U.S. Centers for Disease Control and Prevention COVID-19 Vaccine Safety Monitoring from December 2020 – May 2023

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National Academies of Science Engineering and Medicine

Outline

- Purpose of NASEM Review of Centers for Disease Control and Prevention (CDC)/Immunization Safety Office (ISO) COVID-19 Vaccine Safety
- Background on CDC and public health responses
- COVID-19 Vaccine Safety Monitoring planning and implementation
- Contributions to vaccine policy
- Vaccine safety risk communication
- Immunization Safety Office: safety monitoring Post-COVID-19 response
- Revisit the purpose of NASEM Review of Centers for Disease Control and Prevention (CDC)/Immunization Safety Office (ISO) COVID-19 Vaccine Safety
- Conclusion

Charge to the NASEM Committee: Review of purpose

1) Evaluate vaccine safety systems, analytic methods, and processes used by CDC's ISO to monitor and assess COVID-19 vaccine safety during the U.S. COVID-19 vaccination program: beginning with the start of the vaccination program (December 2020) through the end of the COVID-19 public health emergency declaration (May 2023)
   - Including an evaluation of CDC communications on its safety monitoring systems, findings of COVID-19 vaccine safety monitoring, risk communication around vaccine safety and vaccination, and clinical guidance recommendations to healthcare professionals, public health officials, and the public.
2) Provide recommendations for sustaining, maintaining, and strengthening ISO's current monitoring systems going forward, taking into account that CDC's vaccine safety monitoring is part of a broader national monitoring system.

CDC & Public Health Responses

Levels of response at CDC

Agency-wide response

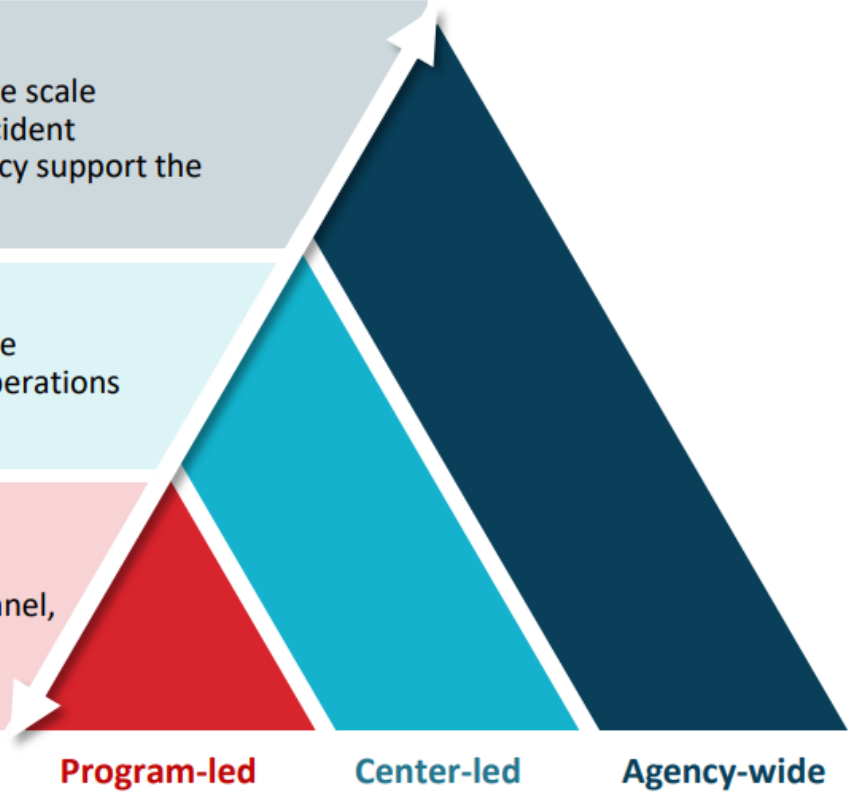
This is the highest GRF level of response and reserved for large scale responses. It requires significant augmentation of the CDC Incident Management System (IMS), where staff from across the agency support the activation.

Center-led response

Centers leverage an IMS structure, which may include multiple functional teams. CIO staff may be redirected from normal operations to support response activities.

