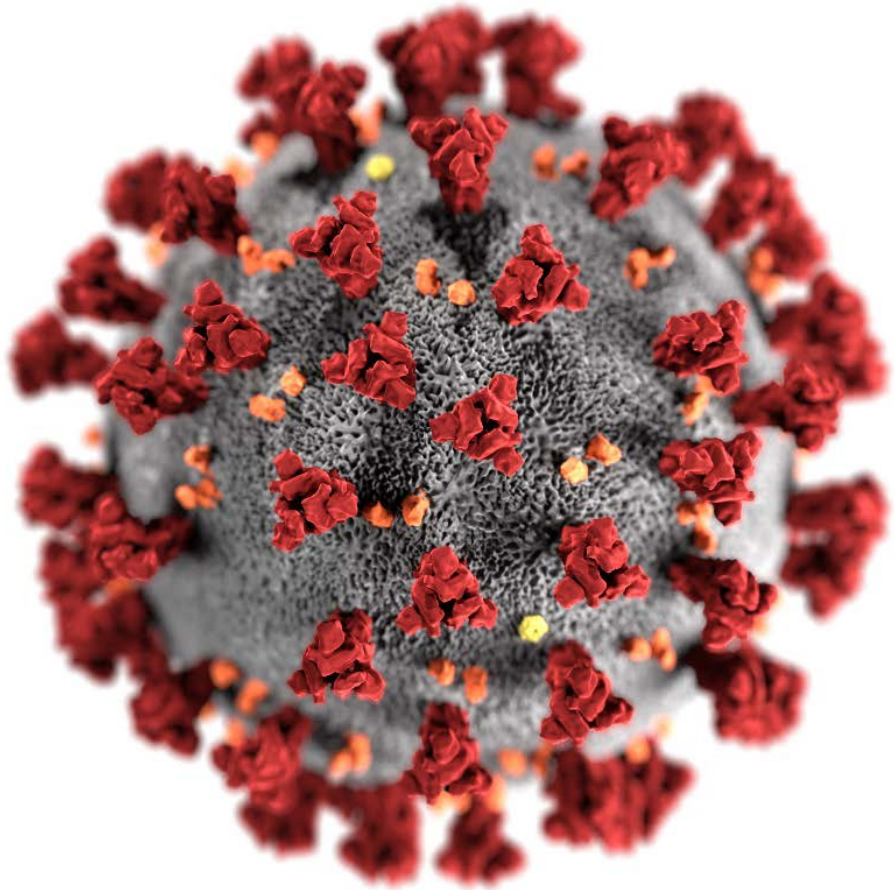
Work Group interpretation and next steps



Sara Oliver MD, MSPH
LCDR, USPHS
ACIP Meeting
December 11, 2020

Clinical Trial Data

Safety data Reviewed by Work Group

Pfizer-BioNTech COVID-19 vaccine: Phase III data

- **Local** reactions occurring within 7 days were common
  - Pain at the injection site most common
- **Systemic** reactions within 7 days were common
  - Fatigue, headache and muscle pain most common
- Symptom onset was usually **1-2 days** post-vaccine receipt
- Most symptoms resolved after **1 day** (median duration)

Safety data Reviewed by Work Group

Pfizer-BioNTech COVID-19 vaccine: Phase III data

Select local reactions in persons aged 16-55 years

	Dose 1		Dose 2	
	Pfizer-BioNTech vaccine N=2291	**Placebo** N=2298	**Pfizer-BioNTech vaccine** N=2098	**Placebo N=2103**
Redness[a], n (%)				
Any	104 (4.5)	26 (1.1)	123 (5.9)	14 (0.7)
Severe (Grade 3)	6 (0.3)	4 (0.2	10 (0.5)	0 (0)
Pain at the injection site[b], n (%)				
Any	1904 (83.1)	322 (14.0)	1632 (77.8)	245 (11.7)
Severe (Grade 3)	24 (1.0)	2 (0.1)	25 (1.2)	0 (0)

