Overview of Postmarketing Safety Monitoring

ADVISORY COMMISSION ON CHILDHOOD VACCINES (ACCV)

March 8, 2024

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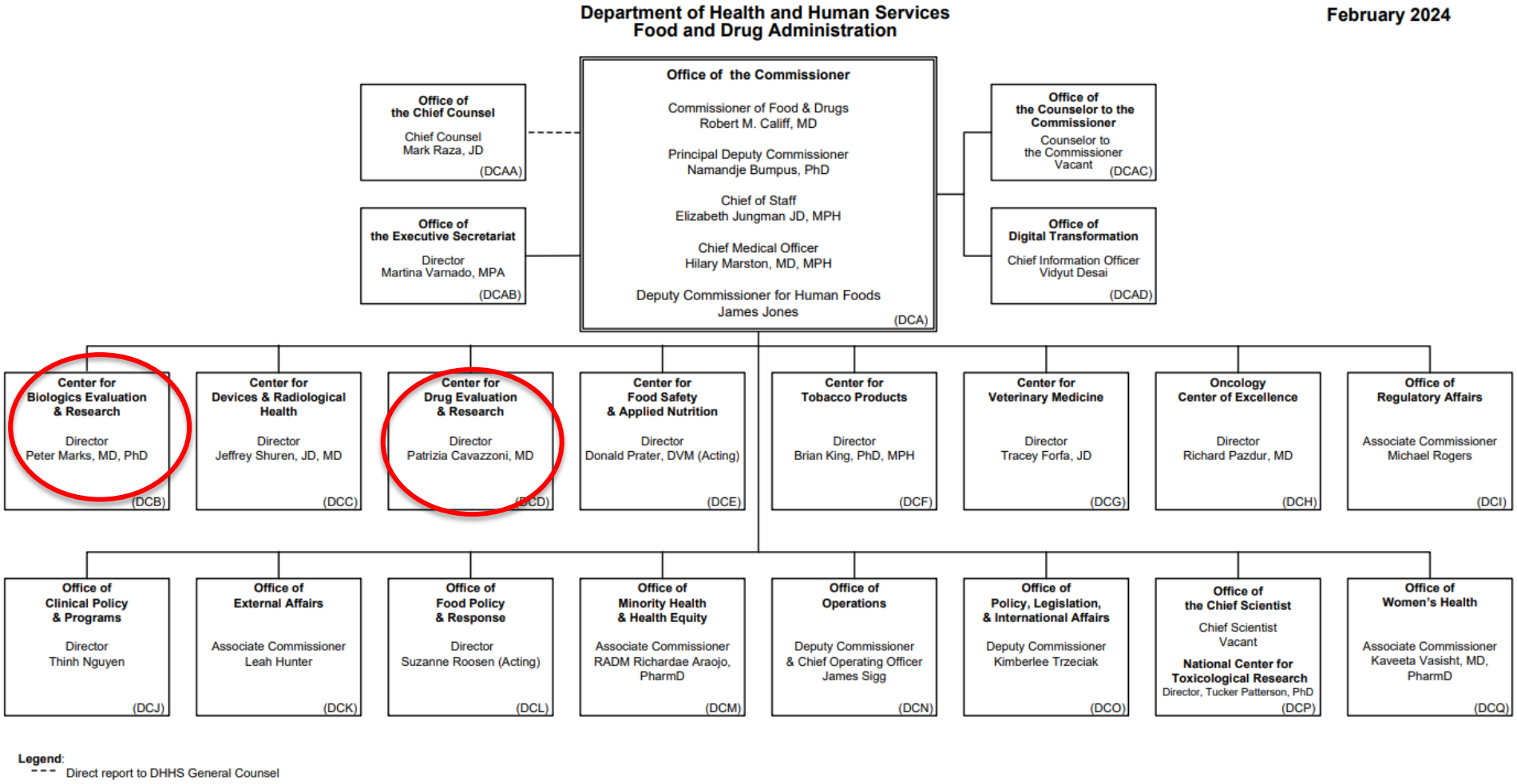
Disclaimer

My comments are an informal communication and represent my own best judgment. These comments do not bind or obligate the US FDA.

Outline

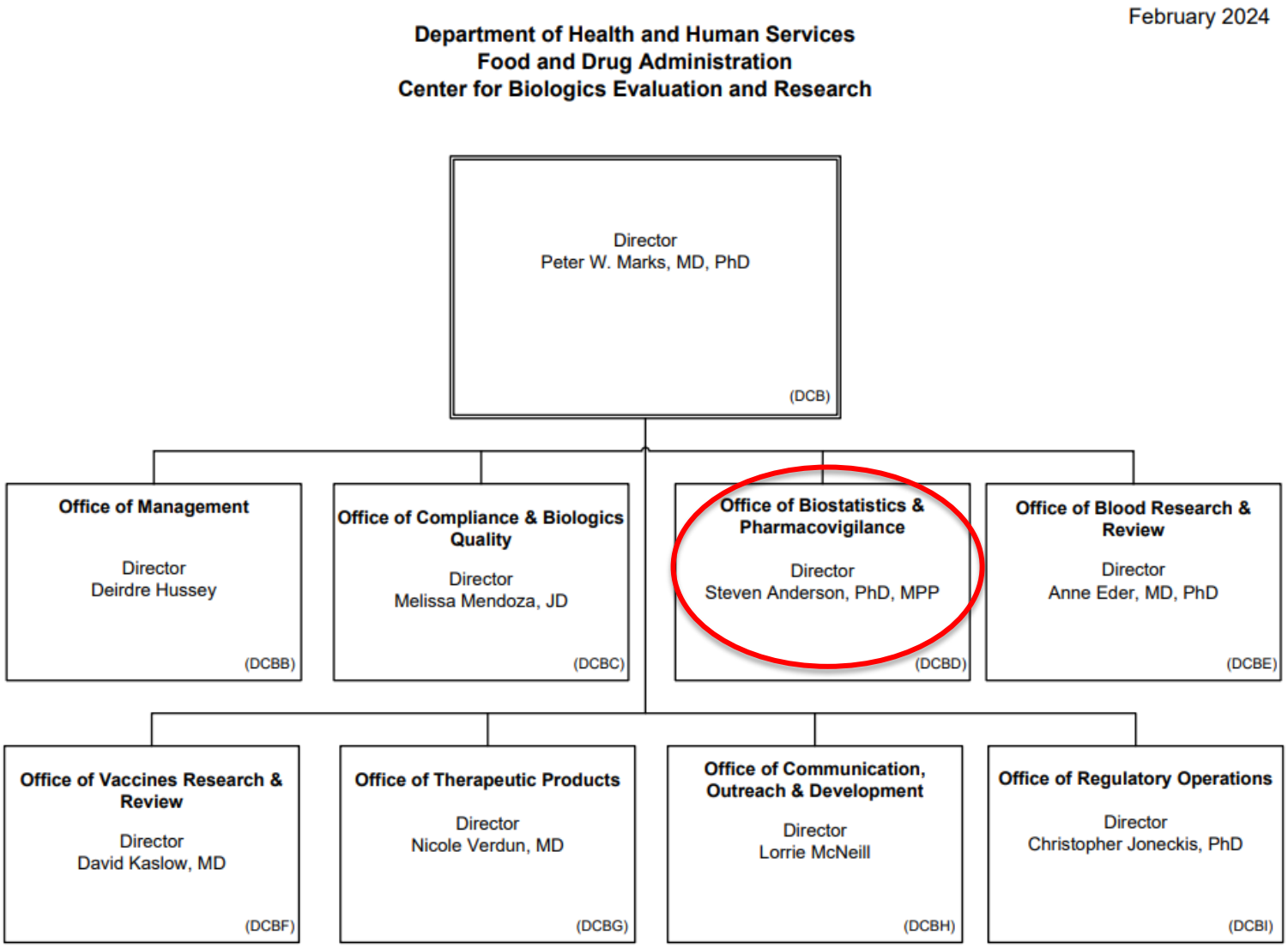
- Organizational chart
- FDA responsibilities during product lifecycle
- Vaccine and therapeutics pharmacovigilance
  - *Passive* surveillance
  - *Active* surveillance
    - Population-based surveillance
    - Observational studies
- Signal evaluation and risk management
- Examples
- Summary

FDA Organization Chart



https://www.fda.gov/about-fda/fda-organization-charts/fda-overview-organization-chart