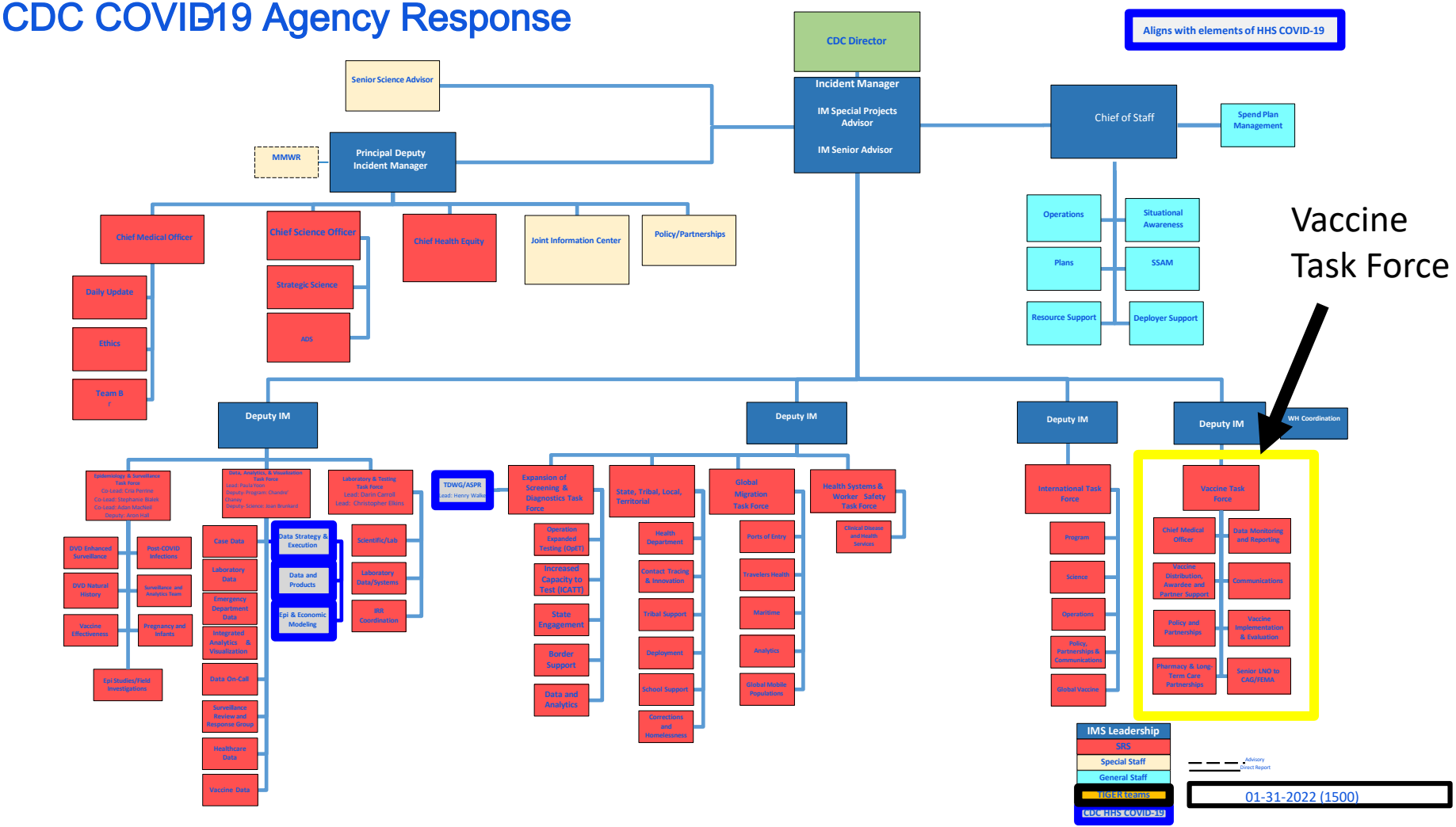
Program-led response

Many responses begin within a program as a result of normal operations and routine surveillance. As resources (i.e., personnel, facilities, and funding) and requirements expand, the response is moved to the center level.



https://www.cdc.gov/about/advisory-committee-director/pdf/2023.05.11_acd-slides.pdf

CDC COVID-19 Agency Response



CDC COVID-19 Vaccine Safety Monitoring: New and existing systems and activities

CDC COVID-19 Response Vaccine Task Force (VTF)

- New systems and activities:
  - V-safe
  - COVID-19 Vaccine Pregnancy Registry
  - Follow-up of Long-term Effects of Myocarditis
  - Long-term care facility monitoring
    - National Healthcare Safety Network (NHSN)
    - Genesis Healthcare
- Development of ACIP* COVID-19 Vaccine Safety Technical Working Group (VaST)

*Advisory Committee on Immunization Practices

Immunization Safety Office

- Existing systems:
  - Vaccine Adverse Event Reporting System (VAERS)
  - Vaccine Safety Datalink (VSD)
  - Clinical Immunization Safety Assessment (CISA) Project

CDC COVID-19 Vaccine Safety Monitoring

Goals of post-licensure or post-authorization vaccine safety monitoring

- Rapidly identify new or rare adverse events of clinical importance
- Monitor changes in patterns of known adverse events
- Assess safety in special populations
- Determine patient risk factors for adverse events
- Provide timely and accurate data to stakeholders, including the ACIP and other advisory bodies

