide
15 three.

16 A dramatic difference in rate of side effects
17 between vaccine and placebo raises questions about how
18 well these trials could be observer-blinded. With a
19 subjective endpoint like symptomatic COVID, blinding is
20 important. But it seems fair to think that people

1 could make reasonable guesses as to which group they
2 were in. Slide four, please.

3 In the real world, the mantra has been to
4 test, test, test but this wasn't the case in the trial.
5 The study protocol says, in the seven days after
6 vaccination do not test unless, in the investigator's
7 opinion, the clinical picture suggests COVID rather
8 than vaccine side effects. This basically amounts to
9 asking investigators to make guesses as to which
10 intervention group patients were in. My question is,
11 was this kind of judgement ever applied in the days it
12 could affect the primary endpoint? And now I'd like to
13 skip to slide six in the interest of time.

14 Possible unblinding would matter less if the
15 trials had been designed to directly test the vaccine's
16 ability to reduce deaths, ICU use and hospitalizations
17 as most people assumed the trials were set up to do.
18 It's great when the data look encouraging, but trials
19 should be directly testing the endpoints that matter.

20 Then there's the duration of protection issue.

1 A vaccine that delivers a 95 percent relative risk-
2 reduction of COVID two to three months after
3 vaccination is one thing. But for the many people who
4 lack natural immunity, and don't get exposed to the
5 virus soon after vaccination, protection needs to last
6 much longer. After six months or a year, will the
7 vaccine still meet the FDA's 50 percent effective
8 requirement? The trials just don't have sufficient
9 data to say.

10 Keeping the trials going with placebo-
11 controlled follow up will help answer the many crucial
12 questions that remain. For those that do not wish to
13 wait for clear evidence that benefits outweigh risk, an
14 expanded access program can be set up. Access doesn't
15 require authorization. And I just want to end by
16 saying that whatever FDA ultimately does, the full
17 trial data must be made publicly available. Thanks for
18 offering me the time to speak.

19 **DR. PRABHAKARA ATREYA:** Okay. The next
20 speaker is Rossi Hassad.

1 **DR. ROSSI A. HASSAD:** Thanks. Thank you. I
2 am Rossi Hassad a professor at Mercy College with
3 expertise in epidemiology, statistics, and mental
4 health. I hereby declare no known potential conflict
5 of interest. Next slide.

6 This vaccine is reported to have an impressive
7 overall efficacy rate of 95 percent consistent across
8 key demographics. However, the primary efficacy
9 endpoint of the trial was symptomatic COVID-19
10 infection. Participants who may have developed
11 asymptomatic infection were not identified in this
12 trial. Therefore, if as expected an Emergency Use
13 Authorization is issued, the spectrum of COVID-19
14 infection that this vaccine is efficacious against must
15 be emphasized. Next slide.

16 Adequate statistical power is necessary for
17 differentiating between an actual vaccine effect and
18 one that occurred by chance. The power of this trial
19 was calculated as 90 percent to detect an overall
20 effect for vaccine efficacy and may not allow for

1 formed conclusions regarding subgroup differences.

2 Next slide. As reported, there were no serious safety
3 concerns, which is quite reassuring. However, there
4 were frequent mild and moderate adverse effects which
5 are recognized as common side effects of vaccines.

6 Next slide.

7 Additionally, participants were blind as to
8 whether they received the vaccine or placebo. But
9 given the common awareness of vaccine side effects,
10 unintentional unblinding may have occurred and this can
11 potentially inflate estimates of vaccine efficacy.

12 Next slide.

13 In conclusion, the potential benefits of this
14 vaccine outweigh the identified risks. Therefore, I
15 support the issuance of an EUA with the stipulation
16 that the vaccine can protect against symptomatic
17 disease. But at this time it is not known if it
18 prevents infection and transmission.

19 Contraindication for those with a history of
20 severe allergic reactions is plausible and should be

1 included in the EUA as well. The continuing need for
2 non-pharmaceutical interventions, particularly mask
3 wearing, should also be noted. Finally, ongoing
4 monitoring of this vaccine is imperative. Thank you.

5 **DR. PRABHAKARA ATREYA:** Okay. The next
6 speaker is Evan Fein.

7 **MR. EVAN FEIN:** Hi. My name's Evan Fein and
8 I'm a Phase 1 participant in the Pfizer-BioNTech trials
9 that was conducted by researchers at NYU. I have no
10 financial or other conflicts of interest to disclose.

11 I'm speaking today because after conversations
12 with friends, family, and coworkers I thought it was
13 important to share my experience in this trial and to
14 do my part to help ease people's fears about the
15 vaccine. I think I got a real vaccine and not a
16 placebo because of mild adverse effects such as fever,
17 chills, and pain in the injection site after the second
18 injection. After reporting the side effects, I was
19 called repeatedly by the doctors and researchers at NYU
20 to see if I was okay, and I was.

1 Nothing felt rushed and I never felt like a
2 guinea pig. The question that everyone asked me is,
3 well what happened in the long term? Are there any
4 long-term side effects? And it's been more than five
5 months now since my first shot and I can happily report
6 that there are none.

7 Since I participated in the trial, I've helped
8 out my older parents, I've gone to work in person, and
9 I've exercised in small groups, and I haven't gotten
10 COVID-19. I also want to emphasize that these
11 activities do not represent changes of behavior that
12 would alter the integrity of the clinical data. These
13 are life activities that I have to do anyway. Not all
14 of us are able to lock down and stay at home
15 indefinitely.

16 I'd still do my best to follow health rules
17 and safety precautions. I understand the concern about
18 whether or not people will trust the vaccine, but there
19 will always be some hold outs. Most Americans will
20 take the vaccine voluntarily as long as we're honest,

1 don't talk down to them and treat them like autonomous
2 adults. But right now, demand for the vaccine exceeds
3 the supply. The skepticism of some does not justify
4 delays for others who desperately want to take it.

5 The best way to get people to take the vaccine
6 is to lead by example. I don't think that the problem
7 was that this vaccine was rushed, the issue is that
8 other important innovations are slowed down too much by
9 delays in scheduling, lack of funding, and other
10 bureaucratic rules that do little to enhance safety
11 protocols.

12 If Pfizer, BioNTech, Moderna or anyone else
13 has an RNA product that can immediately help people
14 with cancer, dementia or AIDS, the FDA should accept
15 the data on a rolling basis and work with these
16 companies to get to and complete Phase 3 clinical
17 trials within a year or two. Five to ten years for
18 these trials is simply not good enough. Pfizer has
19 just set the gold standard for future clinical trials.
20 Let's live up to this.

1 Now, this is an emergency, and the burden of
2 proof is on those who don't want to authorize the
3 vaccine. Absent compelling reason not to authorize it,
4 it is simply immoral and unethical to deny the vaccine
5 to healthcare workers or first responders who want it.
6 An EUA must be granted and it must be granted tonight.
7 As of yesterday, the daily death toll for COVID-19
8 exceeds the death toll on September 11, 2001. Delays
9 on December 10th will be more deaths on January 10th.
10 In the words of Todd Beamer, let's roll. Thank you.

11 **DR. PRABHAKARA ATREYA:** Thank you. The next
12 speaker is Angela Rasmussen.

13 **DR. ANGELA RASMUSSEN:** Thank you for allowing
14 me a few moments to speak. I'm a virologist and
15 affiliate of the Georgetown Center for Global Health
16 Science and Security. I have an advisory relationship
17 with Seamans but I have not been compensated to appear
18 today. I'd like to offer some comments on how serology
19 testing might better inform our knowledge of how these
20 vaccines are working after they are rolled out to the

1 public.

2 So this expedited process has moved
3 considerably faster than the typical vaccine
4 development timeline. And as such, we are inherently
5 limited on the breadth and scope of data that's
6 available on duration, durability, and effectiveness of
7 the immunity as well as the variability of different
8 vaccinee's respective immune responses.

9 Due to exclusion criteria in the clinical
10 trial itself, there's also limited data available on
11 minority and underserved populations as well as
12 pediatric populations, pregnant women, and the elderly.
13 And we don't really know a lot about how these broader
14 populations will develop antibodies to the vaccines.

15 Also with the limited supply of vaccines, at
16 least initially, it's going to be really critical to
17 determine who has already been infected with SARS-CoV-2
18 in order to conserve the vaccine for equitable access
19 for others in the same priority category.

20 Because this rollout will be so highly visible

1 and pivotal, we really need to address potential
2 problems such as outbreaks in nursing homes, hospitals,
3 schools or at other at-risk populations due to a
4 failure to seroconvert. And serology testing could
5 really help limit all of these issues. Next slide,
6 please.

7 Serology testing could help at different
8 phases also, before and after vaccination. But prior
9 to vaccination, serology testing could assist in
10 prioritizing individuals for vaccination as I just
11 mentioned. Also, establishing a serological baseline
12 in the population and help ensure that a scarce supply
13 of vaccines initially reaches the most vulnerable
14 people. Shortly after vaccination, it can confirm
15 initial neutralizing antibody responses to the vaccine.

16 It can also help ensure that antibody response
17 clears the threshold for protective immunity. And over
18 the longer term, three, six and nine months after
19 vaccination, it can confirm the persistence and
20 duration of immunity. It can also provide the means of

1 a bridge trial to additional populations and subgroups.

2 Finally, it can assess the protective efficacy

3 of vaccinations by distinguishing antibodies from

4 vaccinations versus antibodies from natural infection.

5 So by looking for anti-nucleocapsid antibodies, you

6 could actually determine if people who have been

7 vaccinated have been infected after being vaccinated.

8 And finally, annually after vaccination, we

9 can assess better the persistence and duration of

10 immunity. It can also inform the requirements for

11 future vaccinations that are developed on an

12 accelerated timeline such as this one. Thank you so

13 much for allowing time to speak.

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

15 speaker is Jared Krupnick.

16 **MR. JARED KRUPNICK:** Thank you. Before I

17 begin, your next presenter, Dr. David Berger alerted me

18 that he can't get back into the conference. If you

19 could resolve that for him, so thank you. So slide

20 number one, please. My name is Jared Krupnick. I'm

1 the President of Uniting for Action and the founder of
2 the Vaccine Considerations Project. I don't have any
3 conflicts of interest to share. Slide number two,
4 please.

5 As you can see, the Vaccine Considerations
6 Project has been created to highlight health and safety
7 throughout the COVID-19 vaccine evaluation process. I
8 want to acknowledge and thank the incredible team
9 behind all this work. Thank you, Dr. Eric Brown, Dr.
10 David Berger and our incredibly talented, committed,
11 and rapidly growing team of graduate students. Slide
12 number three, please.

13 I don't have to tell you about the challenges
14 this committee and this Agency have been facing, you're
15 living those challenges. I'm bringing up the
16 challenges to highlight that amid all the different
17 reasons for vaccine hesitancy, what remains universal
18 is that widespread concerns must be adequately
19 addressed in order to ensure sufficient buy-in by
20 public health experts, medical professionals, and the

1 public. Slide number four, please.

2 You're seeking to establish trust and
3 confidence in any vaccine you authorize and in the
4 evaluation process by being rigorous, comprehensive,
5 and transparent. There are limits to what can be
6 addressed in a meeting. We're working hard to help you
7 expand those limits. We're creating new ways to
8 organize and share information.

9 Here you can see how we've thoroughly analyzed
10 the transcript of your previous meeting to extract
11 specific concerns expressed by each individual
12 committee member. We're providing the links to our
13 website, vaccineconsiderations.com, where the full
14 process transcript is available for anyone to see.
15 Slide number five, please.

16 As you can see on this slide, our team has
17 plotted specific concerns from specific individuals to
18 develop a matrix of concerns. By plotting each concern
19 as a row and placing each of the committee members in
20 separate columns, you can use this matrix to quickly

1 and easily see which members share concerns, and which
2 concerns have yet to addressed or fully resolved.

3 You can use this document as a living document
4 where each member can continue to add and update their
5 concerns offline, and the FDA staff and other committee
6 members can address those concerns. By making this
7 public, things won't fall through the cracks. This
8 reassures the public and the professionals that are
9 relying on you. The matrix of concerns is available to
10 all at vaccineconsiderations.com. Slide number six,
11 please.

12 We're using this spreadsheet as the model to
13 demonstrate the concepts, but a spreadsheet is limited.
14 That's why we spent over a year programming a custom
15 platform called "Information for Action" that provides
16 this type of functionality at scale. Our team is
17 reaching out to stakeholders all around the country,
18 experts, organizations, and associations, to build and
19 organize a central repository of concerns.

20 We want to invite and encourage this

1 committee, and the FDA staff, to utilize these
2 technological tools to effectively address concerns,
3 build trust and reduce hesitancies. If you appreciate
4 what we've shared we'd like to connect with you.

5 Please reach out to us at

6 team@vaccineconsiderations.com. Thank you. My team
7 and I look forward to working with you.

8 **DR. PRABHAKARA ATREYA:** Great. The next
9 speaker is Mr. David Berger, Dr. Dave Berger.

10 **DR. DAVID BERGER:** Hello. Thank you for
11 allowing me to speak today. My name is David Berger.
12 I am a board-certified pediatrician. I have no
13 conflicts of interest.

14 I am one of the few pediatricians in Florida
15 who does not discharge families from my practice if
16 they have vaccine hesitancy or do not wish to follow
17 the recommended CDC schedule. My comments today are
18 very mindful of the strong, overall benefit our nation
19 will get when most of us have immunity to SARS-CoV-2.
20 Next slide, please.

1 My presentation today is about vaccine
2 hesitancy and steps that can be taken to increase
3 confidence in the COVID vaccine program. And this
4 should be slide three by the way. It is very important
5 that we see ongoing complete transparency about the
6 vaccine in terms of both safety and efficacy. We have
7 seen reports that up to 50 percent of Americans, and 30
8 percent of physicians, have some level of hesitancy
9 about COVID vaccines. We must allow for meaningful
10 public scrutiny to build public confidence in the
11 vaccine program. Next slide, slide four.

12 True informed consent has always been at the
13 core of how I practice medicine. As doctors, we have a
14 duty to inform our patients about the benefits and
15 risks of any medical procedure. If a person feels she
16 is not given sufficient information about a treatment,
17 how can she provide informed consent? I also think
18 it's important to respect people who have concerns
19 about hesitancy about vaccines. I often find that
20 hesitant families will proceed with vaccines if they

1 don't feel like their concerns were blown off or
2 minimized, but instead were respected and tended to.
3 Slide five.

4 While there are many subpopulations that
5 should be studied for increased chances of vaccine side
6 effects, there is particular concern about those with
7 preexisting, allergic, hyper-inflammatory and
8 autoimmune conditions. The Pfizer data shows that four
9 individuals who received the vaccine developed Bell's
10 Palsy whereas there were no incidents in the placebo
11 group. On the first day of England's vaccine program,
12 their government had to tell people not to take the
13 vaccine, the Pfizer vaccine, if they have a history of
14 significant allergic reactions after two significant
15 anaphylactic reactions were seen in recipients. Slide
16 six.

17 It will be difficult to quickly and fully
18 track all 50 states to find the real frequency of
19 adverse reactions. It is important that we have a
20 strong federal program to coordinate this. Please

1 ensure a plan for this. Please provide data for us to
2 know if people who have had COVID infection already
3 have an increased or decreased risk of a vaccine
4 reaction. Please provide comparative data between the
5 different vaccine products to determine if any brand
6 may have more or different reactions than other brands.
7 Slide seven.

8 I implore you to put in place a very long-term
9 post-vaccine surveillance program. Many autoimmune or
10 hyper-inflammatory conditions often take a while to
11 develop significant enough symptoms for a patient to
12 seek medical help. Slide eight. It is also important
13 to have a robust surveillance of COVID IgG antibodies
14 so we will have a way of knowing if immunity is waning.
15 We need to know what is considered a protective
16 antibody level for COVID-19 just like we have for other
17 vaccine titers that can be commercially tested. Slide
18 nine.

19 If the FDA can increase our level of
20 confidence, hesitancy will likely decline and the COVID

1 vaccine program will have a better chance of success.
2 It will take many good people to defeat COVID-19 and I
3 hope I can help you make a difference. Next slide.
4 Thank you very much. I appreciate the time.

5 **DR. PRABHAKARA ATREYA:** Okay. Thank you, Dr.
6 Berger. The next speaker is Sidney Wolfe, Dr. Sidney
7 Wolfe. And he does not have PowerPoint.

8 **MR. MICHAEL KAWCZYNSKI:** Dr. Wolfe? Dr.
9 Wolfe, you can't listen to it on the -- Dr. Wolfe?

10 **DR. SIDNEY WOLFE:** Yes.

11 **MR. MICHAEL KAWCZYNSKI:** Okay. Dr. Wolfe --

12 **DR. SIDNEY WOLFE:** Can you hear me with the
13 speakerphone on?

14 **MR. MICHAEL KAWCZYNSKI:** No. Yeah. You have
15 to turn your TV off or otherwise we're going to hear
16 the delay. So please turn your TV off or whatever
17 you're listening to.

18 **DR. SIDNEY WOLFE:** I will turn it off right
19 now. It's off.

20 **MR. MICHAEL KAWCZYNSKI:** All right.

1 **DR. SIDNEY WOLFE:** Can you hear me on
2 speakerphone? I'm doing speakerphone now.

3 **MR. MICHAEL KAWCZYNSKI:** Yes, we can, sir.
4 Yes, we can.

5 **DR. SIDNEY WOLFE:** Can you hear that?

6 **MR. MICHAEL KAWCZYNSKI:** Go ahead, sir. Yes,
7 we can. Go ahead, sir.

8 **DR. SIDNEY WOLFE:** I'm Dr. Sidney Wolfe,
9 founder, and senior advisor of the Public Citizens
10 Health Research Group. I have no conflicts. With the
11 surging pandemic and interim efficacy and safety
12 results made public two days ago, we now agree with the
13 need for an EUA for Pfizer-BioNTech COVID vaccine.
14 There's an important unresolved conflict though.

15 If an EUA is granted for widespread use,
16 should the 19,000 participants in the trial who
17 received a placebo be notified of this and be offered a
18 vaccine by Pfizer, clearly encouraging them to stay in
19 the trial. Similarly, should blinded vaccine
20 recipients be told of their status, thereby encouraging

1 continuation in the trial? What would you wish if you
2 were subjects in the trial?

3 As status uninformed trial participants, you
4 might otherwise leave the trial to get vaccinated with
5 the Pfizer or any other EUA available vaccine. The
6 unblinding of vaccine providing proposal has important
7 advantages. First, once an EUA's granted, the ethical
8 obligations, as Pfizer says, to both inform all placebo
9 recipients of their status and offer them vaccine
10 within the context of the trial, is met.

11 Second, by retaining more trial participants
12 than if the trial remains blinded after an EUA, more
13 recipients may be followed afterwards. The originally
14 vaccinated group could be compared with the newly
15 vaccinated group to continually compare rates of new
16 COVID-19 infection with increasing duration of
17 vaccination as well as adverse reactions.

18 FDA has said that it doesn't consider
19 availability, as you have all heard, of a COVID-19
20 vaccine under an EUA in and of itself as grounds for

1 immediately stopping a blinded follow up in an ongoing
2 trial or offering a vaccine to all placebo recipients.

3 During the October 22nd meeting, during Dr.
4 Doran Fink's presentation, someone asked, "What about
5 the problem of retaining placebo patients post EUA?"
6 And Dr. Fink responded with regards to mitigating the
7 risk of dropout from ongoing clinical trial, "We do
8 share that concern. I don't have any specific remedies
9 to offer at this time. We've asked the vaccine
10 manufacturers to think carefully about how they would
11 ensure clinical trial retention."

12 Pfizer has stated in a briefing document, "It
13 intends to continue the pivotal Phase 3 study with
14 participants in both the vaccine and placebo groups as
15 originally allocated for as long as possible,"
16 emphasize that. "Nevertheless, we have an ethical
17 responsibility to inform all outgoing" -- all ongoing
18 rather -- "study participants the availability and
19 eligibility criteria of the vaccine made available
20 under an EUA."

1 They would accommodate those trial
2 participants wishing to leave the trial by reviewing
3 which group they are in, but they can receive the
4 vaccine only when practically eligible, depending on
5 the government specified priority group and the
6 available supply. But Pfizer's real preference -- and
7 this is in the briefing documents -- is that such
8 placebo individuals are vaccinated within the study in
9 order that both safety and efficacy data can continue
10 to be collected. We believe this approach will
11 minimize the number of current participants --

12 **MR. MICHAEL KAWCZYNSKI:** Time.

13 **DR. SIDNEY WOLFE:** -- who withdraw from the
14 study. If you were in the trial, would you prefer
15 being unblinded only if you wished to leave the trial
16 to seek possibly available but needed vaccine? Or
17 being automatically unblinded given Pfizer's vaccine if
18 in the placebo group or happy to find out --

19 **MR. MICHAEL KAWCZYNSKI:** You need to wrap it
20 up.

1 **DR. SIDNEY WOLFE:** -- to stay in the trial?

2 Thank you.

3 **DR. PRABHAKARA ATREYA:** Thank you. The next
4 speaker is Kim Witczak.

5 **MS. KIM WITCZAK:** Yes. Good afternoon. My
6 name is Kim Witczak and I'm speaking on behalf of Woody
7 Matters, a drug safety organization started after the
8 death of my husband due to an undisclosed side effect
9 of antidepressants. We represent the voice of families
10 who live every day with the consequences of the current
11 drug safety system. I am also on the board of
12 directors for U.S.A. Patient Network, and independent
13 patient voice advocating for safe, effective, and
14 accessible medical treatments.

15 Right now the world is looking for hope so
16 they can get back to normal. Too many lives and
17 livelihoods have been lost. Like many of us, we put
18 blind faith and hope in the system that ultimately
19 failed us. I have several concerns about rushing novel
20 vaccines to market.

1 The public needs assurances that the FDA's
2 review was thorough and independent. Given the process
3 for reviewing new products usually takes six to ten
4 months. How could the FDA be as rigorous in weeks this
5 time? Is there a process in place if there are
6 dissenting scientific reviews within the Agency? This
7 needs to be available, and FDA scientists need to be
8 protected for whatever their judgment is, and not be
9 political like it has been with many of the past
10 controversies such as antidepressants and suicide has
11 been handled within the Agency.

12 Transparency is everything. Assuming FDA
13 approval, then all trial data must be released and made
14 public. This also includes the process information
15 like Pfizer's data monitoring committee who determined
16 it was safe. Is it public? If not, it should be. We
17 also need a transparent process for catching safety
18 signals and communicating with the public. It needs to
19 be real-time like we saw in the U.K. yesterday with the
20 allergic reactions and not reported in weeks, months,

1 years later like history has shown.

2 Post-market monitoring will be more important
3 than ever. We really don't know what short and long-
4 term harms are given the short duration. Will FDA be
5 staffed to handle the large task of closely monitoring
6 that will be needed? Like MOD, the medical device
7 recording system, which includes patient narratives in
8 the reporting, the FDA needs to do the same for the
9 VAERS. Narratives can help tell a more complete story
10 than just the data without giving away important
11 patient details.

12 Finally, I have huge concerns with possibly
13 unblinding of placebo participants and giving them the
14 actual vaccine as Pfizer's CEO alluded to be willing to
15 do. If this happens, we lose our control group. In
16 closing I'm directing this comment to the news media.

17 You have a huge responsibility to dig deeper
18 ask critical questions, and not be just an extension of
19 the manufacturer's PR department. And accept press
20 releases like the Wall Street Journal article did

1 earlier this week and included a Pfizer-supplied chart
2 showing efficacy by subgroups where blacks had 100
3 percent efficacy. This should have sounded alarms and
4 begged for additional questions. And then they would
5 have dug deeper and realized there weren't a whole lot
6 of blacks in the trial. Please seek out independent
7 researchers, scientists, and others without political
8 or financial agendas.

9 Ultimately, the public is the real-world
10 clinical trial. It is one big human experiment. The
11 only ones that have 100 percent immunity in this will
12 be the pharmaceutical companies. They get all the
13 benefits of sales without any of the legal liability
14 should something go wrong. I'd like to thank you for
15 your careful consideration of my comments. I know
16 firsthand the importance of your advisory committee
17 work. Thank you.

18 **DR. PRABHAKARA ATREYA:** Okay. The next
19 speaker is Ms. Lynda Dee.

20 **MS. LYNDA DEE:** Hi. Thank you. I'm from AIDS

1 Action Baltimore and the AIDS Treatment Activist
2 Coalition. I have no conflicts of interest. The
3 answer to both Agency questions on COVID-19 prevention
4 and the risk benefit ratio are clearly yes in my
5 opinion. Many of the issues submitted in my written
6 comments have been addressed by the sponsor submission.

7 One important ethical issue, involving
8 maintaining participants in the placebo arm after EUA,
9 has been discussed. I think it is very reassuring that
10 the sponsor's proposing the placebo participants be
11 permitted to decide whether to remain on the placebo or
12 to receive the vaccine within the study at the
13 appropriate time. The crossover design will hopefully
14 ensure that the study will not crash.

15 Crossovers are nobody's favorite, but an
16 unblinded crossover is probably much more feasible
17 here. Laypeople have no understanding of the nuances
18 discussed today. Acceptable designs, that will confirm
19 initial EUA data and protect current participants and
20 suspicious future potential participants promoting

1 public trust, are essential.

2 I do have a few important remaining concerns.
3 The DART study for pregnant women should be much
4 further along by now. Also, the sponsor is essentially
5 claiming that safety and efficacy have been established
6 across race and ethnicity. The analysis of 3,800 Phase
7 2/3 participants includes only 0.5 percent Native
8 Americans, 9.3 Black or African Americans and 28 Latinx
9 people. The Native American and Black or African
10 American numbers are especially concerning in these key
11 populations, who are disproportionately affected by and
12 who experience greater adverse COVID-19 related
13 comorbidities and deaths.

14 While my community appreciates the eventual
15 inclusion of people with HIV, HBV, and HCV per
16 Amendment 6, the mere 120 people with HIV enrolled is
17 abysmal. The sponsor has submitted zero separate data
18 on people with HIV, HBV, and HCV or people over 75.
19 Thus, there is absolutely no data to guide vaccine use
20 in these populations.

1 This is especially concerning for people with
2 HIV as there's mounting evidence of disparate, adverse
3 coinfection outcomes. VRBPAC should recommend that the
4 sponsor conduct post-EUA research to establish safety
5 and efficacy in significant numbers of people over 75,
6 and people of color and people with HIV, HBV, and HCV,
7 where feasible, without excluding them from any
8 indication.

9 Finally, I hope we don't begin by lagging
10 behind in the enrollment of people of color in COVID-19
11 research. I sincerely hope Pfizer will include
12 consumers in its vaccine expert safety subcommittee and
13 will convene community meetings to discuss trial
14 designs, as well vaccine education and accrual and
15 retention issues. This practice has served both the
16 HIV community and sponsors very well over many years of
17 successful and mutually beneficial drug development.
18 Thank you and the FDA for such dedicated service and
19 for the opportunity to comment.

20 **DR. PRABHAKARA ATREYA:** Okay. Thank you.

1 Next speaker is Peter Lurie.

2 **DR. PETER LURIE:** Good afternoon. I'm Peter
3 Lurie, president of the non-profit Center for Science
4 in the Public Interest and Associate Commissioner at
5 FDA from 2014 to '17. I have no conflicts of interest
6 to disclose. I would like to thank the FDA for
7 conducting its review in a transparent manner, and for
8 committing to the advisory committee review process
9 particularly under concerted political pressure.

10 I just want to address two issues today.
11 First, based on the data accrued to date, the Pfizer
12 product demonstrates a striking degree of efficacy in
13 preventing confirmed COVID-19, one that is shared
14 across a variety of demographic, clinical and other
15 subgroups. I agree with the FDA reviewers that there
16 is no evidence of a major safety signal. However, the
17 extent of more minor adverse events is notable. These
18 include injection site reactions, fatigue, headache,
19 all in over 50 percent of subjects, and chills in
20 almost a third. All substantially elevated compared to

1 rates in the placebo group.

2 I do not believe that these events should
3 stand between this product and authorization. But I do
4 think the rates of these events are sufficiently
5 elevated to merit open and even-handed discussion with
6 patients. We're already facing significant levels of
7 vaccine hesitancy and, if patients are not forewarned
8 about these adverse events, their word will surely
9 spread rapidly, potentially exacerbating the hesitancy
10 problem. I also welcome FDA's identification of the
11 disproportionate numbers of Bell's Palsy cases, and
12 hypersensitivity-related adverse events observed in the
13 treated group, as matters that should continue to be
14 monitored including in the post-marketing phase.

15 The second issue relates to trial design now
16 that at least one safe and effective vaccine has been
17 identified. The issues are complex, but we ought to be
18 able to agree on this; no subject who has put their
19 body on the line in a vaccine study should be at a
20 disadvantage in terms of vaccine access as a result of

1 their participation. Some observers appear to be
2 advocating for extended periods of blinded follow up
3 even after authorization. This position is hard to
4 justify ethically, if it is inconsistent with public
5 health recommendations at the time, particularly with
6 rapidly rising case rates and the reported levels of
7 effectiveness for the Pfizer and Moderna vaccines. So
8 let me propose the following framework, which I think
9 we can all agree on -- at least most of it.

10 One, subjects should be informed if any
11 vaccine candidate is authorized, not just the one in
12 their trial. Two, like any study subjects, those in
13 vaccine trials should be given the opportunity to leave
14 the trial at any time if they so desire. Three, given
15 the shortages of available product, subjects should be
16 offered vaccination with an authorized vaccine as soon
17 as it is offered to those in their clinical or
18 demographic group in accordance with federal or state
19 guidelines.

20 Four, those for whom the product is not yet

1 recommended can continue to be followed in blinded
2 fashion. And five, vaccination is recommended for an
3 individual, a good option is to do so in a blinded
4 crossover manner as described by Dr. Goodman to
5 facilitate blinded follow up for long term safety and
6 efficacy outcomes. I believe that this will facilitate
7 the collection of essential data while honoring the
8 contributions of the tens of thousands of people whose
9 altruistic efforts have brought us to where we are
10 today. Thank you.

