AGRE

# Association of Graduate Regulatory Educators

Education Webinar

***Emergency Use Authorization During COVID-19 Pandemic***

**Speakers: Kim Walker (SDSU) and Kathleen Thoma (GWU)**

January 19, 2021

# AGRE Global

- Initiated in 2010 through a series of meetings
- Brought together leaders of programs offering graduate training in regulatory affairs and regulatory science that developed a formal organization with several goals:
  - to share best practices in regulatory education and promote the continued development of regulatory education as an academic discipline
  - to provide a forum for discussion of issues of mutual importance for educating stakeholders involved with commercializing products or services in the biomedical product and healthcare industries
  - to support the development of an organizational critical mass that is well-positioned to impact public policies that affect regulatory education in the US and internationally

- **AGRE** is a place to meet and exchange ideas with other regulatory educators internationally.
- **AGRE** is a forum for coordinating input on policy issues of importance to our educational programs.
- **AGRE** is a group that develops and consolidates teaching materials to make your teaching more effective.
- **AGRE** is a community for research on competencies, advancement of the discipline, and development of the profession.

- New members WELCOME ( see website agreglobal.org)

# Today's Webinar Speakers Bios

- **Kim Walker MS, RAC (US & EU), FRAPS; Global Regulatory, Quality and Clinical Consultant and Instructor, California State University at Fullerton and San Diego State University**
  - Ms Walker is an independent Global Regulatory Affairs, Quality Assurance, and Clinical Affairs Consultant and owner of Kim Walker Consulting since 2006. In her consulting practice, she assists clients with pre- and post-market regulatory, clinical, and quality system needs. She is currently assisting the World Health Organization (WHO) as an Innovation COVID-19 Response Team Consultant. Kim has served on the Orange County Regulatory Affairs Discussion Group (OCRA) Program Committee since 2003. Ms. Walker has also participated in the San Diego Regulatory Affairs Network (SDRAN) Mentoring Program since 2009. She has achieved both the US and EU Regulatory Affairs Professional Society (RAPS) Regulatory Affairs Certifications. and has been accepted as a RAPS Fellow in recognition of her contributions and leadership in advancing the regulatory profession. Kim is an instructor and co-developer of many Medical Device Regulation courses.

- **Kathleen Thoma EdD, CCRC, CPH; Assistant Professor and Director of the Undergraduate Program in Clinical Research Administration, The George Washington University School of Medicine and Health Sciences**
  - Dr. Thoma is an assistant professor in the Department of Clinical Research and Leadership and the program director for the undergraduate program in Clinical Research Administration. She has been at GW for almost 4 years. Before that, she was the director of research and a clinical research specialist at the University of Florida Center for HIV/AIDS Research, Education and Services for 10 years. During that time, she managed both industry-sponsored and NIH-funded network trials through the IMPACT, HPTN, ATN and PHACS networks. She is a certified clinical research professional through the Society of Clinical Research Associates and is certified in public health. Her research interests include improving diversity in clinical trials, patient centricity and patient engagement in clinical trials, health literacy, health equity and HIV impacted populations.

# Next AGRE Education Webinar

- Topic: ***Building the Best RA Curriculum***
  - Speaker: **Orin Chisholm**
  - Date: **March 16, 2021**
  - Time: **4pm ET/1pm Pacific**

# EMERGENCY USE AUTHORIZATIONS

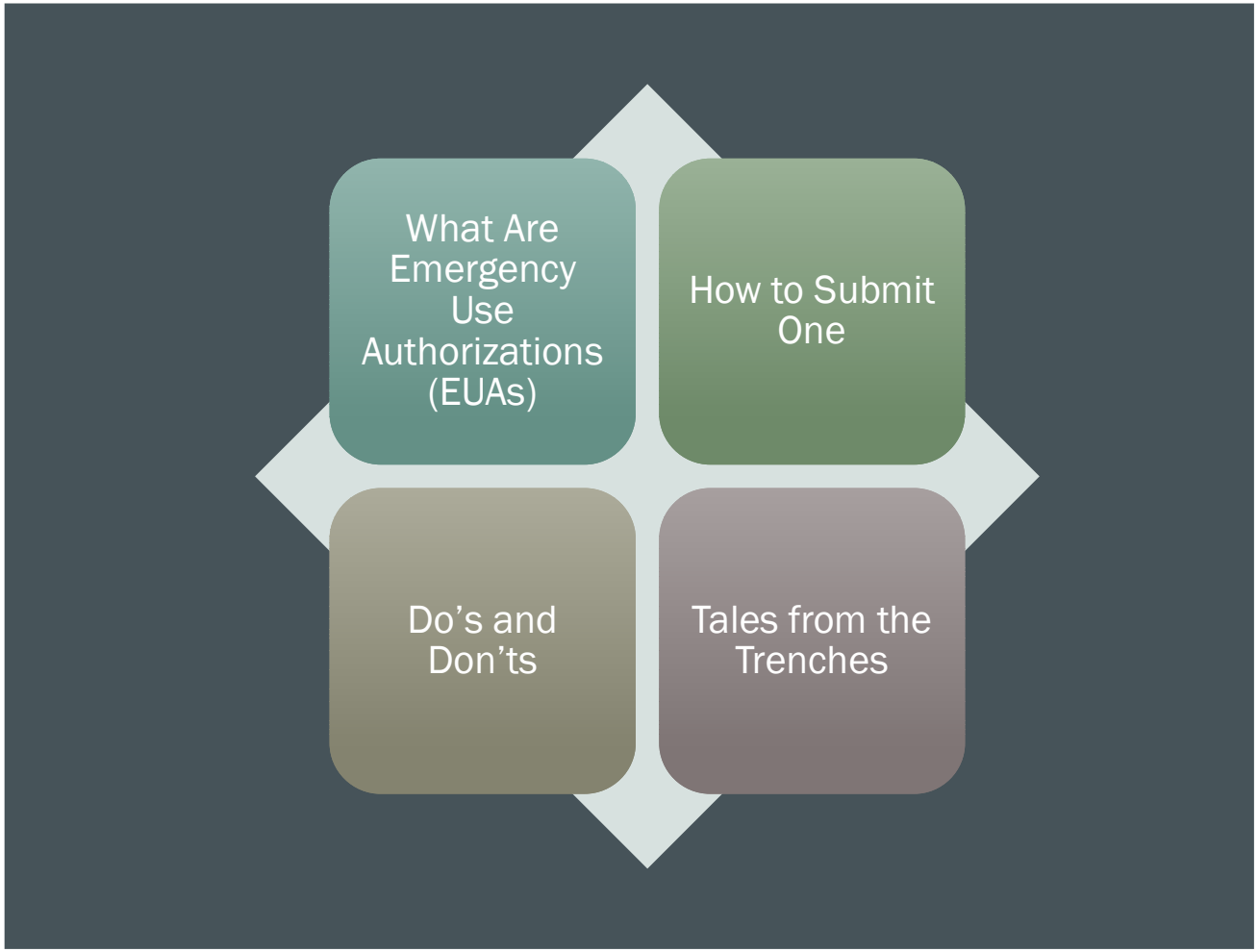
## TALES FROM THE TRENCHES

### ASSOCIATION OF GRADUATE REGULATORY EDUCATORS (AGRE)

### JANUARY 19, 2021

KIM WALKER, MS, RAC (US & EU), FRAPS

# WHAT WE WILL DISCUSS



# WHAT ARE EUAs?

- HHS Secretary Makes Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) FD&C Act
  - Based on emergency determinations by Secretary of Homeland Security, Secretary of Defense, and/or HHS Secretary
  - In consultation with Assistant Secretary for Preparedness and Response (ASPR), Director of the National Institutes of Health (NIH), & Director of CDC
- Section 564 FD&C Act - FDA Commissioner may allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by chemical, biological, radiological, & nuclear (CBRN) agents when there are no adequate, approved, & available alternatives
- Medical products also referred to as “medical countermeasures” or “MCMs”
- Section 564 of the FD&C Act was amended by:
  - Project Bioshield Act of 2004
  - Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA)
  - 21st Century Cures Act of 2016
  - Public Law 115-92 of 2017
- PAHPRA amendments allowed for:
  - Empower FDA to extend the expiration date of MCM stockpiled for use in a CBRN emergency
  - Permit FDA to waive cGMP requirements (e.g., storage or handling) to accommodate emergency response needs;
  - Allow emergency dispensing of MCMs without requiring individual prescriptions or all of the information otherwise required
  - Permit CDC to create and issue “emergency use instructions” (EUI) concerning FDA-approved conditions of use for eligible products
  - Authorize FDA to waive Risk Evaluation and Mitigation Strategy (REMS) requirements
  - Permits government stakeholders to pre-position (e.g., stockpile, forward-deploy) MCMs in anticipation of FDA approval or clearance, authorization of an investigational use, or issuance of EUA, to enable rapid deployment

# CONDITIONS OF AUTHORIZATION

EUA Guidance – January 2017
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities

| Condition | Unapproved Product | Unapproved Use of an Approved Product | FD&C Act Section |
|---|---|---|---|
| **Information ("fact sheets") for healthcare providers administering the product** (significant known/potential benefits/risks of product and extent to which benefits/ risks are unknown; FDA has authorized emergency use) | Required | Required | § 564(e)(1)(A)(i) § 564(e)(2)(A) |
| **Information ("fact sheets") for product recipients** (significant known/potential benefits/risks of product and extent to which benefits/ risks are unknown, option to accept or refuse product, consequences of refusing, available alternatives, FDA has authorized emergency use) | Required | Required | § 564(e)(1)(A)(ii) § 564(e)(2)(A) |
| **Adverse event monitoring and reporting** | Required | Discretionary | § 564(e)(1)(A)(iii) § 564(e)(2)(A) |
| **Recordkeeping and reporting** (by product manufacturers) | Required | Discretionary | § 564(e)(1)(A)(iv) § 564(e)(2)(A) |
| **Recordkeeping and reporting** (by persons other than product manufacturers) | Discretionary | Discretionary | § 564(e)(1)(B)(iv) § 564(e)(2)(A) |
| **Product distribution** (which entities may distribute product and how to perform distribution) | Discretionary | Discretionary[c] | § 564(e)(1)(B)(i) § 564(e)(2)(A) |
| **Product administration** (who may administer product and categories of individuals to whom, and circumstances under which, product may be administered ) | Discretionary | Discretionary[c] | § 564(e)(1)(B)(ii) § 564(e)(2)(A) |
| **Data collection and analysis** (concerning product safety/effectiveness) | Discretionary | Discretionary | § 564(e)(1)(B)(iii) § 564(e)(2)(A) |
| **CGMP and prescription waiver or limit** | Discretionary | Discretionary | § 564(e)(3) |
| **Advertising/other promotional material** | Discretionary | Discretionary | § 564(e)(4) |
| **Other** (any other condition FDA finds necessary or appropriate to protect the public health) | Discretionary | Discretionary | § 564(e)(1)(B) § 564(e)(2)(A) |

