Vaccine Safety: The Process of Protection

Tabitha Hanson, DNP, MPH, RN, NBCSN | Vaccine Clinical Consultant

Objectives

- Participants will:
  - Understand the Food & Drug Administration's role in the licensing of vaccine in the United States.
  - Know the steps taken by vaccine manufacturers to ensure that vaccines are safe and effective.
  - Describe the role of the Advisory Committee on Immunization Practice in recommending licensed vaccines for use in the United States.
  - Identify three ways that the FDA and CDC monitor vaccine safety after the public begins using the vaccine.

Happy National Infant Immunization Week!

Are vaccines safe?

Do vaccines cause autism?

Was COVID-19 vaccine tested before approval?

Do vaccines contain harmful ingredients?

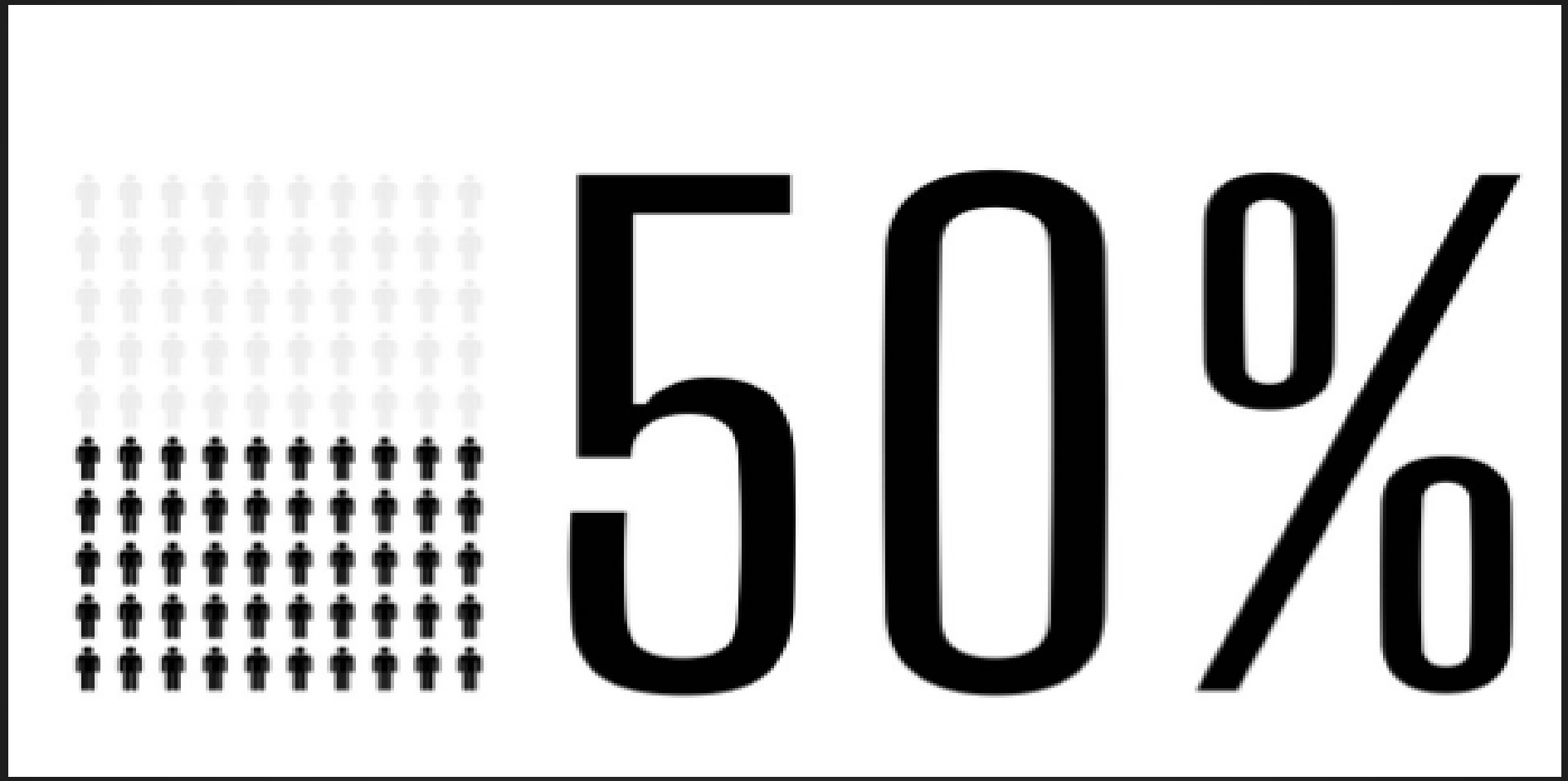
Will COVID-19 vaccines alter my DNA?

Are there microchips in vaccines?

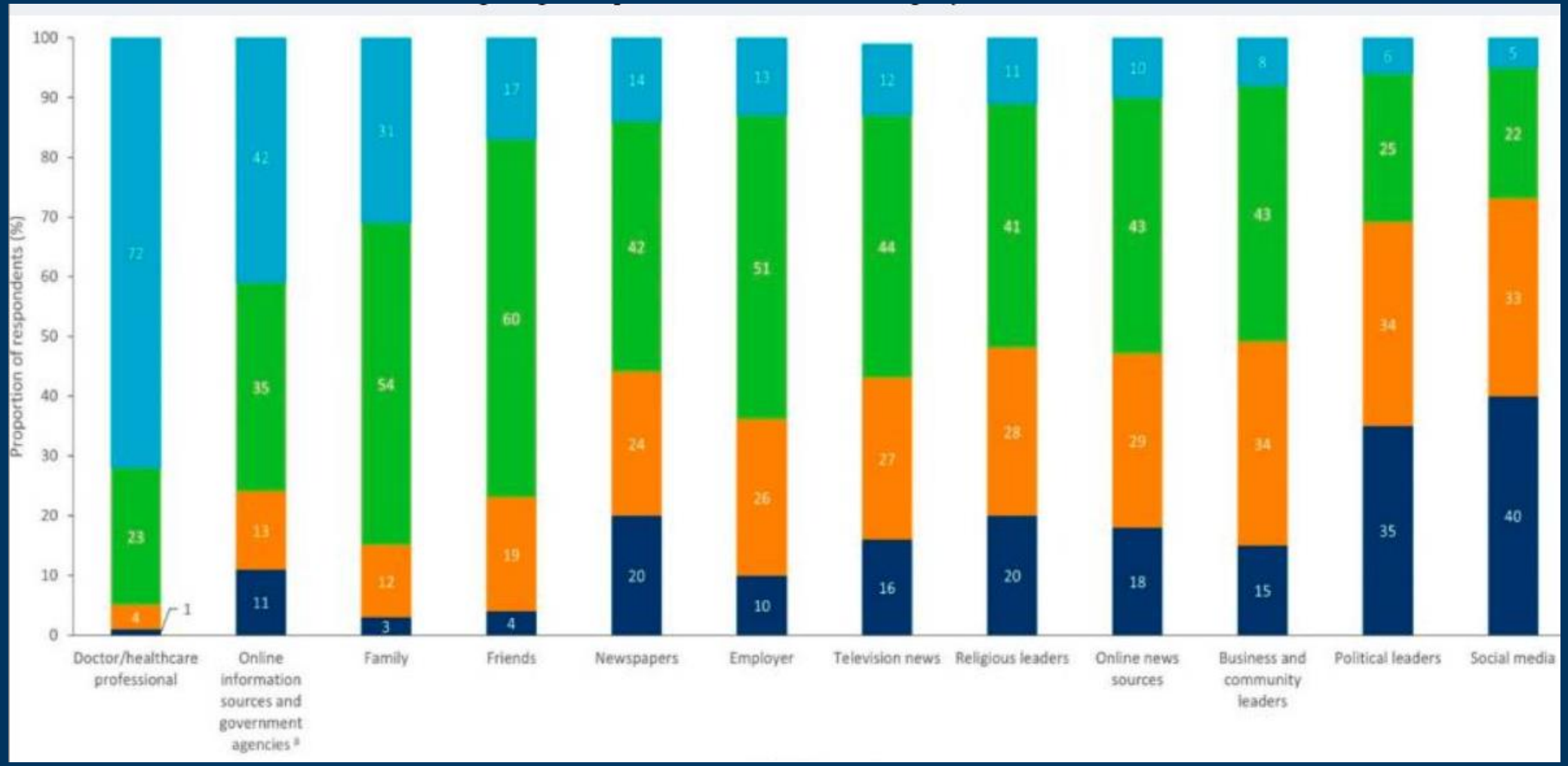
Can you get the disease from the vaccine?

Do vaccines cause SIDS?

