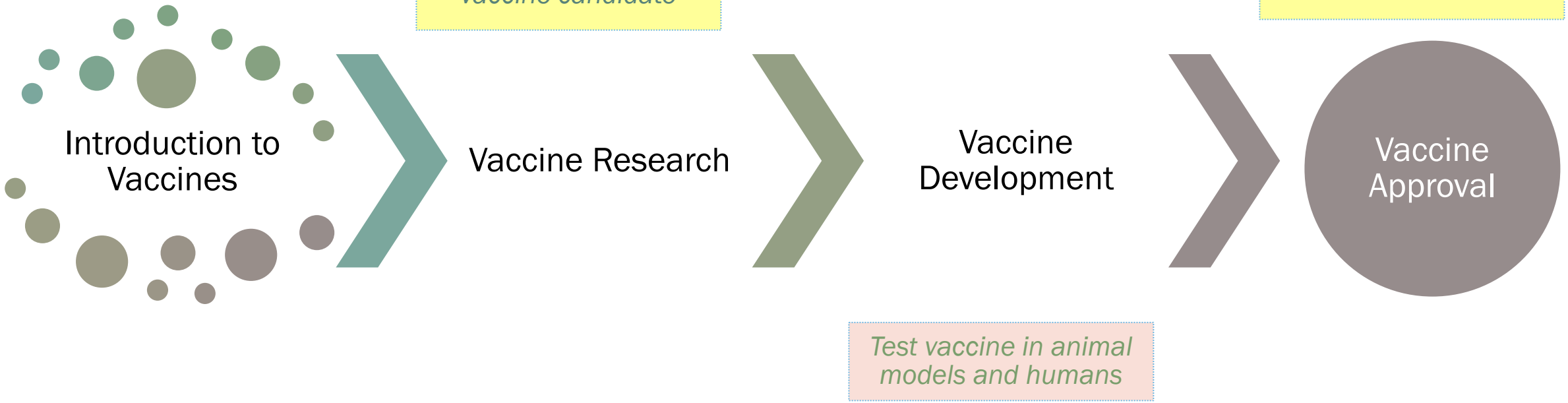
VACCINE RESEARCH, DEVELOPMENT, AND APPROVAL

2021 HOWARD L. BOST MEMORIAL HEALTH POLICY FORUM

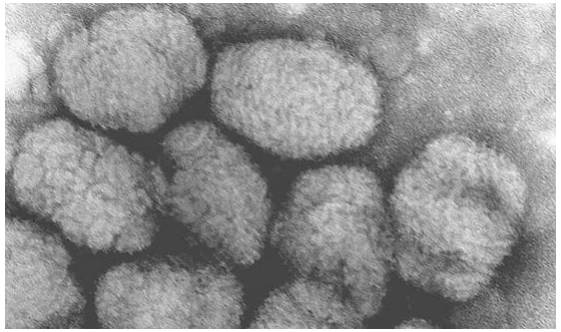
Erome Daniel Hankore, PhD


Introduction to Vaccines
Vaccine Research
Discovery of novel vaccine candidate
Vaccine Development
Test vaccine in animal models and humans
Vaccine Approval
Vaccines approved by FDA

A

Source: Wikipedia

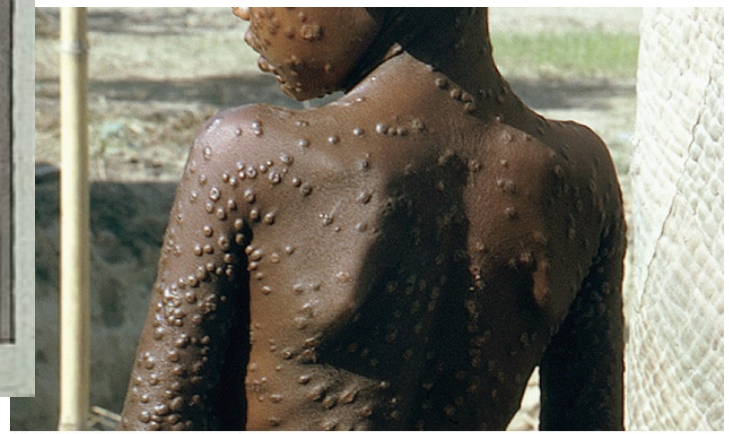
nd



Source: CDC

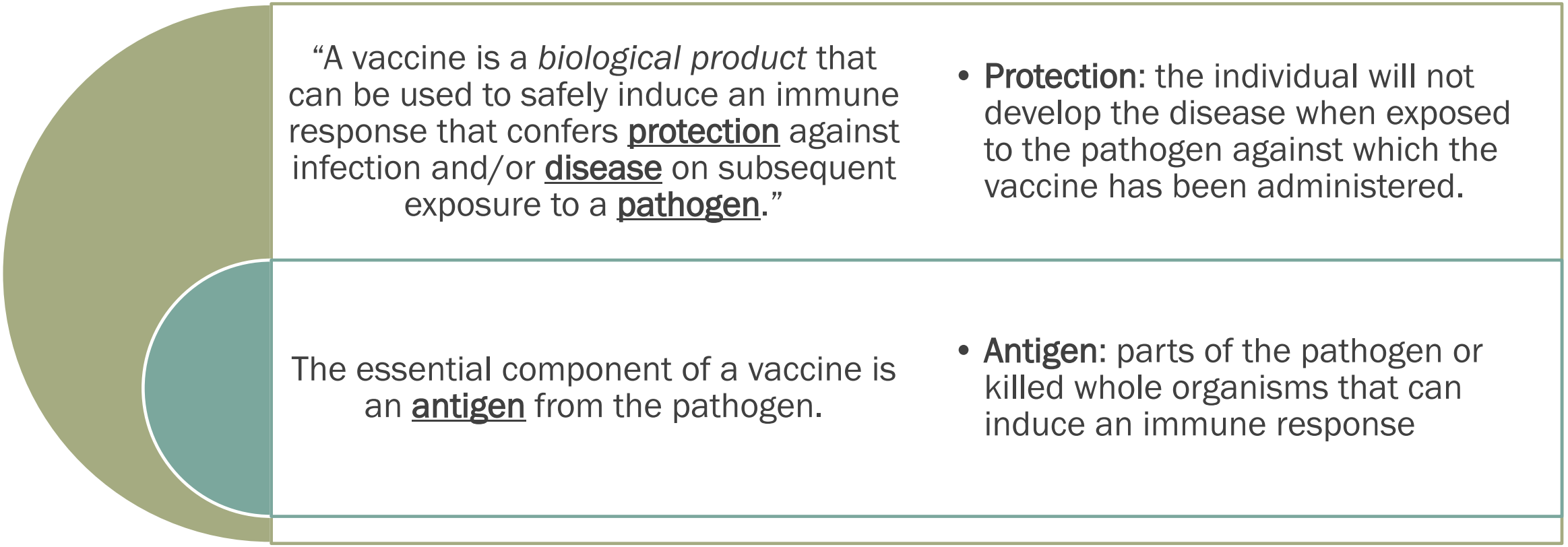
lesions
(~900)

Pathogens: *Variola major* and *Variola minor*
Disease: smallpox



Source: CDC

WHAT IS A VACCINE?