Vaccine safety signal*

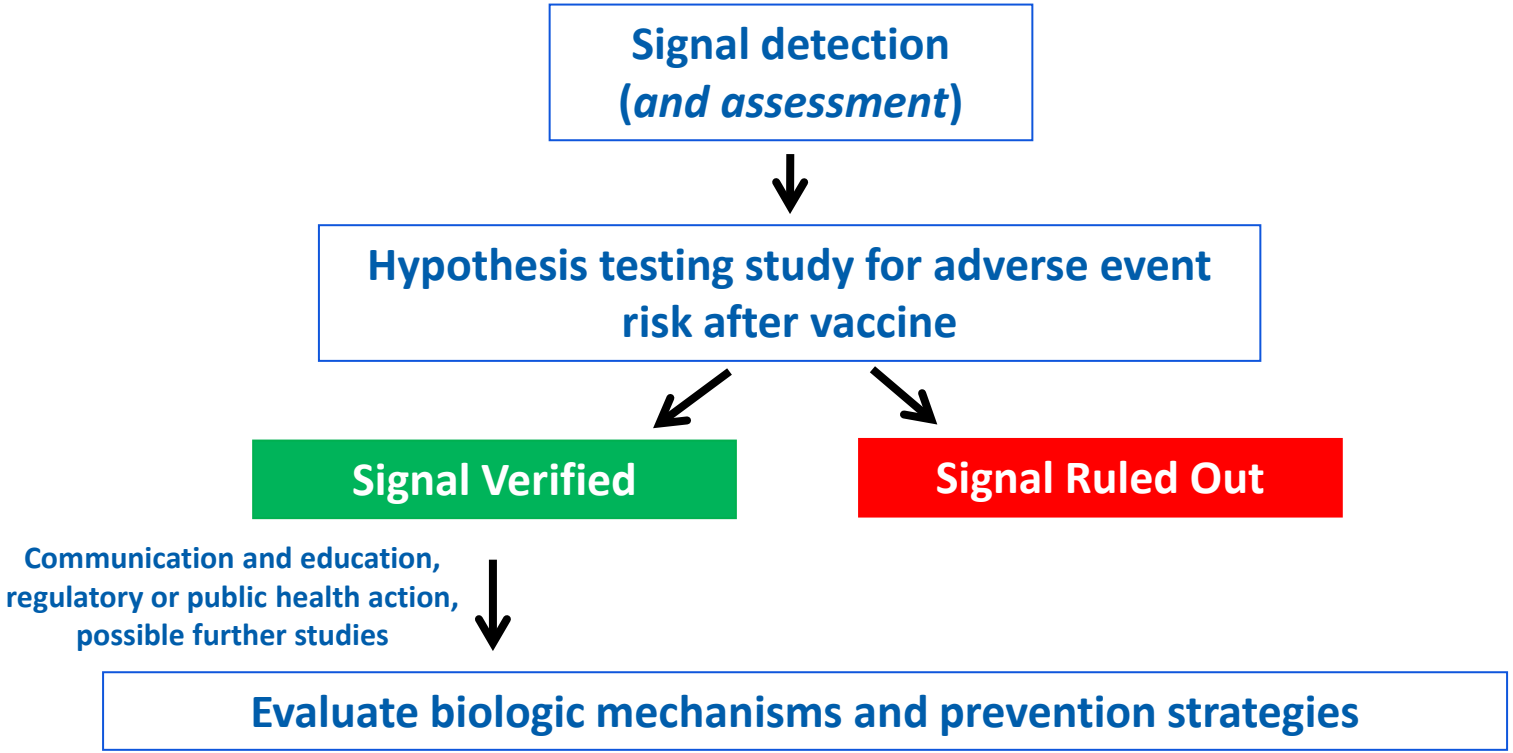
- Different definitions of “signal” in the field of pharmacovigilance
- The Council for International Organizations of Medical Sciences (CIOMS) proposed a signal as:

  “Information…from one or multiple sources …, **which suggests a new potentially causal association, or a new aspect of a known association, between an intervention and an event** or set of related events, either adverse or beneficial, that is judged to be of sufficient likelihood to justify verificatory action.”*

- In practice, efforts focus on detecting signals for “adverse” events

* Practical Aspects of Signal Detection in Pharmacovigilance: Report of CIOMS Working Group VIII – CIOMS. (2010)

Vaccine safety signal pathway



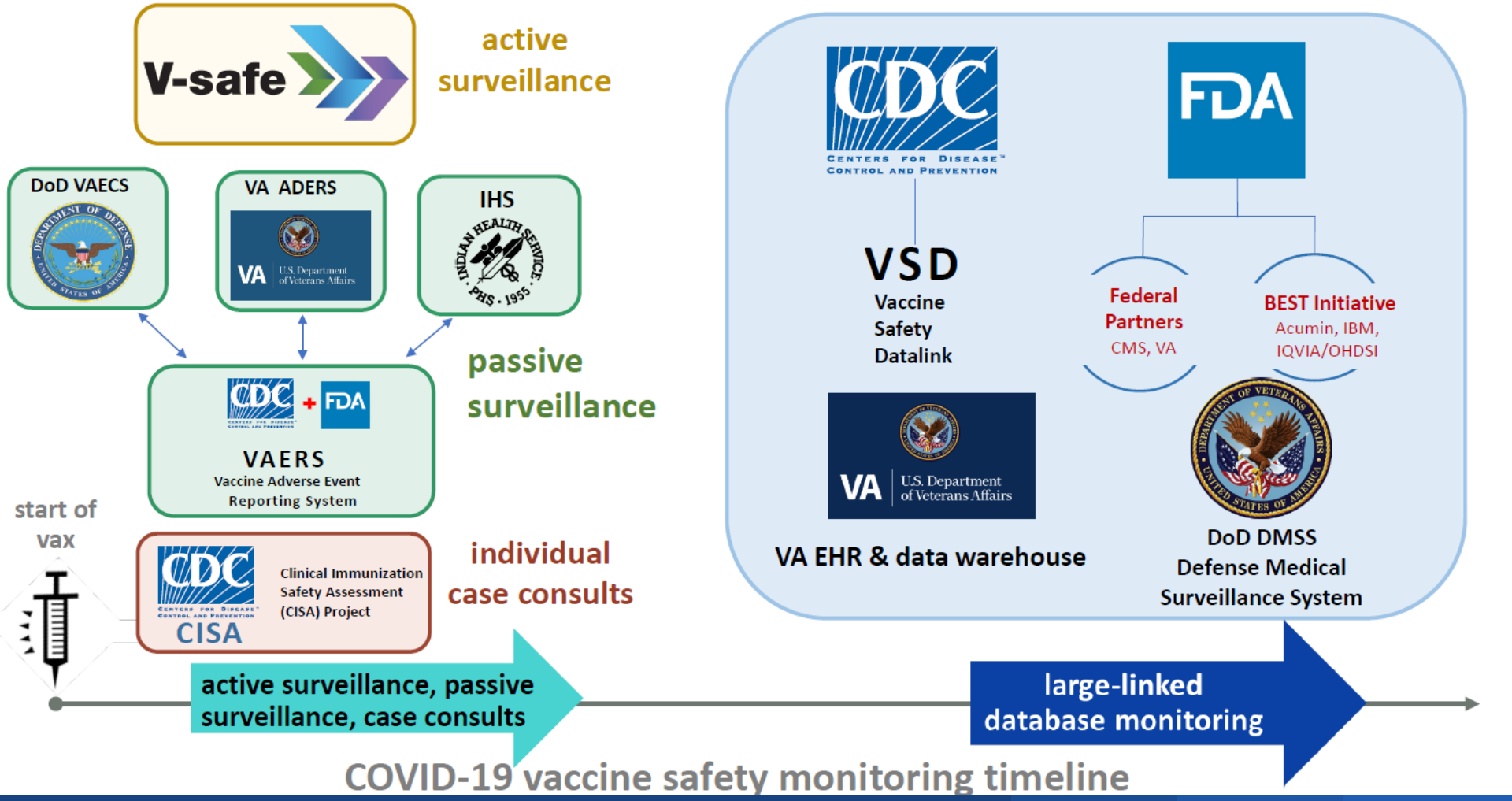
*Adapted from: Practical Aspects of Signal Detection in Pharmacovigilance: Report of CIOMS Working Group VIII – CIOMS. (2010)