Americans have concerns about vaccine safety

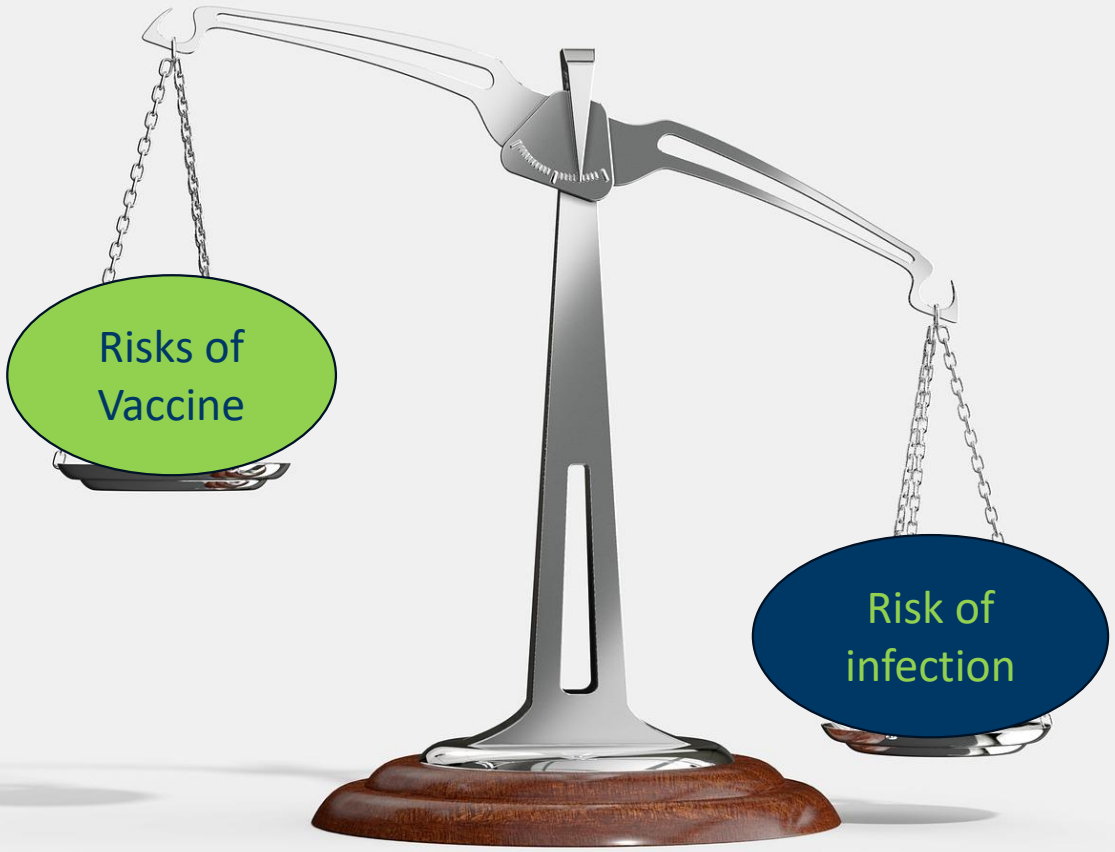


Level of Trust in Vaccine Information Sources



Attitudes and Beliefs around the Value of Vaccination in the United States - PMC (nih.gov)

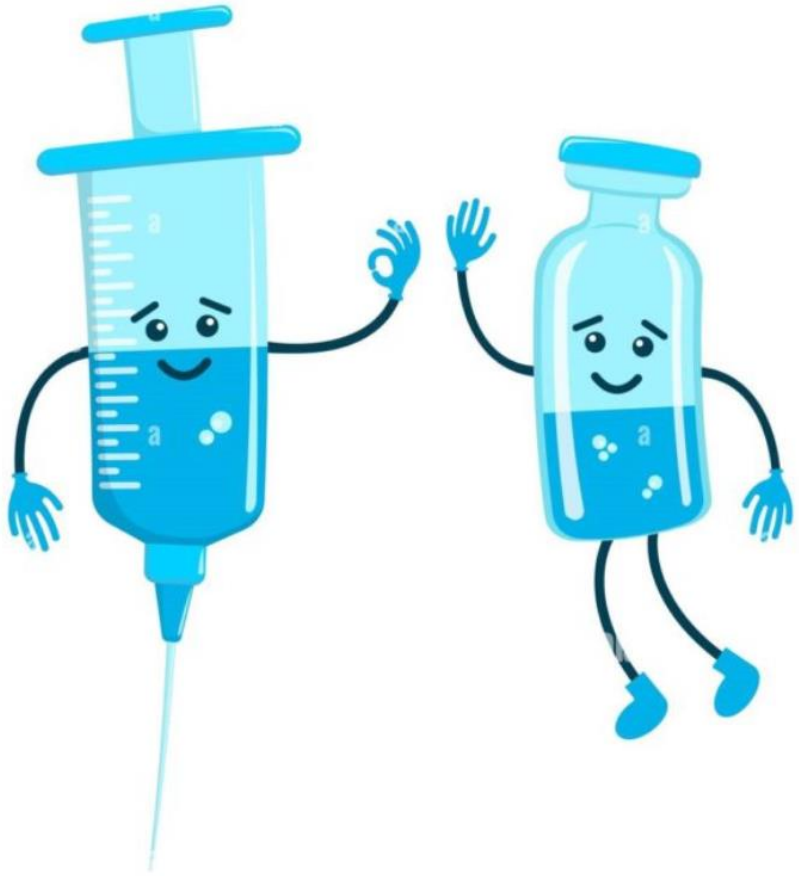
What is “safe”?



Vaccines vs Other Drugs

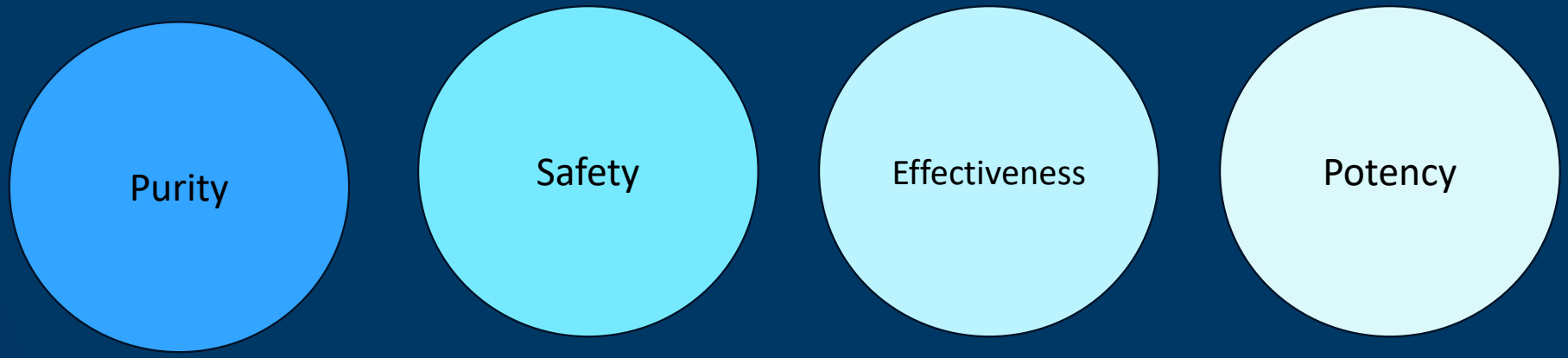
- Higher standard of safety expected of vaccines
  - Vaccinees generally healthy (vs. ill for drugs)
  - Dual role of vaccinations
    - Individual protection
    - Societal protection

