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of PUBLIC HEALTH

Pharmacovigilance: Passive Surveillance

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Contents

What Is Passive Surveillance?

Passive Surveillance—1

- Spontaneous (voluntary) reporting of adverse events / adverse drug reactions directly to either established national or regional centers or to pharmaceutical manufacturers
- The most common form of pharmacovigilance

Passive Surveillance—2

- The use of term “spontaneous” is because the person who initially reports the adverse event / adverse drug reaction chooses what events to report
  - Reporting is entirely dependent on the initiative and motivation of the potential reporters
  - No specific efforts are made to make sure all cases are reported

- Spontaneous reporting systems are labeled as “passive”
  - Based on the argument that the reporting center or manufacturers “passively receive” this information rather than actively seeking it out

Passive Surveillance—3

- However, many pharmacovigilance centers seek to operate, even if resource constraints limit the ability to interact adequately with reporters
- Most countries have mandated reporting from manufacturers
- Clinicians, pharmacists, and community members should be trained on how, when, what, and where to report

Passive Surveillance System in the United States

MedWatch: National Passive Surveillance Program in the United States

- The US Food and Drug Administration (FDA)'s medical product safety reporting program for health care professionals, patients, and consumers (founded in 1993)
- Voluntary reports are submitted by consumers and health care professionals (~6% of all reports)
- Mandatory reports are submitted by manufacturers (~94% of all reports)

Source: Chew, C., for the US Food and Drug Administration. (n.d.). The small print: How to report side effects, find drug information and engage with CDER [presentation]. https://www.fda.gov/media/97287/download

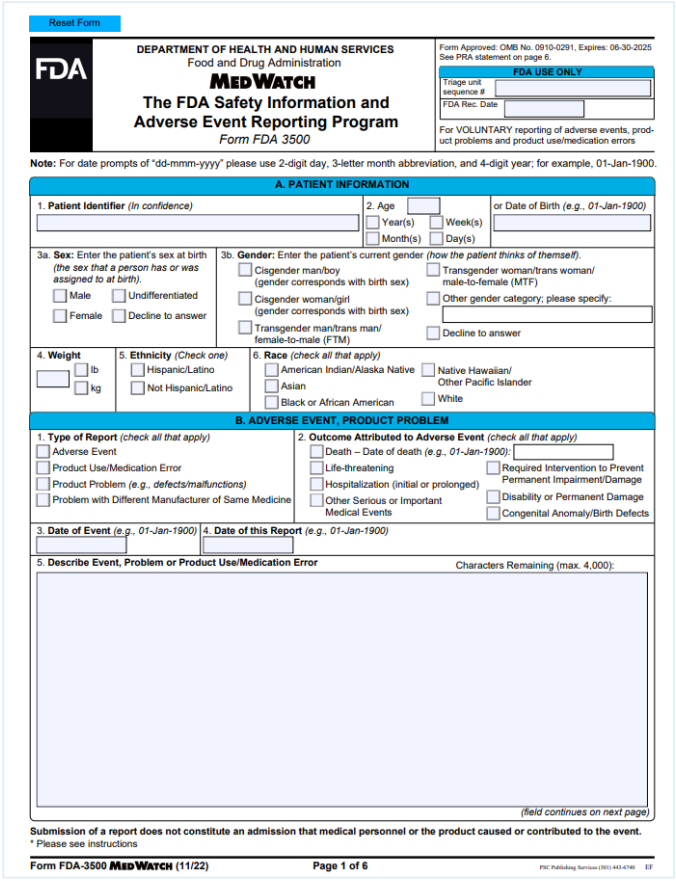
Goals of the MedWatch Program

- Increase awareness of adverse events and importance of reporting
- Clarify what should be reported
- Convenient reporting of adverse drug events (Forms 3500 and 3500A)
  - Available via online and paper (postage-paid) forms
- Provide timely and clinically useful safety information to providers and patients

MedWatch Online Voluntary Reporting Form

Source: US Food and Drug Administration. (n.d.). MedWatch Online Voluntary Reporting Form. https://www.accessdata.fda.gov/scripts/medwatch/index.cfm

MedWatch Voluntary Reporting Form for Health Care Professionals



Reset Form

FDA

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
MEDWATCH
The FDA Safety Information and Adverse Event Reporting Program
Form FDA 3500

Form Approved: OMB No. 0910-0291, Expires: 06-30-2025
See PRA statement on page 6.

FDA USE ONLY
Triage unit sequence #
FDA Rec. Date

For VOLUNTARY reporting of adverse events, product problems and product use/medication errors

Note: For date prompts of "dd-mmm-yyyy" please use 2-digit day, 3-letter month abbreviation, and 4-digit year; for example, 01-Jan-1900.