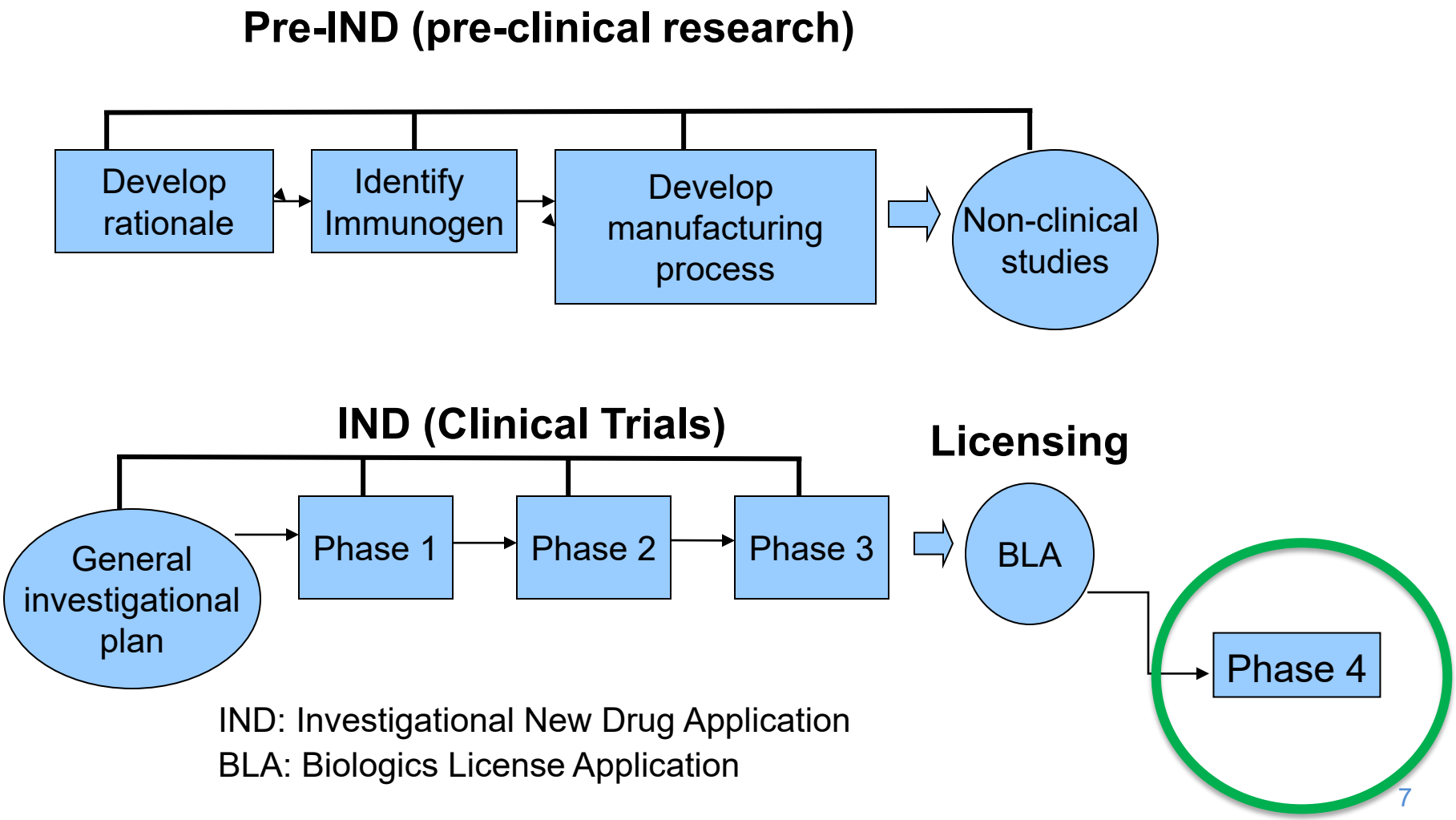
CBER Organization Chart



https://www.fda.gov/about-fda/fda-organization-charts/center-biologics-evaluation-and-research-organization-chart

FDA Responsibilities During Product Lifecycle

Product Development Life Cycle



IND: Investigational New Drug Application
BLA: Biologics License Application

FDA Product Safety Throughout the Life Cycle

- FDA ensures that products are safe for their intended use.
- Product safety activities occur throughout the life cycle
  - Preclinical research (non-human) testing of candidate vaccines
  - Early phase human studies through large phase III clinical trials
  - Inspection of manufacturing facilities
  - Monitoring of lot release
  - Postmarketing adverse event surveillance
  - Inspection of clinical sites for compliance with Good Clinical Practices

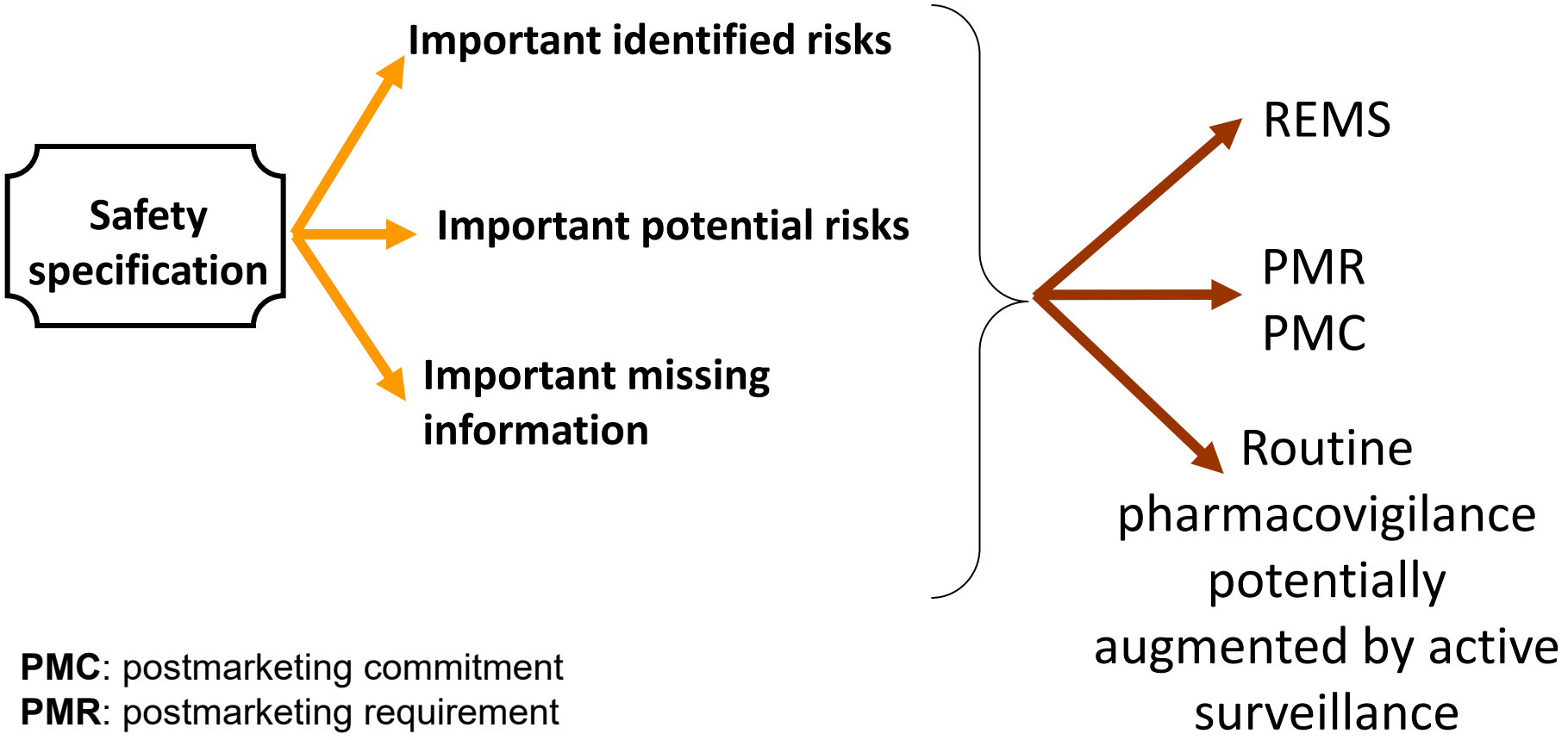
- **Monitoring product safety is equally important during development and during the postmarketing period**

Why does FDA conduct postmarketing safety surveillance?