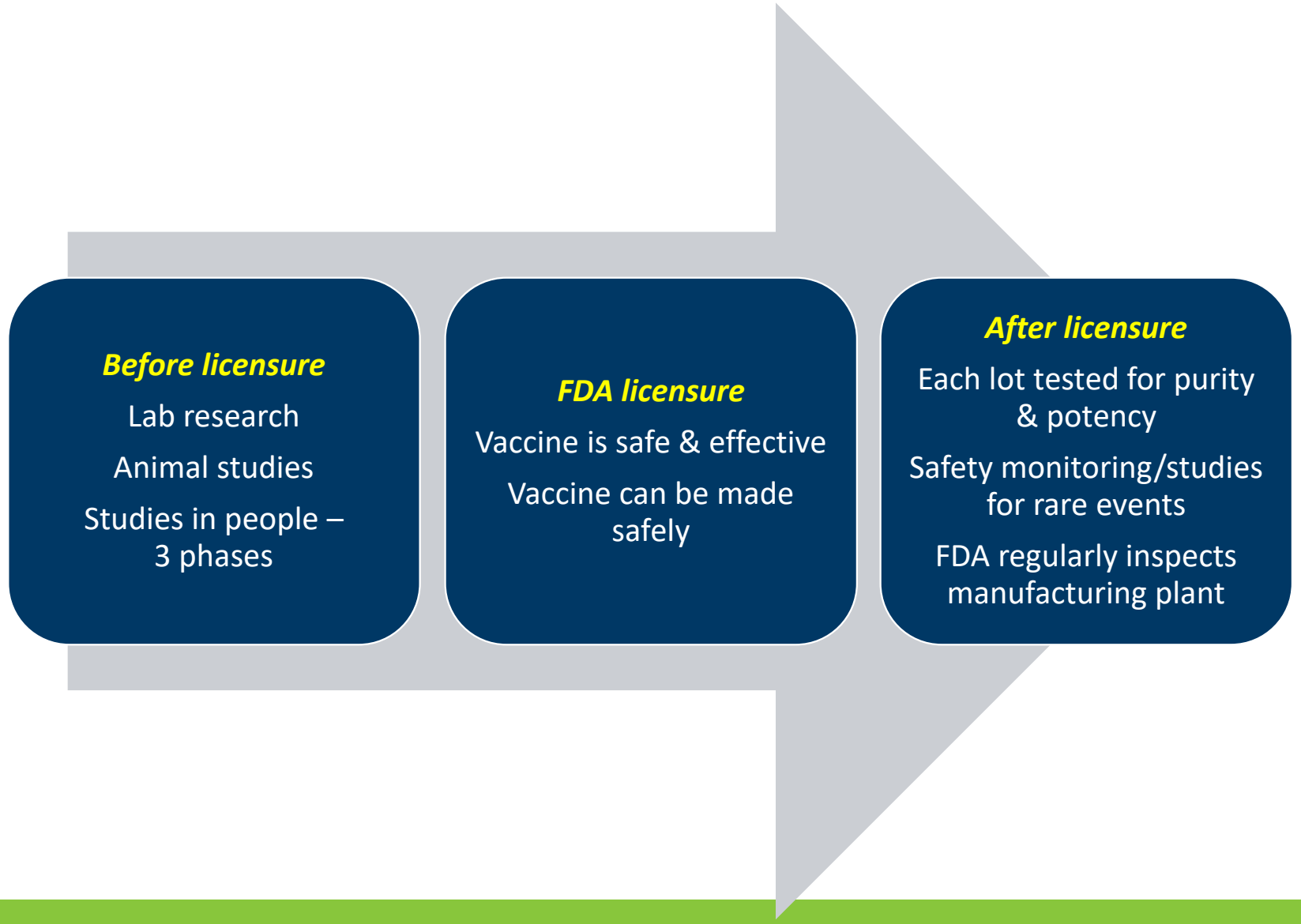
How a Vaccine Becomes a Shot



Food & Drug Administration (FDA)

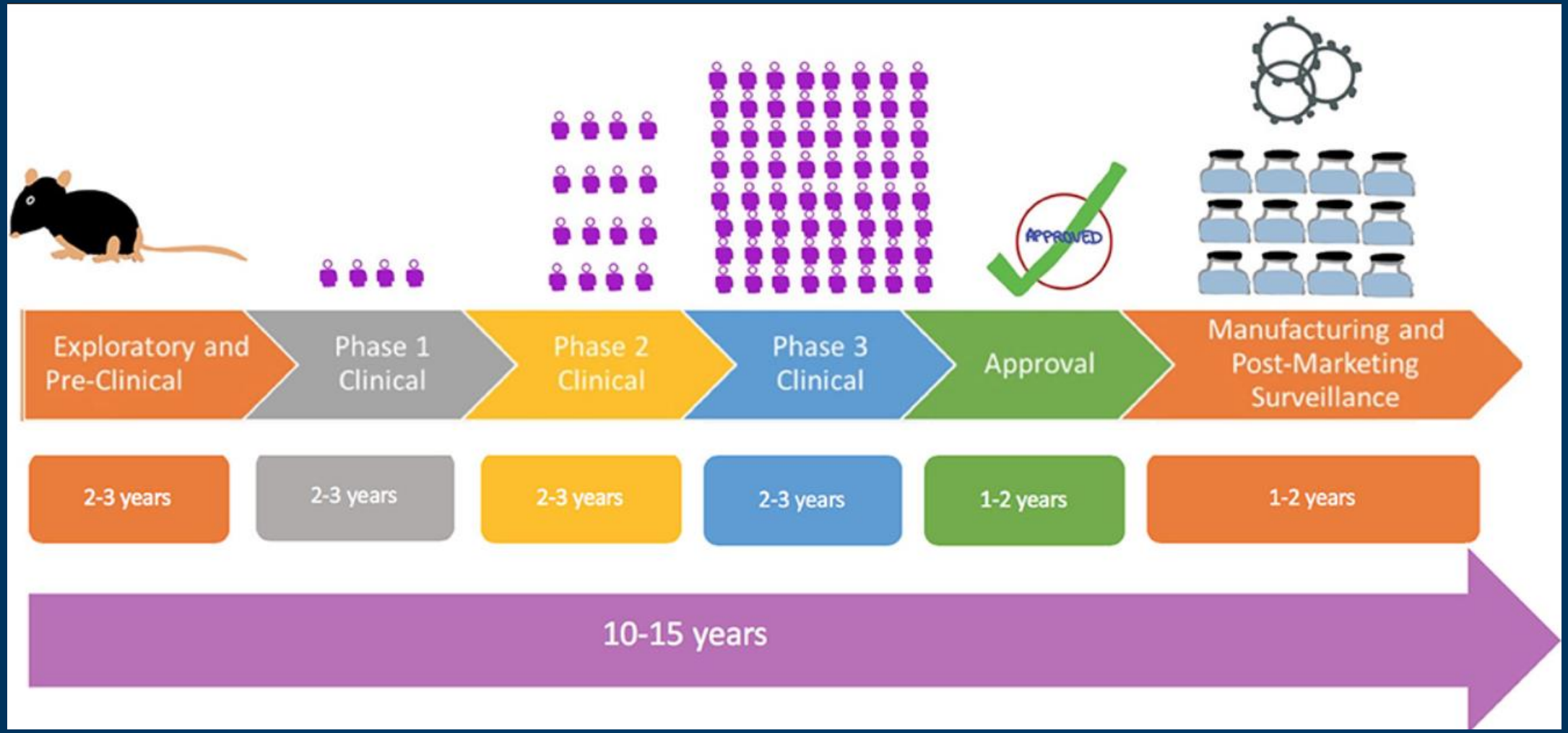
FDA Requirements for Vaccine Licensure





Vaccine safety pathway

Vaccine Development Process



Clinical Trials Pros & Cons

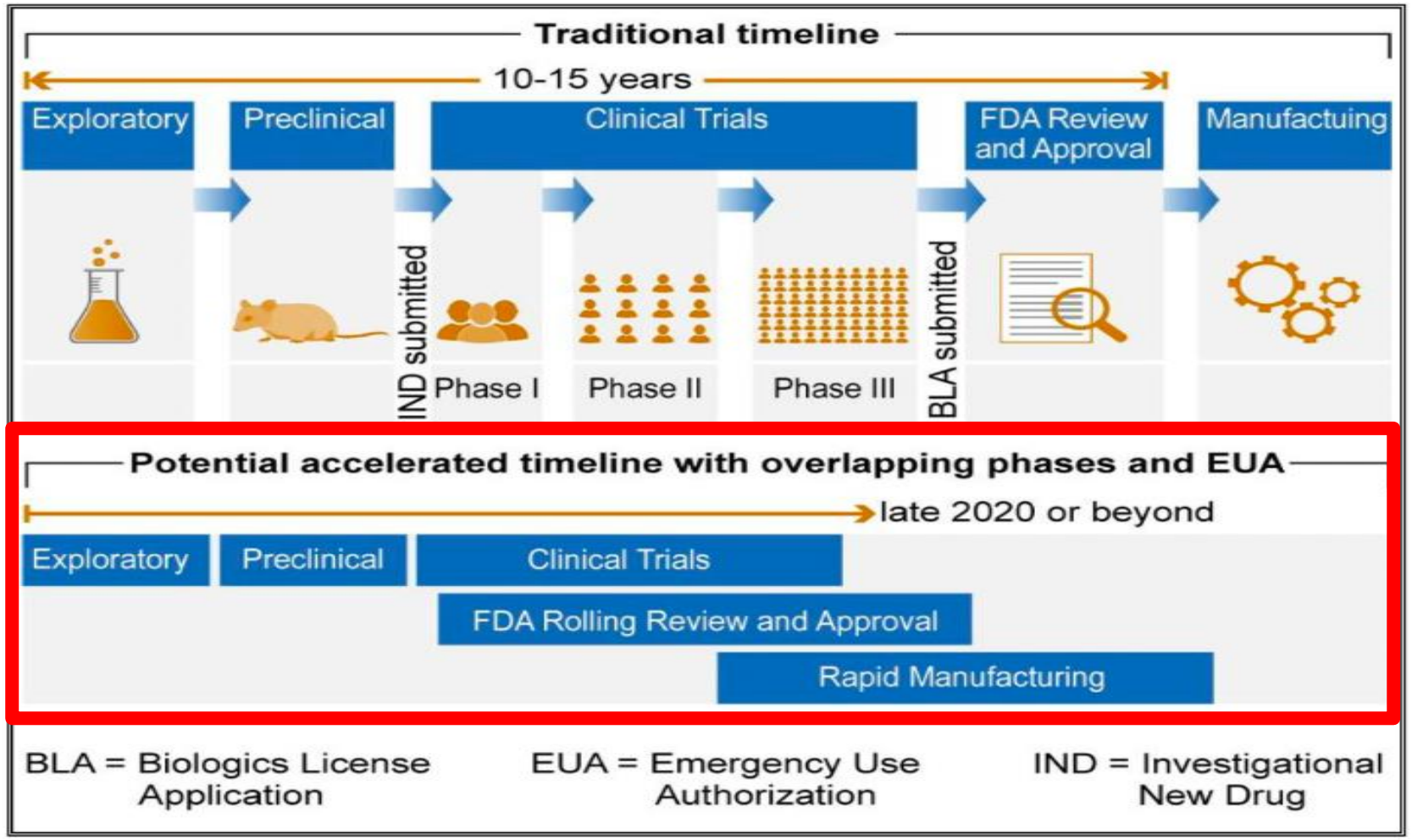
PROS

- Rigorous Step-by-Step Process
- Randomized Controlled Trials
- Gold Standard
- Bias prevention
- Detects efficacy

