IMMUNIZE. PREVENT WHAT'S PREVENTABLE

From the Lab to Your Doctor's Office:

Vaccine Development & Safety Measures

THE IMMUNIZATION PARTNERSHIP

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The Immunization Partnership

Vision

A community protected from vaccine preventable diseases

Mission

To eradicate vaccine-preventable diseases by educating the community, advocating for evidence-based public policy, and supporting immunization best practices

ACKNOWLEDGEMENTS

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- Requirements for successful completion of learning activity
  - Listen to entire presentation
  - Submit online pre-test
  - Submit online evaluation
- Certificate of completion sent via email
- Contact Katy Gore at kgore@immunizeUSA.org with questions

Disclosure and Disclaimer

- The speakers and planning committee have disclosed no conflicts of interest.
- This presentation is for educational use only and does not constitute medical or legal advice.

Agenda

1. Vaccine Development (narrated by Ashley Beale)

2. Vaccine Safety Monitoring (narrated by Rachel Walker)

3. Vaccine Adverse Event Reporting System (VAERS) (narrated by Rachel Walker)

4. Vaccine Injury Compensation Program (narrated by Ashley Beale)

5. Development of the COVID-19 Vaccines (narrated by Rachel Walker)

6. Helpful Resources (narrated by Ashley Beale)

Are vaccines safe?

Vaccine Development

STAGES OF VACCINE DEVELOPMENT

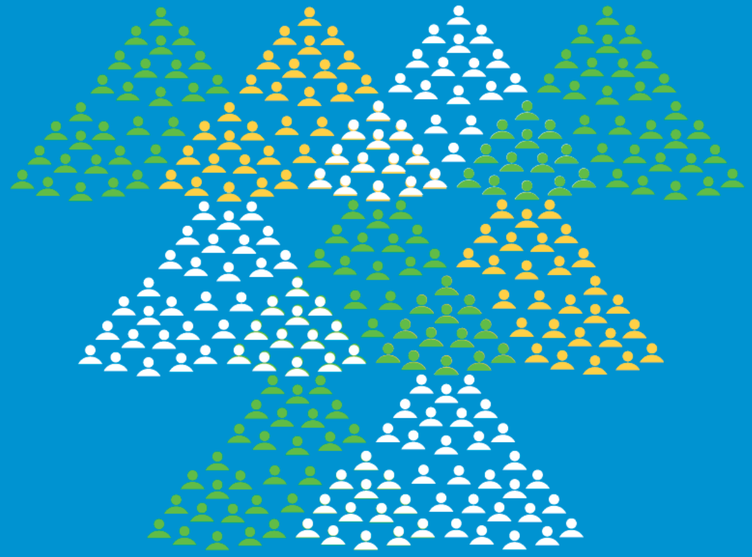
Exploratory Stage

Pre-Clinical Stage

Phase 1 Clinical Trials

Phase 2 Clinical Trials

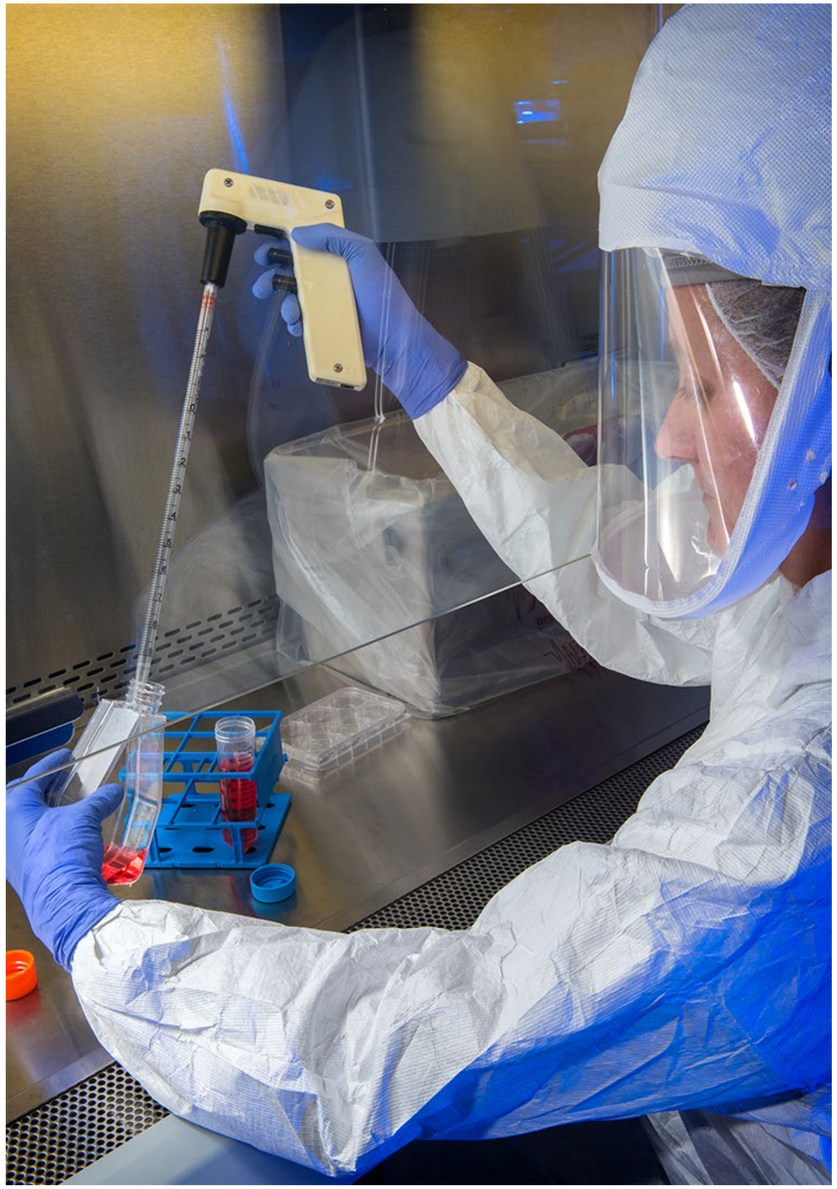
Phase 3 Clinical Trials



Review & Licensure

Exploratory Stage

- Basic **laboratory science**
- Researchers try to **identify antigens** that may help to prevent or treat a disease (either a virus or bacteria)
- **Test their ideas** to find a vaccine candidate
- **2 – 4 years** (but may take longer)



Pre-Clinical Stage

- Before a vaccine can be tested in humans, safety and efficacy **tests are done using**:
  - **Tissue cultures**
  - **Cell cultures**
  - **Animals** (mice, monkeys)

- Helps researchers **understand the immune response** created by the vaccine

- **1 - 2 years** (but may take longer)

Placebo-Controlled Vaccine Trials

(May be present in Phase 1 Clinical Trials, Phase 2 Clinical Trials or Phase 3 Clinical Trials)

- Clinical trials for vaccines are configured to include both a **control group** and an **experimental group** – this is essential for comparison.