Coordination of COVID-19 vaccine safety monitoring efforts among US Federal Agencies

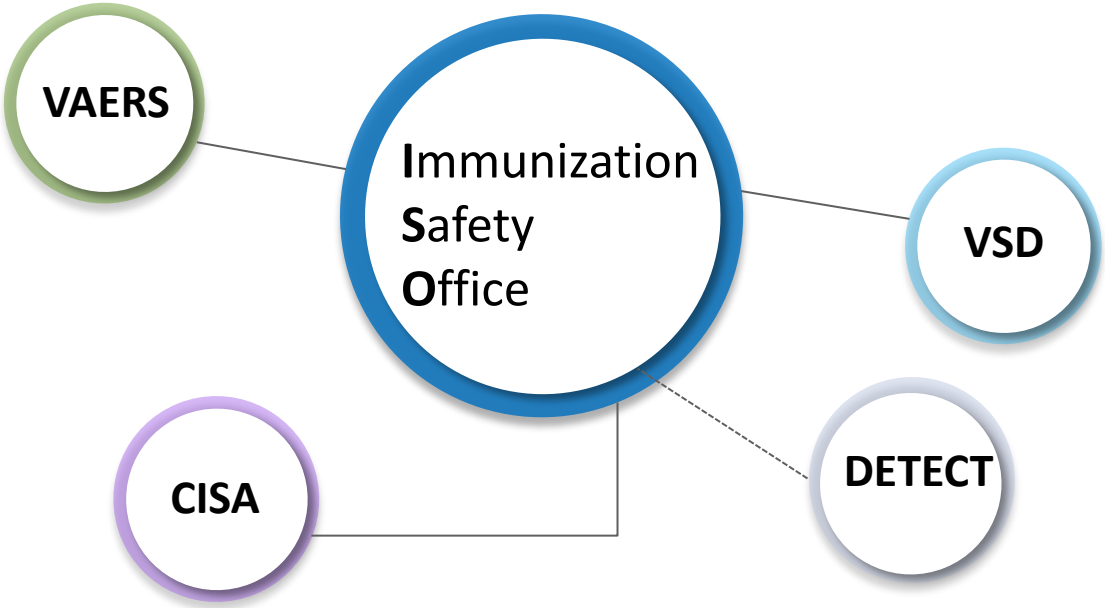
- Federal partners involved:
  - Centers for Disease Control and Prevention (CDC)
  - Food and Drug Administration (FDA)
  - Department of Veterans Affairs (VA)
  - Department of Defense (DoD)
  - Indian Health Service (IHS)
- Recurring meetings to discuss planning and implementation efforts for vaccine safety monitoring and to conduct timely reviews of safety findings as data were collected and analyzed

Coordination of COVID-19 vaccine safety monitoring efforts among US Federal Agencies (continued)

- In advance of the national vaccination program, CDC and FDA developed a core list of adverse events of special interest (AESI) for enhanced safety monitoring based on:
  - Historical concerns for vaccine safety
  - Serious allergic AEs known to be associated with vaccination
  - Theoretical safety concerns and outcomes based on certain COVID-19 disease complications
  - Biological plausibility
  - Findings from COVID-19 vaccine preauthorization clinical trials
- Other AESIs were added for monitoring based on surveillance findings as the vaccination program progressed.


V-safe
active surveillance
DoD VAECS
VA ADERS
IHS
passive surveillance
VAERS
Vaccine Adverse Event Reporting System
start of vax
CISA
Clinical Immunization Safety Assessment (CISA) Project
individual case consults
CDC
Centers for Disease Control and Prevention
FDA
VSD
Vaccine Safety Datalink
Federal Partners
CMS, VA
BEST Initiative
Acumin, IBM, IQVIA/OHDSI
VA
U.S. Department of Veterans Affairs
VA EHR & data warehouse
DoD DMSS
Defense Medical Surveillance System
active surveillance, passive surveillance, case consults
large-linked database monitoring
COVID-19 vaccine safety monitoring timeline

Centers for Disease Control and Prevention (CDC)
Immunization Safety Office



- **Clinical Immunization Safety Assessment (CISA) Project**
- **Vaccine Adverse Event Reporting System (VAERS)**
- **Vaccine Safety Datalink (VSD)**
- **Data Exploration and Technology (DETECT)**
  - V-safe
  - COVID-19 Pregnancy Registry

