International Best Practices and Innovations in Adverse Event Reporting

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September, 2022

Better Protection for Patients and Users

- Harmonization to the international best practice for Adverse Event Reporting:
  - **Improves** patient and user safety.
  - Allow data to be combined and compared to more **quickly identity and react** to potential adverse trends.
  - Improves **efficiency** and allows regulators to **focus** on those cases with the highest risk.
- IMDRF (International Medical Device Regulators Forum)[1] is comprised of regulators around the world who come together, collaborate, and establish recommendations for adoption of global best practices aimed to provide ideal regulatory practices.

1. IMDRF: Australia, Brazil, Canada, China, European Union, Japan, Russia, Singapore, South Korea, United Kingdom, United States of America

IMDRF Adverse Event Reporting Recommendations

- Any event which meets **all of the three** basic reporting criteria should be considered an adverse event and reported to the regulator.
- (1) The manufacturer **becomes aware** of information regarding an event which has occurred with its device
- (2) The Manufacturer's **device is associated** with the event
- (3) The event led to one of the following outcomes:
  - **Death** of a patient, user or other person.
  - **Serious Injury** of a patient, user or other person.
  - No Death or Serious Injury occurred but the event **might** lead to death or Serious Injury of a patient, user or other person if the event recurs (otherwise known as malfunction or near miss).

IMDRF Recommends and Exclusions

- Adverse events which could lead, but have not yet led, to death or serious injury, but **have a negligible likelihood** of causing death or serious injury, and which have been **established and documented as acceptable after risk assessment do not need to be reported**.
- **Use error** related to medical devices, which did **not result in death or serious injury** or serious public health threat, **need not be reported**.
- **Abnormal use need not be reported** under adverse event reporting procedures. Abnormal use should be handled by the health care facility.
- All complaints should be evaluated by the manufacturer to determine reportability.

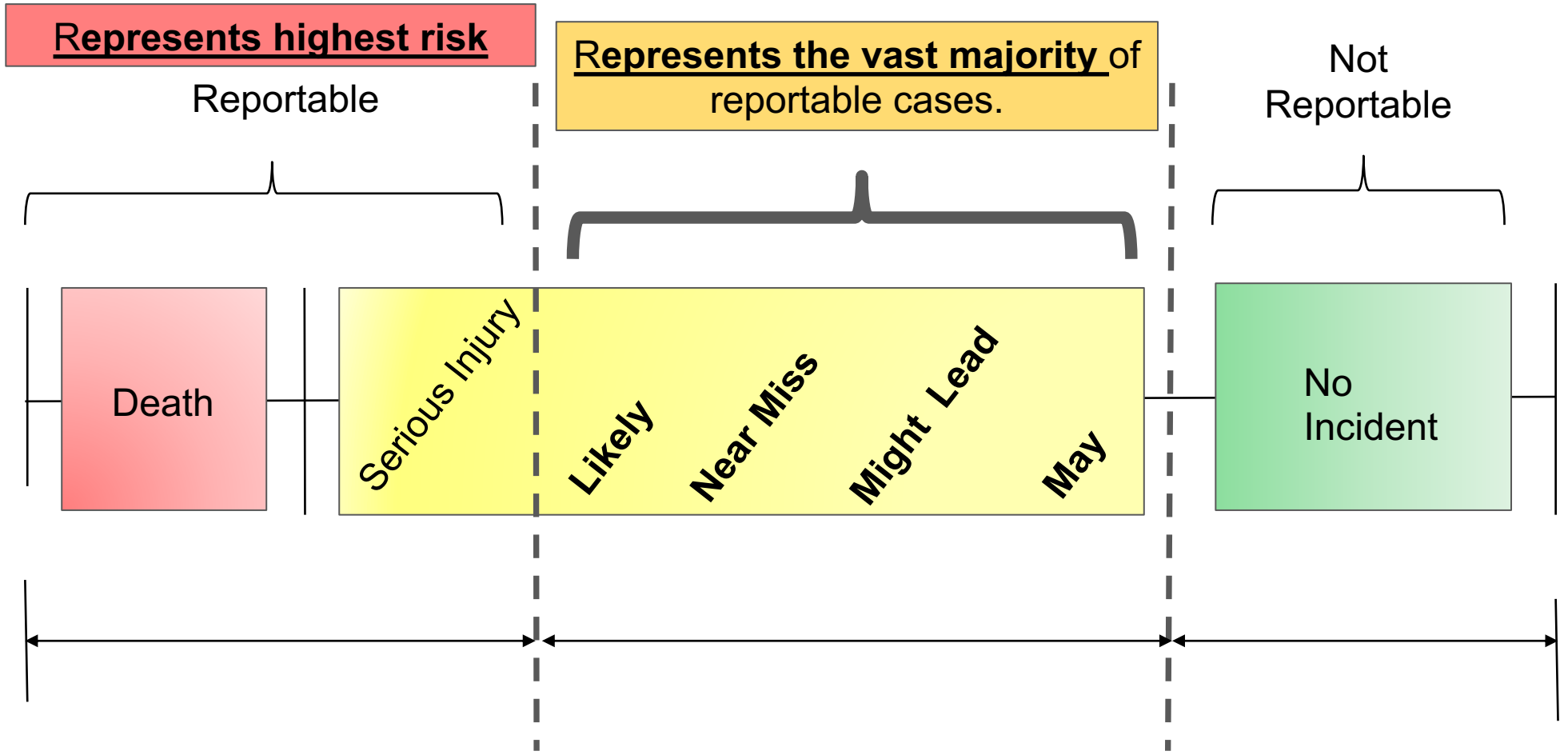
Inaccuracies in promotional material are generally not reportable events unless death or serious injury occurred.