- Limitations of premarket safety database
  - Clinical trials may not detect safety issues that arise when products are marketed to the general population (e.g., postmarketing surveillance may reveal interactions with comorbid conditions)
  - Inclusion criteria may exclude groups within the general population (e.g., pregnant women)
  - Smaller sample sizes and observation periods limit reliable detection to the most common events with shorter latency to onset
  - Unless a trial has a dedicated safety endpoint, inferences about safety are limited by concerns about post hoc analyses with multiple comparisons
- **Postmarketing surveillance further characterizes the safety profile of licensed products**

Pharmacovigilance

Key Decisions in Pharmacovigilance Planning

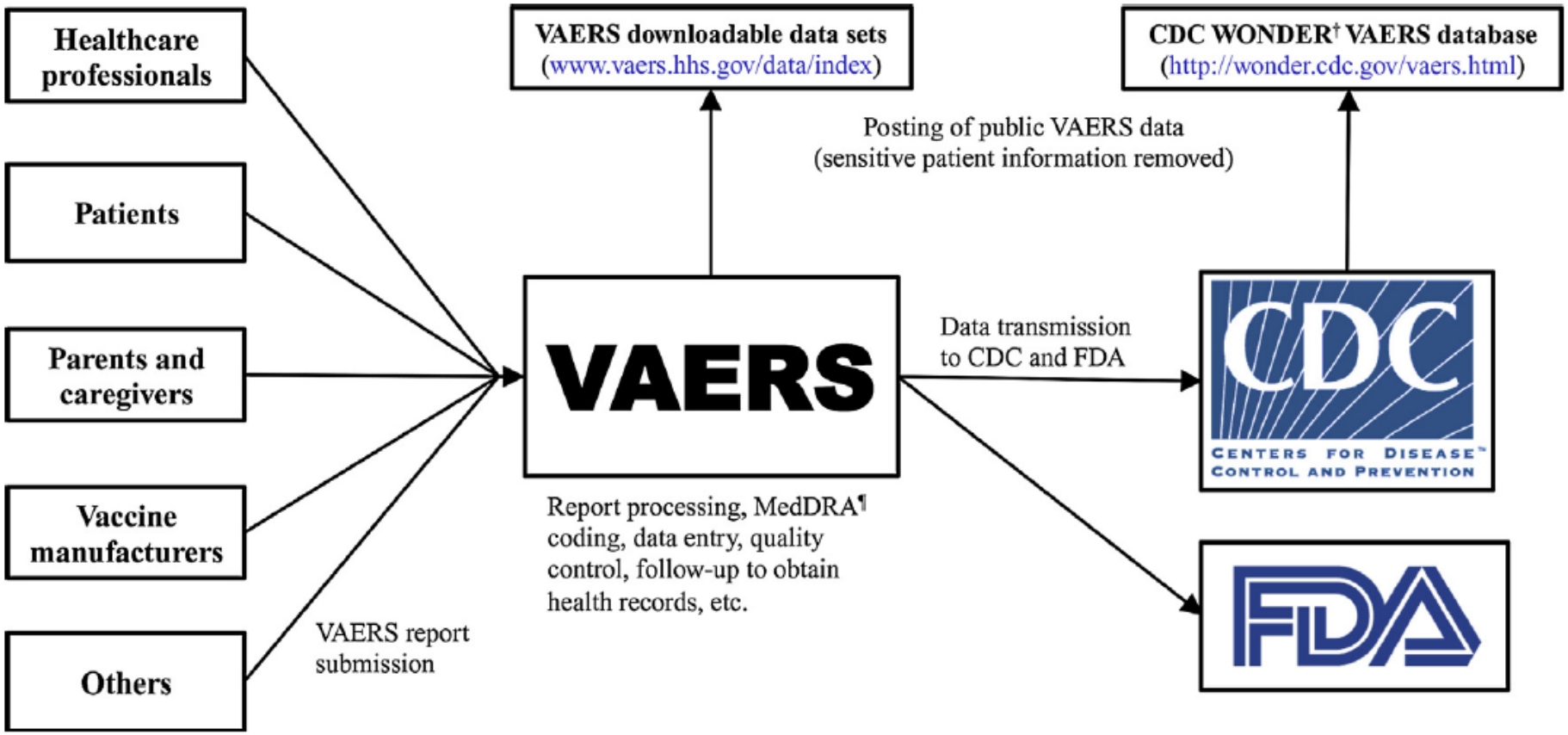


PMC: postmarketing commitment
PMR: postmarketing requirement
REMS: risk evaluation and mitigation strategies

ICH Guideline for Pharmacovigilance Planning E2E Nov 2004 (www.ich.org) International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
FDA Guidance for Industry: Postmarketing Studies and Clinical Trials — Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (April 2011)
FDA's Application of Statutory Factors in Determining When a REMS is Necessary: Guidance for Industry (September 2016)

Passive surveillance databases

FAERS: FDA Adverse Event Reporting System



Shimabukuro T, Nguyen M, Martin D, DeStefano F. Safety Monitoring in the Vaccine Adverse Event Reporting System (VAERS). *Vaccine* doi :10.1016/j.vaccine.2015.07.035.

VAERS Vaccine Adverse Event Reporting System
www.vaers.hhs.gov

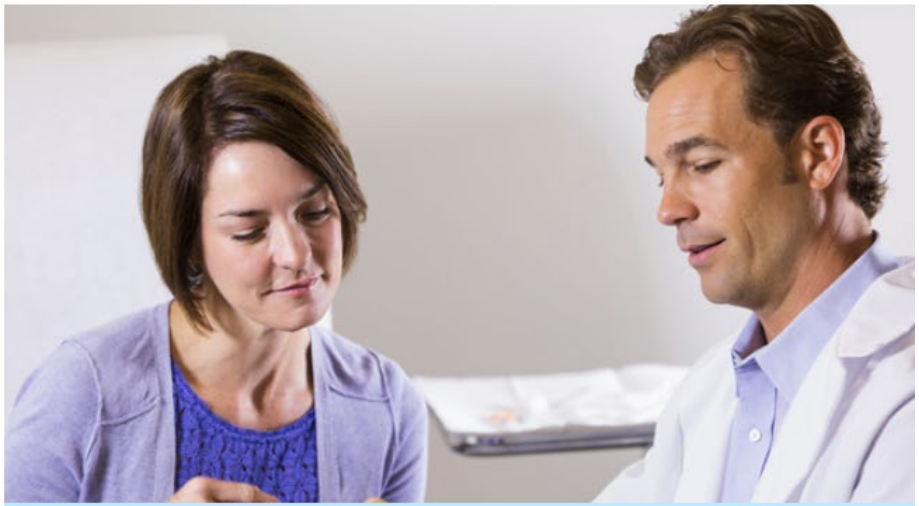
FDA

About VAERS | Report an Adverse Event | VAERS Data | Resources | Submit Follow-Up Information

Have you had a reaction following a vaccination?

1. Contact your healthcare provider.
2. Report an Adverse Event using the VAERS online form or the downloadable PDF. *New!*

Important: If you are experiencing a medical emergency, seek immediate assistance from a healthcare provider or call 9-1-1. CDC and FDA do not provide individual medical treatment, advice, or diagnosis. If you need individual medical or health care advice, consult a qualified healthcare provider.



Reporting requirements for healthcare providers administering COVID-19 vaccines

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Search

CDC WONDER | FAQs | Help | Contact Us | WONDER Search

CDC Wonder: Publicly available VAERS data

About The Vaccine Adverse Event Reporting System (VAERS)

Request Form | Results | Map | Chart | Report | About

Dataset Documentation | Other Data Access | Data Use Restrictions | How to Use WONDER

Note: *Any use of these data implies consent to abide by the terms of the data use restrictions.*

How to Report Adverse Events to FDA

Food and Drug Administration
MEDWATCH

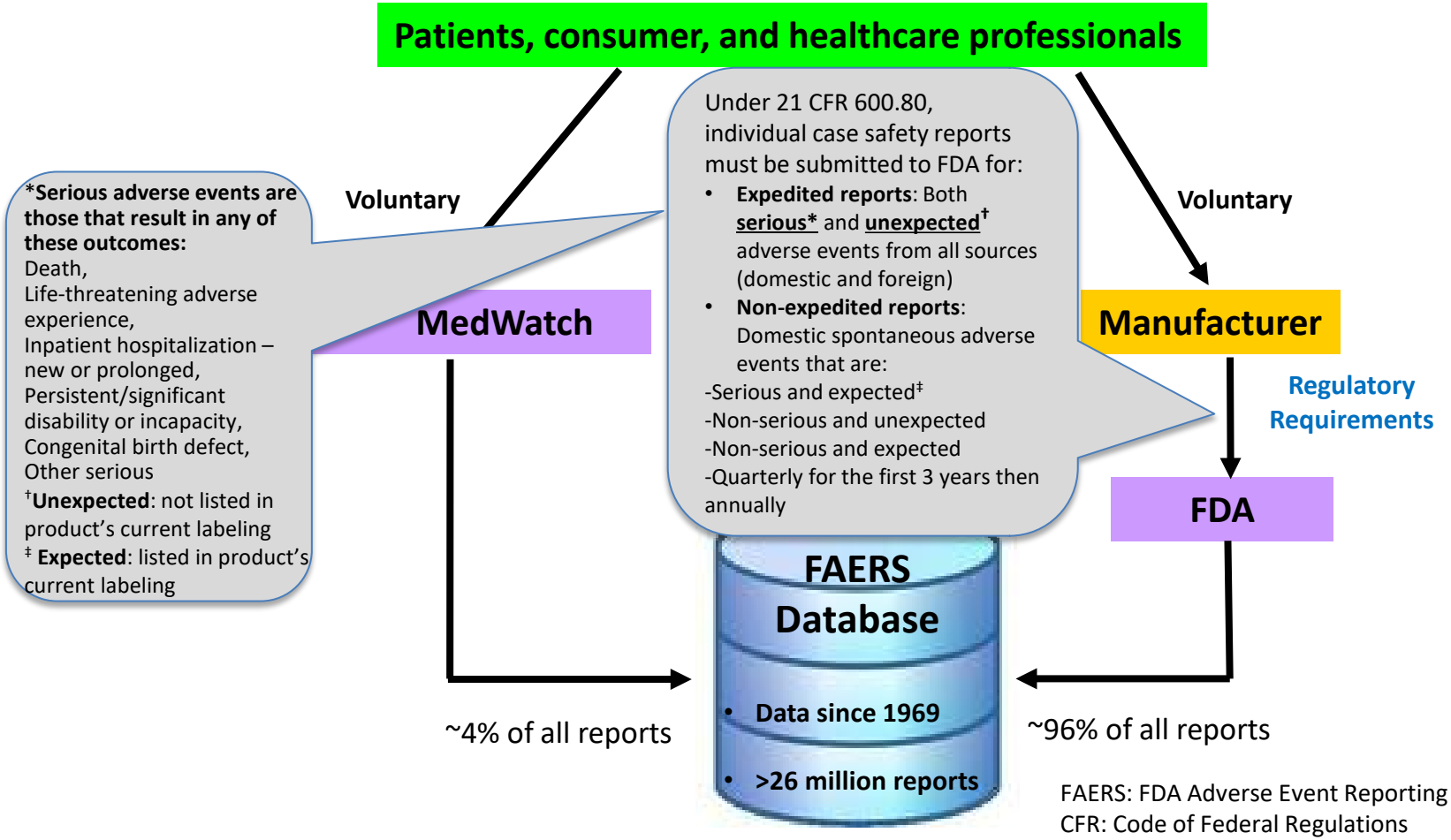
- How to Report:
  - Online (www.fda.gov/medwatch)
  - Download the form
    - Mail
    - Fax 1–800–332–0178
- For questions about the form:
  - 1–800–332–1088

