COVID-19 Vaccine Update

Franklin D. Pratt, MD, MPHTM, FACEP
Medical Director
Vaccine Preventable Disease Control Program
fpratt@ph.lacounty.gov

December 1, 2020

NO FINANCIAL DISCLOSURES

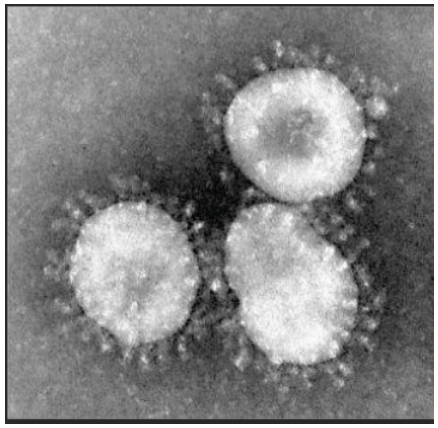
Please note:

- *….every component of the vaccine plan or information presented today, is subject to modification and update on short notice.*

- *We haven't seen any substantive changes yet, but, most likely, there will some in the very near future.*

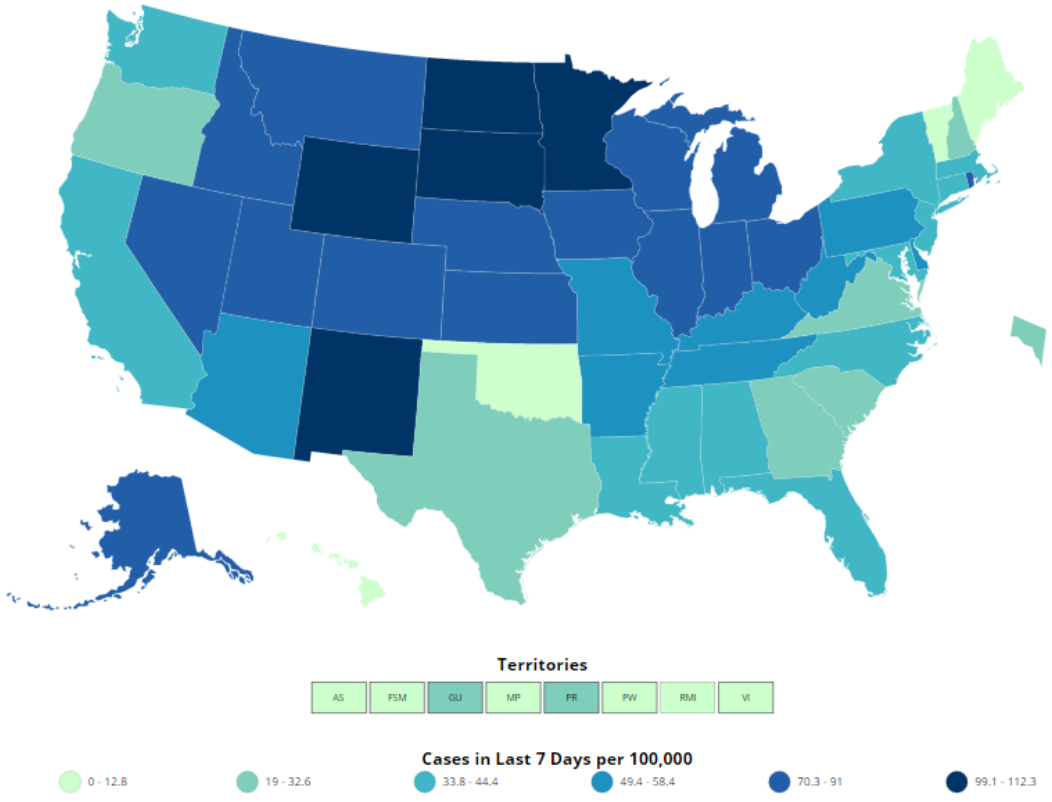
Learning Objectives

1. Describe current status of COVID-19 pandemic in United States
2. Describe basic biology of current COVID-19 Phase III candidate vaccines
3. Describe storage and handling requirements for use of vaccines requiring ultra-low cold storage
4. List steps to permit paramedic scope of practice adjustment to allow COVID-19 vaccine administration



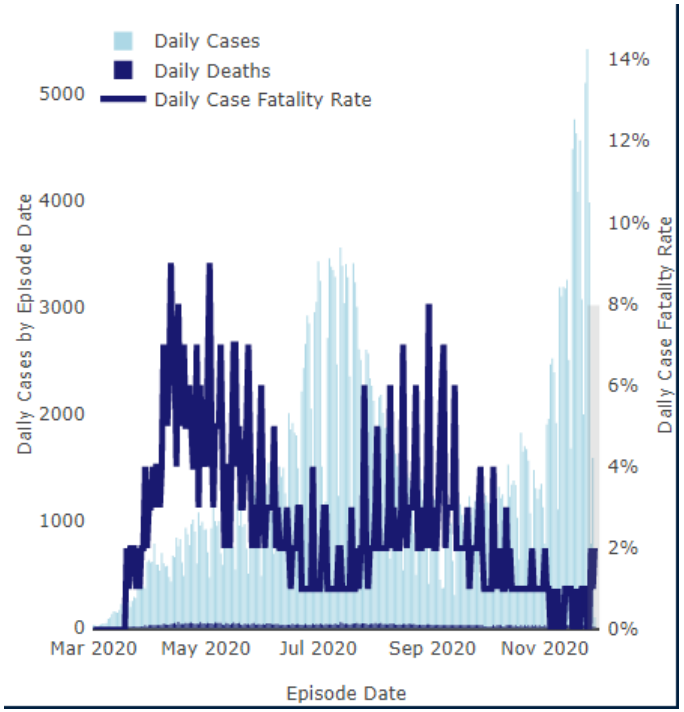
COVID-19 Pandemic United States Information

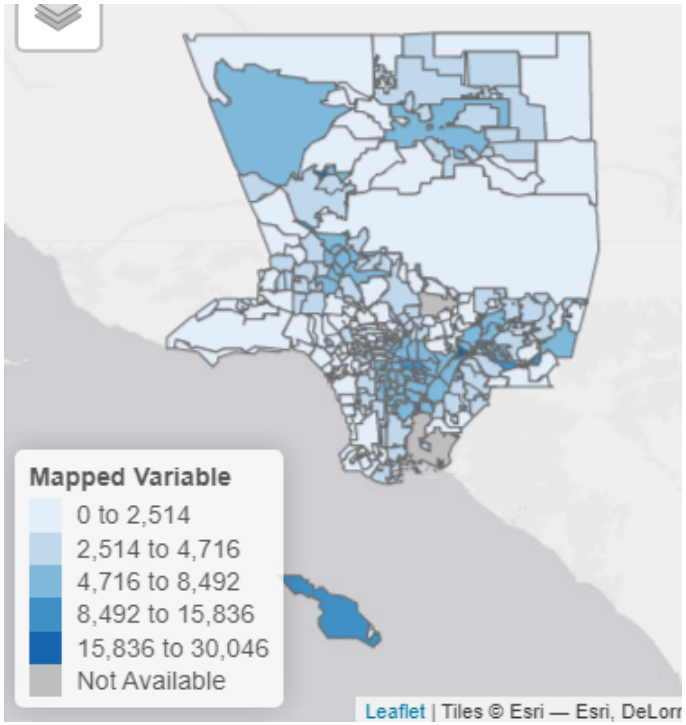
US COVID-19 Case Rate Reported to the CDC in the Last 7 Days, by State/Territory (cases per 100K)