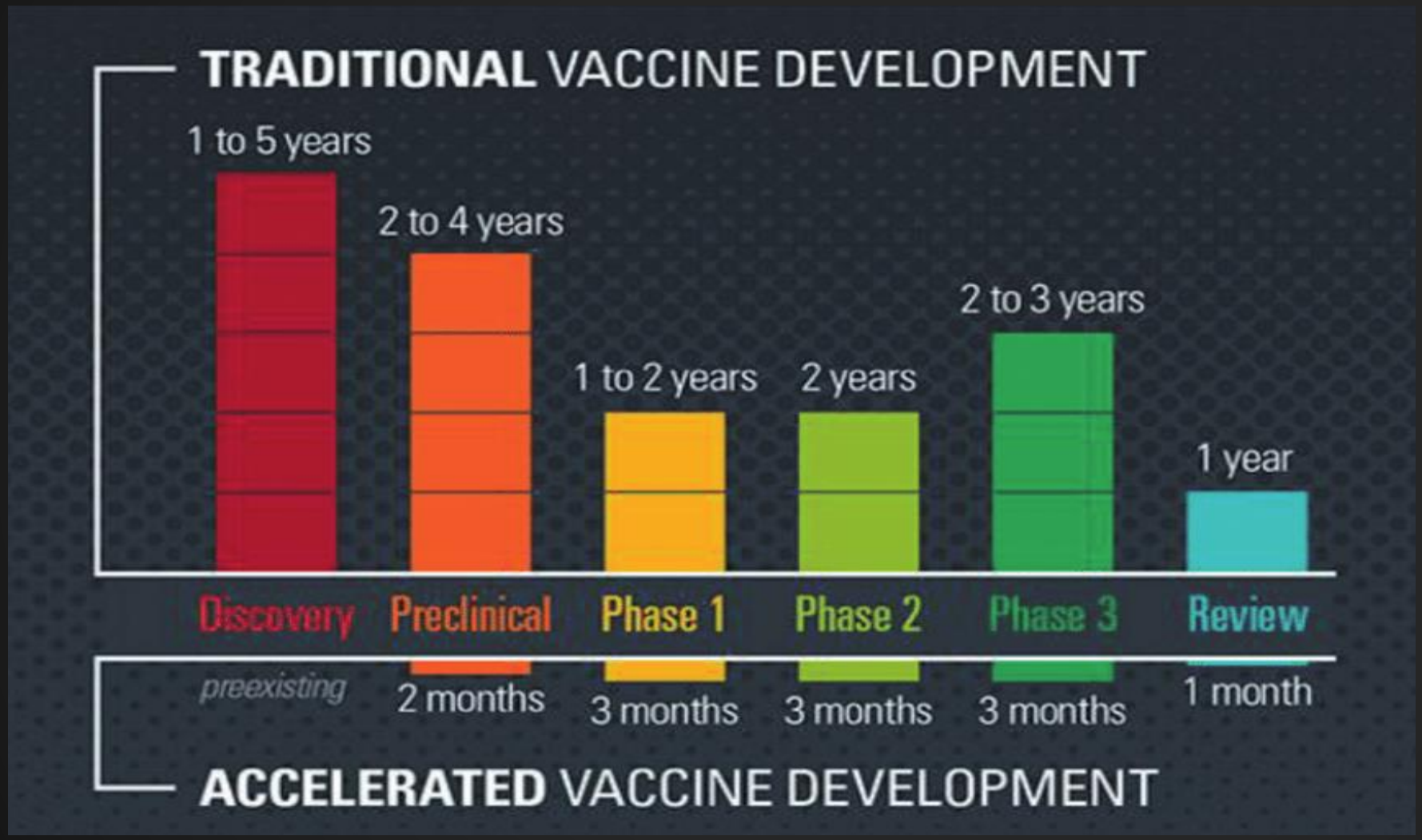
CONS

- Difficult to detect very rare, very late or delayed adverse events
- Expensive
- Time Intensive
- Specialized groups are studied later