11 **DR. PRABHAKARA ATREYA:** Okay. Thank you. The
12 next speaker is Andrew Spiegel.

13 **MR. ANDREW SPIEGEL:** Yes. Thank you. Thank
14 you for allowing me the opportunity to provide comments
15 on this most important day. My name is Andrew Spiegel,
16 and today I present in my role as Chair of the World
17 Patients Alliance. I have no disclosures.

18 The World Patients Alliance is a global
19 umbrella organization of nearly 200 patient
20 organizations from 86 countries representing hundreds

1 of millions of patients across diseases world-wide. My
2 very brief comments today fall into three basic areas,
3 dedication, commitment to science and transparency and
4 innovation.

5 First, we want to applaud the dedication of
6 the scientists both within the private companies and
7 within the FDA. In the last year, scientists and
8 researchers have fought tirelessly to create a vaccine
9 for the Novel Coronavirus and put it through rigorous
10 processes to ensure its safety and its efficacy. We
11 are comforted in knowing that the FDA will require
12 rigorous post-distribution data monitoring, to continue
13 to ensure any approved vaccines will be safe for the
14 population.

15 We know that in these unprecedented times the
16 people of America, and the people of the world, deserve
17 to know that their governments are working to eliminate
18 this threat. And we want to make sure that the FDA
19 knows that we will continue to hope that it keeps the
20 patients at the forefront of all of its policy and

1 approval decisions on these vaccines as well as other
2 medicines. The entire world is watching what the FDA
3 is doing and, as everyone knows, they're relying upon
4 the FDA's commitment to patients.

5 Last, as the Coronavirus vaccines continue to
6 be approved and used in countries around the world, we
7 must continue the process of innovation. Developing
8 countries need access to innovative medicines now more
9 than ever. In future breakthroughs, the vaccine for
10 COVID could be manufactured as a pill, that would be
11 easily distributed and prescribed in those countries
12 with less access to healthcare professionals around the
13 globe.

14 I certainly am in agreement with other
15 speakers before me on the issue of ensuring diversity
16 in clinical trials, and ensuring trial members get
17 access to the vaccine, and will not repeat further
18 comments on that. Thanks again to all the stakeholders
19 who have come together in an unprecedented way, during
20 these unprecedented times, to do what would be

1 unthinkable in the past. On behalf of patients around
2 the globe, we thank you for your hard work and your
3 commitment.

4 **DR. PRABHAKARA ATREYA:** Okay. Great. The
5 next speaker is Nissa Shaffi.

6 **MS. NISSA SHAFFI:** Good afternoon. I'm Nissa
7 Shaffi and I'm here today on behalf of the National
8 Consumers League. I have no relevant conflicts of
9 interest. We extend our gratitude to the Vaccines and
10 Related Biological Products Advisory Committee for the
11 opportunity to present public comment today on behalf
12 of consumers, regarding the deployment of an Emergency
13 Use Authorization for the Pfizer-BioNTech COVID-19
14 vaccine.

15 Firstly, we want to thank the Food and Drug
16 Administration, Centers for Disease Control and
17 Prevention and other public health agencies for their
18 demonstrated commitment to fostering public trust
19 throughout the COVID-19 vaccine development and
20 approval process. As consumer advocates, we have been

1 encouraged by the honesty, transparency and access
2 afforded to the public during this critical time. To
3 that point, there has never been a more critical time
4 for consumers to have confidence in the FDA. The
5 Agency has undergone scrutiny from the scientific
6 community for prematurely issuing EUAs for COVID-19
7 therapeutics.

8 NCL is aware that developing a vaccine for
9 COVID-19 is a time-sensitive priority and appreciate
10 that the FDA recognized that an EUA is not intended to
11 replace long-term, randomized clinical trials data
12 associated with full FDA approval. We look forward to
13 continuing guidance around the vaccine as the trial
14 continues to collect safety and efficacy data two years
15 post-release. We have great trust in the FDA's
16 rigorous vaccine approval process and call on the
17 Agency to perform ongoing post-market surveillance to
18 ensure the vaccine's ongoing safety and efficacy.

19 Post-market surveillance performed in the U.K.
20 yielded that the vaccine is unsafe for individuals with

1 severe allergies. We call on the FDA to heed these
2 warnings and to continue to sustain its robust inter-
3 agency collaboration towards the evaluation, approval,
4 and distribution of the COVID-19 vaccine. Consumers
5 will rely on ongoing guidance from public health
6 agencies regarding any potential adverse events from
7 the vaccine.

8 Additionally, ensuring innovative vaccine
9 delivery methods, such as including oral or nasal
10 options, could address geographic access issues as well
11 as adequately consider diverse health needs increasing
12 overall uptake. We welcome efforts to ensure diversity
13 in the clinical trials for the COVID-19 vaccine, and
14 NCL requests that the FDA continue to prioritize
15 vaccine clinical trial data that reflects diversity as
16 people of color will need to have confidence in the
17 vaccine's efficacy in their communities. This will
18 impact overall uptake of the vaccine.

19 The development of a COVID-19 vaccine in such
20 record time has been a miraculous feat made possible

1 through robust collaboration between private and public
2 entities. NCL will continue to support the FDA and CDC
3 in its efforts to release a COVID-19 vaccine safety and
4 expeditiously. Thank you to the committee for your
5 consideration for our views on this important public
6 health issue.

7 **DR. PRABHAKARA ATREYA:** Okay. Thank you. The
8 next speaker is Julie Omohundro.

9 **MS. JULIE OMOHUNDRO:** Good afternoon. I'm
10 Julie Omohundro, unaware of any conflicts of interest.
11 I will cover two points in the comments I submitted and
12 leave you to read through those as you please. They
13 were submitted under the banner of the Regulatory Watch
14 Cat and easily identified by a cute, black cat.

15 I start with a question. Does the EUA violate
16 Article 37 of the Declaration of Helsinki, which states
17 that unproven interventions should not be used in
18 medical practice without informed consent? This led to
19 the question as to whether authorized products are
20 proven or unproven, and whether their use is medical

1 practice or research. Eventually, I concluded that EUA
2 lies in an ethical gray area, falling along several
3 continuums.

4 I consider a few such continuums and ethical
5 questions that they might raise. I also looked at
6 ethical standards in 21 CFR, the Belmont Report, and
7 the AMA Code of Medical Ethics. Finally, I considered
8 Section 564 of the Food Drug and Cosmetic Act and the
9 current status of both informed and consent for EUA
10 products.

11 Section 564 requires informing patients that
12 the product has been authorized for emergency use. The
13 problem is that patients don't know what the means.
14 Currently, providers and patients are provided with
15 product factsheets, all apparently based on the same
16 template. The language addressing the product has been
17 authorized for emergency use comes directly from
18 Section 564, which was not written to inform patients
19 of anything. It is not in language understandable to
20 patients nor to providers.

1 Currently, there's much confusion among
2 manufacturers, providers, and patients regarding the
3 regulatory status of authorized products and what can
4 reasonably be expected of their safety and
5 effectiveness. It is the latter that patients and
6 providers need to understand and where the factsheets
7 fall far short. If individuals with the appropriate
8 expertise could evaluate concepts such as proven versus
9 unproven, medical practice versus research, as they
10 apply to EUA and as points along a continuum, this
11 could provide a rational framework for addressing
12 ethical concerns that have emerged with the EUA, as
13 well as the appropriate regulatory oversight and the
14 appropriate use of clinical data generated from the use
15 of an EUA product.

16 I don't think this type of evaluation is
17 suited for Warp-Speed. Therefore, in the interim, I
18 ask the committee to consider that the risks presented
19 by the EUA include not only ethical risk but also loss
20 of public trust, a serious risk for any public health

1 program. If issues emerge with the use of a new
2 medical product, patients and providers rarely go back
3 to, "What was I told?"

4 I hope FDA will give serious consideration to
5 moving forward with any COVID-19 vaccine initially
6 under expanded access, rather than EUA, to assure
7 adequate ethical oversight, informed consent, and early
8 access to a vaccine by the populations that most
9 urgently need it. In addition, for the love of Harvey
10 Wiley and Jenna Sock (phonetic), please, please, have
11 an IRB take a look at the template for the patient
12 factsheet. Thank you.

13 **DR. PRABHAKARA ATREYA:** Okay. Great. The
14 next speaker is Dru West.

15 **DR. DRU WEST:** Thank you. Thank you for this
16 opportunity to comment. My name is Dru West and I'm
17 the President of the U.S.A. Patient Network. Our
18 organization is composed of many patients and family
19 members who have been affected by pharmaceutical and
20 medical devices that promised hope but left our members

1 or family members harmed with lifelong side effects and
2 sometimes death. We have no conflicts of interest to
3 report as we are a completely independent voice for
4 patients and their families.

5 Our concerns are based on lived experience.
6 Every person receiving a COVID vaccine needs to know
7 the answers to basic questions such as, will this
8 vaccine prevent the most serious symptoms or the spread
9 of the disease? What side effects or problems might
10 occur immediately, mid-term and long-term? And how
11 long will this vaccine protection last?

12 It's our opinion that at this time there are
13 too many unanswered questions regarding the safety and
14 efficacy to release the vaccine. The release of these
15 vaccines will make participants unwitting subjects in a
16 seemingly uncontrolled clinical trial. That said, we
17 recognize the tremendous pressure being placed on the
18 FDA to act. Therefore, in the absence of reasonable
19 assurances of safety and efficacy, we ask that the
20 release of this vaccine be done cautiously and with

1 thoughtful for the health and well-being of the
2 recipients. We ask that you proceed slowly with
3 release of these vaccines on a voluntary basis until
4 full conclusion of blinded Phase 3 clinical trials.

5 We ask that you exclude populations that have
6 not been studied or thoroughly studied, such as,
7 pregnant women, frail elderly persons and severely
8 immunocompromised persons, among others. We also ask
9 that you continue, or expand existing or new clinical
10 trials, to include groups of people who have not yet
11 been included in any clinical trial to truly determine
12 safety and efficacy. We ask that you monitor the
13 vaccine recipients long term over time, by collecting
14 and analyzing data to identify the real world safety
15 and adverse response results.

16 This includes giving clear instructions and
17 encouragement to vaccine recipients on what, where and
18 how to report adverse response events not just
19 reporting to their doctors. We ask that you give
20 complete, informed consent information that includes

1 full disclosure of the ingredients in the vaccines, all
2 possible adverse responses as well a statement, in
3 plain language, that the current safety and efficacy
4 information is incomplete, and that the vaccines have
5 not yet been studied for safety and effectiveness for
6 everyone or studied for adverse responses or
7 effectiveness over time. We thank you for hearing our
8 concerns.

9 **DR. PRABHAKARA ATREYA:** Okay. Great. Thank
10 you. The next speaker is Sarah Christopherson.

11 **MS. SARAH CHRISTOPHERSON:** Hi. Thank you. My
12 name is Sarah Christopherson. I am the Policy Advocacy
13 Director at the National Women's Health Network. We're
14 a non-profit advocacy organization that has been
15 bringing the voices of women to the FDA for 45 years.
16 We are supported by our members and do not accept
17 financial support from drug or device makers. And I
18 have no conflicts of interest to disclose.

19 We applaud the FDA for their diligent work
20 during this public health emergency on desperately

1 needed vaccines including, yes, over Thanksgiving.
2 However, we do have serious concerns that moving
3 forward with an Emergency Use Authorization, based on
4 so little data for so many of the communities that have
5 been hardest hit by this virus, will do little to
6 assuage legitimate concerns in those communities about
7 taking the vaccine.

8 As we heard this morning, CDC data indicates
9 that Black and Indigenous people living in the U.S. are
10 roughly four times more likely to be hospitalized from
11 COVID-19 and roughly three times more likely to die
12 from the virus than their white counterparts. And as
13 we heard at the October 22nd meeting, members of those
14 communities have also expressed a really strong
15 interest in knowing that the vaccine will work in
16 people like them. Without those assurances, black
17 Americans have expressed high rates of COVID vaccine
18 hesitation, and for good reason.

19 Black Americans don't have to look back to the
20 last century or to the infamous Tuskegee study to see

1 examples of the medical system undervaluing them. And
2 many black and Indigenous people have had multiple
3 discriminatory and negative experiences with the
4 medical system in their own lives. Pew Research found
5 a clear link between confidence in the regulatory
6 process that you all are pursuing and American's
7 willingness to get the vaccine.

8 Before authorization is granted, affected
9 communities need to have confidence that the vaccine is
10 safe and effective for people like them. The efficacy
11 data submitted to this panel includes fewer than 2,000
12 black or African American vaccine recipients, and just
13 131 American Indian or Alaskan Native recipients, not
14 counting the placebo-control population. The safety
15 data included just 206 black seniors, 65 or older, and
16 just 131 American Indian or Alaska Native people of any
17 age.

18 If this advisory committee votes to recommend
19 authorization based on this data, FDA must ensure
20 robust tracking and bold public transparency once the

1 vaccine is taken. Otherwise, the near-term side
2 effects of the vaccine, which have been mentioned
3 earlier, such as fever, chills, pain, fatigue, all of
4 which could be really quite alarming to the public not
5 expecting it, could further fuel distrust among
6 communities that have been given little reason to trust
7 this process. Thank you.

8 **DR. PRABHAKARA ATREYA:** Okay. Thank you. The
9 next speaker is Vicky Pebsworth.

10 **DR. VICKY PEBSWORTH:** My name is Dr. Vicky
11 Pebsworth. I have no financial conflicts. I'm a
12 public health scientist and nurse who has served as
13 consumer representative on VRBPAC. I am the Volunteer
14 Director of Research and Patient Safety for the
15 National Vaccine Information Center and the mother of a
16 child injured by his 15-month well-baby shots in 1998.

17 The normal U.S. vaccine development, testing,
18 and licensing process takes 10 to 20 years. When
19 accelerated and when population studies are not large
20 enough, or do not closely match those targeted to be

1 vaccinated, the public assumes unknown and potentially
2 increased risks. Under the Emergency Use
3 Authorization, COVID-19 vaccines can be approved but
4 remain experimental and unlicensed while manufacturers
5 are shielded from liability if the vaccines cause harm.

6 The EUA factsheet prepared for the public must
7 be transparent, and fully disclose known and unknown
8 risks of the Pfizer-BioNTech COVID-19 vaccine, to
9 guarantee fully informed medical decision making and to
10 ensure public confidence. Specifically, the EUA
11 factsheet should disclose whether the vaccine is at
12 least 94 percent effective in preventing SARS-CoV-2
13 infection and transmission, or only prevents severe
14 COVID-19 disease, hospitalization, and death.

15 Whether there is evidence for antibody
16 acquired and T Cell mediated immunity, and how long it
17 lasts. Whether there is a risk of enhanced COVID-19
18 disease when vaccine recipients are exposed to the
19 SARS-CoV-2 virus or have previously received flu shots
20 or other vaccines. Whether there is evidence for

1 immediate and/or delayed serious vaccine reactions and
2 poor health outcomes, especially in those who have
3 already had COVID-19 disease, have severe allergies,
4 experience severe reactions to previous vaccinations or
5 are chronically ill.

6 The EUA factsheet must clearly identify
7 populations excluded from clinical trials. Over 40
8 criteria excluded certain people from some trials,
9 including pregnant women and children, those with high
10 blood pressure, obesity, diabetes, asthma, heart, lung
11 and kidney disease, neural and immune problems, and
12 those using certain medications or with a history of
13 vaccine reactions or over age 85. Will the vaccine be
14 safe and effective for them?

15 The EUA factsheet must clearly list all
16 vaccine ingredients and disclose that an aborted fetal
17 cell line was used to test the vaccine, as reported in
18 a September 2020 paper published by 61 Pfizer and
19 BioNTech scientists. By law, the EUA factsheet must
20 state that the consumer has the option to accept or

1 refuse the vaccine.

2 It is the position of the National Vaccine
3 Information Center that using coercion and sanctions to
4 persuade adults to take an experimental vaccine, or
5 give it to their children, is unethical and unlawful.
6 Thank you for your consideration.

7 **DR. PRABHAKARA ATREYA:** Okay. Thank you. The
8 next speaker is Martha Nolan.

9 **MS. MARTHA NOLAN:** Good afternoon. Thank you
10 for the opportunity to speak with you today. I am
11 Martha Nolan, Senior Policy Advisor at Healthy Women.
12 Healthy Women is the nation's leading non-profit health
13 organization representing more than 18 million women.
14 We provide consumers and healthcare providers with
15 accurate, evidence-based information about diseases and
16 conditions, innovations in research and science and
17 changes in policy that affects women's access to
18 treatment and care.

19 I'd like to first thank you for the thoughtful
20 and important work you are doing today and all that

1 you've been doing throughout the pandemic. The
2 discussion today is truly historic, and I commend all
3 of you for your leadership and careful consideration of
4 the data that is before you. Whether today or in the
5 future as COVID-19 vaccines are authorized by this
6 body, I know that we are all cognizant of the
7 challenges that lie ahead in terms of public trust.

8 The science being presented today is truly
9 remarkable, and the transparency of this meeting and
10 the sharing of information from all of the companies as
11 they work to develop COVID-19 vaccine candidates is the
12 first step in bolstering public trust. As you're
13 aware, recent surveys among the general public, but
14 also somewhat surprising among healthcare workers
15 reveal concerns around the safety of COVID vaccines and
16 many myths and misconceptions. When you look at
17 communities of color, the level of skepticisms are even
18 higher.

19 All of us who work in public health must look
20 to address this issue and working together will be

1 particularly critical. That is why Healthy Women is
2 co-leading an effort with more than 60 other public
3 health organizations representing patients, caregivers
4 and families, diverse communities, healthcare workers,
5 older Americans, veterans, front line workers and
6 scientists, to work together to alleviate the concerns
7 and hesitancy associated with the COVID vaccines. The
8 COVID-19 Vaccine Education and Equities Project's
9 mission is to educate and raise awareness of the
10 importance of the COVID-19 vaccination for public
11 health, the economy, and the broader society, as well
12 leading the conversation to ensure equitable access to
13 authorized and approved vaccinations.

14 The key to getting our lives back to normal
15 here in the U.S. and across the globe hinge on the
16 success of COVID-19 vaccinations. But we also know
17 that vaccines are only as effective if they are trusted
18 and taken by the majority of the population. We look
19 forward to continuing our work to help build that
20 trust, and thank all of you, again, for the work you're

1 doing to ensure that the coming vaccines are safe and
2 effective. Thank you.

3 **DR. PRABHAKARA ATREYA:** Okay. Great. Thank
4 you must. The next speaker is Mitchell Warren.

5 **MR. MITCHELL WARREN:** Thank you so much. My
6 name is Mitchell Warren and I'm the Executive Director
7 of AVAC, a non-profit organization founded in 1995 to
8 accelerate the ethical development and global delivery
9 of HIV vaccines and other new prevention options. And
10 in March we joined with several organizations to
11 establish the Global COVID Advocates Advisory Board. I
12 have no conflicts to declare and we accept no funding
13 from pharmaceutical companies.

14 AVAC enthusiastically welcomes the safety and
15 efficacy data of the Pfizer-BioNTech mRNA vaccine
16 candidate being presented today. This is terrific news
17 to be sharing on a triumph of science and partnership.
18 While the data to us should clearly warrant an EUA,
19 they also require the maximization of additional data
20 collection to address a number of remaining questions

1 and issues that need to be addressed.

2 One, the critical importance of distinguishing
3 between an EUA and licensure under a BLA, and for you
4 all to help ensure that continued data collection and a
5 clearly articulated pathway and timeline for a BLA is
6 provided. Two, there continues enormous need for the
7 inclusion of diverse populations in COVID vaccine
8 trials generally. And the data under review today
9 provide limited information about the safety and
10 efficacy data in diverse populations, including people
11 living with HIV, other immuno-compromised people and
12 those who are pregnant and breastfeeding. It is
13 essential that specific requirements and timelines be
14 articulated so that these key populations are not left
15 behind. And I want to underscore my colleague, Linda
16 Dee's, earlier comments on the critical importance of
17 equity, diversity and inclusion in research and review.

18 Three, with only two months of follow up data
19 as per EUA guidance, it is essential the future BLAs
20 include at least six months of follow up. Therefore,

1 continued blinded follow up of the trial is warranted
2 while recognizing that some trial participants will
3 want to exercise their rights to leave the trial and,
4 if from the placebo group, seek vaccination.

5 If an EUA is granted, it will be urgent for
6 the FDA and the companies to rapidly develop clear
7 information including an explicit re-consent process
8 outline the benefits, risks, and rights of maintaining
9 in the blinded trial for both public and personal
10 benefit. And strongly encourage the committee to
11 endorse the deferred blinded crossover design proposed
12 by NIAD and presented earlier. In addition, we
13 encourage the FDA to urgently issue guidance to other
14 developers who will need to address this issue.

15 Fourth, perhaps the biggest unknowns remain
16 the durability of vaccine efficacy and whether the
17 vaccine prevents asymptomatic disease and will limit
18 transmission. A clear plan to collect and communicate
19 information to inform answers from within the ongoing
20 trial, as well as in the design of additional trials,

1 is essential and should be clearly articulated when any
2 EUA is announced. And should be strategically linked
3 to other vaccine developers to jointly identify
4 correlates, bridge data to other populations and
5 platforms, and track use. As we've seen repeatedly in
6 this pandemic and throughout HIV, clear evidence-based
7 information is key.

8 In conclusion, AVAC applauds this mRNA vaccine
9 and both this VRBPAC and FDA for its commitment towards
10 transparency, independence and evidence-based
11 scientific decision making. This process is not just
12 about authorization or approval, it is a beacon of
13 independent review and transparency that will help to
14 foster the trust necessary to rebuild confidence in
15 vaccines, in science and in our public institutions.

16 Thank you for what you're doing today and
17 throughout this process. And thank you for the
18 opportunity present and looking forward to continued
19 engagement with scientific and regulatory processes
20 that move with speed of trust.

1 **DR. PRABHAKARA ATREYA:** Okay. Great. Thank
2 you. I think we are almost come to the closure. We
3 tried the last person requested and then we're unable
4 to reach her. I think we can conclude because we
5 already are past 10 minutes past the actual time for
6 the next presentation. But before we go to sponsor
7 presentations, the Director of the Center for
8 Biologics, Dr. Peter Marks, would like to make a few
9 comments. Then we'll go to sponsor presentation.
10 Thank you. Dr. Marks, you're on.

11 **DR. PETER W. MARKS:** Thanks very much Prabha.
12 I just want to take a moment here to offer some thanks
13 to various people. First of all, thanks to anyone from
14 the public who's tuning in today. I think having this
15 as a transparent process is very important as one of
16 the steps we're taking to try to enhance vaccine
17 confidence across the country.

18 I also want to take a moment to thank all of
19 the advisory committee members and the speakers today.
20 They're contributions are immense, and we'll look

1 forward to their discussion later on today. It's also
2 very important for me to take a moment to thank a group
3 of people at FDA; that have put an incredible amount of
4 effort into this advisory committee meeting while
5 they're simultaneously getting ready for another
6 advisory committee meeting and taking care of many
7 other vaccines in various stages of development.

8 The amount of work that has been put into
9 this, by those just setting up these meetings, is
10 tremendous. And I'd like to thank Prabha and all of
11 the advisory committee staff, but also an incredible
12 debt of gratitude to all of our reviewers in various
13 offices and especially in our Office of Vaccine
14 Research and Review. The leadership and the staff in
15 that office have worked tirelessly throughout the past
16 weeks and months to get to this point, and that
17 included working diligently over this past holiday when
18 they could have been spending time with their families.

19 So we're very, very grateful for all of the
20 work and grateful to all of you. So with that, I want

1 to let this proceeding move on since it's going to be a
2 long day anyway. But thank you very much.

3 **DR. PRABHAKARA ATREYA:** Thank you, Dr. Marks.
4 Now, Dr. Monto, back to you to take on from this point
5 on for the next presentation with the sponsors.

6

7

SPONSOR PRESENTATION

8

9 **DR. ARNOLD MONTO:** Right. Next, we have the
10 sponsor presentations. The moderator is Kathrin
11 Jansen, Senior Vice President and Head of Vaccine
12 Research and Development at Pfizer, and William Gruber,
13 Senior Vice President of Vaccine Clinical Research and
14 Development at Pfizer. You're on.

15 **DR. KATHRIN JANSEN:** Good afternoon members of
16 the committee, FDA, and ladies and gentlemen in the
17 audience. It is a real pleasure to be here today. I'm
18 Dr. Kathrin Jansen and I'm a Senior Vice President and
19 head of Vaccine Research and Development for Pfizer. I
20 would like to thank the FDA for organizing the VRBPAC,

1 and the VRBPAC chair and members for their time.
2 Pfizer and our partner, BioNTech, are pleased to be
3 here today to discuss our candidate mRNA COVID-19
4 vaccine program in the context of requesting an
5 Emergency Use Authorization.

6 Our presentation today will follow this
7 agenda; after I give a brief introduction, Dr. William
8 Gruber, Senior Vice President Vaccine Clinical Research
9 and Development, will review the development program
10 for our vaccine including non-clinical, clinical safety
11 and clinical efficacy data. After this, I will come
12 back to review the benefits-risks and provide
13 conclusions for our presentation.

14 We are also pleased to have a principal
15 investigator with us to answer any study-related
16 questions. Dr. Stephen Thomas, who is Professor of
17 Medicine and Microbiology and Immunology, Chief
18 Division of Infectious Diseases, and Director Institute
19 for Global Health and Translational Sciences, from the
20 State University of New York Upstate Medical

1 University.

2 Our COVID-19 mRNA vaccine called BNT162b2 has
3 been developed for the following indications:
4 prevention of COVID-19 in individuals 16 years of age
5 and older. The dose level is 30 micrograms with two
6 doses given 21 days apart. The vaccine presentation is
7 a five dose, multi-dose vial that is preservative free
8 and stored frozen between -80 and -60 degrees Celsius
9 until use. Since the beginning of the year, we have
10 been facing a devastating situation with COVID-19, the
11 disease caused by the new Coronavirus, SARS-CoV-2.

12 Tens of millions of people have been infected
13 globally and over 1.5 million people have already died.
14 No one is safe from this disease and certain groups,
15 such as healthcare workers and first responders, the
16 elderly and people with underlying diseases, are at
17 particularly high risk. It is now becoming very clear,
18 particularly with the recent increasing rates of COVID-
19 19 globally and in the United States as discussed
20 earlier by Dr. Hall, that we need a safe and

1 efficacious vaccine to stem this devastating pandemic
2 while also deploying other prevention strategies such
3 as infection control, including mask wearing and social
4 distancing.

5 SARS-CoV-2, the virus that causes COVID-19, is
6 a new beta-Coronavirus that emerged late in 2019 in
7 China. Shown in red are the Coronavirus glycoprotein
8 spikes called S for short. The spike protein is an
9 important vaccine target or antigen as it mediates
10 first the specific binding of the virus to the H2 host
11 cell receptor and then the fusion of the viral envelope
12 with the host cell membrane. By these actions, the
13 virus enters into human cells where it replicates then
14 spreads to other people and often causing illness in
15 the infected individual.

16 Data available from other Coronaviruses, such
17 as SARS and MERS, have established that antibodies 2S
18 can stop the binding of the virus to cells and prevent
19 the virus infection of the human cell. So we chose the
20 S protein as our vaccine antigen. Specifically, we

1 chose a form of the S protein that was engineered to
2 lock it in the prefusion conformation which is thought
3 to be optimal for eliciting functional virus-
4 neutralizing antibodies.

5 We chose BioNTech's mRNA vaccine platform for
6 a number of reasons and given BioNTech's long
7 experience with messenger RNA vaccines in the oncology
8 space. mRNA vaccines are produced by self-reproduction
9 processes using chemically highly-defined vaccine
10 components, RNA, and lipid. mRNA vaccines can induce
11 broad immune responses well-suited to address a new
12 pathogen in a situation where there's no or limited
13 knowledge of what correlates with protection.

14 The mRNA vaccine platform lacks unwanted viral
15 or vaccine platform antigens that may lower a vaccine-
16 induced immune response. As a consequence, mRNA
17 vaccines can be boosted repeatedly, an important
18 consideration when persistence of vaccine immunity is
19 not yet known. Given that mRNA vaccines are
20 essentially synthesized, they can be developed and

1 scaled up quickly. A clear advantage over cell-based
2 production processes when developing a vaccine in a
3 pandemic setting.

4 So how does an mRNA vaccine work? We have a
5 deep scientific understanding of how such vaccines
6 work. The mRNA code, that means harbors information
7 for the vaccine antigen which is a form of the S
8 protein. The mRNA is stabilized through formulation
9 with lipids to form what we call lipid nanoparticles,
10 or LNP. The LNP formulation is further optimized to
11 allow efficient entry of the LNPs into human cells.

12 This LNP is also optimized to be able to enter
13 antigen-presenting cells that are efficient at
14 simulating a broad immune response which we desired
15 given that we did not know, and still do not know,
16 which response best correlates with protection. Inside
17 the cell, the mRNA is released from the LNP. Just like
18 any other messenger RNA in the cell, the mRNA from the
19 vaccine can direct the synthesis of a protein by the
20 cell's own production machinery.

1 And since our vaccine codes a form of the
2 SARS-CoV-2 spike protein, that protein is also
3 produced. Once produced, the whole S protein and its
4 smaller fragments are presented to the human immune
5 system that recognizes the protein as foreign resulting
6 in simulation of T-Helper Cells or CD4 T Cells that
7 activate other T Cells and antibody producing B-Cells.
8 The antibodies can bind to the S protein on our SARS-
9 CoV-2 and neutralize the virus, which means the virus
10 is no longer capable of infecting a cell.

11 Also produced are CD8 T Cells that can
12 eliminate virally-infected cells. An important feature
13 of mRNA vaccines is that they stimulate affected B-Cell
14 and T Cell memory responses. This ensures longer term
15 protection from viral infection and disease.