- **Control group receives a placebo** (often a vaccine that is already approved or saline solution) and the **experimental group receives the vaccine being tested**.

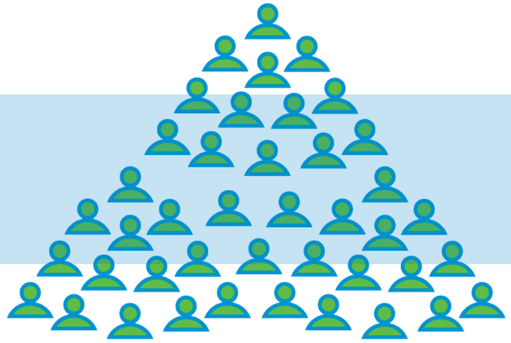
- The **control and experimental groups are made up of similar participants** (age, race, health status, sex) so researchers can compare and determine the true effects of the vaccine.

- Studies are **randomized** and **double-blinded** (meaning neither researchers of participants know which group they are in) **to avoid bias.**

Phase 1 Clinical Trials

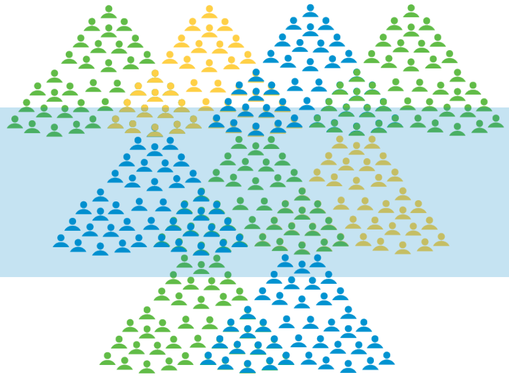
- Begin **testing** the vaccine in **healthy adults**
- Studies start small with **20 – 100 participants**
- Focused on answering 2 questions:
  1. Is the vaccine **safe**?
  2. Is the vaccine **effective**? (does it generate the expected immune response)
- **1 – 2 years**

Volunteer, Jennifer Haller, receives her experimental Moderna COVID-19 vaccine during Phase 1 clinical trials. (Ted S. Warren / Associated Press)



Phase 2 Clinical Trials

- Phase 2 includes **more study participants (several 100)** – those with **different health statuses**, **demographic** backgrounds, and **at risk for acquiring disease** are included.
- Participants may receive the vaccine (of **varying doses**) or a **placebo** as part of **randomized-controlled studies**.
- Focused on vaccine s**afety among diverse populations**, **short-term side effects**, and understanding the vaccine's **immune response**, including **dosing**.
- **2+ years**



Phase 3 Clinical Trials

- Phase 3 **includes hundreds of thousands of people** – **experimental group** (receive the vaccine) and **control** group (receive a placebo).
- The study is **double-blinded** (for researchers AND participants)
- Goal is to **assess vaccine safety in a large group** of people and identify common side effects and any **rare side effects**.
- **Vaccine efficacy** is tested – does the vaccine **prevent disease**, does it **prevent infection**, does it lead to **production of antibodies**?
- **Can last several years**

Review & Licensure

- After successful Phase 3 trials, a vaccine developer submits a **Biologics License Application** to the FDA for review
- FDA reviews the data from a vaccine's clinical trials to determine whether the vaccine has been shown to be both **safe** and **effective.**
- **Manufacturing processes** are also reviewed to **ensure vaccine quality and consistency**
- **FDA will approve** (license) the vaccine for use in the United States if the **benefits of the vaccine outweigh any risks.**

Safety Monitoring

Post-Licensure Safety

Safety monitoring doesn't stop once a vaccine is approved. Vaccine safety is monitored at multiple levels after approval:

1. **Pharmaceutical companies** may continue clinical trials (what is known as **Phase IV**) to continue tracking safety.

2. The **CDC** will have large health departments monitor **recipients of the vaccine** and report back.

3. The **CDC monitors diseases** reported by every health department, so if there is a **large increase of a disease**, they will **investigate** to ensure it is not related to the vaccine.

Post-Licensure Safety, cont'd

4. **Vaccine Safety Datalink (VSD)** - started in 1990. Partnership with the **CDC** and **8 large Healthcare Organizations** mostly in the West Coast. Patient size of over **6 million** to compare who did and did not receive the vaccine and **answer safety questions.**