# DO EUAs EXPIRE?

- Yes!
- When an EUA declaration is terminated, any EUA(s) issued will no longer remain in effect
- HHS Secretary's EUA declaration will terminate on the earlier of:
  - Determination by HHS Secretary that circumstances that precipitated declaration have ceased
    - After consultation as appropriate with the Secretary of Homeland Security or the Secretary of Defense
  - Change in approval status of the product such that the authorized use of the product is no longer unapproved
    - For example, EUA issued for unapproved use of approved product may no longer be needed if product is approved by FDA for use permitted by EUA
- Before EUA declaration terminates, HHS Secretary must provide advance notice sufficient to allow for disposition of unapproved products, and labeling or other information provided related to an unapproved use of an approved product

# CURRENT NON-COVID EUAs

- Anthrax
- Ebola Virus
- Enterovirus D68 (EV-D68)
  - EV-D68 is one of more than 100 non-polio enteroviruses. This virus may cause mild to severe respiratory illness or cause no symptoms in some people. Those most susceptible are infants, children, teenagers, and those with asthma.
- Freeze Dried Plasma
  - Treatment of hemorrhage or coagulopathy of U.S. Military personnel during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical
- H7N9 Influenza
  - The H7N9 flu is a respiratory disease caused by novel influenza virus. Human cases of influenza A (H7N9) virus infection have been identified in China but there has been no sustained human-to-human transmission in China.
- Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
- Nerve Agent
  - Atropine Auto-Injector for the treatment of poisoning by susceptible organophosphorous nerve agents having cholinesterase activity as well as organophosphorous or carbamate
- Zika Virus

# CURRENT COVID EUAs (AS OF JAN 18TH)

- *In Vitro* Diagnostic Products
  - Commercial Molecular – 204 approved
  - LDT Molecular – 32 (5 – OIR rejected) (OIR is no longer accepting LDT EUAs to conserve reviewer resources)
  - Commercial Antibody Serology - 68
  - Commercial Antigen – 13
  - COVID Patient Management – 3 (IL-6 assays)
- Personal Protective Equipment and Related Devices – 270
  - Decontamination Systems for PPE - 14
- Drug/Biologic Products – 8
- Vaccines - 2

# CURRENT COVID EUAS (AS OF JAN 18TH)

- Ventilators and Other Medical Devices
  - Right Ventricular Assist Catheter – 1
  - Left Ventricular Support System – 2
  - ECMO - 1
  - Predictive Screening Software - 2
  - Continuous Renal Replacement Therapy - 3
  - Extracorporeal Blood Purification - 4
  - Remote Patient Monitoring - 6
  - Infusion Pumps - 1
  - ECG Low Ejection Fraction Software Tool - 1
  - Patient Isolation Transport Unit (PITU) - 1
  - Respiratory Muscle Stimulator/Diaphragmatic Pacing Therapy System - 4
  - Ventilators & Accessories - 105

# PRE-EUAs

- Highly recommended
  - Get valuable feedback – Tales from the Trenches example
  - Do not be discouraged if you do not hear back from FDA; it just means they are busy & triaging
- May include discussions about:
  - A potential EUA product
  - Appropriate vehicle to use (e.g., IND or IDE, Master File, pre-EUA submission) for submitting EUA data
- Generally, FDA recommends submitting data as part of "pre-EUA" - should follow recommendations for submitting pre-IND, IND, and device pre-submissions
  - Early in the COVID EUA timeline, FDA was very available and willing to discuss any potential EUA; very helpful and creative conversations
  - As certain offices within CDRH became overwhelmed (i.e. IVD group – OHT7/OIR), they started to recommend submitting pre-EUA using device specific templates & through special email addresses
  - Not going through Doc Control Center for pre-EUAs or EUAs

# EUA GENERAL CONTENT

- Description of the product
- Intended use
- Description of product's FDA approval status
  - Under an investigational application
  - Is product is approved in a foreign country for either the proposed use or another use
  - Information on use by either foreign country or international organization (e.g. WHO)
- Need for product, including ID of any approved alternative product(s) & their availability & adequacy for the proposed use
- Unmet need(s) EUA would address
- Available safety & effectiveness info for the product, including reference to other pre-market submission data
  - This can be very helpful in expediting your EUA review (e.g. IVD controls previously cleared under K123456)
- Risks & benefits, including info on threats posed by CBRN agent(s) involved
- CMC info
- List each manuf site for the product & cGMP status
- Quantity of finished product on hand & surge capabilities of each manufacturing site
  - This is important info for FDA to help triage product reviews
  - If you are not truly capable of ramping up to meet the needs of this emergency, then you should consider not filing EUA; don't waste FDA's time & your money
- Draft IFU/PI & Fact Sheets for health care professionals &/or users/patients

# EUA IVD CONTENT

- EUA IVD Templates - https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas
- Send pre-EUAs and EUAs to CDRH-EUA-Templates@FDA.HHS.GOV
- Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised) Guidance May 11, 2020 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised
- Can distribute IVDs once fully validated and with notification to FDA
  - Molecular tests must submit an EUA within 15 business days
  - Commercially manufactured serology tests must submit an EUA within 10 business days
  - High complexity CLIA lab manufactured serology tests do not have to submit an EUA but do have to notify FDA
  - Beware the temptation to distribute too early – Recalls & False Results Letters to Customers
- FAQs on Testing for SARS-CoV-2 - https://www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-testing-sars-cov-2
- OIR hosts Virtual Town-Hall meetings every Wednesday morning
  - Recordings, transcripts, and schedules can be found at: https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/virtual-town-hall-series-immediately-effect-guidance-coronavirus-covid-19-diagnostic-tests-07152020

# EUA IVD MOLECULAR CONTENT

- EUA Templates - https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas
  - Molecular Diagnostic Template for Commercial Manufacturers (updated July 28, 2020)
  - Molecular Diagnostic Template for Laboratories (updated July 28, 2020)
  - Home Specimen Collection Molecular Diagnostic Template (May 29, 2020)
  - Manufacturers of Molecular and Antigen Diagnostic COVID-19 Tests for Non-Laboratory Use (July 29, 2020)
- Validation Requirements
  - Limit of Detection
    - Dilution series 3 replicates per concentration w/inactivated virus on actual patient specimen (spiked RNA or inactivated virus in artificial matrix also acceptable)
    - Confirm final concentration w/20 replicates in most challenging clinical matrix (for respiratory samples = sputum)
    - LoD = lowest concentration at which 19/20 replicates are positive
  - Clinical Evaluation
    - 30 positive and 30 negative specimens
    - Contrived samples OK but have special requirements
    - Must have 95% agreement at 1x-2x LoD & 100% agreement at all other concentrations & for negative specimens
  - Inclusivity
    - *In silico* analysis 100% of published SARS-CoV-2 sequences will be detectable w/selected primers and probes
  - Cross-reactivity
    - Wet testing on common respiratory flora & other viral pathogens at concentrations of $10^6$CFU/ml or higher for bacteria & $10^5$pfu/ml or higher for viruses

# EUA IVD SEROLOGY ANTIBODY CONTENT

- EUA Templates - https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas
  - Serology Template for Commercial Manufacturers (updated November 24, 2020)
  - Home Specimen Collection Serology Template for Fingerstick Dried Blood Spot (November 24, 2020)
- Validation Requirements
  - Cross-reactivity/Analytical Specificity
    - 100% agreement required
  - Matrix Equivalency
  - Class Specificity
    - 100% agreement required
  - Clinical Agreement Study
    - Use human specimens from patients with microbially confirmed (PCR) COVID infection
    - Use at least 30 unique antibody positive samples from 30 patients for each immunoglobulin claimed & 75 unique antibody negative samples from 75 patients tested for SARS-CoV-2 & confirmed as negative
    - For tests that detect and differentiate IgM and IgG:
      - Overall (i.e., combined IgM/IgG) positive percent agreement (PPA) of 90%, PPA for IgM of 70%, PPA for IgG of 90% and overall (i.e., combined IgM/IgG) negative percent agreement (NPA) of 95%
    - For tests that detect either total antibodies, only IgG or only IgM:
      - PPA of 90% and NPA of 95%
  - Point of Care Studies
- Assay Requirements
  - Must have external positive control for each antibody class claimed (e.g., IgG, IgM)
  - Must have external negative control

# WHAT HAPPENED WITH SEROLOGY TESTS

- FDA provided early market access through its March 16, 2020 guidance but that access was premised on the understanding that tests should be validated before being marketed to fall under the enforcement discretion policy
  - Intended to help support CDC Serology Surveillance Program (seroprevalence – looking to see how common infection is & where)
- Reports started to trickle into FDA about serology tests not being accurate
- Partnered w/NIH-NCI to conduct independent evaluations of serology tests
- On June 16, 2020, FDA revoked EUA for Chembio Diagnostic Systems, Inc.'s DPP COVID-19 IgM/IgG System for detection of IgM and IgG antibodies against SARS-CoV-2
- Then FDA systematically started to revoke other serology tests based on NCI results
- FDA listed on their website the commercial manufacturers who provided notification to the FDA that they validated & intended to distribute a serology test who were now not allowed to continue distributing their product
  - FDA had previously included them on the website notification list of commercial manufacturers distributing serology test kits but they have now been removed from that notification list & placed on the EUA revoked list.
- FDA expects that the tests on this list will not be distributed unless & until an EUA is issued for the test, & the FDA may take additional actions as appropriate.
- FDA also issued a letter on the recommendations for clinical laboratories & health care providers regarding these tests - June 19, 2020, Letter to Clinical Laboratory Staff and Health Care Providers - 71 tests on this list