CDC COVID-19 Vaccine Safety Systems and Activities

V-safe: Self-reported active safety monitoring

v-safe℠

Enroll yourself or your dependent after COVID-19 or RSV vaccine!

https://vsafe.cdc.gov

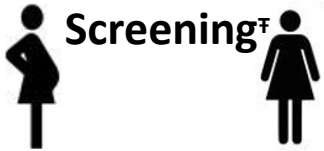
COVID-19 Vaccine Pregnancy Registry

v-safe℠ after vaccination health checker

- Started December 14, 2020 with Phase 1a of vaccine roll out for COVID-19 vaccines

Individual Reporting Pregnancy*

Eligibility Screening†



Pregnant at time of vaccination

Vaccinated during peri-conceptional period

- Reported a pregnancy into v-safe between Dec 14, 2020 – Jun 20, 2021
- 18+ years of age
- Speak English or Spanish

Eligible Individuals

Consent for registry

- Phone interviews conducted
- Data collected prospectively and/or retrospectively
- Consent obtained to request medical records

*Pregnancy questions in v-safe assessments on first survey after each dose and on post-vaccination days 21 and 42 and months 3, 6, and 12

†Eligibility determined from verbal interviews and responses to 3-question web-based v-safe follow-up survey received prior to May 31, 2021. Eligible individuals received COVID-19 vaccination during pregnancy or periconceptional period (≤ 30 days before the first day of the last menstrual period before pregnancy).

Key contributions of v-safe to COVID-19 vaccine safety

February 2021

Rapid preliminary post-authorization data

MMWR

First Month of COVID-19 Vaccine Safety Monitoring — United States, December 14, 2020–January 13, 2021

June 2021

Reactogenicity after primary series and booster doses

JAMA Insights

Reactogenicity Following Receipt of mRNA-Based COVID-19 Vaccines

July 2022

Reactogenicity after simultaneous administration with influenza vaccine

JAMA Network Open

Reactogenicity of Simultaneous COVID-19 mRNA Booster and Influenza Vaccination in the US

September 2022

Menstrual irregularities and vaginal bleeding after COVID-19 vaccination

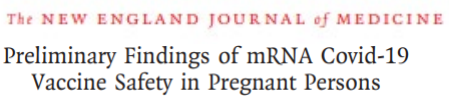
The Lancet Digital Health

Menstrual irregularities and vaginal bleeding after COVID-19 vaccination reported to v-safe active surveillance, USA in December, 2020–January, 2022: an observational cohort study

Key contributions of COVID-19 Pregnancy Registry to COVID-19 vaccine safety

April 2021

mRNA vaccine safety in pregnancy



Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons

September 2021

mRNA vaccines and risk of spontaneous abortion

Receipt of mRNA Covid-19 Vaccines and Risk of Spontaneous Abortion

VAERS in the US early warning system for vaccine safety

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System

http://vaers.hhs.gov

Key contributions of VAERS to COVID-19 vaccine safety

January 2021

Reports of anaphylaxis following mRNA vaccines

JAMA Insights

Reports of Anaphylaxis After Receipt of mRNA COVID-19 Vaccines in the US—December 14, 2020-January 18, 2021

April 2021

Reports of blood clots in the brain after Janssen vaccines

JAMA

US Case Reports of Cerebral Venous Sinus Thrombosis With Thrombocytopenia After Ad26.COV2.S Vaccination, March 2 to April 21, 2021

August 2021

Rapid preliminary post-authorization data

MMWR

COVID-19 Vaccine Safety in Adolescents Aged 12–17 Years — United States, December 14, 2020–July 16, 2021