CDC Nov 29, 2020

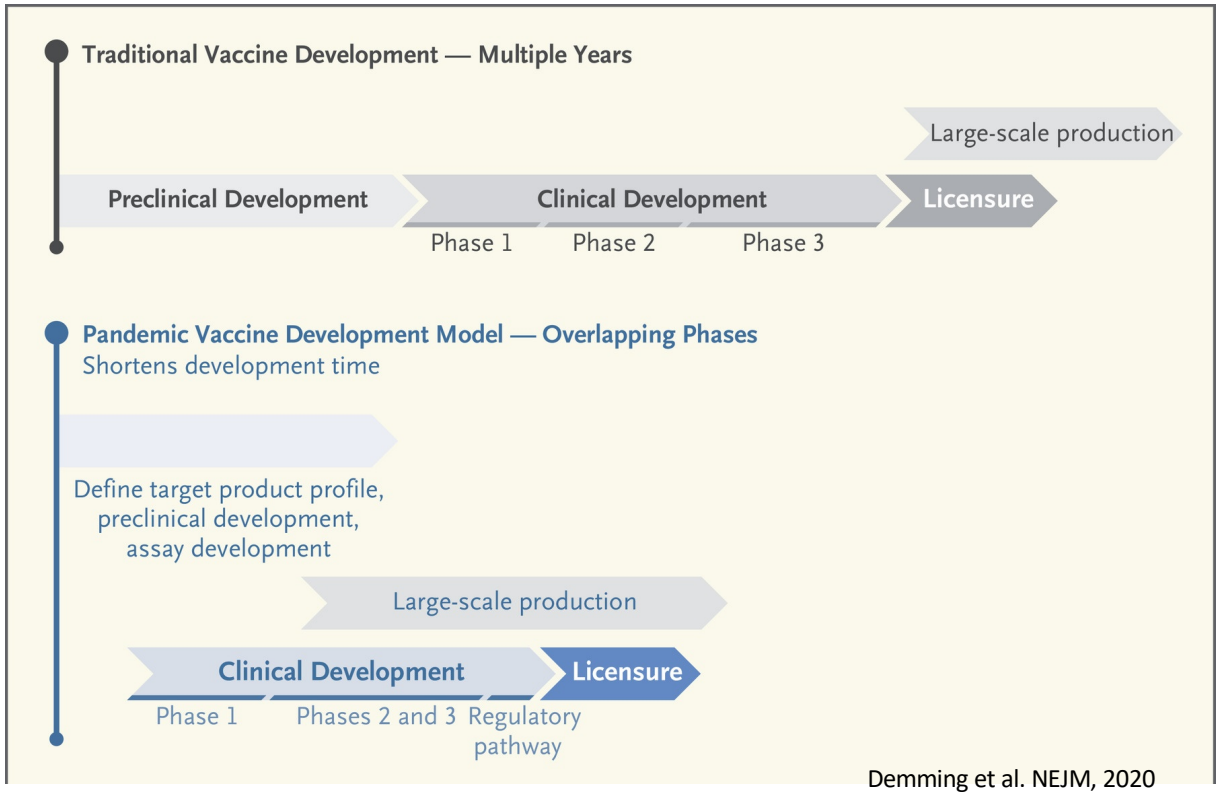
Los Angeles County Information





COVID-19 vaccine development

- Jump started thanks to lessons from vaccine development since 2003 with SARS-CoV then MERS coronaviruses
- Federal Govt. Funding
- No skipped steps: phases 1, 2, 3 completed
- Timeline shortened by simultaneous activities, including manufacturing, rather than completing sequentially



Demming et al. NEJM, 2020

COVID-19 vaccine results

- A collaborative triumph of science, public policy, and politics with better and faster results than expected:

  95% effective

- Reassuringly similar results from two largely similar vaccines

- Extensively studied with 43,000+ (Pfizer) and 30,000+ (Moderna) phase 3 participants

- 42% and 37% respectively from diverse racial and ethnic groups

NEWS / Pfizer and BioNTech Announce Vaccine Candidate Against COVID-19 Achieved Success in First Interim Analysis from Phase 3 Study

PFIZER AND BIONTECH ANNOUNCE VACCINE CANDIDATE AGAINST COVID-19 ACHIEVED SUCCESS IN FIRST INTERIM ANALYSIS FROM PHASE 3 STUDY

Monday, November 09, 2020 - 06:45am

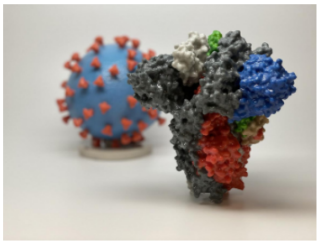
- *Vaccine candidate was found to be more than 90% effective in preventing COVID-19 in participants without evidence of prior SARS-CoV-2 infection in the first interim efficacy analysis*
- *Analysis evaluated 94 confirmed cases of COVID-19 in trial participants*
- *Study enrolled 43,538 participants, with 42% having diverse backgrounds, and no serious safety concerns have been observed; Safety and additional efficacy data continue to be collected*
- *Submission for Emergency Use Authorization (EUA) to the U.S. Food and Drug Administration (FDA) planned for soon after the required safety milestone is achieved, which is currently expected to occur in the third week of November*
- *Clinical trial to continue through to final analysis at 164 confirmed cases in order to collect further data and characterize the vaccine candidate's performance against other study endpoints*

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20201109005539/en/

Monday, November 16, 2020

Promising Interim Results from Clinical Trial of NIH-Moderna COVID-19 Vaccine

An independent data and safety monitoring board (DSMB) overseeing the Phase 3 trial of the investigational COVID-19 vaccine known as mRNA-1273 reviewed trial data and shared its interim analysis with the trial oversight group on Nov. 15, 2020. This interim review of the data suggests that the vaccine is safe and effective at preventing symptomatic COVID-19 in adults. The interim analysis comprised 95 cases of symptomatic COVID-19 among volunteers. The DSMB reported that the candidate was safe and well-tolerated and noted a vaccine efficacy rate of 94.5%. The findings are statistically significant, meaning they are likely not due to chance. 90 of the cases occurred in the placebo group and 5 occurred in the vaccinated group. There were 11 cases of severe COVID-19 out of the 95 total, all of which occurred in the placebo group.



