

HOW TO USE IMDRF GUIDANCE DOCUMENTS

ADVERSE EVENT (AE) TERMINOLOGY

Information Session on IMDRF Guidance Document

*IMDRF terminologies for categorised Adverse Event Reporting
(AER): terms, terminology structure and codes*

IMDRF/AE WG/N43FINAL:2020 (Edition 4) and related documents

September 2023



Training Transcript

Slide 1

Hello, and welcome to this training session on how to use IMDRF Adverse Event Terminology (AET) as set out in the guidance document 'IMDRF terminologies for categorised Adverse Event Reporting (AER): terms, terminology structure and codes, IMDRF/AE WG/N43FINAL:2020 (Edition 4) and related documents which can be found on the IMDRF website.

You will note that throughout this presentation the term 'adverse event' will be used. This term is synonymous with the terms 'incident' or 'serious incident' that are used in some jurisdictions. The precise criteria for reporting adverse events are defined by each regulatory authority and are not subject to this guidance document.

Slide 2

In this session, you'll learn about the IMDRF adverse event terminology and the objectives that the IMDRF had in mind when developing the terminology and coding.

You'll be introduced to the details of the terminology, including the various annexes and the coding structure, and an overview of how the system can be used will be provided.

We'll also look at how the terminology is kept up to date and the steps to follow to request an addition, modification, or deletion of an adverse event term.

Lastly, we will summarise the expected benefits of adopting this globally harmonised system for assisting with adverse event reporting and how the IMDRF Adverse Event Terminology can help in this respect.

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Let's begin with a definition of the IMDRF AE Terminology.

It's a standardised set of terms, with associated alpha-numerical codes, which can be used for reporting medical-device-related adverse events globally.

It is designed to enhance and not replace existing national or regional adverse event reporting requirements.

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The IMDRF had several key aims in mind when it developed the adverse event terminology as a standardised reporting system for global use.

The first was to establish a harmonised terminology and corresponding codes for reporting adverse events related to medical devices that could be used across the world.

Secondly was to establish a harmonised terminology, which would assist in improving the accuracy and consistency of adverse event reporting at global level, thus simplifying the analysis of adverse event related data, and facilitating the early detection of potential safety signals relating to the use of medical devices in the market.

It was envisaged that this would greatly assist in the identification and the initiation of timely and prompt corrective measures by manufacturers where necessary; for example, medical device recalls and field safety corrective actions.

It was also envisaged that it would provide regulators with better oversight of the performance of the devices in the marketplace, allowing them to more easily identify trends and potential safety concerns, and initiate actions where necessary.

Lastly, and most importantly, one of the principle aims of the global harmonised AE terminology was to protect patients by enabling faster local and international responses to issues and/or problems that are identified with medical devices

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The Adverse Event Terminology terms and codes were designed to provide a harmonised global terminology system to assist with adverse event reporting; a system that could complement and enhance national or regional systems, making it easier for those manufacturers and regulators that need to be able to operate and communicate on the global stage.



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The terminologies presented in the IMDRF Adverse Event Terminology guidance document are intended to be used by two key stakeholders:

- By reporters – that is, those who are obliged to report to regulatory authorities in accordance with the relevant regulations of each jurisdiction, whether manufacturers or healthcare professionals; and
- By regulatory authorities themselves, who collect and process information and data to monitor and analyse adverse events so that they can better protect patients and public health.

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While IMDRF's global guidance on adverse event reporting does not provide a definition of an 'adverse event' involving a medical device or IVD, it does, however, provide terms and codes that can help in clearly communicating such events when they arise. As stated earlier, the precise criteria for reporting adverse events are defined by each regulatory authority and are not detailed in this IMDRF guidance document.

When an adverse event occurs, there are several questions that need to be considered by both the healthcare professionals and the manufacturers of any medical devices that may have been in use at the time of the event

- What occurred?
- Did a medical device contribute to, impact, or influence the event?
- Should the event be classified as an adverse event?
- How serious is the event? What is the health impact on the patient or the user of the medical device?
- How should the event be investigated?
- What problem or fault – if any – occurred with the device?
- What is the root cause of this problem?