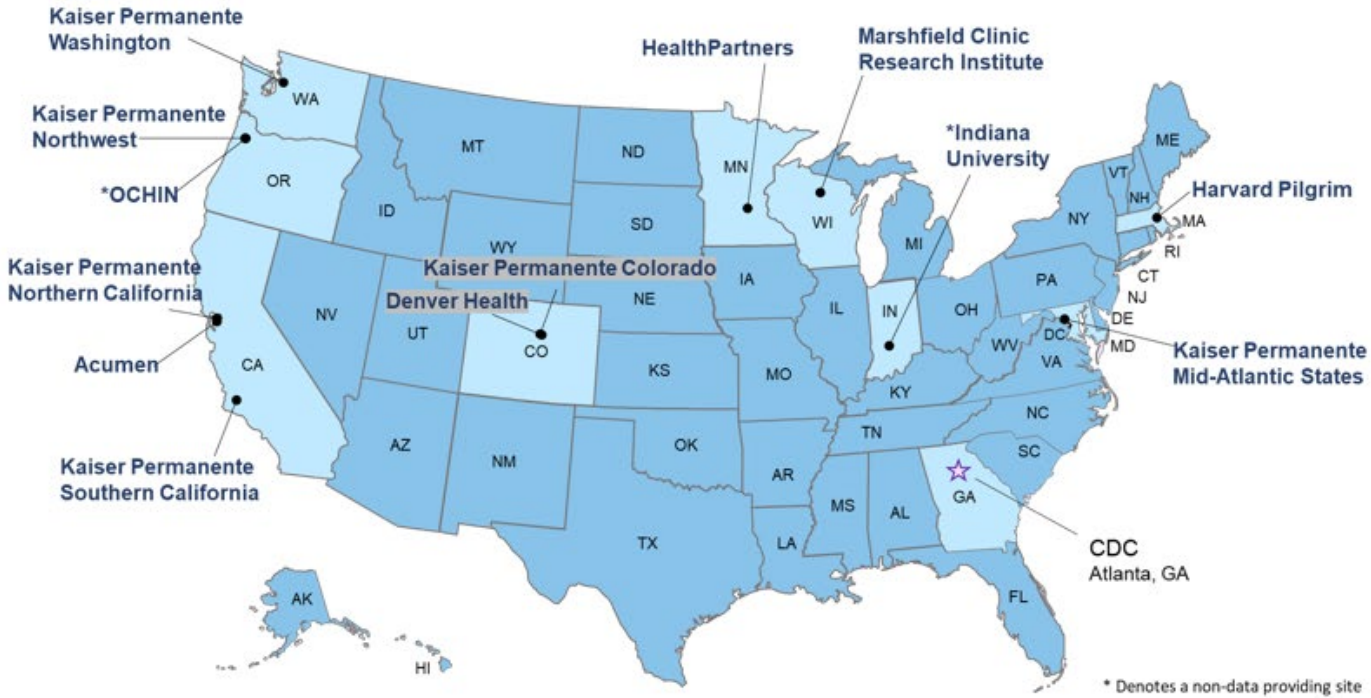
January 2022

Reports of myocarditis following mRNA vaccines

JAMA

Myocarditis Cases Reported After mRNA-Based COVID-19 Vaccination in the US From December 2020 to August 2021

Vaccine Safety Datalink (VSD)



- Collaborative project between CDC and **13** integrated healthcare organizations
- Data on >15 million persons per year
- Conducts rigorous vaccine safety studies and near-real-time monitoring

Key contributions of VSD to COVID-19 vaccine safety

September 2021

Surveillance data on adverse events after mRNA vaccines

JAMA

Surveillance for Adverse Events after COVID-19 mRNA Vaccination

September 2021

Spontaneous abortion after COVID-19 vaccination during pregnancy

JAMA

Spontaneous Abortion Following COVID-19 Vaccination During Pregnancy

August 2021

Risk of mortality following COVID-19 vaccination

MMWR

COVID-19 Vaccination and Non–COVID-19 Mortality Risk — Seven Integrated Health Care Organizations, United States, December 14, 2020–July 31, 2021

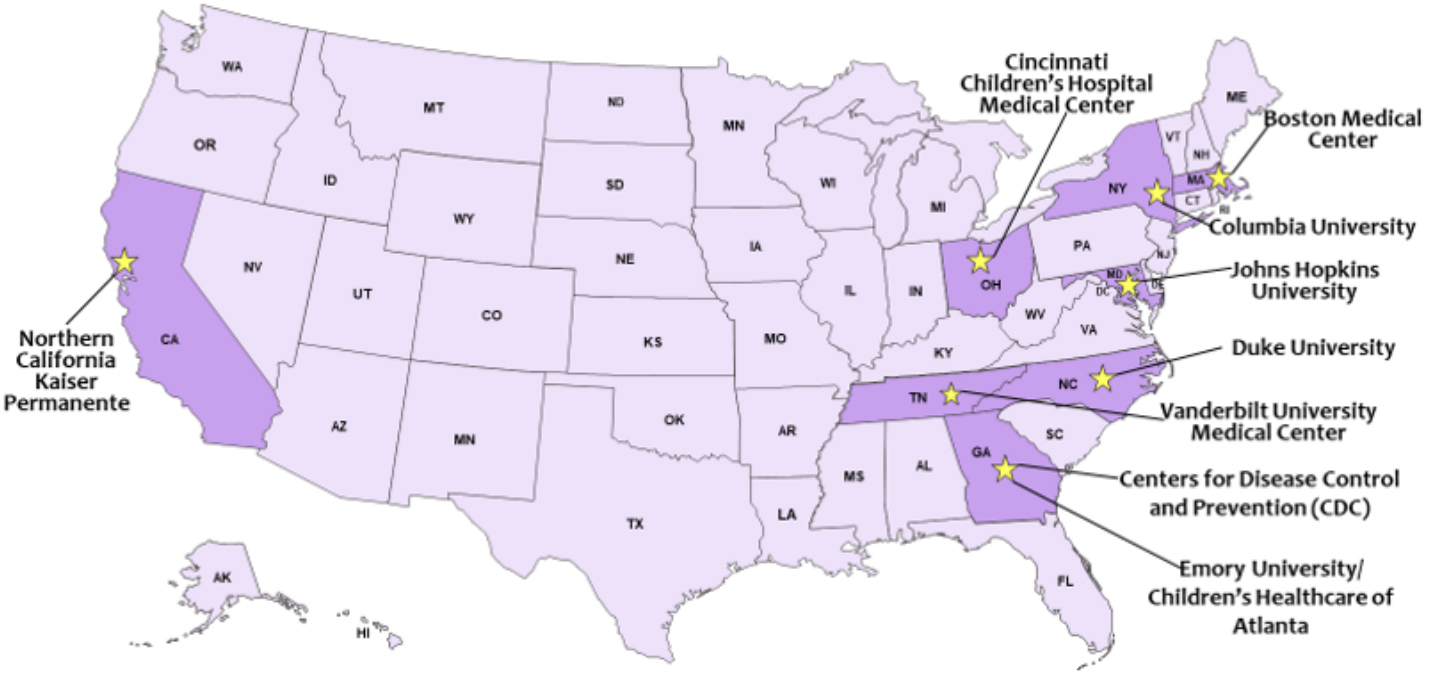
January 2022

GBS following COVID-19 vaccines

JAMA Network Open

Incidence of Guillain-Barré Syndrome after COVID-19 Vaccination in the Vaccine Safety Datalink