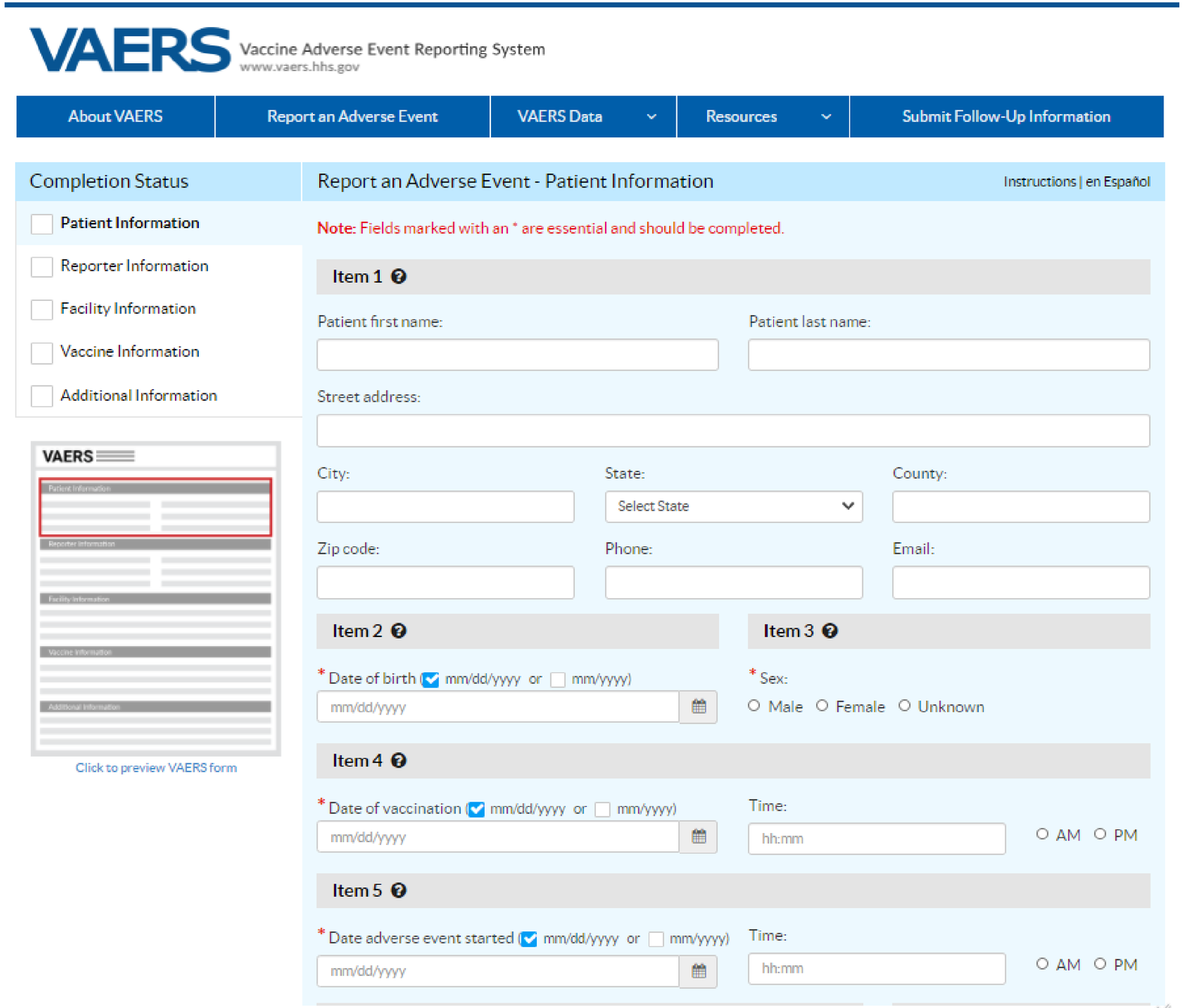
5. **Vaccine Adverse Event Reporting System (VAERS)** - national reporting system maintained by the CDC and FDA. **Anyone** (doctor, nurse, patient) **can submit a report** related to a vaccine side effect. Not perfect but may be a first line of detection of vaccine issues that require further investigation.

Vaccine Adverse Event Reporting System (VAERS)

What is VAERS?

- National reporting system used by the CDC and FDA to collect **adverse event reports** that occurred **after vaccination.**

- **Anyone can submit a report** – healthcare providers, health departments, and individuals.



What VAERS can and can't do

Reports made to VAERS cannot prove causality.

Strengths of VAERS	Weaknesses of VAERS
VAERS **collects data** from **across the United States** and territories	**Determining causality is not possible** – VAERS cannot determine if a vaccine caused the adverse event. Similarly, VAERS data cannot be used to compute rates of adverse events.
Reporting to VAERS is inclusive – **anyone can submit a report**	Some VAERS reports may **lack details** or contain **inaccurate information**
The VAERS report form **collects information** about the **vaccine**, the **person who was vaccinated**, and the **adverse event**	**Reporting of serious adverse events** are much **more likely** than mild events – skews data.
Data from VAERS is **publicly available**	**Media attention** or other forms of awareness (social media, stories) may cause a **flurry of reports to VAERS**

Misuse vs. Success Stories

- Since being established in 1988, multiple **anti-vaccine organizations** have pointed to **VAERS as evidence of significant vaccine-related adverse events**
- Computing rates and **statistics without comparison** groups or presenting VAERS **results as confirmed facts** is **inaccurate and misleading**
- **However, VAERS remains a valuable tool and first alert for researchers.**
  - Discovery of an **intestinal problem** after the first **rotavirus** vaccine was released in 1998.