# EUA IVD ANTIGEN CONTENT

- EUA Templates - https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas
  - Antigen Template for Commercial Manufacturers (updated October 26, 2020)
  - Manufacturers of Molecular and Antigen Diagnostic COVID-19 Tests for Non-Laboratory Use (July 29, 2020)
- Validation Requirements
  - Limit of Detection/Analytical Sensitivity
  - Cross-reactivity/Analytical Specificity
  - Microbial Interference
  - Clinical Agreement Study
    - Should use human specimens from patients with & without COVID infection
- New variants – FDA asking all antigen and molecular who might be affected by new variants to send in data confirming assay can detect new variants

# EUA NON-IVD CONTENT

- EUA Non-IVD Templates
  - Infusion Pump Template - https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/infusion-pump-euas
  - Ventilator Templates - https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/ventilators-and-ventilator-accessories-euas
  - Surgical Masks EUA Template - https://www.fda.gov/media/140896/download
  - General Template - Pre-Emergency Use Authorization (EUA)/EUA Interactive Review Template For Non-IVD Products - https://www.fda.gov/media/137965/download
- Send pre-EUAs and EUAs to : CDRH-NonDiagnosticEUA-Templates@fda.hhs.gov

# EUA REVIEW PROCESS – GUIDANCE DOC

- FDA intends to establish priorities for its review of requests to issue an EUA based on a variety of factors. These include:
  - Seriousness & incidence of the clinical disease or condition
  - Public health need for product &, when known, the safety & effectiveness of other potential MCMs
  - Urgency of treatment need
  - Availability & adequacy of info concerning likelihood product may be safe & effective
  - Potential role that use of product may have in ensuring national security
  - Whether the product is included in government stakeholder stockpiles
  - Extent to which product would serve a significant unmet medical need
  - Whether the request is from (or supported by) a government stakeholder
  - Availability of the product, (e.g., the quantity & manufacturing capacity)
  - Whether other mechanisms, such as developing a clinical study protocol under an IND or IDE for investigational use, might be more appropriate for allowing emergency access to products under development

# EUA REVIEW PROCESS – PERSONAL EXPERIENCE

- In the beginning, EUAs were being approved in 1-2 weeks
- Now (for IVDs) slowed down to 2 months or more
- FDA is resource limited – IVD reviewer told me they had over 2,000 EUAs to review & only 60 reviewers available
  - IVD reviewers are very stressed & feel under the microscope by White House, Congress, Industry, & Media
- Other offices within CDRH much less busy & very willing to help
  - If they cannot justify an EUA, they will fast-track your IDE or Pre-Market Submission
- Review process is very interactive & transparent
- Overall, has been great experience & a helpful window into the inner workings of FDA

# ADVERSE EVENT REPORTING

- Adverse Event Reporting for Medical Devices Under Emergency Use Authorization (EUA) or Discussed in COVID-19-Related Guidance Documents - https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/adverse-event-reporting-medical-devices-under-emergency-use-authorization-eua-or-discussed-covid-19

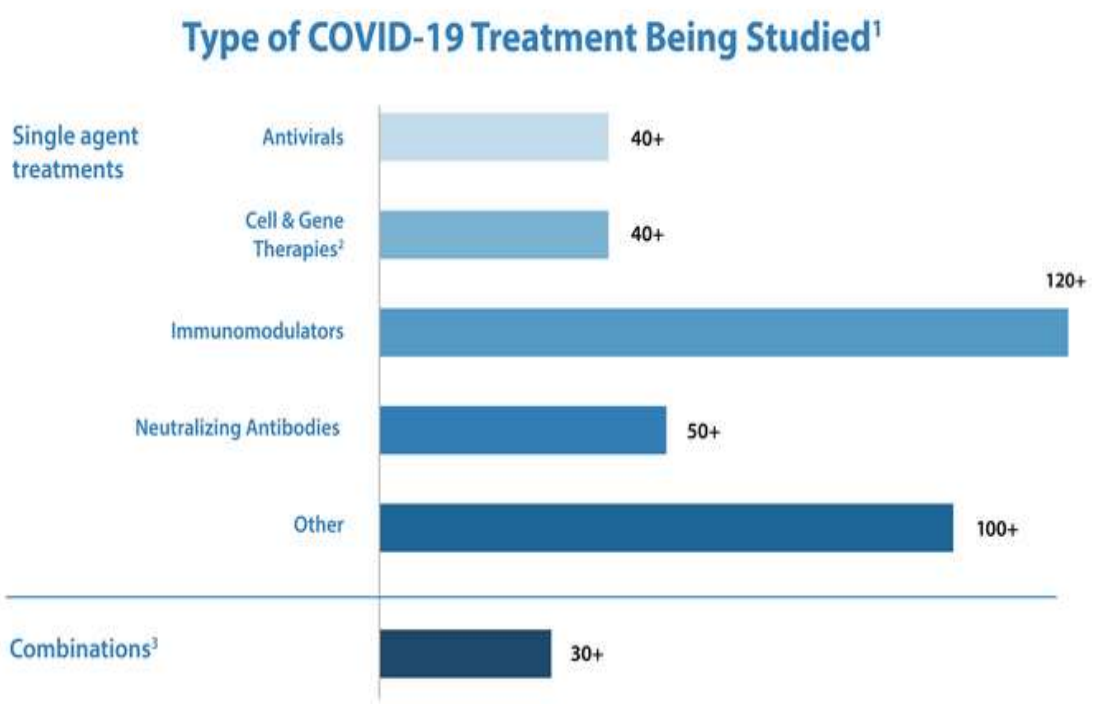
# CBER COVID ACTIVITIES

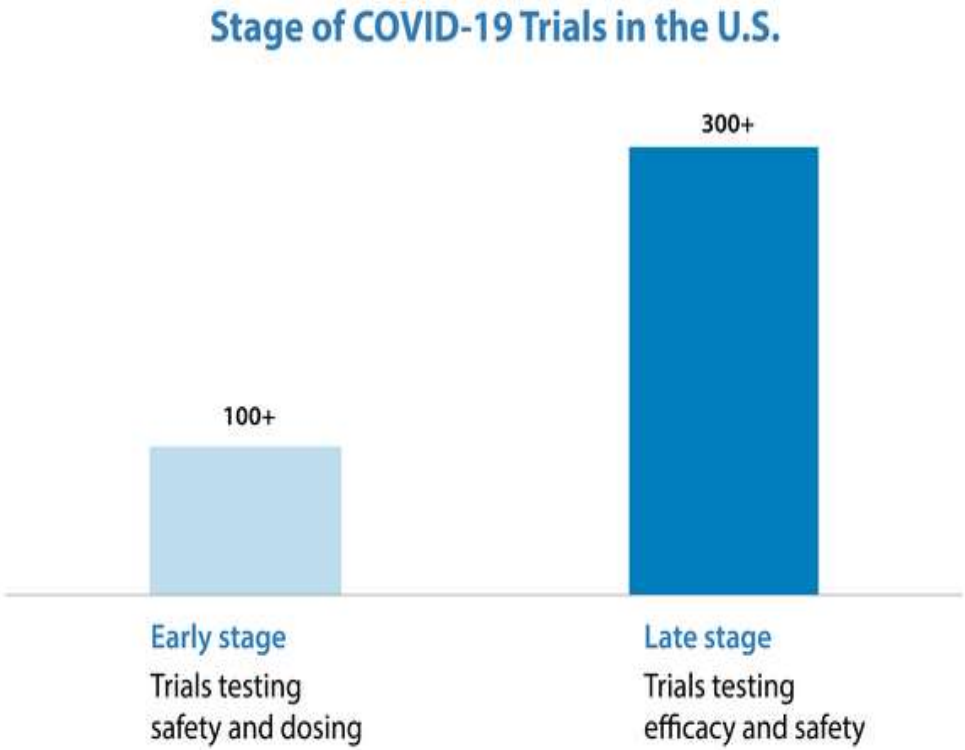
- Expediting clinical trials for preventive vaccines & other therapeutic biological products
- Supporting product development & scaling up of manufacturing capacity for high priority products for COVID-19
- Helping to ensure adequate blood supply
- Facilitating access to convalescent plasma & other investigational products
- Providing info to healthcare providers & researchers to help them submit emergency IND requests

# CTAP

- FDA created special emergency program for possible therapies, the Coronavirus Treatment Acceleration Program (CTAP)
- Uses every available method to move new treatments to patients as quickly as possible, while at the same time finding out whether they are helpful or harmful
- Continue to support clinical trials testing new COVID treatments to gain valuable knowledge about their safety & effectiveness
- As of January 18, 2021:
  - 400+ active trials of therapeutic agents
  - Another 590+ development programs for therapeutic agents in the planning stages
  - 8 EUAs for COVID-19 Treatments
  - 1 Drug approved for use in COVID-19 patients
- More info at: https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap

# CTAP UPDATES



# EUA DO'S & DON'TS

- Be nice!  Reviewers are stressed & appreciate being treated as humans – Tales from the Trenches Example
- Follow the EUA templates & guidance docs
- Create a well organized & easy to navigate submission
  - Tell the story….do not assume they understand your product or data as well as you do
- Help your reviewer keep track of changed docs & send them a final version of everything before approval for their files
  - We need to go above and beyond to help FDA through this
- If you don't get your reviewer assigned within 2 weeks, email FDA
- If you have questions, email or call FDA; they are very responsive
- However, do not waste their time; be judicious
  - Don't pester them about your timeline – Tales from the Trenches Example
- Make sure you follow through with any conditions of approval
  - 7/14 OIR started to contact Molecular Manufs with newly created protocol & reference materials for LoD & traceability testing