Vaccine Development Process

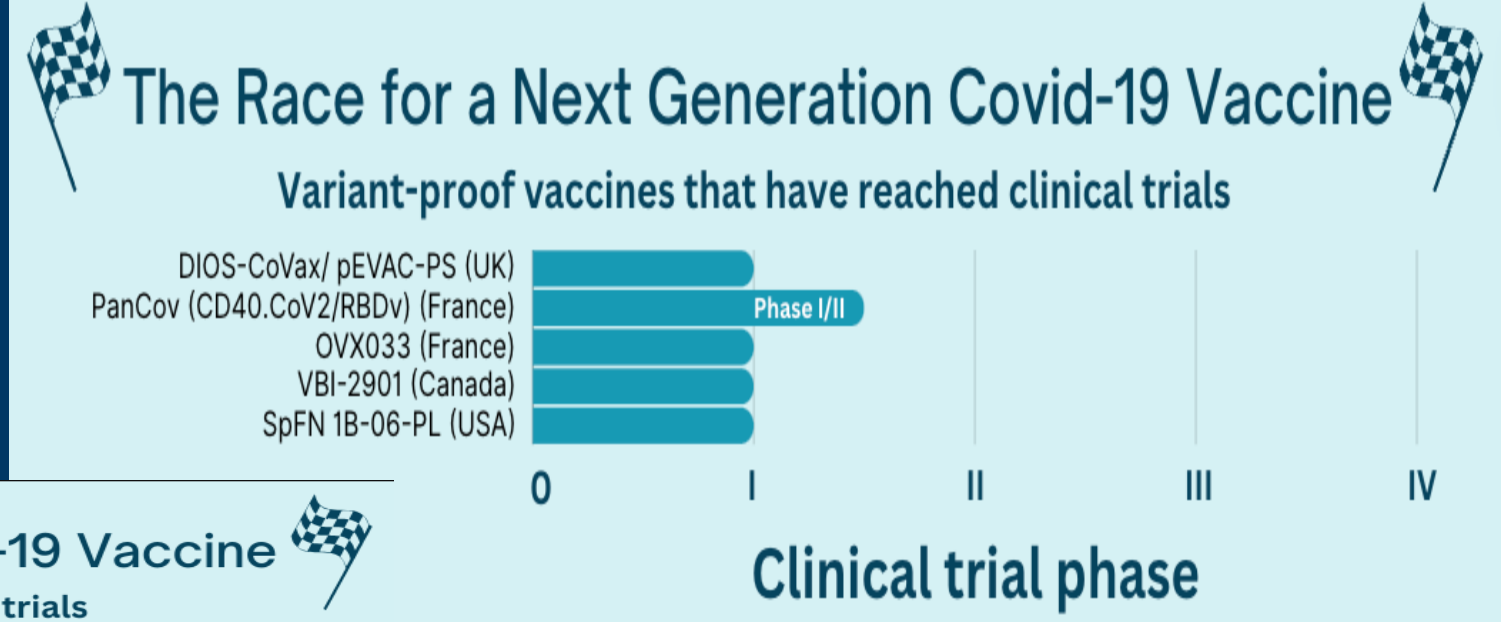


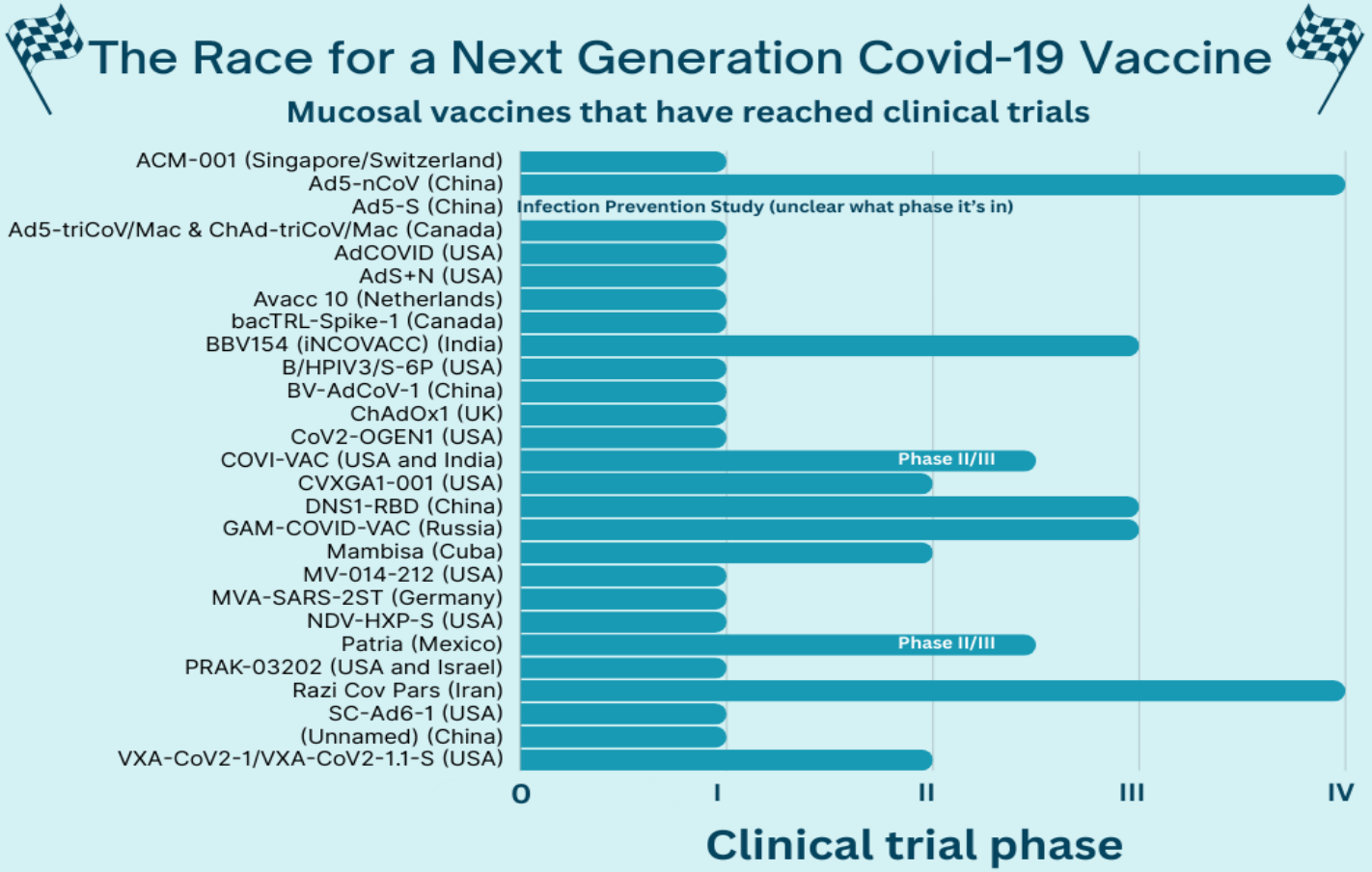
Accelerated Vaccine Development



Traditional vs. (accelerated) Covid-19 vaccine development timeline.... | Download Scientific Diagram (researchgate.net)

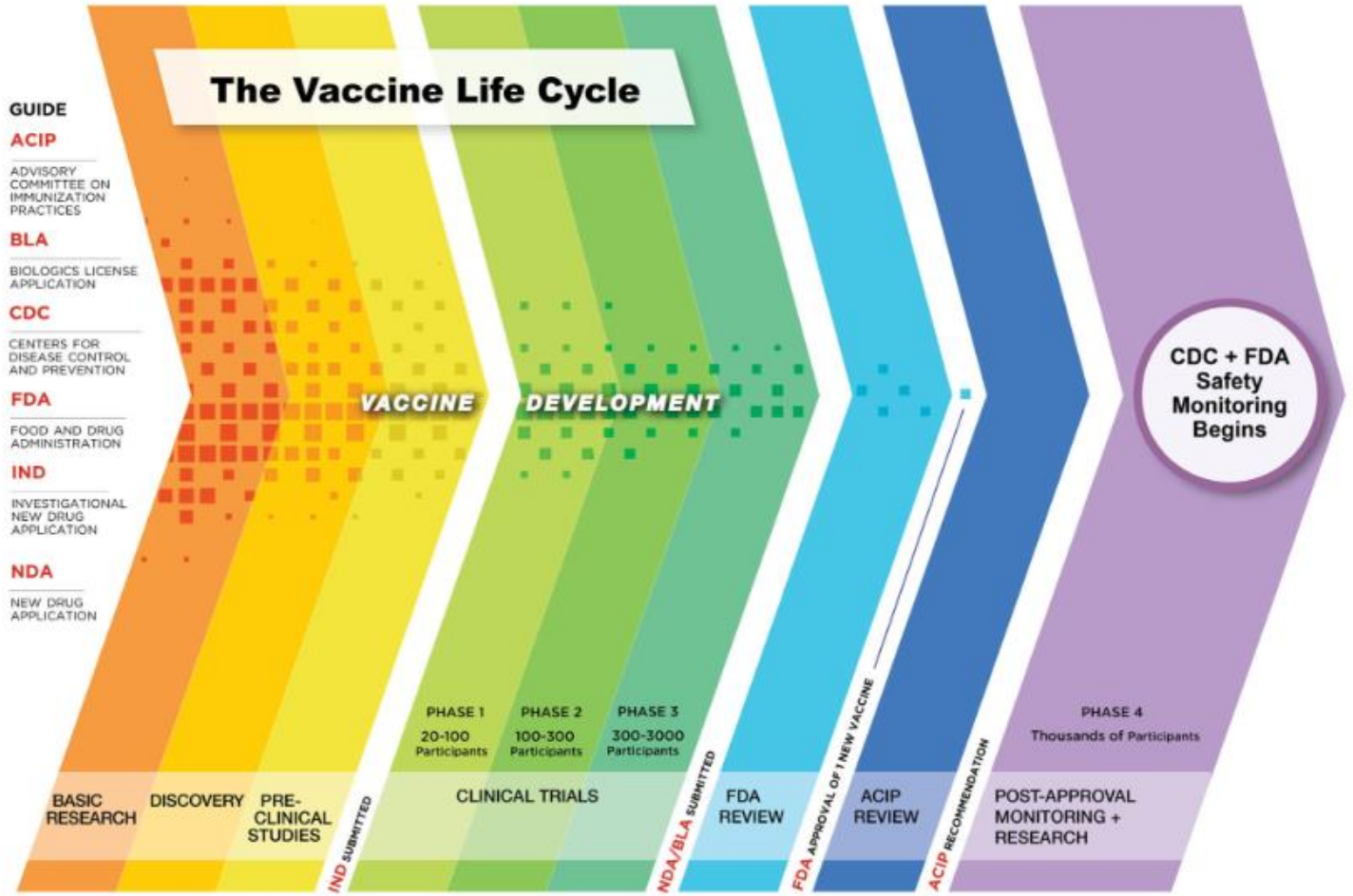
In the Pipeline





- 9 out of 10 products fail
- Universal coronavirus vaccine
- Intranasal COVID-19 vaccines
- Combining COVID-19 + Flu

Next Steps: ACIP & Monitoring



Further Review After Licensure

Vaccines & Related
Biological Products
Advisory Committee
(VRBPAC- informs FDA)

Advisory Committee on
Immunization Practices (ACIP)

Centers for Disease Control
and Prevention (CDC)

Advisory Committee on Immunization Practices

ACIP Process

GRADE

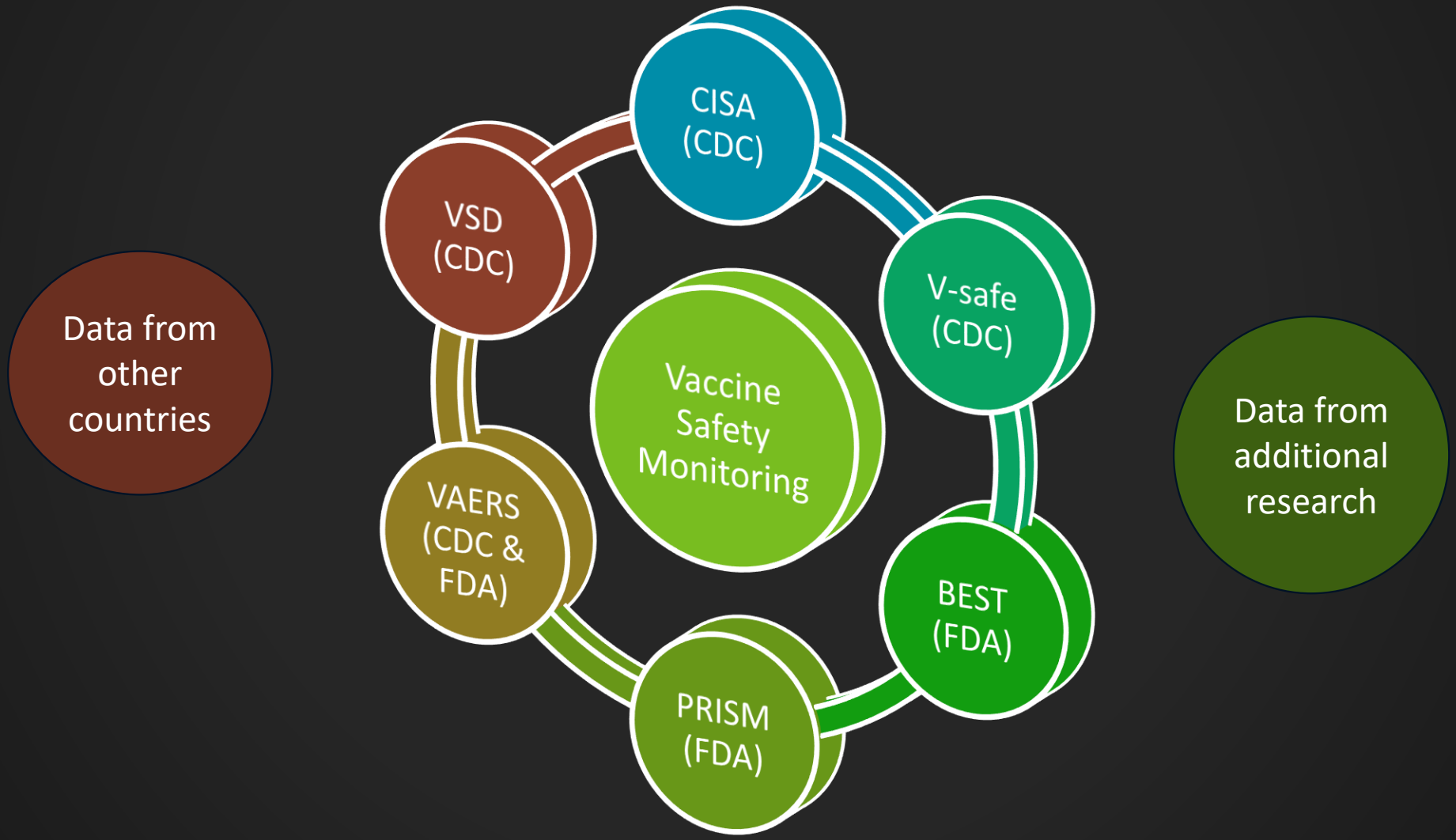
Grading of Recommendations Assessment, Development & Evaluation