3D print of a spike protein of SARS-CoV-2, the virus that

Institute/Center

National Institute of Allergy and Infectious Diseases (NIAID)

Contact

NIAID Office of Communications
301-402-1663

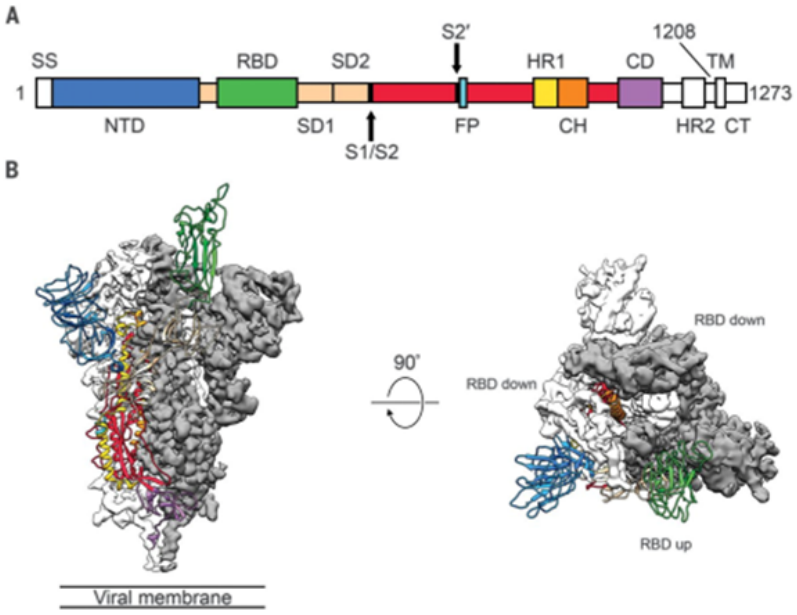
Connect with Us

Subscribe to news releases

RSS Feed

Spike Protein Structure

Fig. 1 Structure of 2019-nCoV S in the prefusion conformation.



Daniel Wrapp et al. Science 2020;367:1260-1263

Science AAAS

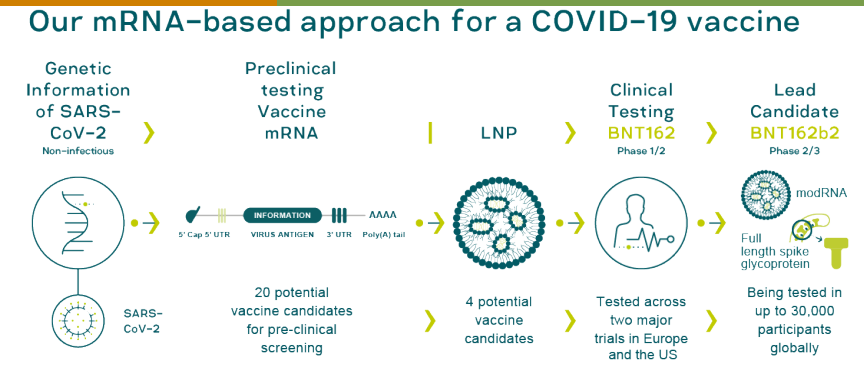
Current Phase III mRNA Vaccine Candidates in US

1. Moderna/NIH – mRNA-1273 – EUA applied for – review Dec 17, 2020
    1. 94.1% efficacy, usual freezer temps
    2. Pre-existing logistics
    3. 2 doses (0, 28d)
    4. IM administration
    5. 18-55, 56+ years
    6. No reconstitution

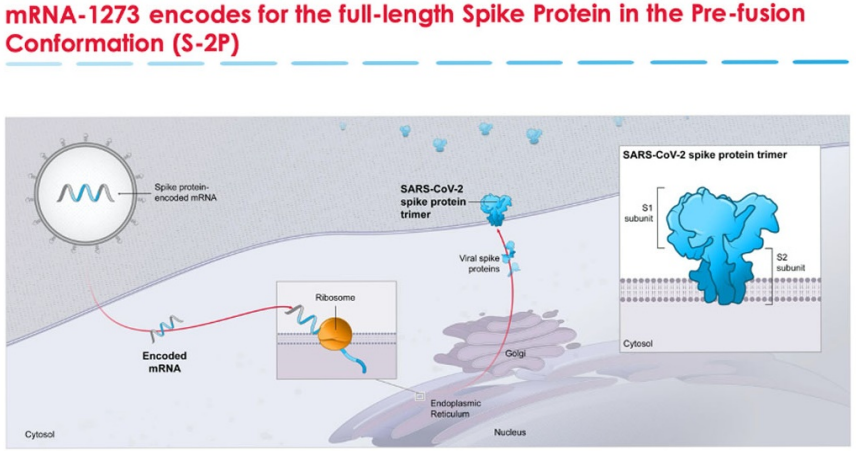
2. Pfizer/BioNTech – mRNA-BNT162b2 – EUA applied for – review Dec 10, 2020
    1. 95% efficacy, ultra-low cold freezer temps
    2. Their own storage and handling logistics
    3. 2 doses (0, 21d)
    4. IM administration
    5. 18-85 years
    6. Needs reconstitution

How Does it Work?

- Synthetic mRNA provides instructions to make viral spike (S) protein which is used to enter human cells through the ACE2 receptor
- Encapsulated in fatty, protective covering (lipid nano-particles) to stabilize and allow cell entry into human cell
- Human cell structures (ribosomes) make spike protein
- Spike protein seen as “foreign” – generates immune response of antibodies and T-cells.
- Similar process to natural infection



BioNTech



Moderna

Comparison of the two leading vaccines

Vaccine	Preparation	Route	Dosing	Storage		Ages	Exclusions*
Pfizer/ BioNTech	30µg in 0.3mL 5 dose vial	IM	2 doses 21d apart	-80°C	6m	12-85	Immunocompromised Pregnancy Prior SARS-COV-2+
				-4°C	5d		
				Room	6h		
Moderna	100µg in 0.5mL 10 dose vial	IM	2 doses 28d apart	-20°C	6m	>18	Immunocompromised Pregnancy Prior SARS-COV-2+
				-4°C	28d		
				Room	12h		

*Excluded in Phase 3 trials, final indications based on EUA

Safety Data: Pfizer

- In >43,000 phase 3 participants:
  No serious adverse events reported
  No evidence of antibody-dependent enhancement

Phase 2 detailed data

- Local events:
  Mostly mild, **pain at site of injection** was common
- Systemic events:
  Mostly mild, **fatigue** was common

- Summary:
  Mild reactions, more after the 2nd dose

Walsh et al. NEJM, 2020

Safety data: Moderna

- In >30,000 phase 3 participants:
  No serious adverse events reported
  No evidence of antibody-dependent enhancement

Phase 2 detailed data

- Local events:
  Mostly mild, **pain at site of injection** was common
- Systemic events:
  Mostly mild, **fatigue** and headache were common with chills, fever, and myalgia presenting after the 2nd dose