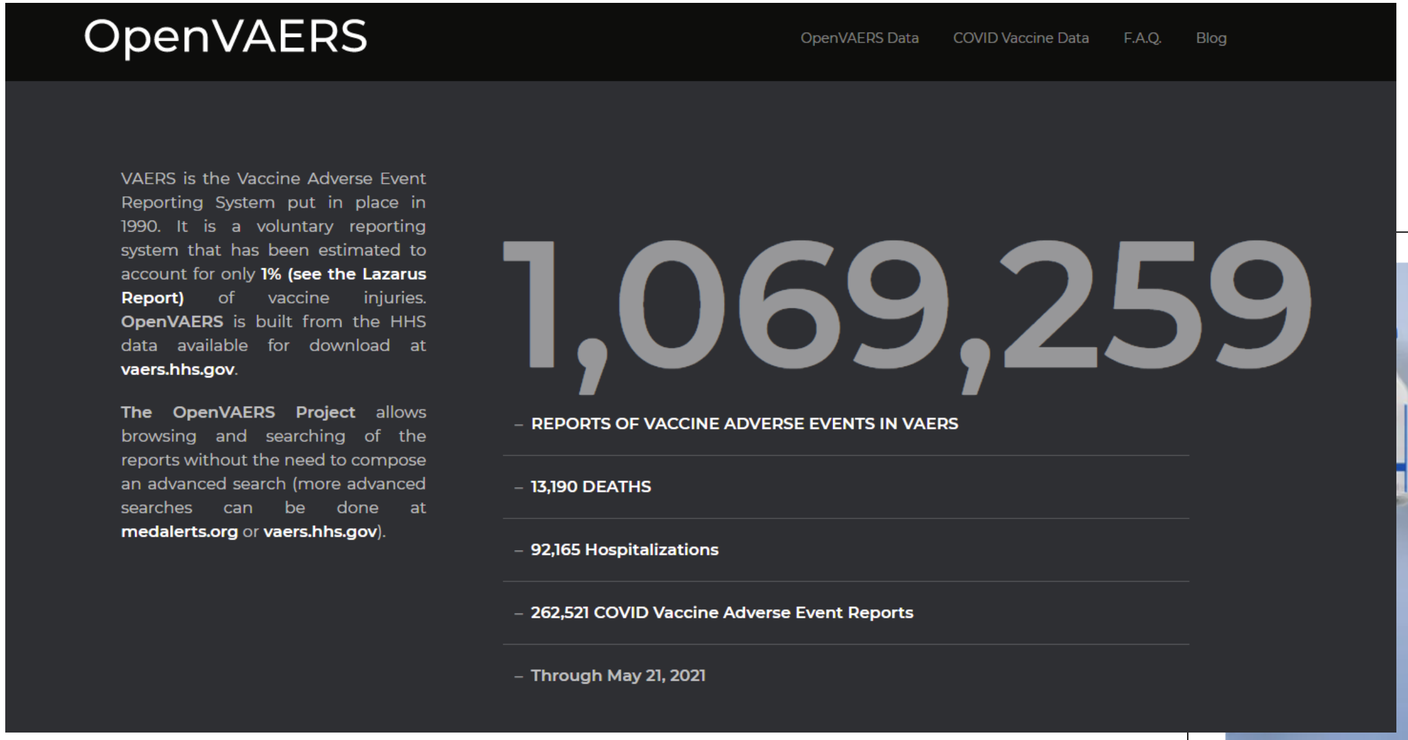


Image from https://www.openvaers.com/

VAERS data **presented without a disclaimer** about the system's limitations can **alarm the public** and **reduce vaccine confidence**, as seen recently with the COVID-19 vaccine.

NEWS

6000% Increase in Reported Vaccine Deaths 1st Quarter 2021 Compared to 1st Quarter 2020

April 1, 2021 4791 views 0

As can be expected when new experimental "vaccines" that are not approved by the FDA are given emergency use authorization to fight a "pandemic" that is now over a year old, reported deaths following the injections of these shots have now skyrocketed in the U.S. population by over 6000% here at the end of the first quarter of 2021, as compared to recorded deaths following FDA-approved vaccines at the end of the first quarter of 2020.

Image from https://truthunmuted.org/6000-increase-in-reported-vaccine-deaths-1st-quarter-2021/

National Vaccine Injury Compensation Program

History of the Vaccine Injury Compensation Program (VCIP)

- Established by Congress through the **National Childhood Vaccine Injury Act of 1986.**

- Sought to find a solution after a **rise in vaccine injury and illness <u>claims</u>** against vaccine manufactures increased and created serious **financial risk to vaccine development** that threatened US vaccine supply.

- Result of program – individuals **file claim with the US government** (Vaccine Injury Compensation Program) <u>instead</u> of individual vaccine manufacturers.

How Does the VICP Work?

Congress created to address vaccine-claims “quickly, easily, and with certainty and generosity.”[11]

- Any individual who received a covered vaccine and believes they were injured as a result may file a petition (parents/guardians may file on behalf of children, disabled adults, and those who are deceased)

- Three government entities are involved in the VCIP
  1. **The Department of Health and Human Services (HHS)** administers the VICP
  2. The **Department of Justice (DOJ)** represents HHS in Court
  3. The **U.S. Court of Federal Claims (the Court)** makes the final decision regarding whether a petitioner should be compensated.

Claims Process in Detail

Claim is filed

Individual files claim with the **U.S. Court of Federal Claims**.

HHS reviews petition & makes preliminary recommendation

Medical staff with HHS review the petition to **determine if it meets medical criteria for compensation** and makes preliminary recommendation.

DOJ develops report and submits to the Court

Department of Justice develops report that includes both the **medical recommendation** and **legal analysis**. Report is submitted to the Court.

Report presented to Court for consideration of compensation

Report presented to a **court-appointed special master** to **decide whether petitioner** (individual) **should be compensated**. A hearing is held in which both parties may present evidence. If compensation is awarded, special master determines the amount and type of compensation.

Court may order compensation from HHS / petitioner may appeal decision

If required, the **Court will order HHS to award compensation**. Petitioners may still **appeal the decision and file new claim in civil court**.

Compensation Numbers and what they mean

- A **2015** analysis found that roughly a **quarter of petitions were compensated**.
- Recent **increase** in portion of **claims being compensated**.
  *2015-2019 saw **77% of claims compensated**.*
- **Vaccine Injury Table** – helps **standardize compensation process** and lists illnesses, disabilities and injuries that are presumed to be caused by a vaccine, if **no other cause is found**. May lead to ***presumption of causation*** – all the VCIP requires for compensation.
- **Being awarded compensation does not mean the vaccine caused the injury** – HHS estimates that 70% of compensation cases are the result of a settlement between the two parties. The Program **averages about 500 petitions a year**.

Development of the COVID-19 Vaccines

- EUA authorized: Dec. 11, 2020
- 2 doses

- EUA authorized: Dec. 18, 2020
- 2 doses

- EUA authorized: Feb. 11, 2021
- 1 dose

EUA APPROVAL PROCESS

(Emergency Use Authorization)

1 DETERMINATION OF EMERGENCY

2 DECLARATION OF EMERGENCY

3 FDA REVIEWS EUA REQUEST

4 ISSUANCE OR DENIAL OF EUA REQUEST

5 TERMINATION OF DECLARATION & EUA

mRNA Technology & mRNA Vaccines

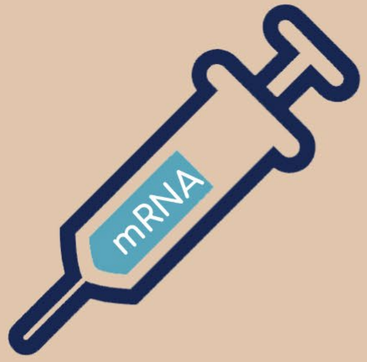
- Utilize messenger RNA (mRNA) technology

- In development as a **vaccine platform** since the **early 1990s**, with decades of established research. As recent as **2015**, mRNA technology used in **early clinical trials for a Zika vaccine**.

Benefits associated with mRNA technology:

- It does **not generate infectious particles**.
- It requires a **shorter manufacturing time** compared to other vaccines.
- It has the potential for **targeting multiple diseases** with one vaccine.

