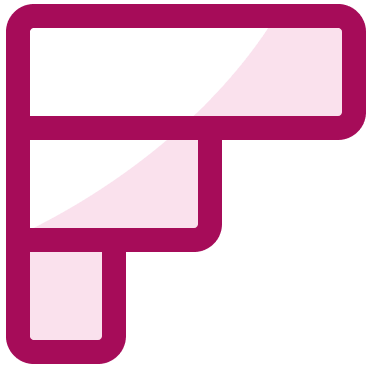
Post Market *Adverse Event Reporting*

Tammy Steuerwald, MT (ASCP), JD
Head of Global Regulatory Policy, Foundational Principles & Supranational Orgs.
Roche Diagnostics
tammy.steuerwald@roche.com

USAID FROM THE AMERICAN PEOPLE · ANSI American National Standards Institute · Standards Alliance · FDA U.S. FOOD & DRUG ADMINISTRATION · AUDA - NEPAD AFRICAN UNION DEVELOPMENT AGENCY

slido



How Familiar Are You with Post Market Controls for Medical Devices and In Vitro Diagnostics?

ⓘ Start presenting to display the poll results on this slide.

Complaint monitoring, adverse event reporting and corrective actions are a critical to protect patient safety.

Complaint Handling

A complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution.

Reportable Events

- Death, Serious Injury
- Malfunctions
  - Summary Reporting

Recalls

Field Safety Corrections

- Update design & risk documents

Risk Management
Design Control
Labeling
Training
Education

Increasing Risk

At a minimum regulators should be set up to receive and handle death, serious injury cases and have the authority to require a recall.