16 An additional advantage of the mRNA platform
17 is that the vaccine induces a Th 1-biased, CD4-positive
18 T Cell response that is linked to protection from
19 viruses and thus minimizes a theoretical risk of
20 vaccine-enhanced disease. The Th 1-biased response is

1 characterized by secretion of cytokines involved in
2 fighting a viral infection such as interferon gamma and
3 IL-2. So in a nutshell, the immune responses induced
4 by the mRNA vaccine are similar to what you may get in
5 response to a viral infection. But of course, the mRNA
6 vaccine is non-infectious and cannot cause disease.

7 When we started our COVID-19 vaccine
8 partnership with BioNTech, we had the choice of a
9 number of different mRNA vaccine candidates, different
10 flavors of the mRNA, and different forms of the Spike
11 protein. Given the enormity of our mission, clinical
12 data were important to us in deciding on the right
13 candidate for a COVID-19 vaccine. So we evaluated not
14 just one but four different candidates, in Phase 1, to
15 be able to make real time scientific decisions to
16 select the best candidates based on the following major
17 selection criteria.

18 With regard to safety, we were looking for the
19 most favorable safety and tolerability profile in both
20 younger and older adults. With regard to

1 immunogenicity, we were looking for the broadest
2 antiviral immune responses most likely associated with
3 efficacy. And with regards to a rapid pandemic
4 response, we were looking for the candidate that could
5 be developed and produced most efficiently. Using
6 these criteria, we selected BNT162b2 which contains a
7 modified RNA that expresses a code on optimized, full-
8 length, pre-fusion stabilized Spike protein of SARS-
9 CoV-2.

10 The top priorities for vaccine development in
11 general and for a COVID-19 vaccine, in particular, are
12 as follows: we must demonstrate that the vaccine is
13 highly effective, meaning that it can help prevent
14 COVID-19 in at least the majority of vaccinated people.
15 We must demonstrate that the vaccine is safe with a
16 robust safety dataset generated in a very large,
17 pivotal efficacy study. And we also must demonstrate
18 that we can consistently manufacture the vaccine to the
19 highest standards.

20 Throughout 2020 we have been asked often, how

1 can this be done in a year or less when the process
2 normally takes many years? Well, vaccine development
3 or anything else in a pandemic setting is not normal.
4 It requires a completely different way of thinking and
5 a strategy of parallel versus sequential R&D.

6 Instead of waiting for pre-clinical and
7 clinical data to emerge, substantial efforts and
8 resources were poured into process development and
9 manufacturing scale-up well before any clinical data
10 were available. This has been an unprecedented
11 investment early in development. In planning clinical
12 development, we worked with the FDA and other
13 regulators on a seamless trial which collapsed Phases
14 1, 2, and 3 clinical development also in an
15 unprecedented way, with close to real time
16 communications and decision making, without ever
17 stopping the trial.

18 We are grateful to FDA and other regulatory
19 agencies who have lent us their enormous support to
20 work on these seamless development timelines. With

1 substantial work on the mRNA platforms already done at
2 BioNTech, we were able to quickly start clinical
3 development and advance to Phase 2/3 start at the end
4 of July this year. And we have support from CDC to
5 provide real data on regional SARS-CoV-2 and COVID-19
6 attack rates, in the United States, to optimize our
7 selection of trial size.

8 Last but certainly not least, was a dedication
9 of investigators and site staff as well as the
10 motivation of tens of thousands of trial participants.
11 We were able to enroll over 40,000 participants in a
12 record six weeks, give them each two doses of vaccines,
13 and ensure their safety while conducting the trial with
14 strict compliance and uncompromising quality.

15 And now, let me introduce for you the clear
16 and compelling data package you will hear about today
17 that we believe satisfy the FDA guidance for COVID-19
18 vaccine's Emergency Use Authorization. We have
19 submitted all of the information required to meet the
20 EUA guidance and you will hear about them this morning.

1 As for manufacturing data, FDA has reviewed
2 the C&C data submitted to date for our vaccine and has
3 determined that the C&C information is adequate to
4 ensure the vaccine's quality and consistency for
5 authorization of the product under an EUA. And now,
6 Dr. Bill Gruber will discuss the non-clinical and
7 clinical datasets with you as well as our future plans.

8 **DR. WILLIAM GRUBER:** Thank you, Kathrin. It's
9 my pleasure to share with you today the development
10 program for our vaccine candidate BNT162b2. I'm going
11 to begin with a very brief summary of the non-clinical
12 data that encouraged us to move forward into the
13 clinic. This includes both toxicity studies as well as
14 a study looking at a challenge study in Rhesus-
15 Macaques. These studies are described in the briefing
16 documents.

17 Two toxicity studies in rats, including the
18 BNT162b2 vaccine construct, were completed with no
19 safety concerns. Development and reproductive toxicity
20 studies are ongoing with preliminary results available

1 by mid-December. In a SARS-CoV-2 Rhesus challenge
2 model, the BNT162b2 construct provided complete
3 protection in the lungs as determined by nucleic acid
4 amplification testing for SARS-CoV-2 and
5 bronchoalveolar lavage fluid. This information is now
6 published. And importantly, there was no radiologic or
7 histopathologic evidence of vaccine-elicited disease
8 enhancement.

9 Despite limitations of animal models, these
10 findings anticipated results in our Phase 3 clinical
11 trial in which there is no evidence of enhanced
12 disease. These results were encouraging, satisfied FDA
13 guidance criteria, and permitted progression of human
14 clinical trials. I'm now going to share with you the
15 clinical safety, immunogenicity, and efficacy data from
16 our overall clinical development program.

17 First, I will cover safety and immune response
18 from the German and U.S. studies and then cover aspects
19 of the Phase 2/3 trial finishings with the safety and
20 efficacy results. So let's begin with the two Phase 1

1 studies. The German Phase 1 dose-ranging study was
2 conducted in individuals 18 to 55 years of age. 12
3 subjects received the active BNT162b2 vaccine for each
4 dose level cohort. This study evaluated safety,
5 binding, and neutralizing antibody responses, as well
6 as cell-mediated immune response to look for the
7 potential for Th 1-biased, CD4, and CD8 T Cell
8 responses.

9 The U.S. study is a seamless study where we
10 have a Phase 1 portion that moved into Phase 2 and then
11 Phase 3. For the Phase 1 dose-ranging portion, we
12 included 18 to 55 and 65 to 85-year-old individuals.
13 Twelve of whom received vaccine and 3 received placebo
14 per dose-level cohort. We looked at safety and
15 immunogenicity with both binding and neutralizing
16 antibody responses and followed reactogenicity by
17 electronic diary.

18 These individuals will continue to be followed
19 for a full two years after the second dose. The
20 results from the Phase 1 experience have now been

1 published and you have details in your briefing
2 documents.

3 I'll just summarize for you briefly the
4 reactogenicity from Phase 1. Mild to moderate
5 injection site pain was observed frequently and was
6 consistent with local reactions observed with other
7 commonly licensed and recommended adult vaccines.
8 Fever and chills along with other systemic
9 manifestations were observed. Reactogenicity was
10 generally higher after dose two than dose one, and
11 reactogenicity events after each dose of the vaccine in
12 older adults were milder and less frequent than those
13 observed in younger adults.

14 Now I'd like to summarize for you the antibody
15 responses in Phase 1 to two 30 microgram doses of the
16 chosen BNT162b2 vaccine, focusing on the neutralizing
17 antibody titers from the U.S. based trials. These
18 results have been published in a peer review journal
19 and are described in your briefing document.

20 By day 28, or seven days after the second 30

1 microgram dose, through 50 percent neutralizing
2 antibody responses are observed. GMTs are shown at the
3 top of each column. Antibody responses are well
4 maintained, out to day 52, approximately one month
5 after dose two, in both this younger 18 to 55 years of
6 age group and the older 65 to 85 years of age group.
7 GMTs are again shown at the top of each column. The
8 GMTs in vaccinated participants ranged from 1.5 to 3.8-
9 fold higher than the virus neutralizing GMT of 94,
10 observed in a panel of 38 convalescent sera labeled
11 HCS.

12 So this was very encouraging to us, that we
13 were achieving a functional antibody response that
14 could be associated with protection. It was also very
15 important for us to examine cell-mediated immune
16 response to be confident that we were getting a Th 1-
17 biased CD4 and strong CD8 T Cell response.

18 These are data from the German trial. This
19 first panel shows gamma interferon intracellular
20 cytokine analysis data. We see a substantial increase

1 in gamma interferon, very consistent with Th 1, and at
2 levels above responses following natural infection
3 labeled HC. If you look at the middle panel, you can
4 see a relatively higher proportion of S specific CD4
5 cells expressing gamma interferon, IL-2, or both,
6 compared to a lower proportion expressing IL-4.

7 So once again, this emphasizes a Th 1-biased
8 that could be associated with protection. And
9 likewise, not only is it important to demonstrate the
10 CD4 responses and the concomitant potential for
11 inducing memory, it was important to demonstrate CD8 T
12 Cell response indicating potential for virus killing of
13 infected cells. And in the right-hand panel, you see a
14 robust CD8 T Cell response that exceeds responses
15 observed from natural infection, again labeled HC.

16 So on the basis of promising neutralizing
17 antibody response, Th 1-biased, CD4 response as well as
18 the robust CD8 immune response, we were encouraged to
19 move into the Phase 2/3 portion of the study with the
20 BNT162b2 vaccine construct.

1 Outlined here for you, at a very high level,
2 are the fundamental elements of the trial where our
3 goal is to enroll approximately 44,000 healthy
4 subjects. Stable, chronic disease is allowed because
5 we find it important to make sure that those
6 individuals with underlying diseases are included.
7 They stand to have the greatest benefit from a vaccine
8 because of their high morbidity associated with COVID-
9 19. We also have included individuals with stable HIV,
10 Hepatitis B, and Hepatitis C virus infections.

11 At least 40 percent of participants are 56
12 years of age or older. This is important because we
13 recognize that this population is also particularly
14 vulnerable to severe disease. We also recognized the
15 importance of conducting the study in people of color;
16 so we have adopted an approach that assures a diverse
17 racial and ethnicity profile, including Black and
18 African American populations, Asians, and
19 Hispanic/Latinx populations. We've excluded
20 immunocompromised individuals because it's yet to be

1 determined if different dosing might be required in
2 this population. And as you'll see later, we plan to
3 evaluate those populations in future studies.

4 So here are the demographics displayed for the
5 full population data (audio skip) on over 43,000
6 subjects as of November the 14th, with good
7 representation of gender, race, ethnicity and age, with
8 even splits between vaccine and placebo recipients.
9 The age breakdown is highlighted to show the different
10 age groups above and below 55 years old, and in the
11 older 65 and above age group. Note that over 9,000, or
12 20.9 percent of the 43,000 participants, were over 65
13 years of age.

14 So now let me share with you the safety data
15 from our Phase 2/3 portion of the clinical trial. I
16 wanted to highlight something familiar to members of
17 the VRBPAC committee. We have ongoing safety reviews
18 by an independent data monitoring committee of
19 unblinded safety data. And in fact, these are
20 occurring weekly. This makes sense in the context of a

1 rapidly enrolling trial with this new vaccine
2 candidate.

3 The DMC consists of four adults or pediatric
4 infectious disease experts and one statistician, all
5 with expertise in assessing vaccine safety, immune
6 response, and efficacy. And the DMC, as recently as
7 this past week, has identified no safety concerns
8 during the duration of the clinical trial and has
9 recommended that the study continue as planned at all
10 of their safety reviews.

11 This figure summarizes the safety database
12 populations submitted to the FDA for this review.
13 Starting at the bottom, there are over 43,000 study
14 participants with safety data collected in the trial as
15 of the data cutoff on November the 14th. Moving up the
16 figure, nearly 38,000 of these represent a subset with
17 median safety follow up time of two months post dose
18 two, meeting FDA guidance.

19 This means that there are over 19,000
20 participants for whom safety follow up data is

1 available for at least two months, post dose two, shown
2 in the second bar from the top. Of the total safety
3 population there are over 8,000 subjects, shown at the
4 top, from whom seven days of solicited local and
5 systemic reactions were obtained by electronic diary.

6 Shown here is a schematic of how safety of
7 subjects was monitored. On the left-hand side at the
8 top, vaccination of doses were given 21 days apart.
9 The first dose of vaccine was followed by very intense
10 active surveillance for potential COVID-19 symptoms
11 that would trigger a telehealth or in person visit and
12 nasal swab. This was done both as a safety measure as
13 well as to evaluate efficacy.

14 Individuals could either be swabbed at the
15 investigative site or obtain a self-swab. We were very
16 intent, of course, on otherwise tracking safety
17 comprehensively, and you can see at the bottom left of
18 the slide that we used an electronic diary to address
19 common reactions seen after vaccine administration,
20 encompassing at least 6,000 subjects and at least 500

1 in each of the countries that are included in the
2 trial.

3 We also captured non-serious adverse events
4 one month post dose two. We will actively collect
5 serious adverse events for at least six months post
6 dose two, and deaths and related SAEs after the end of
7 the trial at two years after the second dose. So now
8 let me share with you electronic diary data related to
9 local adverse events.

10 This represents data that were captured over
11 seven days after dose one and dose two in 16 to 55 and
12 56 to 85-year-olds. I think you can quickly appreciate
13 looking at the two panels which represent dose one and
14 dose two, that for redness, swelling and pain at the
15 injection site, the type of local reactions are very
16 consistent to those seen with commonly licensed and
17 recommended vaccines with very little redness or
18 swelling. Pain was largely mild to moderate in
19 severity. No grade four local reactions were observed.
20 Again, a very satisfactory safety profile as far as

1 local reactions.

2 We also, of course, used the electronic diary
3 to look at systemic events. The orientation of this
4 slide is different in that we are looking first at
5 events seven days after dose one. And those who
6 received the vaccine on the top panel compared to those
7 who received placebo on the bottom.

8 Looking at both the 16 to 55-year-olds, as
9 well as the 56 to 85-year-olds, you can see that the
10 reactions fall within a tolerable range compared to
11 other adult vaccines. I would highlight fever and
12 chills because these appear to be the most
13 discriminating, as you can see, compared to placebo.
14 But both were within an acceptable range.

15 Now we are looking at systemic events seven
16 days after dose two. And you can see a somewhat higher
17 incidence of fever and chills as well as other systemic
18 manifestations compared to placebo. The only grade
19 three or severe solicited adverse event, greater than
20 or equal to 2 percent in frequency after the first or

1 second dose, were fatigue at 3.8 percent and headaches
2 at 2.0 percent following dose two.

3 One vaccine recipient reported a fever of 41.2
4 degrees Centigrade only on day two, after dose two, and
5 reported no fevers for all other reporting days. One
6 vaccine recipient reported a fever of 40.7 degrees, on
7 day four after dose one, with no fever at the end of
8 the seven day reporting period. Otherwise, no grade
9 four systemic reactions were observed. There was a
10 difference between younger individuals and older
11 individuals. Younger individuals tended to have more
12 reactions. But in all age groups the vaccine was well
13 tolerated and the reactions were within an acceptable
14 range.

15 If we consider how these events peak and
16 declined over the seven day post dose two period, in
17 the BNT162b2 group, it can be seen that the duration is
18 short lived. Participants are vaccinated on day one.
19 Fever, the left-most dark blue bar, typically appears
20 on the day after vaccination and lasts only a single

1 day. Otherwise, systemic events shown as the other
2 colored bars peak at day two then rapidly decline over
3 the next two days in both age groups.

4 We captured spontaneously-reported adverse
5 events by System Organ Class in the nearly 38,000
6 subjects subset, for which median safety follow up was
7 two months after dose two. This slide shows adverse
8 events by System Organ Class occurring in one percent
9 or more of the study population. More details are
10 included in your briefing document.

11 The most common adverse events observed were
12 general disorders and administration of site
13 conditions. As shown in the footnotes, the top four
14 classes of unsolicited reactions in this nearly 38,0000
15 participant dataset, mirror the common reactions
16 captured by electronic diary in the 8,000 participant
17 subset previously described. For example, these
18 include reports of injection pain, fever, myalgia. For
19 nervous disorders, the highest proportion is headache.
20 For GI disorders, not diarrhea and vomiting.

1 When we exclude those terms reflecting local
2 reactions and systemic events typically occurring
3 within seven days of vaccination, we see a more even
4 split of adverse events between the active vaccine and
5 placebo, apart from general disorders and
6 administration site conditions where the predominant
7 remaining event is unspecified pain in the vaccine
8 group, 2.4 percent versus 0.2 percent. In general,
9 adverse events by System Organ Class are infrequent and
10 within range of such reactions reported after other
11 licensed vaccines.

12 Rounding out this part of the safety reviews,
13 serious adverse events shown here by System Organ Class
14 are consistent with what we typically see in
15 populations that not only include 40 percent of
16 individuals being older than 55, but over 50 percent of
17 the population being obese and/or having at least one
18 underlying comorbidity. SAEs have been balanced
19 between vaccine and placebo recipients. These include
20 observed, serious adverse events of special interest

1 designated by the CDC, which are few in number and
2 comparable between vaccine and placebo recipients.

3 A total of six deaths have occurred in this
4 population with four of these in the placebo group.
5 None of these have been considered related by the
6 investigators. Further description of these deaths and
7 the full safety data available, as of November the
8 14th, are included in your briefing documents.

9 So in summary, the tolerability and safety
10 profile of the BNT162b2 vaccine, at 30 micrograms,
11 administered in a two dose regimen 21 days apart is
12 favorable, and no clinically significant safety
13 findings other than mostly mild or moderate
14 reactogenicity have been identified. I'd now like to
15 turn to our efficacy evaluation.

16 So let me now summarize how we went about
17 determining efficacy for the first primary efficacy
18 endpoint. Again, the vaccine doses were administered
19 21 days apart. And to qualify for the first primary
20 efficacy endpoint evaluation, individuals needed to

1 have no evidence of prior or current infection before
2 each dose.

3 And that was determined either by obtaining a
4 swab at the time of each dose, to identify evidence of
5 SARS-CoV-2 by nucleic acid amplification testing, or
6 obtaining a blood specimen for N-antigen antibodies at
7 the time of the first dose to indicate evidence of
8 prior infection that may have preceded vaccination by
9 months.

10 So this allowed us to be confident that the
11 individuals, for the purpose of this primary endpoint,
12 had no evidence of prior or current infection at the
13 time of each dose. And again, this is important
14 because this is the group that we would all anticipate
15 is most vulnerable to SARS-CoV-2 disease or COVID-19.
16 And then of course as I already mentioned, we have
17 active surveillance for potential COVID-19 symptoms
18 that trigger a telehealth or in person visit and a
19 nasal swab. And we will continue to do this for up to
20 two years after the second dose.

1 So now let me summarize for you what
2 constitutes a case definition. To qualify as a case
3 for the first primary endpoint case definition,
4 individuals had to be baseline negative by serology and
5 PCR for prior or current infection. And then we
6 characterized the illness as needing to include one or
7 more of these symptoms. And these should be familiar
8 to you because they largely coincide with symptoms that
9 are captured by the CDC case definition, but with a bit
10 more potential specificity. Comparable efficacy
11 observed encompassing all the CDC criteria are shown in
12 the briefing documents.

13 And then on the right-hand side, once an
14 individual qualifies for those first two categories,
15 they need to have a positive validated PCR; either in
16 our central laboratory or results will be accepted from
17 a local laboratory if it's approved as a type of
18 testing that we agreed is valid. All testing was
19 performed blinded to treatment assignment. And so it's
20 this combination that determines the case definition

1 for the efficacy results that I'll now be sharing with
2 you.

3 We performed an interim analysis at 94 cases
4 in individuals without prior infection and observed
5 efficacy of 95.7 percent. We have now also performed
6 the final vaccine efficacy evaluation against COVID-19
7 occurrence from seven days after dose two in 170 cases
8 without evidence of prior infection. Observed efficacy
9 is high at 95 percent, with high confidence based on
10 the parameters shown in the two right-hand columns.

11 There's 95 percent probability that efficacy
12 falls in the intervals shown; meaning, that over 97.5
13 percent likelihood that efficacy is greater than 90
14 percent. Likewise, the probability that vaccine
15 efficacy is at least greater than 30 percent greatly
16 exceeds FDA COVID-19 vaccine guidance.

17 This efficacy trial is not powered to evaluate
18 efficacy based on age, stratum, gender, racial or
19 ethnic group. Nonetheless, we think it would be useful
20 for the VRBPAC committee to see vaccine efficacy broken

1 down by these parameters. As you can see, observed
2 efficacy was high regardless of age and consistent with
3 overall results. Fifteen cases were seen in adults 65
4 to 74 years of age, and only one was in the vaccine
5 group. Five cases were observed in participants
6 greater than or equal to 75 years of age, and all were
7 in the placebo group.

8 Likewise, as shown on this slide, efficacy was
9 high in both males and females. And efficacy was high
10 across racial and ethnic groups. Comparable high
11 observed efficacy was observed across white, Black,
12 African American, other racial groups, and likewise
13 also across Hispanic and non-Hispanic ethnicity with
14 lower bounds of the confidence intervals above 80
15 percent across these ethnic groups. There were also
16 comparable values of observed efficacy seen across
17 geographies.

18 This efficacy trial was also not powered to
19 evaluate efficacy based on risk groups. Nonetheless,
20 we think it would be useful for the VRBPAC committee to

1 see vaccine efficacy broken down by these parameters.

2 The risk groups included individuals with body
3 mass index greater than or equal to 30 kilograms per
4 meter squared, and/or those with Charlson Comorbidity
5 index which included malignancies, chronic pulmonary
6 disease, chronic cardiovascular disease, diabetes,
7 renal disease, and many others. As you can see,
8 observed efficacy was high regardless of whether the
9 participants were at risk or not, consistent with
10 overall results.

11 Likewise, as shown on this slide, efficacy was
12 high across age groups with and without risk, as well
13 as those with or without obesity. If we break out
14 comorbidity, we see that regardless of category, past
15 history of malignancy, cardiovascular disease,
16 pulmonary disease, diabetes, or additional category of
17 hypertension, point estimates of observed efficacy
18 remain high, and for some, the nominal lower bound of
19 the confidence intervals are well above zero. Hence,
20 we can be confident that the vaccine is likely to work

1 well in older or debilitated individuals.

2 Likewise, we have now evaluated efficacy
3 against COVID-19 from seven days after dose two in
4 those with and without prior infection, the second of
5 our two primary endpoints. Efficacy remains high at
6 94.6 percent with similarly high confidence based on
7 the parameters shown in the right hand columns. It was
8 also important for us to define severe cases both for
9 evaluation of safety and for determinations of
10 efficacy. And for this, we used the definition of
11 severe COVID-19 based on FDA guidance. And that's
12 summarized here for you in bullet form.

13 ICU admission, clinical signs of severe
14 disease, organ or respiratory failure, and death are
15 key features. Using the FDA definition of severe
16 disease, let's first look at this top table. Although
17 not statistically significant, due to a small number of
18 cases, protection against the few cases of severe
19 disease occurring at least seven days after dose two is
20 consistent with the overall efficacy results, with one

1 case in the vaccine group and three cases in the
2 placebo group in those without prior infection, shown
3 here.

4 However, if one examines the All-available
5 population for first severe COVID-19 cases after dose
6 one, the bottom table, only one case is seen in the
7 vaccine group and nine cases are observed in the
8 placebo group for an observed vaccine efficacy of 88.9
9 percent. The vaccine recipient only met a single FDA
10 criterion for severe disease of O₂ saturation below 93
11 percent and was not hospitalized.

12 In contrast, out of the nine placebo
13 recipients with severe disease, six met two or more
14 criteria, six were hospitalized, three were admitted to
15 the ICU, and one was intubated or mechanically
16 ventilated. This is consistent with overall vaccine
17 efficacy seen seven or more days after the second dose,
18 and indicates that the BNT162b2 vaccine is likely to
19 protect well against serious disease.

20 The FDA's definition does not include

1 hospitalization as a specific criterion for severe
2 disease. However, the CDC definition of severe
3 disease, shown in the light blue box, includes
4 hospitalization, more severe outcomes of
5 hospitalization, and death. We thought it would be
6 useful to perform a post hoc analysis of severe disease
7 using the CDC definition to further assess the impact
8 of vaccines on this outcome.

9 Using this parameter, efficacy against severe
10 disease greater than or equal to seven days after dose
11 two was observed, with zero cases in the vaccine group
12 and five cases in the placebo group with confidence
13 interval as shown. Once again, protection was also
14 observed for first severe COVID-19 occurrence after
15 dose one of 92.9 percent with a 1 to 14 case split, and
16 lower bound of the 95 percent confidence interval well
17 above zero. One vaccine recipient was hospitalized 12
18 days after receiving the first dose of the vaccine, but
19 without additional CDC defined morbidity.

20 In contrast, of the 14 placebo recipients

1 hospitalized, three were admitted to the ICU, and one
2 was intubated or mechanically ventilated. This
3 analysis provides further evidence for vaccine
4 protection against hospitalization and attended
5 morbidity.

6 This curve shows the cumulative incidents of
7 all available COVID-19 cases beginning after dose one.
8 Placebo cases are in red, vaccine cases in blue.
9 Darker dots represent severe cases using the FDA
10 guidance definition, nine in the placebo group and one
11 in the vaccine group, with two instances where cases
12 overlap dramatically at day eight and day 67 in the
13 placebo group.

14 One can see that by at least 14 days, the
15 curves begin to spread indicating some efficacy after
16 the first dose. Placebo cases continue to increase,
17 out to 105 days at the time of this data cut, while the
18 vaccine case curve remains relatively flat. One can
19 see in this expanded view, from dose one to day 21,
20 that the curves begin to spread by as soon as day 12

1 and at least by day 14 after the first vaccine dose.

2 This graphic provides -- (Audio cuts out).

3 **DR. ARNOLD MONTO:** Hold on a second, Pfizer.

4 We are not hearing you at the moment. So let's just

5 take a moment here to just check on Pfizer's

6 connection. Just out of curiosity, can I get a

7 soundcheck from somebody else, please?

8 **UNIDENTIFIED MALE:** Can you hear me?

9 **UNIDENTIFIED MALE 2:** Test, test.

10 **DR. ARNOLD MONTO:** Okay. Thank you. That's

11 what I wanted. Alright. Hold on a second. We are on

12 a --

13 **UNIDENTIFIED MALE 3:** It's them, it's not us.

14 **MR. MICHAEL KAWCZYNSKI:** Yep. I figured as

15 much. Pfizer, we are -- we are going to reach out to

16 our sponsor here and tell them that they have to

17 connect their audio. They just -- it looks like they

18 are back up -- they're backup dropped so Pfizer, please

19 go to your backup audio. Here it comes. Are you

20 there, Pfizer?

1 **DR. WILLIAM GRUBER:** We're here.

2 **MR. MICHAEL KAWCZYNSKI:** Alright. There you
3 go. So, sir just go back about one slide -- just to
4 the beginning of this slide, please. We don't want to
5 lose any of your content. Okay?

6 **DR. WILLIAM GRUBER:** Alright. Alright. Thank
7 you.

8 **MR. MICHAEL KAWCZYNSKI:** Not a problem.

9 **DR. WILLIAM GRUBER:** So apologies --

10 **MR. MICHAEL KAWCZYNSKI:** So we'll --

11 **DR. WILLIAM GRUBER:** -- to everyone. Are we
12 ready to roll?

13 **MR. MICHAEL KAWCZYNSKI:** Alright. So we'll
14 hand it back to -- we're going to -- yep. We're going
15 to hand it back to Pfizer whenever you're ready.

16 **DR. WILLIAM GRUBER:** I'm ready. Okay?

17 **MR. MICHAEL KAWCZYNSKI:** Alright. Take it
18 away. Yep. Take it away.

19 **DR. WILLIAM GRUBER:** Alright. Okay. Great.
20 Thank you. Sorry for the technical difficulties. So

1 our efficacy conclusions are as follows; both primary
2 efficacy objectives met the success criteria. In
3 individuals without prior SARS-CoV-2 infection observed
4 vaccine efficacy against COVID-19 occurring at least
5 seven days after dose two was 95 percent with high
6 probability, 97.5 percent that the true vaccine
7 efficacy is at least 90 percent. And again, this meets
8 the pre-specified FDA criteria for Emergency Use
9 Authorization.

10 Observed vaccine efficacy was greater than 93
11 percent for the first primary endpoint across age,
12 race, ethnicity, and at-risk subgroups. Per the FDA
13 definition, nine severe COVID-19 cases were observed in
14 the placebo group and one in the vaccine group as of
15 the interim analysis cutoff dates, and 14
16 hospitalizations and associated morbidities were seen
17 in placebo recipients versus one vaccine recipient
18 hospitalization in a post hoc analysis, providing
19 further evidence to support efficacy against severe
20 disease consistent with that seen against all COVID-19.

1 From the cumulative incidents curve, there is
2 early onset of protection with divergence of the
3 placebo group from the BNT162b2 group as soon as 12
4 days, and by at least 14 days with steady accumulation
5 of cases in the placebo group while the vaccine group
6 remains virtually flat. Overall, the efficacy results
7 show that the vaccine at 30 micrograms provides
8 protection against COVID-19 in participants who had, or
9 did not have, prior SARS-CoV-2 infection and COVID-19.

10 Our Emergency Use Authorization application is
11 based on our satisfactory safety profile and efficacy
12 against COVID-19. The Emergency Use Authorization will
13 be seeking an indication for individuals who are 16
14 years of age and older. This safety data includes
15 reactogenicity in over 8,000 individuals.

16 Adverse events and serious adverse events in
17 over 37,000 individuals with a median of two months of
18 follow up post dose two, and adverse events and serious
19 adverse events at over 43,000 individuals 16 years of
20 age and older with varying degrees of follow up. The

1 BLA, which we plan to submit in 2021 will encompass
2 reactogenicity in over 8,000 individuals and AEs and
3 SAEs in at least 44,000 total participants. Of these,
4 safety data will be provided from at least 6,000
5 participants with six months or more of safety follow
6 up post dose two.

7 Additional data will include safety in a 12 to
8 15 year old population which is currently undergoing
9 study as part of our current Phase 2/3 trial. The
10 efficacy that we have presented to you today is based
11 on more than 164 SARS-CoV-2 cases and immune response
12 in adults 18 years of age and older. This also serves
13 as the foundation of data for the BLA which we plan to
14 file by April of 2021. Additional planned analyses
15 include efficacy against asymptomatic infection,
16 evaluation for persistence of protection, and a 12 to
17 15 year old immuno-bridging study.