# WHAT ARE OTHER COUNTRIES DOING?

- EU – Emergency Route
  - Up to individual member states
  - Several EU-wide guidelines published:
    - Current performance of COVID-19 test methods and devices and proposed performance criteria - https://ec.europa.eu/docsroom/documents/40805?locale=en
    - COMMISSION RECOMMENDATION (EU) 2020/403 of 13 March 2020 on conformity assessment and market surveillance procedures within the context of the COVID-19 threat - https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32020H0403&from=EN
    - How to verify that medical devices and personal protective equipment can be lawfully placed on the EU market and thus purchased and used – also in the COVID-19 context - https://ec.europa.eu/docsroom/documents/41385/attachments/1/translations/
- UK – Medicines and Healthcare products Regulatory Agency (MHRA) – Regulatory Flexibilities
  - Has expedited review processes - https://www.gov.uk/guidance/mhra-regulatory-flexibilities-resulting-from-coronavirus-covid-19
- China - National Medical Products Administration (NMPA) - https://covid-19.chinadaily.com.cn/
  - Fast Track Product Reviews
  - Allow products to be approved at provincial level
  - Import exceptions
  - Expanded insurance to cover telemedicine services

# WHAT ARE OTHER COUNTRIES DOING?

- Australia – Therapeutic Goods Administration (TGA) - https://www.tga.gov.au/collection/covid-19
  - Exemptions from Listing on Australian Register of Therapeutic Goods (ARTG)
  - Expedited Reviews
- Japan – Pharmaceuticals and Medical Devices Agency (PMDA) - https://www.pmda.go.jp/english/about-pmda/0002.html
  - Expedited reviews
- Canada – Health Canada - https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/regulatory-response-health-product-access.html
  - Streamlined Clinical Trials
  - Expedited Reviews
  - Reduced Administrative Requirements
  - Published Several Guidelines
- South Korea – Ministry of Drug & Food Safety (MDFS) - https://www.mfds.go.kr/eng/index.do
  - Expedited Reviews
  - Published Several Guidelines
- Many Other Countries with Special COVID Product Processes

# FDA GUIDANCE DOCUMENTS

- Emergency Use Authorization of Medical Products and Related Authorities January 2017 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities
- Pandemic and All-Hazards Preparedness Reauthorization Act of 2013(PAHPRA) Medical Countermeasure (MCM) Authorities: FDA Questions and Answers for Public Health Preparedness and Response Stakeholders January 2014 - https://www.fda.gov/media/87718/download
- Effects of the COVID-19 Public Health Emergency on Formal Meetings and User Fee Applications for Medical Devices - Questions and Answers - Guidance for Industry and Food and Drug Administration Staff 06/22/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/effects-covid-19-public-health-emergency-formal-meetings-and-user-fee-applications-medical-devices
- Notifying CDRH of a Permanent Discontinuance or Interruption in Manufacturing of a Device Under Section 506J of the FD&C Act During the COVID-19 Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff (Revised) 06/19/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/notifying-cdrh-permanent-discontinuance-or-interruption-manufacturing-device-under-section-506j-fdc
- Enforcement Policy for Non-Invasive Remote Monitoring Devices Used to Support Patient Monitoring During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency (Revised) - Guidance for Industry and Food and Drug Administration Staff 06/05/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-non-invasive-remote-monitoring-devices-used-support-patient-monitoring-during
- Recommendations for Sponsors Requesting EUAs for Decontamination and Bioburden Reduction Systems for Face Masks and Respirators During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff 05/26/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recommendations-sponsors-requesting-euas-decontamination-and-bioburden-reduction-systems-face-masks

# FDA GUIDANCE DOCUMENTS

- Enforcement Policy for Face Masks and Respirators During the Coronavirus Disease (COVID-19) Public Health Emergency (Revised) - Guidance for Industry and Food and Drug Administration Staff 05/26/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-face-masks-and-respirators-during-coronavirus-disease-covid-19-public-health
- Supplements for Approved Premarket Approval (PMA) or Humanitarian Device Exemption (HDE) Submissions During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff 05/21/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/supplements-approved-premarket-approval-pma-or-humanitarian-device-exemption-hde-submissions-during
- Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised) - Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff 05/04/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised
- Enforcement Policy for Remote Digital Pathology Devices During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry, Clinical Laboratories, Healthcare Facilities, Pathologists, and Food and Drug Administration Staff 04/24/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-remote-digital-pathology-devices-during-coronavirus-disease-2019-covid-19-public
- Enforcement Policy for Imaging Systems During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff 04/23/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-imaging-systems-during-coronavirus-disease-2019-covid-19-public-health-emergency
- Enforcement Policy for Non-Invasive Fetal and Maternal Monitoring Devices Used to Support Patient Monitoring During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff 04/23/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-non-invasive-fetal-and-maternal-monitoring-devices-used-support-patient

# FDA GUIDANCE DOCUMENTS

- Enforcement Policy for Telethermographic Systems During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff 04/16/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-telethermographic-systems-during-coronavirus-disease-2019-covid-19-public-health
- Enforcement Policy for Digital Health Devices For Treating Psychiatric Disorders During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff 04/14/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-digital-health-devices-treating-psychiatric-disorders-during-coronavirus-disease
- Enforcement Policy for Extracorporeal Membrane Oxygenation and Cardiopulmonary Bypass Devices During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff 04/06/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-extracorporeal-membrane-oxygenation-and-cardiopulmonary-bypass-devices-during
- Enforcement Policy for Remote Ophthalmic Assessment and Monitoring Devices During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff 04/06/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-remote-ophthalmic-assessment-and-monitoring-devices-during-coronavirus-disease
- Enforcement Policy for Infusion Pumps and Accessories During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff 04/05/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-infusion-pumps-and-accessories-during-coronavirus-disease-2019-covid-19-public

# FDA GUIDANCE DOCUMENTS

- Enforcement Policy for Clinical Electronic Thermometers During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff 04/04/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-clinical-electronic-thermometers-during-coronavirus-disease-2019-covid-19-public
- Enforcement Policy for Gowns, Other Apparel, and Gloves During the Coronavirus Disease (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff 03/30/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-gowns-other-apparel-and-gloves-during-coronavirus-disease-covid-19-public-health
- Enforcement Policy for Sterilizers, Disinfectant Devices, and Air Purifiers During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff 03/29/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-sterilizers-disinfectant-devices-and-air-purifiers-during-coronavirus-disease
- Enforcement Policy for Ventilators and Accessories and Other Respiratory Devices During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff 03/22/20 - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-ventilators-and-accessories-and-other-respiratory-devices-during-coronavirus

# FDA EUA WEBSITES

- Emergency Use Authorization Main Page - https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization
- IVD EUAs - https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas
- FAQs on Testing for SARS-CoV-2 - https://www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-testing-sars-cov-2
- OIR Virtual Town-Hall Meetings - https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/virtual-town-hall-series-immediately-effect-guidance-coronavirus-covid-19-diagnostic-tests-07152020

# THANK YOU FOR YOUR ATTENTION!

# QUESTIONS????

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# Clinical Trials & Emergency Use Authorization Information for COVID-19 Vaccines

Kathy Thoma, EdD, CCRP, CPH

Association of Graduate Regulatory Educators (AGRE) Webinar

January 19, 2021

# Learning Objectives:

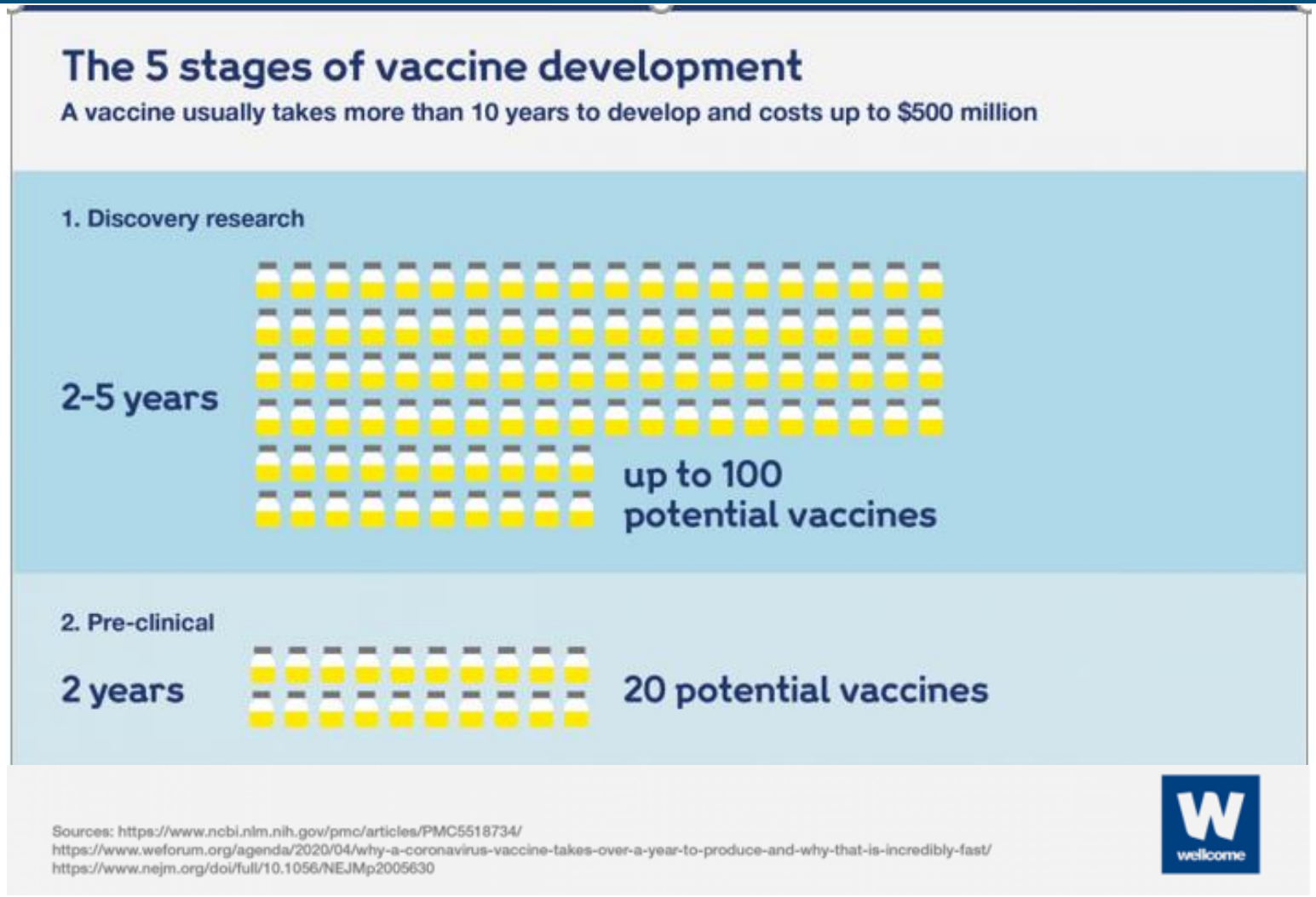
- Describe the accelerated timeline for the development, testing and production of COVID-19 vaccines.
- Discuss the different public-private partnerships that have been an essential component of the process along with the level of funding in the U.S. for the partners.