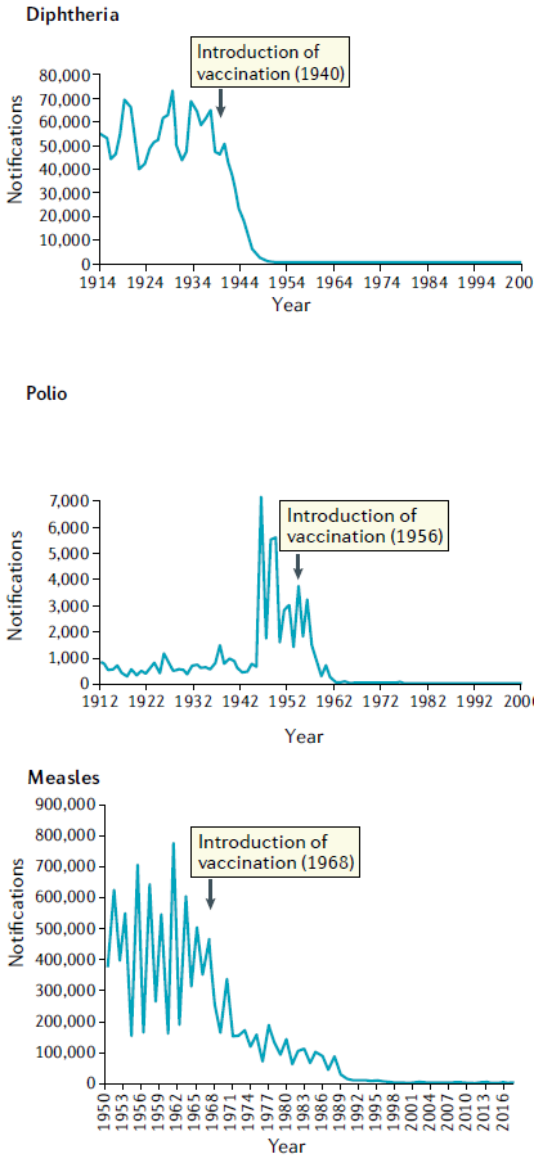
"A vaccine is a *biological product* that can be used to safely induce an immune response that confers **protection** against infection and/or **disease** on subsequent exposure to a **pathogen**."

- **Protection**: the individual will not develop the disease when exposed to the pathogen against which the vaccine has been administered.

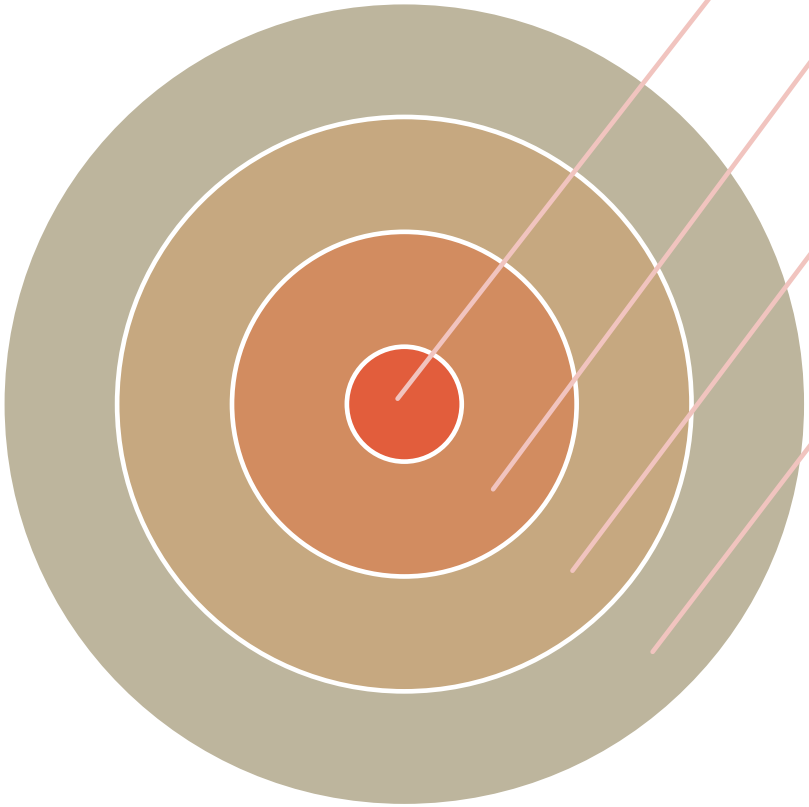
The essential component of a vaccine is an **antigen** from the pathogen.

- **Antigen**: parts of the pathogen or killed whole organisms that can induce an immune response

Pollard, A. J., and Bijker, E. M. *Nature Reviews.* **2021**. 21, 83-100



Disease	Pathogen
Diphtheria	*Corynebacterium diphtheriae*
Polio (poliomyelitis)	poliovirus (*Enterovirus C* subtype)
Measles	*Measles morbillivirus*



Exposure to pathogen
- Viruses
- Bacteria
- Fungi
- Parasites

Vaccine intervention

Disease manifestation

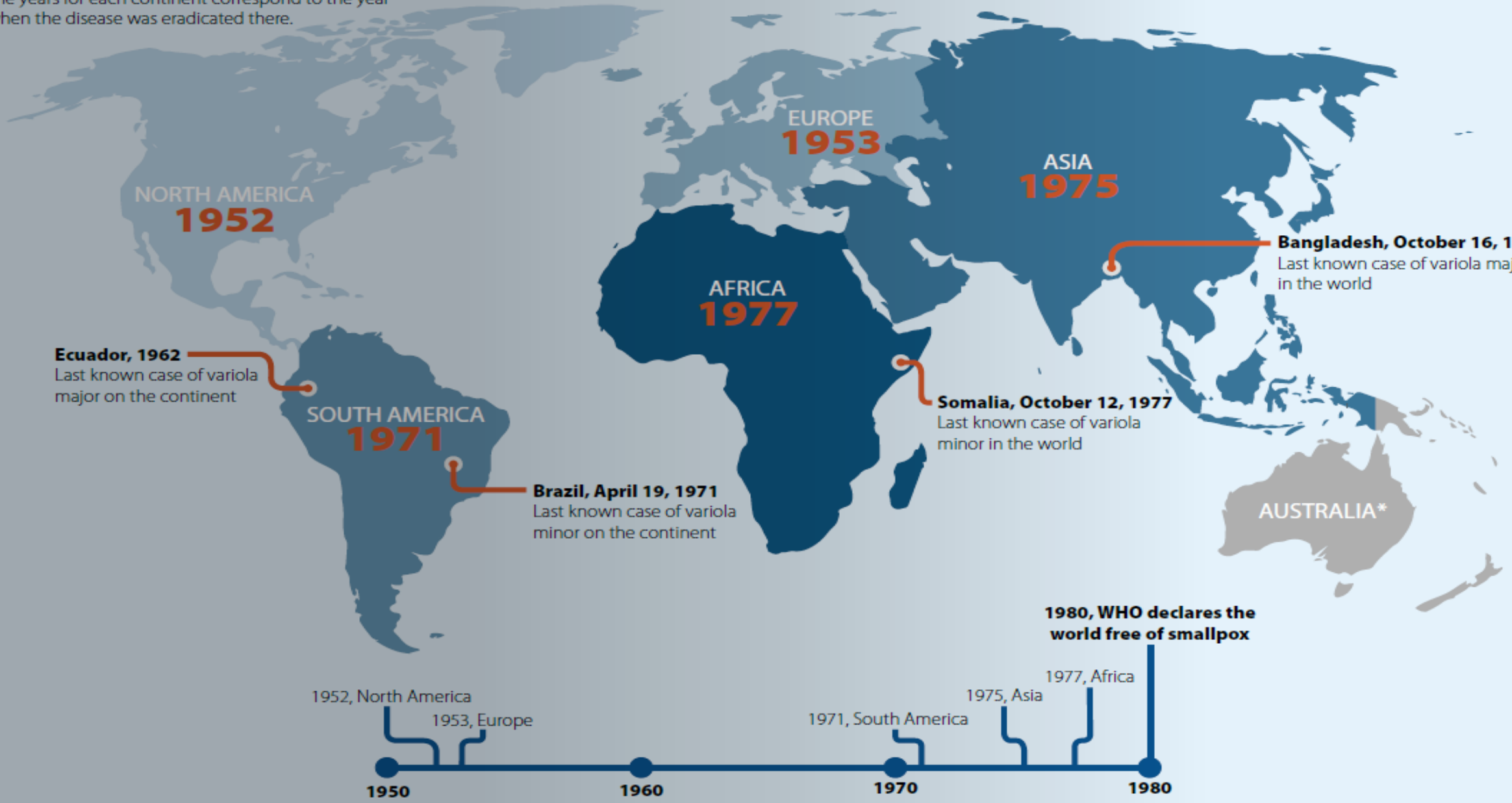
Medical intervention

Treatment course

Outcome
- Full recovery
- Recovery with side effects
- Death

Pollard, A. J., and Bijker, E. M. *Nature Reviews.* **2021**. 21, 83-100

The years for each continent correspond to the year when the disease was eradicated there.