How mRNA Technology Works

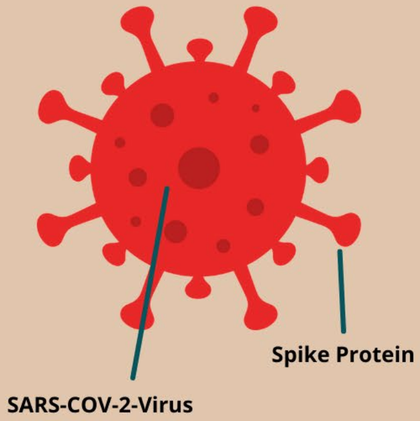


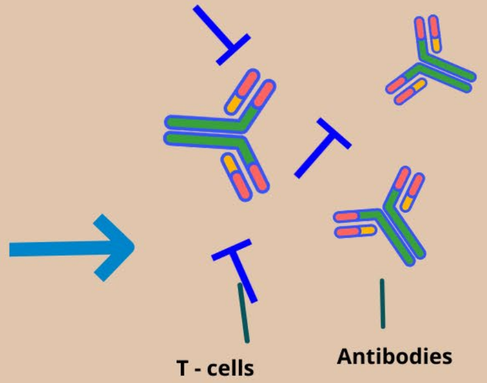
VACCINE

messenger RNA (mRNA) from virus's genetic code is injected into patient.

VIRUS

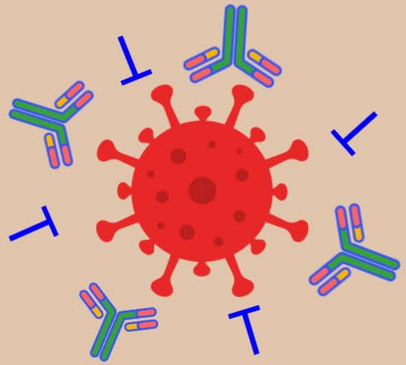
The mRNA instructs human cells to create part of the SARS-CoV-2 virus called the "spike" protein. The cell gets rid of the protein once it breaks down mRNA instructions.





PROTECT

Our immune system reacts to the protein (because it doesn't belong) by producing antibodies and activating T-cells to destroy the spike proteins.



PRODUCE

The T-cells and antibodies will remember how to fight the virus, and protect you from getting sick if you are exposed in the future.

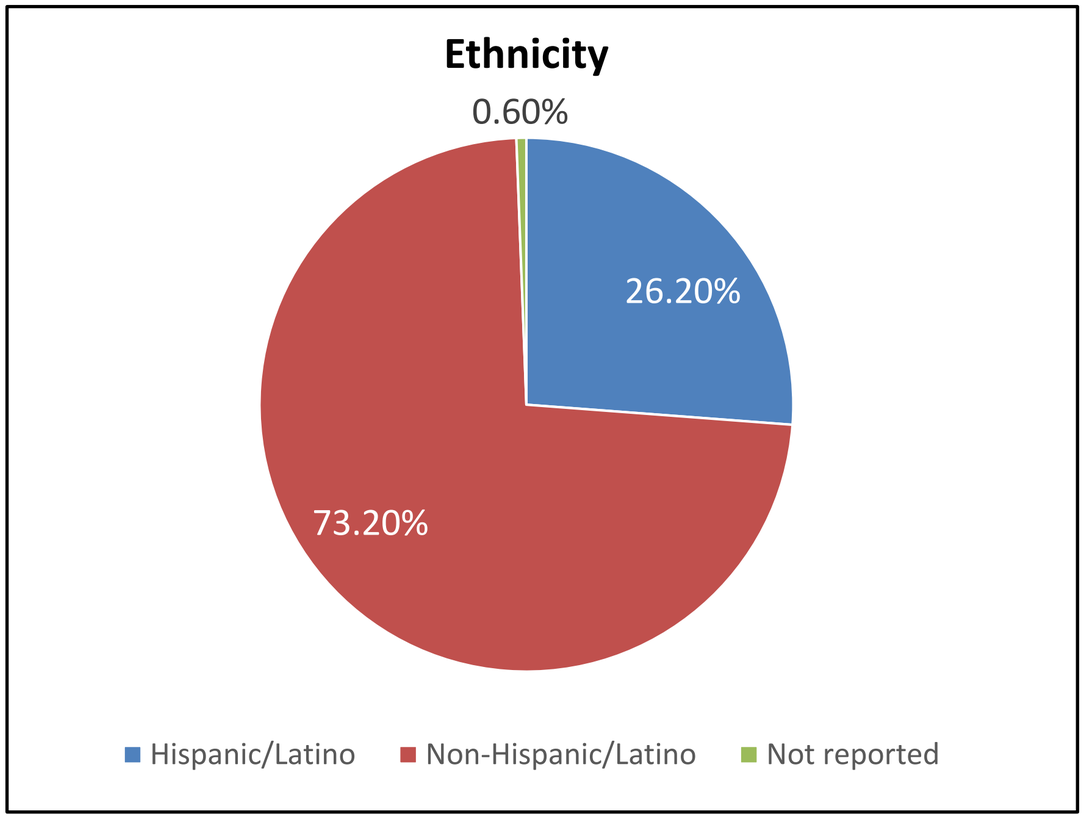
Image adapted from: https://www.michigan.gov/documents/coronavirus/2020_MDHHS_COVIDVaccine_Infograph_3.0_710373_7.pdf