EtR Framework

Evidence to Recommendation

- Public Health Importance
- Benefits & Harms
- Values & Preferences
- Acceptability
- Resource Use
- Equity
- Feasibility

Vaccine Safety Monitoring After Licensure



Active vs Passive Surveillance

PASSIVE

- VAERS
- Reports submitted without solicitation
- Serves as an alerting system
- Can be submitted by anyone without screening for qualifying condition
- Can miss cases

ACTIVE

- VSD & PRISM & BEST
- Aims to detect every case
- Can verify safety signals from VAERS
- Inclusive of population
- Proactive

National Childhood Vaccine Injury Act of 1986

- Vaccine Adverse Event Reporting System (VAERS)
  - Accepts reports of AEs following vaccination
- Vaccine Information Statements (VIS)
  - Required for childhood vaccines
- National Vaccine Injury Compensation Program (NVICP)
  - Compensates those injured by vaccines on a "no fault" basis

Vaccine Adverse Event Reporting System (VAERS)

https://vaers.hhs.gov

What is a vaccine adverse event?

- A health problem that happens after vaccination that may or may not be caused by a vaccine.
- May be any unfavorable or unintended condition
  - Sign
  - Symptom
  - Abnormal laboratory finding
  - Disease
- Does not necessarily have a causal relationship with vaccination

What to report to VAERS

- Any medically important health event/AE following vaccination even if you are not sure the vaccine caused the event
  - Local: redness, swelling, pain at injection site
  - Systemic: fever, myalgia, headache
  - Allergic: hives, pruritis, anaphylaxis
  - Vaccination errors (ex. wrong drug administered)

- National Childhood Vaccine Injury Act mandates reporting of any event found in the *VAERS Table of Reportable Events*
  - https://vaers.hhs.gov/docs/VAERS_Table_of_Reportable_Events_Following_Vaccination.pdf

Types of vaccine adverse events

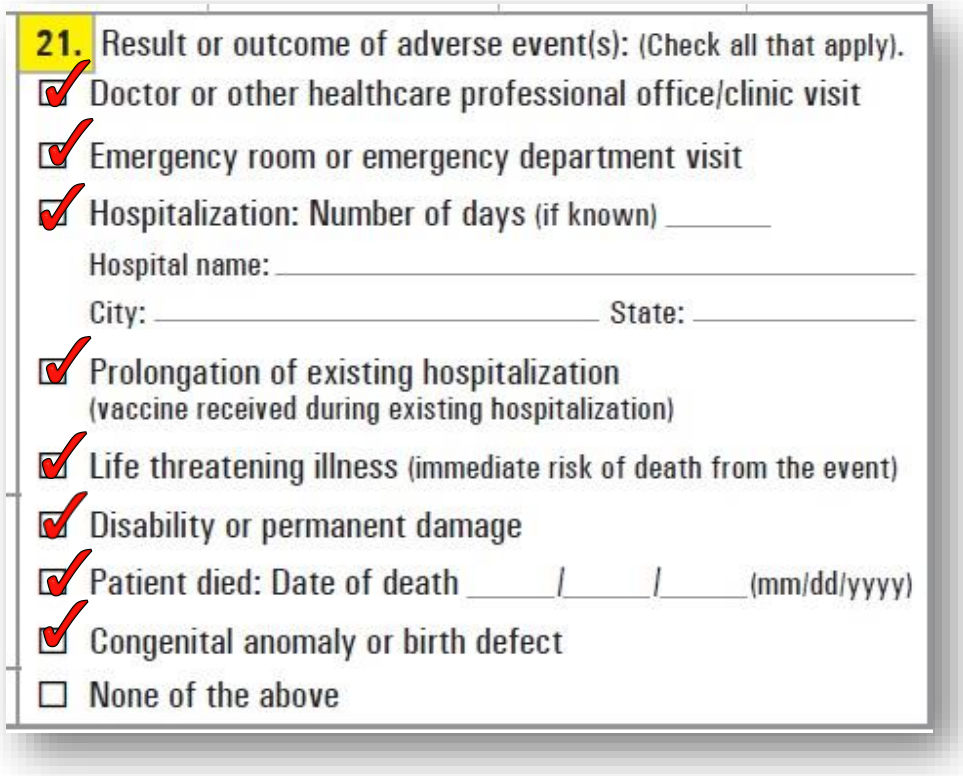
Category	Cause
Vaccine quality defect-related reaction	Due to one or more quality defects of the vaccine product including its administration device as provided by the manufacturer
Immunization error-related reaction	Inappropriate vaccine handling, prescribing, or administration
Immunization anxiety-related reaction	Arises from anxiety about the immunization
Vaccine product-related reaction	Due to one or more of the inherent properties of the vaccine product
Coincidental event	Something other than the vaccine product, immunization error, or immunization anxiety

VAERS follow-up

- VAERS staff follow up with health care providers on serious reports[1]
  - Medical records
  - Death certificates/autopsy reports
- FDA and CDC review medical records and VAERS reports for serious reports

[1]FDA reviews all serious reports; CDC reviews selected serious reports

VAERS form Box 21 – Serious status



21. Result or outcome of adverse event(s): (Check all that apply).

- ☑ Doctor or other healthcare professional office/clinic visit
- ☑ Emergency room or emergency department visit
- ☑ Hospitalization: Number of days (if known) _____
  - Hospital name: _____
  - City: _____ State: _____
- ☑ Prolongation of existing hospitalization (vaccine received during existing hospitalization)
- ☑ Life threatening illness (immediate risk of death from the event)
- ☑ Disability or permanent damage
- ☑ Patient died: Date of death ____/____/____(mm/dd/yyyy)
- ☑ Congenital anomaly or birth defect
- ☐ None of the above

VAERS strengths and limitations

Strengths

- National data; accepts reports from anyone
- Rapid signal detection
- Can detect rare AEs
- Collects information about vaccine, characteristics of vaccinee, AE
- Data available to public

Limitations

- Reporting bias
- Inconsistent data quality and completeness
- Lack of unvaccinated comparison group
- Generally cannot assess if vaccine caused an AE
- Pregnancy inconsistently reported