For example, in this image we see an unconscious patient lying on a bed connected to an infusion pump.

- Has an adverse event occurred?
- Did the pump malfunction?
- Was there an over infusion?
- Was the over infusion the result of a device problem or a user error?
- How should this adverse event be investigated?
- Will the event need to be reported to a regulatory body?

The IMDRF codes have been designed and structured to assist both healthcare professionals and manufacturers to describe the various aspects of adverse event or incident investigations and investigation findings.

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The IMDRF AE Terminology coding structure consists of 'terms' and 'codes' that are clearly defined within a hierarchical coding structure.

The '**Terms**' describe events clearly and precisely, thus reducing the possible ambiguity that can arise when interpreting narrative text. The IMDRF terms are based on existing terminologies that already exist in different regions globally. In creating the IMDRF terms, these existing terminologies were reviewed, improved, expanded and/or simplified.

Each term is explained with a definition, and, in some instances, examples are provided.

The level of detail incorporated into the current IMDRF terminology is based on what was considered to be the most appropriate level for regulatory purposes. It does not intend to set the level of detail appropriate for manufacturers. Manufacturers are welcome to create additional levels of granularity for their own internal tracking purposes.

Code/coding: To ease the use of this terminology, in particular in databases, and to reduce possible ambiguities of meaning, each term is uniquely identified by an alpha-numerical code.

The **hierarchical coding structure** allows for the coded terms to be logically set out in branching structures consisting of several levels.

Although the hierarchical arrangement has been referred to as a 'coding structure' (similar to ISO TS 19218), it is important to note that it is primarily the *terms* and their descriptions that are of interest, while the codes are merely used to unambiguously identify the terms.

In such a hierarchical term structure (a coding structure), more general terms comprise the entry level, for example, Level 1. From each Level 1 term, second and in some cases third level terms, Levels 2 and 3, branch off, which allow for various, more detailed, options for a finer description of the Level 1 term.

Therefore, with an increasing number of levels, the resolution and descriptive power of the hierarchical system grows. The advantage of a hierarchically arranged terminology, or 'coding structure', is that a large variety of terms can be selected by users in a relatively accessible way, without the need to know all terms before using the system.

Inevitably, there had to be a trade-off between the *resolution* of the number of levels and number of terms or codes and the *practical use* of such a system by users, including healthcare workers, manufacturers, and regulatory authorities.

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The IMDRF Adverse Event Terminology is composed of seven annexes, covering four sets of terms and their associated codes.

It is designed to facilitate the accurate description and reporting of four main areas relating to adverse events:

- the medical device problem;
- the associated component problems;
- the health impact for the patient;
- the investigation into the cause of the adverse event.

The general terminology, combined with the specific codes, facilitates the reporting of investigations into possible causes of the event and causal links between use of the device – independent of whether it malfunctioned or not – and the adverse health effects experienced.

All terms are closely aligned to a subset of MedDRA terms, through close collaboration between the IMDRF and MedDRA.

It is recommended that adverse events should be coded to the most detailed level possible. The most appropriate code may be a Level 1 or Level 2 code depending on the circumstances and the information known. It is likely that it will be necessary to use multiple terms from each annex in combination to adequately code the adverse event, in agreement with the requirements of each relevant jurisdiction.

An overview of the terminologies and associated codes is given in the following slide.

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This schematic illustrates how the IMDRF codes work together.

The IMDRF codes were developed and introduced in a sequence - Annex A to Annex G. However, in practice, the codes are not necessarily used in this sequence.

The IMDRF Annex A, Annex E and Annex F codes are usually the first codes that may be considered by a healthcare professional or a manufacturer. For example, in the previous scenario that was outlined in Slide 7, in assessing the adverse event with the infusion device, the healthcare professional and the manufacturer would first consider the following.

- How did the problem manifest itself – the medical device problem? Did the infusion pump fail, was the infusion pump programmed correctly?
- What impact did the problem have on the patient? What were the patient's symptoms and the negative consequences for the patient? What is the patient's current state of health? Was this caused or impacted by the performance or lack of performance of the device?

The manufacturer would then consider what method(s) of investigation they would need to use to find out more information about the event – Annex B: Cause Investigation.