:

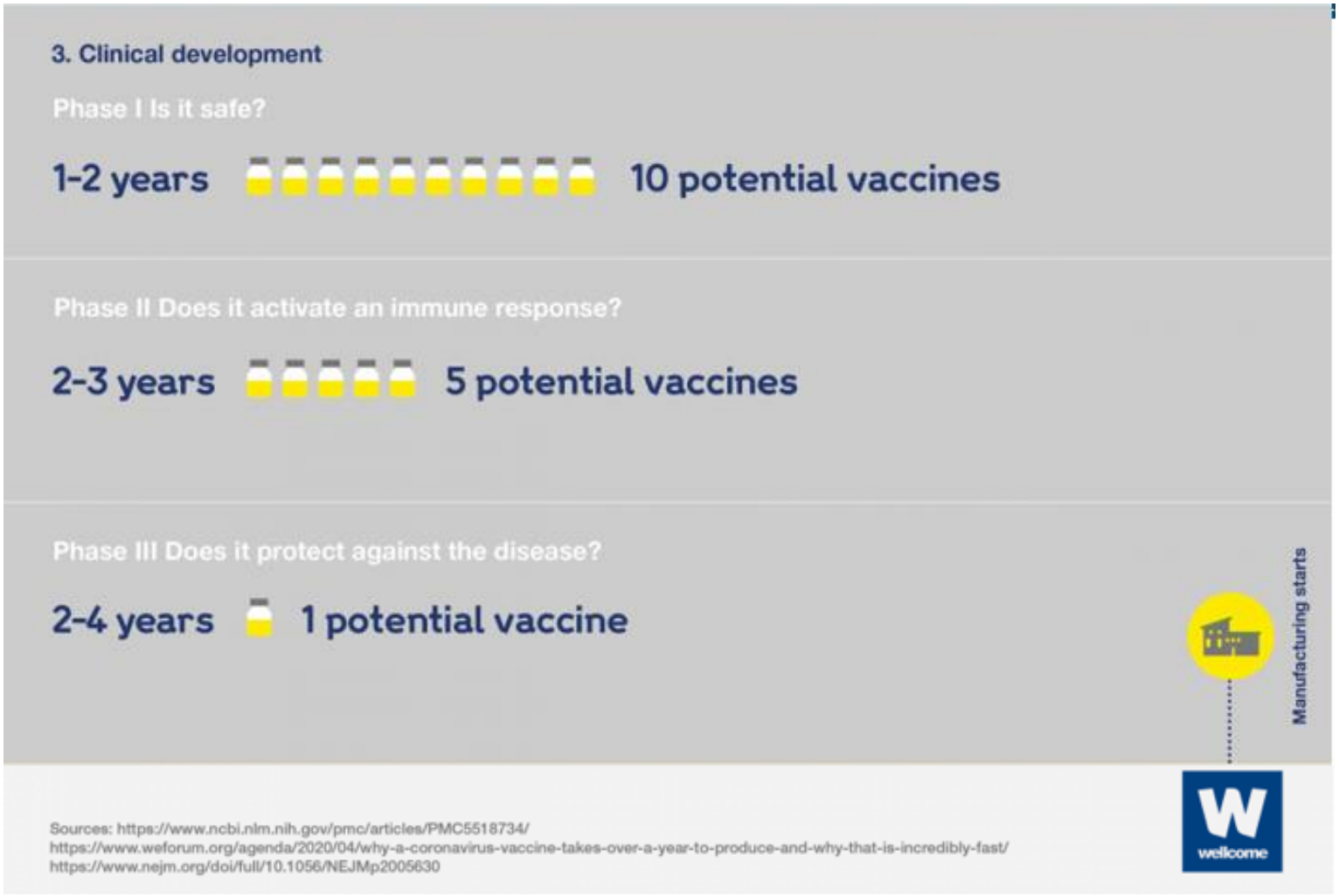
- Discuss the justification and criteria for the issuance of EUAs for the Pfizer-BioNTech and Moderna COVID-19 vaccines.
- Identify some of the other vaccines that are in the pipeline.