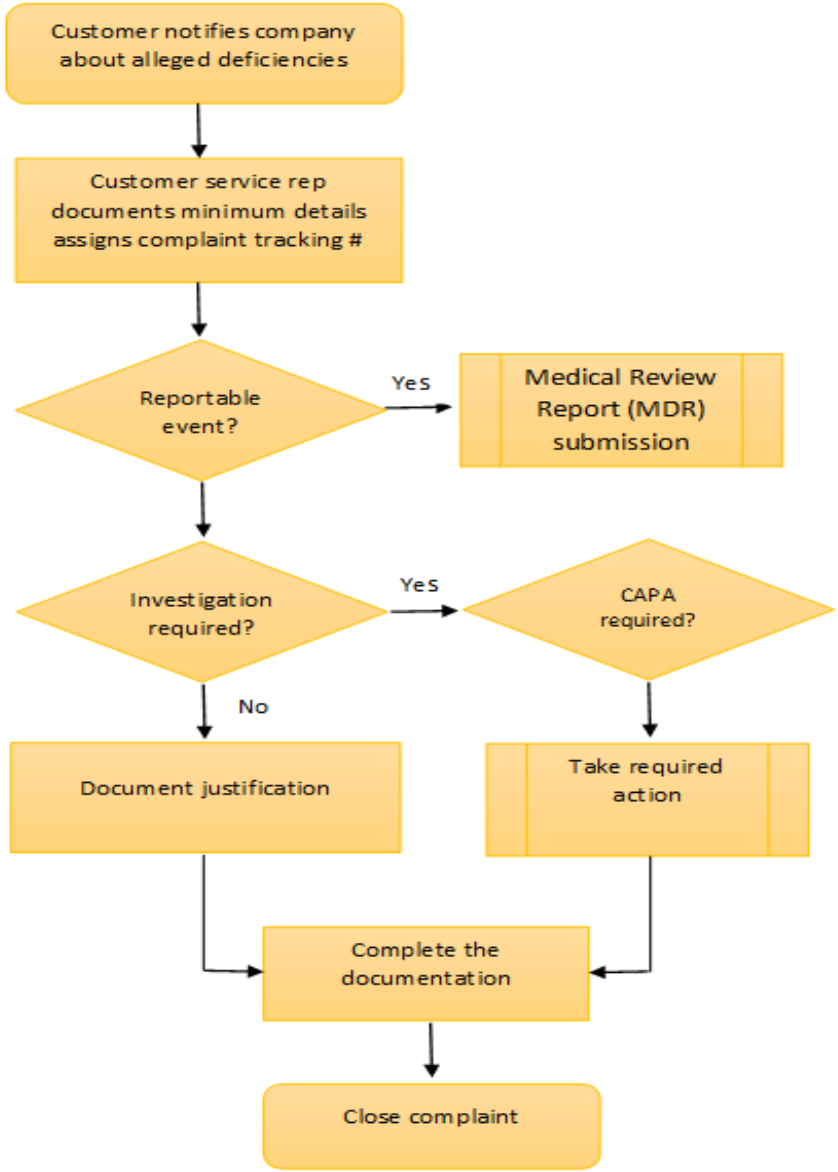
Complaint Handling

Document, Evaluate, Investigate, report, take action.

- **Document** all complaints.
- **Evaluate** complaints and determine if an investigation is needed (nexus to the device, complaint may already have been investigated).
- **Investigate** the complaint.
- Take appropriate **action** when needed (CAPA, field corrective action e.g., updates to the device, removal).

Inspections review a sampling of complaint files to ensure manufacturers are following their documented process as required by the QMS, justifying their decision, and making accurate decisions (e.g., reportability decision).

Document rational throughout the process! If its not documented, it didn't happen.



* Flowchart provided by https://www.complianceonline.com/resources/medical-device-complaint-handling.html

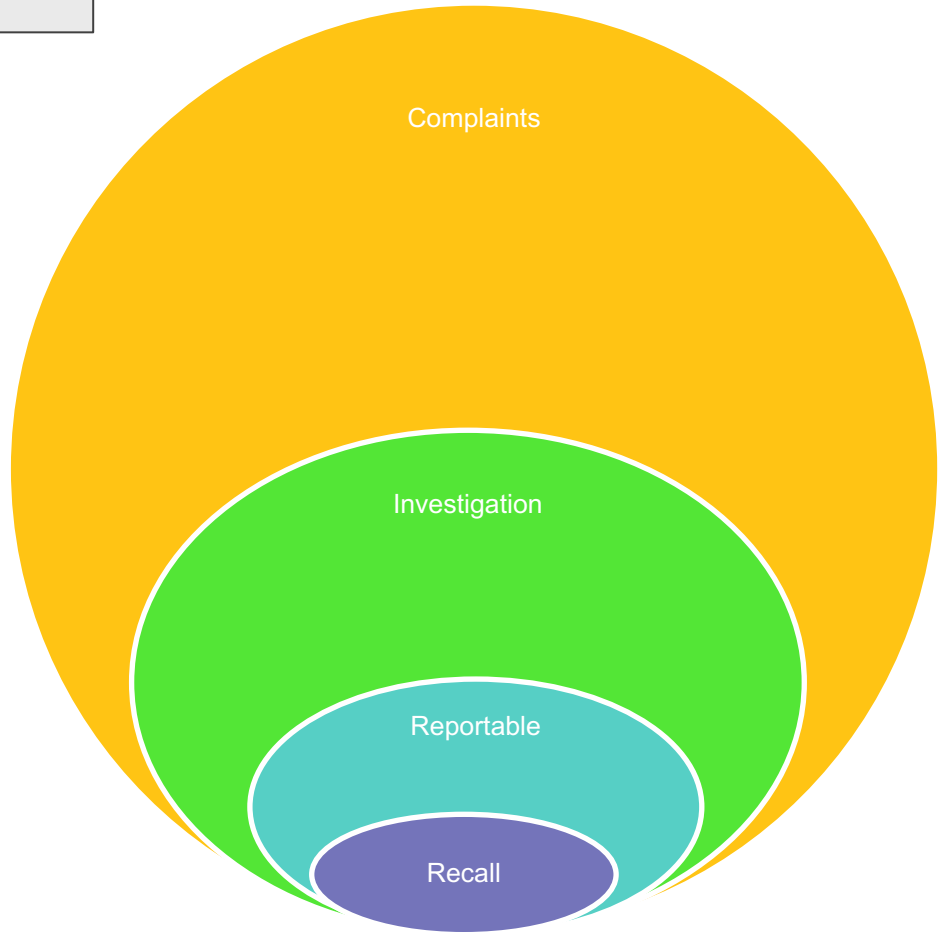
ISO 13485 Includes a Section Dedicated to Complaint Handling & Reporting Requirements.