IMDRF Recommended Exclusions

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**

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

Malfunctions/Near Misses



Report to drive meaningful changes that improve patient and user safety

- **Malfunctions**/Near misses represent the **vast majority** of reported cases.
  - Yet there is **little to no evidence** to show that **these cases lead to meaningful changes** to protect patients and users (e.g., labeling changes, field actions, recalls).
  - And these cases consume the majority of regulator time and **detract from more serious adverse events** (death, serious injury).
- Advances are being made to better utilize malfunction information.

Summary Reporting for Malfunctions

- **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.

Voluntary Malfunction Summary Reporting Program

The Voluntary Malfunction Summary Reporting (VMSR) program was established in 2018 and permits manufacturers to report certain device malfunction medical device reports (MDRs) in summary form on a quarterly basis. It reflects a pilot program conducted in response to changes made by Section 227 of the Food and Drug Administration Amendments Act of 2007 and the goals for streamlining malfunction reporting outlined in the commitment letter agreed to by the FDA and industry and submitted to Congress, as referenced in the Medical Device User Fee Amendments of 2017 (MDUFA IV) Commitment Letter. The FDA believes the program will enhance the FDA's capacity to effectively monitor many devices.

In the ***Federal Register*** of December 26, 2017 (82 FR 60922), the FDA issued a notification outlining the FDA's proposal to grant an alternative under 21 CFR 803.19 to permit reporting by a manufacturer of certain device malfunctions in summary form on a quarterly basis, subject to certain conditions, and requested comments from the public. On August 17, 2018, (83 FR 40973) the FDA issued a notification granting this alternative and describing the overarching principles for the VMSR program. Key among these principles is transparency of this information to the FDA and to the public, regardless of whether the information is reported as an individual Medical Device Report (MDR) or VMSR.

Under the VMSR program, manufacturers submit separate summary reports for each unique combination of brand name, device model, and problem code(s). Each summary report identifies the total number of reportable malfunctions, and the summary reports are available to the public in MAUDE. Importantly, mandatory submission of individual reports of death or serious injury events continues to be required, under sections 803.50 and 803.52, or 803.53, as applicable.

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

Summary Reporting for Malfunctions

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.

Summary reporting has also been implemented in Saudi Arabia. We recommend Indonesia consider implementing this innovative approach.