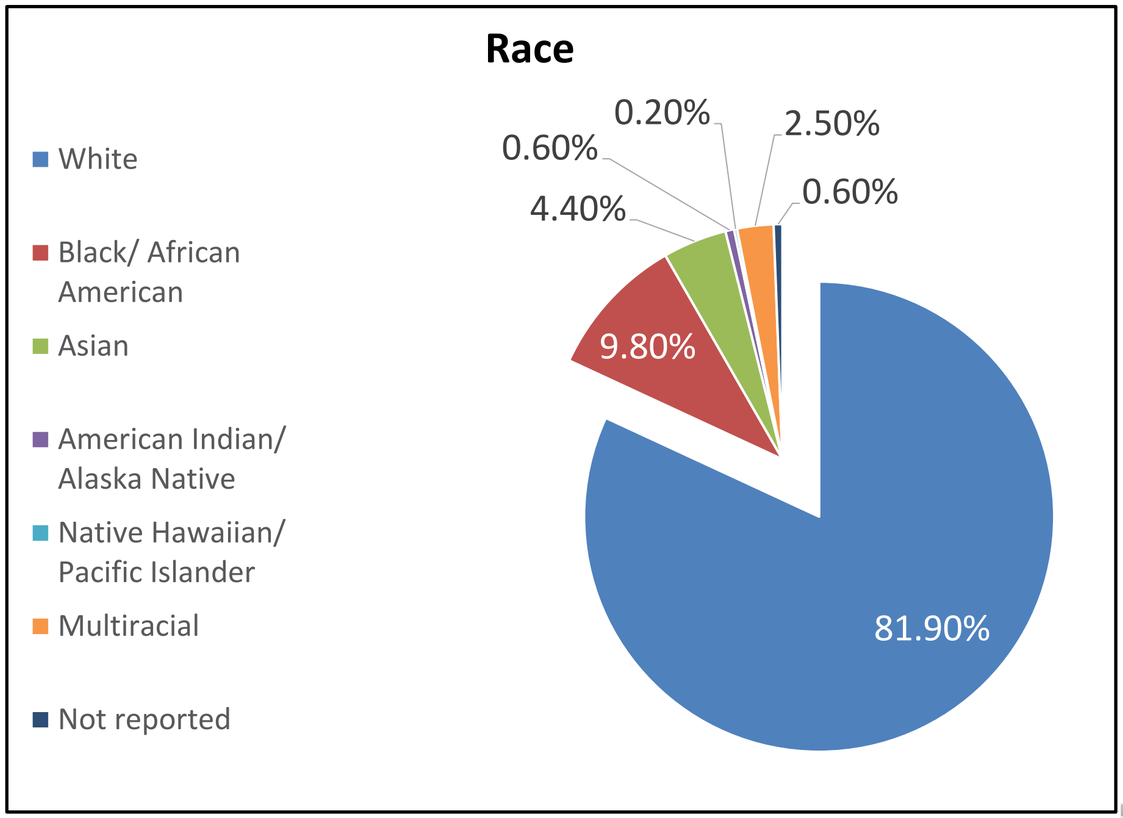
Pfizer/BioNTech Clinical Trial Demographics

Participants: 40,277	Sex: Male: 50.6% Female: 49.4% Median age at vaccination: 51