Select local reactions in persons aged >55 years

	Dose 1		Dose 2	
	Pfizer-BioNTech Vaccine N=1802	**Placebo** N=1792	**Pfizer-BioNTech Vaccine** N=1660	**Placebo** N=1646
Redness[a], n (%)				
Any	85 (4.7)	19 (1.1)	120 (7.2)	12 (0.7)
Severe (Grade 3)	3 (0.2)	2 (0.1)	8 (0.5)	1 (0.1)
Pain at the injection site[b], n (%)				
Any	1282 (71.1)	166 (9.3)	1098 (66.1)	127 (7.7)
Severe (Grade 3)	4 (0.2)	0 (0)	8 (0.5)	0 (0)

Safety data Reviewed by Work Group

Pfizer-BioNTech COVID-19 vaccine: Phase III data

Select systemic reactions in persons aged 16-55 years

	Dose 1		Dose 2	
	Pfizer-BioNTech vaccine N=2291	**Placebo** N=2298	**Pfizer-BioNTech vaccine** N=2098	**Placebo** N=2103
Fever, n (%)				
≥38.0°C	85 (3.7)	20 (0.9)	331 (15.8)	10 (0.5)
≥38.0°C to 38.4°C	64 (2.8)	10 (0.4)	194 (9.2)	5 (0.2)
>38.4°C to 38.9°C	15 (0.7)	5 (0.2)	110 (5.2)	3 (0.1)
>38.9°C to 40.0°C	6 (0.3)	3 (0.1)	26 (1.2)	2 (0.1)
>40.0°C	0 (0)	2 (0.1)	1 (0)	0 (0)
Fatigue[a], n (%)				
Any	1085 (47.4)	767 (33.4)	1247 (59.4)	479 (22.8)

Select systemic reactions in persons aged >55 years

	Dose 1		Dose 2	
	Pfizer-BioNTech Vaccine N=1802	**Placebo** N=1792	**Pfizer-BioNTech Vaccine** N=1660	**Placebo** N=1646
Fever				
≥38.0°C	26 (1.4)	7 (0.4)	181 (10.9)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.3)	2 (0.1)	131 (7.9)	2 (0.1)
>38.4°C to 38.9°C	1 (0.1)	3 (0.2)	45 (2.7)	1 (0.1)
>38.9°C to 40.0°C	1 (0.1)	2 (0.1)	5 (0.3)	1 (0.1)
>40.0°C	1 (0.1)	0 (0)	0 (0)	0 (0)
Fatigue[a], n (%)				
Any	615 (34.1)	405 (22.6)	839 (50.5)	277 (16.8)

Safety data Reviewed by Work Group

Pfizer-BioNTech COVID-19 vaccine: Phase III data

- **Lymphadenopathy**
  - higher frequency in vaccine group (n=64), compared to placebo (n=6)
  - As localized lymph nodes are involved in the vaccine response, it is plausible this could be related to the vaccine
- **Bell's palsy**
  - higher frequency in vaccine group (n=4), compared to placebo (n=0)
  - Incidence within vaccine group consistent with expected population rates
  - No known causal relationship
- Serious adverse events similar between vaccine and placebo

Efficacy data Reviewed by Work Group

Pfizer-BioNTech COVID-19 vaccine: Phase III data

- Primary efficacy endpoint: Subjects without evidence of prior infection
  - Efficacy: **95.0**% (90.3–97.6%)
- **High** efficacy (≥92%) for additional efficacy analysis, including those with evidence of prior infection, and across age, sex, race, and ethnicity categories, and those with underlying medical conditions
  - Efficacy among adults ≥65 years of age: **94.7**% (66.7–99.9%)
- Most recipients received 2 doses of the Pfizer-BioNTech vaccine
  - Efficacy of **52.4**% (29.5–68.4%) noted between dose 1 and dose 2

Efficacy data Reviewed by Work Group

Pfizer-BioNTech COVID-19 vaccine: Phase III data

- Efficacy noted against severe disease as well
  - FDA definition*: **66.4**% (-124.8–96.3%)
  - CDC definition**: **100**% (-9.9–100%)