- **8.2.2 Complaint handling**. The organization shall document procedures for timely complaint handling in accordance with applicable regulatory requirements. These procedures shall include at a minimum requirements and responsibilities for:
  - a) receiving and **recording** information;
  - b) **evaluating** information to determine if the feedback constitutes a complaint;
  - c) **investigating** complaints;
  - d) **determining the need to report** the information to the appropriate regulatory authorities;
  - e) **handling** of complaint-related product;
  - f) determining the need to initiate **corrections or corrective actions**.
- If any complaint is not investigated, justification shall be documented. Any correction or corrective action resulting from the complaint handling process shall be documented.
- If an investigation determines activities outside the organization contributed to the complaint, **relevant information shall be exchanged between the organization and the external party involved**.
- 8.2.3 Reporting to regulatory authorities. If applicable regulatory requirements require notification of complaints that meet specified reporting criteria of adverse events or issuance of advisory notices, the organization shall document procedures for providing notification to the appropriate regulatory authorities.

Correction means repair, modification, adjustment, relabeling, destruction, or inspection (including patient monitoring) of a product without its physical removal to some other location. For more information see the US FDA website: https://www.fda.gov/medical-devices/postmarket-requirements-devices/recalls-corrections-and-removals-devices#:~:text=Correction%20means%20repair%2C%20modification%2C%20adjustment,removal%20to%20some%20other%20location.

Not all complaints are adverse events.
Not all complaints need to be reported.

- A complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution.
- Not all complaints are reportable events.
- Risk based approach.



slido

Which of the following examples is a complaint?
Pick all that apply.

ⓘ Start presenting to display the poll results on this slide.

Which of the following examples is a complaint?

- A. I didn’t test my blood sugar today because I was too busy.
- B. I don’t trust the results I am getting from my device.
- C. I don’t think the device result was correct.
- D. When I ran the controls, I could not get them to come into range.
- E. Patient uses test strips according to IFU. Readings provide incorrect values leading to incorrect insulin dosage & hospitalization.