- Summary:
  Mild to moderate reactions, more after the 2nd dose

Jackson et al. NEJM, 2020

Pfizer/BioNTech Vaccine Packaging

Product Packaging Overview

1 Primary Packaging

- 2 mL type 1 glass preservative free multi-dose vial (MDV)
- MDV has 0.45 mL frozen liquid drug product
- 5 doses per vial after dilution

2 Secondary Packaging "Single Tray"

- Single tray holds 195 vials
- 975 doses per tray
- A smaller tray, containing 25 vials (125 doses) is in development with estimated availability in early 2021

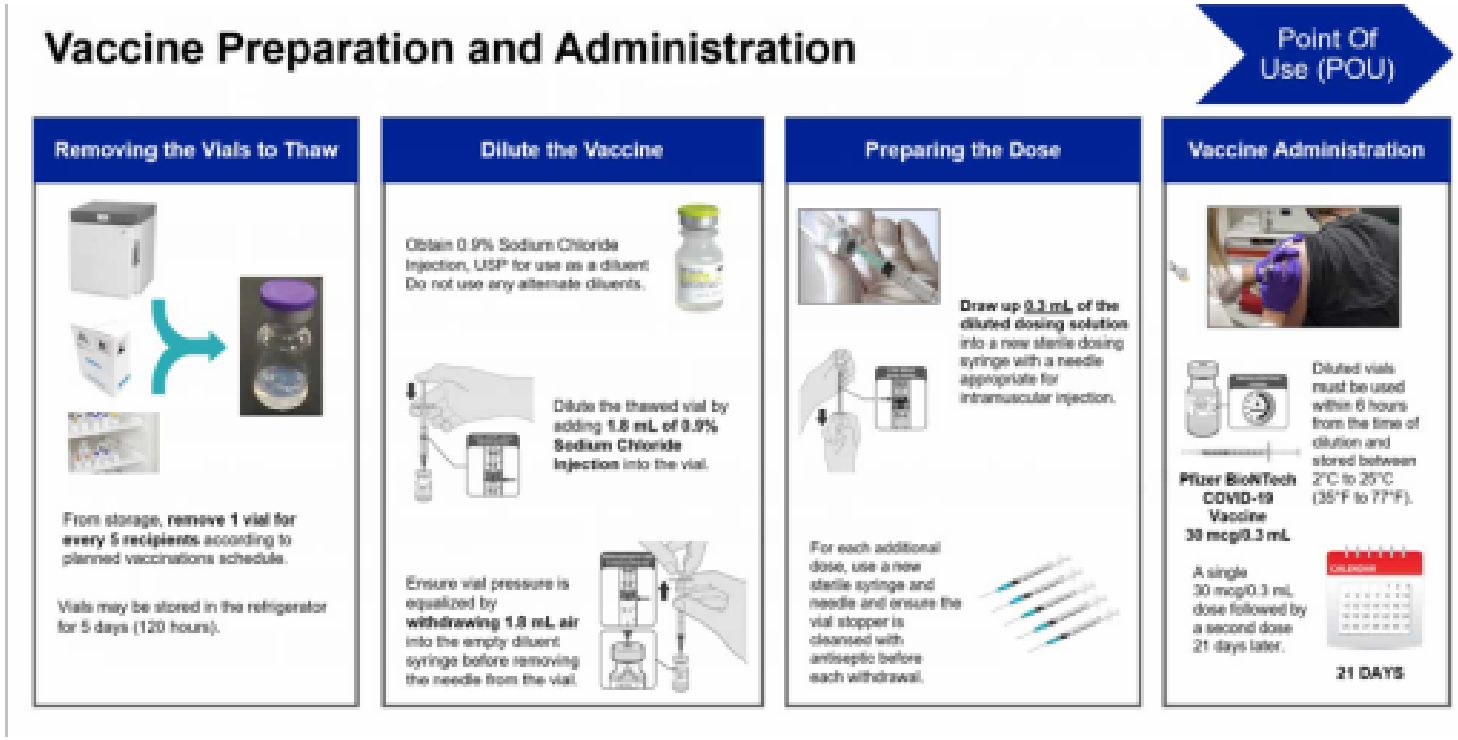
3 Tertiary Container: Thermal Shipper

Item	Description
1	Dry Ice Pod
2	Payload (Vial Trays)
3	Inner Lid
4	Payload Sleeve
5	Outer Carton

- Minimum 1 tray (975 doses) or up to 5 trays (4875 doses) stacked in a payload area of the shipper
- Payload carton submerged in dry ice pellets
- Thermal shipper keeps ULT (-75±15°C) up to 10 days if stored at 15°C to 25°C temperatures without opening.
- Thermal shippers are reusable and designed to be a temporary storage containers by replenishing dry ice

*subject to change, per CDC presentation by Pfizer/BioNTech 11/3/2020

Pfizer/BioNTech Vaccine Preparation & Administration



*subject to change, per CDC presentation by Pfizer/BioNTech 11/3/2020

COVID-19 Vaccine Roll-Out

mRNA VACCINES

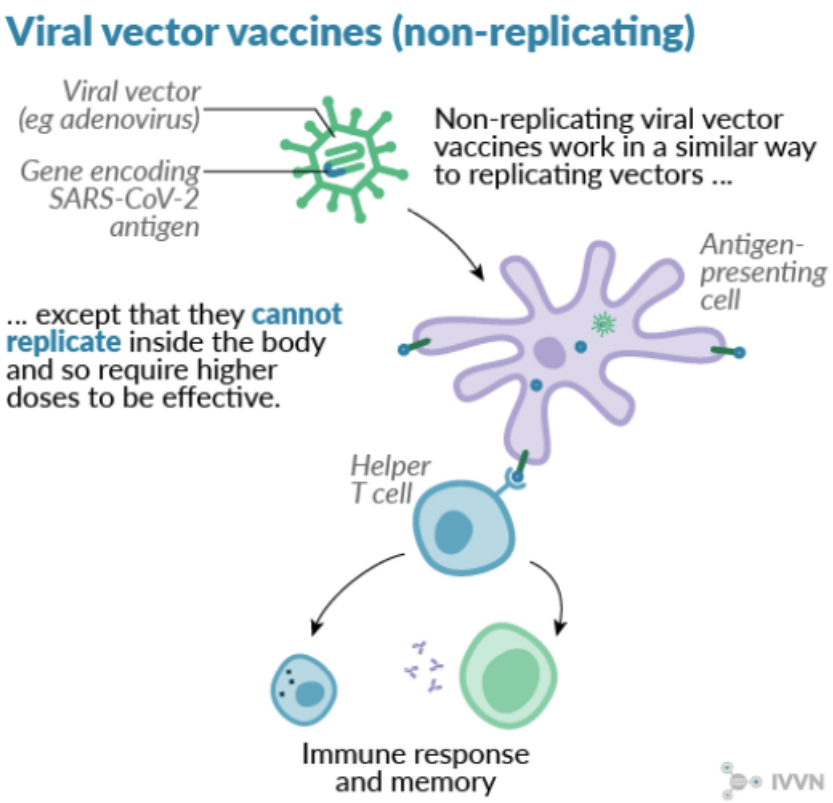
Pros –

1. Quickly create vaccine components
2. Precise antigen definition
3. Good immune response

Cons -

1. Less stable – need ultra low cold - minus 80 degrees Centigrade
2. No human vaccines before
3. Second dose needed

How Viral Vector Works



https://www.intvetvaccnet.co.uk/blog/covid-19/vaccine-eight-types-being-tested

Current Phase III Viral Vector Vaccine Candidates in United States

1. AstraZeneca/Oxford
    1. AZD1222
    2. 2 doses (0,28 days)
    3. IM administration
    4. 18+

2. Johnson & Johnson
    1. Ad26COVS1
    2. 2 dose and 1 dose studies (0,56d)
    3. IM administration
    4. 18-55, 65+

After dosing mix-up, latest COVID-19 vaccine success comes with big question mark

Vials of the University of Oxford's and AstraZeneca's vaccine candidate in a facility in Anagni, Italy, which will participate in large-scale production of the vaccine after regulatory approval.