- Phase III trial not powered to assess efficacy of the vaccine to prevent **hospitalization** or **death**

*__FDA definition__: Respiratory Rate ≥ 30, Heart Rate ≥125, SpO2≤ 93% on room air at sea level or PaO2/FIO2< 300 mm Hg; OR Respiratory failure or Acute Respiratory Distress Syndrome (ARDS), defined as needing high-flow oxygen, non-invasive or mechanical ventilation, or ECMO; OR evidence of shock (systolic blood pressure <90mmHg, diastolic BP<60mmHg or requiring vasopressors); OR Significant acute renal, hepatic or neurologic dysfunction; OR Admission to an intensive care unit or death

**__CDC definition__: Hospitalization, admission to ICU, intubation or mechanical ventilation or death

Work Group Interpretation:
Phase III safety and effectiveness data

- Communications around expected **local** and **systemic reactions** after vaccine receipt will be important
- Post-authorization **safety** and **effectiveness** studies will be important
  - Surveillance for Bell's Palsy will help determine any possible causal relationship
- >90% efficacy among adults ≥65 years of age is reassuring
- Continued studies are needed to assess **duration of protection**
- Additional studies are needed to assess the impact of the Pfizer-BioNTech vaccine on **viral shedding** and **transmission**

EtR Domain: Benefits and Harms

Evidence to Recommendations Framework:
Benefits and Harms

- Full Evidence to Recommendations (EtR) Framework presented at upcoming meeting
- Previously, not discussed “Benefits and Harms” Domain of the EtR Framework and Work Group interpretations

Evidence to Recommendations Framework:

Benefits and Harms

- **Criterion 1**: Magnitude of desirable anticipated effects

How substantial is the anticipated effect for each main outcome for which there is a desirable effect?

Work Group felt that the desired anticipated effects were **large**

Evidence to Recommendations Framework:

Benefits and Harms

- **Criterion 2**: Magnitude of undesirable anticipated effects

How substantial is the anticipated effect for each main outcome for which there is an undesirable effect?

Work Group felt that the desired anticipated effects were **small**

Evidence to Recommendations Framework:

Benefits and Harms

- **Criterion 3**: Balance of the desirable versus undesirable anticipated effects

What is the balance between the desirable effects relative to the undesirable effects?

Work Group felt that the balance of effects **favored the intervention**:

Pfizer-BioNTech COVID-19 vaccine

Safety Surveillance

Anaphylaxis

- Anaphylaxis/anaphylactoid reactions in 2 UK recipients: 2 healthcare workers with history of severe allergic reaction; first to eggs and other food items and the second to a drug. A third healthcare worker, with no history of allergies, developed tachycardia, and erythema
- CDC is following up with Public Health England to understand these cases
- CDC convened an external group with expertise in vaccine safety, immunology and allergy (Clinical Immunization Safety Assessment, CISA), to collate expert knowledge regarding possible causes
- FDA is obtaining more data from U.K. regulatory authority (MHRA), and will consider if additional contraindications or precautions needed

COVID-19 Vaccine Safety Technical (VaST) Subgroup

- Built off lessons learned from H1N1 vaccine safety monitoring
- Consensus VaST would ensure transparency, independence, and public accountability
- Composition
  - Co-chairs: Grace Lee (ACIP member) and Bob Hopkins (NVAC Chair)
  - ACIP and NVAC representation
  - 7 independent expert consultants
  - ACIP ex officio members (NIH, FDA, OIDP, CMS, HRSA, IHS)
  - VA and DoD liaison
  - CDC co-leads

COVID-19 Vaccine Safety Technical (VaST) Subgroup

Objectives

- Review, evaluate, and interpret post-authorization/approval COVID-19 vaccine safety data
- Serve as the central hub for technical subject matter experts from federal agencies conducting post-authorization/approval safety monitoring
- Advise on analyses, interpretation, and data presentation
- Liaise with the ACIP COVID-19 Vaccines Working Group on issues of safety data presentation to the ACIP and application of safety data to policy decisions