18 As you will note in the Pfizer briefing
19 document, we plan to administer vaccines to placebo
20 recipients. We have an ethical obligation to inform

1 study participants of COVID-19 vaccine availability
2 under Emergency Use Authorization. We are currently in
3 discussions with the FDA about the best way to
4 vaccinate placebo recipients to further inform safety
5 and efficacy of the vaccine while meeting our ethical
6 obligations to participants. Eligible participants in
7 the placebo group will have the option to receive the
8 vaccine.

9 Since it will take to provide vaccines to over
10 22,000 placebo recipients, we plan to first offer
11 vaccines to those individuals satisfying FDA Emergency
12 Use Authorization and current CDC recommendations.
13 Vaccination of other participants will expand over
14 time. Participants will be given the option to remain
15 blinded if they chose to do so through study
16 completion. The study will continue for the planned 24
17 months regardless. Pfizer plans to meet FDA EUA
18 guidance for risk and benefit during use of the vaccine
19 under the Emergency Use Authorization.

20 First, let's talk about pharmacovigilance.

1 Since this vaccine is likely to be administered in a
2 short time, we've expanded our capacity to process AE
3 reports with an online adverse event reporting portal.
4 Our signal detection activities will occur on a more
5 frequent site. We have plans for future clinical
6 studies to expand to more vulnerable populations.

7 Second, proactive risk minimization. Clear,
8 comprehensive labeling and education materials for
9 vaccine providers will emphasize key messages about
10 appropriate handling, storage, and preparation of the
11 vaccine. And for vaccinees, emphasize the importance
12 of following up for their second dose to maximize their
13 protection. Product in cold-chain will be monitored in
14 real time.

15 Third, pharmacoepidemiology studies. Several
16 safety studies are planned to continue safety data
17 collection. These will access healthcare information
18 from millions of lives to monitor safety events
19 including adverse events of special interest. We know
20 our vaccine works in the clinical study setting and

1 plan to investigate its effectiveness in real world
2 use.

3 And finally, collaborating with vaccine safety
4 stakeholders. At a previous VRBPAC and this morning,
5 we've heard about the FDA and CDC's planned programs
6 for pharmacovigilance, including VAERS, CISA Network,
7 V-SAFE, and VSD, and we've shown you some of our plans
8 which are intended to be complimentary to CDC and FDA
9 planned pharmacovigilance activities. After approval,
10 Pfizer will conduct test-negative design studies to
11 demonstrate real world effectiveness against severe
12 disease with important endpoints like hospitalizations
13 and emergency department visits in specific populations
14 and to understand vaccine efficacy when vaccine is used
15 in real world conditions and in broader populations.

16 These studies will complement the CDC planned
17 effectiveness studies. We also intend to conduct a
18 number of studies recognizing that there are other
19 populations that stand to benefit and there are other
20 things that we need to learn about the vaccine. These

1 include boost-ability, studies in pediatrics and
2 pregnancy, and use in immuno-compromised populations.
3 We also plan to explore a refrigerator stable next
4 generation formulation that can combine use with
5 influenza vaccine.

6 We look forward to expanding the safety,
7 immunogenicity, and efficacy profile demonstrated
8 today. So now that ends my summary of the clinical
9 development program and I'm pleased to turn our
10 presentation back over to Dr. Kathrin Jansen.

11 **DR. KATHRIN JANSEN:** -- Dr. Gruber. We
12 believe that our data have satisfied the EUA
13 requirements for a COVID-19 vaccine as you see here on
14 the green checkmarks. We are seeking Emergency Use
15 Authorization for our vaccine for prevention of COVID-
16 19 caused by SARS-CoV-2 in individuals 16 years and
17 older with or without evidence of prior infection with
18 SARS-CoV-2.

19 We have demonstrated the positive benefit-risk
20 profile for our BNT162b2 vaccine given the high overall

1 vaccine efficacy of 95 percent with high efficacy
2 observed in both younger and older adults, as well as
3 diverse demographics with and without underlying
4 comorbidities. And we observed efficacy against severe
5 COVID-19. In addition, we have demonstrated a
6 favorable safety and tolerability profile in more than
7 40,000 individuals.

8 So why are we applying an Emergency Use
9 Authorization for BNT162b2 now? With the high efficacy
10 and good safety profile shown for our vaccine and the
11 pandemic essentially out of control, vaccine
12 introduction is an urgent need. Dramatic increases in
13 cases have occurred all over the country and it is
14 estimated that about 55,000 deaths will likely occur
15 every month over the next few months. Modeling from
16 the CDC shows that a vaccine with high efficacy can
17 save many lives.

18 However, a pandemic vaccine must be
19 introduced before the peak of cases to have maximal
20 impact which is best achieved under EUA. We at Pfizer

1 and BioNTech wish to thank all of our sites,
2 investigators, and their dedicated staff. And we want
3 to thank our clinical trial participants without whom
4 we would not be here today. We are also grateful for
5 the guidance provided by the CDC, the FDA, and other
6 regulatory bodies, and members of Operation Warp Speed.

7 Finally, we want to thank our colleagues at
8 BioNTech, Pfizer, and other companies for their
9 tireless work and dedication to develop our COVID-19
10 vaccine candidate. Thank you for your attention and we
11 would be happy to take any questions.

12 **DR. ARNOLD MONTO:** Thank you very much to both
13 of you. I wanted first to ask Dr. Gruber about how he
14 is going to be measuring asymptomatic infections. In
15 addition, I wanted to let everybody know that Bill
16 Gruber is not related to Marion Gruber. So, Bill.

17 **DR. MARION GRUBER:** That's correct. Not to my
18 knowledge.

19 **DR. KATHRIN JANSEN:** Alright. If I understood
20 you or heard you correctly because there was a little

1 bit of a delay, you were asking about our plans how to
2 monitor asymptomatic infections.

3 **DR. ARNOLD MONTO:** Correct.

4 **DR. KATHRIN JANSEN:** So indeed, our protocol,
5 our trial was actually designed not just to look for
6 symptomatic COVID-19, but also to monitor and explore
7 whether our vaccine is efficacious against asymptomatic
8 infection. And we are monitoring individuals and
9 screening them with a serological test that measures
10 exposure to SARS-CoV-2 infection N-protein test.

11 **DR. ARNOLD MONTO:** Right. The N-protein.
12 Yes.

13 **DR. KATHRIN JANSEN:** And we hope -- yes -- and
14 we hope that we will have those analysis completed very
15 soon in the new year.

16 **DR. ARNOLD MONTO:** And you were also looking
17 then at correlates of protections?

18 **DR. KATHRIN JANSEN:** That is correct. Our --
19 in our large study with collecting serological samples
20 throughout the study up to study conclusion, which is

1 24 months duration, we have the opportunity to look for
2 correlates of protection provided that we see enough
3 breakthrough cases over time --

4 **DR. ARNOLD MONTO:** (Audio distortion).

5 **DR. KATHRIN JANSEN:** That's right. So of
6 course with a vaccine that is highly efficacious, and
7 if it continues to be highly efficacious over time, it
8 may be a little bit more difficult to define a
9 correlate of protection but nevertheless we are trying.
10 We are trying to do that.

11 **DR. ARNOLD MONTO:** Okay. We have many, many
12 questions and we're going to have to limit them and
13 hope you -- and expect you to stay on for our open
14 discussion in about an hour or so because I think we
15 can get to some of the other issues at that point. So
16 Dr. Levy.

17 **DR. OFER LEVY:** Hi. Thank you. I'm Dr. Ofer
18 Levy with the Precision Vaccines Program at Boston
19 Children's Hospital. I'd like to thank Pfizer for its
20 impressive effort and excellent presentation. I have

1 the following questions. For Dr. Jansen, one regarding
2 mechanism of action. RNAs, in principle, can be
3 recognized via the innate immune system. Specifically,
4 potential RNA boost activation of Toll-like receptor 7
5 and 8 could induce interferons, which may explain the
6 transient lymphocytopenia that was observed in the
7 study and may provide an adjuvant effect contributing
8 to robust immune responses and the protection observed.

9 Recognizing that the vaccines contains
10 modified RNA that may have blunted innate immune
11 activating potential, what is known regarding the
12 ability of the lead mRNA to activate Toll-like
13 receptors such as TLR-7 and 8? Has the mRNA vaccine
14 induced BLR activation been assessed in vitro in cell
15 culture?

16 And my question for Dr. Bill Gruber regarding
17 the safety, the briefing document alludes to numerical
18 imbalances of AEs potentially representing allergic
19 reaction. What is Pfizer's knowledge regarding any
20 potential vaccine AE relating to allergic reactions

1 from either animal models or human data? And finally,
2 regarding immunogenicity, Dr. Gruber described the
3 adaptive response. What about the innate? Were
4 plasma, cytokines, chemokines measured and did these
5 correlate with any of the study endpoints? Thank you.

6 **DR. KATHRIN JANSEN:** Yeah. So I would like to
7 actually have Dr. Sahin describe in detail what we know
8 about the mechanisms of action. Let me just start out
9 while Dr. Sahin is getting ready to say that one of the
10 reasons that we chose the modified RNA platform for the
11 -- for our vaccine is the reason that indeed it tempers
12 if you want -- tunes down if you want, the innate
13 immune system. Because as I mentioned earlier, we were
14 looking for a candidate that would allow us to have a
15 very -- or would give us a vaccine with a very
16 favorable safety profile. If I could ask Dr. Sahin
17 please to come -- to comment on the more detailed
18 questions about signaling pathways for the mRNA vaccine
19 candidate.

20 **DR. UGUR SAHIN:** Yeah. Can you hear me? It's

1 good volume?

2 **DR. KATHRIN JANSEN:** Yes.

3 **DR. UGUR SAHIN:** Yeah.

4 **DR. KATHRIN JANSEN:** Yes.

5 **DR. UGUR SAHIN:** Thanks, Kathrin. This is
6 indeed an excellent question broached. The nucleotide
7 modified mRNA does not directly activate TR-7 and TR-8
8 in the human setting. And adjuvant activity is driven
9 by a combination of the recognition of messenger RNA
10 component (inaudible) lipid nanoparticle formulation,
11 which disrupts the integrity of the plasma membrane,
12 which integrates innate immune stimulation signals that
13 will start an activation of the (inaudible) pathway.
14 And this starts in cytokine secretion with starting in
15 the lymphocyte recirculation from the blood into the
16 peripheral tissue.

17 **DR. KATHRIN JANSEN:** Thank you. Bill, you
18 want to touch on the other part of the question?

19 **DR. WILLIAM GRUBER:** Sure, Kathrin. And we
20 can obviously, if there are additional questions,

1 follow up in terms of pharmacovigilance. But I think
2 the first question was about adverse events within the
3 study. Amongst the 44,000 subjects, we saw no serious
4 allergic reactions to the vaccine.

5 There were no substantive differences in
6 standard measure queries in numbers between the BNT
7 construct and the placebo groups analyzed on the 38,000
8 subject database. So within the clinical trial, we've
9 actually not seen evidence to suggest a signal related
10 to allergic reaction to the vaccine. Obviously, we're
11 conscious of the report that's occurred with use in the
12 U.K. and perhaps Patrick Caubel can speak to that.

13 As far as the -- and maybe while he's
14 preparing let me just deal with the second part of your
15 question, which was the nature of cytokine measurement
16 and the like. The measurements that were obtained were
17 the ones that I shared with you. And I think,
18 actually, as of today it's my understanding that it's
19 now being published from the Phase 1 trial -- from the
20 German trial, some of which I shared with you in

1 talking about the CD4 responses. But we have not as
2 part of either our Phase 1 trial in the United States
3 or the Phase 2/3 expansion looked specifically at
4 cytokines as part of that trial.

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

6 **DR. KATHRIN JANSEN:** Thank you.

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

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

9 **DR. PATRICK MOORE:** -- exciting data. Thank
10 you very much. Perhaps the most interesting data I've
11 heard in this epidemic. There -- I have two questions
12 for you. One is related to Ofer's question, which is
13 modified RNAs in this vaccine.

14 Do we know anything about whether the modified
15 RNAs undergo salvage, could be reincorporated into, for
16 instance, DNA, or if cellular reverse transcriptases
17 could possibly amplify them or turn them into DNA?
18 That's one question. The second one is, among the
19 eight people that were vaccine failures, do you have --
20 did -- were you able to sequence the virus that came

1 from those people, and was there evidence of antibody
2 escape from your antigen?

3 **DR. KATHRIN JANSEN:** Yeah. So I will start to
4 -- with answering the last -- your last question and
5 then I'd like to get Dr. Phil Dormitzer to be ready to
6 address your first question. So as of the eight
7 individuals that had a vaccine failure in our study, we
8 have not yet analyzed, for example immune responses or
9 anything else for those individuals but we plan to do
10 this. But we don't have the data today. And if I
11 could ask Dr. Dormitzer to answer the question that you
12 had about the RNA.

13 **DR. PHILLIP DORMITZER:** Yes. I guess there
14 were two questions. One is of the modified nucleotides
15 recycled, the RNAs? The second about the possibility
16 of reverse transcriptase change -- transforming the RNA
17 to DNA. We do not have data on recycling of the
18 modified nucleotide.

19 Although it's theoretically possible for a
20 reverse transcriptase to act on RNA, we think that the

1 probability is actually quite low that this would
2 occur. mRNAs have no signals that would make them
3 preferential substrates for a reverse transcriptase.
4 They are present transiently in literally low amounts.

5 And we actually have very recent data
6 indicating that actually, it's a very modest amount of
7 RNA that gets into the cell. We actually don't see it
8 hitting the nucleus where this would occur so there
9 don't seem to be any greater likelihood that a vaccine
10 RNA would end up reverse transcribed than a cellular
11 RNA.

12 **DR. KATHRIN JANSEN:** Thank you.

13 **DR. ARNOLD MONTO:** Okay. Thank you. Dr.
14 Offit.

15 **DR. PAUL OFFIT:** Yes. Thank you. So this
16 question is probably for Bill. First of all, thank you
17 for an excellent presentation. The -- one thing that's
18 been raised is that there roughly were 162 participants
19 who got sick that were in the placebo group, which
20 would mean a disease rate of about 0.74 percent. It

1 seems like that might be low.

2 But -- so would be interesting to know whether
3 that was lower than the disease rate in the area where
4 the participants were being recruited. Because the
5 concern that if that is true, if it is lower than
6 typical, that we may have an example of volunteer bias
7 where people who volunteer for this trial are more
8 likely to physically distance, more likely to wear a
9 mask, and therefore, more likely to be exposed to a
10 lower inoculum.

11 So could you comment on that? Was that 0.74
12 percent disease rate lower than you were seeing in that
13 area? Was that typical for the areas where you were
14 recruiting?

15 **DR. KATHRIN JANSEN:** Bill?

16 **DR. WILLIAM GRUBER:** Yeah. I think, of
17 course, it's a good question, Dr. Offit. I -- the rate
18 of disease that we were seeing I think was relatively
19 typical of not only the area but thinking ahead to the
20 nature of this population, on the one hand, this is a

1 population that we recruited because they were at
2 increased risk. But they were also voting with their
3 feet to be part of a vaccine trial and hence we assume
4 that of course, they were, and we certainly encouraged
5 them to take the appropriate sorts of social distancing
6 measures and masking. So I expect it was probably some
7 combination of the two.

8 The other thing to keep in mind is that this
9 trial, although it's been very, you know, short
10 duration in terms of being able to get our efficacy
11 endpoint, did span a period of time particularly in the
12 United States where rates dropped. And then of course
13 we now know the horrific situation we're in now with
14 over 3,000 deaths a day. But it's my sense that part
15 of this is the nature of the span of the trial both
16 during a time when the rates were high and low, as well
17 as the precautions that individuals in the trial, even
18 though they were high risk, took to further reduce that
19 risk.

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

1 **DR. KATHRIN JANSEN:** Thank you.

2 **DR. ARNOLD MONTO:** Okay. Dr. Pergam.

3 **DR. STEVEN PERGAM:** Thanks. First of all, I
4 just want to thank Pfizer again for first of all
5 presenting this data. And I want to -- I really thank
6 them for providing this data to the public as well
7 because I think the way that they present this data to
8 the community was really important for many different
9 reasons. I've been curious about enrollment related to
10 risk categories.

11 It, you know, the large proportion of people
12 in this trial are white and there's about, I think I
13 characterized 46 percent had a comorbidity and a
14 certain number were of older age, et cetera. My
15 curiosity is about timing of enrollment and on those
16 high-risk groups. Were they more likely to be enrolled
17 in latter portions of the trial and therefore had less
18 time accumulated and at risk? Do you have data about
19 how many people have been followed for two months versus
20 four months, et cetera, in the time and risk strata?

1 I'd be curious if that makes a difference in terms of
2 the outcomes we're seeing.

3 **DR. KATHRIN JANSEN:** Yeah. So we have the --
4 all the individuals 18 and older were part of our study
5 right from the get-go as well as all of the risk
6 groups. The only individual participants that were
7 invited later as part of the study were the younger age
8 group, the 12 to 15-year-olds, the 16 to 18-year-olds,
9 and individuals that had stable underlying infectious
10 disease conditions such as stable HIV, Hepatitis-B or
11 Hepatitis-C.

12 **DR. ARNOLD MONTO:** Okay. Thank you. Dr.
13 Banacloche.

14 **DR. JUAN GEA-BANACLOCHE:** Thank you. My
15 question is, how sure are you that you need the second
16 dose, the booster dose? And the reason I'm asking is
17 that clearly in the Neurological for Medicine paper,
18 you can see that the responses are much better after
19 the second dose, but in the graph where you show the
20 two curves separating, they separate at 14 days. And

1 they -- the curve remains flat so you cannot see any
2 effect of the second dose on the curve and I wonder if
3 there's a possibility that one dose is enough. If it
4 is not, how do you know it's not?

5 **DR. KATHRIN JANSEN:** So we are obviously
6 interested to evaluate in our vaccine study the
7 persistence of protection over time and so the data
8 that we have so far, and if could have up the Kaplan-
9 Meier curve, not the insert but the whole curve,
10 please? If someone could have that slide up. What you
11 see on that slide that so far, we have -- slide three
12 up, please. So you see that so far, we were able to
13 observe high degree of efficacy for up to 105 days or
14 so. And I think it's really important that we do
15 understand what the persistence is of our protection.

16 So we cannot conclude to say that after single
17 dose we would see a similar persistence of infection.
18 So, therefore -- and we also have seen that protection
19 was most mature and was highest after two doses were
20 given. So therefore, while we won't have the data to

1 look at one dose versus two doses, but since we started
2 this study with two doses we, of course, cannot predict
3 how a single dose would affect vaccine persistence or
4 protection of persistence which is very -- which is of
5 course very important in this setting.

6 **DR. ARNOLD MONTA:** Okay. I'm going to -- the
7 last question that we're going to have in this session,
8 and we'll try to pick this up when we have more time in
9 the discussion later on is Dr. Hildreth. Dr. Hildreth,
10 the floor is yours.

11 **MR. MICHAEL KAWCZYNSKI:** Dr. Hildreth, make
12 sure you don't have your own phone muted. You are
13 unmuted in the system.

14 **DR. JAMES HILDRETH:** I'm sorry. I did not
15 have a question. My question was asked and answered
16 already.

17 **DR. ARNOLD MONTA:** Okay. Well, in that case,
18 we'll move on, at least temporarily. Please stay
19 available so we can return to some of these questions
20 in the first part of our discussion. Now I'd like to

1 call on Dr. Wollersheim from FDA who is going to give
2 us FDA's presentation of the data and also describe the
3 questions we are going to address in the discussion.
4 Dr. Wollersheim.

5

6 **FDA PRESENTATION AND VOTING QUESTIONS**

7

8 **DR. SUSAN WOLLERSHEIM:** Thank you so much, Dr.
9 Monto, and good afternoon everyone. I'll go ahead and
10 present our FDA review of the clinical data submitted
11 with the Pfizer-BioNTech COVID-19 vaccine Emergency Use
12 Authorization request. Alright. So brief outline here
13 just to walk you through what we're going to present
14 today.

15 I'll start with a brief introduction of the
16 product and an overview of the clinical development
17 program followed by our efficacy and safety data
18 analyses. Then review the pharmacovigilance plans and
19 plans for future and ongoing studies. And finally,
20 ending with our benefit-risk assessment to help prepare

1 the advisory committee to discuss and vote on the
2 topics presented earlier today by Dr. Fink.

3 So first we will begin with a brief
4 introduction and Pfizer just walked us through this.
5 The vaccine is based on the SARS-CoV-2 spike
6 glycoprotein S antigen encoded by RNA and it is a
7 formulated in lipid nanoparticles. It's administered
8 by two intramuscular injections 21 days apart with
9 proposed indication and usage under the EUA. It's for
10 active immunization for the prevention of COVID-19
11 caused by SARS-CoV-2 in individuals 16 years of age and
12 older.

13 And moving on to a brief overview of their
14 clinical development programs to date. There are two
15 ongoing studies of the vaccine candidate. Study
16 BNT16201 is an ongoing Phase 1 dose-finding safety and
17 immunogenicity study in adults 18 to 50 years of age.
18 And study C4591001 is an ongoing Phase 1/2/3 randomized
19 placebo controlled, observer blinded study in
20 individuals 12 years of age and older.

1 I'll note now, as Pfizer also pointed out,
2 that their Phase 1 studies did begin at approximately
3 the same time earlier this year, BNT16201 in Germany
4 and C4591001 in the U.S. The overlap of vaccine
5 candidates and dose levels in the two studies allowed
6 for phasing immunogenicity from each study to provide
7 data and support in real time to change vaccine
8 candidates and dose levels to be evaluated in a larger
9 study that began in the U.S.

10 So looking at study BNT16201, this study
11 evaluated 60 participants who received the vaccine
12 candidate BNT162b2 at the various dose levels listed in
13 the table. There are 12 participants per dosage cohort
14 and no placebo group. The safety results showed a
15 similar safety profile for the vaccine candidate
16 between both Phase 1 studies. There are no serious
17 adverse events reported in the safety database for
18 BNT162b2.

19 And moving on to the immunogenicity results.
20 These results were obtained seven days after dose two

1 and show that two doses of the vaccine candidate induce
2 SARS-CoV-2 neutralization antibodies, with geometric
3 mean titers comparable to or higher than GMTs from a
4 human convalescent serum panel from recovered COVID-19
5 patients. The GMTs are highest with the 30 microgram
6 dose.

7 Two doses of BNT162 also induced S-1 binding
8 immunoglobulin G antibodies and a T-Helper 1 skewed
9 secretion of interferon gamma and or IL-2. The
10 immunogenicity data demonstrated a prospect of benefit
11 to support enrollment of larger numbers of subjects.
12 And thus the data from study BNT16201 helped support
13 the final vaccine candidate, selected dose, and
14 vaccination schedule that was determined in tandem with
15 the Phase 1 data from study C4591001.

16 We'll move on to that study design next. And
17 initially, the study was designed to include
18 approximately 30,000 adults 18 to 85 years of age. And
19 this study population was expanded after the study was
20 already underway to later include participants down to

1 12 years of age and those with stable, chronic medical
2 conditions, and infections such as HIV, Hepatitis B or
3 C.

4 All participants were planning to receive two
5 doses of the vaccine or placebo 21 days apart. The
6 Phase 1 portion of this study was designed for dose-
7 finding and vaccine candidate selection based on
8 evaluations of safety and immunogenicity. 90
9 participants are randomized 4 to 1 to receive vaccine
10 of placebo in cohorts of 15 per dose-level separated
11 into two age groups of participants 18 to 55 years of
12 age and 65 to 85 years of age. The dosing began at the
13 lower dose levels and participants in the younger age
14 group, and the doses escalated only after safety
15 review. In the older age group was vaccinated with the
16 same vaccine dose and candidate following a
17 satisfactory safety review of the same dose in the
18 younger age group.

19 The numbers of participants who received the
20 various dose levels of the two vaccine candidates

1 evaluated are displayed there. These Phase 1 results
2 in combination with the study BNT16201 determine the
3 final vaccine candidate to move forward into Phase 2
4 and 3. Alright. Let me go one back here.

5 And the study design for Phase 2 and 3
6 included a randomization of 1 to 1 for participants to
7 receive either the vaccine candidate or placebo and to
8 evaluate the safety and efficacy of a vaccine
9 candidate. The first 360 participants enrolled were
10 specified as an expanded cohort to further evaluate
11 safety and immunogenicity. And any COVID-19 cases from
12 these participants also contributed to the overall
13 Phase 3 efficacy population.

14 Enrollment was stratified by age as displayed
15 with a goal of 40 percent in the oldest age group
16 representing a population at risk for COVID-19. The
17 total number of participants 60 years of age or older
18 that were randomized in the Phase 2 and 3 as of
19 November 14th was 43,551. And here is a graphic to
20 show the overall study designed as planned with a point

1 in time for the data cut off identified in yellow for
2 which we have the data to present to you today.

3 Participants either received vaccine or
4 placebo 21 days apart and surveillance for potential
5 COVID-19 symptoms began after the first dose. The
6 presence of any of these symptoms would trigger an
7 illness visit for collection of the details about the
8 symptoms and collection of a nasal swab for PCR
9 testing. Additionally, participants had blood drawn
10 prior to dose one as well as nasal swabs prior to each
11 dose for SARS-CoV-2 PCR testing to evaluate for the
12 evidence of baseline infection.

13 Participants were vaccinated and followed
14 immediately after each vaccination for 30 minutes for
15 any acute reactions, and then also followed for
16 unsolicited adverse events for one month after their
17 last dose, and for serious adverse events for six
18 months after their last dose. A subset of participants
19 were designated as the reactogenicity subset and
20 reported daily solicited adverse reactions for seven

1 days following each dose. All participants are planned
2 to have two years of follow up for possibly related
3 serious adverse events or deaths as well.

4 Moving on to the case definitions here. On
5 the right-hand side of the slide is the case
6 definitions of the primary endpoints which included at
7 least one of the listed symptoms and a positive SARS-
8 CoV-2 PCR test obtained within four days of the
9 symptomatic period. And on the right side of the
10 screen is the case definition for one of the secondary
11 efficacy endpoints which is severe COVID-19 disease.

12 This case definition was met for confirmed
13 COVID-19 cases as shown on the right who also had any
14 one of the listed more severe criteria based on vital
15 signs, the need for medical intervention for
16 respiratory failure, shock, intensive care unit
17 admissions, or death. And moving on to the primary
18 efficacy endpoints. The primary endpoint definition
19 was using the case definition from the previous slide,
20 confirmed COVID-19 cases that occurred at least seven

1 days after dose two were counted towards the primary
2 endpoint. From the first primary efficacy endpoint was
3 described in terms of COVID-19 incidence per 1,000
4 years of follow up and those without serological or
5 virological evidence of past SARS-CoV-2 infection
6 before or during the vaccine regimen.

7 Evidence of past SARS-CoV-2 infection was
8 based on the result from the baseline blood draw to
9 evaluate for the presence of SARS-CoV-2 antibodies
10 prior to dose two, and the results from each PCR test
11 done prior to each dose. All of which needed to be
12 negative results for participants to be included in the
13 first primary endpoint. The second primary endpoint --
14 efficacy endpoint was described in the same terms but
15 in participants with and without evidence of prior
16 infection. The secondary efficacy endpoints are listed
17 here based on different case definitions and time cut
18 off for counting those cases.

19 The first endpoint listed is for confirmed
20 COVID-19 cases that occurred at least 14 days after

1 dose two and those without, and with and without
2 evidence of past infections. The second endpoint is
3 confirmed severe COVID-19 cases that occurred at least
4 seven or 14 days after dose two, and those with and
5 without evidence of past infections. The final
6 endpoint is confirmed COVID-19 based on the CDC case
7 definitions occurring at the same two timepoints and
8 two participant populations.

9 And now the next slide will review the
10 statistical considerations for the primary endpoints.
11 The vaccine efficacy was evaluated in participants
12 without evidence of prior infection before two -- seven
13 days following the second dose in the evaluable
14 efficacy populations, which I will define for you on
15 the next slide. And vaccine efficacy was defined in
16 terms of illness rate ratio, or IRR, where the IRR is
17 calculated as a ratio of the first confirmed COVID-19
18 illness rate in the vaccine group to be -- to the
19 corresponding illness rate in the placebo group.

20 For the interim and final efficacy analyses

1 the success criterion was met if the lower bound of the
2 vaccine efficacy was greater than 30 percent based on
3 the numbers listed for the interim and final analyses
4 above. Interim analyses were planned after the accrual
5 of at least 32, 62, 92, and 120 cases, but in reality,
6 the first interim analysis was conducted upon accrual
7 of 94 cases on November 4th and it met the success
8 criterion outlined here. The final analysis was
9 planned after accrual of at least 164 cases. And in
10 reality, it was conducted upon accrual of 107 cases on
11 November 14th.

12 And now to define for you the analysis
13 populations that will show from our data analyses
14 today. The populations and the numbers of participants
15 who were included in these populations are presented
16 here. The All-available efficacy populations included
17 all Phase 2 and 3 randomized participants who received
18 at least one or two study vaccinations and the
19 invaluable -- hello? Okay.

20 The evaluable efficacy populations was a

1 subset of this group. The participants who received
2 all vaccines within the predefined time window without
3 important protocol deviations and with follow up
4 through November 14th. The evaluable efficacy
5 population was used for the primary efficacy
6 population.

7 In terms of the safety populations analyzed,
8 the All-enrolled populations included all enrolled
9 participants regardless of the duration of follow up
10 who received at least one study vaccination. And the
11 study population was -- the safety population was a
12 subset of this group for participants who received at
13 least one study vaccination and were enrolled through
14 October 9th with follow up through November 14th.

15 So to review the duration of follow up for the
16 Phase 2 and 3 participants in terms of our guidance for
17 the EUA for the COVID-19. For this study, I think it's
18 important that the sponsor submitted protocol revisions
19 while the study was underway to increase the sample
20 size and to expand the study population. So there was

1 a late enrollment for participants in the adolescent
2 age group, and those over 85 years of age, and those
3 with stable, chronic infections such as HIV, Hepatitis
4 B or C. So these specific study populations do have
5 less follow up than the general study population.