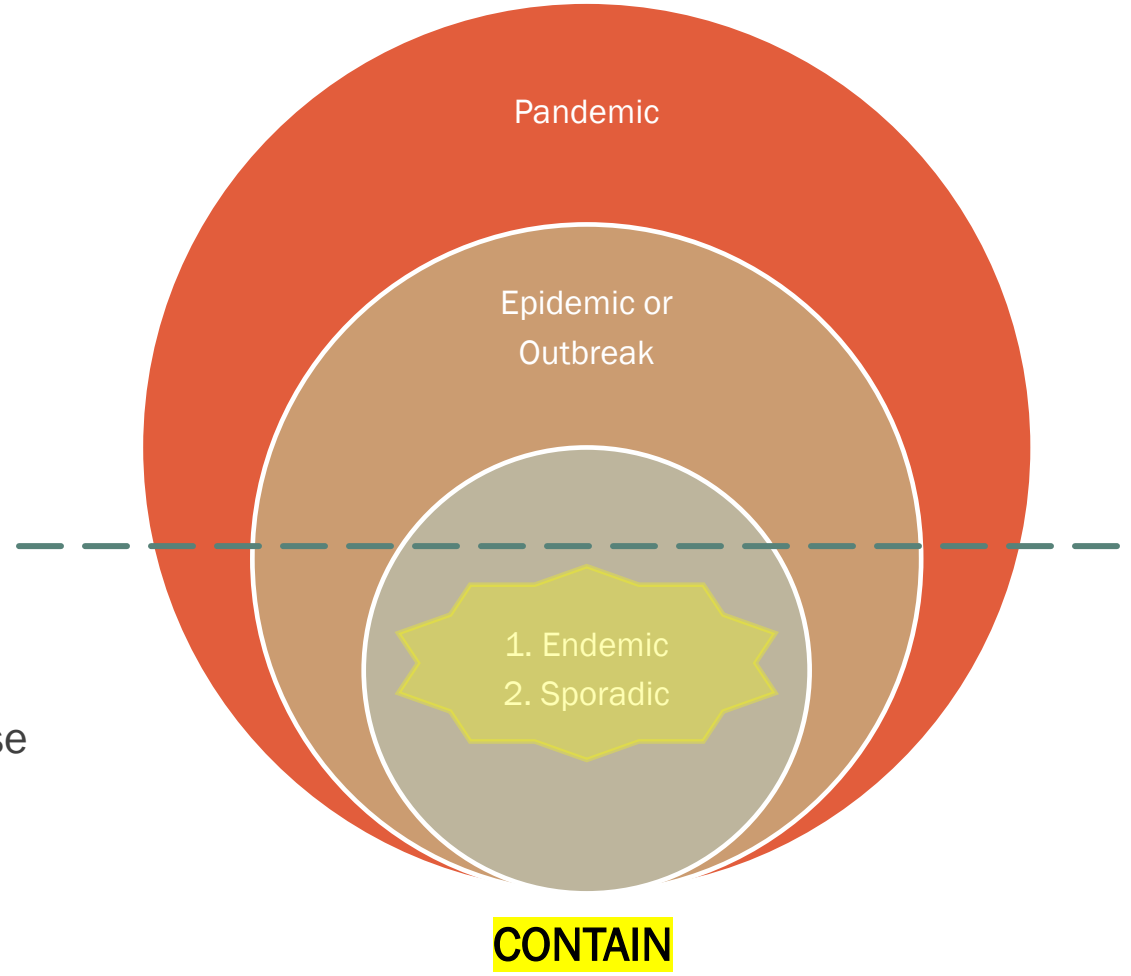


* Smallpox was never endemic (widespread) in Australia

CS265471-A

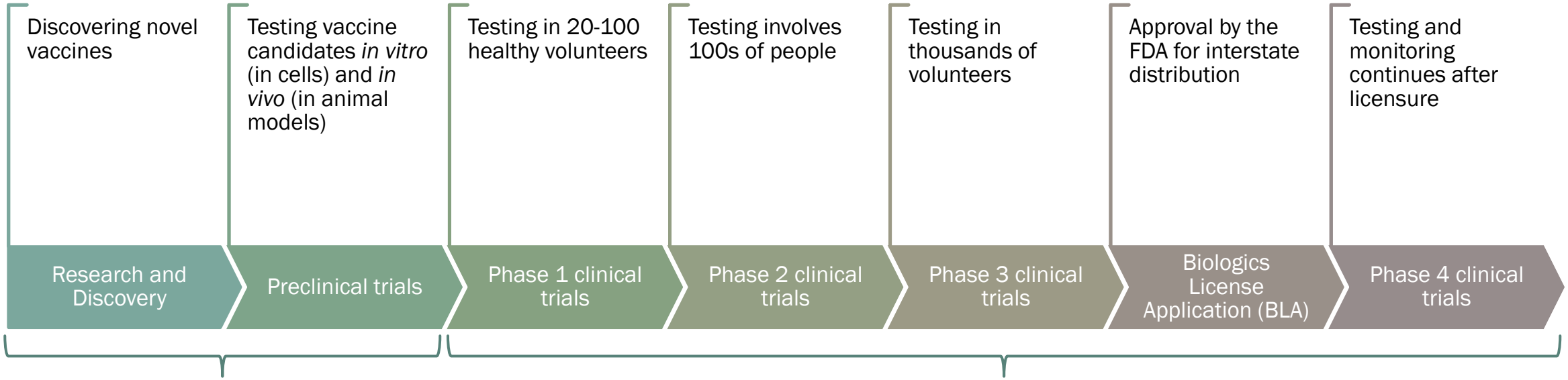
BENEFITS OF VACCINES

- Reduce transmission rate in communities
- Reduce disease severity and long-term negative outcomes
- Reduce case-fatality rates among infected individuals
- Prevent emergence of more virulent and pathogenic strains
- Proven and safe means of building an effective immune response



VACCINE RESEARCH, DEVELOPMENT AND APPROVAL PROCESS

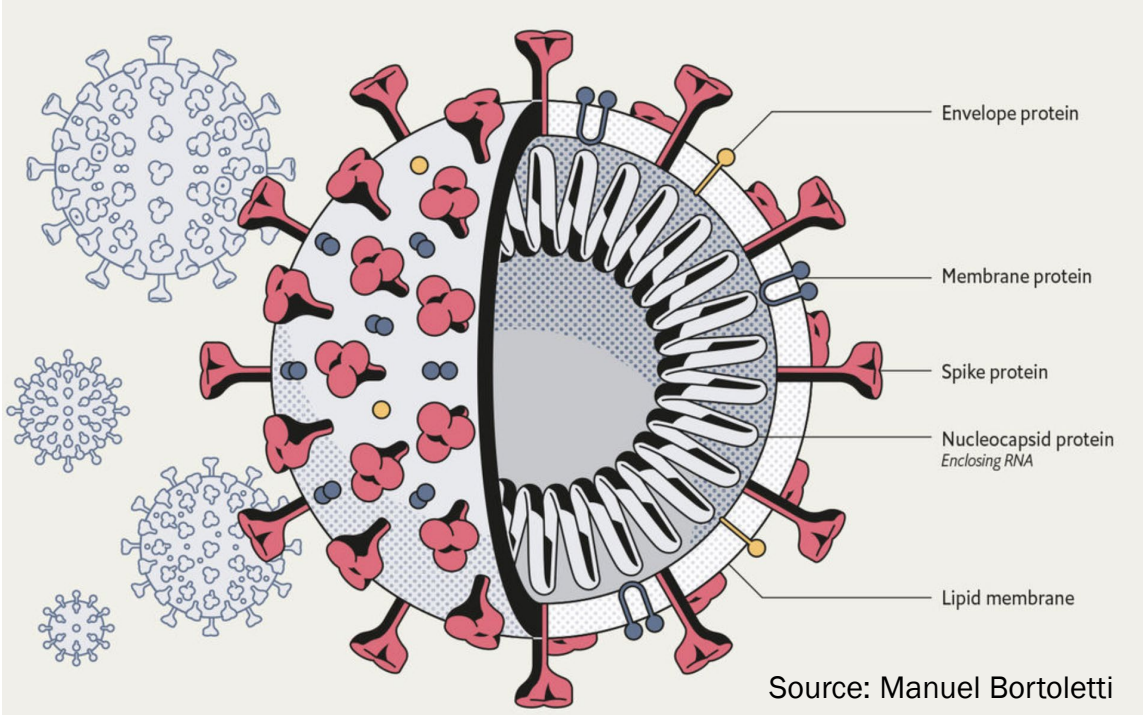
Safety
Immunogenicity (inducing an immune response)
Protective efficacy (capacity to prevent disease)



RESEARCH AND DISCOVERY STAGE

"A vaccine is a *biological product* that can be used to safely induce an immune response that confers **protection** against infection and/or **disease** on subsequent exposure to a **pathogen**."