Reportability

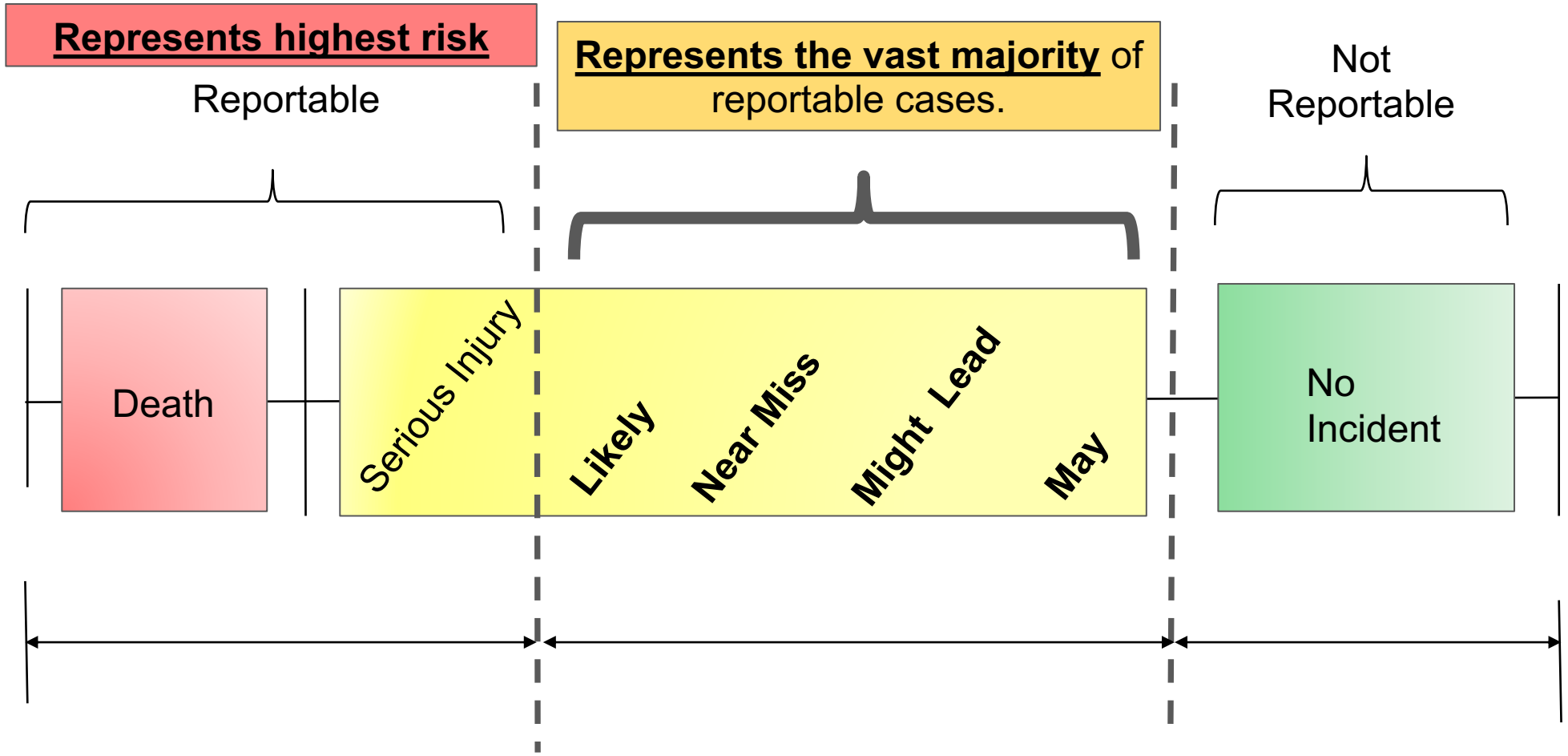
Generally, manufacturer responsibility for Adverse Event reporting is consistent around the globe.

An event becomes reportable to the Regulatory Authorities when the **manufacture becomes aware** of an event involving their device:

- May have caused or **contributed to a death, serious injury** or serious deterioration in health of a patient, user or other person.
- Has malfunctioned and would be **likely** to cause or contribute to a death, serious injury or serious deterioration in health if the malfunction were to recur.

…However, opportunities still exist.

Inconsistent Regulatory Triage of high risk cases. Malfunction criteria is a “gray area” and presents a challenge for manufactures.



IMDRF is driving harmonization in adverse event reporting

- Through collaboration, they have created a **common framework** for adverse event reporting that includes:
  - Criteria
  - Timelines
  - Exclusions
  - Definitions
  - Coding
  - Periodic reporting

To help converge global requirements, IMDRF developed a common framework for Adverse Event reporting

Medical Devices Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices. 30 November 2006.
IMDRF terminologies for categorized Adverse Event Reporting (AER): terms, terminology structure and codes. 18 March 2020 .

IMDRF (GHTF) Criteria for Reportability

- An **event**;
  - i.e., malfunction, out of specification result, discovery of design flaw, inaccuracy in labeling
- **Associated** with the manufacturer's device; **and**
- The **event led to** either:
  - **Death, serious injury**; or
- No death or serious injury but the event **might lead** to D/SI if it were to reoccur

Medical Devices Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices. Nov 2006.
Serious Injury - Life threatening illness or injury. Permanent impairment of a body function or permanent damage to a body structure. A condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure.

IMDRF Timing for Reportability

- Public health threat, **death and serious injury** cases – **10 days**
- Event that **might lead** to D/SI if it were to reoccur – **30 days**
- These timelines **allow sufficient time** for manufacturers to gather information, investigate the complaint, send out a field service agent etc.
- **Shorter timelines can result in many unnecessary reportable reports**.
  - Overshadows those cases with the highest risk.
  - Unnecessarily uses regulator and manufacturer resources.
  - "*While it is desirable that adverse event reports be timely, it is also desirable that the information be accurate*."[1]

1. Medical Devices Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices. Nov 2006.

IMDRF is driving convergence for AE terminology and report coding.