6 But for the evaluable efficacy population, the
7 participants included in the interim analysis conducted
8 on November 4th at a follow up duration of less than
9 two months. And the interim analysis was successful
10 with a vaccine efficacy of 95.5 percent after the
11 accrual of 94 cases. The participants included in the
12 final analysis conducted on November 14th also had a
13 follow up duration of just less than two months.

14 However, this time point included all of the
15 participants included in the interim analysis, and the
16 duration of follow up for the participants included an
17 interim analysis at the time of the final analysis is
18 two months. We focused our review, however, on the
19 data from the final efficacy data cutoff, which
20 includes those from the interim analysis, because the

1 results of the final analysis were consistent with
2 those from the interim analysis and they provided more
3 robust data from a greater number of participants.

4 The Phase 2/3 safety populations includes only
5 Phase 2/3 participants enrolled by October 9th with a
6 follow up through November 14th, and the median follow
7 up duration is two months. The All-enrolled population
8 includes all enrolled participants regardless of the
9 duration of follow up. And the median duration of
10 follow up for this group is less than two months. But
11 additional safety analyses from this larger database of
12 All-enrolled participants was also reviewed to evaluate
13 for differences compared with the smaller Phase 2/3
14 safety population.

15 And this is just a duplicate slide. So moving
16 on to one additional consideration that we wanted to
17 point out was implemented for vaccine-induced enhanced
18 respiratory disease. There's oversight from the data
19 monitoring committee from day one. And an unblinded
20 team supporting the DMC reviewed cases of severe COVID-

1 19 at least weekly to evaluate the case splits of the
2 number of severe cases in each treatment group in terms
3 of the study design alert criteria and stopping rules
4 that are outlined in this slide.

5 Neither the alert trigger nor the study
6 stopping criteria were met, which suggests that vaccine
7 administration was associated with more severe COVID-19
8 disease to date. And now I will go ahead and move on
9 to our efficacy data analyses. And the first slide
10 here is showing the demographics of our efficacy
11 population by demographic subgroup such as sex, age,
12 race, ethnicity, and the presence of comorbidity.

13 For age, you can see that the elderly
14 population is represented with approximately 20 percent
15 of the population being 65 years of age and older. For
16 race, approximately 10 percent of participants
17 identified themselves as Black or African American.
18 And there are smaller numbers of participants of
19 American Indian, Alaska Native, Native Hawaiian,
20 Pacific Islander, and multiracial backgrounds.

1 In terms of ethnicity, approximately 25
2 percent of the population identified themselves as
3 Hispanic or Latino. And approximately 45 percent of
4 the population had medical comorbidities, specifically,
5 35 percent of the population was obese. You can also
6 see here that there are 153 total adolescents, 16 to 17
7 years of age that were included in the efficacy
8 population. The demographics are similar for the
9 safety population.

10 So moving on to the dispositions of the
11 efficacy population. To identify the reasons for
12 exclusion from the evaluable efficacy population for
13 analysis of our primary endpoint. Starting at the top
14 of the slide, from the total number of randomized
15 participants and moving down the table you will see how
16 many subjects received each dose and were included
17 because they did not have evidence of prior infections,
18 in addition to how many subjects were excluded with the
19 reason for exclusion listed toward the bottom of the
20 slide.

1 Most of the exclusions were because
2 participants did not receive both vaccinations within
3 the predefined windows, and the number of participants
4 affected was balanced between treatment groups. There
5 were more protocol deviations in the vaccine group than
6 the placebo group, and most of them were medication
7 errors such as product storage errors, incorrect dosage
8 administration, or the wrong product being
9 administered.

10 The next slide here shows the results of the
11 primary efficacy analysis with a total 170 cases, 8 in
12 the vaccine group and 162 in the placebo group giving a
13 vaccine efficacy of 95 percent for the prevention of
14 COVID-19 from seven days after dose two. And the
15 criterion for success was met. The prespecified age
16 stratifications are also shown here with similar
17 results for vaccine efficacy.

18 On this slide the first row shows the overall
19 second primary efficacy endpoint, which is COVID-19
20 cases at least seven days after dose two in subjects

1 with and without prior infection as most people who
2 will receive the vaccine most likely will not know
3 their baseline infection status. The vaccine efficacy
4 was similar to the primary endpoints and had nine cases
5 in the vaccine group and 169 in the placebo group,
6 giving a vaccine efficacy of 94.6 percent.

7 Subgroup analyses of this second primary
8 endpoint are also shown here by age, obesity as a
9 comorbidity, and by sex. The vaccine efficacy was
10 consistently high across different subgroup analyses
11 with limitations on the adolescent age group because of
12 small numbers of cases and participants as compared to
13 the adult population. The vaccine point estimates were
14 uniformly high across the subgroups examined, with the
15 exception of participants identifying as multi-racial
16 and participants with evidence of prior SARS-CoV-2
17 infection at enrollment, for which too few COVID-19
18 occurred to interpret efficacy data for these
19 subgroups.

20 So continuation of the subgroup analyses for

1 the second primary endpoints are shown here. I think I
2 just described that with the prior slide. So the
3 vaccine efficacy point estimates were uniformly high so
4 you can see the numbers here on this slide.

5 And moving on to one additional subgroup
6 analysis of the vaccine efficacy by comorbidity to show
7 that the vaccine efficacy point estimates, again, were
8 uniformly high across subgroups, again, that increase
9 the risk of COVID-19 such as chronic pulmonary disease,
10 diabetes, obesity, and hypertension. The next slide
11 here is to show that the secondary efficacy analyses
12 have similar case splits. And the vaccine efficacy
13 results are consistent with the primary efficacy
14 endpoint for these secondary efficacy endpoints, as
15 well, based on the case definitions with cases being
16 counted at 14 days following dose two as well as using
17 the CDC case definitions.

18 The other secondary efficacy to discuss is
19 severe COVID-19 and this table breaks down the numbers
20 of severe cases that occurred in the All-available

1 efficacy populations at each range of timepoints shown
2 following dose one. In the All-available efficacy
3 population, 10 participants have severe COVID-19
4 disease after dose one; one subject who received the
5 vaccine, and two subjects who received placebo. The
6 vaccine efficacy was 88.9 percent but within a wide 95
7 percent confidence interval that goes down to 20
8 percent.

9 Based on review of the case managers overall,
10 and the All-available efficacy populations, two placebo
11 recipients met severe criteria based on vital signs and
12 no other criteria. Six placebo recipients who had
13 severe COVID-19 disease were hospitalized, three of
14 which were admitted to intensive care unit and seven
15 placebo recipients had at least one risk factor for
16 severe disease. In the bottom row of this table, you
17 see the case splits for the primary endpoint
18 evaluations at least seven days after dose two, in
19 which four placebo recipients and one vaccine recipient
20 had severe COVID-19 disease.

1 The vaccine recipient who had severe COVID-19
2 disease met the severe case definition because of
3 oxygen saturations at the time of the COVID-19 illness
4 visit being less than 93 percent on room air. The
5 subject was not hospitalized, did not seek further
6 medical care, and did not have risk factors for severe
7 disease.

8 The four placebo recipients who had severe
9 COVID-19 disease met the severe case definition for the
10 following reasons: one subject had oxygen saturation of
11 92 percent on room air and one had a heart rate of 125
12 without other severe criteria; one subject was
13 hospitalized for non-invasive positive pressure
14 ventilation with bilateral pneumonia; one subject had
15 an oxygen saturation of 92 percent and ICU admission
16 for heart block. Two of these placebo recipients with
17 severe disease also have obesity as a risk factor while
18 the other two participants did not have any risk
19 factors for severe disease.

20 The total number of severe cases is small,

1 which does limit the overall conclusions that can be
2 drawn. However, the case split does suggest protection
3 from severe COVID-19 disease. We'll move on to one
4 post hoc analysis that we ran on the timing of COVID-19
5 cases following dose one and the All-available efficacy
6 population.

7 The timing of cases is presented similarly to
8 the prior slide for severe cases. Vaccine efficacy and
9 participants in the All-available efficacy population
10 were similar to results in the evaluable efficacy
11 population. And the vaccine efficacy for prevention
12 COVID-19 disease after dose one is 82 percent.

13 Based on the number of cases accumulated after
14 dose one and before dose two you can see that there
15 does seem to be some protection against COVID-19
16 disease following one dose. However, these data do not
17 provide information about longer term protection beyond
18 21 days after a single dose because the vast majority
19 of subjects received dose two. And our next slide here
20 shows one additional post hoc analysis of the vaccine

1 efficacy based on baseline SARS-CoV-2 status in the
2 dose one All-available efficacy population.

3 Only three percent of participants had
4 evidence of prior infection at study enrollment, and
5 additional analyses showed that very few COVID-19 cases
6 occurred in these participants over the course of the
7 entire study; 10 in the vaccine group and nine in the
8 placebo group. Only one of the 10 cases in the vaccine
9 group occurred seven days or more after completion of
10 the two-dose vaccine regimen. Some participants with
11 prior evidence of infection also had confirmed COVID-19
12 during the study conduct.

13 These data do suggest that previously infected
14 individuals can be at risk of COVID-19 reinfection.
15 The small numbers of participants with baseline
16 positive status limits the interpretation of the
17 efficacy at this timepoint. Moving on, we will now
18 focus our attention on the safety data, and here's a
19 quick reminder from the graphic about the general study
20 design.

1 And first, we'll review, the reactogenicity
2 results collected daily for the first seven days
3 following each dose in the reactogenicity subset. Dose
4 one reactogenicity is shown here on this first slide
5 and it's separated by the pre-defined age
6 stratification. For both age groups, injection site
7 pain was the most frequent solicited local adverse
8 reaction. After dose two, the younger age group
9 reported any pain more frequently than the older group,
10 and pain was characterized as moderate with a similar
11 pattern observed after dose one.

12 Injection site redness and swelling after each
13 dose was generally similar for both age groups. For
14 each age group in the reactogenicity subset, the
15 younger subjects and overall the median onset of local
16 reactions in the vaccine group was from the day of
17 vaccination to two days after the dose and lasted for a
18 median duration between one and doses -- one and two
19 days. Local reactogenicity following dose two is shown
20 here with consistent reports of pain, redness, and

1 swelling. An analysis by various demographic subgroups
2 showed consistent results.

3 The next slide here shows -- my slides are a
4 little behind. I'm sorry. So here are solicited
5 adverse events within seven days following dose one.
6 I'm caught up. I apologize for that. These are -- let
7 me catch up here.

8 These are reports of joint pain, diarrhea, and
9 vomiting which were reported pretty equally between the
10 age groups and the... Following dose two the systemic
11 reactogenicity is shown here. The frequency and
12 severity of systemic AEs was higher after dose one than
13 in dose two -- was higher after dose two than dose one
14 except for vomiting and diarrhea, which is generally
15 similar regardless of dose. And again, analyses by
16 various demographic subgroups showed consistent
17 results.

18 This slide is a continuation of the dose two
19 solicited systemic adverse reactions within seven days
20 showing the numbers for joint pain, diarrhea, and

1 vomiting. Here are the numbers for our adolescents 16
2 and 17 years of age. It's important to note that the
3 majority of adolescents 16 and 17 years of age enrolled
4 by October 9th, local reactions, and systemic AE data
5 were collected as unsolicited AEs with the preferred
6 terms showed here, rather than from prespecified
7 prompts for reactions which were solicited daily for
8 seven days for each vaccination as was done for the
9 adult population just shown.

10 So the same details are not available for
11 reactogenicity in 16 and 17-year-olds as compared to
12 the adults in the study at this timepoint. So based on
13 the unsolicited AEs shown here, in general, the 16 and
14 17-year-olds had similar symptoms reported but to a
15 lesser degree than the adult population. Moving on to
16 the unsolicited adverse events. Subjects were
17 monitored for 30 minutes immediately following each
18 vaccination and no subjects had an acute allergic
19 reaction.

20 For the unsolicited non-serious adverse events

1 that were reported more frequently in the vaccine group
2 than the placebo group, they're consistent with
3 solicited reactions recorded from the reactogenicity
4 subset; 18 percent in the vaccine group versus three
5 percent in the placebo group, which would be expected.
6 Additionally, lymphadenopathy occurred more in the
7 vaccine group than the placebo group with a plausible
8 relationship to vaccination.

9 And finally, Bell's Palsy occurred in four
10 vaccine recipients and no placebo recipients, two
11 within one month of vaccination and two after one
12 month. More details here include that three cases
13 occurred at 3, 9, and 37 days after vaccination and
14 participants with no prior history of Bell's Palsy.
15 The case with the onset at three days post-vaccination
16 was reported as resolved without (inaudible) within
17 three days of onset.

18 The other case -- the other three cases were
19 reported and continuing or resolving as of the November
20 14th data cutoff with ongoing duration of 15 -- 10, 15,

1 and 21 days, respectively. The fourth case had an
2 onset at 48 days after vaccination in a participant
3 with prior history of Bell's Palsy. And it was
4 reported as ongoing with a duration of 21 days at the
5 time of the data cutoff.

6 In addition, we independently conducted
7 standard measure queries, SMQs, using FDA developed
8 software to evaluate for a constellation of unsolicited
9 adverse events -- event preferred terms that could
10 represent various diseases and conditions including but
11 not limited to; allergic, neurologic, inflammatory, and
12 autoimmune conditions. The SMQs conducted on the Phase
13 2/3 All-enrolled safety population revealed a slight
14 numerical imbalance of adverse events potentially
15 representing allergic reaction, with more participants
16 reporting hypersensitivity adverse events in the
17 vaccine group with 137 or 0.63 percent compared with
18 the placebo group with 111 or 0.51 percent. There are
19 no imbalances between treatment groups that were
20 evident for any other SMQs evaluated.

1 Moving on to serious adverse events. There
2 were six deaths reported in the study, two in the
3 vaccine group, and both of these were in participants
4 over 55 years of age. One death was following a
5 cardiac arrest 62 days after dose two and the other was
6 due to atherosclerotic disease three days after dose
7 one. Neither of these deaths were considered related
8 to the vaccine.

9 For non-fatal SAEs, these reported -- these
10 included appendicitis in eight vaccine recipients and
11 four placebo recipients. For the vaccine group, two
12 participants were 55 or over 55 years of age and one of
13 these had a perforated appendicitis. None of these
14 events were considered related to vaccination.

15 One shoulder injury in the same arm as the
16 vaccine administration was reported as an SAE which we
17 attributed as possibly related to the vaccine
18 administration or to the vaccine itself. My next slide
19 here focuses on pregnancy because women were screened
20 for pregnancy prior to each vaccination and were

1 excluded or not vaccinated if they had a positive
2 result. So as of November 14th, there were 23
3 pregnancies reported, 12 in the vaccine group and 11 in
4 the placebo group.

5 The time interval between vaccination as it
6 relates to the date of the woman's last menstrual
7 period are shown here. Two placebo recipients had
8 known pregnancy outcomes, one of which was a
9 spontaneous abortion, and the other was retained
10 product of conception. The pregnancy outcomes are
11 otherwise not known at this time as the pregnancies are
12 ongoing.

13 Our next slide here shows other safety
14 evaluations. Clinical laboratories commit -- such as
15 hematology and chemistry were assessed in Phase 1
16 participants. The only common laboratory abnormality
17 reported was a transient decrease in lymphocytes one to
18 three days after dose one, which were mostly grade one
19 to two in severity, and they generally normalized
20 within six to eight days, and did not occur after dose

1 two.

2 And among the Phase 1 participants in this
3 study who received the 30 microgram dose, transient
4 decreases in lymphocytes post dose one occurred in 5 of
5 12 participants in the younger age group, 18 to 55
6 years of age, and in 4 of 12 participants in the older
7 age group 65 to 85 years of age. These transient
8 hematological changes were not associated with clinical
9 symptoms. Additionally, overall subgroup analyses of
10 the previous safety results were assessed by race,
11 ethnicity, medical comorbidities, and prior SARS-CoV-2
12 infection without any safety concerns identified by the
13 subgroup analyses.

14 So in summary, our efficacy conclusions are
15 that the totality of the clinical data submitted with
16 the EUA request meets the expectations for the duration
17 of follow up. In the final S-50 analysis, vaccine
18 efficacy after seven days post dose two was 95 percent
19 in participants without prior evidence of SARS-CoV-2
20 infection. Efficacy outcomes were consistently greater

1 than 93 percent across demographic subgroups, and
2 efficacy against severe COVID-19 occurring after the
3 first dose was 88.9 percent. The small number of
4 severe cases is a limitation to these data.

5 A trend of potential efficacy following a
6 single dose is observed in the data. However,
7 conclusion is limited because almost all participants
8 received a second dose. On our summary for safety
9 here, is that the totality of the clinical data
10 submitted with the EUA request meets the expectations
11 for follow for duration of follow up and evaluation of
12 the All-enrolled population. And this provided
13 additional safety data from a total of greater than
14 43,000 participants.

15 Reactogenicity was generally more frequent
16 after dose two in all ages, mostly mild to moderate
17 with less frequency and severity in adults over 55
18 years of age than in the younger adults. There were no
19 specific safety concerns identified in subgroup
20 analyses by age, race, ethnicity, medical

1 comorbidities, or prior SARS-CoV-2 infection. As of
2 the data cut off, four cases of Bell's Palsy were
3 reported in vaccine recipients and none in the placebo
4 recipients.

5 Although there is no clear basis upon which to
6 conclude a causal relationship at this time, we do
7 recommend further surveillance if the vaccine is
8 authorized for widespread use. We're moving on in the
9 outline here. I will move on to the pharmacovigilance
10 plans, future studies, and ongoing study plans.

11 The sponsor submitted a pharmacovigilance plan
12 to monitor safety concerns that could be associated
13 with the vaccine. The sponsor identified vaccine-
14 associated enhanced disease including vaccine-
15 associated enhanced respiratory disease as an important
16 potential risk. The use in pregnancy and lactation are
17 areas the sponsor identified as missing information.

18 In addition to the safety concerns specified
19 by the sponsor, FDA is requested that the sponsor
20 update their pharmacovigilance plan to include missing

1 information in pediatric participants less than 16
2 years of age, which the applicant agreed to. We also
3 recently requested that the sponsor add anaphylactic
4 reactions including anaphylaxis to the
5 pharmacovigilance plan based on the recent post-market
6 reports of anaphylactic reactions. Next slide is a
7 graphic here to outline pharmacovigilance activities.

8 AE reporting under the EUA may come from
9 vaccine recipients, vaccination providers, or from the
10 sponsor. First, vaccine recipients will be notified
11 that AEs can be reported to VAERS through the
12 factsheets, or recipients and caregivers. Another
13 source of AE reports from recipients is the V-SAFE
14 program, which is a smart phone based program that uses
15 text messaging and web surveys from the CDC to check in
16 with vaccine recipients for health problems after
17 vaccination. Reports from vaccine recipients are
18 voluntary.

19 AE reporting by vaccination providers and the
20 sponsor is mandatory. Both the sponsor and vaccine

1 providers administering the Pfizer-BioNTech COVID-19
2 vaccine must report to VAERS the following information
3 associated with the vaccine; any vaccine administration
4 errors whether or not associated with an adverse event,
5 serious adverse events irrespective of attribution to
6 the vaccination, cases of multi-system inflammatory
7 syndrome in children and adults, cases of COVID-19 that
8 result in hospitalization or death.

9 In addition, the applicant will also conduct
10 periodic aggregate review of safety data and submit
11 period safety reports at monthly intervals for FDA
12 review. Each periodic safety report is required to
13 contain a narrative summary and an analysis of adverse
14 events submitted during reporting interval, including
15 interval and cumulative counts by age groups, special
16 populations, i.e., pregnant women, and adverse events
17 of special interest, newly identified safety concerns
18 in the interval and actions taken since the last result
19 because of adverse experience.

20 Both FDA and CDC will take a collaborative and

1 complementary approach on reviewing AEs. FDA will
2 individually review all serious adverse events on a
3 daily basis. And FDA will also examine other sources
4 for adverse events such as the literature and will
5 perform data mining to determine if adverse events are
6 disproportionately reporting for the candidate vaccine
7 compared to all other vaccines in VAERS. Any potential
8 safety signals identified will be investigated.

9 The next slide outlines the sponsor's
10 pharmacovigilance activities that are also included as
11 active surveillance studies, each of which will be
12 conducted over a 30-month time period. The first study
13 will be conducted in a survey of 20,000 healthcare
14 workers. Incident rates of adverse events will be
15 compared to expected rates.

16 The second study listed will be conducted
17 within the Department of Health, Health System
18 Databases for U.S. military and their families. Rates
19 of adverse events of special interest in vaccine
20 recipients will be compared to unvaccinated

1 comparators. The final study listed will evaluate for
2 AEs of special interest using the Veteran's Health
3 Administration's electronic medical record database.
4 Vaccine recipients will be compared to unvaccinated
5 participants, or to recipients of the seasonal
6 influenza vaccine.

7 Moving on. The next slide here will outline
8 the proposed revisions to the study protocol if an EUA
9 is issued. The study design figure shows the current
10 study design, and for participants that originally
11 received the vaccine candidate or for placebo
12 recipients who decline receiving the vaccine under the
13 EUA when it is made available, there is no change to
14 the study design. Participants will continue to be
15 followed as previously proposed through two years post
16 dose two.

17 The next slide here shows Pfizer's proposal
18 for subjects eligible to receive the vaccine under
19 local and national recommendations at the time of EUA.
20 They can contact their investigator to confirm that

1 they meet eligibility criteria. They would then be
2 unblinded to know if they received vaccine or placebo.
3 If they received placebo, they would then receive the
4 vaccine within the study conduct and continue with the
5 study for 18 months of follow up.

6 At visit four -- alternatively, at visit four
7 or six months after dose two, subjects that had not met
8 local or national recommendations for the EUA issuance
9 would then be offered the option to receive the vaccine
10 at that timepoint. And if they accept, both the
11 sponsor and the participant would be unblinded and
12 participants who originally received placebo would then
13 receive vaccine. Participants who cross over from the
14 placebo group to receive the vaccine would then get
15 baseline blood drawn from immunogenicity prior to the
16 first dose, a nasal swab for PCR prior to each dose.

17 They would then have phone follow up at 1, 6,
18 and 18 months following dose two, as indicated in the
19 figure, in addition to any illnesses for potential
20 COVID-19 symptoms that meet the case definitions. So

1 the total study duration would still be approximately
2 two years for these participants.

3 So moving on I will wrap up now with our
4 benefit and risk assessment in the context of the
5 proposed EUA. The known benefits of the vaccine at
6 this time include a reduced risk of confirmed COVID-19
7 at least seven days after completing a two dose
8 vaccination regimen in individuals without prior
9 history of SARS-CoV-2 infection. Efficacy findings are
10 consistent across subgroups, including racial and
11 ethnic minorities, adults 65 years of age and older,
12 and individuals with one or more of the following
13 conditions: obesity, diabetes, hypertension, and
14 chronic cardiopulmonary disease.

15 Efficacy data in adolescents, 16 and 17 years
16 of age are limited but could be extrapolated from the
17 efficacy observed in adults 18 to 55 years of age. In
18 addition, here is a for our risks. The known risks of
19 the vaccine include local and systemic adverse
20 reactions. In all age groups these were generally mild

1 to moderate and more frequent following dose two than
2 following dose one. In adults over 55 years of age,
3 they were less frequent and less severe compared to the
4 younger adult age group.

5 Severe adverse events that were possibly
6 related to the vaccinations included the shoulder
7 injury that we attributed to vaccine administration or
8 to the vaccine itself, and lymphadenopathy that was
9 thought to be temporarily associated and biologically
10 plausible. There are no specific safety concerns
11 identified in analyses of subgroups described or by
12 prior SARS-CoV-2 infection. The data are limited from
13 adolescents 16 and 17 years of age but could be
14 extrapolated from the safety profile in adults 18 to 55
15 years of age.

16 The risk assessment is also limited by the
17 duration of follow up at this snapshot in time and the
18 fact that pregnant and breastfeeding women were
19 excluded from the study. In addition, we are aware of
20 the reports of anaphylactic reactions and we are

1 continuing to collect information to monitor this
2 situation closely. I will now move on to my final
3 slides here to remind the advisory committee of the
4 items that we would like for them to discuss without a
5 vote.

6 The first of which is that Pfizer has proposed
7 a plan for continuation of blinded placebo controlled
8 follow up in ongoing trials if the vaccine were made
9 available under the EUA. Please discuss Pfizer's plan,
10 including how loss of blinded placebo controlled follow
11 up in ongoing trials should be addressed. The second
12 item to discuss is to discuss any gaps in plans
13 described today and in the briefing documents for
14 further evaluation of vaccine safety and effectiveness
15 in populations who would receive the Pfizer-BioNTech
16 vaccine under EUA.

17 And the final slide here is our questions for
18 the advisory committee to vote on. Based on the
19 totality of the scientific evidence available to the
20 benefit of the Pfizer-BioNTech COVID-19 vaccine both

1 outweigh its use for risks in individuals 16 years of
2 age and older. With that, I will conclude my
3 presentation and welcome questions. Thank you.

4 **DR. ARNOLD MONTO:** Thank you very much. Let's
5 have questions for about 10 minutes or so. We're
6 running late but I think it's critical for us to
7 entertain some questions now. And if anybody I shut
8 off questions to the sponsors so we might want to
9 follow up with questions to the sponsor as well and we
10 can sort it out, the direction of the questions,
11 whether it goes to FDA or to the sponsor. Let's start
12 out with Mr. Toubman.

13 **MR. SHELDON TOUBMAN:** Thank you. So I raised
14 this before and that is that the data is now 26 days
15 old, that was the closing date. And I asked a question
16 about, you know, do we have more recent data and Dr.
17 Fink said it hasn't been requested. However, the
18 sponsor is here, and based upon my experience they will
19 have updated data and some other folks may want to ask
20 them about it.

1 But I have one specific set of data I'd like
2 to ask about in terms of update, probably for them and
3 not for you Dr. Wollersheim, but we'll see. It's about
4 this question is severe disease. And the takeaway --
5 there's a lot -- I mean, Pfizer suggested it's been
6 demonstrated that their vaccine is effective with
7 severe disease but that's really not the case.

8 And your conclusion just now was that the case
9 split does suggest protection from severe COVID-19
10 disease but as stated in your briefing document you
11 just don't have enough data to know that. Well, it's
12 been 26 days, and the question is, do we have such
13 data? All we have based upon what we've -- with the
14 cases 26 days ago, was actually a vaccine efficacy of
15 66 percent on the actual endpoint, not the other data
16 you talked about which was from dose one. And then you
17 got to 88 percent.

18 But the actual endpoint that was in the study,
19 and it's been, analyzed came up with a 66 percent
20 vaccine efficacy. And that's concerning the thing that

1 really matters to me. They care about severe disease.
2 Frankly, almost nobody cares about COVID-19 that all it
3 does is give you a sore throat.

4 So I think it's really in the public's
5 interest to know what is the story on this vaccine in
6 preventing severe disease, and we really don't have
7 sufficient data to conclude that as of November 14th.
8 So can we get data? Is there data from Pfizer right
9 now, as of yesterday, which shows additional cases that
10 gives us more data such that we can actually -- they
11 conclude in their document that the data does not meet
12 prescribed (inaudible) criteria, the endpoint of severe
13 disease?

14 Maybe that new data does. And then the second
15 question is, if it's not sufficient yet, at what point
16 do we project we might have sufficient data so we could
17 really look at that critical question of, does this
18 vaccine really prevent severe disease?

19 **DR. ARNOLD MONTO:** Could I ask the Pfizer team
20 to respond about additional data?

1 **DR. KATHRIN JANSEN:** -- comes to the
2 relevance. I'd like Dr. Gruber to respond to the first
3 question in terms of additional data. And then also
4 when it comes to severe disease, I would like to invite
5 Dr. Stephen Thomas to give his perspective of the
6 medical importance of preventing --

7 **DR. ARNOLD MONTO:** We really need to keep this
8 -- we need to keep it brief.

9 **DR. KATHRIN JANSEN:** Alright. Just Bill then.

10 **DR. ARNOLD MONTO:** Okay. Just --

11 **DR. WILLIAM GRUBER:** Yeah. I can be fairly
12 brief here.

13 **DR. KATHRIN JANSEN:** Go ahead.

14 **DR. WILLIAM GRUBER:** The answer to the
15 question as we heard earlier, it takes quite a bit of
16 work to essentially prepare a data package for
17 comprehensive review by the FDA. So since November the
18 14th we obviously have not done the additional
19 unblinded analysis. We will do that obviously at the
20 direction of the FDA.

1 And there is obviously potential over time at
2 an appropriate time in collaboration with the FDA to
3 look at that again. I can tell you that we don't have
4 enough additional cases post second dose to greatly
5 enlarge that data. But I would emphasize that the data
6 where we see the 1 to 9 split using the FDA guidance
7 after the first dose and the 1 to 14 split, I think in
8 my view, and it seems to be in the FDA's view, is
9 compelling for evidence of protection. I think it's
10 just a matter of getting enough cases and we have the
11 potential to have more cases over time but we've not
12 analyzed those yet. Everything --

13 **DR. ARNOLD MONTO:** Dr. Wollersheim, anything
14 to add?

15 **DR. SUSAN WOLLERSHEIM:** No. I agree. At
16 some point, I guess we'll have those discussions in
17 terms of when additional data will be requested but
18 that's not the topic for today's EUA discussion.

19 **DR. ARNOLD MONTO:** Okay. Let's go on to --

20 **MR. SHELDON TOUBMAN:** If I could follow up --

1 **DR. ARNOLD MONTO:** No follow ups. We -- we're
2 pressed for time. I got 10 people who want to talk --
3 ask questions. Dr. Kurilla.

4 **DR. MICHAEL KURILLA:** Yeah. I've got -- I'd
5 like FDA to make two comments. One, with the clinical
6 findings of loss of smell and taste which also involved
7 cranial nerves, is Bell's Palsy that odd in your mind
8 that it could not be associated with some immunological
9 response to the antigen? And the second is, in looking
10 at the data package, we don't as yet have a recognized
11 or accepted correlative protection.