1. Develop the vaccine candidate
2. Test vaccine in preclinical trials



Source: Manuel Bortoletti

RESEARCH AND DISCOVERY STAGE

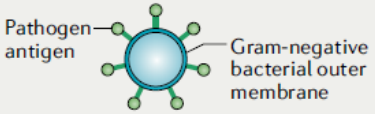
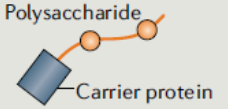
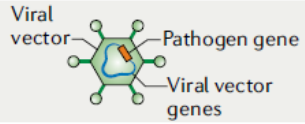
1. DEVELOP VACCINE

"A vaccine is a *biological product*..."

Vaccines

- **Live**
  Chance of uncontrolled replication in compromised individuals
- **Non-live (inactivated)**
  No risk of uncontrolled replication in immunocompromised individual

Non-live (inactivated) vaccines

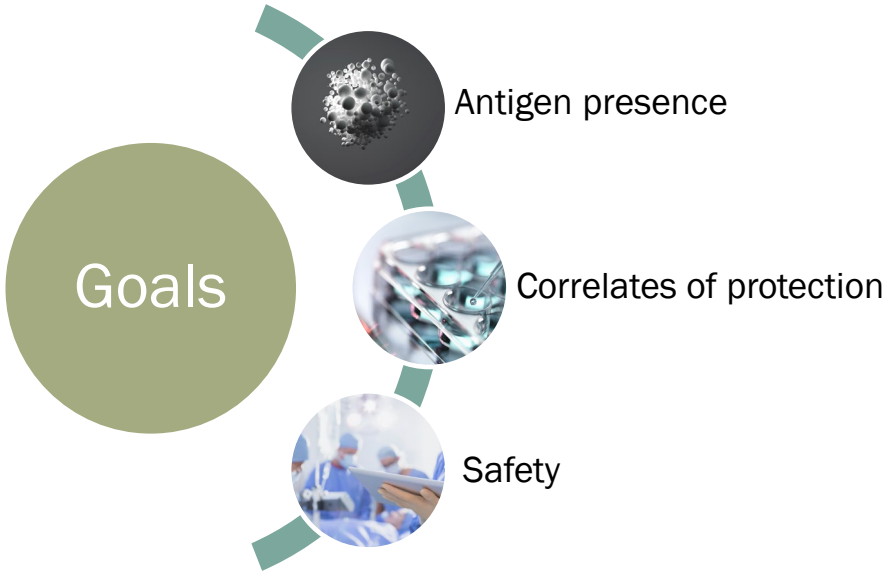
Type of vaccine		Licensed vaccines using this technology	First introduced
Live attenuated (weakened or inactivated)		Measles, mumps, rubella, yellow fever, influenza, oral polio, typhoid, Japanese encephalitis, rotavirus, BCG, varicella zoster	1798 (smallpox)
Killed whole organism		Whole-cell pertussis, polio, influenza, Japanese encephalitis, hepatitis A, rabies	1896 (typhoid)
Toxoid		Diphtheria, tetanus	1923 (diphtheria)
Subunit (purified protein, recombinant protein, polysaccharide, peptide)		Pertussis, influenza, hepatitis B, meningococcal, pneumococcal, typhoid, hepatitis A	1970 (anthrax)
Virus-like particle		Human papillomavirus	1986 (hepatitis B)
Outer membrane vesicle		Group B meningococcal	1987 (group B meningococcal)
Protein–polysaccharide conjugate		*Haemophilus influenzae* type B, pneumococcal, meningococcal, typhoid	1987 (*H. influenzae* type b)
Viral vectored		Ebola	2019 (Ebola)
Nucleic acid vaccine		SARS-CoV-2	2020 (SARS-CoV-2)

Pollard, A. J., and Bijker, E. M. *Nature Reviews.* **2021**. 21, 83-100

RESEARCH AND DISCOVERY STAGE

2. TEST VACCINE IN PRECLINICAL TRIALS

1. Confirm expression of antigen
2. Characterize immune response
3. Check for any adverse effects



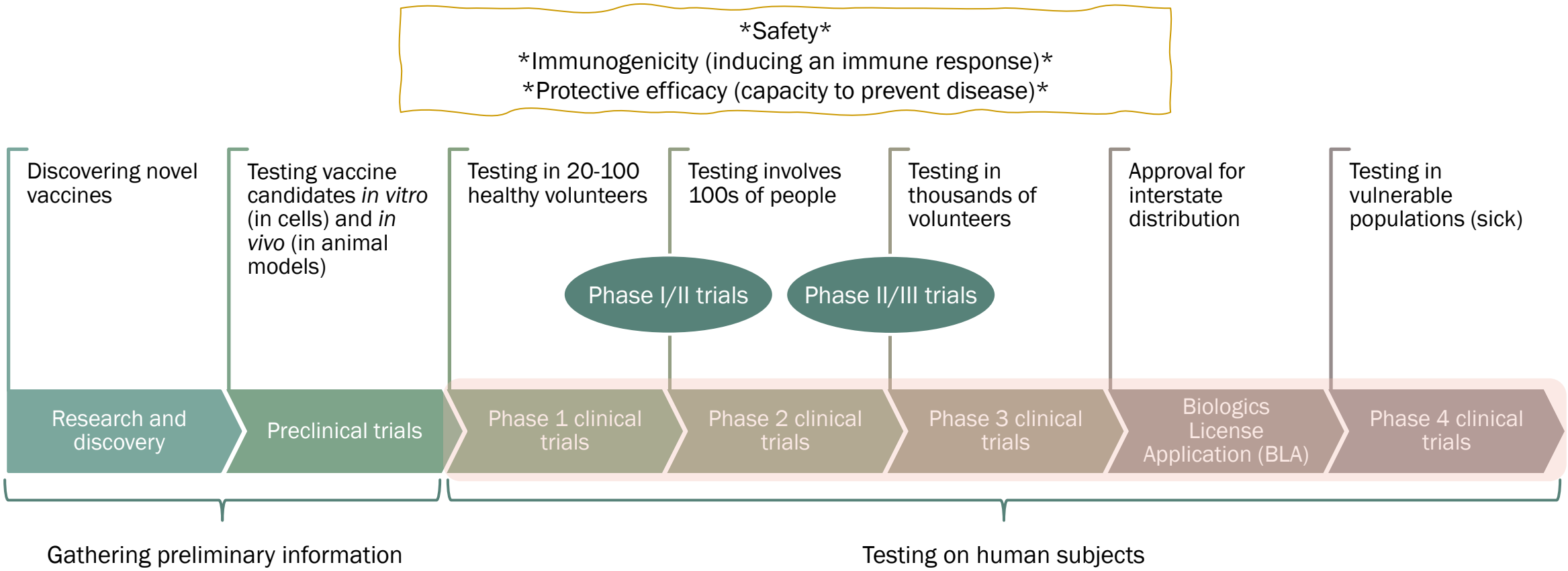
PFIZER AND BIONTECH ANNOUNCE DATA FROM PRECLINICAL STUDIES OF MRNA-BASED VACCINE CANDIDATE AGAINST COVID-19