A. PATIENT INFORMATION

1. **Patient Identifier** *(In confidence)*
2. Age ☐ Year(s) ☐ Week(s) ☐ Month(s) ☐ Day(s) or Date of Birth *(e.g., 01-Jan-1900)*

3a. **Sex:** Enter the patient's sex at birth *(the sex that a person has or was assigned to at birth).*
☐ Male ☐ Undifferentiated ☐ Female ☐ Decline to answer

3b. **Gender:** Enter the patient's current gender *(how the patient thinks of themself).*
☐ Cisgender man/boy (gender corresponds with birth sex)
☐ Cisgender woman/girl (gender corresponds with birth sex)
☐ Transgender man/trans man/female-to-male (FTM)
☐ Transgender woman/trans woman/male-to-female (MTF)
☐ Other gender category; please specify:
☐ Decline to answer

4. **Weight** ☐ lb ☐ kg
5. **Ethnicity** *(Check one)* ☐ Hispanic/Latino ☐ Not Hispanic/Latino
6. **Race** *(check all that apply)* ☐ American Indian/Alaska Native ☐ Asian ☐ Black or African American ☐ Native Hawaiian/Other Pacific Islander ☐ White

B. ADVERSE EVENT, PRODUCT PROBLEM

1. **Type of Report** *(check all that apply)*
☐ Adverse Event
☐ Product Use/Medication Error
☐ Product Problem *(e.g., defects/malfunctions)*
☐ Problem with Different Manufacturer of Same Medicine

2. **Outcome Attributed to Adverse Event** *(check all that apply)*
☐ Death – Date of death *(e.g., 01-Jan-1900)*:
☐ Life-threatening
☐ Hospitalization (initial or prolonged)
☐ Other Serious or Important Medical Events
☐ Required Intervention to Prevent Permanent Impairment/Damage
☐ Disability or Permanent Damage
☐ Congenital Anomaly/Birth Defects

3. **Date of Event** *(e.g., 01-Jan-1900)*
4. **Date of this Report** *(e.g., 01-Jan-1900)*

5. **Describe Event, Problem or Product Use/Medication Error** Characters Remaining (max. 4,000):

(field continues on next page)

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.
* Please see instructions

Form FDA-3500 MEDWATCH (11/22) Page 1 of 6

C. PRODUCT AVAILABILITY

1. **Product Available for Evaluation?** *(Do not send product to FDA)* ☐ Yes ☐ No ☐ Returned to Manufacturer on *(e.g., 01-Jan-1900)*
2. **Do you have a picture of the product?** (Check if you are including a picture) ☐ Yes

D. SUSPECT PRODUCTS

SUSPECT PRODUCT #1

This report involves: ☐ Cosmetic ☐ Dietary supplement ☐ Food/medical food ☐ Other

1. **Name, Strength, Manufacturer/Compounder** *(from product label).*
Product Name | Strength | Unit
NDC # or Unique ID | Manufacturer/ Compounder Name | Lot #
2. **Dose or Amount** | **Frequency** | **Route**
Unit | **Other Frequency** | **Other Route**
3. **Treament Dates/Therapy Dates** *(give best estimate of length of treatment (start/stop) or date of dose reduction.)*
Therapy started on *(e.g., 01-Jan-1900)* | Therapy stopped on *(e.g., 01-Jan-1900)* | Dose reduced on *(e.g., 01-Jan-1900)* | **OR** Duration | Unit
Is therapy still on-going? ☐ Yes ☐ No
4. **Diagnosis for use** *(indication)*
5. **Product Type** *(check all that apply)* ☐ OTC ☐ Compounded ☐ Generic ☐ Biosimilar
6. **Expiration Date** *(e.g., 01-Jan-1900)*
7. **Event Abated after use Stopped or Dose Reduced?** ☐ Yes ☐ No ☐ Doesn't apply
8. **Event Reappeared after Reintroduction?** ☐ Yes ☐ No ☐ Doesn't apply

SUSPECT PRODUCT #2

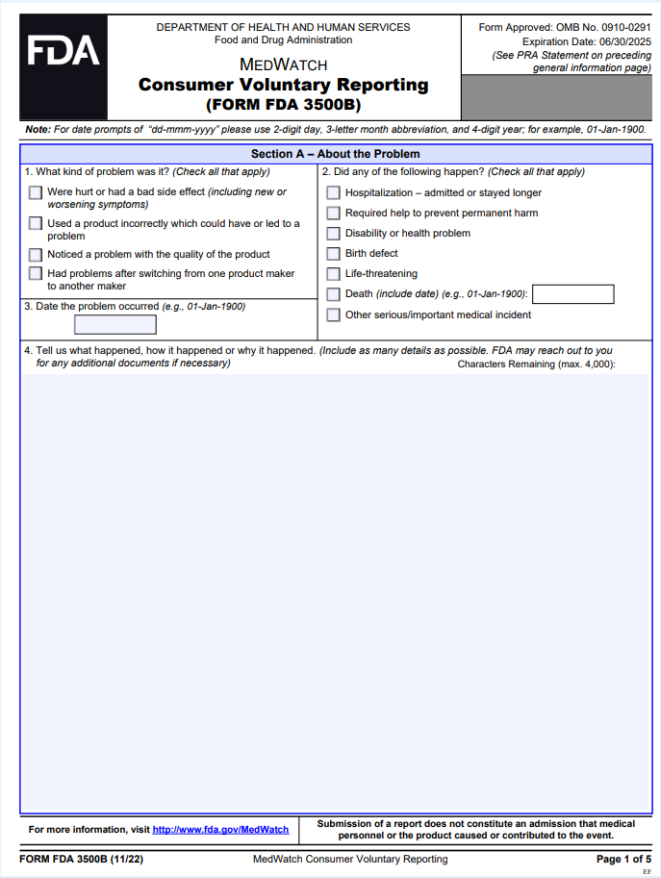
This report involves: ☐ Cosmetic ☐ Dietary supplement ☐ Food/medical food ☐ Other