12 And the panel of human convalescent plasma, if
13 I recall it was derived from 38 individuals, 35 of
14 which had mild disease. Only one was hospitalized.
15 I'm assuming the other two were asymptomatic. But we
16 know that the antibody titers do scale with the
17 severity of infection.

18 So it seems like a little bit of a low bar to
19 be comparing against people who had mild disease who
20 may be mediating other innate immune responses. And so

1 I'm just trying to get a sense of who we can move
2 forward following people who get vaccinated when we
3 don't really have a recognized correlative protection.
4 And then for the Pfizer group, the question I wanted to
5 ask before is, you have tripled in terms of innate
6 immune responses of the vaccine, but is that in general
7 innate immune responses, or is that related
8 specifically to Toll-like receptor responses?

9 Given that the younger individuals had more
10 reactogenicity, it sounds more inflammatory. And I
11 wonder if generation of interferon responses and
12 potentially natural killer responses from the
13 vaccination and antigen non-independent response, or an
14 antigen period? And since you're period of time for
15 overall efficacy is very short are you actually not
16 measuring the true efficacy of your adaptive immune
17 response that you are clearly generating?

18 **DR. ARNOLD MONTO:** Dr. Wollersheim, please.
19 Responses kind of brief. Okay? Dr. Wollersheim first.

20 **DR. SUSAN WOLLERSHEIM:** Sure. Thank you. I

1 think your first question is regarding causality with
2 Bell's Palsy and just given the small numbers of cases
3 that we have it would be difficult to attribute
4 causation at this time. I do see correlating
5 potential, but I think that this is unclear at this
6 time to attribute to the vaccine. And your second
7 question was regarding comparison of GMTs to the
8 convalescent plasma panel. I do see your point with the
9 symptomology comparison of correlating potential, of
10 GMTs to the convalescent plasma panel.

11 And I might actually ask Pfizer to address
12 this question because I know that they had two
13 different panels of convalescent plasma that they
14 (audio skip) data and I don't recall off the top of my
15 head which one was used in today's presentation, and
16 what the composition of those patients that submitted
17 to those panels were. So I will actually let Pfizer
18 address that question, please.

19 **DR. KATHRIN JANSEN:** Yeah. If it's okay I can
20 answer this. So it was a panel of 38 (audio skip)

1 they were collected 14 days after PCR confirmed COVID-
2 19 case at a time when the donors were asymptomatic.
3 We had 35 symptomatic infections. In that, three
4 asymptomatic infections, one individual was
5 hospitalized. And we -- I just want to stress that we
6 used that panel initially to give us guidance of how a
7 vaccine-induced immune response compares to a panel of
8 individuals that had contracted COVID-19. We did not
9 use that to make any decisions or draw any conclusion
10 in terms of a correlate of protection.

11 **DR. ARNOLD MONTO:** Okay. We're going to not
12 worry about adaptive and innate immune responses right
13 now. We'll take that off-line. Dr. Perlman, your
14 question.

15 **DR. STANLEY PERLMAN:** Yeah. Yeah. Okay.
16 Yes. I just had a question about pregnant women,
17 because if an EUA is of pregnant women not being
18 immunized but we have no data --

19 **DR. SUSAN WOLLERSHEIM:** I will defer that
20 question here to Dr. Fink who is here.

1 **DR. DORAN FINK:** Hi. Thanks for asking that
2 question. I'm trying to activate my video but the --

3 **DR. ARNOLD MONTO:** We know what you look like,
4 Doran.

5 **DR. DORAN FINK:** Alright. So in the --

6 **DR. ARNOLD MONTO:** Let's go ahead.

7 **DR. DORAN FINK:** -- interest of time -- right.
8 So in the interest of time. You are correct that we
9 have very limited data on the use on pregnancy. We are
10 expecting results of a developmental and reproductive
11 toxicity study in animals to be submitted to us later
12 this month. That type of data typically precedes
13 licensure of a vaccine.

14 In terms of inclusion of pregnant women in the
15 EUA, we recognize that among the groups first
16 prioritized for vaccine use under EUA there will be
17 many women of childbearing potential including women
18 who are pregnant, either knowingly or unknowingly. And
19 we have really no data to speak to risks specific to
20 the pregnant woman or the fetus, but also no data that

1 would warrant a contraindication to use in pregnancy at
2 this time.

3 And so in the interest of allowing women of
4 childbearing potential who would consider vaccination
5 to be right for them, we could consider including them
6 in the EUA population -- the population approved for
7 use under EUA. They would be then free to make their
8 own decision in conjunction with their healthcare
9 provider.

10 **DR. ARNOLD MONTO:** Thank you. Dr. Sawyer.

11 **DR. MARK SAWYER:** Thanks very much and I'd
12 like to thank all the presenters and all the many, many
13 people who contributed the work to the presentations.
14 My question is for FDA and it is about the 16 to 17
15 year old group. I am concerned about the lack of data,
16 particularly reactogenicity, and I'm not aware of any
17 other vaccine where we've interpreted or extrapolated
18 adult data down into the adolescent years.

19 I appreciate that 16 and 17-year-olds are big
20 and hairy and pretty close to adults, but they're not

1 exactly the same. And so my specific question is, if
2 this data holds six months from now and there's no
3 safety concern and we have this level of evidence of
4 effectiveness, one case in a placebo group and no cases
5 in the vaccine group, would that be sufficient for a
6 BLA to be down to the age of 16? Thanks.

7 **DR. WILLIAM GRUBER:** Maybe I can --

8 **DR. KATHRIN JANSEN:** Yeah. I'm not --

9 **DR. WILLIAM GRUBER:** -- that question. So
10 that's a decision that we would have to make at the
11 time that we are considering a licensure application.
12 Our regulations and laws do allow us to extrapolate
13 effectiveness and safety from adult populations into
14 pediatric populations as you mentioned. The ages of 16
15 and 17 are those adolescents that are closest in age to
16 adults and so the extrapolation becomes biologically
17 all that more reasonable.

18 As well, 16 and 17-year-olds are at increasing
19 risk of exposure to SARS-CoV-2 because of activities
20 that they typically engage in. So as outlined in Dr.

1 Wollersheim's presentation, for the purpose of this EUA
2 we do consider that safety and effectiveness from
3 adults, in particular younger adults, could be
4 extrapolated to older adolescents ages 16 and 17.

5 **DR. ARNOLD MONTA:** Thank you. The last
6 question that we have time for right now before we have
7 a very short break is from Dr. Rubin. Please.

8 **DR. ERIC RUBIN:** Thank you for your -- thank
9 you for your careful analysis. It gets to one of the
10 post hoc analyses you did. It looks as if 19
11 participants regardless of their -- whether they were
12 placebo or vaccine recipients got -- developed disease
13 within the first 28 days. If you calculate that rate,
14 play with the numbers as much as we have them, that's a
15 pretty high rate of infection. It's actually a little
16 higher than the rate in the group that was allegedly
17 not immune.

18 And I wonder if that brings into question
19 whether or not the anti-nucleic acid antibody is
20 actually a very good test because there's a lot of

1 independent evidence suggesting that people with anti-
2 spike protein antibody have -- are relatively
3 protected. Since the entire evaluation of asymptomatic
4 disease is going to depend on that, I wonder if the
5 test is any good.

6 **DR. SUSAN WOLLERSHEIM:** That's a good question
7 and at this point those antibody tests have been
8 qualified for that stage of development. It's not part
9 of their final analysis at this point so they've not
10 been validated to a certain extent. So that would be
11 something that we will be discussing further.

12 **DR. ARNOLD MONTO:** Right. And there's also
13 the issue of seasonal Coronaviruses.

14 **DR. SUSAN WOLLERSHEIM:** Yes.

15 **DR. ARNOLD MONTO:** When you get into --

16 **DR. SUSAN WOLLERSHEIM:** I would give Pfizer
17 the opportunity to address the assays as well if they
18 wish.

19 **DR. ARNOLD MONTO:** Pfizer representative
20 please and we'll call it -- then we're going to take a

1 break.

2 **DR. KATHRIN JANSEN:** Yes. Sorry. I was on
3 mute. Yes. So we have used the N-protein assay to
4 distinguish it from a vaccine in dose response. But we
5 need to demonstrate a prevention of asymptomatic
6 infection and we can't use the spike protein for this
7 purpose because, you know, otherwise everyone would be
8 positive that received the vaccine. The second
9 question I believe that you were asking I'm blanking
10 right now was -- the second part of your question --

11 **DR. ERIC RUBIN:** Well, it was whether it was
12 really -- whether it was a good correlate of prior
13 infection, the N-protein.

14 **DR. KATHRIN JANSEN:** Yes. So it is our
15 understanding that N-protein positivity does indeed
16 develop within probably two weeks after becoming
17 infected. There's of course another way to determining
18 infection, which is by more frequent sampling using
19 PCR. Both are I think valid approaches from our
20 perspective.

1 In terms of cross-reactivity with other
2 seasonal Coronavirus, it was very important to
3 demonstrate it. So we have carefully looked at the N-
4 protein assay that we are using. It's a commercial
5 test. And have evaluated a relatively large number of
6 sera that were collected prior to the appearance of
7 SARS-CoV-2 and we have not seen any evidence of cross-
8 reactivity to seasonal Coronaviruses.

9 **DR. ARNOLD MONTO:** Okay. Well, let us now
10 take a -- looking at the clock, a break until 10
11 minutes to four. Hard start at 10 minutes to four.
12 The meeting on October 22nd went on until a quarter to
13 seven eastern and I don't think we want to go on that
14 late tonight.

15 **MR. MICHAEL KAWCZYNSKI:** Alright. With that,
16 we're going to take a break.

17

18

19

[BREAK]

20

1 **COMMITTEE DISCUSSION AND VOTING**

2

3 **MR. MICHAEL KAWCZYNSKI:** All right. Welcome
4 back and we are now ready to start our Committee
5 discussion. So with that, Dr. Monto, would you like to
6 take it away?

7 **DR. ARNOLD MONTO:** Right. And I guess there
8 we are. Could you put the discussion questions up,
9 please, Mike?

10 **MR. MICHAEL KAWCZYNSKI:** Yes, I just did, sir.

11 **DR. ARNOLD MONTO:** All right. I don't see
12 them yet.

13 **MR. MICHAEL KAWCZYNSKI:** It may take a moment
14 as you just came in. Just give it a moment, sir.

15 **DR. ARNOLD MONTO:** Okay. Let's discuss what
16 we're going to do in the discussion. Because I've had
17 to cut off questions that were going to be addressed to
18 the presenters, the sponsor and FDA. What I would
19 suggest, since we are running quite late, is that we
20 have a discussion of these two items and ask the

1 sponsor and FDA, as we go through, of any items of fact
2 that they can help us in this discussion. So I don't
3 need to read to you the discussion items.

4 Item one is please discuss Pfizer's plan,
5 including how loss of blinded placebo-controlled
6 follow-up in ongoing trials should be addressed. So
7 we're talking here about plans for giving dose three
8 and dose four as was shown in the last presentation.
9 And also gaps in plans described today for further
10 evaluation of vaccine safety and effectiveness.

11 So I think they're related, and I think we
12 need to continue our discussion around both of these
13 points, plus any other specific questions you have of
14 the sponsors or FDA. I think we want to stay away from
15 more discussions about immune response and other things
16 that could be taken offline. So with that
17 introduction, Dr. Gans?

18 **DR. HAYLEY GANS:** I had a question regarding
19 the unblinding, if we go through with the EUA as number
20 one. The actual unblinding in any manner -- so if we

1 did the crossover -- how is that actually going to
2 affect the BLA? Because all of the data that was
3 presented today on how they would move forward on the
4 BLA is assuming that there isn't an unblinding (audio
5 distortion). So I think that would be important for us
6 to understand the impact it's having on an EUA. And my
7 follow up question (audio skip) because I think we've
8 seen a lot of conversations --

9 **DR. ARNOLD MONTA:** You're breaking up. Are
10 other people able to hear?

11 **MR. MICHAEL KAWCZYNSKI:** No, she is breaking
12 up a little bit, Dr. Gans.

13 **DR. HAYLEY GANS:** Sorry about that. Is this
14 better? Hello?

15 **MR. MICHAEL KAWCZYNSKI:** Go ahead. Continue.

16 **DR. HAYLEY GANS:** Okay. My second question
17 was we had a lot of questions about the use of the
18 vaccine and, as we've heard, a systemic -- continued --
19 that would be to asymptomatic (inaudible) and therefore
20 being contagious to those outlets. And it would be

1 very important to understand even if they had any data
2 from Health (inaudible) in terms of people who're
3 already vaccinated at the rates (inaudible) situation.

4 **DR. ARNOLD MONTO:** Let's keep the second part
5 of your question, which we had problems hearing anyway,
6 to the discussion before we get to the voting question.
7 Because we're going to want to have a second round of
8 discussions before we get to the voting question. So
9 is there anybody from FDA who wants to address the
10 issue of how the unblinding issue could affect the BLA?

11 **MR. MICHAEL KAWCZYNSKI:** Anyone? Dr. Gruber?
12 Dr. Gruber, let's just make sure that we unmute you.
13 There we go.

14 **DR. MARION GRUBER:** I know. It took me a
15 minute. I just wanted to say that starting with a
16 general comment that, of course, the gold standard for
17 doing phase 3 studies to demonstrate the safety and the
18 efficacy of a product is by randomized controlled
19 trial, ideally the placebo-controlled study. And this
20 is why, from a regulatory perspective, of course, we

1 would welcome continuing the placebo-controlled follow
2 up for as long as feasible, recognizing the
3 complexities thereof. And that was, I think, very
4 nicely discussed by Dr. Goodman this morning.

5 So we would of course be looking at
6 potentially losing longer term safety follow up. But
7 realizing the gravity of the pandemic, and if we really
8 looking at having to think about other designs and
9 modifications of the protocol, we would be looking at
10 that and to see and make sure that we have sufficient
11 data regarding safety. I'm not that worried about
12 effectiveness, but regarding safety then to support the
13 BLA application. So, I think, if it's no longer
14 feasible to really keep the blind -- to really get
15 those data from a placebo-controlled efficacy study, we
16 would, of course, look at other approaches to get these
17 data. And I'll stop it here and, I think, perhaps Dr.
18 Fink wants to add to that.

19 **DR. DORAN FINK:** I actually don't have much to
20 add. I was trying to jump in, and the platform wasn't

1 letting me. It seems to be a delay, so nothing more.

2 **DR. ARNOLD MONTA:** Okay. Thank you. Dr.
3 Fuller? And let's try to keep to one-part questions
4 until we catch up at least. Dr. Fuller?

5 **DR. OVETA FULLER:** Yes, thank you. This is a
6 simple question. Risk assessment is going to be very
7 critical for uptake of the community. Was the placebo
8 including the LNT, or did it only have other materials?
9 So in other words, are the side effects that we've seen
10 in the limited amount of risk assessment, that's been
11 done in two months, due to only the spiked protein
12 because the placebo has the lipid material? Or is that
13 due to both the lipid and the spiked protein expression
14 and we don't know what the lipid does alone? This will
15 be really critical considering that most of the people
16 who are getting vaccinated have not yet seen multiple
17 exposures to the coronavirus. So what does that mean
18 for long-term effects that cannot even be looked at
19 right now because we just got this into people?

20 **DR. ARNOLD MONTA:** Okay. I don't know who

1 wants to take that. Dr. Krause?

2 **DR. PHILIP KRAUSE:** Just to answer quickly,
3 the placebo control was a saline control, so the
4 vaccine is being compared against a complete placebo,
5 not against the lipid. So the side effects that were
6 observed are due to the combination of the lipid and
7 the mRNA.

8 **DR. ARNOLD MONTO:** Okay.

9 **DR. OVETA FULLER:** So we have no idea what
10 putting a messenger RNA lipid vaccine into people does
11 long term? It's not been done before. And we're going
12 from 20,000 people who get this vaccine to millions who
13 get this vaccine, with a very limited amount of risk
14 assessment. Is that correct?

15 **DR. ARNOLD MONTO:** Dr. Krause?

16 **DR. PHILIP KRAUSE:** I apologize. I'd
17 accidentally muted you when I was trying to get off
18 here, and so I did not hear that question.

19 **DR. ARNOLD MONTO:** A limited database.

20 **DR. OVETA FULLER:** Yes, we have very little

1 information about what happens to people who get the
2 vaccine, and then subsequently get exposed to COVID-19.
3 Because we've only looked for two months, and that
4 didn't include -- it included the vaccine with a lipid
5 and the messenger RNA. So we don't even know what's
6 going to happen long-term to people who get these lipid
7 particles plus the vaccine. There's such a limited
8 risk assessment that I think the uptake in the
9 community is going to be fairly poor unless something
10 better is done.

11 **DR. PHILIP KRAUSE:** Pfizer may comment, but
12 there has been a number of other vaccines, that have
13 been mRNA vaccines, that have been studied where people
14 have gotten these lipids and have been followed for
15 considerably longer periods of time. Although, not the
16 very large numbers of people that you might be looking
17 for here. But perhaps we can give Pfizer an
18 opportunity to comment on that.

19 **DR. OVETA FULLER:** Also, we know that COVID-19
20 is a multi-organ disease, so it's not like some of the

1 previous lipid vaccines.

2 **DR. PHILIP KRAUSE:** Yup.

3 **DR. OVETA FULLER:** This is something we don't
4 know very much about the pathology of this coronavirus.

5 **DR. ARNOLD MONTO:** Dr. Jansen and then we'll
6 move on, please. I think you're muted.

7 **DR. KATHRIN JANSEN:** We actually have
8 evaluated what happens after -- when individuals are
9 being exposed by COVID-19 in our last study. So while
10 we have relatively few cases of individuals that had
11 (inaudible) interactions with COVID-19, nevertheless,
12 those individuals showed, as we saw, a much lower
13 profile of severity comparing to the many other -- the
14 162 individuals that received placebo.

15 The other point I would make, is that we have
16 stated multiple times that we will follow our trial
17 participants up to the end of the study, which is
18 planned to last for the full duration of 24 months.

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

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

1 **DR. ARNOLD MONTO:** Dr. Offit?

2 **DR. PAUL OFFIT:** Okay. Thanks. My question
3 is for Bill from Pfizer. I'm worried about the severe
4 anaphylactic reactions for this reason. We don't know
5 the details of those two cases. We don't know
6 specifically what it was they were allergic to or what
7 their history with severe allergies was, we just know
8 that they carried EpiPens. The public health people in
9 the UK said if you had a history of severe allergies,
10 you can't get this vaccine. Similarly, Moncef Slaoui
11 here, head of Warp-Speed, said the same thing. If you
12 have a history of severe allergies, you can't get this
13 vaccine.

14 There are tens of millions of people in this
15 country who carry EpiPens with them -- because they
16 have peanut allergies, because they have egg allergies
17 -- who are going to believe now that they can't get
18 this vaccine. That's a lot of people.

19 So what I would suggest is first we need to
20 drill down on those two people in the UK. But I think

1 more importantly, Dr. Gruber, you had said that there
2 were no cases of severe allergy in your trial. Did you
3 exclude people with a history of severe allergy?

4 That's question one.

5 **DR. WILLIAM GRUBER:** Let me address question
6 one, and then I think maybe what I'll do, Dr. Offit, is
7 defer to our head of safety at Pfizer who can describe
8 more about what we know about the cases that occurred
9 in the UK and then the nature of our plans for moving
10 forward. And perhaps we can even include the
11 regulatory view.

12 So the nature of what was actually excluded
13 from the trial was really restricted to those
14 individuals who had had a severe allergic reaction to a
15 vaccine -- any vaccine previously. Or if, obviously,
16 during the course of the trial they'd gotten the first
17 dose and they had a significant type 1 hypersensitivity
18 response, then that would preclude giving a second
19 dose. And we did not encounter that circumstance in
20 the trial.

1 The first circumstance, I don't know how many
2 people we actually screened out who'd had a prior issue
3 with having had an anaphylactic reaction to a vaccine,
4 but we didn't have to exclude anybody from getting the
5 second dose. So as I said, at least during the course
6 of the trial, we have not seen anything that alerted us
7 to a safety signal associated with the vaccine or
8 potential for anaphylaxis. But maybe what I can do is
9 -- yeah. Go ahead.

10 **DR. PAUL OFFIT:** So Bill, what I'm asking is
11 this. Do you know whether there were people in the
12 trial who were in the vaccine group who had a history
13 of severe anaphylaxis, period, not necessarily to a
14 vaccine. Or if they had a history of carrying an
15 EpiPen? Do you have those data?

16 **DR. WILLIAM GRUBER:** Yeah. Let me ask Dr.
17 Caubel to share with you what we do know in terms of
18 the nature of pre-existing allergic conditions and the
19 outcomes in the trial. To my knowledge, we didn't have
20 anybody that had had a prior history of anaphylaxis.

1 But let me ask Dr. Caubel to actually share with you
2 the information that we do have.

3 **DR. PATRICK CAUBEL:** Good afternoon. I'm Dr.
4 Patrick Caubel. I'm the head of safety here for Pfizer
5 and also the Chief Safety Officer for Pfizer.

6 Actually, we know more about these two cases that
7 occurred in the UK, so let me give you more detail
8 about these two cases.

9 So these two cases, in fact, were reported in
10 the UK from December 8, so which means -- because they
11 have the vaccination campaign in the UK. So the same
12 day, 6,000 people were vaccinated, and all these
13 vaccinations were performed in hospital settings
14 because the primary target for the vaccination in the
15 UK are healthcare providers. In fact, it happened that
16 these two subjects were not only -- as I say,
17 healthcare workers, they were 49 and 40 years old. The
18 first subject, in fact, had a medical history of
19 serious allergic reactions, so he had a severe allergic
20 reaction with anaphylaxis.

1 But not following drugs, she had, in fact,
2 food allergy with allergy to eggs and to cheesecake and
3 lemon and lime. But in fact, the last episode of the
4 cheesecake led her to the emergency room where she
5 needed to have resuscitation and administration of
6 epinephrine. So in fact for research patients of the
7 case of anaphylaxis occurred only two minutes after the
8 vaccination. She required an administration of
9 epinephrine, corticosteroids, and finally the patient
10 fully recovered.

11 The second patient, in fact, was a little bit
12 milder, but it was a patient who also had a medical
13 history of allergy to drugs. We don't which drug yet,
14 but she was under the care of an immunologist before
15 receiving the vaccination. So it was mostly, in this
16 case, shortness of breath, (inaudible), and finally she
17 required also the administration of epinephrine.

18 Again, these two cases occurred the first day
19 of vaccination. We have also a third case that was
20 reported the second day of vaccination, which was not

1 really a case of anaphylaxis. It was just a patient
2 who developed a (inaudible). She had some skin
3 redness. She was given (inaudible) and antihistamines,
4 and then she went back into a similar mode and finally
5 also fully recovered. At this stage, we don't think
6 that this case developed (inaudible).

7 **DR. PAUL OFFIT:** Can I ask Dr. Gruber how FDA
8 is going to respond to these reports?

9 **DR. PATRICK CAUBEL:** Do you want to answer or
10 --

11 **DR. ARNOLD MONTO:** I think he was speaking of
12 Marion Gruber. I think this is the FDA --

13 **DR. PAUL OFFIT:** I was speaking of Marion
14 Gruber.

15 **DR. MARION GRUBER:** Okay. I just also wanted
16 to say I am not aware that we are related, Bill, so we
17 had that discussion before. So yeah. So first of all,
18 we have been in communication with the Medical
19 Healthcare Products regulatory Agency, MHRA, in the
20 United Kingdom who made us aware of these two cases of

1 anaphylactic reactions. And what was just reported
2 about what is known about these was also transmitted to
3 us.

4 At this point, we are seeking further
5 information from the MHRA under our confidentiality
6 agreement to learn more about this and to really tease
7 that out. I also wanted to remind the Committee -- and
8 I think Dr. Wollersheim really presented that nicely --
9 of the safety analysis that the FDA independently
10 conducted by doing standard medical queries. And we
11 looked at events that could potentially include or
12 present allergic reactions. We found a slight
13 numerical imbalance there that Susan reported and
14 presented on.

15 I want to stress that none of these were
16 considered to be serious. None of them received
17 epinephrine injections, and none of these events
18 occurred in the immediate post-vaccination period.
19 That being said, over the last couple of weeks, we have
20 been working with Pfizer on generating fact sheets and

1 prescribing information.

2 And we -- FDA and the sponsor -- we agreed for
3 the fact sheets and the prescribing information for
4 this vaccine to include information under
5 contraindications and under warnings. So the fact
6 sheets and the prescribing information will state that
7 this vaccine should not be administered to individuals
8 with known history of severe allergic reactions to any
9 components of Pfizer's COVID-19 vaccine. And the
10 warning statement will say, appropriate medical
11 treatment used to manage immediate allergic reactions
12 must be immediately available in the event an acute
13 anaphylactic reaction occurs following administration
14 of the Pfizer COVID-19 vaccine.

15 So that has made it already in these fact
16 sheets and prescribing information weeks ago. We,
17 however, will consider any additional information that
18 we're going to be receiving over the next couple of
19 days, and factoring this into our decision making to
20 decide whether the fact sheets and the prescribing

1 information may need to be further revised to include
2 additional precautionary statements. And I'll leave it
3 here. Thank you.

4 **DR. PAUL OFFIT:** Marion, could I just offer
5 one thing and then I'll stop? If you look at the
6 components of that vaccine, which has probably the
7 longest chemical name of any vaccine I've ever seen in
8 terms of that lipid, nobody's going to look at that
9 name and think, you know, I'm allergic to that.

10 So here's what I would suggest, moving
11 forward, just as a practical solution. I think a study
12 should be done by Pfizer or whomever where you take
13 people who have a known history of severe egg allergy,
14 a known history of severe peanut allergy and given them
15 these vaccines under careful observation to prove that
16 this is not going to be a problem for them. Because
17 you're talking about tens of millions of people who are
18 going to not get this vaccine because of the comments
19 that were made both by the UK and both by Moncef Slaoui
20 here. I just think it's a practical solution because

1 this issue is not going to die until we have better
2 data.

3 **DR. ARNOLD MONTO:** Okay. Let's -- Marion, do
4 you have anything to add? And then we'll go to Dr.
5 Meissner.

6 **DR. MARION GRUBER:** Yeah. Just in response to
7 that, I hear your suggestion, Paul, and I think so did
8 Pfizer. We, however, need to decide on the issuance of
9 an EUA the next couple of weeks and/or days -- days
10 more than weeks. And we are looking at the question
11 whether the benefits outweigh the risks, you know --

12 **DR. PAUL OFFIT:** I agree. The benefits -- I
13 mean, I'm fine with that.

14 **DR. MARION GRUBER:** -- not determine if this
15 product is safe and effective for the purpose of
16 licensing it. I just wanted to remind you that.

17 **DR. PAUL OFFIT:** I agree.

18 **DR. MARION GRUBER:** Thank you.

19 **DR. ARNOLD MONTO:** Okay. Let's move on to Dr.
20 Meissner. You're muted.

1 **DR. CODY MEISSNER:** First of all, in terms of
2 our current discussion of anaphylaxis, remember that's
3 recommended for any vaccine that's administered. The
4 vaccinator should be able to handle anaphylactic
5 reaction from any vaccine. It wouldn't be just for a
6 COVID-19 vaccine, number one. And, Paul, I'm not sure
7 that an allergic reaction to ovalbumin would have much
8 bearing on the risk of a reaction to this vaccine.

9 Number two, going back to the pregnancy
10 discussion, my concern is that during pregnancy there's
11 a great deal of replication, of DNA replication,
12 cellular replication that's occurring in the fetus.
13 And vaccinating a pregnant woman with this messenger
14 RNA gives me a little bit of pause. We certainly --
15 and I understand the response, but could there be a
16 retrovirus somehow around -- a migrant retrovirus and
17 reverse transcribe this RNA into the chromosome of the
18 baby? That is one thought.

19 The next point, I agree very much with Dr.
20 Mark Sawyer in his comment about a 16- and 17-year-old.

1 There are only 163 subjects who have been enrolled in
2 the randomized trial, and we have heard that the
3 inflammatory response is higher in younger people than
4 it is in the elderly. I think we need more information
5 before we think about that.

6 And then the final point I want to make -- and
7 thank you for your patience -- back to Dr. Gans, it's
8 so important -- an EUA -- we need this vaccine. We
9 need to do our very best to develop herd immunity. We
10 need this vaccine. But we need to move it from an EUA
11 to a BLA as soon as it satisfies the threshold that the
12 FDA will hold this vaccine to. But there are many
13 reasons to move it to a BLA, such as it will be
14 included in the vaccine injury compensation program if
15 the CDC recommends it for adults and for children. So
16 I think we need to move in that direction. Thank you.

17 **DR. PAUL OFFIT:** Cody, I just want to say one
18 thing. I'm not talking -- I completely agree with you,
19 but I don't think --

20 **DR. ARNOLD MONTTO:** Very quickly.

1 **DR. PAUL OFFIT:** Okay. Quickly. I just think
2 that I'm talking about perception more than reality.
3 With those two statements out there -- that people who
4 have severe allergic reactions shouldn't get this
5 vaccine -- I think we just need to offer people some
6 solace that this is not going to be a problem for them.

7 I'm not saying this should stop us moving
8 forward at all with approving this vaccine. I'm just
9 saying, when it rolls out there, this is going to be an
10 issue, and we need to have some data that we arm
11 ourselves with so we can address it. That's all. I'm
12 not saying it's biologically sound. I'm just saying
13 that we need data to argue against -- any more than
14 vaccines cause autism was biologically sound. We just
15 need data to address it. That's all I'm saying.

16 **DR. CODY MEISSNER:** I agree.

17 **DR. ARNOLD MONTO:** Thank you. I think we
18 agree, perception is everything. Facts may be
19 important, but perception drives a lot of decisions.
20 Dr. Annunziato?

1 **DR. PAULA ANNUNZIATO:** Thank you. I have a
2 question for Dr. Bill Gruber. Bill, in your study can
3 you describe for us how the non-solicited adverse
4 experiences that were collected up until one month
5 after dose two were collected? In other words, was
6 there active surveillance for those events as well?