- IMDRF also established IMDRF terminologies for categorized Adverse Event Reporting (AER): terms, terminology structure and codes with the purpose to:
  - Improve, harmonize and where necessary expand the terminology and systems being used to code information relating to medical device adverse events, and
  - Establish IMDRF adverse event terminology composed of the following three parts: terms for medical device malfunction, terms for patient/user outcome and terms for part/component of medical device.
- Widespread use of a single, appropriate adverse event terminology and coding system is **expected to improve information sharing among regulators and improve response by both industry and regulatory authorities.**

IMDRF terminologies for categorized Adverse Event Reporting (AER): terms, terminology structure and codes. April 2020.

Reportable Event Terminology and Coding Implementation can be iterative.

- Implementation of Annexes can be iterative and can increase accuracy and efficiency over time.
- Training can be found here.
- US FDA mapped to IMDRF codes.

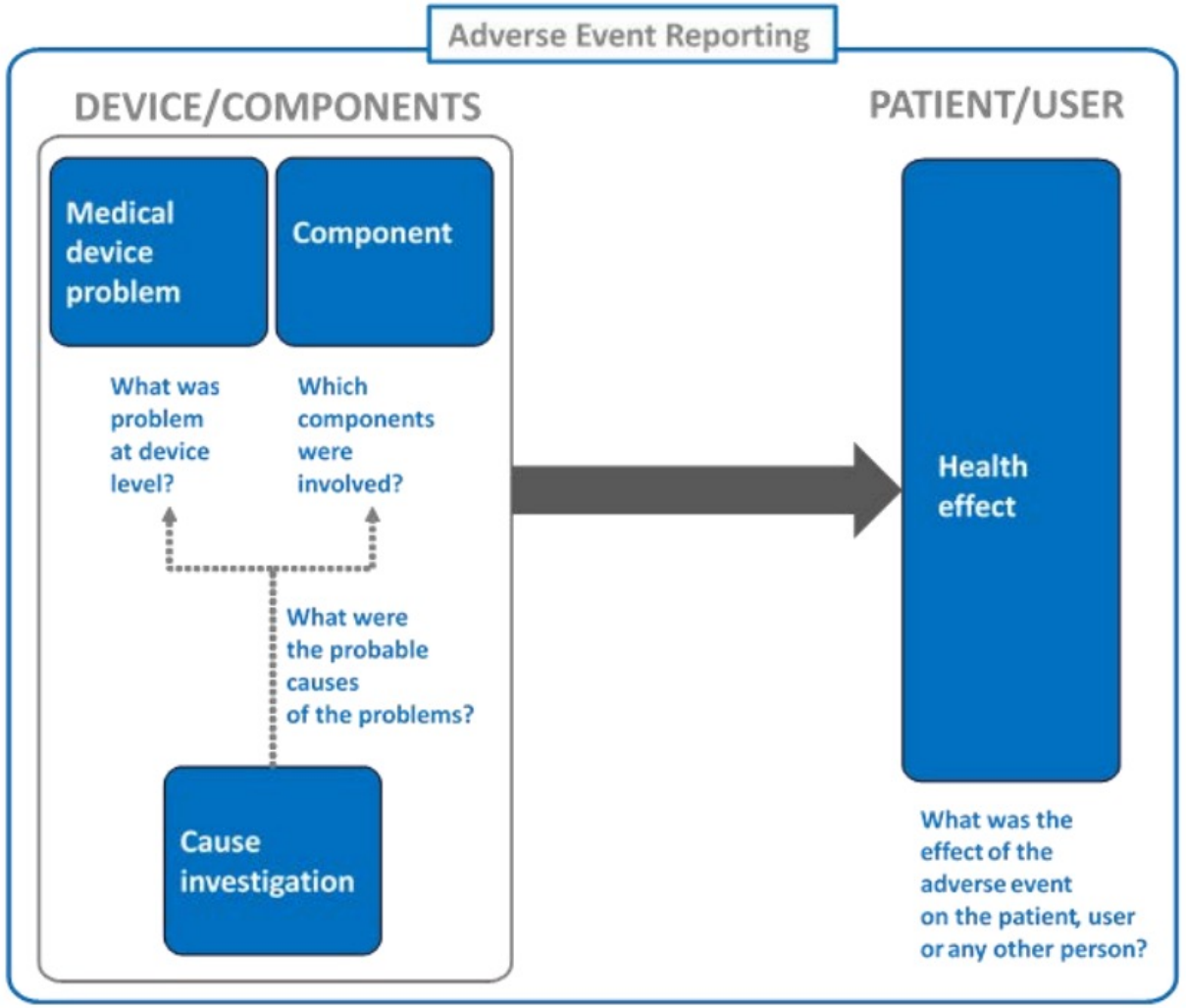
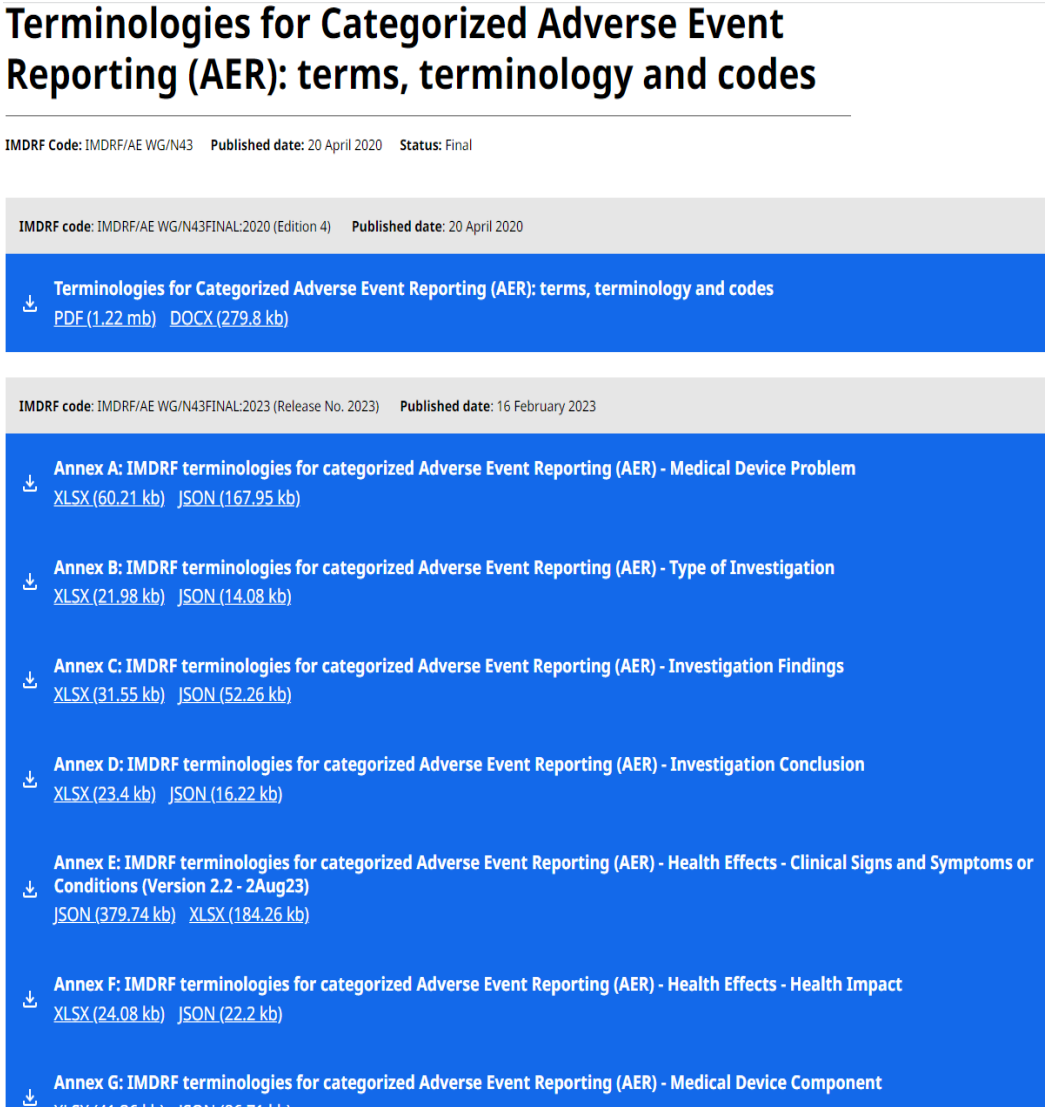