U.S. Food and Drug Administration. MedWatch: The FDA Safety Information and Adverse Event Reporting Program. Available at: https://www.fda.gov/Safety/MedWatch/default.htm

Source: https://www.fda.gov/media/169322/download

Acknowledgement: Neha Gada, PharmD, BCPS, Cross Discipline Safety Advisor, Office of Surveillance and Epidemiology/CDER

Postmarketing Adverse Events & FAERS Submission



FAERS: FDA Adverse Event Reporting System
CFR: Code of Federal Regulations

Source: https://www.fda.gov/media/169322/download

Acknowledgement: Neha Gada, PharmD, BCPS, Cross Discipline Safety Advisor, Office of Surveillance and Epidemiology/CDER

Passive Surveillance

- Continuous safety monitoring for licensed products
- Spontaneous adverse event reports
- Reporting regulations:
  - Voluntary AE reporting for healthcare providers and the public
  - Mandatory AE reporting for manufacturers (21 CFR 600.80)
    - Expedited reporting of serious and unlabeled AEs in 15 days

    Seriousness: death, hospitalization, life-threatening, disability, congenital anomaly, other medically important event
    - Non-expedited reports
    - Periodic safety reports
- Systems involved
  - Vaccine Adverse Event Reporting System (VAERS); FDA Adverse Event Reporting System (FAERS)
  - Global pharmacovigilance, WHO Vigibase, public health agencies, other regulators

Adverse Event Following Immunization (AEFI)

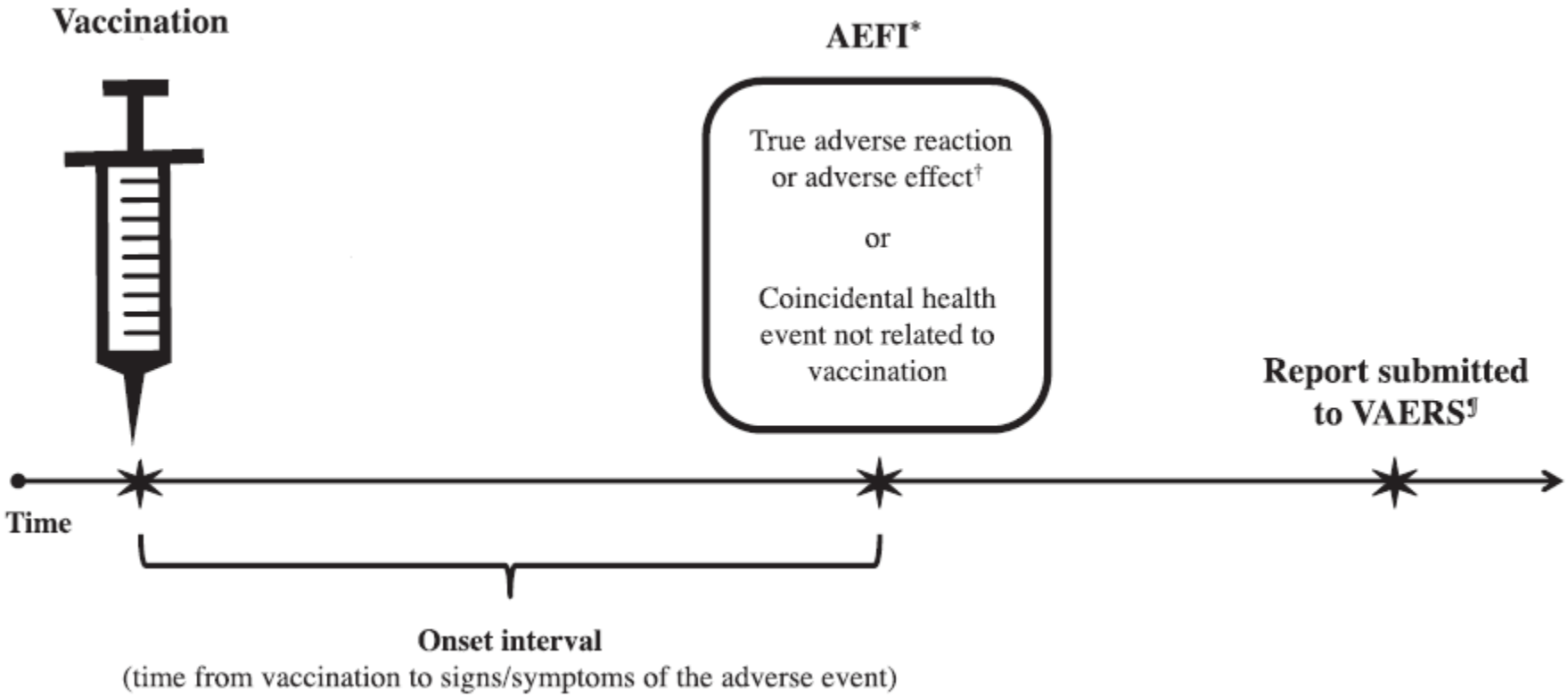


Fig. 1. Adverse event following immunization (AEFI) and the VAERS reporting timeline. *AEFI indicates only that the event happened after vaccination (i.e., a temporal association). †"Vaccine adverse reaction" and "vaccination adverse effect" are also AEFIs, but imply that the vaccine caused the event (i.e., a causal association). ¶There are no deadlines or time limits for the submission of a VAERS report, but reports should be submitted promptly after an adverse event occurs to facilitate surveillance and review. The National Vaccine Injury Compensation Program (VICP) is administered by the Health Resources and Services Administration (HRSA). The VICP is separate from the VAERS program and reporting an adverse event to VAERS does not constitute filing a claim for compensation to the VICP (see www.hrsa.gov/vaccinecompensation/index.html).

Shimabukuro T, Nguyen M, Martin D, DeStefano F. Safety Monitoring in the Vaccine Adverse Event Reporting System (VAERS). *Vaccine* doi :10.1016/j.vaccine.2015.07.035.