1. **Name, Strength, Manufacturer/Compounder** *(from product label).*
Product Name | Strength | Unit
NDC # or Unique ID | Manufacturer/ Compounder Name | Lot #
2. **Dose or Amount** | **Frequency** | **Route**
Unit | **Other Frequency** | **Other Route**
3. **Treament Dates/Therapy Dates** *(give best estimate of length of treatment (start/stop) or date of dose reduction.)*
Therapy started on *(e.g., 01-Jan-1900)* | Therapy stopped on *(e.g., 01-Jan-1900)* | Dose reduced on *(e.g., 01-Jan-1900)* | **OR** Duration | Unit
Is therapy still on-going? ☐ Yes ☐ No
4. **Diagnosis for use** *(indication)*
5. **Product Type** *(check all that apply)* ☐ OTC ☐ Compounded ☐ Generic ☐ Biosimilar
6. **Expiration Date** *(e.g., 01-Jan-1900)*
7. **Event Abated after use Stopped or Dose Reduced?** ☐ Yes ☐ No ☐ Doesn't apply
8. **Event Reappeared after Reintroduction?** ☐ Yes ☐ No ☐ Doesn't apply

Form FDA-3500 MEDWATCH (11/22) Page 3 of 6 *(continued on next page)*

Source: US Food and Drug Administration. (2024). MedWatch Forms for FDA Safety Reporting. https://www.fda.gov/safety/medical-product-safety-information/medwatch-forms-fda-safety-reporting

MedWatch Voluntary Reporting Forms for Consumers/ Patients and Industry



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Form Approved: OMB No. 0910-0291
Expiration Date: 06/30/2025
(See PRA Statement on preceding general information page)

MEDWATCH
Consumer Voluntary Reporting
(FORM FDA 3500B)

Note: *For date prompts of "dd-mmm-yyyy" please use 2-digit day, 3-letter month abbreviation, and 4-digit year; for example, 01-Jan-1900.*

Section A – About the Problem

1. What kind of problem was it? *(Check all that apply)*
   - Were hurt or had a bad side effect *(including new or worsening symptoms)*
   - Used a product incorrectly which could have or led to a problem
   - Noticed a problem with the quality of the product
   - Had problems after switching from one product maker to another maker

2. Did any of the following happen? *(Check all that apply)*
   - Hospitalization – admitted or stayed longer
   - Required help to prevent permanent harm
   - Disability or health problem
   - Birth defect
   - Life-threatening
   - Death *(include date)* *(e.g., 01-Jan-1900)*:
   - Other serious/important medical incident

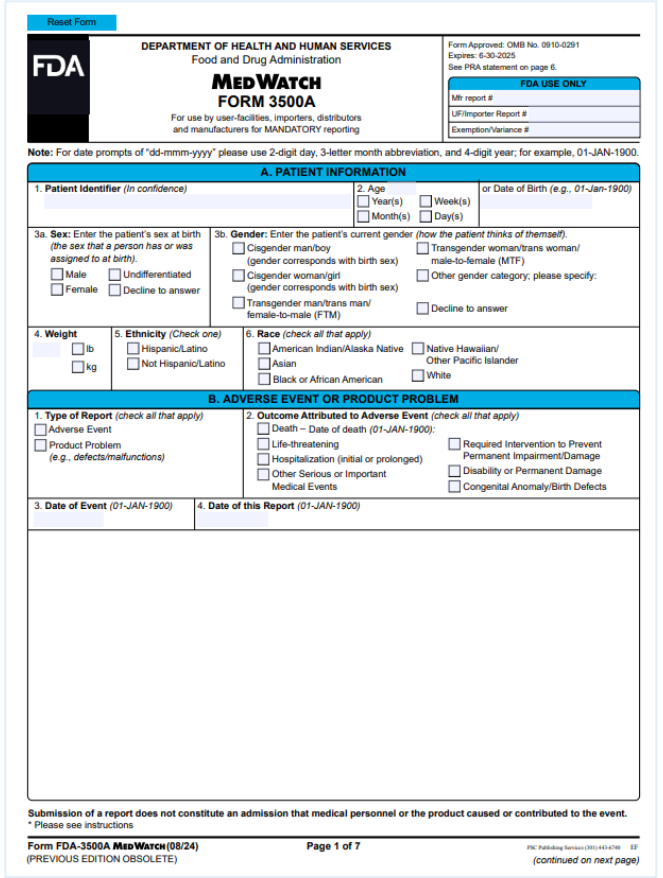
3. Date the problem occurred *(e.g., 01-Jan-1900)*

4. Tell us what happened, how it happened or why it happened. *(Include as many details as possible. FDA may reach out to you for any additional documents if necessary)*
   Characters Remaining (max. 4,000):

For more information, visit http://www.fda.gov/MedWatch

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

FORM FDA 3500B (11/22) MedWatch Consumer Voluntary Reporting **Page 1 of 5**



Reset Form

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Form Approved: OMB No. 0910-0291
Expires: 6-30-2025
See PRA statement on page 6.