# U.S. Vaccines with an EUA


# Vaccine Development Timeline



# Vaccine Development Timeline

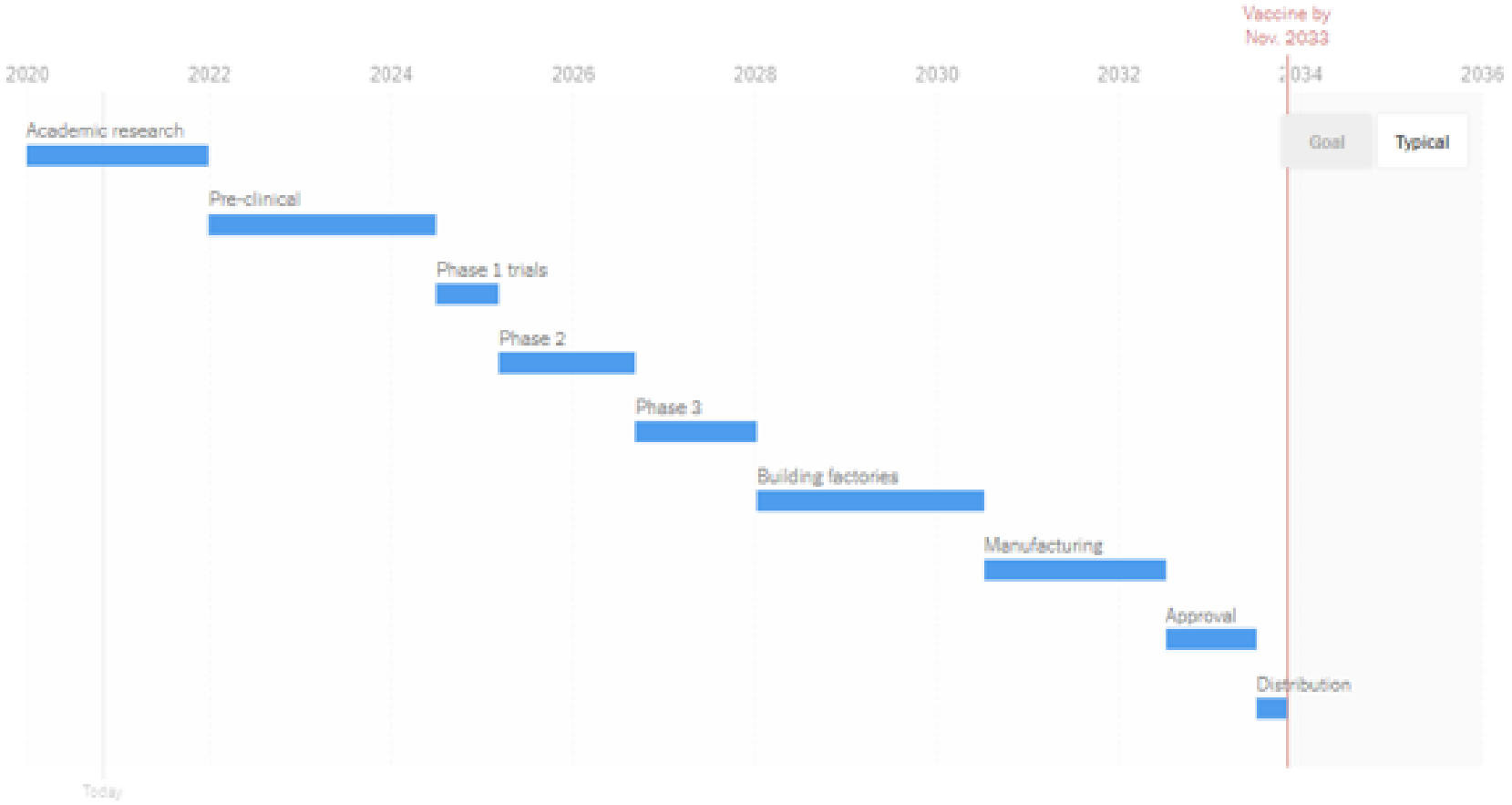


# Vaccine Development Timeline

The New York Times

# How Long Will a Vaccine Really Take?

By Stuart A. Thompson
April 30, 2020



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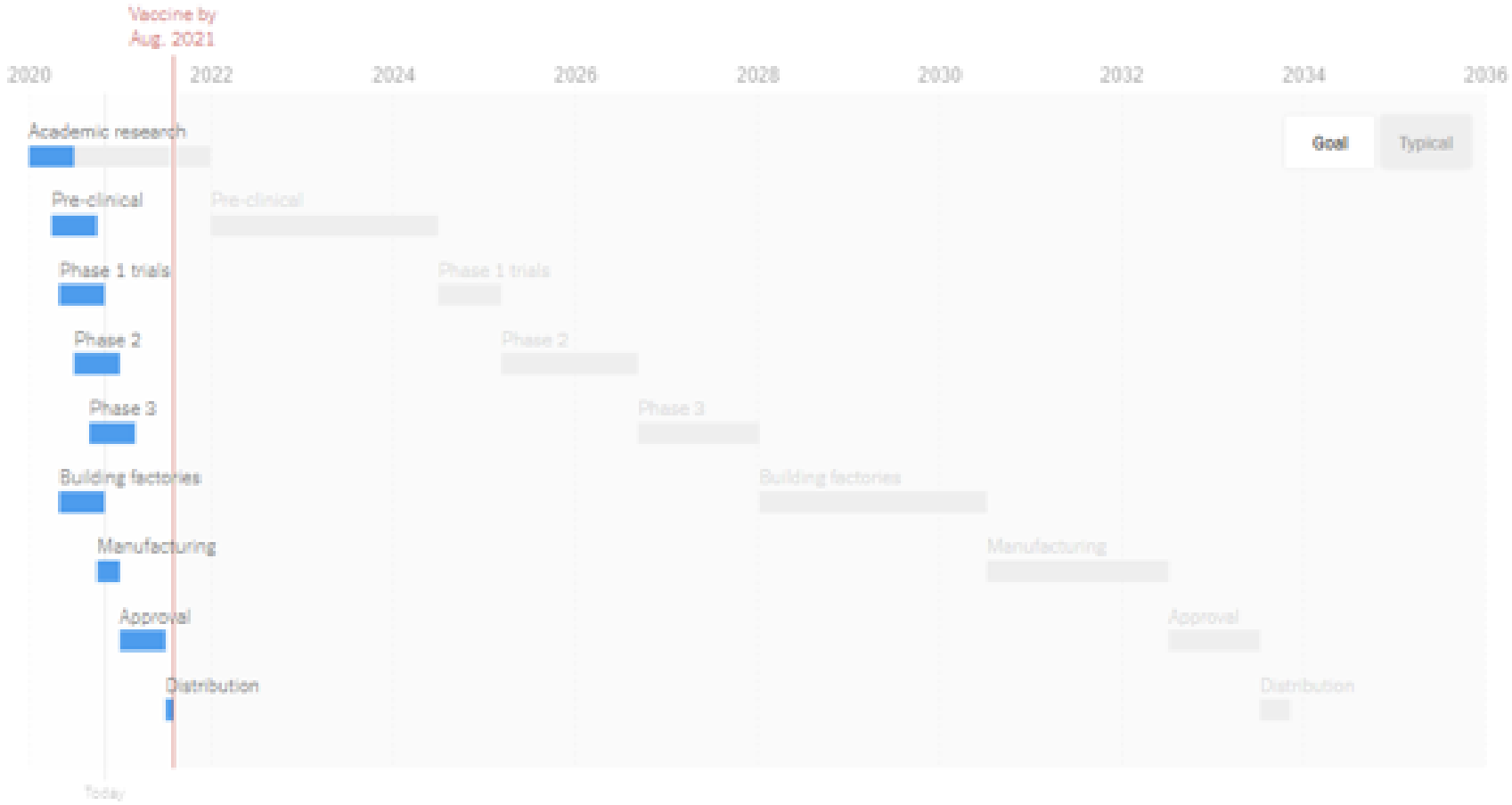
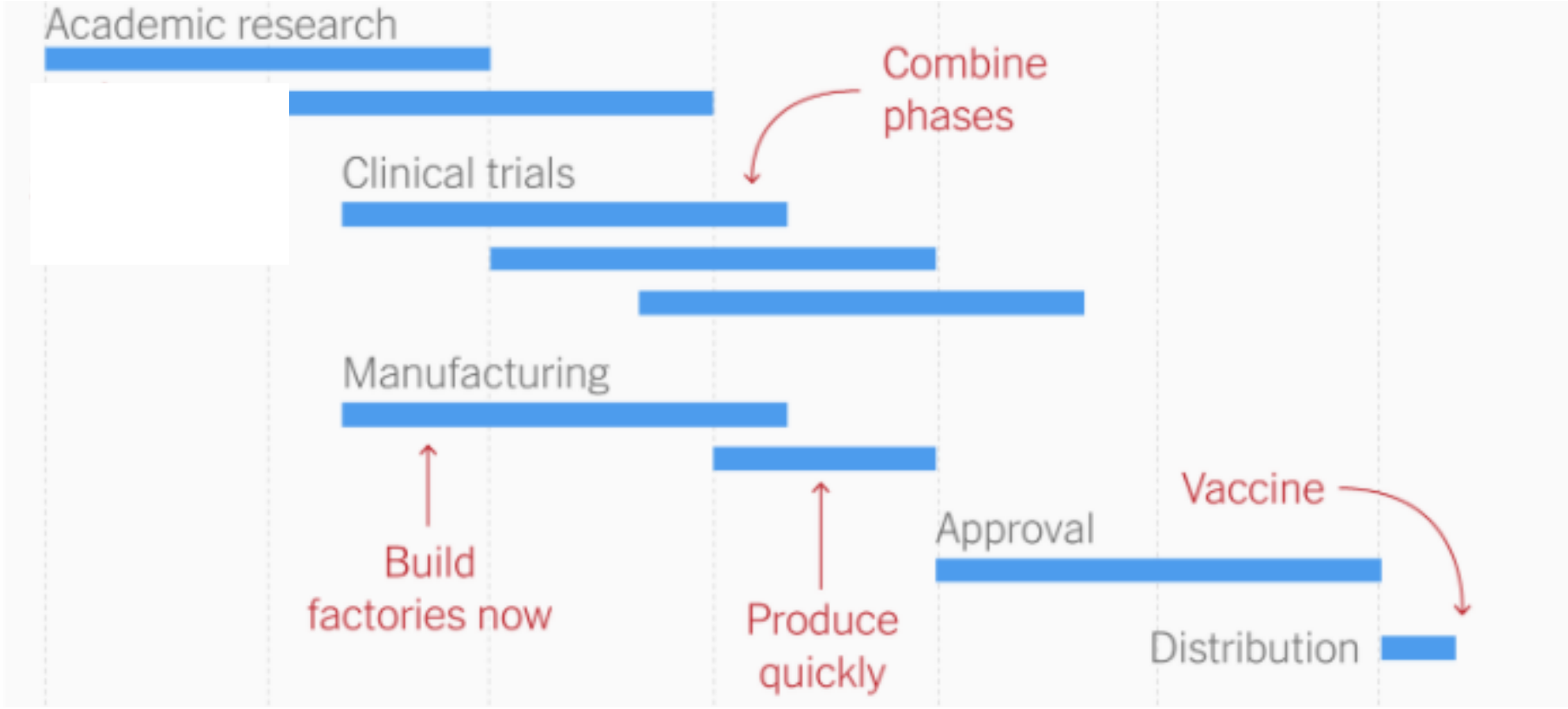
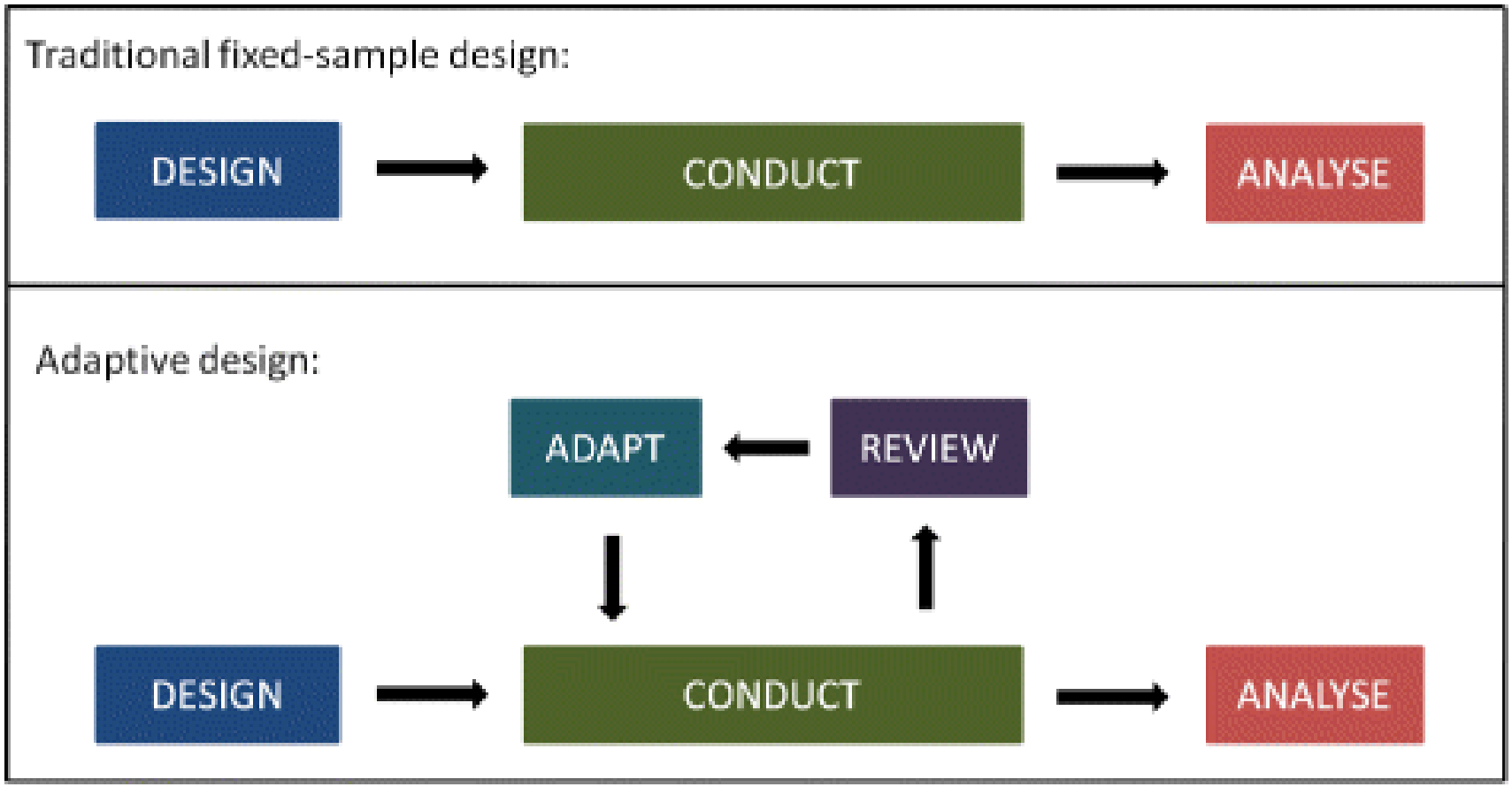


2020


Academic research
Combine phases
Clinical trials
Manufacturing
Build factories now
Produce quickly
Approval
Vaccine
Distribution