VINCENZO PINTO/AFP via Getty Images

By Jon CohenNov. 25, 2020 , 11:40 AM

News

AstraZeneca likely to conduct new global low-dose Covid-19 vaccine trial

27 November 2020 (Last Updated November 27th, 2020 08:04)

AstraZeneca may initiate an additional global trial to evaluate the efficacy of its Covid-19 vaccine candidate, AZD1222, using a lower dosage.

AstraZeneca's production and manufacture facility. Credit: AstraZeneca.

AstraZeneca may initiate an additional global trial to evaluate the efficacy of its Covid-19 vaccine candidate, AZD1222, using a lower dosage.

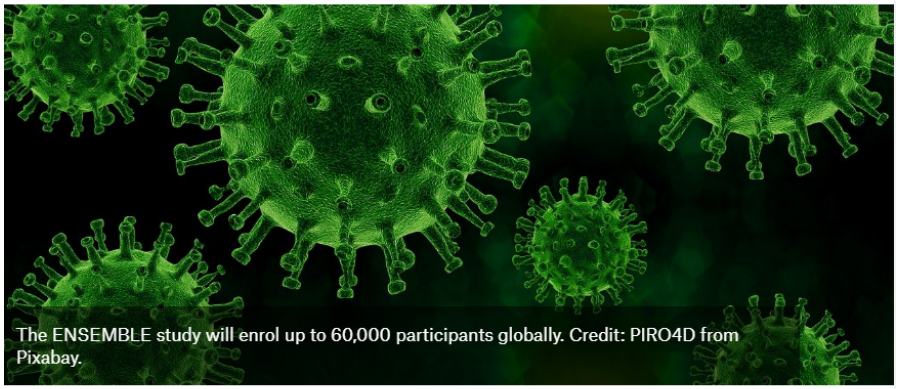
Pharmaceutical Technology 27 Nov 2020

News

Janssen begins second Phase III Covid-19 vaccine trial

16 November 2020 (Last Updated November 16th, 2020 06:40)

The Janssen Pharmaceutical Companies of Johnson & Johnson (J&J) has initiated enrolment and dosing of participants in the Phase III ENSEMBLE 2 trial of a two-dose regimen of JNJ-78436735, an investigational vaccine candidate for preventing Covid-19 infection.



The ENSEMBLE study will enrol up to 60,000 participants globally. Credit: PIRO4D from Pixabay.

The Janssen Pharmaceutical Companies of Johnson & Johnson (J&J) has initiated enrolment and dosing of participants in the Phase III ENSEMBLE 2 trial of a two-dose regimen of JNJ-78436735, an investigational vaccine candidate for preventing Covid-19 infection.

Pharmaceutical Technology 26 Nov 2020

Viral vector vaccine

Pros:

1. Viruses great at invading cells - use their machinery to make more copies of themselves = strong immune response.
2. Chimpanzee adenovirus. Believed to be safe, not been used before in a vaccine.

Cons:

? Anti vector immunity

Now What??

At least two vaccines available soon

Need to authorize use (FDA – EUA or approve)

Need to determine who will receive and how vaccines should be allocated (CDC/ACIP)

Review by CDPH Advisory Groups

What is an Emergency Use Authorization (EUA)?

- Mechanism to facilitate the availability and use of medical countermeasures, including vaccines, during public health emergencies.
- Under an EUA, FDA may allow use of unapproved medical products, or unapproved uses of approved medical products in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions when certain statutory criteria have been met, including that there are no adequate, approved, and available alternatives.
- Taking into consideration input from the FDA, manufacturers decide whether and when to submit an EUA request to FDA.

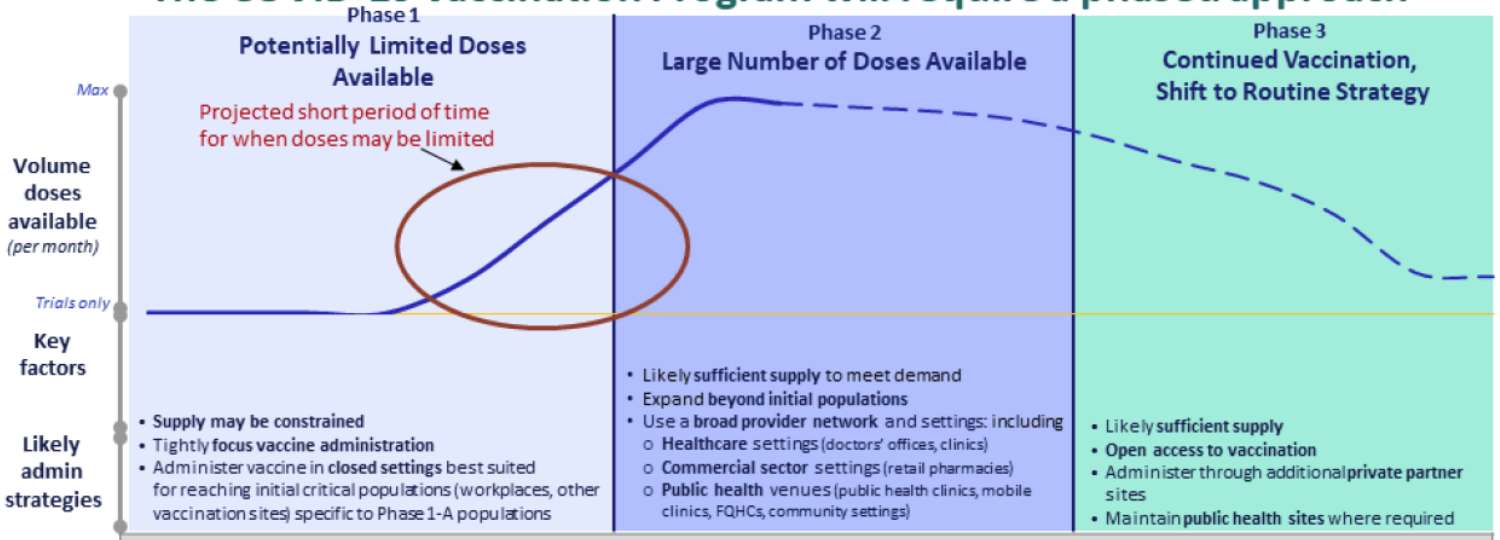
What is an Emergency Use Authorization (EUA)?