Adverse Event Reporting Systems

- Passive surveillance of vaccines
- Nation's early warning system for vaccine safety
- Pharmacovigilance databases accept all reports regardless of the plausibility of the product causing the event or the clinical seriousness of the event

Strengths

- Rapidly detects potential safety problems
- Potential detection of rare adverse events
- Open-ended for hypothesis generation
- Geographic diversity
- Capability to monitor production lots

Limitations

- Missing and/or inaccurate data
- Reported diagnoses are not verified
- Under-reporting
- Reporting bias (stimulated reporting)
- Absence of unvaccinated control group
- Inability to assess causation
- Not likely to detect long latency events

Role of Product Utilization Data

- Sponsor distribution data provides context for AE reports
  - Accounts for total amount distributed in US
  - Lot-specific
- Interpret with caution
  - Cannot calculate incidence
  - Not all doses distributed were administered
  - Does not include information on age groups (pediatric versus adult)

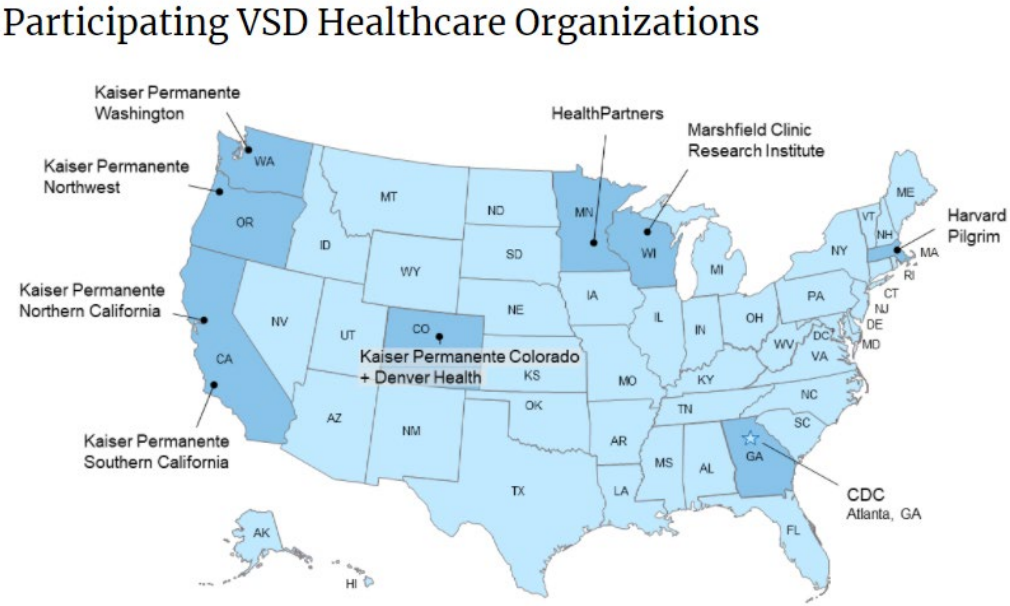
Active surveillance and postmarketing studies

FDA CBER Active Surveillance Program

Biologics Effectiveness and Safety Initiative

BES

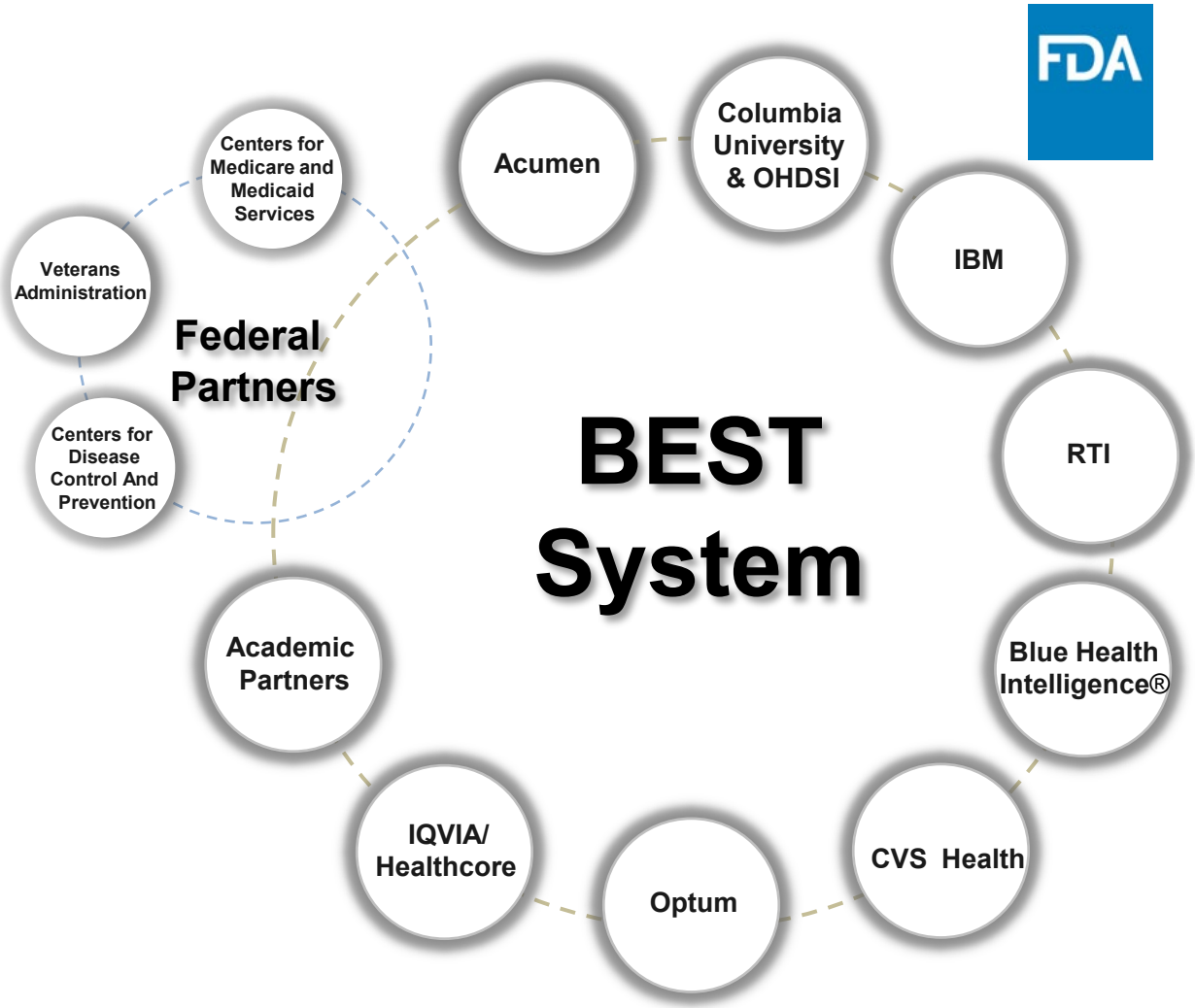
www.bestinitiative.org



CMS.gov

Centers for Medicare & Medicaid Services

FDA CBER Active Surveillance Program



CBER: Center for Biologics Evaluation and Research
BEST: Biologics Effectiveness and Safety

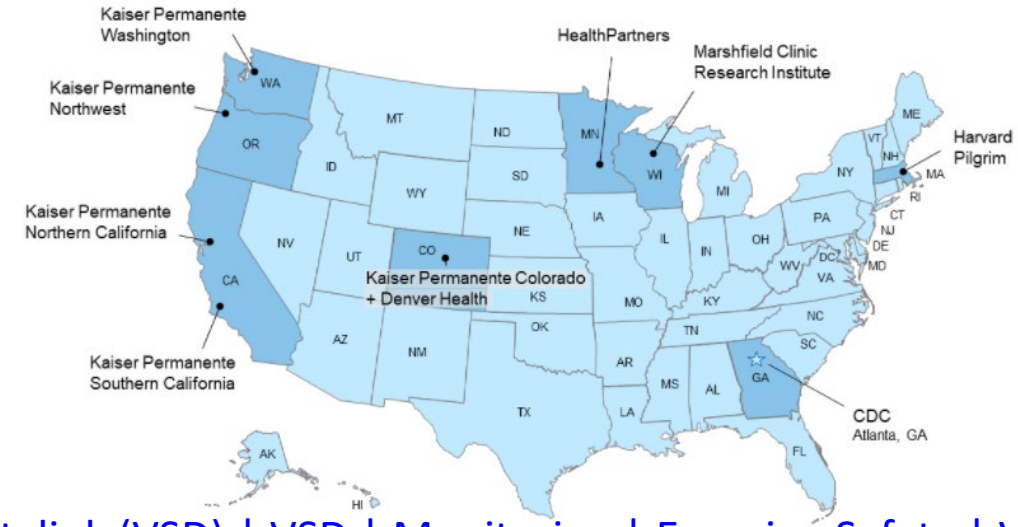
BEST System Data Sources

Data Source*	Database Type	Number of Patients Covered (Millions)	Time Period Covered
CMS- Medicare	Claims	105	2005 - present
MarketScan Commercial and Medicare Supplemental	Claims	254	1999 - 2019
MarketScan Medicaid	Claims	48	1999 - 2019
Blue Health Intelligence	Claims	33.6	2012 - present
Optum - Adjudicated	Claims	66	1993 - present
Optum - Pre adjudicated	Claims	22	2017 - present
HealthCore	Claims	76	2006 - 2020
CVS Health	Claims	26	2014 - 2020
OneFlorida Clinical Research Consortium - Medicaid	Claims	6.7	2012 - present
OneFlorida Clinical Research Consortium - EHR	EHR	5.6	2012 – present
Optum EHR	EHR	102	2007 - 2020
MedStar Health Research Institute	EHR	6	2009 - present
PEDSnet	EHR	6.2	2009 - present
IBM CED	Linked EHR Claims	5.4	2000 - present
Optum Integrated Claims - EHR	Linked EHR Claims	25	2007 - 2020
OneFlorida Clinical Research Consortium – Linked EHR Claims	Linked EHR Claims	1.5	2012 - present

*Data lag varies for different databases, and it is approximately 3 months.