Final efficacy analysis: Nov. 14, 2020

95% effective



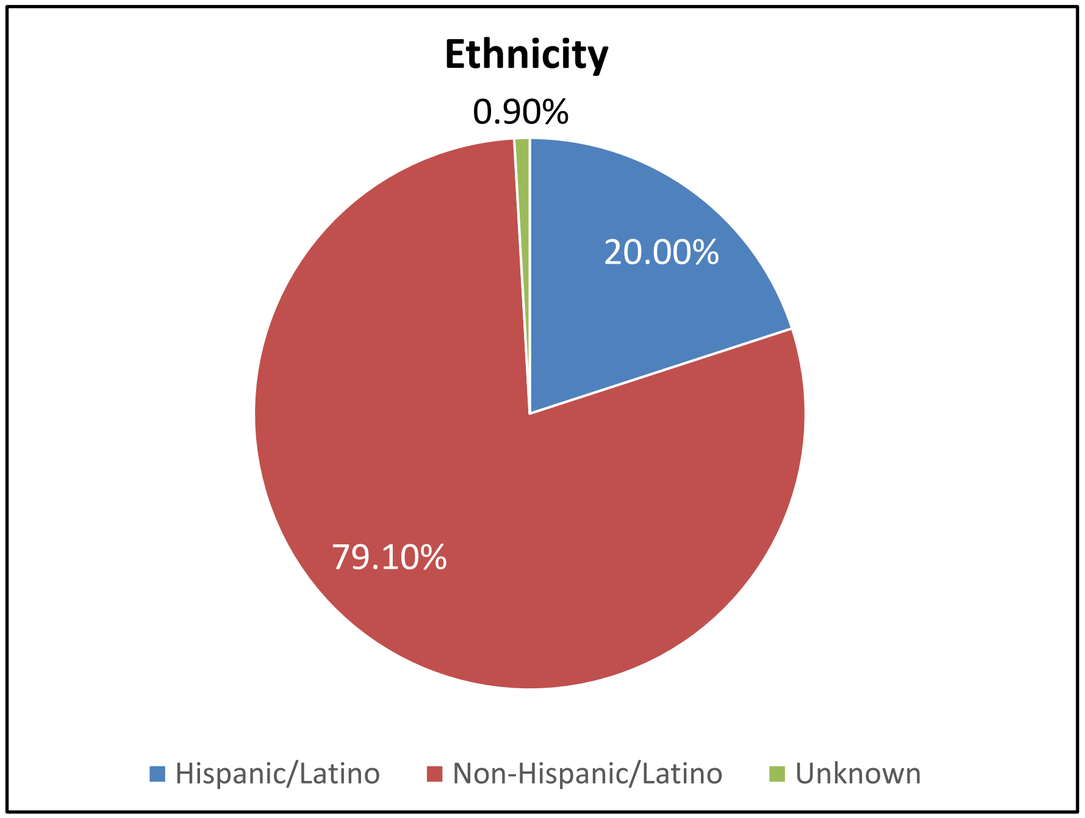


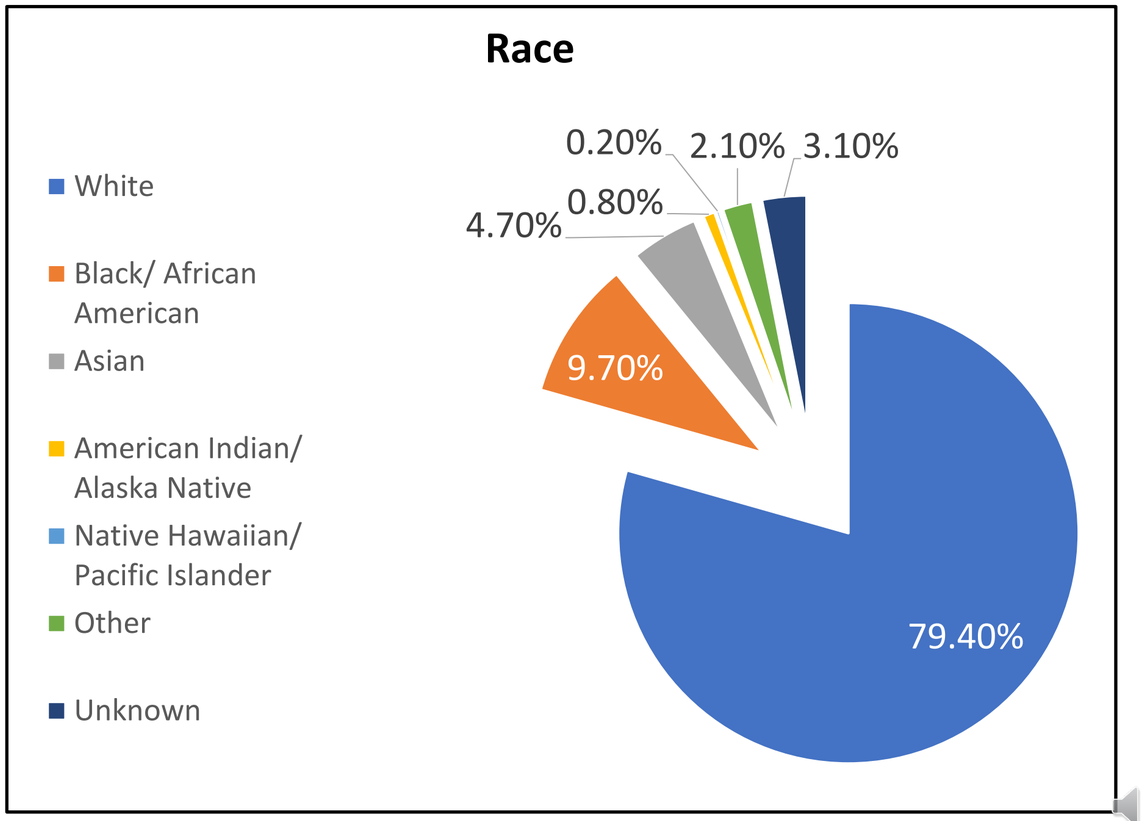
Moderna Clinical Trial Demographics

Participants: 27,817	Sex: Male: 52.6% Female: 47.4% Median age at vaccination: 53

Final efficacy analysis: Nov. 25, 2020

94.1% effective

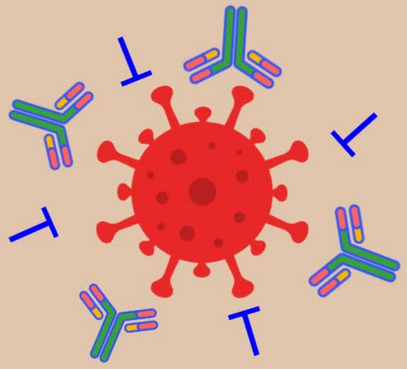




How AdVac® Technology Works

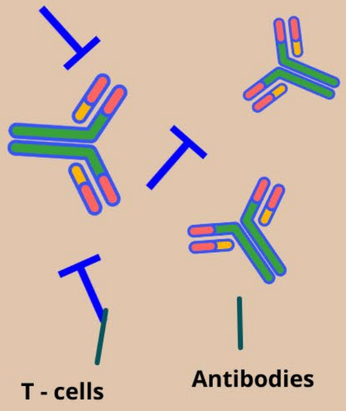
VACCINE

An adenovirus vector (a carrier) from an antigen's genetic code, used to mimic the virus, is injected into the patient.



PRODUCE

The T-cells and antibodies will remember how to fight the virus, and protect you from getting sick if you are exposed in the future.



PROTECT

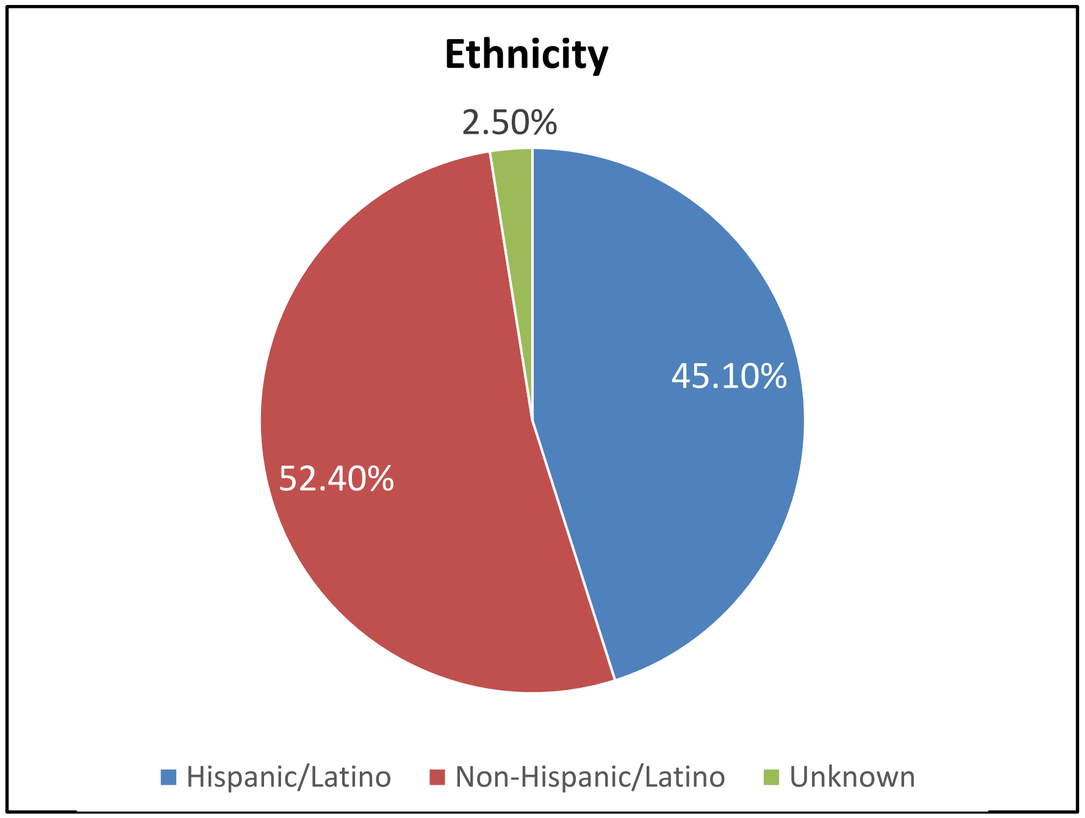
Our immune system reacts to the antigen (because it doesn't belong) by producing antibodies and activating T-cells.