Wednesday, September 09, 2020 - 07:45am

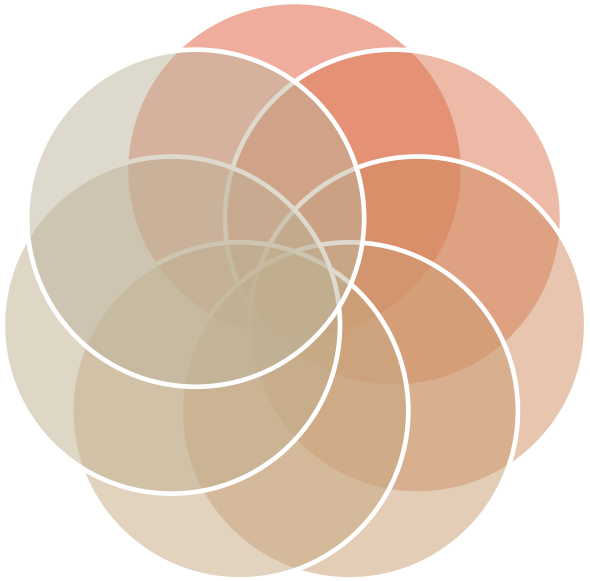
- *Immunization of non-human primates (rhesus macaques) with BNT162b2, a nucleoside-modified messenger RNA (modRNA) candidate that expresses the SARS-CoV-2 spike glycoprotein, resulted in strong anti-viral effects against an infectious SARS-CoV-2 challenge*
- *BNT162b2 immunization prevented lung infection in 100% of the SARS-CoV-2 challenged rhesus macaques, with no viral RNA detected in the lower respiratory tract of immunized and challenged animals. The BNT162b2 vaccination also cleared the nose of detectable viral RNA in 100% of the SARS-CoV-2 challenged rhesus macaques within 3 days after the infection*
- *The BNT162b2 vaccine candidate induced SARS-CoV-2 neutralizing antibodies in rhesus macaques, pseudovirus neutralizing antibodies in mice, and strong, antigen-specific CD4+ and CD8+ T cells in mice and macaques*

bioRxiv 2020.09.08.280818; doi: https://doi.org/10.1101/2020.09.08.280818
Vogel, A. B., Kanevsky, I., Che, Y., et al. *Nature.* **2021**. 592, 283-289

CLINICAL TRIALS



ALL CLINICAL TRIALS



Guidance for Industry

Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials

Clinical or Laboratory abnormalities
Grade 1: Mild
Grade 2: Moderate
Grade 3: Severe
Grade 4: Potentially life threatening

Additional copies of this guidance are available from the Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or from the Internet at http://www.fda.gov/cber/guidelines.htm.

For questions on the content of this guidance, contact the Division of Vaccines and Related Products Applications, Office of Vaccines Research and Review at 301-827-3070.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
September 2007

https://www.fda.gov/media/73679/download

RESOURCES

Article | Published: 12 August 2020

Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults

Mark J. Mulligan, Kirsten E. Lyke, Nicholas Kitchin, Judith Absalon, Alejandra Gurtman, Stephen Lockhart, Kathleen Neuzil, Vanessa Raabe, Ruth Bailey, Kena A. Swanson, Ping Li, Kenneth Koury, Warren Kalina, David Cooper, Camila Fontes-Garfias, Pei-Yong Shi, Özlem Türeci, Kristin R. Tompkins, Edward E. Walsh, Robert Frenck, Ann R. Falsey, Philip R. Dormitzer, William C. Gruber, Uğur Şahin & Kathrin U. Jansen

Nature **586**, 589–593 (2020) | Cite this article

328k Accesses | **349** Citations | **3452** Altmetric | Metrics

A Publisher Correction to this article was published on 19 January 2021

This article has been updated

Abstract

In March 2020, the World Health Organization (WHO) declared coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1], a pandemic. With rapidly accumulating numbers of cases and deaths reported globally[2],

IgG concentrations and SARS-CoV-2 neutralizing titres in sera increased with dose level and after a second dose. Geometric mean neutralizing titres reached 1.9–4.6-fold that of a panel of COVID-19 convalescent human sera, which were obtained at least 14 days after a positive SARS-CoV-2 PCR. These results support further evaluation of this mRNA vaccine candidate.

NIH U.S. National Library of Medicine

ClinicalTrials.gov

Find Studies | About Studies | Submit Studies | Resources | About Site | PRS Login

ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

Explore 389,077 research studies in all 50 states and in 219 countries.

See listed clinical studies related to the coronavirus disease (COVID-19)

ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine.

Find a study (all fields optional)

Status

- Recruiting and not yet recruiting studies
- All studies

Condition or disease (For example: breast cancer)

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Recruiting	Study to Describe the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals	• SARS-CoV-2 Infection • COVID-19	• Biological: BNT162b1 • Biological: BNT162b2 • Other: Placebo • Biological: BNT162b2SA	• North Alabama Research Center, LLC Athens, Alabama, United States • Birmingham Clinical Research Unit Birmingham, Alabama, United States • Medical Affiliated Research Center Huntsville, Alabama, United States • (and 163 more...)

PHASE I: PROTECTIVE EFFICACY TRIALS

- Vaccine must have already been tested in preclinical trials
- Small number of healthy, immunocompetent volunteers
- Intended to investigate underlying immunological mechanisms (e.g., immunological memory and antibody production postvaccination)
- Gain experience with vaccine before testing in larger populations (e.g., mode of administration, injection site, etc.)
- May or may not be controlled

"The enrollment of healthy volunteers warrants a very low tolerance for risk in those clinical trials."
FDA

PHASE I: FIRST TRIALS IN HUMANS

Phase I

- **Objectives:**
  - Establish safety: symptoms associated with immune response such as fever, swelling, etc.
  - Collect data on immune response
  - Administration protocol
    - Delivery method
    - Dose
- **Test group**
  - Size: A small group of 20-100 of naïve and immunocompetent human subjects
  - Age group: first trials in humans, target population

Phase I: Pfizer–BioNTech mRNA vaccine

- **Objectives:**
  - Establish safety: primary event was pain at injection site
  - Immune response: neutralizing antibodies observed in sera
  - Administration protocol
    - Delivery method: 10, 20, 30 or 100 μg into the deltoid (arm)
    - 2 doses at 21-day intervals
- **Test Group:**
  - Size
    - 13 groups of 15 participants (total 195)
    - 12 received vaccine and 3 received placebo
  - Age group: 18-55 and 65-85

medRxiv 2020.08.17.20176651; doi: https://doi.org/10.1101/2020.08.17.20176651
Walsh, E. E., Frenck, R. W., Falsey, A. R. *NEJM.* **2020**. 383, 2439-2450

PHASE II: TESTING IN A TARGET POPULATION

- Safety and immunogenicity
- Larger number of participants, typically in the 100s of people
- Intended to extract as much information about the vaccine as possible (dose, vaccine schedule, vaccine composition, age-specific responses, duration of immune response, reactions to the vaccine)
- Continue gaining experience with vaccine before testing in larger populations
- Control and vaccine groups
- Clinical evaluators, laboratory staff and participants themselves are unaware about who is in the control or vaccine groups until trail has been completed.