IMDRF Recommendations for Timing to Report

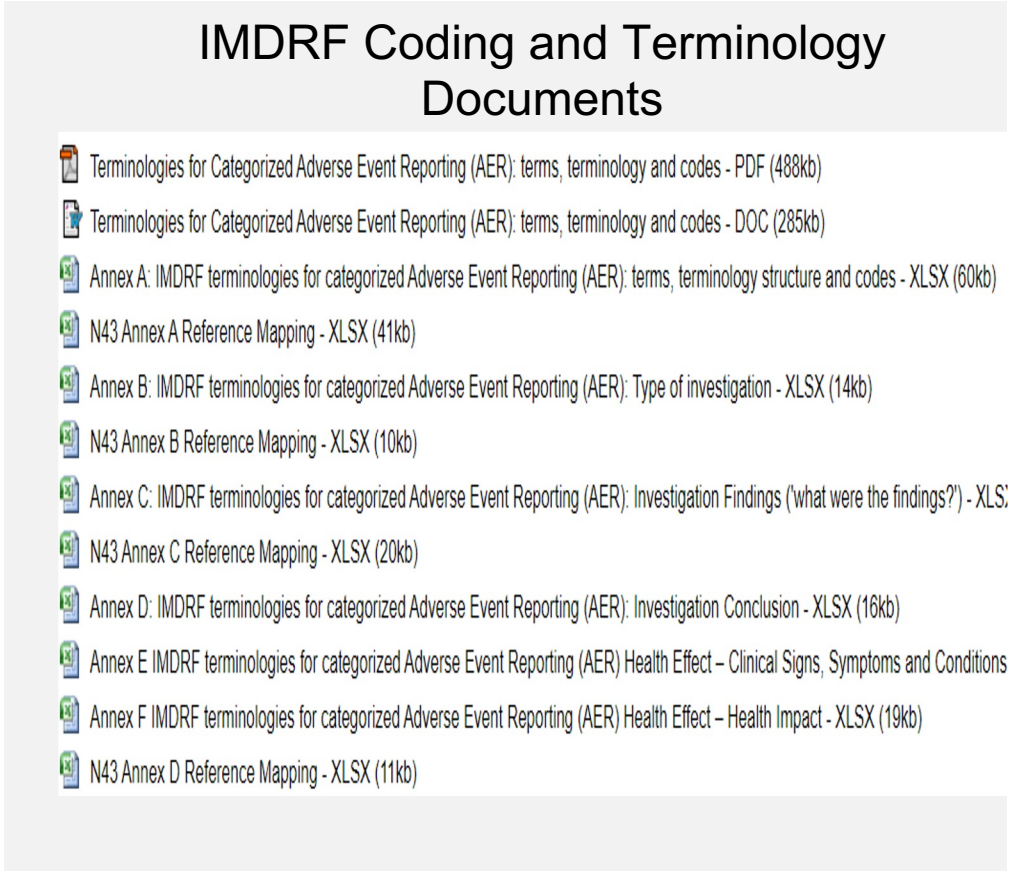
- IMDRF recommends that those events that pose a public health threat, result in death, or serious injury be reported to the regulator within **10 days**.
- IMDRF recommends all malfunctions/near misses be reported within **30 days**.
- There remains global variability in reporting timelines that can result in significant over-reporting of events that fail to drive improved patient safety.

Example of Reporting Timelines and Their Impact

- **Example**: The **IVDR** changed malfunction reporting **from 30 days to 15 days**. This means that manufacturers must report potential adverse events within 15 days of becoming aware of the issue.
- This very short timeline results in a large number of unnecessary adverse event reports.
- To illustrate this, we conducted an internal **study that included of 2,794** events that were reported to the regulatory authority.
- Following the completion of the investigation, **less than 8% of the events needed to be reported**.
- This study shows the importance of reasonable reporting timeframes. In order to focus resources on those cases with the highest safety risk, and drive results that better protect patients, **we urge Regulators to implement IMDRF timelines**.