Clinical Immunization Safety Assessment (CISA) Project



- **8** participating research centers with vaccine safety experts
- Clinical consult services* and clinical research studies

CISA clinical consultations*

- Clinical consultation service for U.S. healthcare providers and health departments with complex vaccine safety questions/issues that are:

  (1) about an individual patient(s) residing in the United States

  (2) not readily addressed by CDC or ACIP guidelines**

- For COVID-19 vaccines 24/7 on-call consultation available for vaccine safety emergencies

* Clinical Immunization Safety Assessment (CISA) Project | CISA | Monitoring | Ensuring Safety | Vaccine Safety | CDC

**Interim Clinical Considerations for Use of COVID-19 Vaccines | CDC

Key contributions of CISA to COVID-19 vaccine safety

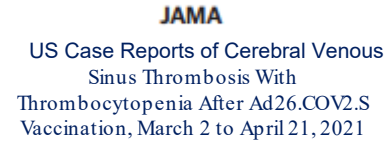
January 2021

Interim clinical considerations on anaphylaxis and allergic reactions

Interim Clinical Considerations for Use of COVID-19 Vaccines: Appendices, References, and Previous Updates | CDC

April 2021

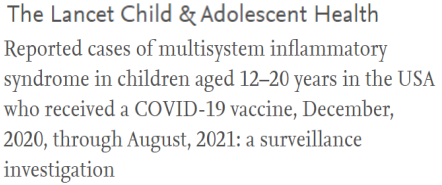
Reports of Venous Thrombosis with Thrombocytopenia after Janssen vaccine


JAMA

US Case Reports of Cerebral Venous Sinus Thrombosis With Thrombocytopenia After Ad26.COV2.S Vaccination, March 2 to April 21, 2021

August 2021

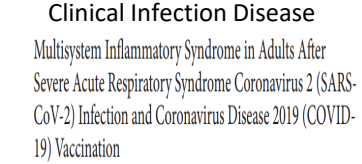
Reports of Multisystem Inflammatory Syndrome in Children


The Lancet Child & Adolescent Health

Reported cases of multisystem inflammatory syndrome in children aged 12–20 years in the USA who received a COVID-19 vaccine, December, 2020, through August, 2021: a surveillance investigation

January 2022

Reports of Multisystem Inflammatory Syndrome in Adults


Clinical Infection Disease

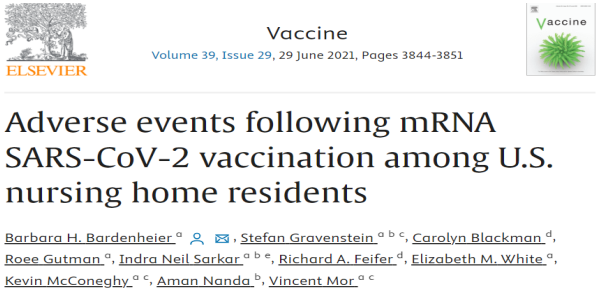
Multisystem Inflammatory Syndrome in Adults After Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection and Coronavirus Disease 2019 (COVID-19) Vaccination

Follow-up of outcomes of myocarditis reported to VAERS after mRNA COVID-19 vaccination

- Purpose: Assess functional status and clinical outcomes among individuals reported to have developed myocarditis after mRNA COVID-19 vaccination
- Methods: A two-component survey conducted at least 90 days after the onset of myocarditis symptoms
  - Patient survey: Focused on ascertaining functional status, clinical symptoms, quality of life, and need for medication or other medical treatment
  - Healthcare provider (e.g., cardiologist): Gather data on cardiac health and functional status
- CDC also conducted telephone surveys of both patients and cardiologists or other healthcare providers to describe outcomes at least 1 year after symptom onset

COVID-19 Vaccine Safety Monitoring in Long-Term Care Facilities (LTCF)

- Enhanced monitoring conducted for elderly populations residing in LTCF during the initial rollout of COVID-19 vaccination program
- Data sources:
  - VAERS
  - NHSN: supplemented reporting to VAERS
  - Genesis Healthcare



ELSEVIER

Vaccine

Volume 39, Issue 29, 29 June 2021, Pages 3844-3851

Adverse events following mRNA SARS-CoV-2 vaccination among U.S. nursing home residents

Barbara H. Bardenheier [a], Stefan Gravenstein [a b c], Carolyn Blackman [d], Roee Gutman [a], Indra Neil Sarkar [a b e], Richard A. Feifer [d], Elizabeth M. White [a], Kevin McConeghy [a c], Aman Nanda [b], Vincent Mor [a c]

Contributions to COVID-19 Vaccine Policy

U.S. Vaccine Advisory Committees

- **FDA Vaccine and Related Biologic Products Advisory Committee (VRBPAC)**
  - Evaluates data regarding the safety, effectiveness, and appropriate use of vaccines and related biological products to the FDA Commissioner
    - Vaccine approval/licensure and authorization
- **CDC Advisory Committee on Immunization Practices (ACIP)**
  - Develop recommendations on the use of vaccines
- **HHS National Vaccine Advisory Committee (NVAC)**
  - Provides peer review, consultation, advice, and recommendation to the Assistant Secretary for Health
- **HRSA Advisory Commission on Childhood Vaccines (ACCV)**
  - Advises and makes recommendations on issues related to the National Vaccine Injury Compensation Program