PHASE II: TESTING IN A TARGET POPULATION

Phase II

- **Objectives:**
  - Optimize vaccine use and delivery conditions
    - Optimal dose
  - Plan for phase 3 trials
- **Test group**
  - Size: A small group of 50-500 of naïve and immunocompetent human subjects
  - Age group: Vaccine target population

Phase I/II: Pfizer BioNTech (mRNA)

- **Objectives:**
  - Optimize vaccine use and delivery conditions
    - Optimal dose test: 10, 30 or 100 µg, 1 or 2 doses 21 days apart
    - Also tested single doses of 100 µg
  - Prepare for Phase II/III trials
- **Test group**
  - Size: 76 participants
  - Age group: 19-54 years

medRxiv 2020.08.17.20176651; doi: https://doi.org/10.1101/2020.08.17.20176651
Walsh, E. E., Frenk, R. W., Falsey, A. R. *NEJM.* **2020**. 383, 2439-2450
Mulligan, M. J., Lyke, K. E., Kitchin, N., et al. *Nature.* **2020**. 586, 589-593

PHASE I/II: INITIAL SAFETY TRIALS AND TARGET POPULATIONS

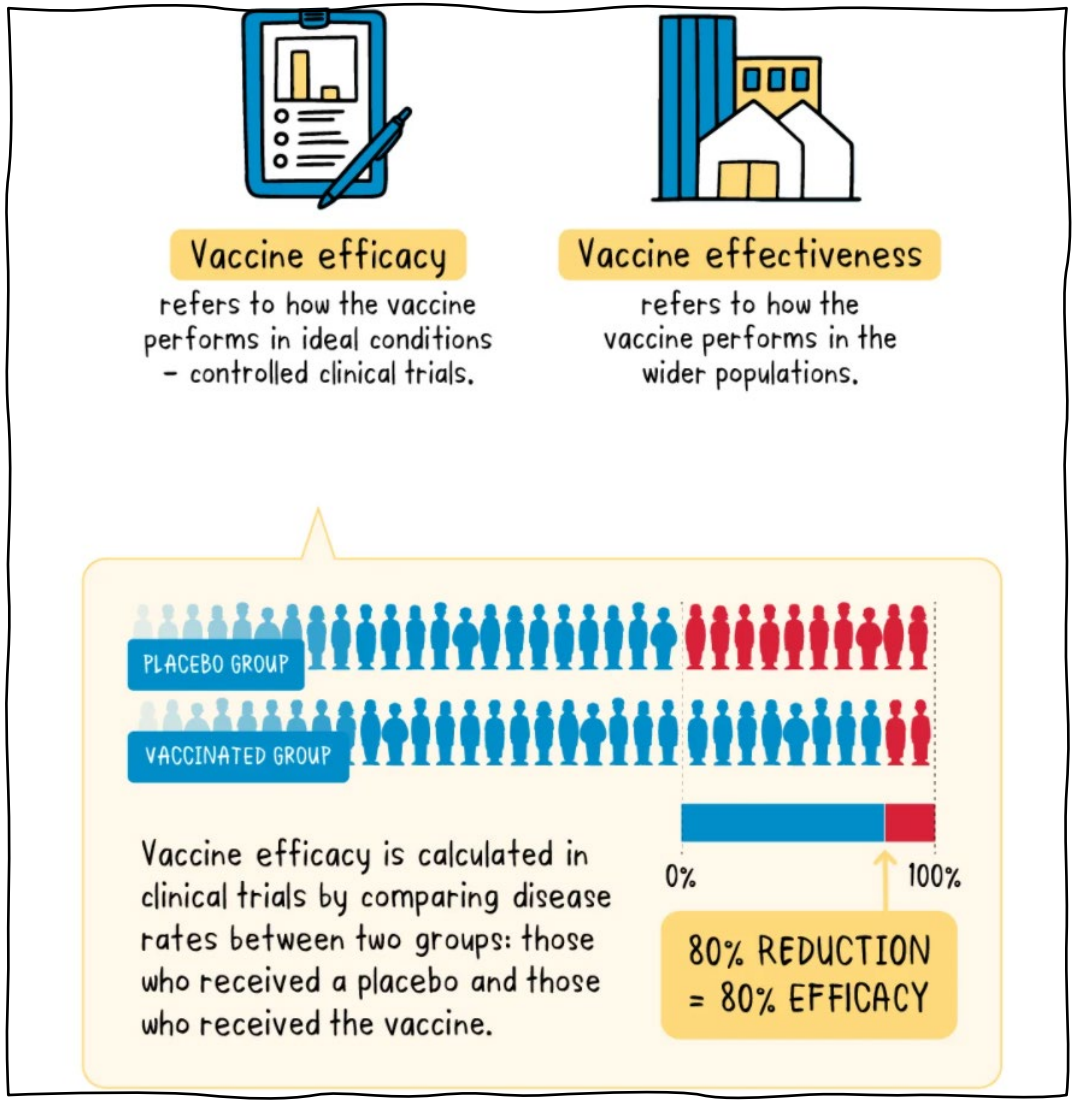
PFIZER AND BIONTECH SHARE POSITIVE EARLY DATA ON LEAD MRNA VACCINE CANDIDATE BNT162B2 AGAINST COVID-19

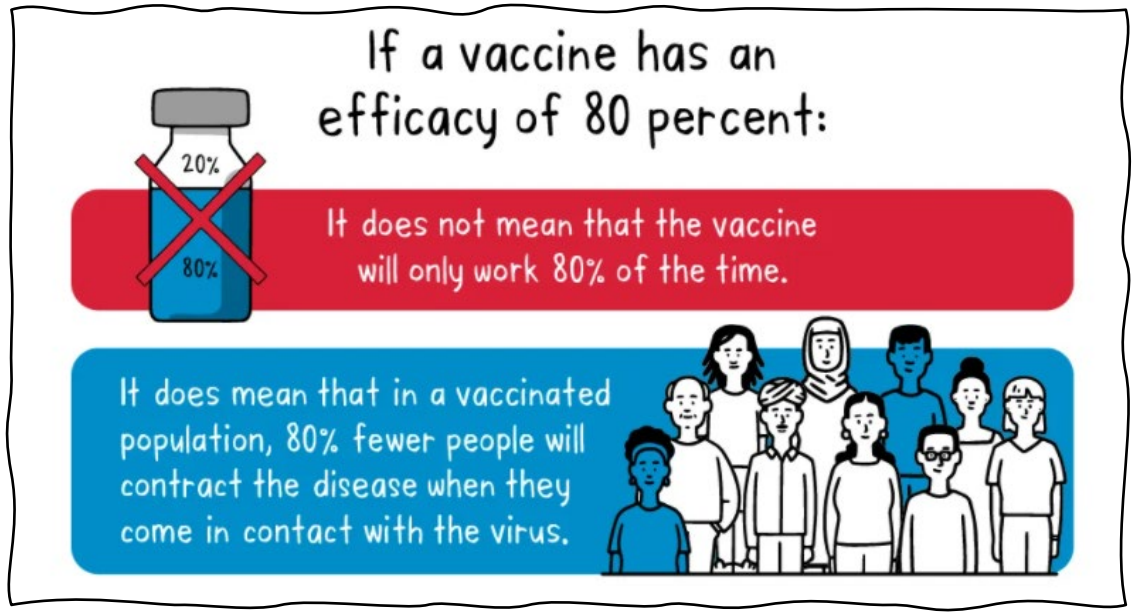
Thursday, August 20, 2020 - 08:00pm

- *In a Phase 1 study in the U.S., at 7 days after a second dose of 30µg, BNT162b2 elicited SARS-CoV-2–neutralizing geometric mean titers (GMTs) in younger adults (18-55 years of age) that were 3.8 times the GMT of a panel of 38 sera of SARS-CoV-2 convalescent patients, and in older adults (65-85 years of age) the vaccine candidate elicited a neutralizing GMT 1.6 times the GMT of the same panel, demonstrating strong immunogenicity in younger and older adults.*
- *The companies previously announced that BNT162b2-vaccinated human participants displayed a favorable breadth of epitopes recognized in T cell responses specific to the SARS-CoV-2 spike antigen, and that BNT162b2 demonstrated concurrent induction of high magnitude CD4+ and CD8+ T cell responses against the receptor binding domain (RBD) and against the remainder of the spike glycoprotein*
- *Across all populations, BNT162b2 administration was well tolerated with mild to moderate fever in fewer than 20% of the participants*
- *These results informed the selection of the BNT162b2 candidate for the pivotal Phase 2/3 global study in up to 30,000 participants that started in July 2020, which has to date enrolled more than 11,000 participants, including in areas with significant SARS-CoV-2 transmission*
- *Assuming clinical success, Pfizer and BioNTech are on track to seek regulatory review of BNT162b2 as early as October 2020 and, if regulatory authorization or approval is obtained, currently plan to supply up to 100 million doses worldwide by the end of 2020 and approximately 1.3 billion doses by the end of 2021*