IMDRF Also Recommends Aligned Coding

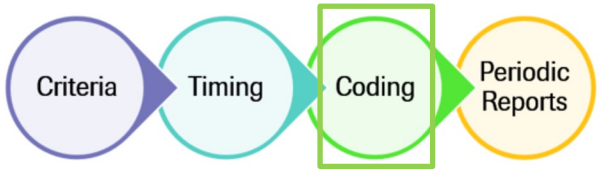
- IMDRF members have created a **comprehensive** coding framework.
- Includes definitions, terminology and a unique alpha-numerical code for each adverse event type.
- **Benefits**:
  - Consistent reporting.
  - Effective trending.
  - Better signal detection.
  - Faster response times.



IMDRF coding documents can be found here.

Aligned Coding

U.S. FDA Harmonizing IMDRF Codes



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US FDA is **harmonizing** to the IMDRF coding system.

- Will **enable comparison and trending** of common data sets.
- Strengthen **predictive power**.
- Allow **quicker reaction** to adverse trends identified by the data.

FDA U.S. FOOD & DRUG ADMINISTRATION

FDA is in the process of harmonizing the FDA adverse event coding system with the new IMDRF Adverse Event Reporting terminologies, a new international guideline for coding medical device adverse events. As the first step in this process, FDA updated four of its code sets (Device Problem Code, Manufacturer Evaluation Method Code, Manufacturer Evaluation Result Code, and Manufacturer Evaluation Conclusion Code) to have a one-to-one matching with the first four code sets from IMDRF on July 5, 2018. Future updates will harmonize all remaining FDA adverse event codes with IMDRF as the remaining annexes are published.

See full article here.

Periodic Reporting

Great variability exists in periodic reporting. This divergence is leading to a significant increase in workload at both the regulator and manufacturer and little value to improve patient or users is being seen.

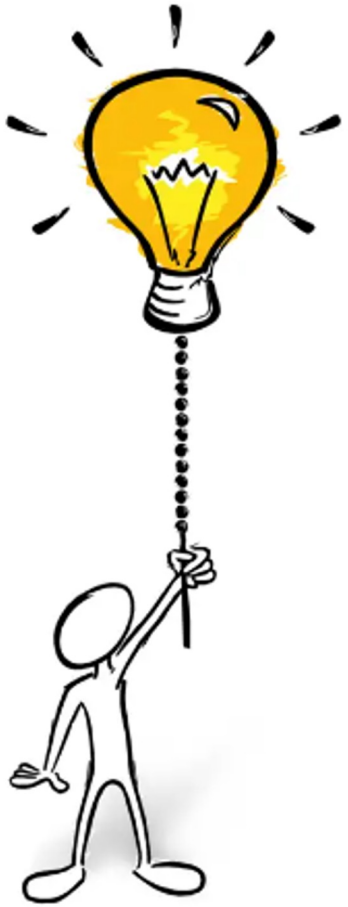
We recommend regulators pause on implementing periodic reporting so that best practices can emerge.

Periodic Reporting

- Periodic Reports are a **redundant, retrospective** review of data already assessed and trended by the manufacturer.
- The Quality Management System already requires the manufacturer to evaluate each product complaint and determine if an investigation is necessary.
- This process also requires the manufacturer to assess same or similar products and determine adverse event reportability.
- Therefore, **almost in real time, manufacturers already assess each complaint and when necessary update the risk information, undertake a Corrective and Preventive Action, initiate review by executive management or a Safety Review Board, or issue a Recall**.
- All of this activity has already occurred by the time a periodic report comes into play.

IMDRF Recommendations for Periodic Reporting

"*The decision to file a trend report should be based on the occurrence of a significant increase in the number of adverse events.*"[2]



2. Medical Devices Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices, 30 November 2006, page 25. This long standing GHTF Guidance was adopted by IMDRF and remains the industry best practice recommendation from INDRF today.

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- IMDRF is comprised of regulators around the world who come together, collaborate, and establish recommendations for adoption of global best practices aimed to provide ideal regulatory practices.
- Therefore, we recommend continued alignment to IMDRF adverse event recommendations.

Thank you for you time!!

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