- FDA will undertake a comprehensive evaluation of non-clinical, clinical, and manufacturing data information submitted by a vaccine manufacturer.

- An EUA request for a COVID-19 vaccine can be submitted to FDA based on a final analysis of a phase 3 clinical efficacy trial or an interim analysis of such trial, i.e., an analysis performed before the planned end of the trial once the data have met the pre-specified success criteria for the study's primary efficacy endpoint.

1. Emergency Use Authorization for Vaccines Explained | FDA

The COVID-19 Vaccination Program will require a phased approach



Populations of Focus*		
Phase 1	**Phase 2**	**Phase 3**
Phase 1-A: • Paid and unpaid persons serving in healthcare settings who have the potential for direct or indirect exposure to patients or infectious materials and are unable to work from home.	• Remainder of Phase 1 populations • Critical populations** • General population	• Remainder of Phase 1 populations • Critical populations** • General population
Phase 1-B: • Other essential workers • People at higher risk of severe COVID-19 illness, including people 65 years of age and older		

9/4/20

**Planning should consider that there may be initial age restrictions for vaccine products.*

***See Section 4: Critical Populations for information on Phase 1 subset and other critical population groups.*

Consensus values guiding the phases

- Goals for vaccination while supply is limited
  - Decrease death and serious disease as much as possible
  - Preserve functioning of society
  - Reduce the extra burden the disease is having on people already facing disparities
  - Increase the chance for everyone to enjoy health and well-being

- Ethical principles while supply is limited
  - Maximize benefits and minimize harms — Respect and care for people using the best available data to promote public health and minimize death and severe illness
  - Mitigate health inequities — Reduce health disparities in the burden of COVID-19 disease and death, and make sure everyone has the opportunity to be as healthy as possible
  - Promote justice — Treat affected groups, populations, and communities fairly. Remove unfair, unjust, and avoidable barriers to COVID-19 vaccination
  - Promote transparency — Make a decision that is clear, understandable, and open for review. Allow and seek public participation in the creation and review of the decision processes

Source: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations-process.html

Final - November 27, 2020

MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)

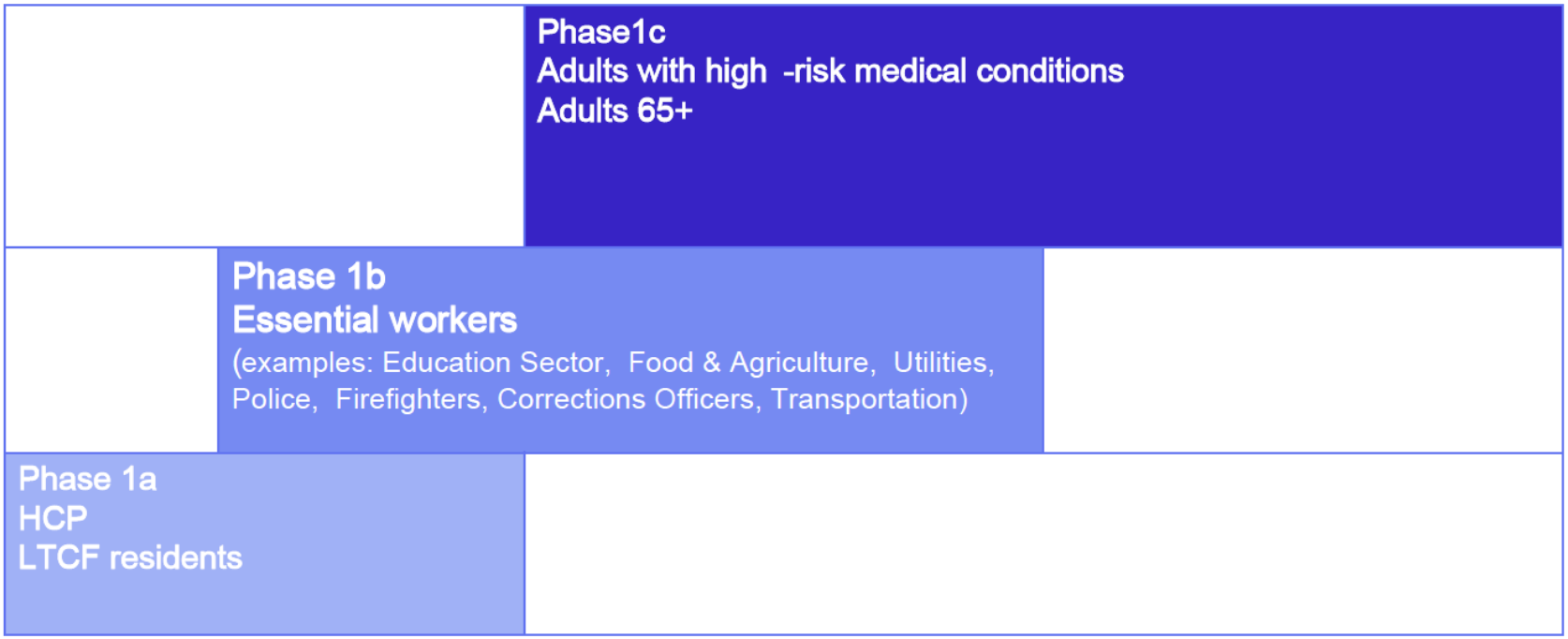
Centers for Disease Control and Prevention
Atlanta, Georgia 30329
December 1, 2020

	AGENDA ITEM	PRESIDER/PRESENTER(s)
Tuesday, December 1, 2020		
2:00	**Welcome & Introductions**	Dr. José Romero (ACIP Chair) Dr. Amanda Cohn (ACIP Executive Secretary, CDC)
	Coronavirus Disease 2019 (COVID-19) Vaccines	
	Introduction	Dr. Beth Bell (ACIP, WG Chair)
	Allocation of initial supplies of COVID-19 vaccine: Phase 1a	Dr. Kathleen Dooling (CDC/NCIRD)
	Clinical considerations for populations included in Phase 1a	Dr. Sara Oliver (CDC/NCIRD)
	Post-authorization safety monitoring update	Dr. Tom Shimabukuro (CDC/NCEZID)
	Discussion	
4:00	***Break***	
4:10	Public Comment	
4:40	**VOTE**	
	Allocation of initial supplies of COVID-19 vaccine: Phase 1a	Dr. Kathleen Dooling (CDC/NCIRD)
5:00	**Adjourn**	

Acronyms

CDC	Centers for Disease Control and Prevention
COVID-19	Coronavirus disease 2019
NCIRD	National Center for Immunization & Respiratory Diseases [of CDC/OID]
NCEZID	National Center for Emerging and Zoonotic Diseases [of CDC/OID]
WG	Work Group