7 And then for your plans for under an EUA, if a
8 subject is unblinded and vaccinated, could you also
9 just reiterate for us what safety surveillance you will
10 be conducting in that situation?

11 **DR. WILLIAM GRUBER:** Yes, thanks, Paula. I
12 may call upon Nick Kitchin to help with some of the
13 details. He's the clinical lead for the program. But
14 the e-diary information was solicited and collected for
15 the first seven days, and then investigators were
16 encouraged to potentially collect adverse events but in
17 an unsolicited fashion for the first month after
18 administration. And then, I'm sorry, the second
19 question was what, again?

20 **DR. PAULA ANNUNZIATO:** Was what are the plans

1 for safety collection for the subjects who may opt to
2 be unblinded and then vaccinated after the EUA is
3 issued?

4 **DR. WILLIAM GRUBER:** Right. So I'm going to
5 defer to Dr. Kitchin who's helped put together our
6 latest amendment that deals with management of the
7 placebo recipients to address both questions, but
8 particularly the second one. Dr. Kitchin?

9 **DR. NICHOLAS KITCHIN:** Thank you, Bill. This
10 is Nick Kitchin from Pfizer. Can you hear me okay?

11 **DR. PAULA ANNUNZIATO:** Yes.

12 **DR. NICHOLAS KITCHIN:** Okay. Yeah. So with
13 respect to elicitation of adverse events and
14 specifically the reactogenicity type events that you
15 were asking about for subjects that were not in the
16 subset, they were elicited in the same way as other
17 adverse events. There weren't specific leading or
18 directed questions to elicit specifically for those
19 events, and that's why you typically would expect to
20 see them -- seen at a lower rate when reported as

1 adverse events rather than when it's actively solicited
2 daily for seven days immediately after vaccination in
3 the diary. So for reactogenicity, the data from the
4 subset gives us the best picture of the profile.

5 With respect to our plans for safety
6 surveillance for subjects that would be receiving the
7 BNT162b2 as a result of being eligible, for example,
8 under EUA, our intention is to use the same safety
9 surveillance as those not in the subset. So we would
10 not use e-diaries for those subjects that were moving
11 across, but they would have all adverse events elicited
12 for one month after what would be their fourth
13 vaccination but their second active dose and six months
14 post previous adverse.

15 **DR. WILLIAM GRUBER:** I might just add, Paula,
16 as you can well recognize, 8,000 subjects set for
17 common events that are being solicited routinely like
18 fever, headache, fatigue, the chills. We probably have
19 -- in fact, I'd argue we do have -- sufficient
20 precision on those common sorts of events. So it makes

1 less sense, I think, to essentially say come back and
2 to also now have to essentially do the e-diaries again.
3 I don't think it really will add value, and it
4 potentially could mitigate against individuals wanting
5 to participate.

6 **DR. PAULA ANNUNZIATO:** Sure. Thank you.

7 **DR. ARNOLD MONTA:** Dr. Lee?

8 **DR. JEANNETTE LEE:** So my question is really
9 for Pfizer about their blinded follow up, or unblinding
10 the placebo recipients. And I think one question I
11 have is why in your unblinding is there not
12 incorporated some sort of scale, or whatever you want
13 to call, for severity, rare, or risk factor either
14 based on age, co-morbidity or so forth? Instead,
15 you're relying on local and national guidelines, and I
16 can tell you they're going to vary state by state,
17 county by county here. And you're going to have a
18 hodge-podge. So it seems if you were going to
19 incorporate something about the risk factors, you might
20 have a little bit more consistency on the follow up for

1 various risk groups. And I didn't know if Pfizer had
2 considered that at all.

3 **DR. ARNOLD MONTA:** I'm glad you asked this
4 question because it moves us back to the discussion
5 topic. Can we have Pfizer respond please?

6 **DR. KATHRIN JANSEN:** Yes, could I please ask
7 Dr. Anezden (phonetic) to explain in detail how we are
8 going to follow vaccine recipients over time?

9 **DR. JEANNETTE LEE:** No, it wasn't a question
10 of follow up. It was a question of identifying when
11 somebody would be eligible to be unblinded that would
12 include their risk factors, not just local and national
13 criteria because they will vary tremendously in this
14 country and I suspect elsewhere.

15 **DR. KATHRIN JANSEN:** Okay. That may be Dr.
16 Gruber. Please continue.

17 **DR. WILLIAM GRUBER:** Yeah. And again, I may
18 call upon Nick to help with this, too. We obviously --
19 as you heard this morning from Dr. Goodman, this is an
20 incredibly challenging area for us to put forward the

1 right path. We want to be contentious about providing
2 vaccine to individuals who would qualify. So the onus
3 is on us to take the emergency use authorization and
4 the recommendations to heart. If you happen to live in
5 an area where in fact you are eligible, we'd be hard
6 pressed to say, "Well, because we've taken a national
7 recommendation, you don't fit because we're just going
8 by the national recommendation."

9 I think we have yet to see how that will work
10 in practice, but it is our intent to try to do what we
11 think is right to follow the guidance and local
12 recommendation. We're also, obviously, facing this
13 issue, as you can perceive, not just on a national
14 level but internationally since we have a number of
15 countries involved. So we have to look at each of
16 those issues and weigh them to make that type of
17 decision. I don't know, Nick, if you have anything
18 else to add to that.

19 **DR. ARNOLD MONTO:** I know that you will be in
20 discussion, Bill, with FDA about these as well.

1 **DR. WILLIAM GRUBER:** Right. Right. I mean,
2 that's clearly, in part, why I'm glad this is a topic
3 for discussion.

4 **DR. ARNOLD MONTO:** Exactly.

5 **DR. NICHOLAS KITCHIN:** Sorry, Bill. Yeah.
6 This is Nick Kitchin again from Pfizer just to add. So
7 yes, our intention, at least initially, we would
8 anticipate in terms of the recommendations following
9 the initial ACIP recommendations. So we will provide
10 specific guidance -- more specific than applying to
11 local and national recommendations. But certainly to
12 start with, I imagine, it would follow how ACIP would
13 recommend allocation of the initial doses.

14 **DR. ARNOLD MONTO:** Thank you. And as we go
15 forward, please mainly pay attention to the discussion
16 items because, as many have stated, we'd like to move
17 to a BLA submission promptly or as smoothly -- I won't
18 say promptly -- as smoothly as possible. And the
19 answer to some of these issues is going to affect that.
20 So Dr. Moore?

1 **DR. PATRICK MOORE:** Hi, yes. One question
2 that addresses these two discussion items, I find is
3 really, really central, and important, is that FDA did
4 not ask in its guidance and Pfizer has presented no
5 evidence in its data today that the vaccine has any
6 effect on virus carriage or shedding, which is the
7 fundamental basis for herd immunity. And so even
8 though the individual efficacy of this vaccine is very,
9 very, very high, we really, as of right now, do not
10 have any evidence that it will have an impact, social-
11 wide, on the epidemic.

12 So I would like to ask, before the unblinding,
13 that Pfizer seriously consider performing nucleic acid
14 assays on the vaccinees and the placebo patients. I
15 don't know whether the point estimate for shedding is
16 going to be high enough that you're going to see a
17 significant difference, but at least one should try
18 because that's one piece of data that we're going to
19 completely lose once the unblinding occurs.

20 **DR. ARNOLD MONTA:** Let me just interrupt and

1 tell you that these questions are being addressed by
2 CDC in the observational studies as we go forward,
3 because of sample size issues and a lot of issues that
4 are not possible when you're not looking at households
5 where transmission will take place.

6 **DR. PATRICK MOORE:** Right. And with the CDC,
7 they certainly would like to have a toe-in to the
8 vaccine companies to be able to help perform these very
9 types of studies if at all possible. And so that
10 industry-CDC collaboration would be tremendous. But it
11 is so important as of right now as to whether or not
12 this vaccine can have an impact on the non-vaccinated
13 persons who are at risks for acquiring infection. We
14 don't know that.

15 **DR. ARNOLD MONTA:** Dr. Jansen, you want to
16 comment?

17 **DR. KATHRIN JANSEN:** Yes, we actually are
18 looking into this to do precisely that. Not just to
19 look for prevention of asymptomatic infection but also
20 doing the PCR testing to look for virus equation -- or

1 prevention of virus acquisition.

2 I may remind, though, that we have data, not
3 from humans but from or non-human primate study, that
4 would argue that the vaccine does prevent infection.
5 We have seen that it prevents infection of the lung,
6 and we have also seen some evidence that it has a more
7 transient -- that the virus is more transiently
8 detected in the vaccinated animals compared to the
9 control animals.

10 **DR. ARNOLD MONTO:** Okay. We're going to have
11 move on. Dr. Kim?

12 **DR. DAVID KIM:** I think this relates to
13 discussion item number two. Vaccine efficacy data
14 might not be evident for HIV positive study
15 participants given they're small number, but presumably
16 preliminary vaccine safety data are available. After
17 all, trial participants were enrolled in October, and
18 EUA application was made on November 20. Would Pfizer
19 please comment are there any updated information, since
20 people with HIV infection, or other conditions that are

1 stable and meet the criteria for vaccination, will be
2 standing in line for the vaccine in short time?

3 **DR. KATHRIN JANSEN:** Bill, could you please
4 comment?

5 **DR. WILLIAM GRUBER:** Yeah. So obviously, we
6 included individuals, as I mentioned and Dr. Jansen
7 mentioned, with HIV, HCV, and HBV if they had stable
8 infection. And we included additional evaluation
9 beyond the core group that we're looking for solicited,
10 non-solicited adverse events. So within the population
11 that we have so far, we have -- within the 38k database
12 -- about 120 of these and 196 in the total 43,000-plus
13 database.

14 So we're getting to a point where we will have
15 enough of those individuals to look at, and we would
16 propose, obviously, doing that in association with the
17 filing that goes into BLA, if not sooner. We just need
18 to have enough of them. As you may know, we amended
19 the protocol in flight, so there was a little bit of
20 delay. That was really the only population apart from

1 the 12- to 15-year-olds that were a little bit delayed
2 in terms of enrollment in the trial because of the way
3 that was staggered. But yes, it is our intent to
4 essentially have more information on that population.

5 **DR. ARNOLD MONTA:** Okay. Dr. Pergam?

6 **DR. STEVEN PERGAM:** Thanks. So I had a
7 question about since this vaccine is going to be rolled
8 out through the EUA, there's going to be a fair number
9 of people who might have access the vaccine who've had
10 previous COVID exposure, may not know they've been
11 positive, or have known history of positivity. There's
12 limited data in the trial, at least, because of
13 enrollment, for people that are previously positive.

14 Two questions kind of relating to both of
15 these things is, thinking about potentially looking at
16 side effects within the group that potentially gets
17 this, is there an increase enhancement of the side
18 effects? It didn't look like it in the initial data
19 you showed.

20 But looking at that a little more carefully in

1 people that have known prior positivity. And then
2 secondarily, I'm curious what are you going to do with
3 patients in the clinical trial who did develop COVID?
4 Are they going to also be offered the vaccine, just as
5 a question for Pfizer?

6 **DR. ARNOLD MONTO:** Dr. Jansen, I think you're
7 muted.

8 **DR. KATHRIN JANSEN:** I'm sorry. Can you hear
9 me now?

10 **DR. ARNOLD MONTO:** Yes.

11 **MR. MICHAEL KAWCZYNSKI:** Yes, we can hear you
12 Kathrin.

13 **DR. KATHRIN JANSEN:** Yeah. So I think we may
14 have lost the link.

15 **DR. ARNOLD MONTO:** No, we can hear you.

16 **DR. KATHRIN JANSEN:** Oh, you now can? Oh,
17 good. Okay. Thank you. I would like to take the
18 first part of the question and then have Dr. Gruber
19 comment on the second one. So while we have excluded
20 individuals with known COVID-19 -- so meaning PCR

1 confirmed COVID-19 -- we actually do have in our trial
2 individuals that are seropositive. In other words,
3 they were prior exposed to COVID-19. And so our
4 estimate is about 2 to 3 percent of the individuals who
5 are participating in our trials were seropositive at
6 baseline. Bill, if you want to take the second?

7 **DR. WILLIAM GRUBER:** I think the second
8 question was about the nature of the safety profile in
9 individuals that had evidence of a prior SARS-
10 coronavirus infection or were PCR positive at the time
11 they adhered to their first or second dose. And the
12 bottom line is -- and this has been submitted to the
13 FDA -- if you just separate out that group -- and,
14 again, it's a small proportion of the total population
15 but still fairly sizable. When you look at the total
16 group, we had, I guess, well over 150, I think, in the
17 reactogenicity subset and over 500 in the larger
18 database of looking at unsolicited adverse events.

19 And when you compare that to the individuals
20 that had no prior evidence of infection, it looks

1 basically the same. The point estimates actually look
2 a little bit better, but obviously within the realm of
3 statistical significance, we can't make much of that.
4 But clearly these individuals did not fare worse from
5 the vaccine. And I think we've not seen anything in
6 terms of, as those individuals had tracked through the
7 study, a particularly high attack rate or severe
8 disease that would suggest to us that there's a problem
9 in that group.

10 **DR. ARNOLD MONTO:** Okay. Dr. Kurilla, one
11 part only.

12 **DR. MICHAEL KURILLA:** Thank you. If Pfizer
13 were to receive an EUA and you lost all of the
14 participants in the trial who were healthcare workers,
15 would the remainder still allow you to have -- be
16 adequately powered to carry on? That would be my first
17 question. The other --

18 **DR. ARNOLD MONTO:** I said one part only.

19 **DR. MICHAEL KURILLA:** Well, I'm just going to
20 put my hand up again, then, Arnold.

1 **DR. ARNOLD MONTO:** Then you go to the bottom
2 of the queue. Okay. Please, that's an important
3 question.

4 **DR. KATHRIN JANSEN:** So I would like to have
5 Bill address this, and then we may also need help from
6 Dr. Ken Currie (phonetic).

7 **DR. WILLIAM GRUBER:** Yeah. Thanks, Kathrin.
8 So I think it's our current estimate, as best we can
9 determine, that about maybe 20 percent or something
10 north of that may fit into the health provider
11 category. However, that still leaves, of course, 80
12 percent, given the highest attack rate, presuming that
13 those placebo recipients remained in the trial for a
14 while longer. We know that we would be in a good
15 position, which is particularly sad given the high
16 attack rate, that we could still track out and get a
17 good measure both for safety and efficacy over the
18 longer term.

19 I think the bigger challenge really relates to
20 how quickly the CDC moves forward to the additional

1 tiers and how quickly those populations, again, get
2 encompassed with an emergency use authorization and
3 would be covered if we conform to the plan that we've
4 outlined. But it's my sense -- and I'll ask Ken
5 Currie, who's our head of stats just to comment on
6 this. But it's my sense that, yes, even with 20
7 percent loss, we won't have that much difficulty. If
8 we were sort of in the 50 to 60 percent efficacy
9 category, that could potentially prove more
10 challenging. I don't know. Dr. Currie.

11 **DR. KEN CURRIE:** Hi, this is Ken Currie. I
12 lead the vaccines stats for Pfizer, and those answers
13 are correct. The study is well positioned to continue
14 to accrue more cases and to be able to answer some of
15 these questions with more precision.

16 **DR. ARNOLD MONTO:** Thank you. Dr. Hildreth?
17 And please, let's keep it mainly to the discussion
18 items.

19 **DR. JAMES HILDRETH:** Thank you, Dr. Monto. My
20 question is for Pfizer, and it relates to the

1 recruitment of minorities into the study, which is
2 relevant to number two. My understanding is that the
3 minorities were recruited fairly late in the process.
4 Do we have an adequate follow up to that group compared
5 to the majority of the participants? The two-month
6 median is what I'm referring to. Can someone address
7 that for me? Thank you.

8 **DR. KATHRIN JANSEN:** I'd like Dr. Gruber to
9 comment on the demographics.

10 **DR. WILLIAM GRUBER:** Thanks, Kathrin. Let me
11 correct one, perhaps, incorrect assumption, which is
12 that we actually from the very start were focused on
13 targeting in recruitment from racial and ethnic
14 minorities. What we decided to do, after we proved
15 successful in terms of the overall success in getting
16 to 30,000 and deciding how to move forward, we decided
17 at that point, given that we'd had some success but we
18 wanted to have more, we actually informed sites that to
19 preferentially, beyond what they'd already done, in any
20 new recruitment that they provided was really targeted

1 to minority communities. So it was a fact that we
2 started from the very beginning, but then we further
3 enriched at the end.

4 So I would say you can feel confident that
5 minority communities were recruited throughout, perhaps
6 with a bit more towards the end. But I'm convinced and
7 I think the data supports that we had individuals from
8 those communities followed for a long enough time,
9 certainly to demonstrate efficacy, within the limits,
10 of course, of some of the groups having a smaller
11 number of total cases.

12 But it's not the right assumption that we
13 didn't start from the very beginning. That was a key
14 ingredient we advertised, both on our website and
15 everywhere else that we could, about our intent to
16 bring people of color into the trial.

17 **DR. ARNOLD MONTA:** Okay. Dr. Levy on the
18 discussion items, please.

19 **DR. OFER LEVY:** Hi. My webcam isn't working.
20 Can you hear me?

1 **DR. ARNOLD MONTO:** We can hear you. We don't
2 need to see you.

3 **DR. OFER LEVY:** Okay. Fair enough. So my
4 question is, in terms of gaps, this is a very big
5 picture question. If we want to have a safe and
6 effective vaccine deployed and make a huge dent in this
7 pandemic, eventually what will be needed is high
8 vaccine penetrance, right? 60, 70, 80 percent of the
9 vulnerable population immunized. Would we
10 realistically get there -- given the structure of the
11 United States and the tendency of adults in the United
12 States -- would we realistically get there without a
13 pediatric vaccine?

14 And I realize there are all sorts of
15 challenges and hurdles and counterarguments, but I'd be
16 interested to hear from FDA and Pfizer if they've given
17 long-term thought to the ultimate endgame here.
18 Because if there were a safe and effective pediatric
19 vaccine, obviously the infrastructure for vaccine
20 delivery and penetration of vaccine is very favorable

1 in that regard. Thank you.

2 **DR. ARNOLD MONTO:** Let's keep the answer
3 relatively short. That's a very big question. So
4 Pfizer, pediatric plans?

5 **DR. KATHRIN JANSEN:** Bill, you want to take
6 that?

7 **DR. WILLIAM GRUBER:** Sure. I'm happy to. We
8 obviously recognize the importance of moving into the
9 pediatric population. I touched base on this briefly
10 in the main presentation.

11 We thought so strongly about this that, as you
12 know, we obviously are trying to seek an indication in
13 16- to 17-year-olds, which we think is supported by
14 what you've heard from us and the FDA. In addition to
15 which, we already have 12- to 15-year-olds in the
16 trial. Which not only informs the ability to move
17 forward in that group where we're going to recruit
18 2,000 individuals, but actually also preliminary
19 information which was submitted to the FDA from the
20 first 100 individuals looks quite good compared to the

1 reactogenicity we're seeing in 18- to 25- and 18- to
2 55-year-olds.

3 So we're already embarking on that path, and
4 then it's are intention, if all continues to go well --
5 and so far it has from a safety point of view -- to
6 move down to 5- to 11-year-olds. Based on the nature
7 of the data becoming available, the completion of where
8 we are with the 12-to-15-year-olds, we anticipate that
9 that will commence by April of 2021. And the idea
10 would be to start there and then, as is typical for
11 pediatric trials, once we have documented safety in
12 that group move down.

13 It's our expectation, although I'm encouraged
14 it might not necessarily be the case, that we may need
15 to do dose ranging in the 5- to 11-year-olds. We
16 thought that might happen in the 12 to 15, but they
17 seem to tolerate the 30 microgram well. But once we
18 move down to 5 to 11, we'll be very judicious just as
19 we were in the 12 to 15, doing small sample of
20 sentinels and then working our way down. And then,

1 ultimately, we propose to move down in younger age
2 groups below five years of age. And again, we'd do
3 that in a judicious fashion.

4 **DR. ARNOLD MONTO:** Dr. Krause?

5 **DR. PHILIP KRAUSE:** I just want to comment, if
6 I can, on behalf of FDA, and that is Pediatric Research
7 Equity Act actually requires there to be a plan for
8 evaluating products in pediatric patients and in
9 children. But, of course, there's also a requirement
10 that you can't do research in children unless you have
11 a prospect of benefit. And so, you can't do these
12 studies initially in children, but I think moving
13 quickly now the benefit of the vaccine has been
14 established is a very reasonable thing to do. And
15 that's something that we'll be working with the sponsor
16 on. I'm wondering, while I have the floor, though,
17 that I might drive things back towards the actual
18 discussion items a little bit more.

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

20 **DR. PHILIP KRAUSE:** And in that regard, we

1 heard this morning from Dr. Goodman suggestions that we
2 might look towards, instead of an unblinding when
3 people become eligible for receipt of vaccine outside
4 of a trial, a crossover design in which blinding is
5 maintained. And of course, if one is to do something
6 like that, that is the last opportunity in which one
7 might be able to draw serum on people in the trial in
8 order to determine whether they've seroconverted, which
9 would then give a chance to look at the question raised
10 earlier as to whether or not people have gotten
11 infected while one still can compare a vaccine versus
12 placebo.

13 So I don't know if anyone at Pfizer is
14 prepared to opine on this, but do these seem like
15 reasonable things for you to do? Instead of unblinding
16 to do a crossover when people become eligible for a
17 vaccine. But also to draw serum on these individuals
18 before that happens to allow for this kind of
19 additional look at the last moment before placebos, in
20 essence, disappear and one then loses that opportunity

1 to compare also in the blood what happened to vaccinees
2 versus placebo recipients?

3 **DR. KATHRIN JANSEN:** I can take that first
4 question and comment. So we are fully planning to
5 actually do the analysis of vaccine protection against
6 asymptomatic infections very soon, as I noted, probably
7 at the beginning or very early in 2021. So we can take
8 under advisement to see if there is an opportunity or
9 value based on our routine serum sample that we do in
10 the participants anyway, if an additional blood draw
11 would be of value. And then for the blinding question
12 that you have, I would also give it back to Dr. Gruber
13 to comment.

14 **DR. WILLIAM GRUBER:** Yes, thanks, Kathrin.
15 Obviously, the considerations that were discussed by
16 Dr. Goodman have been front and center for us in
17 thinking about how we would move forward. We have
18 looked at the issue of a potential crossover. And
19 although there is some potential advantage, I think
20 some things that are being advertised may be sort of a

1 false premise. Once, for instance, individuals know
2 that they've received vaccine in both groups you sort
3 have essentially equalized them in terms of their
4 perception about whether they need to come in for
5 illness visits or not. So that's a challenge.

6 Deferral in the circumstances is not an option
7 for ACIP recommended groups, so that's a challenge in
8 terms of, obviously, solving for our ethical
9 obligations to vaccinate folks. There's also a
10 logistic approach.

11 As I mentioned, when we're enrolling 22,000
12 individuals, somebody has to be first in line. We
13 can't bring them all in on day one. So the idea was,
14 okay, with the EUA authorization, we can kind of bring
15 them in as that authorization and recommendation
16 expands. On the other hand, if you're talking about a
17 crossover where everybody is now going to have to come
18 in for two additional visits, you're talking about --

19 **DR. PHILIP KRAUSE:** Well, of course, it'd be
20 twice as many people. Of course, I think that what he

1 proposed was you'd only bring them in for crossover as
2 they otherwise become eligible.

3 **DR. WILLIAM GRUBER:** Good point. Forty four
4 thousand individuals would have to be brought in for
5 two additional visits, and those individuals that are
6 receiving vaccine would have to do this -- in essence,
7 be reconsented, essentially agree to come back for two
8 additional visits. Now, I heard Dr. Goodman
9 appropriately saying that some of these people -- and
10 we would hope that this would be the case if you chose
11 that path -- would do this out of the goodness of their
12 heart. But it does mean that they have to come back
13 for an otherwise unintended -- or a visit back to a
14 medical facility -- and the risks of exposure just from
15 that sort of experience in and of itself.

16 So the notion of these -- what we're concerned
17 about is that when we add this additional piece of work
18 that these individuals have to not only agree to but
19 provide informed consent for two additional visits for
20 both groups, that creates -- potentially from their

1 perspective, maybe the risk-benefit equation isn't such
2 a great idea for me, I'm going to just go ahead and
3 wait my turn and get the vaccine.

4 So those are things -- you know, the logistics
5 are something that are not trivial because we've got to
6 bring in basically a lot of people to be vaccinated.
7 And if we now add this to 88,000 visits, that's a
8 challenge.

9 Obviously, we've enrolled 44,000 people and
10 done 88,000 visits, but it took us a number of months
11 to do that. So if the notion is trying to strike the
12 right balance between getting people timely vaccination
13 when their eligible, there are some advantages to be
14 gained by just having to vaccinate the placebo
15 recipients.

16 **DR. PHILIP KRAUSE:** Of course, one of the
17 questions, and the way this is being put to the
18 Committee, is that if you can't do this and you then
19 lose the ability, for instance, to look more directly
20 at the ratio of efficacy and already even in the

1 crossover design lose the ability to do in many people
2 longer term follow up for safety -- and, of course, as
3 it is the people who are at highest risk who are those
4 who are also going to be suggested for earliest
5 vaccination. And so you'll then lose the ability in
6 continuing your trial to look at further impact on
7 severe disease.

8 What are the ways in which the inability to
9 get that information from continued follow up in the
10 trial will be addressed? How can, well, the American
11 people as well as the FDA and the CDC recommending
12 bodies be sure that we have enough information to
13 proceed with the vaccine, and understand exactly what
14 the longer-term safety, durability, and efficacy
15 against severe disease is?

16 **DR. WILLIAM GRUBER:** I mean, those are all
17 reasonable questions and ones that we're wrestling
18 with. But I think we've already sort of addressed the
19 common reactogenicity. I don't think there's
20 likelihood that you'll get much more precision related

1 to that. So if you set that aside, there is this
2 period of time where we would expect we would continue
3 to be able to collect information as the EUA rolls out
4 and those individuals remain.

5 As I said, maybe 20 percent of the population
6 would be vaccinated, and it will still take some time
7 to do that. So I imagine we might be able to do that
8 within one or two months. That's still -- even within
9 that population, the time where we would be continuing
10 to collect cases.

11 As far as safety is concerned, the same thing
12 applies. You still would have a proportion of these
13 individuals for looking for longer term events. As we
14 move farther and farther out, the likelihood that
15 you've got a vaccine related event, I think, becomes
16 diminishingly small.

17 Part of the reason I think we were enamored
18 with the idea of a median follow up of two months, is
19 it's our perspective that if you're going to see
20 something specifically related to vaccine, it's more

1 likely to happen in that time span. And you've already
2 got a significant database to look at that.

3 And, of course, you don't lose the ability to
4 look at efficacy over the long period of time. Let's
5 suppose that all the placebo recipients ended up moving
6 over to the trial relatively quickly. One of the key
7 features is looking at durability of response, and you
8 can look comparatively at the newly vaccinated -- and I
9 think we heard this from Dr. Goodman this morning. You
10 can look comparatively at the newly vaccinated compared
11 to the previously vaccinated and determine whether or
12 not you're beginning to see those individuals that --
13 previous vaccinees, if their curve basically starts
14 sloping up and it becomes -- suggesting that you're
15 losing protection.

16 **DR. PHILIP KRAUSE:** Although that analysis was
17 based on a premise of blinded follow up.

18 **DR. WILLIAM GRUBER:** I'm sorry. I didn't hear
19 that last comment.

20 **DR. PHILIP KRAUSE:** I think the analysis that

1 was put forward by Dr. Follmann of the NIH was based on
2 a premise of blinded follow up, not of unblinded follow
3 up.

4 **DR. WILLIAM GRUBER:** Yeah. But I'm talking
5 about a circumstance where you would just be able to
6 compare the attack rates in the respective groups based
7 on the difference in terms of time as far as -- of
8 course, that's predicated on what's happening with the
9 pandemic.

10 It'd like nothing better than that the
11 pandemic had gone away if we did that. But I think
12 based on what I'm hearing from the experts, some of
13 whom we heard from today, it's our expectation over the
14 span of time we would plan to conduct this, that we
15 would badly be in a position where we would likely be
16 able to determine if in fact those attack rates for
17 those people who were more remotely vaccinated went up.

18 **DR. ARNOLD MONTO:** Okay. Going to have two
19 more questions, and then we are going to move into
20 discussion of our voting question. So Dr. Chatterjee

1 and then Dr. Cohn.

2 **DR. ARCHANA CHATTERJEE:** Thank you, Dr. Monto.
3 I'd like to address discussion item number two. Dr.
4 Gruber, in your presentation, slide number CC58 I
5 believe, you spoke about different studies that Pfizer
6 might be conducting. But I did not see long-term care
7 facility residents listed. They are obviously at high
8 risk because of which they've been prioritized to
9 receive the vaccine.

10 And the other one was inclusion of any
11 concomitant use trials, particularly with influenza
12 vaccines. At least in the Northern Hemisphere, this
13 vaccine will be rolled out at a time when influenza
14 vaccines are also being given. So does the sponsor
15 have studies planned for those two populations or those
16 two types?

17 **DR. WILLIAM GRUBER:** Kathrin, do you want me
18 to go ahead and take it?

19 **DR. KATHRIN JANSEN:** Yeah. It was addressed
20 to you, Bill.

1 **DR. WILLIAM GRUBER:** Okay. So let me address
2 the second question first. I think it was on the
3 slide. We do have a plan to potentially look at
4 concomitant influenza vaccines, recognizing just the
5 issue that you raised. It'll be great if you find that
6 this vaccine manages to provide protections that's
7 durable and no one requires an additional dose. And as
8 we said, we're going to be looking very intently at the
9 durability of protection.

10 But if that's not the case -- and the
11 presumption is that over the course of the coming
12 months we'll begin to get a clue about that -- then we
13 would be considering looking at co-administration of
14 influenza vaccine, assuming that that would be a timely
15 period for annual vaccination if protection was not
16 inferred.