# Adaptive Clinical Trial Designs



# Adaptive Clinical Trial Designs

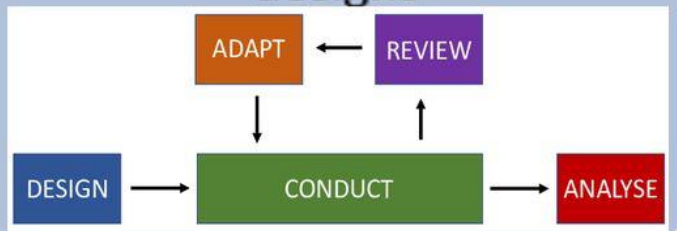
## Flexible

- Use accumulated data to modify the trial's course
- Without undermining integrity or validity

## Ethical

- More patients treated at higher doses or better performing treatments

## Benefits of adaptive trial designs




## Efficient

- Shorter trial duration
- Fewer patients
- More precise estimates

## Reflects real world medical practice

- Learn and react as events happen

# Operation Warp Speed (OWS)

**Government Partners:**

- NIH, FDA, CDC, BARDA, DoD, VA & European Medicines Agency

**Industry Partners:**

- AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Eisai, Eli Lilly, Evotec, Gilead, GSK, J & J, Merck, Moderna, Novartis, Pfizer, Roche-Genentech, Sanofi, Takeda, Vir Biotech

**Nonprofits & Academia**

- Gates Foundation, Fred Hutchinson Cancer Research Center, RTI International and many academic medical center sites

Purpose: coordinate development, manufacturing and distribution

# Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)

**Government Partners:**

- NIH, OWS, FDA, CDC, BARDA, DoD, VA & European Medicines Agency

**Industry Partners:**

- AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Eisai, Eli Lilly, Evotec, Gilead, GSK, J & J, Merck, Moderna, Novartis, Pfizer, Roche-Genentech, Sanofi, Takeda, Vir Biotech

**Nonprofits & Academia**

- Gates Foundation, Fred Hutchinson Cancer Research Center, RTI International and many academic medical center sites

Purpose: coordinate research and clinical trials strategy

# ACTIV Vaccine Trials

- Moderna mRNA vaccine
- Sanofi/GSK adjuvanted recombinant protein-based vaccine
- Oxford University & AstraZeneca adenovirus vaccine
- Novavax recombinant nanoparticle vaccine
- Janssen Pharma/Johnson & Johnson non-replicating adenovirus vaccine

# NIAID's COVID-19 Prevention Network (CoVPN)

- A functional unit of OWS.
- Uses harmonized vaccine protocols developed by ACTIV.
- Merges 4 existing NIAID-funded clinical trial networks that includes over 100 clinical trial sites:
  - HIV Vaccine Trials Network (HVTN),
  - HIV Prevention Trials Network (HPTN),
  - Infectious Diseases Clinical Research Consortium (IDCRC)
  - AIDS Clinical Trials Group

# Congressional Funding

- Congress:
  - $10 billion in supplemental funding for OWS partners
  - $6.5 billion for countermeasure development through Biomedical Advanced Research Development Authority (BARDA)
  - $3 billion for NIH research

| | Vaccine Development & Testing | Vaccine Supplies | Manufacturing/ Distribution |
|---|---|---|---|
| J & J (Jansen) | $456 million | | Up to $1 billion |
| Moderna | $955 million | | Up to $1.5 billion |
| AstraZeneca/U of Oxford | $1.2 billion | | |
| ApiJect | | $138 million | |
| Corning | | $204 million | |
| SiO2 Materials Science | | $143 million | |
| Emergent BioSolutions | | | $628 million task order |

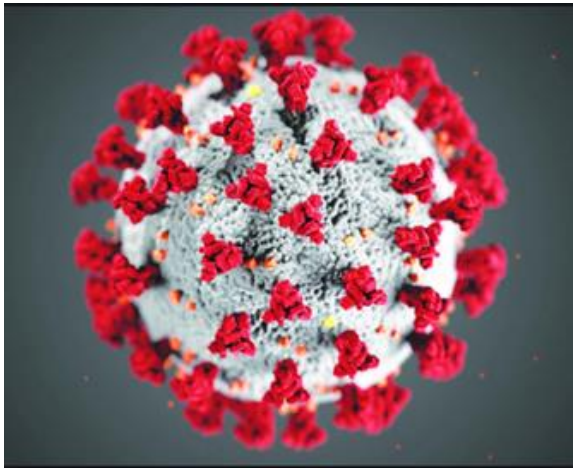
Source: DHHS & DOD. (2020). *Explaining Operation Warp Speed.* https://www.hhs.gov/sites/default/files/fact-sheet-operation-warp-speed.pdf

| | Vaccine Development & Testing | Vaccine Supplies | Manufacturing/ Distribution |
|---|---|---|---|
| Texas A&M/Fujifilm | | | $265 million task order |
| Regeneron | | | $450 million to manufacture antiviral/antibody treatment |
| Novavax | | | Up to $1.6 billion |
| Pfizer | | | Up to $1.95 billion |
| Sanofi/GSK | Up to $2 billion | | |
| Grand River Aspectic, Inc. | | | $160 million contract |
| Cytiva | | $31 million agreement | |

Source: DHHS & DOD. (2020). *Explaining Operation Warp Speed.* https://www.hhs.gov/sites/default/files/fact-sheet-operation-warp-speed.pdf

# mRNA COVID-19 Vaccines

- Contains a piece of the SARS-CoV-2 virus' mRNA genetic material
- Instructs our cells to make the virus' spike protein which triggers our immune system to respond and produce antibodies.



# EUA Justification & Criteria for Issuance*

- The HHS Secretary must declare a domestic, military or public emergency that involves a chemical, biological, radiological & nuclear (CBRN) agent.
- The CBRN agent that is creating the public health emergency must be capable of creating a serious or life-threatening condition.
- Based on totality of current scientific evidence, the Medical Countermeasures (MCM) "may be effective" in preventing, diagnosing, treating or mitigating the serious or life-threatening condition.
  - lower level of evidence required than for full product approval
- **FDA has conducted a risk/benefit analysis and has determined that the potential benefits of the MCM outweighs the known/potential risks**
- There are no adequate, approved & available alternatives.

*FDA. (2017). *Emergency use authorization of medical products and related authorities: Guidance for industry and other stakeholders.* Author.

# FDA Review

- FDA Vaccines & Related Biological Products Advisory Committee (VRBPAC):
  - Main FDA review & evaluation committee for vaccines and biologics
  - Oct. 22, 2020: open meeting to discuss COVID-19 vaccine
  - Dec. 10, 2020: open meeting where an EUA for Pfizer-BioNTech COVID-19 vaccine was discussed
    - Dec. 11, 2020: EUA was issued for 16 years of age and older
    - Data from clinical trials met the June & October guidance
  - Dec. 17, 2020: open meeting where an EUA for Moderna, Inc., COVID-19 vaccine was discussed
    - Dec. 18, 2020: EUA was issued for 18 years of age and older

# Pfizer-BioNTech Trial: NCT04368728

- @44,000 participants were randomized 1:1 into vaccine & placebo arms
- 155 sites (mostly U.S.); 4/29/2020 – 1/27/2023
- Triple blinded: participant, provider, investigator
- Eligibility criteria:
  - Healthy adults at high risk for COVID-19 infection
  - Phase 1: 18 years of age and older
  - Phase 2/3: 12 years of age and older
  - Phase 1: no hypertension, diabetes, COPD, asthma, smokers, high BMI
  - Phase 1 & 2: no HIV, HCV or HBV
  - No history of severe vaccine reactions

# Pfizer-BioNTech EUA Review

- FDA analyzed safety data from 37,586 participants (mostly from U.S.)
  - 18,801 received vaccine & 18,785 received saline placebo
  - Followed for two months after receiving 2nd dose
  - Common side effects: injection site pain, headache, fatigue, muscle pain, joint pain, chills, fever.
    - Side effects more common after 2nd dose

# Pfizer-BioNTech EUA Review

- FDA analyzed effectiveness data from 36,523 participants 12 years of age and older (mostly from U.S.)
  - 18,198 received vaccine; 18,325 received placebo
  - No evidence of SARS-CoV-2 infection w/in 7 days of 2nd dose & confirmed it was **95% effective** in preventing infection.
- No data yet about length of protection and if it prevents transmission between people.

# Pfizer-BioNTech EUA Parameters

- Issued for individuals 16 years of age and older
- Dosing schedule: 2 doses, 3 weeks apart
- Storage: -80C to -60C & protected from light
- Handling: must be used w/in 6 hours of thawing

# Moderna Trial: NCT04470427

- @30,000 participants were randomized 1:1 into vaccine & placebo arms
- 100 COVID-19 Prevention Network (CoVPN) locations; 7/27/2020 – 10/27/2022
- Quadruple masked: participant, provider, investigator, outcomes assessor
- Eligibility criteria:
  - Healthy adults & those with pre-existing medical conditions (stable for 3 months)
  - At risk for COVID-10 infection due to location or circumstances for exposure
  - Not immunosuppressed or immunocompromised
  - Negative pregnancy test

# Moderna Trial EUA Review

- FDA analyzed safety data from 30,351 participants 18 year & older; conducted in the U.S. at CoVID network sites
  - 15,185 received vaccine; 15,166 received saline placebo
  - Two reviews of the safety data: @ 7 weeks after 2nd dose and @ 9 week after 2nd dose
- Most common side effects: infection site pain, fatigue, headache, muscle pain, joint pain, chills, swollen lymph nodes, nausea, vomiting, fever.
  - Side effects more common after 2nd dose

# Moderna Trial EUA Review

- FDA analyzed efficacy data from 28,207 participants 18 years of age and older
  - 14,134 received vaccine; 14,073 receive placebo
  - No evidence of SARS-CoV-2 infection w/in 14 days after 2nd dose & confirmed it was **94.1% effective** at preventing infection
  - No long term protection or transmission data

# Moderna EUA Parameters

- Issued for individuals 18 years of age and older.
- Dosing schedule: 2 doses, 1 month apart
- Storage: -25C to -15C & protect from light
- Handling: must be used w/in 6 hours of dilution

# General EUA Requirements

- Sponsor & vaccine providers must report the following events to the Vaccine Adverse Event Reporting System (VAERS) within 15 calendar days of receipt by Sponsor
  - All vaccine administration errors
  - All serious adverse events
  - All cases of Multisystem Inflammatory Syndrome (MIS)
  - All COVID-19 hospitalizations & deaths

# General EUA Requirements

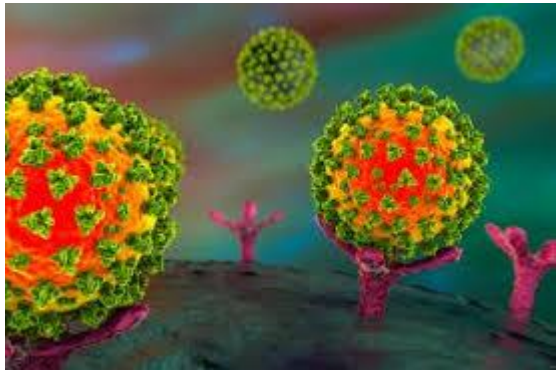
- Must provide “fact sheets” w/ dosing & benefit/risk information to all vaccine providers & recipients
- Must submit a pharmacovigilance plan for the long-term safety follow-up of participants & product to FDA
- Must continue clinical trials to collect additional safety/efficacy data & pursue approval
- All vials must be labeled for “Emergency Use Authorization”

# General EUA Requirements

- Sponsors cannot change the description, manufacturing process, facilities or equipment without notification to & concurrence by FDA
- Manufacturing must comply with GMP
- Sponsors must submit quarterly manufacturing report to FDA
- Sponsors must maintain records of distribution (lot, quantity, etc.)