FDA USE ONLY
Mfr report #
LIF/Importer Report #
Exemption/Variance #

MEDWATCH
FORM 3500A
For use by user-facilities, importers, distributors and manufacturers for MANDATORY reporting

Note: For date prompts of "dd-mmm-yyyy" please use 2-digit day, 3-letter month abbreviation, and 4-digit year; for example, 01-JAN-1900.

A. PATIENT INFORMATION

1. **Patient Identifier** *(In confidence)*
2. Age ☐ Year(s) ☐ Week(s) ☐ Month(s) ☐ Day(s) or Date of Birth *(e.g., 01-Jan-1900)*

3a. **Sex:** Enter the patient's sex at birth *(the sex that a person has or was assigned to at birth)*.
☐ Male ☐ Female ☐ Undifferentiated ☐ Decline to answer

3b. **Gender:** Enter the patient's current gender *(how the patient thinks of themself)*.
☐ Cisgender man/boy (gender corresponds with birth sex)
☐ Cisgender woman/girl (gender corresponds with birth sex)
☐ Transgender man/trans man/ female-to-male (FTM)
☐ Transgender woman/trans woman/ male-to-female (MTF)
☐ Other gender category; please specify:
☐ Decline to answer

4. **Weight** ☐ lb ☐ kg
5. **Ethnicity** *(Check one)* ☐ Hispanic/Latino ☐ Not Hispanic/Latino
6. **Race** *(check all that apply)* ☐ American Indian/Alaska Native ☐ Asian ☐ Black or African American ☐ Native Hawaiian/ Other Pacific Islander ☐ White

B. ADVERSE EVENT OR PRODUCT PROBLEM

1. **Type of Report** *(check all that apply)*
   ☐ Adverse Event
   ☐ Product Problem *(e.g., defects/malfunctions)*

2. **Outcome Attributed to Adverse Event** *(check all that apply)*
   ☐ Death – Date of death *(01-JAN-1900)*:
   ☐ Life-threatening
   ☐ Hospitalization (initial or prolonged)
   ☐ Other Serious or Important Medical Events
   ☐ Required Intervention to Prevent Permanent Impairment/Damage
   ☐ Disability or Permanent Damage
   ☐ Congenital Anomaly/Birth Defects

3. **Date of Event** *(01-JAN-1900)*
4. **Date of this Report** *(01-JAN-1900)*

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.
* Please see instructions

Form FDA-3500A MEDWATCH (08/24) **Page 1 of 7**
(PREVIOUS EDITION OBSOLETE)
(continued on next page)

Source: US Food and Drug Administration. (2024). MedWatch Forms for FDA Safety Reporting. https://www.fda.gov/safety/medical-product-safety-information/medwatch-forms-fda-safety-reporting

What Should Be Reported to MedWatch

- Unexpected side effects or adverse events (e.g., everything from skin rashes to more serious complications)
- Product quality problems
- Product use/medication errors that can be prevented (e.g., choosing the wrong product because of labels of packaging that look alike or have similar brand or generic names)
- Therapeutic failures

Source: US Food and Drug Administration. (n.d.). MedWatch Online Voluntary Reporting Form. https://www.accessdata.fda.gov/scripts/medwatch/index.cfm

Types of Products That Should Be Reported to MedWatch

- Events associated with:
  - Prescription and over-the-counter medicines, including those administered in a hospital or outpatient infusion centers
  - Biologics (e.g., blood components, blood/plasma derivatives, blood transfusions, gene therapies, and human cells and tissue transplants)
  - Medical devices (e.g., diabetes glucose-test kit, hearing aids, breast pumps)
  - Combination products (e.g., prefilled drug syringe, auto-injectors, metered-dose inhalers, contact lens coated with a drug, and nasal spray)
  - Cosmetics (e.g., moisturizers, makeup, shampoo, conditioners, hair dyes, and tattoos)
  - Food (e.g., beverages and ingredients added to foods)

Source: US Food and Drug Administration. (n.d.). MedWatch Online Voluntary Reporting Form. https://www.accessdata.fda.gov/scripts/medwatch/index.cfm

US Mandatory Reporting Requirements for Manufacturers

- All adverse events must be reported to FDA by industry
  - 15-day alert reports: serious and unexpected adverse events from all sources (foreign and domestic)
  - Periodic adverse events reports (domestic only): quarterly for the first three years, then annually
    - Serious and expected
    - Nonserious and unexpected
    - Nonserious and expected