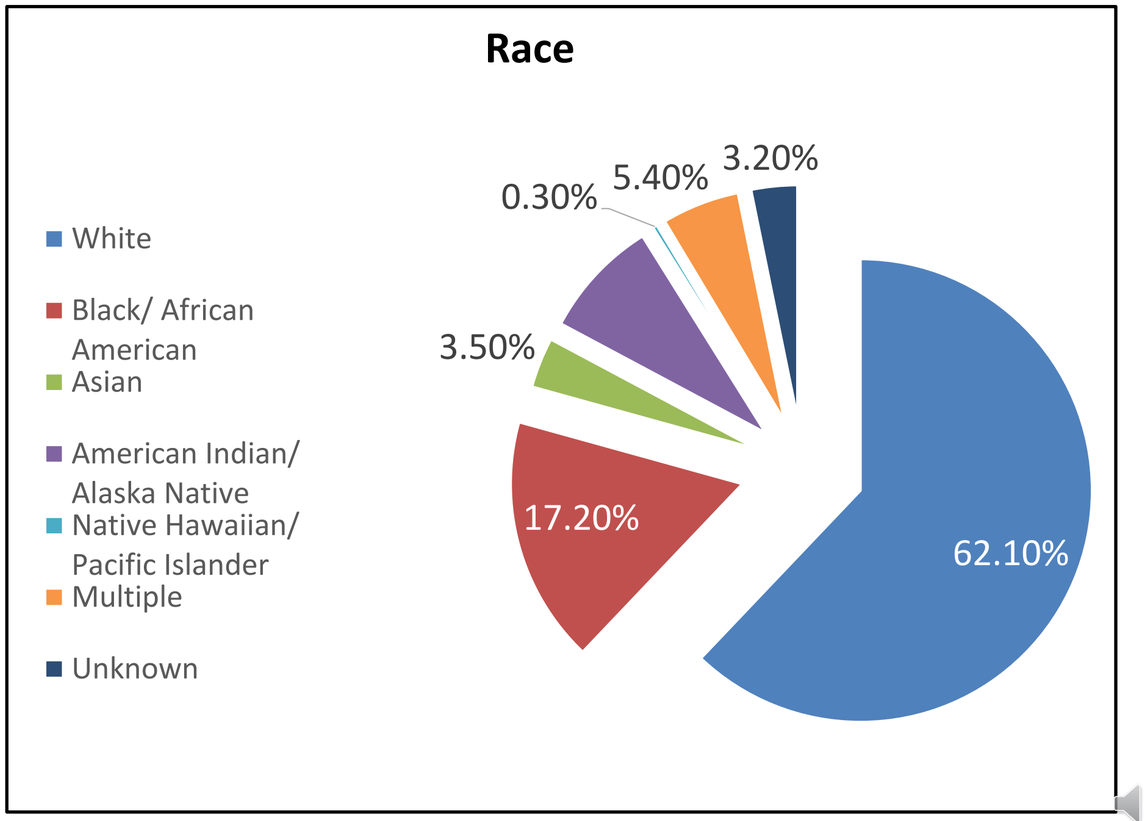
J&J Clinical Trial Demographics

Participants: 39,321	Sex: Male: 55.5% Female: 44.5% Undifferentiated, <0.1% Unknown, <0.1% Median age at vaccination: 53

Final efficacy analysis: Jan. 22, 2021

85% effective





J&J Pause & Ongoing Safety Monitoring

The CDC and FDA recommended a temporary pause of the J&J vaccine on April 13th following several reports of a **rare blood clot condition**, thrombosis with thrombocytopenia syndrome (TTS), 1-2 weeks following vaccination.

- As of July 12, 2021 , **38 cases of TTS (submitted to VAERS)** have occurred among the more than 12.8 million doses of the J&J in the United States. Majority of cases occurred among women between 18 – 59 years.
- Pause was lifted on April 23rd after review of all available data showed that the J&J/Janssen COVID-19 Vaccine's known and **potential benefits outweigh its known and potential risks.**
- Women 50 and younger should be aware of this rare but adverse event risk.

Factors of Vaccine Development Speed

1. **Global public health threat - #1 priority**
   - **Unprecedented** number of **vaccine candidates** / public and private **funding**
   - Included **"Operation Warp Speed"**

2. **Decades of research informed work for COVID-19 vaccines:**
   - Other coronaviruses (**SARS** and **MERS**)
   - Previous vaccine research using **mRNA technology** for other viruses such as **Zika**, **rabies**, and **influenza**

Helpful Resources

CDC, “Vaccine Testing and the Approval Process”: https://www.cdc.gov/vaccines/basics/test-approve.html

CDC, “Vaccine Safety Monitoring”: https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/index.html

Children’s Hospital of Philadelphia, “Making Vaccines: Process of Vaccine Development”: https://www.chop.edu/centers-programs/vaccine-education-center/making-vaccines/process-vaccine-development

Children’s Hospital of Philadelphia, “Vaccine Safety References”: https://www.chop.edu/centers-programs/vaccine-education-center/vaccine-safety-references

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24. https://www.fda.gov/news-events/press-announcements/joint-cdc-and-fda-statement-johnson-johnson-covid-19-vaccine
25. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/JJUpdate.html
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27. https://www.houstonmethodist.org/blog/articles/2020/dec/how-was-the-covid-19-vaccine-developed-so-fast/
28. https://news.uchicago.edu/story/how-were-researchers-able-develop-covid-19-vaccines-so-quickly

World Health Organization

Protected Together

#VACCINESWORK

Thank You!

THE IMMUNIZATION PARTNERSHIP

If you have any questions about this presentation please email Ashley Beale at abeale@immunizeUSA.org or Rachel Walker at rwalker@immunizeUSA.org