# General EUA Requirements

- Sponsors must conduct post-authorization observational studies to evaluate the association between the vaccine and a pre-specified list of adverse events of special interest, COVID-related deaths, hospitalizations and severe cases.



# EUA Limitations

- EUAs will be in effect until the COVID-19 public health emergency declaration is terminated
- EUAs may be revised or revoked by FDA at any time due to safety & effectiveness issues or they no longer meet criteria for issuance

# Vaccines in the Pipeline (AVAC; 1/6/2021)

| Primary sponsor(s) | Description | Platform | Funders | Status |
|---|---|---|---|---|
| Pfizer / BioNTech | **Comirnaty**<br>*mRNA that encodes for SARS-CoV-2 spike protein.* | mRNA | Pfizer ($500M)<br>USG ($1.9M)<br>*Warp Speed Finalist* | Ph. I/II ongoing: 456/Germany<br>Ph. II planned: 960/China<br>Ph. II/III ongoing: 44K US +5<br>**Authorization:** EUA in EU, US, +9; WHO Emergency Validation<br>**Approval:** Bahrain, Saudi Arabia, Switzerland |
| Moderna | **mRNA-1273**<br>*Synthetic messenger RNA that encodes for SARS-CoV-2 spike protein.* | mRNA | USG ($2.48B)<br>CEPI/GAVI (Undisclosed)<br>*Warp Speed Finalist*<br>*COVAX Portfolio* | Ph. I ongoing: 155/US<br>**Ph. II ongoing:** 600/US; 3000/US (planned)<br>Ph. III ongoing: 30,000/US<br>**Authorization:** EUA in Canada, EU, Israel, US<br>**Approval:** None |
| U. of Oxford AstraZeneca | **AZD1222**<br>*Chimpanzee Adeno vector expressing SARS-CoV-2 spike protein.* | Viral vector | USG ($1.2B)<br>CEPI/GAVI ($750M)<br>EU ($923M)<br>*Warp Speed* Finalist*<br>*COVAX** Portfolio* | **Ph. I/II ongoing:** Japan, Kenya, RSA, UK<br>**Ph. II/II ongoing:** 12,390 vols/UK; 1700/ India<br>Ph. III ongoing: 40K /US+; 10K/Brazil<br>**Authorization:** EUA in Argentina, India, UK<br>**Approval:** None |
| Sinopharm / Beijing Institute of Biologic Products / Wuhan Institute | **BBIBP-CorV x 2** | Whole inactivated | No Funding Disclosed | Ph. I/II: ongoing: 640/China<br>**Ph III ongoing:** 45K/UAE. Bahrain, Jordan, Egypt; 3K/Argentina; 6K/Peru<br>**Authorization:** EUA in Egypt<br>**Approval:** Bahrain, China, UAE |
| Gamaleya Research Institute | **Sputnik V**<br>*Combination Ad5 and Ad26 vector expressing the SARS-CoV-2 spike glycoprotein* | Viral vector | Ministry of Health- Russia | **Ph. I complete:** 38/Russia; 38/Russia<br>**Ph. II/III planned:** 1600/ India<br>**Ph. III ongoing:** 40K/Russia<br>**Ph. III planned:** 100/Belarus;1000/UAE; 2000/ Venezuela<br>**Authorization:** EUA in Argentina; Early/ limited use in Belarus, Russia<br>**Approval:** None |

# Vaccines in the Pipeline (AVAC; 1/6/2021)

| Primary sponsor(s) | Description | Platform | Funders | Status |
|---|---|---|---|---|
| Bharat Biotech/ Indian Council of Medical Research | **Covaxin** | Whole inactivated | No funding disclosed | **Ph. I/II ongoing:** 755/ India<br>**Ph. III ongoing:** 25.8K/ India<br>**Authorization:** EUA in India; still pending final Ph. III efficacy data<br>**Approval:** None |
| CanSino Biologics | **Convidecia**<br>*Ad5 vector expressing SARS-CoV-2 spike glycoprotein.* | Viral vector | No funding disclosed. | **Ph. I complete:** 108/China<br>**Ph. II ongoing:** 508/China<br>Ph.III ongoing: 40K/ Argentina, Chile, Mexico, Pakistan, Saudi Arabia<br>**Authorization:** Limited use in Chinese military as a "specially needed drug"<br>**Approval:** None |
| Novavax | **NVX-COV2373**<br>*Full-length recombinant SARS-CoV-2 glycoprotein nanopartical vaccine adjuvanted with Matrix M.* | Protein Subunit | CEPI ($388M)<br>USG ($1.6B)<br>*Warp Speed Finalist*<br>*COVAX Portfolio* | **Ph. I ongoing:** 130/Australia<br>**Ph. II ongoing:** 2900/ RSA<br>Ph. III ongoing: 15,000/ UK; 30K/US, Mexico |
| Sinovac Biotech | **CoronaVac** | Whole inactivated | No Funding Disclosed | **Ph. I/II ongoing:** 1166/China<br>**Ph III ongoing:** 8K/Brazil, 1600/ Indonesia, 4K/Bangladesh, 13K/Turkey, 1K/China<br>**Authorization:** EUA for limited use in China<br>**Approval:** None |

# Vaccines in the Pipeline (AVAC; 1/6/2021)

| Primary sponsor(s) | Description | Platform | Funders | Status |
|---|---|---|---|---|
| **J&J** | **JNJ-78436735**<br>*Ad26 vector expressing SARS-CoV-2 spike protein.* | Viral vector | J&J investment (~$500M)<br>USG ($1.45B)<br>*Warp Speed Finalist* | **Ph. I and I/II ongoing:** 250/Japan; 1045/Belgium, US<br>**Ph. II ongoing:** 550/Germany, Netherlands, Spain<br>Ph. III ongoing: 30K (2 dose)/France, Germany, RSA+6; 60K(1 dose)/Argentina, Brazil, Chile+7 |
| **Inovio** | **INO-4800**<br>*DNA plasmid vaccine with electroporation.* | DNA | CEPI ($17.2M)<br>BMGF ($5M)<br>USG ($83M)<br>*COVAX Portfolio* | Ph. I ongoing: 40/US<br>**Ph. II/III ongoing:** 160/S Korea<br>**6K/US** |
| **CureVac** | **CVnCoV**<br>*mRNA vaccine that encodes for the spike protein formulated with lipid nanoparticles.* | mRNA | CEPI ($8.3M)<br>EU ($$421M)<br>USG. (Undisclosed)<br>*COVAX Portfolio* | Ph. I ongoing: 284/Belgium, Germany<br>Ph. II ongoing: 691/Panama, Peru |
| **Imperial College** | *Synthetic self-amplifying RNA producing SARS-CoV-2 spike protein.* | Self-amplifying RNA | UK ($50.7M)<br>Philanthropies ($6.2M) | **Ph. I/II ongoing**: 300/UK<br>**Ph. III planned**: 6000/UK |
| **Merck / Themis / Pasteur Inst.** | **V591**<br>*Uses a weakened measles virus carrying a gene for the coronavirus spike protein.* | Replicating Viral Vector | *USG: ($19M)* | Ph. I/II ongoing: 260 vols/Belgium, Austria, US |

# Vaccines in the Pipeline (AVAC; 1/6/2021)

| Primary sponsor(s) | Description | Platform | Funders | Status |
|---|---|---|---|---|
| Merck / IAVI | **V590**<br>*VSV vector expressing SARS-CoV-2 spike protein* | Replicating Viral Vector | *USG: ($19M)* | Ph. I ongoing: 252 vols |
| Sanofi / GSK | *DNA from the surface protein of the SARS-CoV-2 virus is inserted into insect cells, which express antigen that is then purified and combined with GSK's pandemic AS03 adjuvant.* | Subunit | USG ($2.1B)<br>*Warp Speed Finalist* | Ph. I/II ongoing: 440/US<br>**Ph. III planned:** 30K/ US+ (Delayed) |
| Clover BioPharma / GSK | **SCB-2019**<br>*A trimeric subunit spike protein developed by China-based Clover, delivered alongside an adjuvant.* | Subunit | CEPI ($3.5M) | **Ph. I ongoing:** 150/Australia<br>**Ph. II/III planned** |

# Summary

- There have been many factors that have assisted in the acceleration of the development of a safe and effective COVID-19 vaccine:
  - large public-private partnerships
  - extensive funding by the U.S. federal government
  - adaptive trial designs and other design methods
  - using clinical trial networks
  - focusing recruitment on individuals and areas at high risk for COVID-19 infection for the clinical trials
  - accelerated regulatory review and authorization methods like the EUA.

- Two vaccines in the U.S. have been issued an EUA and several more are in the pipeline.

- The current hurdle is the efficient and timely distribution of the vaccines to the public along with public acceptance.

# Q & A

## Thank you for attending!

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