Figure taken from IMDRF terminologies for categorized Adverse Event Reporting (AER): terms, terminology structure and codes.

IMDRF AE Coding consists of 7 Annexes

- Annex A: Medical Device Problem Terms and Codes
- Annex B: Cause Investigation – Type of Investigation Terms and Codes
- Annex C: Cause Investigation – Investigation Findings Terms and Codes
- Annex D: Cause Investigation – Investigation Conclusion Terms and Codes
- Annex E: Health Effect – Clinical Signs, Symptoms and Conditions Terms and Codes
- Annex F: Health Effect – Health Impact Terms and Codes
- Annex G: Medical Device Parts and Component Terms and Codes



Complete list of IMDRF AE Terminology and Coding Annexes can be found here.

IMDRF guidance also includes recommended exemption rules (event does not need to be reported).

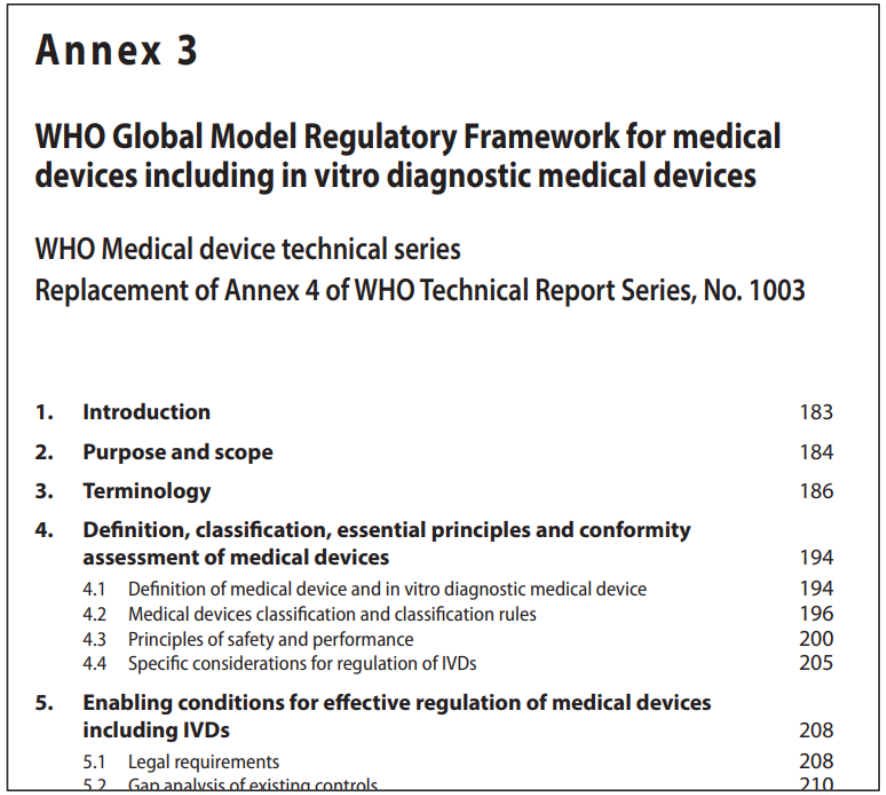
IMDRF Exclusions
Adverse event caused by **patient condition**
Service **life exceeded**
Design feature protected against adverse event
Negligible likelihood of death or serious injury
Documented expected **foreseeable** side effect
Adverse event described in **advisory notice** (corrective action, recall)
Use error, and no death or actual serious injury
Abnormal use
Those requested and **approved by authority**

NOTE: Further explanation and examples of these exemptions rules can be found on page 9 of the IMDRF (GHTF) Global Guidance for Adverse Event Reporting for Medical Devices.