CBER: Center for Biologics Evaluation and Research
BEST: Biologics Effectiveness and Safety System

Vaccine Safety Datalink (VSD)



[Vaccine Safety Datalink (VSD) | VSD | Monitoring | Ensuring Safety | Vaccine Safety | CDC]

- The Vaccine Safety Datalink (VSD) is a collaborative project between CDC's Immunization Safety Office and nine health care organizations.
- Established in 1990
- Large linked database with data on vaccination and medical outcomes
- Objectives of the VSD
  - To conduct research on important vaccine safety questions in large populations
  - To conduct vaccine safety studies that come from questions or concerns in the medical literature or from other vaccine safety systems, like VAERS
  - To monitor possible adverse events when new vaccines are licensed or when there are new vaccine recommendations
  - To provide information to committees who make recommendations for the nation

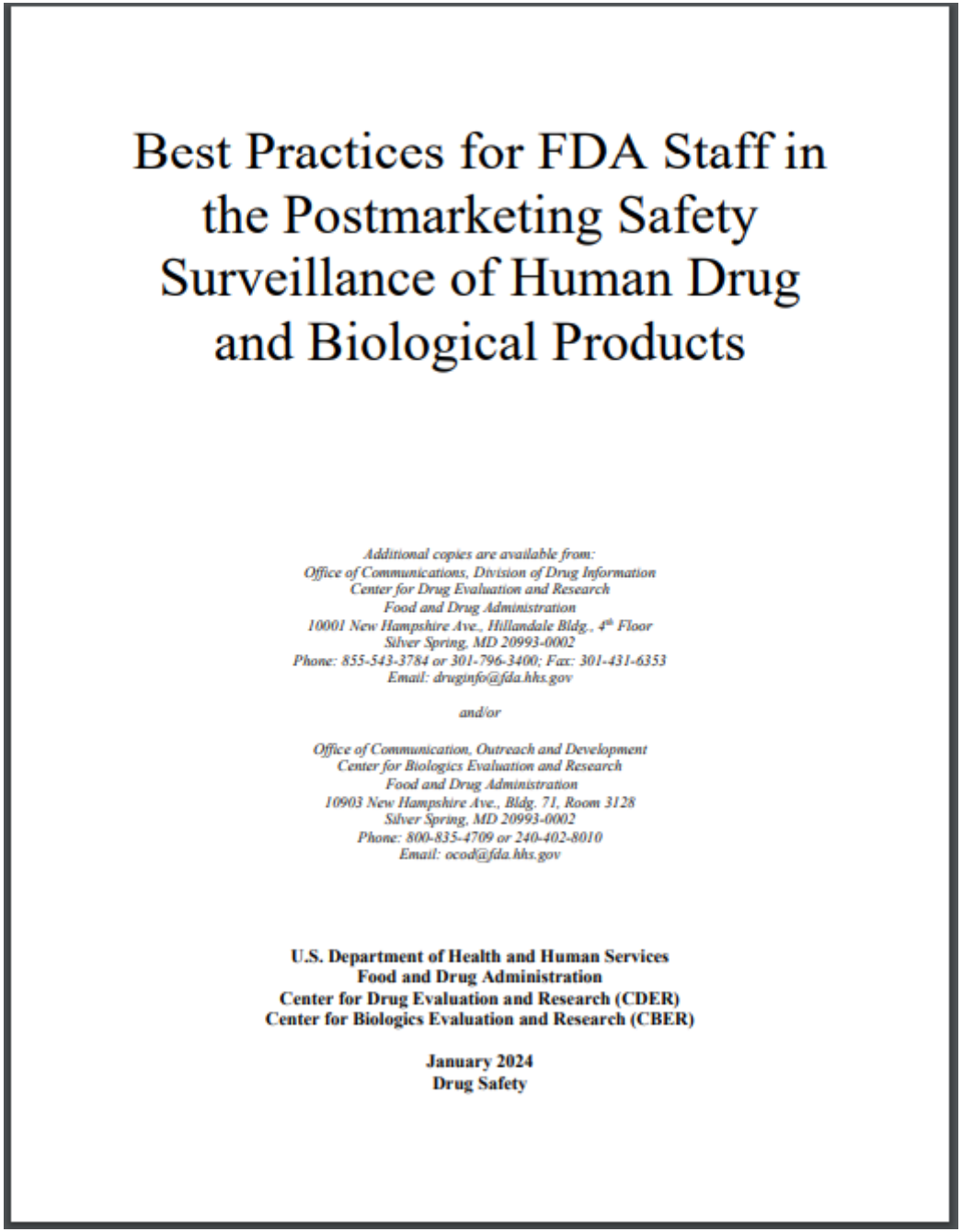
CMS.gov
Centers for Medicare & Medicaid Services

FDA

- Medicare beneficiaries
  - 43 million persons age ≥65 years
  - 9 million persons age <65 with disability or end stage renal disease

- Near real-time surveillance
  - Active surveillance for signal detection
  - Conducted for Guillain Barré syndrome (GBS) after influenza vaccination

Signal Evaluation and Risk Management



Best Practices for FDA Staff in the Postmarketing Safety Surveillance of Human Drug and Biological Products

Additional copies are available from:
Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov

and/or

Office of Communication, Outreach and Development
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 71, Room 3128
Silver Spring, MD 20993-0002
Phone: 800-835-4709 or 240-402-8010
Email: ocod@fda.hhs.gov

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

January 2024
Drug Safety

https://www.fda.gov/media/130216/download

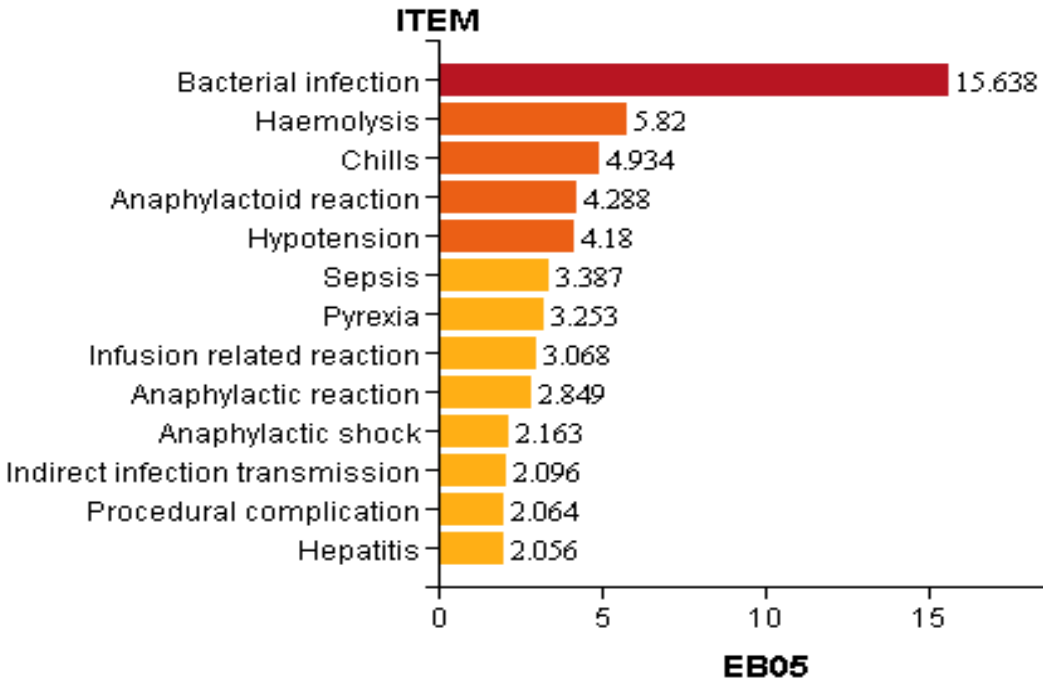
Signal Evaluation

- Postmarket safety issue is defined broadly as information from one or multiple sources which suggests a new potentially causal association, or a new aspect of a known association…that is judged to be of sufficient likelihood to justify verificatory action.
- Medical officers and epidemiologists in CBER perform:
    - Individual case review and aggregate review
    - Case series analysis
        - Unexpected clinical or demographic clustering
        - Is this event new for this product?
        - Biologic plausibility of causal association
        - "Positive re-challenge" reports
        - Absence of alternative explanations (concomitant medications, co- or pre-morbid conditions)
        - How do reporting rates compare with background rates?
    - Aggregate data analysis, including disproportionality analyses
    - Review data from other sources (literature, postmarketing studies)

Data Mining

- Assess the proportion of reports with a specific vaccine –AE pair
- An elevated score does not mean there is a causal association between a product and event, although such an association might exist. This graph shows adverse events, reported for a specific product, with high statistical scores, alerting staff that further investigation may be warranted.
- If data mining score is elevated, the product-AE pair is further evaluated.
  - Unexpected and/or unlabeled?
  - Confounding by indication?
  - Case series analysis