FDA Adverse Event Reporting System (FAERS)

- A computerized database designed to support FDA's postmarketing safety surveillance program for human drug and therapeutic biologic products
- Contains information on spontaneous adverse event reports and medication error reports submitted to FDA
- FAERS data is available to the public
  - FAERS dashboard: a highly interactive web-based tool that allows for the querying of FAERS data in a user-friendly fashion
  - FAERS data files: provide raw data extracted from the FAERS database
  - Individual case safety reports from the FAERS database can also be obtained by sending a request to FDA

Source: US Food and Drug Administration. (2024). FDA's Adverse Event Reporting System (FAERS). https://www.fda.gov/drugs/surveillance/questions-and-answers-fdas-adverse-event-reporting-system-faers

FAERS Public Dashboard

FDA Adverse Events Reporting System (FAERS) Public Dashboard

U.S. FOOD & DRUG ADMINISTRATION

Home | Search | Disclaimer | Report a Problem | FAQ | Site Feedback

Total Reports: 29,153,222

Serious Reports (excluding death): 16,130,758

Death Reports: 2,650,057

Reports by Report Type

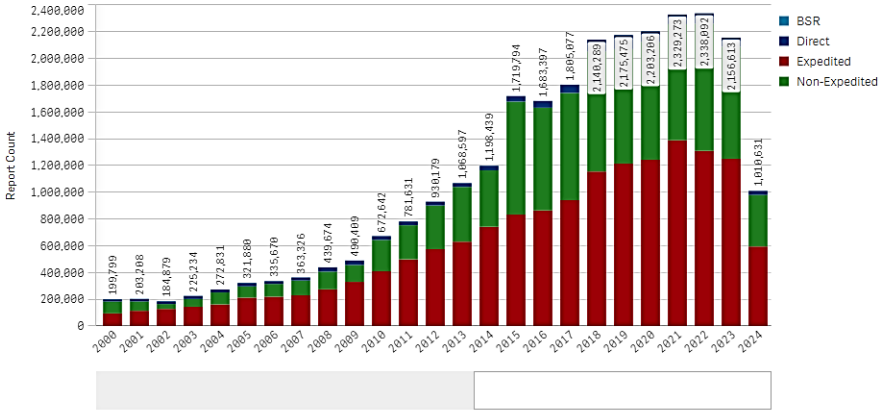
All Years | Last 10 Years

Reports received by Report Type

Year | Report Type

	Total Reports	Expedited	Non-Expedited	Direct	BSR
Total Reports	**29,153,222**	**15,957,059**	**11,911,258**	**1,284,042**	**863**
2024	**1,010,631**	595,177	385,238	30,216	-
2023	**2,156,613**	1,249,616	838,367	68,630	-
2022	**2,338,092**	1,309,886	950,927	78,079	-
2021	**2,329,273**	1,388,575	868,149	72,549	-
2020	**2,203,206**	1,242,465	882,181	78,560	-
2019	**2,175,475**	1,215,211	854,876	105,388	-
2018	**2,140,289**	1,155,398	897,340	87,551	-
2017	**1,885,077**	941,842	801,205	62,030	-
2016	**1,683,397**	863,293	769,113	50,991	-
2015	**1,719,794**	833,115	845,020	41,659	-
2014	**1,198,439**	741,485	422,724	34,230	-
2013	**1,068,597**	631,162	409,045	28,390	-
2012	**930,179**	574,943	326,224	29,012	-
2011	**781,631**	498,424	255,165	28,042	-
2010	**672,642**	409,065	234,633	28,944	-