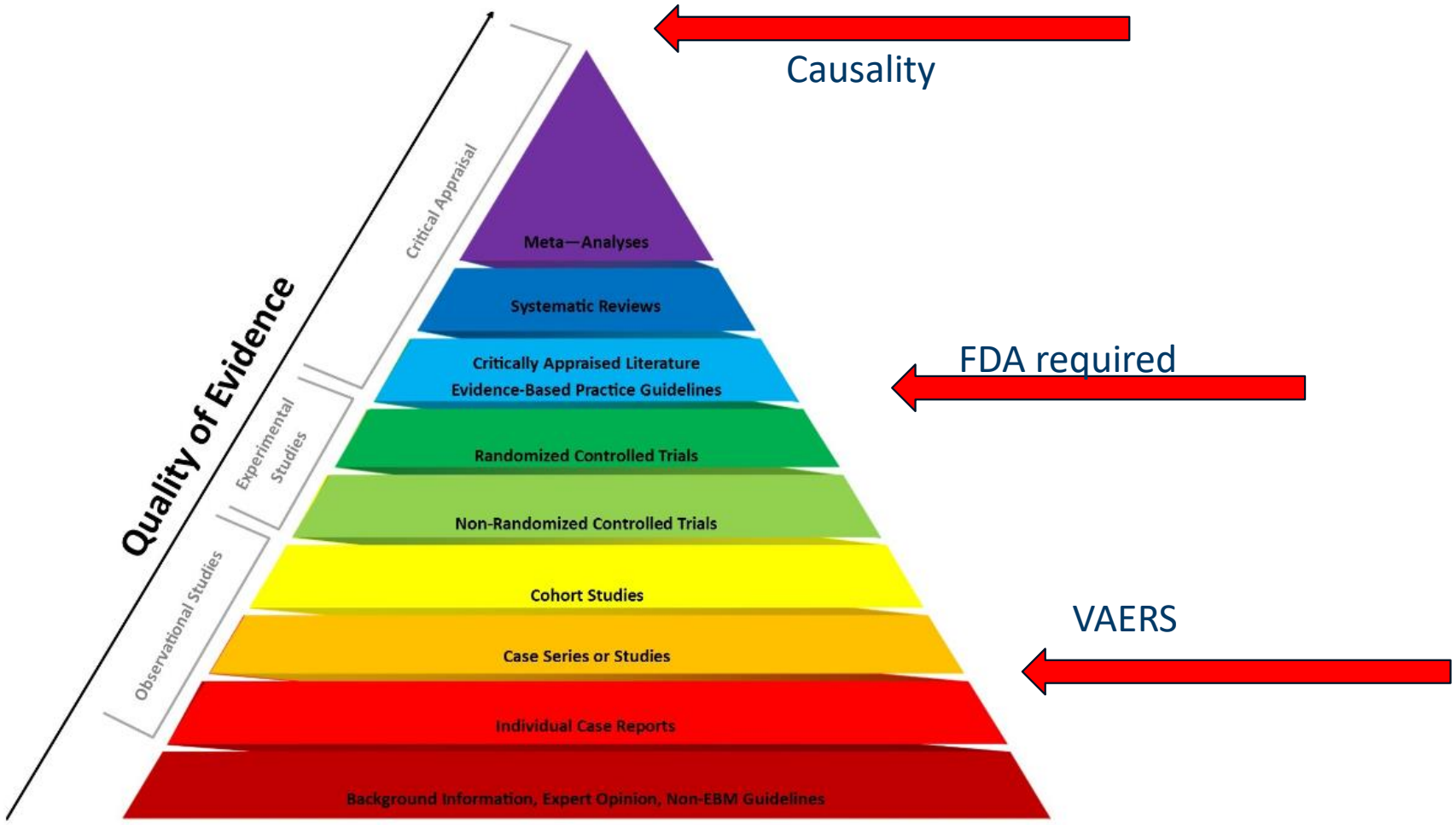
Limitations of VAERS data

Vaccinated with AE, reported to VAERS	Vaccinated no AE
Not vaccinated with AE	Not vaccinated no AE

Does a certain vaccine cause a certain side effect?

- Green cell only contains partial data - incomplete population data
  - Not able to calculate rates of occurrence of AEs
  - Not able to determine increased risk for AEs

Evidence Hierarchy of Evidence



What is the Hierarchy of Evhttps://www.researchsquare.com/blog/what-is-the-hierarchy-of-evidence?continueFlag=3b41b853df05eb0d1faf5743baddbf7cidence? | Research Square

Key Factors to Establish Causality

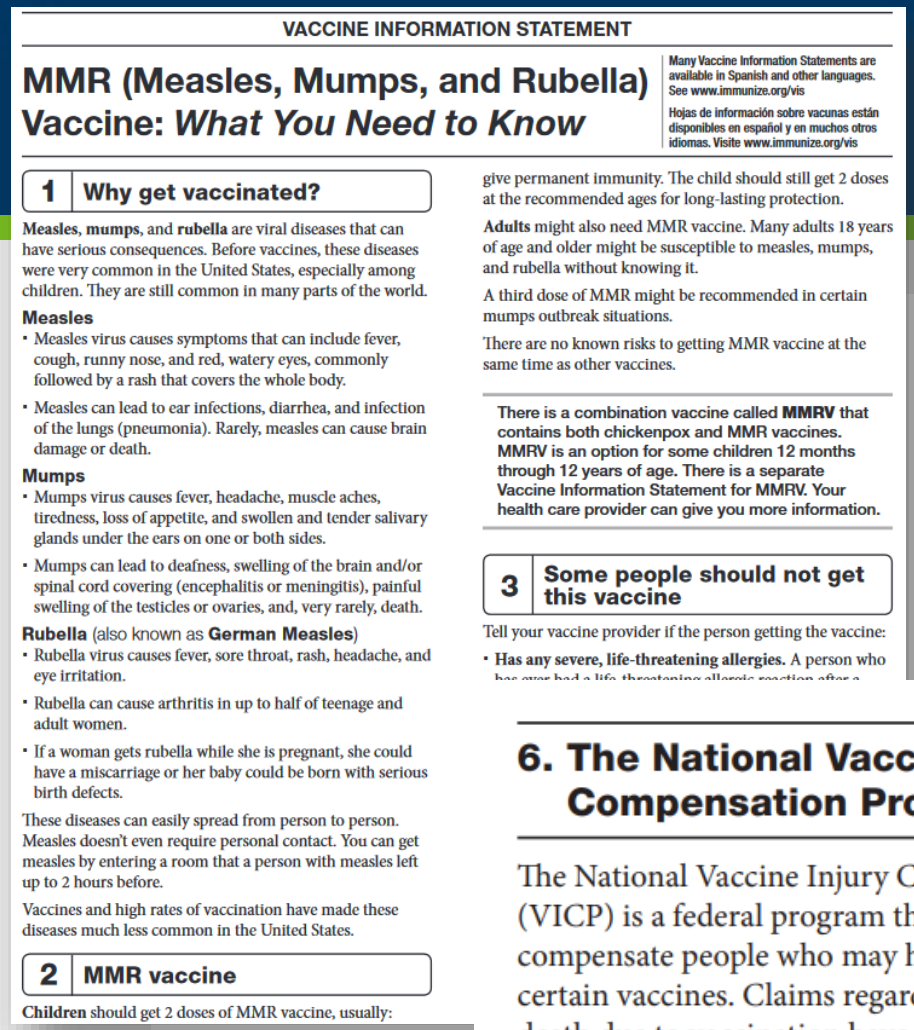
Temporal association does not prove causation.

Adverse Events Associated with Vaccination

Vaccine	Event	Risk
Any	Anaphylaxis	1 : 1,000,000
Influenza (Inactivated)	G-B Syndrome	1-10 : million
MMR	ITP	1 : 40,000
MMR MMRV	Febrile Seizures 12-47 mos old	1 : 2,500 1 : 1,250
RRV-TV (Rotashield)	Intussusception	1 : 11,000
RV1 and RV5 (Rotateq)	Intussusception	1: 100,000

Bohlke. Pediatrics 2003;112:815;
Mantadakis. J Pediatr 2010;156:623; Peter. Pediatrics 2002;110:e67;
Klein. Pediatrics 2010;126:e1ACIP Meeting. June 2013

Vaccine Information Statement (VIS)



VACCINE INFORMATION STATEMENT

MMR (Measles, Mumps, and Rubella) Vaccine: *What You Need to Know*

Many Vaccine Information Statements are available in Spanish and other languages. See www.immunize.org/vis

Hojas de información sobre vacunas están disponibles en español y en muchos otros idiomas. Visite www.immunize.org/vis

1 Why get vaccinated?

Measles, **mumps**, and **rubella** are viral diseases that can have serious consequences. Before vaccines, these diseases were very common in the United States, especially among children. They are still common in many parts of the world.

Measles

- Measles virus causes symptoms that can include fever, cough, runny nose, and red, watery eyes, commonly followed by a rash that covers the whole body.
- Measles can lead to ear infections, diarrhea, and infection of the lungs (pneumonia). Rarely, measles can cause brain damage or death.

Mumps

- Mumps virus causes fever, headache, muscle aches, tiredness, loss of appetite, and swollen and tender salivary glands under the ears on one or both sides.
- Mumps can lead to deafness, swelling of the brain and/or spinal cord covering (encephalitis or meningitis), painful swelling of the testicles or ovaries, and, very rarely, death.

Rubella (also known as **German Measles**)

- Rubella virus causes fever, sore throat, rash, headache, and eye irritation.
- Rubella can cause arthritis in up to half of teenage and adult women.
- If a woman gets rubella while she is pregnant, she could have a miscarriage or her baby could be born with serious birth defects.

These diseases can easily spread from person to person. Measles doesn't even require personal contact. You can get measles by entering a room that a person with measles left up to 2 hours before.

Vaccines and high rates of vaccination have made these diseases much less common in the United States.

2 MMR vaccine

Children should get 2 doses of MMR vaccine, usually:

give permanent immunity. The child should still get 2 doses at the recommended ages for long-lasting protection.

Adults might also need MMR vaccine. Many adults 18 years of age and older might be susceptible to measles, mumps, and rubella without knowing it.

A third dose of MMR might be recommended in certain mumps outbreak situations.

There are no known risks to getting MMR vaccine at the same time as other vaccines.

There is a combination vaccine called **MMRV** that contains both chickenpox and MMR vaccines. MMRV is an option for some children 12 months through 12 years of age. There is a separate Vaccine Information Statement for MMRV. Your health care provider can give you more information.

3 Some people should not get this vaccine

Tell your vaccine provider if the person getting the vaccine:

- **Has any severe, life-threatening allergies.** A person who

6. The National Vaccine Injury Compensation Program

The National Vaccine Injury Compensation Program (VICP) is a federal program that was created to compensate people who may have been injured by certain vaccines. Claims regarding alleged injury or death due to vaccination have a time limit for filing, which may be as short as two years. Visit the VICP website at www.hrsa.gov/vaccinecompensation or call **1-800-338-2382** to learn about the program and about filing a claim.