PHASE III: PROTECTIVE EFFICACY TRIALS

- Study **protective efficacy**
  - "The primary purpose of a phase III trial is to assess the protective efficacy of the vaccine in the target population."
  - Monitor vaccinated and unvaccinated participants for disease incidence over various periods of time to determine protection levels
- 1000-150,000 participants (determined by incidence of disease)
- Randomized, double-blind control trial: participants randomly allocated to placebo or vaccine groups or groups that receive nothing
- Mimic "field" conditions
- Large trials that may last up to several years
- Sufficient data allows for application of license with the FDA





https://www.who.int/news-room/feature-stories/detail/vaccine-efficacy-effectiveness-and-protection

PHASE III: TESTING IN A TARGET POPULATION

Phase III

- **Objectives:**
  - Protective efficacy
    - Define clinical trial **endpoint**
- **Test group**
  - Size: 1,000 – 150,0000
  - Age group: Vaccine target population
  - Vaccine locations

Phase III: Pfizer–BioNTech mRNA vaccine

- **Objectives:**
  - Protective efficacy
    - COVID-19 disease symptoms as outlined by the FDA and laboratory tests
    - Dosage: placebo or 30 µg of vaccine, 21 days apart
- **Test group**
  - Size
    - 43,548 participants
    - 21,720 received vaccine, 21,728 received placebo
  - Age group: 16 years old or older
  - Vaccine locations:
    - Multi-site (United States, Brazil, Argentina, South Africa, Germany, and Turkey)

Polack, F. P., Thomas, S. J., Kitchin, N., et al. *NEJM*. **2020**. 383, 2603-2615

PHASE III : TESTING IN A TARGET POPULATION

"The **safety profile** of BNT162b2 (vaccine) was characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache."

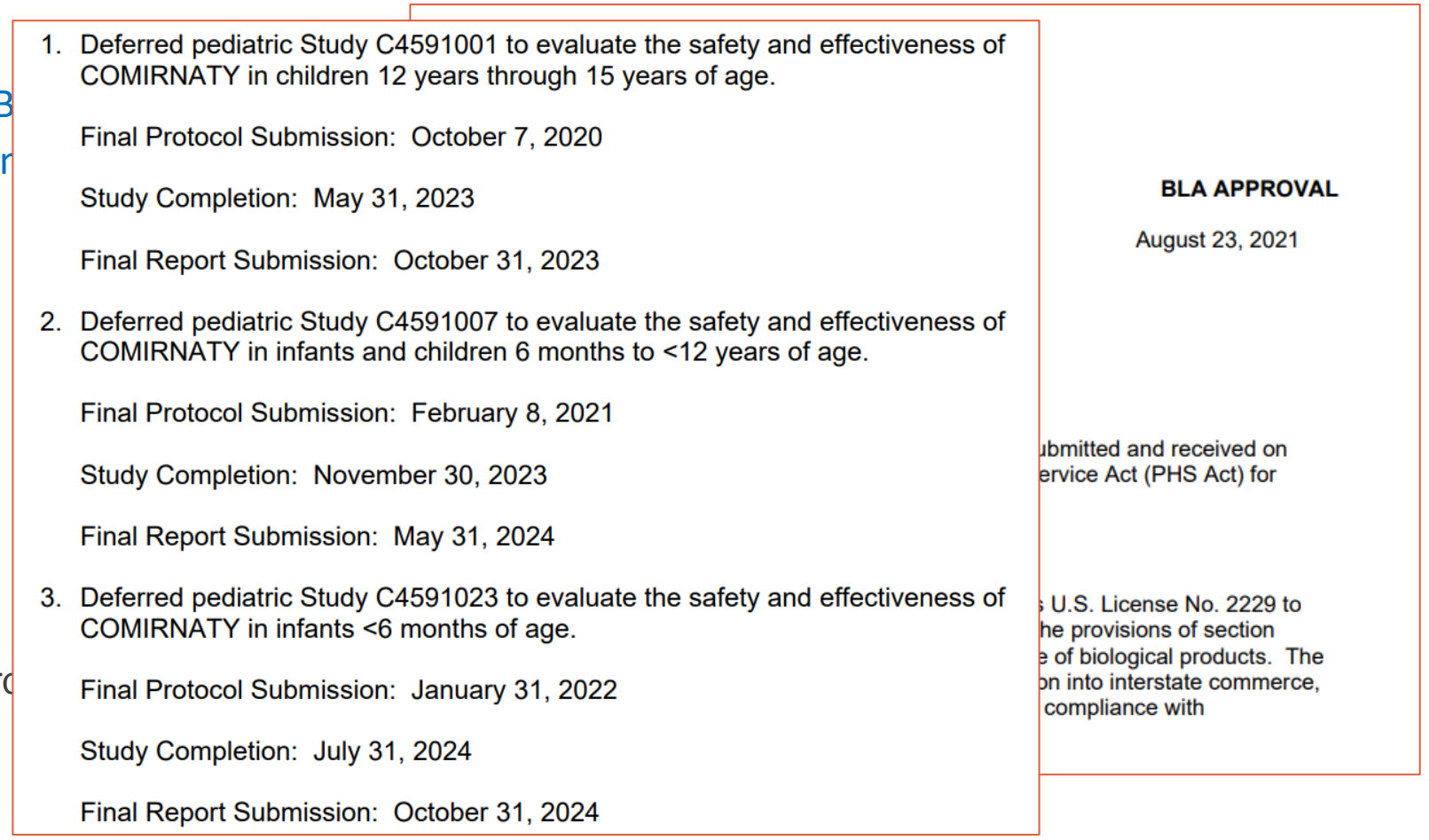
Table 2. **Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.***

Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability (Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
		(N=18,198)		(N=18,325)		
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.3–97.6)	>0.9999
		(N=19,965)		(N=20,172)		
Covid-19 occurrence at least 7 days after the second dose in participants with and those without evidence of infection	9	2.332 (18,559)	169	2.345 (18,708)	94.6 (89.9–97.3)	>0.9999

Polack, F. P., Thomas, S. J., Kitchin, N., et al. *NEJM*. **2020**. 383, 2603-2615

BLA SUBMISSION TO THE FDA

- "The Biologics License Application (B
  biologic product into interstate comr
  manufacture.
- Requirements for a BLA
  - Applicant information
  - Product/Manufacturing information
  - Pre-clinical studies
  - Clinical studies
  - Labeling
- BLA for Pfizer BioNTech vaccine appr



1. Deferred pediatric Study C4591001 to evaluate the safety and effectiveness of COMIRNATY in children 12 years through 15 years of age.

   Final Protocol Submission: October 7, 2020

   Study Completion: May 31, 2023

   Final Report Submission: October 31, 2023

2. Deferred pediatric Study C4591007 to evaluate the safety and effectiveness of COMIRNATY in infants and children 6 months to <12 years of age.

   Final Protocol Submission: February 8, 2021

   Study Completion: November 30, 2023

   Final Report Submission: May 31, 2024

3. Deferred pediatric Study C4591023 to evaluate the safety and effectiveness of COMIRNATY in infants <6 months of age.

   Final Protocol Submission: January 31, 2022

   Study Completion: July 31, 2024

   Final Report Submission: October 31, 2024

BLA APPROVAL

August 23, 2021

ubmitted and received on
ervice Act (PHS Act) for

s U.S. License No. 2229 to
he provisions of section
e of biological products. The
on into interstate commerce,
compliance with