Source: Medical Devices Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices.

WHO Global Model Regulatory Framework also includes criteria for Adverse Event reporting aligned to IMDRF.

- Manufacturers should be obliged to report to the NRA if any of the following events associated with the use of their medical device occur within their jurisdiction:
  - discovery of a **serious public health threat**;
  - **death, serious deterioration in the state of health of a patient, user or other person**; or
  - no death or serious deterioration in health of a user, patient/client or other person but the failure, **malfunction**, improper or inadequate design, manufacture, labelling or user error of the medical device that **could lead to death or serious deterioration in the health of a user, patient/client or other person.**



Annex 3

WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices

WHO Medical device technical series

Replacement of Annex 4 of WHO Technical Report Series, No. 1003

World Health Organization, Global Model Regulatory Framework, Annex 3, May 2023, page 233

US FDA Reporting Criteria is also aligned to IMDRF.

Criteria	Requirement
Who Must Report	Manufacturers[2]
What Must be Reported	• Death • Serious injury • Non-death/SI ***likely*** to lead to death/SI if reoccur (“Malfunction”)
Potential Reporting Exclusions	• Malfunctions not likely to cause or contribute to a death or serious injury if they recur, solely user error with no performance issue, expired product use, off label use.
Reporting Times	• **5 days**: Unreasonable risk of substantial harm to the public health or FDA makes written request • **30 days**: All others • **30 days**: Supplemental reports
Rest of World Adverse Events Reportable	Yes.

2. Requirements for importers and User Facilities not included in the presentation.

slido

Which of the following examples is a reportable event? Select all that apply.

ⓘ Start presenting to display the poll results on this slide.

Which of the following examples is a reportable event?

A. Loss of sensing after a pacemaker has reached end of life. Elective replacement indicator did not show up in time, although it should have according to device specification.

B. The arm of an X-ray system during use had uncontrolled motion. The patient was hit by the device and his nose broke. The system was installed, maintained, and used according to manufacturer's instructions.

C. An infusion pump stops due to a malfunction but fails to give an alarm. Patient receives under-infusion of needed fluids and requires extra days in hospital to correct.

Efficiencies in Reporting
Summary Reporting

- **Program:** US FDA Voluntary Malfunction Summary Reporting (VMSR)*.
- **Purpose**: Enhance ability to effectively monitor devices.
- **Method**: Voluntary program that allows manufacturers to submit quarterly summary reports for potential adverse events.
- **Impact**:
  - Significant reduction in one off reporting.
  - Visibility to important trends.
  - Wise use of authority and manufacturer resources.

EU IVDR also allows summary reporting.

- Periodic summary reports are permitted for **similar serious incidents**.
- Requires:
  - **Same device or device type**, and either:
    - The root cause to be identified
    - A field safety action implemented, or
    - The incidents are common and well documented.
- Authority must agree to the format, content, and frequency.

*Certain exclusions apply (i.e., product subject to recall). See exclusions here.

Manufacturer – Distributor Responsibilities

Who does what and who fulfills the QMS obligations?

- Who in your country is legally responsible to maintain the safety, quality and effectiveness of the device (QMS requirements)?
- Does your legal framework require a designated agent/authorized representative/registered importer?
- How does the manufacturer – designated agent – distributor work together to fulfill QMS requirements?
- Who in the end is held accountable if something happens from a safety perspective?

Risk Management

ISO 14971:2019 Risk Management

Thank you for your time!!

Tammy Steuerwald, Head of Regulatory Policy,
Foundational Principles & Supranational Orgs.
Tammy.Steuerwald@roche.com
(317) 727-5966

Question & Answers