Work Group Proposed Interim Phase 1 Sequence



Phased Allocation of COVID-19 Vaccines
ACIP COVID-19 Vaccines Work Group
Kathleen Dooling, MD, MPH
ACIP meeting
November 23, 2020

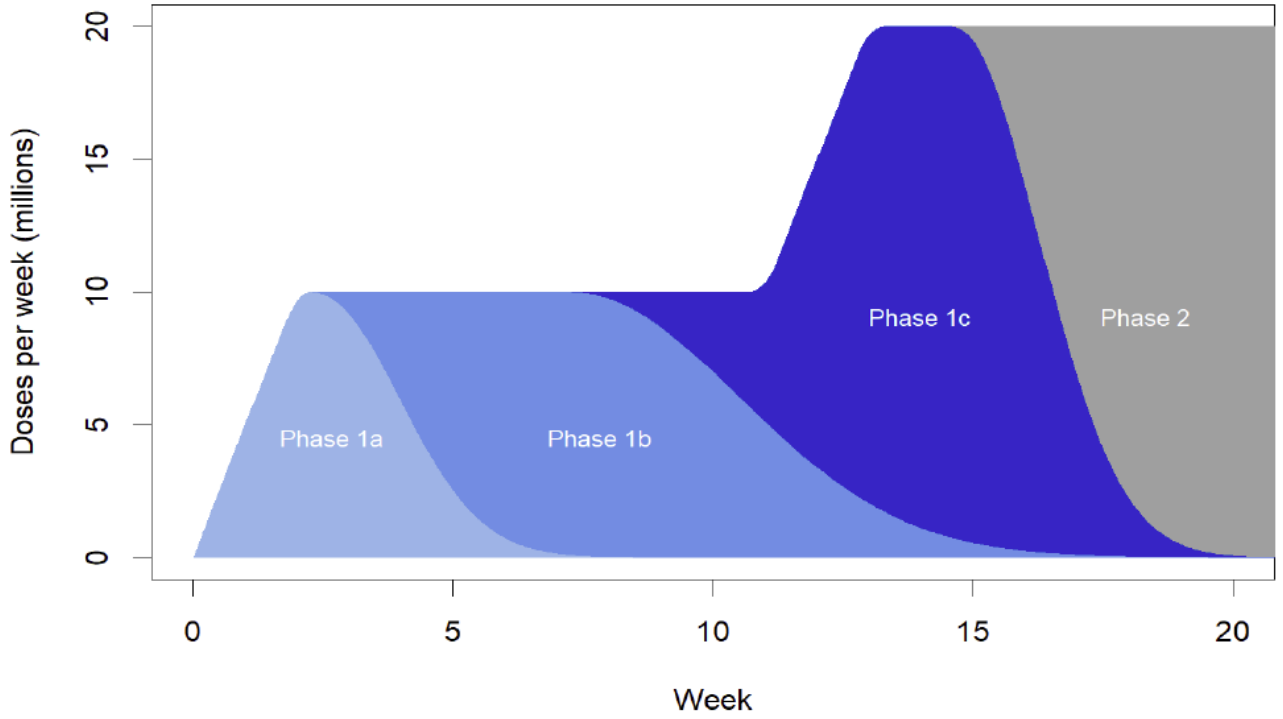
Hi-Risk Pre-Existing Medical Conditions

- Cancer
- Chronic kidney disease
- COPD (chronic obstructive pulmonary disease)
- Heart conditions, such as heart failure, coronary artery disease, or cardiomyopathies
- Immunocompromised state (weakened immune system) from solid organ transplant
- Obesity (body mass index [BMI] of 30 kg/m^2 or higher but < 40 kg/m^2)
- Severe Obesity (BMI ≥ 40 kg/m^2)
- Pregnancy
- Sickle cell disease
- Smoking
- Type 2 diabetes mellitus

Maybe at Increased Risk from COVID-19

- Asthma (moderate-to-severe)
- Cerebrovascular disease (affects blood vessels and blood supply to the brain)
- Cystic fibrosis
- Hypertension or high blood pressure
- Immunocompromised state (weakened immune system) from blood or bone marrow transplant, immune deficiencies, HIV, use of corticosteroids, or use of other immune weakening medicines
- Neurologic conditions, such as dementia
- Liver disease
- Overweight (BMI > 25 kg/m^2, but < 30 kg/m^2)
- Pulmonary fibrosis (having damaged or scarred lung tissues)
- Thalassemia (a type of blood disorder)
- Type 1 diabetes mellitus

Example of a possible Phase 1 sequence



Phased Allocation
of COVID-19 Vaccines
ACIP COVID-19 Vaccines Work Group
Kathleen Dooling, MD, MPH
ACIP meeting
November 23, 2020

Sources of COVID-19 vaccine supply

- Pre-positioned vaccine:
  - Shipped before EUA so its ready to go once FDA and CDC/ACIP approvals made
- Pharmacy partnership for Long-Term Care facilities
- Direct orders
  - Health facilities registered through CDPH
- Retail pharmacy program
  - 19 chains and independent as of now
  - 38,000 retail pharmacies covering 60% of the US population

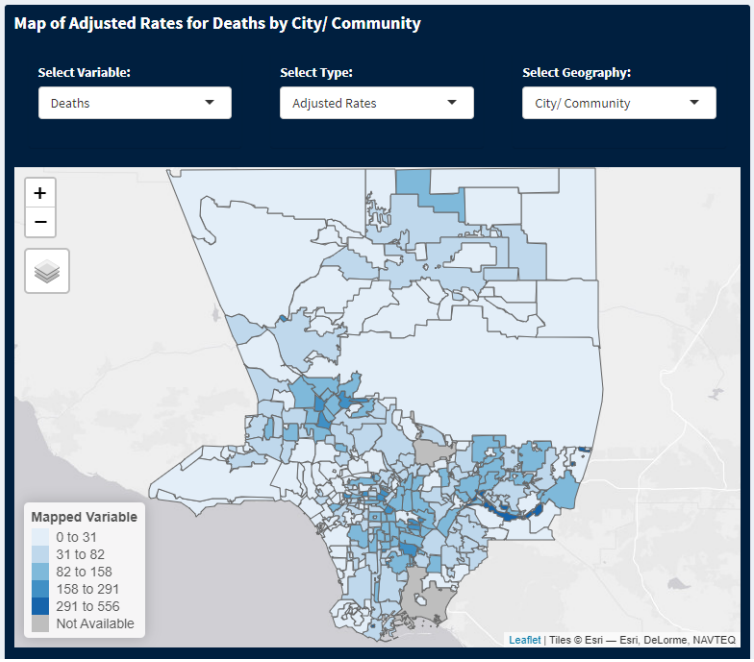
LA County specifics

- Need for further definition within phase 1 until more vaccine supplies available
- Planning in process for specifics within facility and between facility
- Social vulnerability information, healthcare worker surveillance and other data sources - subject to modification as pandemic epidemiology and vaccine availability changes.
- Significant community involvement
- More to follow