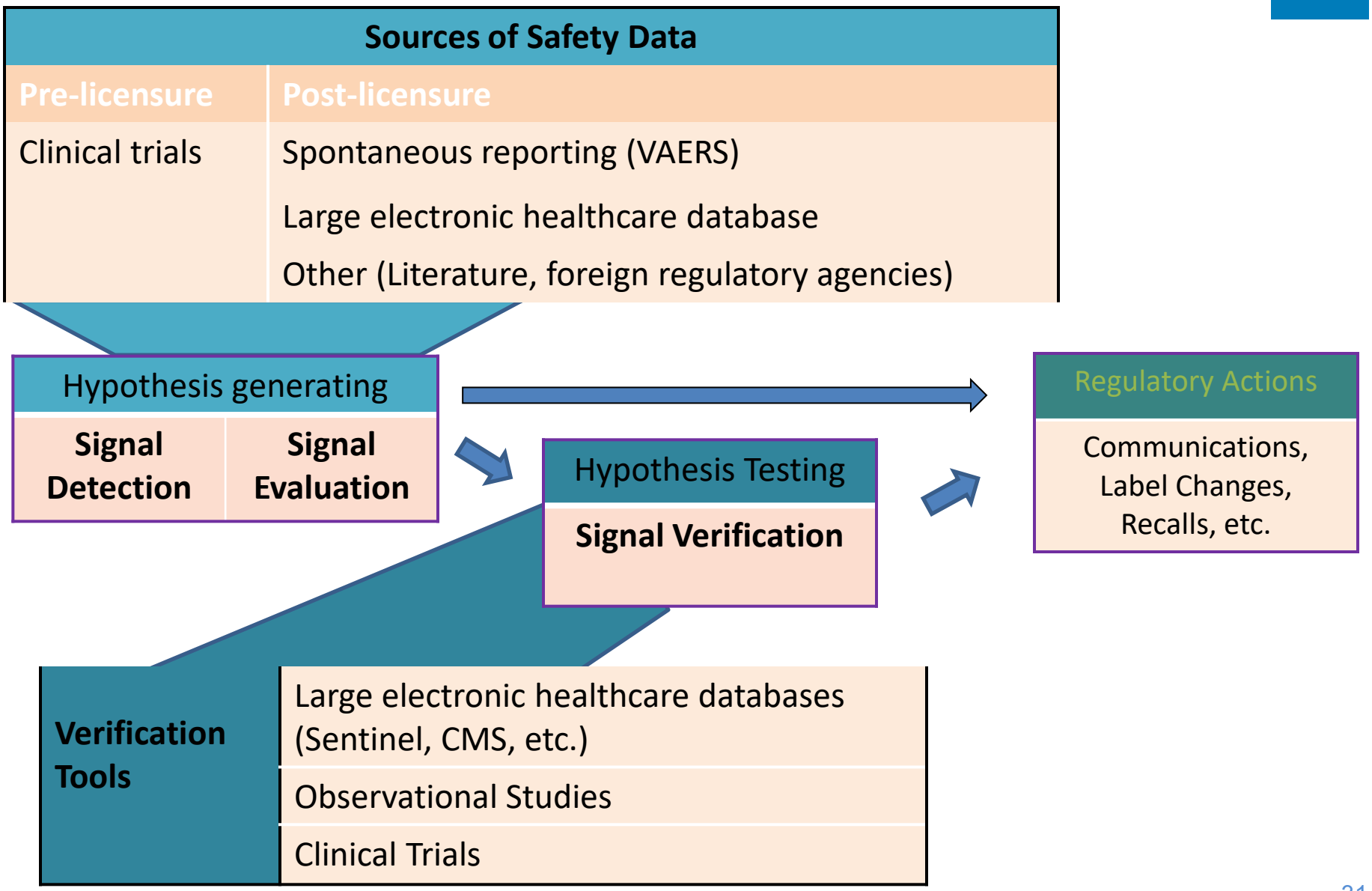
  or epidemiologic study



Signal Evaluation and Risk Management

- Signals generally indicate the **need for further investigation, which may or may not lead to the conclusion that the product caused the event.** After a signal is identified **it should be further assessed** to determine whether it represents a potential risk and whether other action should be taken.
- Regulatory actions include:
  - Communications
  - Label changes
  - Lot recalls
  - Postmarketing requirement (PMR) studies under FDAAA to *assess known serious risk; signals of serious risk; or identify an unexpected serious risk when available data indicates the potential for a serious risk*
  - Postmarketing commitment (PMC) studies agreed upon by FDA and applicant
  - FDA may require sponsors to develop and comply with risk evaluation and mitigation strategies (REMS) to ensure benefits outweigh risks

Signal Detection, Evaluation, and Verification



Examples

U.S. FOOD & DRUG ADMINISTRATION

Original Investigation

FREE

October 7, 2021

Association of Receipt of the Ad26.COV2.S COVID-19 Vaccine With Presumptive Guillain-Barré Syndrome, February-July 2021

Emily Jane Woo, MD, MPH[1]; Adamma Mba-Jonas, MD, MPH[1]; Rositsa B. Dimova, PhD[1]; et al

» Author Affiliations | Article Information

JAMA. 2021;326(16):1606-1613. doi:10.1001/jama.2021.16496

JAMA Network™
JAMA. 2021;326(16):1606-1613. doi:10.1001/jama.2021.16496

From: **Association of Receipt of the Ad26.COV2.S COVID-19 Vaccine With Presumptive Guillain-Barré Syndrome, February-July 2021**

Table 3. Observed to Expected Analysis of Guillain-Barré Syndrome After the Ad26.COV2.S COVID-19 Vaccine[a]

Age groups, y	No.[b]	Vaccine doses administered[c]	Person-years[c]	Background rate per 100 000 person-years	Expected cases	Rate ratio (95% CI)
Onset within 21 days after vaccination						
All (≥18)	105	13 209 858	751 904	2	15.0	6.98 (5.71-8.45)
18-<65	91	11 169 018	635 740	2	12.7	7.16 (5.76-8.78)
18-29	3	2 388 973	135 980	0.88	1.2	2.51 (0.52-7.33)
30-39	10	2 277 609	129 641	1.07	1.4	7.21 (3.46-13.26)
40-49	22	2 345 471	133 504	1.29	1.7	12.77 (8.01-19.34)
50-64	56	4 156 965	236 614	2	4.7	11.83 (8.94-15.37)
≥65	14	2 040 840	116 164	2.4	2.8	5.02 (2.74-8.43)
Onset within 42 days after vaccination						
All (≥18)	123	13 209 858	1 472 162	2	29.4	4.18 (3.47-4.98)
18-<65	105	11 169 018	1 244 722	2	24.9	4.22 (3.45-5.11)
18-29	4	2 388 973	266 237	0.88	2.3	1.70 (0.47-4.37)
30-39	12	2 277 609	253 826	1.07	2.7	4.42 (2.28-7.72)
40-49	25	2 345 471	261 389	1.29	3.4	7.41 (4.80-10.94)
50-64	64	4 156 965	463 270	2	9.3	6.91 (5.32-8.82)
≥65	18	2 040 840	227 440	2.4	5.5	3.30 (1.95-5.21)

[a] In this table, the results using the highest published background rates for each age group were used to illustrate the lowest observed to expected ratio, representing the most conservative estimate of the potential association with the vaccine.

[b] Reports with missing age, missing onset, or onset after 42 days are not included in these calculations. One report had missing age, sex, and onset information but was still deemed a valid report of Guillain-Barré syndrome. For 6 people, the onset time was more than 42 days: 62, 70, 75, 85, 89, or 94 days after vaccination.

[c] Cumulative Vaccine Administration Data.[9] Please see the Methods section. Age-specific dose administration data were obtained from the Centers for Disease Control and Prevention and are shown with permission (F. Lee, MPH, statistician, Centers for Disease Control and Prevention, email September 3, 2021).

Updated Janssen COVID-19 Vaccine EUA Fact Sheets

- July 12, 2021: Authorized EUA Fact Sheets were updated to include new information about GBS

EUA Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers)

5 WARNINGS AND PRECAUTIONS

Subsection '5.3 Guillain-Barré Syndrome' including the following information was added: Reports of adverse events following use of the Janssen COVID-19 Vaccine under emergency use authorization suggest an increased risk of Guillain-Barré syndrome during the 42 days following vaccination.

Section 6 OVERALL SAFETY SUMMARY and *subsection 6.2 Post Authorization Experience* were also updated with information about GBS.

EUA Fact Sheet for Recipients and Caregivers

Section on "WHAT ARE THE RISKS OF THE JANSSEN COVID-19 VACCINE?" was updated to include information under a new subsection entitled "Guillain Barré syndrome"

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CDC 24/7: Saving Lives, Protecting People™

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Vaccines

- Your Vaccination +
- Types of Vaccines Available +
- Possible Side Effects
- After You're Fully Vaccinated +
- Safety & Monitoring −

Selected Adverse Events Reported after COVID-19 Vaccination

Updated Nov. 24, 2021 Languages Print

Safety of COVID-19 Vaccines

Some people have no side effects. Many people have reported side effects that are generally mild to moderate and should go away within a few days.