Reports received by Report Type



Data as of June 30, 2024

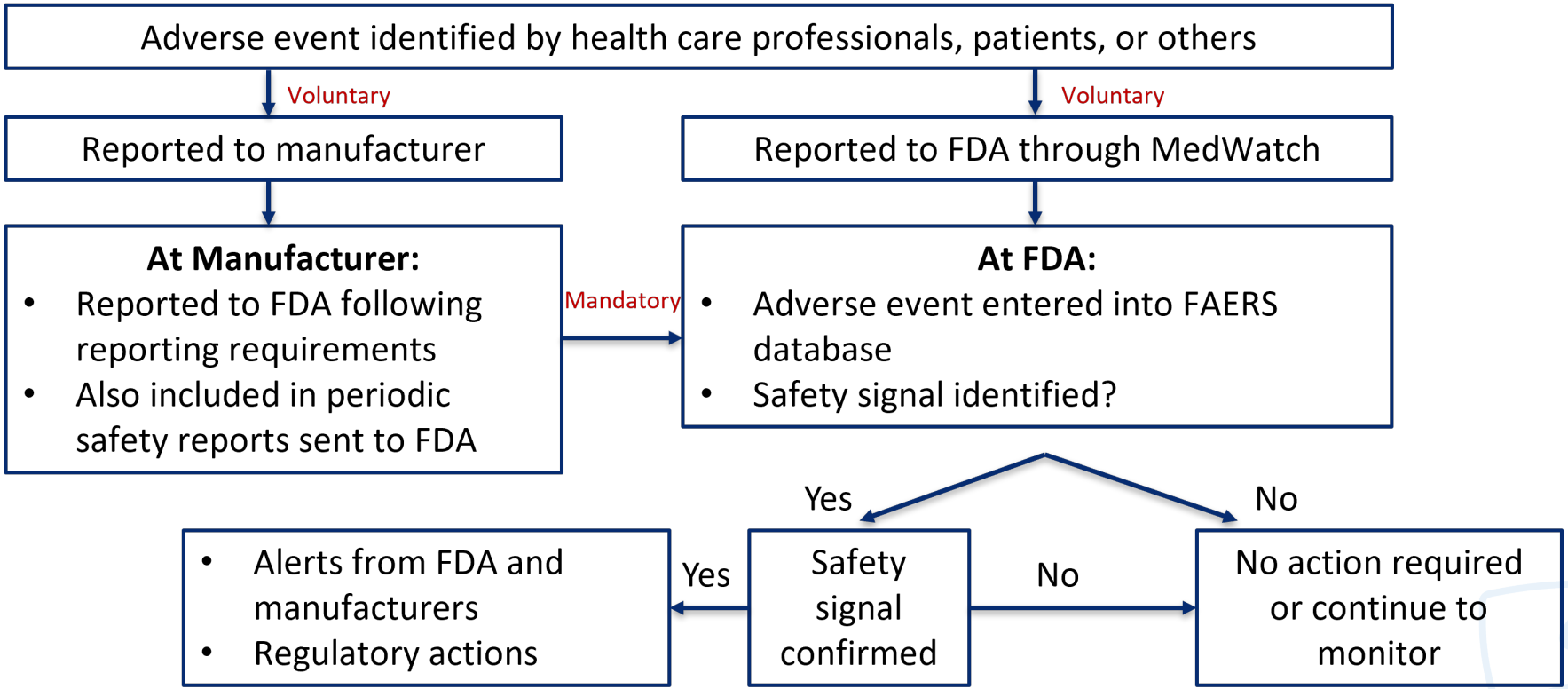
Vulnerability Disclosure Policy

Source: US Food and Drug Administration. (n.d.). FDA Adverse Events Reporting System (FAERS) Public Dashboard. Data as of June 30, 2024. https://fis.fda.gov/sense/app/95239e26-e0be-42d9-a960-9a5f7f1c25ee/sheet/7a47a261-d58b-4203-a8aa-6d3021737452/state/analysis

What Happens After a Report Is Made to MedWatch?

- FDA staff in Center for Drug Evaluation and Research (CDER) regularly monitor FAERS database
- Potential serious risks are communicated in a quarterly report
- FDA continues evaluation and issues public communications as appropriate

Summary


Adverse event identified by health care professionals, patients, or others
Voluntary
Voluntary
Reported to manufacturer
Reported to FDA through MedWatch
At Manufacturer:
• Reported to FDA following reporting requirements
• Also included in periodic safety reports sent to FDA
Mandatory
At FDA:
• Adverse event entered into FAERS database
• Safety signal identified?
Yes
No
• Alerts from FDA and manufacturers
• Regulatory actions
Yes
Safety signal confirmed
No
No action required or continue to monitor

Other Reporting Systems in the United States

- Joint Commission Sentinel Event Reporting System
- Maryland Department of Health and Human Hygiene
- Institute for Safe Medication Practices (ISMP) Medication Errors Reporting System
- US Pharmacopeia (USP) MEDMARX
- Veteran Affairs Patient Safety Reporting System

Worldwide Passive Surveillance System

The World Health Organization Programme for International Drug Monitoring (WHO PIDM)

- A global collaboration for patient safety
- Established in 1968
- The goals are
  - To monitor and identify medicine- and vaccine-related safety problems
  - To establish worldwide pharmacovigilance standards and systems
- >170 full members and associate members in the programme (countries and regions)
- Covers ~99% of the world's population

Source: World Health Organization. (n.d.). Regulation and Prequalification: What Is Pharmacovigilance? https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance

Uppsala Monitoring Centre (UMC)

- The WHO Collaborating Centre for International Drug Monitoring
  - Self-funded, nonprofit organization, founded by WHO and the Swedish government in 1978

- Activities include:
  - Supporting WHO in scientific development and in its activities in the WHO PIDM relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem
  - Under WHO's guidance, providing pharmacovigilance tools and services and delivering efficient access to information in VigiBase, WHO's global database of reported potential side effects of medicinal products
  - Assisting WHO by contributing to capacity-building activities relevant to the framework of the WHO PIDM
  - Supporting WHO drug-risk mitigation strategies for low-and middle-income countries in the WHO PIDM

Source: Uppsala Monitoring Centre (UMC). (n.d.). A global collaboration for patient safety. https://who-umc.org/about-the-who-programme-for-international-drug-monitoring/about-the-who-pidm/