COVID-19 Positive Healthcare Workers and First Responders Data, Los Angeles County

Table 2. Occupational Setting of COVID-19 Positive Healthcare Workers and First Responders[1]

Setting	Count	Percent
Skilled Nursing/Assisted Living/Senior Living Facility	5754	32.6%
Hospital	4530	25.7%
Outpatient	1787	10.1%
EMS/First Responder	914	5.2%
Home Health	764	4.3%
Corrections/Detention	709	4.0%
Dental	486	2.8%
Mental Health	457	2.6%
Other Congregate	164	0.9%
Other	156	0.9%
Dialysis	153	0.9%
Pharmacy	137	0.8%
Urgent Care	114	0.6%



Vaccine information systems and documentation

- Multiple information needs currently across multiple different systems:
  - Scheduling
  - Ordering
  - Inventory
  - Reporting

- Local and federal reporting requirements
  - Record all individual level vaccine administration in EMR within 24 hours
  - Report all EMR data within 72 hours

- Goal is for an integrated end-to-end system without the need for duplication. May be fragmented initially with progressive improvement.

CAIR California Immunization Registry
Connected & Protected

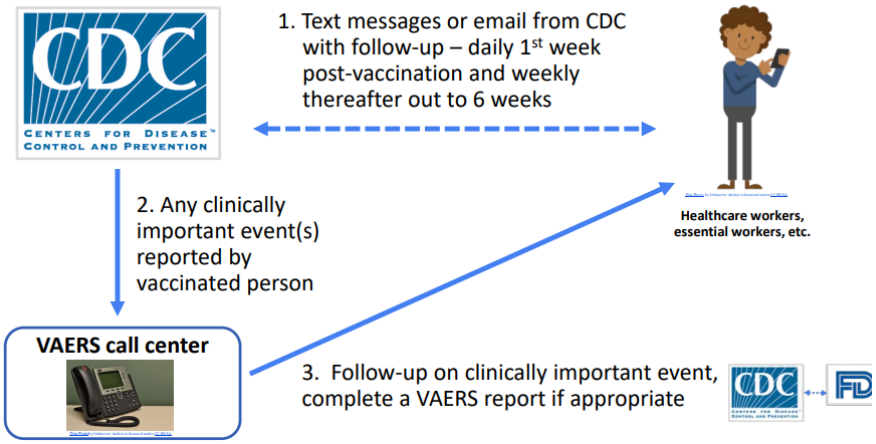
PrepMod SM

VTrckS

Adverse event monitoring and reporting

- New voluntary, self-reporting system V-SAFE
  - Linked to VAERS
- VAERS online reporting as usual
- CDC's National Healthcare Safety Network
- FDA: Other large insurer/payer databases
- [Adverse Event Monitoring and Reporting CDC]

Vaccine safety assessment for essential workers (V-SAFE)



CDC + FDA

VAERS

Vaccine Adverse Event Reporting System

Co-managed by CDC and FDA

http://vaers.hhs.gov

Paramedic Scope of Practice Addition

- Paramedics permitted by State upon request of LEMSA Medical Director to administer influenza and COVID-19 Immunizations during declared emergency (which we have now with the pandemic)
- Provider Agency Medical Director oversight
- Training
- Can immunize public safety personnel and community people
- Tremendous benefit to community

Paramedic Authorization for Influenza and COVID-19 Vaccination

STATE OF CALIFORNIA – HEALTH AND HUMAN SERVICES AGENCY — GAVIN NEWSOM, Governor

EMERGENCY MEDICAL SERVICES AUTHORITY
10901 GOLD CENTER DR., SUITE 400
RANCHO CORDOVA, CA 95670
(916) 322-4336 FAX (916) 324-2875

September 21, 2020

Marianne Gausche-Hill, MD, FACEP, FAAP, FAEMS
EMS Medical Director
Los Angeles County Emergency Medical Services Agency
10100 Pioneer Boulevard, Suite 200
Santa Fe Springs, CA 90670

Dear Dr. Gausche-Hill:

On March 4, 2020, California Governor Gavin Newsom declared a State of Emergency in response to the prevention of the spread of the COVID-19 outbreak. The emergency declaration provides the Director of the Emergency Medical Services Agency the authority to approve the expansion of local optional scope of practice for Emergency Medical Technicians (EMT), Advanced EMTs (AEMT), and paramedics in order to aid in the prevention of the spread of the virus.

This letter is to inform you that the Los Angeles County EMS Agency's request to add the administration of intramuscular influenza vaccination and COVID-19 vaccination, when available, to your paramedic local optional scope of practice has been approved. This authorization allows trained paramedics to administer these vaccines to emergency medical services providers and the public in accordance with your agency's policies and procedures. Your approval for the use of this practice shall conclude the date the emergency declaration is terminated.

If you have any questions, please contact Austin Trujillo of my staff by phone at (916) 431-3727 or by email at Austin.Trujillo@emsa.ca.gov.

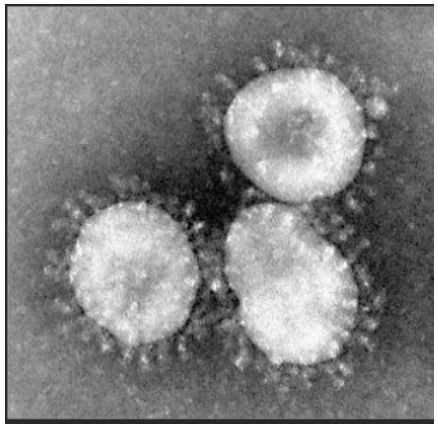
Sincerely,

Dave Duncan, MD
Director

cc: Cathy Chidester, EMS Director, Los Angeles County EMS Agency
Nichole Bosson, MD, MPH, FAEMS, Assistant Medical Director, Los Angeles County EMS Agency

Learning Objectives

1. Describe current status of COVID-19 pandemic in United States
2. Describe basic biology of current COVID-19 Phase III candidate vaccines
3. Describe storage and handling requirements for use of vaccines requiring ultra-low cold storage
4. List steps to permit paramedic scope of practice adjustment to allow COVID-19 vaccine administration



Selected Links

- https://www.pfizer.com/news/hottopics/covid_19_vaccine_u_s_distribution_fact_sheet
- COVID-19 Vaccination | CDC
- COVID-19 Vaccine Planning - Questions and Answers (ca.gov)

Trust, Transparency, Safety, Confidence, Acceptance

Thank you!

fpratt@ph.lacounty.gov

PedAc Educational Session:
COVID-19 Vaccine Update

Access evaluation & post-test for BRN/EMS CE by scanning QR code or entering link into your web browser.

Must have entered name in chat to be eligible for CE credit

Direct link:

https://forms.gle/FmV1JNSabT2aDqop8

Evaluation with passing post-test (5/6) must be submitted by 1200 on December 4th, 2020, to receive CE for this event

BRN CE Questions: rgoodmanrn@yahoo.com

EMS CE Questions: dwells@dhs.lacounty.gov