17 I think the challenge that we encountered when
18 we thought seriously about the long-term care
19 facilities for a prospective trial, given the closed
20 nature of that, getting the informed consent -- a lot

1 of logistic issues. And I think this isn't unique to
2 us, I think it's common to a number of the other
3 sponsors, except maybe the monoclonal antibody trial.
4 That didn't prove to be fertile ground for us to be
5 able to move forward to get a good answer.

6 I think we can take some comfort -- in fact,
7 I'd say a great deal of comfort -- that when we look at
8 the older populations that are engaged in our trial,
9 that were showing efficacy, particularly, not only in
10 people that are older but people older with comorbid
11 conditions. Like obesity and Charlson Comorbidity
12 conditions that I think would translate well into a
13 high likelihood of protecting against individuals in
14 long term care facilities. I might defer to Dr. Luis
15 Jodar, who I know he and his team have thought about
16 more long term follow up in terms of the nature of
17 surveillance. I'm sure the CDC and others will be
18 looking at those populations as well.

19 **DR. LUIS JODAR:** Thank you very much, Dr.
20 Gruber. I'm Luis Jodar --

1 **DR. ARNOLD MONTO:** Very brief, please.

2 **DR. LUIS JODAR:** -- Chief Medical Officer for
3 Vaccines. I do not have much to add, but I should say
4 that we plan post-EUA studies in the next few weeks,
5 the conduct of case-controlled test negative designs in
6 which we can measure real world effectiveness,
7 selecting specific populations. And we are thinking
8 very much indeed to select long-term care facilities in
9 those studies. Thank you.

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

11 **DR. ARNOLD MONTO:** Thank you. Dr. Cohn and
12 then we are going to start discussing the voting
13 question. You're muted.

14 **MR. MICHAEL KAWCZYNSKI:** We still can't hear
15 you, Amanda. Amanda, we can't hear you.

16 **DR. AMANDA COHN:** Okay. I apologize. Can you
17 hear me now?

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

19 **DR. AMANDA COHN:** I was wondering if you could
20 tell us what the timelines may be for authorization or

1 approval in the other countries that you have enrolled
2 trial participants in, which are Argentina, Brazil,
3 Germany, South Africa, and Turkey? And what is the
4 plan in terms of those countries, people continuing in
5 this placebo randomized controlled design versus
6 unblinding those participants as well at the same time
7 as unblinding in the U.S.?

8 **DR. KATHRIN JANSEN:** Bill, please take that.

9 **DR. WILLIAM GRUBER:** Yeah. I think the brief
10 answer is, again, our whole unblinding process is going
11 to be done in cooperation with regulatory authorities,
12 both here as well as elsewhere. I think we will take
13 into account national recommendations, as well as local
14 recommendations. So it is conceivable that we would be
15 in a position to continue individuals in a placebo-
16 controlled fashion in a blinded way in those countries.

17 But we have to be mindful of the fact of our
18 ethical obligations regardless of geography. So it's
19 going to involve a balance. If there's subtle
20 differences, that's going to be probably easier for us

1 to make those sorts of adjustments than if, you know,
2 take healthcare providers, chances are we might be
3 providing this to healthcare providers across the
4 board. But this is something we'll engage in based on
5 our conversations with regulatory authorities both
6 foreign and domestic.

7 **DR. ARNOLD MONTO:** Okay. Thank you. We are
8 now going to close discussion of the discussion items
9 and move onto discussion of the voting question. And
10 could we bring up the voting question? So anybody who
11 has their hands raised now should lower them because
12 the next discussion is going to be about the voting
13 question. And, Mike, can you bring that up?

14 I think we better see it before we start
15 talking about it. Wording is very important. And I
16 will even read it, even though you can all read it.

17 Based on the totality of scientific evidence
18 available, do the benefits of the Pfizer-BioNTech
19 COVID-19 vaccine outweigh its risks for use in
20 individuals 16 years of age and older? Okay? Amanda,

1 is that -- are you asking to be recognized again, or is
2 this the old one?

3 **DR. AMANDA COHN:** Yes, thank you. No, this is
4 a new one. I got my hand up quickly this time.

5 **DR. ARNOLD MONTA:** Okay. Let's start with
6 you.

7 **DR. AMANDA COHN:** I just wanted to comment
8 that I do believe that the benefits outweigh the risks.
9 I think that some language that I would prefer to be
10 added to this language is, "based on the totality of
11 scientific evidence available at this time."

12 And I do want to ask FDA to comment on
13 potential other contraindications, besides history of
14 anaphylaxis to a vaccine or warnings such as persons
15 with a history of Bell's palsy or other things that
16 they are including in the considerations.

17 **DR. ARNOLD MONTA:** FDA? Marion, Phil, Doran?

18 **DR. DORAN FINK:** Hi, so this voting question
19 is what we would like the Committee to consider at this
20 time, which is an all-inclusive authorization for ages

1 16 and above. If the Committee has concerns that the
2 benefit-risk balance is not able to be assessed, or
3 unfavorable such that it would preclude inclusion of a
4 specific subgroup, then, clearly, we would want to hear
5 about that and would consider those recommendations in
6 contraindications or in the parameters of the
7 population authorized for use.

8 **DR. ARNOLD MONTO:** The question is about
9 groups within this 16 years of age and older, such as
10 with some kind of underlying condition. Is that
11 usually handled by FDA with information warnings,
12 labels, or something like that?

13 **DR. DORAN FINK:** Well, it depends on what the
14 reason for concern is. So if there is a clear risk
15 that would make the benefit-risk balance so unfavorable
16 that persons in that group should never be vaccinated,
17 then that would be a contraindication. For lesser
18 concerns than that, that might merit a warning or a
19 precaution.

20 **DR. ARNOLD MONTO:** Right. Is that usually

1 something that is voted on by an advisory committee,
2 those specifics?

3 **DR. DORAN FINK:** Typically, no. Those are
4 handled through labeling.

5 **DR. ARNOLD MONTO:** All right. Okay. Let's go
6 on to next Mr. Toubman.

7 **MR. SHELDON TOUBMAN:** Yes, thank you. So I'm
8 going to ask the Committee or the other members
9 listening this, I'm a consumer rep so maybe I'm a good
10 indicator of how things are perceived by the public.
11 But I have spent a lot of time reviewing the material
12 trying to understand the data. And in light of
13 concerns with the data expressed by my colleagues, many
14 commentators, and in the literature, I do have a
15 compromise proposal that's not (inaudible) the whole
16 thing that was just suggested or even questioned. But
17 rather it would be that EUA be limited to the groups
18 that the CDC ACIP committee has already identified as
19 priority.

20 And the data is limited, as we know. It's

1 limited in so many ways. The severe disease thing that
2 I was talking about before, it's not compelling at all.
3 I mean, FDA says all we can do is suggest protection
4 from severe COVID-19 disease. We need to know that it
5 does that. So that's one bit of data we need to get.

6 The safety issues are only two months of data.
7 And I know it's been said many times that six weeks is
8 usually the amount of time before we have a problem,
9 but this is a completely untested technology with this
10 vaccine in humans. And then the FDA says as far as a
11 vaccine-enhanced disease over time, that's unknown. So
12 there's a few of these missing pieces of data.

13 Given that we don't have good data on
14 effectiveness on the thing that really matters, which
15 is preventing severe disease and the safety issues, and
16 that there's a question of duration of protection,
17 which more time would give us, I think that what we
18 absolutely need, as other people have said, phase 2/3
19 trial to continue. And we've also discussed at length
20 how, if we grant EUA broadly, than it's going to really

1 present a problem.

2 I know that there's work arounds, and I
3 understand -- it makes sense -- the blinded crossover
4 people we're going to lose at that point, thereafter,
5 the placebo benefit.

6 It's been suggested by Pfizer and others that
7 we can go with the standard, that's wait until -- that
8 people in the study will only be told and unblinded, or
9 offered the crossover option, if it is authorized for
10 their particular demographic to get the vaccine at that
11 point. But what's been talked about is state and local
12 standards. And as Dr. Lee pointed out, that is really
13 problematic and variable. And I can tell you as an
14 advocate on the state level, we can lobby successfully
15 to get things change on the state level.

16 And maybe that's not so good. Maybe you need
17 a clear standard of EUA. And as I pointed out earlier,
18 a lot of the trial participants who are writing to us
19 and complaining are viewing, "If EUA is granted, then
20 that means I should get it." And we can disagree with

1 that.

2 But clearly, if EUA is officially granted
3 initially only for the two high risks groups, which is
4 identified by the CDC, which was healthcare workers and
5 the nursing home residents to start, that will give us
6 time -- give FDA time to review more thoroughly the
7 data. It can be just a few weeks. And they could
8 either come back to this Committee or on their own
9 decide, okay, we now have enough to go forward and
10 expand it to a larger population.

11 And the reason I'm suggesting this is
12 obviously because the risk-benefit analysis changes,
13 and you're talking about the hardest populations of
14 persons (inaudible) given all the uncertainty. And the
15 other piece of it is that we know there's just not
16 enough to go around.

17 So even if you agree to what I'm saying, it
18 makes no difference in terms of what's going to happen
19 on the ground in terms of getting vaccine out, because
20 it's only going to go, initially, to the healthcare

1 workers and nursing home residents anyway. But the
2 reason why I think it's important, is it will allow the
3 FDA the opportunity to get real data.

4 I did ask for the data for November 14 to
5 today, just on severe disease. We know there were only
6 10 cases before November 14, and I couldn't get, when I
7 asked, more recent data. I'm sure Pfizer today, right
8 now, knows how many severe cases there were since
9 November 14 in both groups. But that's the kind of
10 data we really need to see, I think. And that's why
11 I'm suggesting it.

12 **DR. ARNOLD MONTO:** Doran?

13 **DR. DORAN FINK:** Yeah. I'd like to make one
14 point about this question of severe disease. I think
15 it's important, and it was covered to some extent at
16 the last VRBPAC meeting in October. And that's that we
17 have able experience of examples of vaccines that
18 protect just as well, if not better, against severe
19 disease as they do against mild to moderate disease.

20 And so, protection against disease of any

1 severity is actually a pretty good predictor of
2 protection against severe disease. We have a pretty
3 strong result in terms of efficacy with this vaccine,
4 based on the available data. And those data that we do
5 have for severe disease are all point in the right
6 direction and corroborate what history has shown us. I
7 think that's important to --

8 **DR. ARNOLD MONTO:** Not only that, we'll get
9 more data as we start using the vaccine more
10 extensively, because with rare outcomes you have to
11 start using the vaccine in order to see them under
12 proper circumstances. I'd like to move on to -- Dr.
13 Meissner's got the next question.

14 **DR. CODY MEISSNER:** Thank you. I would like
15 to concur with what Dr. Fink just said that, if a
16 vaccine prevents mild disease, I think we can assume it
17 will prevent severe disease. So I understand that's
18 the most important endpoint. But because the rarity of
19 the severe disease, it may be difficult to reach that.

20 The other point I wanted to make about long

1 term safety. We know about the safety of this vaccine
2 through 60 days. And it's pretty hard to think of a
3 vaccine reaction that occurs after 60 days. And I
4 looked through the vaccine injury table for
5 conventional vaccines, and all of the injuries, except
6 for one, were only up to six weeks, not even eight
7 weeks. The one exception was a polio vaccine -- a live
8 polio vaccine -- administered to an immunocompromised
9 host. And this is obviously not a live vaccine.

10 So I think we cannot -- no one could say that
11 there is no long term enhance immunity when the
12 vaccinee experiences the vaccine. But to me, I think
13 the safety is pretty well demonstrated. And balance
14 that against over 2,000 deaths a day or 2,500 deaths a
15 day, I'm comfortable. And if I could make one more
16 point, Arnold. I'm sorry.

17 **DR. ARNOLD MONTTO:** Go ahead.

18 **DR. CODY MEISSNER:** Yes. I am uncomfortable
19 about the question as its written. I do not believe we
20 have sufficient data for 16- and 17-year-olds. I would

1 prefer to say, "for use in individuals 18 years of age
2 and older." 16- and 17-year-old children, as we saw,
3 or adolescents do not get very sick, seldom get
4 hospitalized, and I'll bet it's a very small number of
5 deaths.

6 **DR. ARNOLD MONTO:** Phil, would you like to
7 make a comment? And then I think we should talk about
8 the 16- and 17-year-olds specifically. Phil?

9 **DR. PHILIP KRAUSE:** Yeah. I just wanted to
10 make a specific comment about vaccine safety and
11 duration of follow up. Because, I think, one of the
12 important things to remember when we're rolling out a
13 vaccine to many people, is that it's not just the side
14 effects that the vaccine is causing that are important,
15 but it may also be the vaccine side effects that are
16 attributed to the vaccine, but which the vaccine didn't
17 actually cause that are important.

18 That's one of the reasons why we typically to
19 follow people in clinical trials for six months or
20 more, and where that placebo-controlled follow up can

1 be very important in showing that whatever happened in
2 the vaccine group also happened in the placebo group.
3 Because that's our best way of knowing. And very
4 often, it's the fact that we have that placebo-
5 controlled follow up over time, that gives us the
6 ability to say that the vaccine didn't cause something
7 at a longer period of time after vaccination.

8 One could, in fact, argue that one could even
9 get more placebo-controlled safety follow up over the
10 shorter run, which then could expand the total safety
11 database. This was proposed at a WHO meeting a few
12 weeks ago where, as long as vaccine supplies are
13 limited, there shouldn't be a prohibition against
14 getting additional placebo-controlled follow up in
15 people who don't have immediate eligibility for
16 vaccine. And that then could expand the safety
17 database to a much larger number than even what one is
18 capable of doing in these trials.

19 But very often, these kinds of studies work
20 very much to the benefit of the manufacturers because,

1 if one has this data, it actually allows one to say
2 fairly definitively that a side effect that somebody
3 thinks the vaccine is causing is not being caused by
4 the vaccine.

5 And of course, this is something that is a big
6 concern with rapid roll out of a vaccine -- this kind
7 of thing caused big problems in 1975 and 1976. The
8 swine flu vaccine where there were rapid cases of
9 Guillain-Barre syndrome, where if there were more
10 placebo-controlled data, one might have been able to
11 address that at a different level. Although, that
12 would have required very many patients.

13 But I'm just pointing out that it's not just
14 the two months follow up in these phase 3 trials, which
15 are important, but really placebo-controlled safety
16 follow up can play a big role in helping us determine
17 what the vaccine doesn't cause, which is often at least
18 as important as our ability to determine what it does
19 cause.

20 **DR. CODY MEISSNER:** Thank you, Dr. Krause.

1 **DR. ARNOLD MONTO:** Thank you. Does anybody in
2 particular want to talk about the 16- and 17-year-old
3 issue? I think that's an important one to get settled
4 because it may be affecting how people would like to
5 vote on this.

6 **DR. OFER LEVY:** Yeah. This is Ofer Levy. I
7 want to speak to that issue. Is that okay?

8 **DR. ARNOLD MONTO:** Yeah. Please. And then
9 Dr. Gans.

10 **DR. OFER LEVY:** Yeah. So a complicated topic,
11 and it can be argued either way. Cody correctly
12 pointed out that the incidence of severe COVID in 16/17
13 years of age is not high. On the other hand, we've
14 already heard from Pfizer -- and this is quite typical
15 -- that if they do eventually want to get a pediatric
16 indication and the endgame could look -- we don't know.
17 We don't have a crystal ball. But it's possible if you
18 demonstrate safety in pediatrics that eventually you
19 get this as a pediatric vaccine, and it's incorporated
20 into the pediatric immunization schedule. That is a

1 very practical model because that's how most vaccines
2 are distributed, around the world, through the
3 infrastructure of vaccinology.

4 So in terms of achieving population
5 penetration. So the loss, if we take away the 16- and
6 17-year-olds here, we lose what is the effort to climb
7 down in age eventually, and we might lose one of our
8 tools to eventually really conquer this pandemic. So
9 I'm not so sanguine about removing that group.

10 **DR. ARNOLD MONTO:** Dr. Gans.

11 **DR. CODY MEISSNER:** Can I respond?

12 **DR. ARNOLD MONTO:** Dr. Meissner, go ahead.

13 **DR. CODY MEISSNER:** Thank you, Ofer. That's a
14 very interesting point. So I think you're suggesting
15 that if the 16- and 17-year-old subjects are not
16 included then that will delay an approval, or
17 authorization for young children? I don't think that's
18 the case. You're muted.

19 **DR. OFER LEVY:** Okay. Hi. It will reduce the
20 amount of information we have about the 16- and 17-

1 year-olds. It will slow down getting the vaccine to
2 them. And if we don't have that information, it makes
3 it that much harder to go down in age beyond that.

4 So I'm thinking about what the endgame here is
5 for the entire world. As we know, these viruses don't
6 know national borders. What's realistic is, you know,
7 getting vaccines eventually that are safe and effective
8 through the typical vaccine infrastructure in the
9 world. Most vaccines are delivered in early life.

10 **DR. CODY MEISSNER:** But we don't know if the
11 benefit outweighs the risk in that two-year age group,
12 offer.

13 **DR. ARNOLD MONTO:** Let me interrupt. There
14 were data in our briefing documents about studies going
15 down to, I think, 12 years of age. If anything, there
16 were larger numbers there than in some of the -- in the
17 16- and 17-year-olds. Anybody --

18 **UNKNOWN SPEAKER:** I'm sorry. Dr. Levy, why
19 are you saying that a vaccine would have to have an
20 emergency use authorization in 16-year-olds when they

1 probably -- where they're not going to be in the group
2 that's going to get the vaccine. They're not going to
3 be prioritized, but they'll continue to be studies in
4 the trials. So I don't see how this interferes with
5 the eventual total licensure for that age group.

6 **DR. HAYLEY GANS:** I think that's the important
7 point here is, like, when they come into the phase. I
8 think it's very important to study this group, and I
9 think that we will have ongoing data on them. The
10 question is does the risk-benefit actually outweigh it
11 as this point?

12 And being a pediatrician -- and Ofer knows
13 this very well -- I'm obviously a big proponent of any
14 kind of studies that we can get into children, and we
15 certainly need it for herd immunity. But they're not
16 going to be first in line, and I do think we should
17 allow the studies to continue that have been proposed
18 and probably allow the people who have already been
19 vaccinated to actually have sole safety data. So I
20 would support not including them in this round.

1 **DR. ARNOLD MONTO:** Other pediatricians? Dr.
2 Sawyer, did you have something you were -- Dr.
3 Chatterjee?

4 **DR. ARCHANA CHATTERJEE:** Thank you. I've been
5 trying to get in for a while to put in a word in
6 edgewise.

7 **DR. ARNOLD MONTO:** Yeah. Well, it's hard.

8 **DR. ARCHANA CHATTERJEE:** I agree completely
9 with what Dr. Gans and Dr. Meissner said. I have the
10 same concern which is, among all the scientific data
11 presented, I thought that the thinnest was for the 16-
12 and 17-year-olds. Who, if they were eligible under
13 this EUA, would not be granting permission themselves.
14 Their parents are responsible, so they're not making
15 the decisions themselves to get vaccinated or not.

16 The other group I had concerns with was the
17 people who are 75 and older. But because of the very
18 high risk for that group, I think it's reasonable to
19 not put an upper limit on the age. But I too would
20 vote for putting that age limit up to 18 and older.

1 **DR. MARK SAWYER:** This is Mark. I would like
2 to just join that lineup of people advocating for that.
3 I think the data is very thin, and it's inadequate to
4 really say we have safety, given the low incidence of
5 disease. I know the argument was they're going to
6 going off to college, but I'm not sure how many are
7 going to receive vaccine between now and then, given
8 the staging of release of vaccine. So I would favor
9 delay.

10 **DR. ARNOLD MONTO:** Dr. Rubin and then I'm
11 going to ask FDA to respond. You're muted.

12 **DR. ERIC RUBIN:** I'm not a pediatrician, so I
13 say this with some trepidation, but we're looking at
14 lots of subgroups here. And I think we don't want to
15 lose sight of we're very focused on safety, as we
16 should be, because these are healthy people. But the
17 efficacy is overwhelming for this vaccine. It's very,
18 very strong.

19 And remember that we're going to be voting, if
20 we vote for this, to approve this for Native Americans

1 -- and there were very few of those -- for nursing home
2 residents, which weren't in the study at all. And we
3 think that it's likely to work and it's likely to be
4 safe because of what we know.

5 There are more 16- and 17-year-olds in the
6 study than there are Native Americans, I suspect. And
7 I'm not sure why we wouldn't want to provide clinicians
8 the option of using those. Some of these kids are
9 working in supermarkets and are going to be EMTs and
10 essential workers. So I hate to take that tool away
11 from clinicians.

12 **DR. CODY MEISSNER:** Can I comment, Arnold?

13 **DR. ARNOLD MONTTO:** Yes, please, and then we
14 want to hear from the FDA, what they would suggest at
15 this point.

16 **DR. CODY MEISSNER:** Thank you very much for
17 your comment, Dr. Rubin. I think the difference, for
18 example, between American Indians and children is
19 American Indians have a high rate of disease. 16- and
20 17-year-old children do not have high rates of disease.

1 So, it becomes a risk/benefit balance that worries me.

2 **DR. PAUL OFFIT:** As another pediatrician I'd
3 like to chime in -- as the last pediatrician to chime
4 in.

5 **DR. ARNOLD MONTO:** Here's what I would say. I
6 think I support this statement actually as written. I
7 think it's never an issue of when do you know
8 everything, the question is when you know enough? We
9 certainly know that this vaccine is highly effective
10 for three months after dose one. We know that we have
11 a lot of safety data and can say, as Cody pointed out,
12 that at least we don't have a relatively uncommon
13 serious side effect problem.

14 And in terms of safety, we're going to be
15 doing follow up to make sure that issues like Bell's or
16 anaphylaxis will be attended to. The fact of the
17 matter is 16- and 17-year-olds can get this infection.
18 And when they get it, we've seen, certainly, reports as
19 well as children in our hospital who have had cardiac
20 anomalies as 16- and 17-year-olds. And if you can

1 prevent this disease safely and effectively -- I mean,
2 we have clear evidence of benefit. All we have on the
3 other side is theoretical risk. So I frankly would
4 support this as written. And I agree with Dr. Rubin.

5 **DR. CODY MEISSNER:** Can I respond to Paul?
6 Arnold?

7 **DR. ARNOLD MONTO:** Yes, go ahead. Go ahead.

8 **DR. CODY MEISSNER:** Paul, the rates of MIS-C,
9 at least as far as we know, and as was published in the
10 *New England Journal* regarding New York State, the rates
11 of MIS-C were two cases per 100,000 people under 20
12 years of age.

13 **DR. PAUL OFFIT:** Okay. But I'm not just
14 saying MIS-C. There is also vasculitis that doesn't
15 necessarily meet the operational criteria for MIS-C.

16 **DR. CODY MEISSNER:** Well, and that is
17 certainly true. But I'm just saying that the rate of
18 disease is so small, and we know so little in this age
19 group. It's real. Believe me, we've had them, too.
20 But I have a little more trouble justifying it in

1 children who are so unlikely to get the disease.

2 **DR. ARNOLD MONTO:** Can we hear someone from
3 FDA, Doran, or Phil?

4 **DR. CODY MEISSNER:** Amanda's a pediatrician.

5 **DR. ARNOLD MONTO:** -- comment on this. I'd
6 just like to hear what -- or Marion. Come on.

7 **DR. MARION GRUBER:** Okay. This is Marion. So
8 I think I really don't want to throw in my own opinion
9 on this. I hear the Committee's concern. I just think
10 that, as Dr. Fink has discussed earlier on, our laws
11 and regulations do also permit extrapolations to
12 younger age groups. And we have been, I think, pretty
13 forthcoming even in our briefing document that we would
14 support an extrapolation.

15 One should also consider that 16- and 17-year-
16 olds are out there. They may transmit disease. And
17 the last comment that I wanted to make on this one is
18 really, if the argument is made that 16- and 17-year-
19 olds are really not the ones who are high risk group
20 and would get in line to get this vaccine because

1 they're not within the recommended group, I think you
2 can make the same argument for an 18- to 25-year-old.
3 So to me, I don't find that that compelling.

4 I wonder, however, looking at it is 5:30 and,
5 Arnold, we have a strategy -- I would like, provided
6 that other Committee members do no longer want to weigh
7 in -- I would like for the Committee to really vote on
8 this question as is, to really hear -- because we have
9 23 members. And I would like to see the results and
10 then we go to next, Arnold. That's my recommendation.

11 **DR. ARNOLD MONTO:** That is -- thank you very
12 much. I was hoping for some direction because we are
13 moving around in circles right now. So we are going to
14 move to the vote. And again, the process is going to
15 be this. We will vote on our computers. The votes
16 will be announced, and then we will have an explanation
17 of vote from those who wish to give an explanation of
18 their vote. Okay? Kathleen, am I correct in the
19 process?

20 **MS. KATHLEEN HAYES:** Yes, thank you, Dr.

1 Monto. So our members and temporary voting members
2 that you'd be able to see on this slide, excluding the
3 industry representative, will be voting in this
4 meeting. And in regard to the voting process, Dr.
5 Monto, as you mentioned, you'll read the question for
6 the record. And then afterwards, all members and
7 temporary voting members will cast their vote by
8 selecting one of the voting options, which will include
9 yes, no, or abstain.

10 You'll have two minutes to cast your vote
11 after the question is read. And once all of the votes
12 have been placed, we will broadcast the results and
13 read the individual votes aloud for the record. So
14 just please note that you have two minutes timeframe,
15 and you can change your vote within that period of
16 time. But after the vote has closed, all votes will be
17 considered final. So are there any questions related
18 to voting?

19 **DR. CODY MEISSNER:** Yes. Kathleen, can I ask
20 a question? Cody Meissner.

1 **DR. ARNOLD MONTO:** Please.

2 **DR. CODY MEISSNER:** I want to vote for this
3 vaccine. I just would like to remove the 16 to 17 -- I
4 don't want to vote against the EUA just because I'm
5 uncomfortable 16 -- can we modify the wording if this
6 doesn't pass?

7 **DR. ARNOLD MONTO:** I think that's what Dr.
8 Gruber was saying. Marion, would you confirm that?

9 **DR. OVETA FULLER:** I thought we just said we
10 were not going to modify the wording so that we could
11 get to a vote.

12 **DR. MARION GRUBER:** I would recommend voting
13 on this question as is for now because we have not
14 heard from all the Committee members.

15 **MS. KATHLEEN HAYES:** Thank you, Dr. Gruber.

16 **UNKNOWN SPEAKER:** Kathleen, can I ask one last
17 question before we vote?

18 **MS. KATHLEEN HAYES:** If it's related to the
19 voting process, sure.

20 **UNKNOWN SPEAKER:** Well, it is.

1 **DR. ARNOLD MONTO:** Only about the voting
2 process, not the question. Okay. I think we are going
3 to vote.

4 **MS. KATHLEEN HAYES:** Great. Let's pull up the
5 voting question on the slide, and Dr. Monto you can
6 read the question for the record.

7 **DR. ARNOLD MONTO:** Based on the totality of
8 scientific evidence available, do the benefits of the
9 Pfizer-BioNTech COVID-19 vaccine outweigh its risks for
10 use in individuals 16 years of age and older? Your
11 vote possibilities are yes or no, and if you want to
12 abstain, you just don't vote. Is that it? Because I
13 thought there was an abstention possibility.

14 **MS. KATHLEEN HAYES:** There's an abstain
15 selection. The no vote just shows your name if you
16 haven't made a selection.

17 **DR. ARNOLD MONTO:** Okay. So we have two
18 minutes to vote.

19 **MS. KATHLEEN HAYES:** Yes. Go ahead and please
20 cast your vote.

1 **DR. CODY MEISSNER:** How do we return the vote
2 to you? Can you see what we've voted?

3 **MS. KATHLEEN HAYES:** Yes, once you select the
4 radio button, I can see the vote. Mm-hmm. We have
5 one minute remaining. 30 seconds. Okay. At this
6 time, the two minutes is up, so if we could please
7 close the vote and broadcast the results. And I will
8 read the votes aloud for the record.

9 Dr. Moore voted yes. Dr. Cohn voted yes. Dr.
10 Gans voted yes. Dr. Perlman voted yes. Dr. Kurilla
11 voted no. Dr. Rubin voted yes. Dr. Levy voted yes.
12 Dr. Pergam voted yes. Dr. Chatterjee voted no. Dr.
13 Fuller voted no. Dr. Meissner abstained. Dr. Sawyer
14 voted yes. Dr. Hildreth voted yes. Dr. Kim voted no.
15 Dr. Monto voted yes. Dr. Tripp voted yes. Dr. Wharton
16 voted yes. Dr. Gea-Banacloche voted yes. Dr. Offit
17 voted yes. Dr. McInnes voted yes. Dr. Lee voted yes.
18 Mr. Toubman voted yes.

19 And that concludes the vote, so we do have a
20 favorable vote. And that concludes this portion of the

1 meeting, so I will now hand the meeting back over to
2 Dr. Monto. Thank you, everybody.

3 **DR. ARNOLD MONTO:** Okay. Marion, do you have
4 anything you want to add at this point?

5 **MR. MICHAEL KAWCZYNSKI:** We can't hear you,
6 Marion.

7 **DR. MARION GRUBER:** I apologize. Double
8 muted. I just wanted to thank the Committee for voting
9 on this very complex topic. I wanted to thank the
10 Committee for their discussion and their suggestions.
11 We very much appreciate their input on this very
12 important topic, and we will take what we've heard
13 today into consideration when deciding on not only the
14 EUA issuance here but also how to move on in the
15 development and licensure of this product. Thank you
16 so much.

17 **DR. ARNOLD MONTO:** And therefore, our work for
18 the day is done. I wanted to thank the Committee. And
19 I want especially to thank the FDA because they have
20 been laboring long and hard, in doing the analysis,

1 dealing with some of the issues such as the recent
2 anaphylaxis episodes. And I will therefore close the
3 meeting, and I believe most of us are going to be
4 revising some of these issues in about a week. So
5 thank you very much. Goodnight and see you soon.

6

7 **[WHEREUPON THE MEETING WAS ADJOURNED]**