VigiBase

- The richest source of pharmacovigilance data in the world
- WHO PIDM members submit reports of suspected adverse drug reactions to WHO's database, VigiBase
- A few million reports annually
- VigiBase is used to find "signals" of potential adverse effects of medicines and vaccines (VigiFlow: internet-based data management tool)
- Has benefit of pooling reports in a big, global database
  - Safety signals might emerge from the large account of worldwide data that might not be evident in smaller national databases
  - Includes US databases FAERS and VAERS (Vaccine Adverse Event Reporting System), Europe's EudraVigilance, and many national databases from across Asia, Africa, Latin America, and Oceania

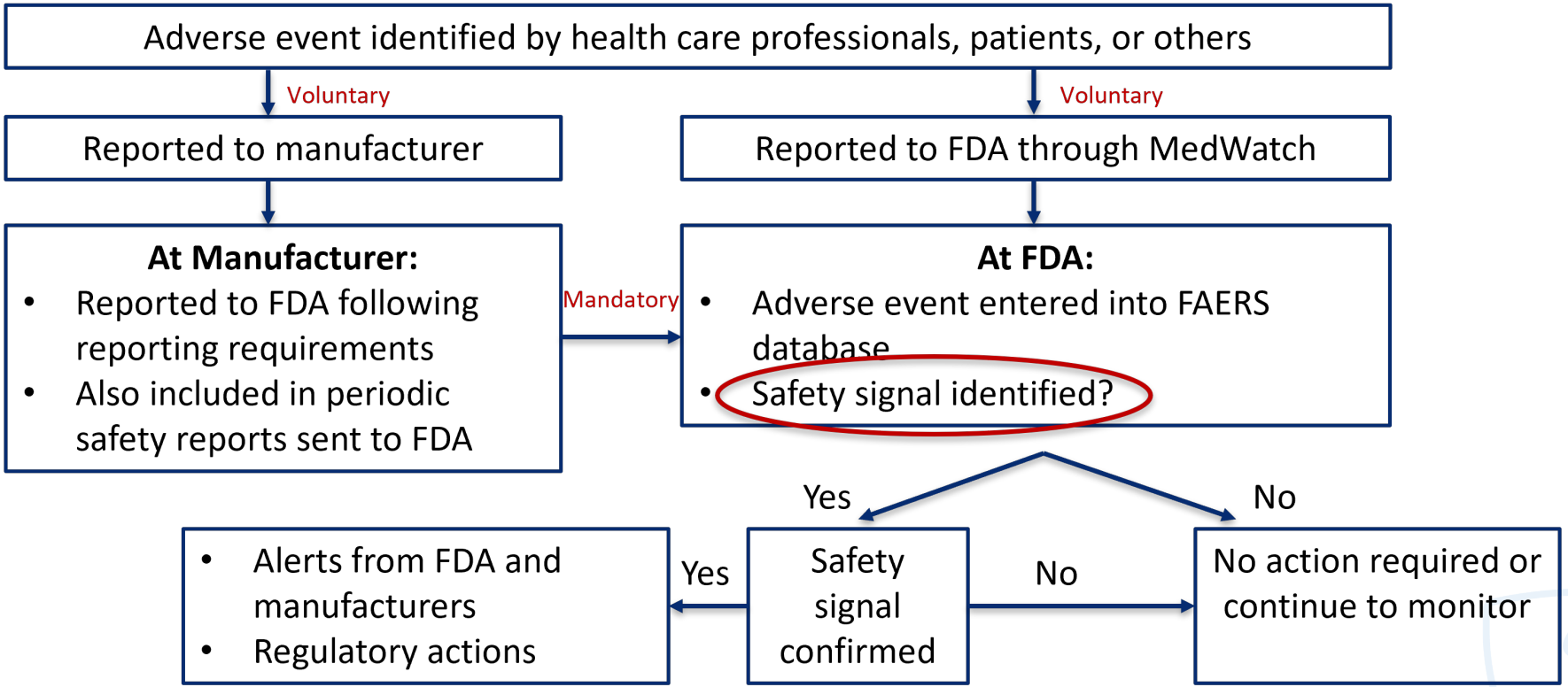
Source: Uppsala Monitoring Centre (UMC). (n.d.). VigiBase Services. https://who-umc.org/vigibase/vigibase-services/

The WHO PIDM in Focus: Building a Global Community

Source: Uppsala Monitoring Centre. (n.d.). The WHO PIDM in Focus—Building a global community—YouTube. Retrieved February 27, 2025, from https://youtu.be/9Gtc9Nno6X8

Analyses of Passively Reported Events

Summary (Revisit)



Safety Signal (Revisit)

- "Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously" (WHO)
  - Usually supported by multiple case reports
  - New unlabeled adverse events
  - An observed increase in a labeled event or a greater severity
  - New interactions
  - Newly identified at-risk population

- Generates hypothesis, which calls for future work to be performed to evaluate that hypothesis

Source: World Health Organization. (2002). *The Importance of Pharmacovigilance. Safety Monitoring of Medicinal Products*. Geneva: WHO.