ACIP COVID-19 Vaccine Safety Technical (VaST) Work Group

- **Objectives:**
  - Review, evaluate, and interpret post-authorization/approval COVID-19 vaccination safety data
  - Serve as the central hub for technical subject matter expertise from federal agencies conducting post-authorization/approval safety monitoring
  - Advise on analyses, interpretation, and presentation of vaccine safety data
  - Provide updates to the ACIP COVID-19 Vaccines Work Group and the entire ACIP on COVID-19 vaccine safety
- **During December 21, 2020 through February 24, 2023:**
  - 71 independent meetings to review vaccine safety data
  - 17 joint meetings with ACIP COVID-19 Vaccines Work Group
  - 22 ACIP meeting presentations or reports with VaST assessment

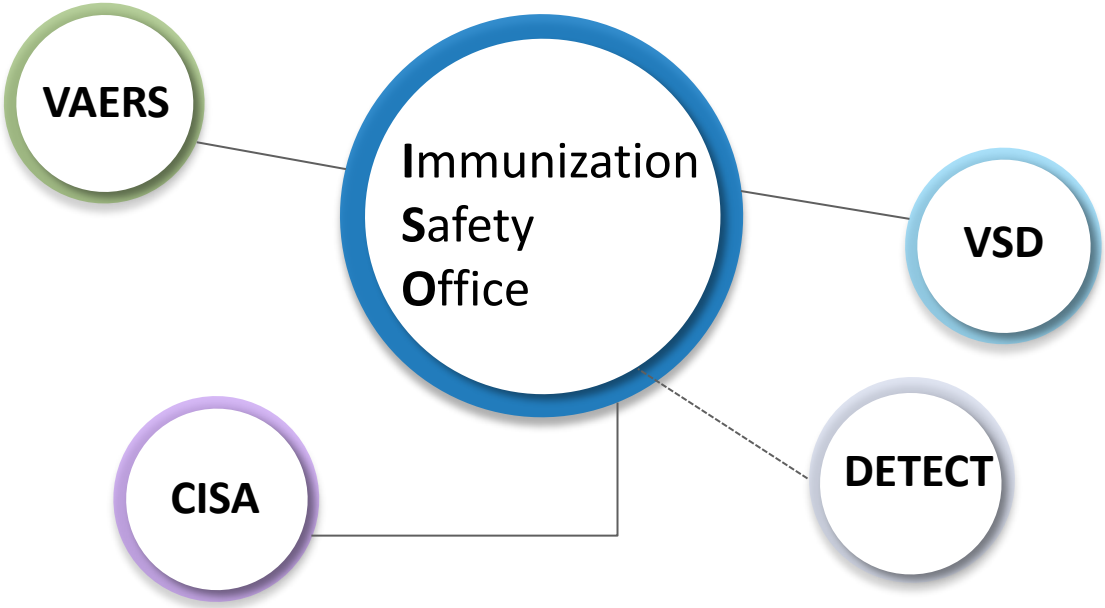
Vaccine Safety Risk Communications

Vaccine Safety COVID-19 Risk Communication

- CDC and FDA posted COVID-19 vaccine safety monitoring protocols online
- VaST reports were publicly posted summarizing discussions and data interpretation from the various data systems at ACIP meetings
- Publications on preprint servers, CDC's Morbidity and Mortality Weekly Report, and peer-reviewed biomedical journals to ensure timely dissemination of information.
- CISA provided input to CDC's Interim Clinical Considerations for Use of COVID-19 Vaccines
- Plain language, lay-friendly communications:
  - CDC COVID-19 webpages to communicate timely information on selected AEs reported after COVID-19 vaccination to the pubic and to healthcare providers
  - Digital and social media channels, and to public and private partners

CDC’s Vaccine Safety Monitoring: Post- COVID-19 Public Health Emergency

Centers for Disease Control and Prevention (CDC)
Immunization Safety Office



- **Clinical Immunization Safety Assessment (CISA) Project**
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- **Data Exploration and Technology (DETECT)**
  - V-safe
  - COVID-19 Pregnancy Registry

Challenges and Needs

- Scaling ISO staff and activities post-COVID-19 pandemic
- Stable funding
- Exploring new data sources and methodologies for vaccine safety monitoring
- Countering vaccine hesitancy

Conclusion

- The U.S. COVID-19 vaccine program demonstrated that vaccines were administered under **the most intensive vaccine safety monitoring effort in U.S. history** (>600 million doses COVID-19 vaccine doses administered in United States)
- Rapid assessment of COVID-19 vaccine safety data during the pandemic has informed vaccination policy and clinical considerations in near real-time.
- CDC provided rapid communication of COVID-19 vaccine safety data to healthcare providers and the public through multiple channels.
- Strong, complementary vaccine safety monitoring systems are in place to rapidly detect and assess potential safety concerns, and to evaluate individual cases of complex adverse events.
- There is well-established coordination of vaccine safety monitoring efforts with other federal agencies, including the FDA.
- Experience during the COVID-19 pandemic has demonstrated that CDC vaccines safety systems can adapt to meet public health needs.

Charge to the NASEM Committee: Review of Purpose

1) Evaluate vaccine safety systems, analytic methods, and processes used by CDC's ISO to monitor and assess COVID-19 vaccine safety during the U.S. COVID-19 vaccination program: beginning with the start of the vaccination program (December 2020) through the end of the COVID-19 public health emergency declaration (May 2023)
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Thanks!

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the U.S. Centers for Disease Control and Prevention.