Are the Vaccines Safe?

[Selected Adverse Events Reported after COVID-19 Vaccination | CDC]

FDA

Get vaccinated. Get your smartphone. Get started with v-safe.

Use your smartphone to tell CDC about any side effects after getting the COVID-19 vaccine. You'll also get reminders if you need an additional dose.

v-safe Overview

V-safe is a smartphone-based tool that uses text messaging and web surveys to give personalized health check-ins after you receive a COVID-19 vaccine. Through **v-safe**, you can quickly tell CDC if you have any side effects after getting a COVID-19 vaccine.

This information helps CDC monitor the safety of COVID-19 vaccines in near real time. Depending on your answers to the **v-safe** questions, someone from CDC may call to check on you or your child and get more information. **V-safe** will also remind you to get additional COVID-19 vaccine doses if you or your child needs one.

[V-safe After Vaccination Health Checker | CDC]

Pediatric Advisory Committee (PAC) meetings

Charter of the Pediatric Advisory Committee to the Food and Drug Administration

Objectives and Scope of Activities

The Pediatric Advisory Committee advises and makes recommendations to the Commissioner or designee in discharging responsibilities as they relate to matters in pediatric therapeutics (including drugs and biological products) and medical devices, pediatric research, pediatric ethical issues and other matters involving pediatrics for which the Food and Drug Administration has regulatory responsibility. The Committee also advises and makes recommendations to the Secretary pursuant to 45 CFR 46.407 on research involving children as subjects that is conducted or supported by the Department of Health and Human Services.

Charter of the Pediatric Advisory Committee to the Food and Drug Administration | FDA

Vaccines and Related Biological Products Advisory Committee (VRBPAC) meetings

The Committee reviews and evaluates data concerning the safety, effectiveness, and appropriate use of vaccines and related biological products which are intended for use in the prevention, treatment, or diagnosis of human diseases, and, as required, any other products for which the Food and Drug Administration has regulatory responsibility. The Committee also considers the quality and relevance of FDA's research program which provides scientific support for the regulation of these products and makes appropriate recommendations to the Commissioner of Food and Drugs.

- Advisory Committee Vacancies, Qualifications, and Experience
- Advisory Committee Calendar

Vaccines and Related Biological Products Advisory Committee | FDA

Examples of Publications

Original Investigation ONLINE FIRST

November 1, 2021

Risk of Guillain-Barré Syndrome Following Recombinant Zoster Vaccine in Medicare Beneficiaries

Ravi Goud, MD, MPH[1]; Bradley Lufkin, MPA, MSES[2]; Jonathan Duffy, MD, MPH[3]; et al

» Author Affiliations

JAMA Intern Med. Published online November 1, 2021. doi:10.1001/jamainternmed.2021.6227

Key Points

Question Is there an increased risk of developing Guillain-Barré Syndrome (GBS) following vaccination with the recombinant zoster vaccine (RZV)?

Findings In an observational study of Medicare beneficiaries, a medical record-based, self-controlled analysis of GBS cases after RZV vaccination identified a rate ratio of 2.84 between the risk and control windows, resulting in an attributable risk of 3 cases per million RZV (Shingrix) doses.

Meaning These findings suggest that there is an increased risk of developing GBS following vaccination with RZV.

RESEARCH LETTER

Administration of the GSK Respiratory Syncytial Virus Vaccine to Pregnant Persons in Error

Moro, Pedro L. MD, MPH; Gallego, Ruth RN, MPH; Scheffey, Anne MPH, BSN; Fleming-Dutra, Katherine E. MD; Hall, Elisha PhD, MS; Zhang, Bicheng MS; Marquez, Paige MSPH; Jones, Jefferson M. MD; Nair, Narayan MD, BS; Broder, Karen R. MD

Author Information

Obstetrics & Gynecology ():10.1097/AOG.0000000000005551, February 23, 2024. | ***DOI:*** 10.1097/AOG.0000000000005551

BUY SDC PAP Metrics

Abstract **In Brief**

The GSK and Pfizer respiratory syncytial virus (RSV) vaccines are both indicated for adults aged 60 years and older, but only the Pfizer product is approved for use in pregnancy to prevent RSV-associated lower respiratory tract disease in infants aged younger than 6 months. To assess for vaccine administration errors (ie, administration of the GSK RSV vaccine to pregnant persons) VAERS (Vaccine Adverse Event Reporting System), a U.S. passive reporting system, was searched for the time period from August 2023 to January 2024. A total of 113 reports of these administration errors were identified. Most reports (103, 91.2%) did not describe an adverse event. These administration errors are preventable with proper education and training and other preventive measures.

Example of a Protocol-Based Assessment in Sentinel, Leading to FDA Safety Communication and Label Change

FDA Releases Final Study Results of a Mini-Sentinel Postlicensure Observational Study of Rotavirus Vaccines and Intussusception

FDA Safety Communication — June 13, 2013

FDA Releases Final Study Results of a Mini-Sentinel Postlicensure Observational Study of Rotavirus Vaccines and Intussusception

FDA Approves Required Revised Labeling for RotaTeq Based on the Study Results

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 6, 2014 VOL. 370 NO. 6

Intussusception Risk after Rotavirus Vaccination in U.S. Infants

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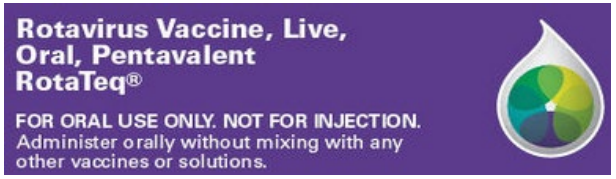
"The risks of intussusception must be considered in light of the demonstrated benefits of rotavirus vaccination."



RotaTeq label change:

"Cases of intussusception were observed in temporal association within 21 days following the first dose of RotaTeq, with a clustering of cases in the first 7 days. …Approximately 1 to 1.5 excess cases of intussusception occur per 100,000 vaccinated US infants within 21 days following the first dose of RotaTeq. In the first year of life, the background rate of intussusception hospitalizations in the US has been estimated to be approximately 34 per 100,000 infants."

FDA: Drug Safety Information to the Public

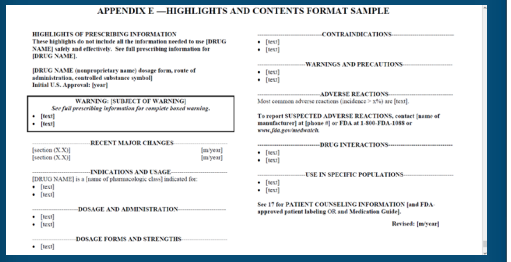
FAERS Public Dashboard [1]

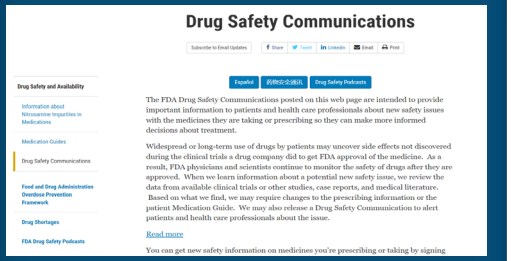
An interactive web-based tool that allows for the querying of FAERS data

Potential Signals [2]

FDA shares early safety signals or potential signals identified through FAERS

Communications [3, 4]





U.S. Prescribing information, Drug Safety Communications, and other communication tools

Resources

[1] https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard
[2] https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/potential-signals-serious-risksnew-safety-information-identified-fda-adverse-event-reporting-system
[3] https://www.fda.gov/drugs/drug-safety-and-availability/drug-safety-communications
[4] https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm

All accessed May 4, 2023

Source: https://www.fda.gov/media/169322/download

Acknowledgement: Neha Gada, PharmD, BCPS, Cross Discipline Safety Advisor, Office of Surveillance and Epidemiology/CDER

Examples of Postmarketing Studies

- Postmarketing **commitment** (PMC) study

- Fluarix Quadrivalent (Approval letter, December 14, 2012)

AGREED UPON POSTMARKETING COMMITMENTS

"To establish a pregnancy registry to prospectively collect data on spontaneously-reported exposures to Fluarix® Quadrivalent during pregnancy."

- **Required** postmarketing (PMR) safety study

- Comirnaty (Approval letter, August 23, 2021)

Section 505(o) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)).

"Study C4591036, a prospective cohort study with at least 5 years of follow-up for potential long-term sequelae of myocarditis after vaccination (in collaboration with Pediatric Heart Network)."

Summary and Conclusions

Summary

- Despite rigorous safety evaluation during premarket phases of clinical development, postmarketing safety monitoring is necessary due to limitations of clinical trials.
- Postmarketing surveillance includes many approaches including passive and active surveillance.
- FDA may require postmarketing studies by manufacturers.
- New databases have expanded population-based surveillance capabilities
- FDA and CDC share many vaccine surveillance activities.
- **Our overall goal to ensure safe and effective products!**