Disproportionality Analysis: Proportional Reporting Ratio (PRR)

- The degree of disproportionate reporting of an adverse event for a product of interest compared with this same event for a comparison drug in the database

$$PRR = \frac{\%\ of\ all\ adverse\ drug\ event\ reports\ that\ are\ the\ event\ of\ interest\ with\ exposure\ to\ a\ drug\ of\ interest}{\%\ of\ all\ adverse\ drug\ event\ reports\ that\ are\ the\ event\ of\ interest\ with\ exposure\ to\ a\ comparison\ drug\ or\ class\ of\ drugs}$$

- Proportional reporting ratio (PRR) >1 indicates increased risk of the drug of interest

Calculation of Proportional Reporting Ratio (PRR)

	Event of interest	All other events	Total
Drug A	a	b	a + b
Comparison drugs	c	d	c + d

$$PRR = \frac{a/(a+b)}{c/(c+d)}$$

Example: Proportional Reporting Ratio (PRR)

- Want to assess whether myocardial infarction is more strongly associated with drug A versus other drugs in its drug class

	Myocardial infarction	All other events	Total
Drug A	83	1,273	1,356
Other 4 drugs in the same class	1,489	52,300	53,789

$$PRR = \frac{83/1{,}356}{1{,}489/53{,}789} = \frac{6.1\%}{2.8\%} = 2.18$$

Disproportionality Analysis: Reporting Odds Ratio (ROR)

	Adverse event of interest	All other adverse events
Drug A	a	b
Comparison drugs	c	d

$$ROR = \frac{a/b}{c/d}$$

Example: Reporting Odds Ratio (ROR)

- Want to assess whether myocardial infarction is more strongly associated with drug A versus other drugs in its drug class

	Myocardial infarction	All other events	Total
Drug A	83	1,273	1,356
Other 4 drugs in the same class	1,489	52,300	53,789

$$ROR = \frac{83/1{,}273}{1{,}489/52{,}300} = 2.29$$

Real-World Example: Alpha-Chymotrypsin in Vietnam

- Alpha-chymotrypsin: a biological product commonly used in Vietnam for numerous conditions
- Significant safety signals related to hypersensitivity, including anaphylactic reactions:
  - ROR (95% CI) = 2.12 (1.26–3.07) from the Vietnamese national spontaneous reporting database
- Since 2010, 249 adverse event reports for this product were received nationwide, of which 65 cases were related to anaphylactic reactions (this is approximately equal to all spontaneous reports related to alpha-chymotrypsin obtained from VigiBase)
- The National Centre sent an official letter to the Drug Administration of Vietnam, Ministry of Health, to advocate a safety revision for this product

Source: World Health Organization. (2017). 40th Annual Meeting of Representatives of National Pharmacovigilance Centres, Kampala, Uganda, 2017.

Factors to Consider in Assessment of a Safety Signal (Is It a Risk?)

- Strength of association
  - Generally speaking, PRR >2 indicates a potential safety signal
- Temporal relationship
- Consistency of findings with other data sources
- Evidence of dose–response or rechallenge effect
- Biological plausibility
- Seriousness of the event
- Potential to mitigate the risk
- Degree of benefit of this and other therapies

Strengths and Limitations of Passive Methods

Strengths of Spontaneous Reporting System

- It enables early detection of events not observed in clinical trials
- It is large scale, broad scope, and relatively inexpensive
  - It covers all medicines used in the population
  - It received adverse event reports throughout a medicine's life cycle
- It generates signals, which led to hypothesis and further investigation
- As few as one event can trigger further evaluation
- It provides opportunity for the public (e.g., consumers and patients) to report adverse events
  - e.g., US MedWatch program

Limitations of Spontaneous Reporting System

- Information is incomplete
- Denominators (number of individuals exposed to a drug) are unknown
  - Population-based rates of an adverse event cannot be estimated from spontaneous reporting data
- Some adverse events are difficult to recognize
- Underreporting
- Reporting biases

Factors Affecting the Reporting of Adverse Events for a Given Drug–Event Pair

- Duration since drug's approval (e.g., Weber effect: reports peak in the second year after approval and decline thereafter, even though the drug might be used more widely)
  - More adverse event reports received from the new drug compared to an older, widely used drug, even if there is no true difference in risk between them

- Publicity about an important new adverse event often causes a large number of reports shortly after the publicity
  - Changes in the number of adverse event reports for a give drug–event pair can not reliably be interpreted as a change in the population-based frequency of the adverse event

Summary

- Passive surveillance
  - Spontaneous reporting of adverse events / adverse drug reactions
  - The most common form of pharmacovigilance
- MedWatch: National Passive Surveillance Program in the United States
  - FDA Adverse Event Reporting System (FAERS)—a computerized database designed to support FDA's postmarketing safety surveillance program
- Worldwide passive surveillance systems: WHO Programme for International Drug Monitoring (WHO-PIDM)
  - VigiBase—the richest source of pharmacovigilance data in the world
- The Proportional Reporting Ratio (PRR) is the foundational concept for many disproportionality methods