- Provides benefits and risks
- Give before vaccination
- Updated with new licensure indications or new information regarding adverse events
- Available in over 40 languages

http://www.immunize.org/vis/

National Vaccine Injury Compensation Program

- An alternative to the tort system for resolving vaccine injury petitions.
- No fault basis
- Vaccine Injury Table or
  - Proof vaccine caused problem
  - Proof vaccine aggravated existing health condition
- 1-800-338-2382
- https://www.hrsa.gov/vaccine-compensation/about

Vaccine Safety Post-Licensure Monitoring

Vaccine Adverse Events Reporting System (VAERS)

- **Passive** surveillance (CDC & FDA)
- Rapid signal detection
- Cannot draw conclusions about reports

Vaccine Safety Datalink (VSD)

- **Active** surveillance (CDC)
- Multiple managed care organizations
- Helps determine if side effects identified using VAERS are actually related to vaccination.
- 2.5% of the US population (24 million people)

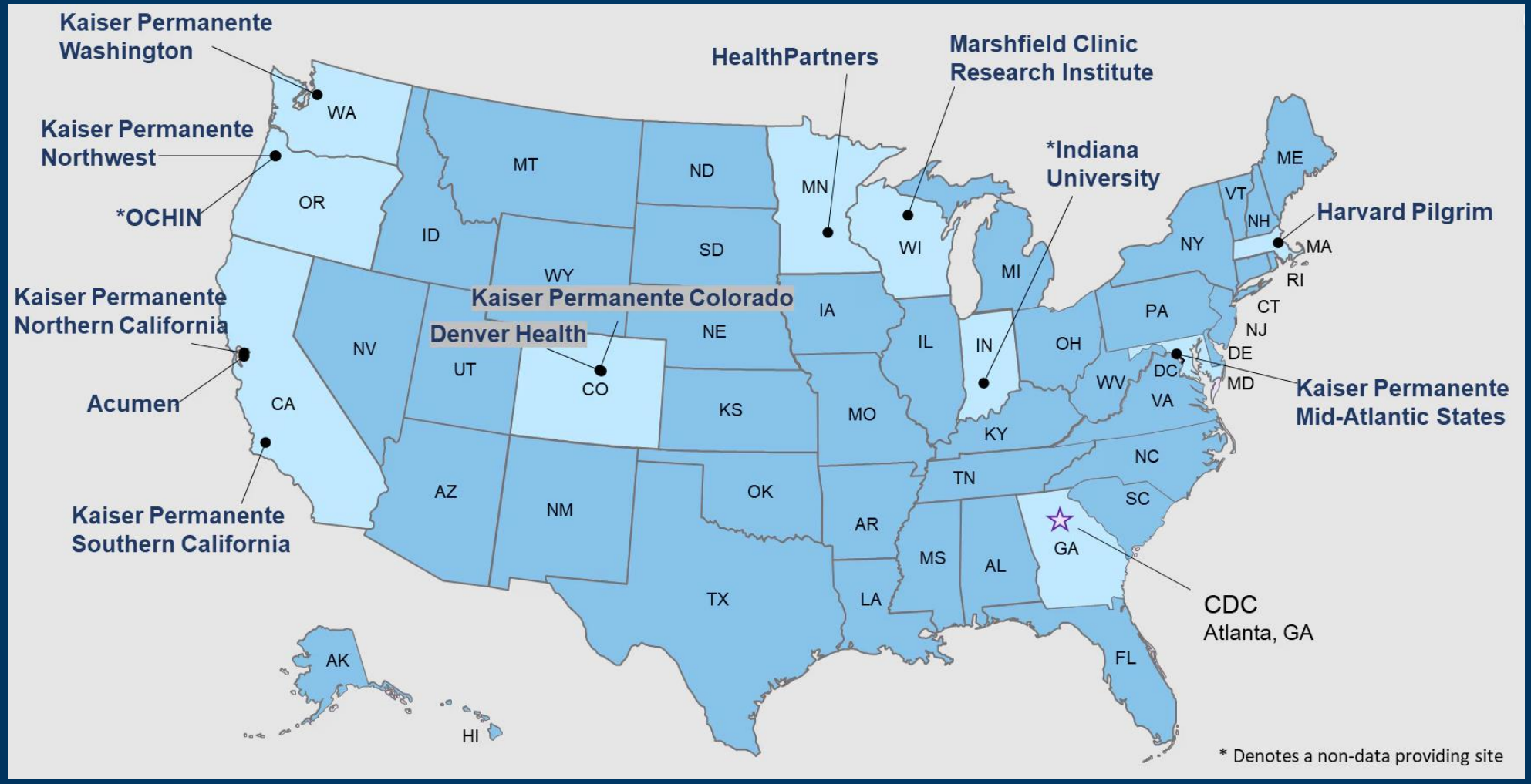
Post-Licensure Rapid Immunization Safety Monitoring (PRISM)

- **Active** surveillance (FDA) & city/state immunization information systems
- 190 million people
- ID and analyze rare events

Clinical Immunization Safety Assessment System (CISA)

- CDC & academic research centers
- Individual clinical assessment and clinical research
- Evaluate unusual or compelling events
- Identify prevention strategies for adverse events
- 7 research centers

Vaccine Safety Data (VSD) Link



Clinical Immunization Safety Assessment (CISA) Project

- Collaboration between the CDC and multiple medical research centers
- Vaccine safety experts serve as consultants for:
  - Individual case reviews to assist with immunization decision-making
  - Clinical research studies about vaccine safety and identification of risk factors (particularly in special populations)
  - Development of strategies to assess individuals who may be at increased risk for adverse events following immunization (AEFI)

https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html

Requesting a CISA consultation

To request a CISA Clinical Consultation:

If you are a US healthcare provider with a vaccine safety question about a specific patient residing in the US, you can contact CISA at CISAeval@cdc.gov to request a case evaluation. This service is provided free of charge. View here for more information.

https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/evaluation.html

V-Safe

https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/v-safe/participate.html

- Active Surveillance (CDC)
- Smart phone-based safety monitoring system
- COVID-19 & RSV
- Voluntary
- Sends regular reminders and surveys
- Quickly validate safety data and potential safety issues
- Follow-up with participants

PRISM & BEST

Post Licensure Rapid Immunization Safety Monitoring (PRISM)

- Active surveillance system (FDA) founded in 2009
- Data from health insurance claims and immunization registries
- Focus on possible safety issues for licensed vaccines
- Access to data on over 190 million people

Biologics Effectiveness and Safety (BEST) System

- Active surveillance system (FDA) founded in 2017
- Data from large-scale claims data and electronic health records (EHR)
- Used to detect or evaluate adverse events related to vaccine

https://www.hhs.gov/immunization/basics/safety/index.html

Example: Surveillance works

- VAERS: Increased signal for febrile seizures following MMRV among infants 12-24 months old
- VSD: Confirmed association with MMRV and febrile seizures
  - Among 12-23 month old children, 5-12 days after MMRV
  - One additional febrile seizure occurred per 2,300-2,600 first MMRV dose
- ACIP changed recommendation for first dose MMR and varicella vaccination at 12-15 months.
  - Recommended MMR and varicella be given separately for first dose
  - Still recommend MMRV at age 4-6 years

What committee licenses vaccine?

a. The American Association of Vaccine Safety (AAVS)

b. The Scientific Study Investigators of America (SSIA)

c. The Food and Drug Administration (FDA)

d. The Center for Vaccine Safety (CVS)

What committee makes recommendations for vaccines?

a) The Committee for Vaccine Recommendations

b) The Advisory Committee for Immunization Practices

c) Vaccine Recommendation Committee

d) International Vaccine Organization

An early version of what vaccine was discontinued because some infants experienced intestinal blockage?

a) MMR vaccine

b) DTaP vaccine

c) Shingles vaccine

d) Rotavirus vaccine

Vaccines have been shown to cause what disease?

a) Autism

b) Diabetes

c) Multiple Sclerosis

d) None of the above

What is the vaccinator's role in vaccine safety monitoring?

a) Provide risk/benefit information (Vaccine Information Statements)

b) Screen for contraindications and precautions

c) Re-evaluate vaccine administration skills regularly

d) Report adverse events

e) Provide support to patient/parent

f) All of the above

References

- CDC: Vaccine Safety: https://www.cdc.gov/patientsafety/features/vaccine-safety.html
- CDC: How Vaccines are Developed and Approved for Use://www.cdc.gov/vaccines/basics/test-approve.html#research-discovery
- CDC: Historical Vaccine Safety Concerns: https://www.cdc.gov/vaccinesafety/concerns/concerns-history.html
- Attitudes and Beliefs around the Value of Vaccination in the United States - PMC (nih.gov)
- Understanding Vaccine Safety and the Roles of the FDA and the CDC | New England Journal of Medicine (nejm.org)
- Building the Supply Chain for COVID-19 Vaccinehttps://www.globalhealthdelivery.org/publications/building-supply-chain-covid-19-vacciness | The Global Health Delivery Project
- The Journey of Your Child's Vaccine (cdc.gov)
- https://www.immunize.org/wp-content/uploads/catg.d/p2073.pdf

Thank You!

Tabitha K. Hanson

Tabitha.hanson@state.mn.us

Cutter Incident-1955

- In 1955, some batches of polio vaccine given to the public contained live polio virus, even though they had passed required safety testing.
- Over 250 cases of polio were attributed to vaccines produced by one company: Cutter Laboratories.
- This case, which came to be known as the Cutter Incident, resulted in many cases of paralysis.
- The vaccine was recalled as soon as cases of polio were detected.

Problems with which vaccine led to the “Cutter incident”?

a) Polio vaccine

b) Haemophilus influenzae type B (Hib) vaccine

c) Rotavirus vaccine

d) Mpox vaccine