Current status

- Meeting weekly to refine procedures and hear updates on monitoring systems
- Plans include periodic safety data summaries to COVID-19 Vaccine WG, ACIP and public

v-safe℠ after vaccination health checker

active surveillance

CDC + FDA

VAERS Vaccine Adverse Event Reporting System

passive surveillance

CDC CISA Clinical Immunization Safety Assessment (CISA) Project

individual case consults

CDC

VSD Vaccine Safety Datalink

Genesis

NIH National Institute on Aging

BROWN

VA EHR & data warehouse

VA U.S. Department of Veterans Affairs

FDA Vaccine Surveillance Program

FDA

Federal Partners CMS, VA

BEST Initiative Acumen, IBM, IQVIA/OHDSI

PRISM Harvard Pilgrim Healthcare Institute

DoD DMSS Defense Medical Surveillance System

start of vax

active surveillance, passive surveillance, case consults

large-linked database monitoring

safety monitoring timeline

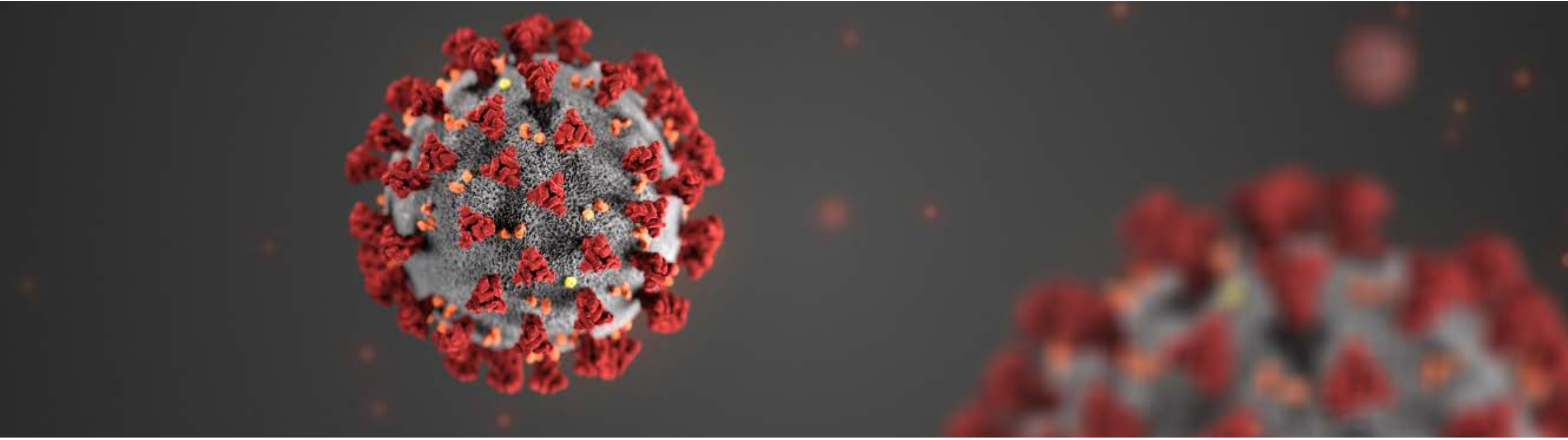
Next Steps

Next Steps

- Await final decision from FDA regarding issuance of EUA
- After an FDA decision, ACIP will have an emergency meeting
- Full Evidence to Recommendation framework presented
- Clinical considerations presentation, including:
  - Dosing intervals
  - Coadministration with other vaccines
  - Vaccination of special populations, including persons with immunodeficiencies and pregnant women
- Vote on recommendations for Pfizer-BioNTech COVID-19 Vaccine

Question

1. What is the balance between the desirable effects relative to the undesirable effects for the Pfizer-BioNTech COVID-19 vaccine?



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Thank you

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.