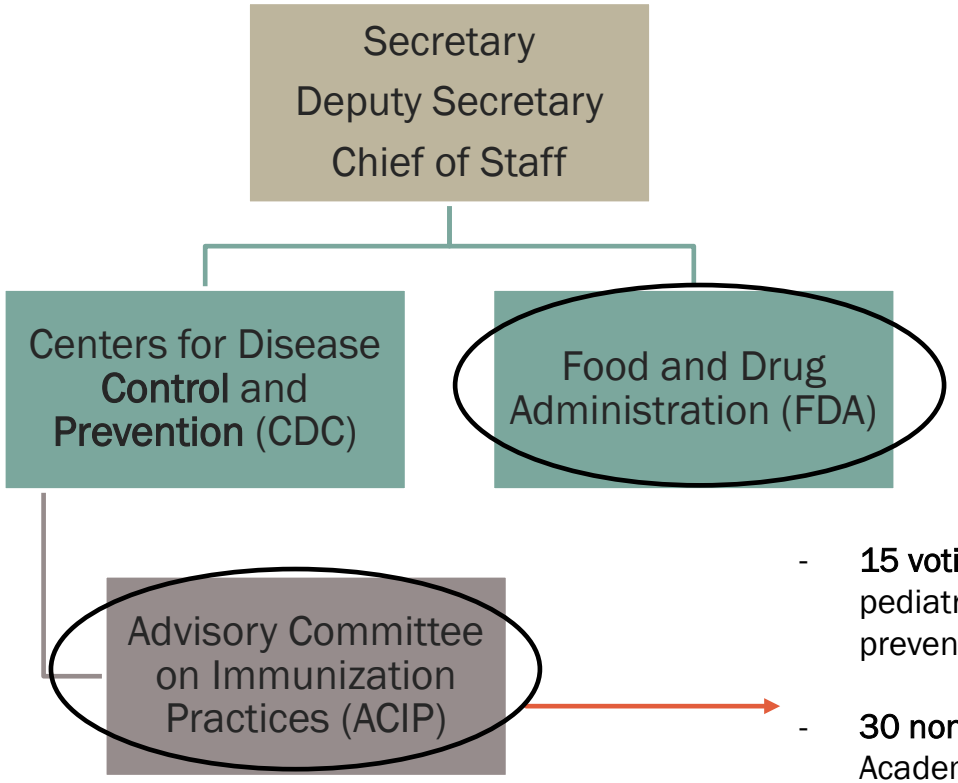
https://www.fda.gov/media/151710/download

PHASE IV: CLINICAL TRIALS

- Postlicensure surveillance, i.e., monitoring continues following FDA approval
  - Safety
  - Vaccine effectiveness
  - Population level effects
- More focused on epidemiological studies
- Trials can be on-going for some substudies
  - Trials are still on-going for groups of ages 12 and under for the Pfizer–BioNTech vaccine

https://www.pfizer.com/science/clinical-trials/children

HEALTH AND HUMAN SERVICES ORGANIZATIONAL STRUCTURE



- **15 voting members** selected by DHHS (experts in vaccinology, immunology, pediatrics, internal medicine, infectious diseases, virology, family medicine, preventative medicine, a consumer representative)
- **30 non-voting representatives** from professional organizations (American Academy of Pediatrics, American Academy of Family Physicians, American College of Nurse Midwives, American College of Obstetricians and Gynecologists, American College of Physicians)

https://www.cdc.gov/vaccines/acip/committee/role-vaccine-recommendations.html

WHAT HAPPENS WHEN NATIONAL AND GLOBAL HEALTH EMERGENCIES OCCUR?

EMERGENCY USE AUTHORIZATION (EUA)

Emergency Use Authorization of Medical Products and Related Authorities

Guidance for Industry and Other Stakeholders

U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner
Office of the Chief Scientist
Office of Counterterrorism and Emerging Threats

January 2017

Procedural
OMB Control No. 0910-0595
Expiration Date 08/31/2022
See additional PRA statement in section IX of this guidance.

A. EUA DECLARATION JUSTIF

1. Determinations to Suppo

Before FDA may issue an EUA, the HHS
justifying the authorization (section 564(
an "EUA declaration"),[12] must be based

1. A determination by the Secret
emergency, or a significant po
heightened risk of attack with a CBRN agent(s);[13]

2. A determination by the Secretary of Defense that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to United States military forces of attack with a CBRN agent(s);[14]

3. A determination by the Secretary of HHS that there is a public health emergency, or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of United States citizens living abroad, and that involves a CBRN agent or agents, or a disease or condition that may be attributable to such agent(s);[15] or

SUMMARY:

The Secretary of Health and Human Services (HHS) is issuing this notice pursuant to section 564 of the Federal Food, Drug, and Cosmetic (FD&C) Act. On February 4, 2020, the Secretary determined pursuant to his authority under section 564 of the FD&C Act that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad and that involves a novel (new) coronavirus (nCoV) first detected in Wuhan City, Hubei Province, China in 2019 (2019-nCoV). On the basis of this determination, he also declared that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of this novel coronavirus (2019-nCoV) pursuant to section 564 of the FD&C Act, subject to the terms of any authorization issued under that section.

DATES:

The determination and declaration took effect February 4, 2020.

https://www.fda.gov/media/97321/download
https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency

EMERGENCY USE AUTHORIZATION (EUA)

December 11, 2020
Worldwide
Deaths: 13,141
New cases: 692,116
USA
Deaths: 2,955
New cases: 280,513

PFIZER AND BIONTECH CONCLUDE PHASE 3 STUDY OF COVID-19 VACCINE CANDIDATE, MEETING ALL PRIM… ENDPOINTS

Wednesday, November 18, 2020 - 06:59am

- *Primary efficacy analysis demonstrates BNT162b2 to be 95% effective against COVID-19 beginning 28 days after th… with 162 observed in the placebo group versus 8 in the vaccine group*
- *Efficacy was consistent across age, gender, race and ethnicity demographics; observed efficacy in adults over 65 ye…*
- *Safety data milestone required by U.S. Food and Drug Administration (FDA) for Emergency Use Authorization (EUA)…*
- *Data demonstrate vaccine was well tolerated across all populations with over 43,000 participants enrolled; no seri… greater than 2% in frequency was fatigue at 3.8% and headache at 2.0%*
- *Companies plan to submit within days to the FDA for EUA and share data with other regulatory agencies around th…*
- *The companies expect to produce globally up to 50 million vaccine doses in 2020 and up to 1.3 billion doses by the…*
- *Pfizer is confident in its vast experience, expertise and existing cold-chain infrastructure to distribute the vaccine a…*

FDA NEWS RELEASE

FDA Takes Key Action in Fight … By Issuing Emergency Use Authorization for First COVID-19 Vaccine

Action Follows Thorough Evaluation of Available Safety, Effectiveness, and Manufacturing Quality Information by FDA Career Scientists, Input from Independent Experts

Share | Tweet | Linkedin | Email | Print

For Immediate Release: December 11, 2020

Español

Today, the U.S. Food and Drug Administration issued the first emergency use authorization (EUA) for a vaccine for the prevention of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. The emergency use authorization allows the Pfizer-BioNTech COVID-19 Vaccine to be distributed in the U.S.

Emergency Use Authorization (EUA)
"allows FDA to help strengthen the nation's public health protections against chemical, biological, radiological and nuclear (CBRN) threats including infectious diseases by facilitating the availability and use of medical counter measures (MCMs) needed during public health emergencies

FACTORS THAT AFFECT SPEED OF VACCINE APPROVAL

- Adequate number of participants in Phase I/II/III trials
- Single or multicenter trials
- Cost
  - The CARES (**C**oronavirus **A**id, Relief, and **E**conomy **S**ecurity) Act was used to fund vaccine research
    - Johnson & Johnson
    - AstraZeneca
    - Moderna
    - Novavax
- Collaboration across the globe
- Emergency Use Authorizations (EUA)
  - Use of Pfizer–BioNTech vaccine for ages 16 and above
  - Comirnaty is currently approved under an EUA for administration to 12–15-year-olds
    - Based on Phase III trials with 2,260 adolescents, with vaccine efficacy of 95%.
  - Comirnaty is still investigating the vaccine for children ages 12 and under.

Frenck, R. W., Klein, N. P., Kitchin, N., et al. *NJEM*. **2021**. 385, 239-250

CONCLUSION

- Vaccines are biological products that confer protection against symptomatic disease.
- Before authorization for use by the FDA, vaccines undergo rigorous safety, immunogenicity and protective efficacy tests in Phase I, Phase II and Phase III clinical trials.
- Vaccines are studied and monitored closely by the FDA, the ACIP and vaccine manufacturers even after licensure and approval for use.
- Emergency Authorization Use (EUA) can be declared by the Secretary of HHS during a public health crisis or a potential public health crisis to increase the speed with which vaccines are authorized by the FDA.