They would then have to identify and categorise the investigation outcome – Annex C: Investigation Findings – before finally concluding the root cause – Annex D Root Cause.

Throughout this process they may also consider specific components or parts that have contributed to the event – Annex G: Component parts.

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Annex A : Annex A includes terms and codes for describing problems associated with a medical device or IVD – for example malfunction, deterioration of function, or failures – that have occurred with medical devices.

The IMDRF codes were specifically developed for use in post-market adverse events, however they can be used to describe problems that occur during clinical studies or clinical evaluations.

Examples of problems include, for instance:

- problems associated with the interaction between the patient's physiology or anatomy and the device that affects the patient and/or the device;
- problems related to the interaction between the patient and the device;
- problems associated with undesirable local or systemic effects due to exposure to medical device materials or leachates from those materials by a patient who has an implant or is receiving treatment with a device made from them.

It is recognised that not all jurisdictions may want to code to such detailed levels. The hierarchical structure allows users to choose the level of coding best suited to their needs.

These terms are largely based on the FDA's device issue terms and are harmonised with ISO Technical Specifications 19218-1, where possible.

In cases where the root cause is unknown and it is not possible to find an appropriate Level 1 category, it is still appropriate to code. Using Level 2 or Level 3 codes, for example, a 'mechanical problem' term could be selected as the device problem, even if the device is still under investigation and it is not clear that the root cause was a mechanical problem.

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Annex B : Annex B covers terms and codes for describing **the type of investigation** carried out on the device involved in the reported event.

For example: The investigation employed relevant empirical testing of the actual device suspected in the reported adverse event in order to establish its functional and other properties, and to identify possible causes for the adverse event. Relevant testing would typically be based on test methods used for evaluating safety and performance as described in the latest relevant standards.

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Annex C: Annex C covers terms and codes for describing **the findings** of the investigation carried out on the device involved in the reported event.

For example, this may describe a biological problem relating to natural biological processes or living organisms. This may be due to a biocompatibility issue where the device causes a cellular or tissue response that elicits an undesirable local or systemic effect in the recipient or beneficiary of that therapy. The cause of this may be that the device was contaminated in some way by the undesirable presence of toxins associated with certain bacteria, for example gram negative bacteria.

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Annex D: Annex D covers terms and codes used for describing **the conclusion** of the investigation. Was the cause of the event traced back to the design of the device itself or the design specifications? For example, in the requirements, testing processes, hazard analysis, or implementation strategy. And, if so, is it that the design of the device is not actually fit for purpose?

Again, in all three investigation annexes, the hierarchical levels allow users to choose the most appropriate level of coding to use.

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Annex E: Annex E covers terms and codes for describing the health impact – so, the clinical signs, symptoms and conditions of the affected person appearing as a result of the medical device adverse event.

These terms should not be used to describe signs, symptoms, or conditions that existed prior to the adverse event. These terms are closely aligned to a subset of MedDRA terms, through close collaboration between the IMDRF and MedDRA.

This annex is organised into categories along organ systems, as well as physiological problems. Some terms appear in more than one category to make it easier to find the proper term. In these cases, each repeated term will only have one unique code assigned on the basis of its primary category.

For example, if the event gives rise to a nervous system problem in the patient, how does this present exactly in terms of symptoms, and what has the investigation determined is the physiological cause of these symptoms?

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Annex F: Annex F covers terms and codes for describing the health consequences of the medical device adverse event for the person affected.

These can include final patient outcomes, or interventions and procedures required as a result of the clinical signs, symptoms, and conditions captured using Annex E. It is likely that multiple terms will be required to fully describe the situation.

For example, in the case of radiation treatment, there may have been a change in response to treatment. The investigation could reveal that there had been a reduction in the desirable beneficial effects expected from a medical treatment and that this was due to a lower than intended dose of radiation being delivered to a single field.

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Annex G: Annex G covers terms and codes for describing the specific parts and components that were involved in, or affected by, the medical device adverse event.

Could a very small component, such as a simple cable grip or tie used for tensioning, pulling, holding or stringing of wires and cables have been involved?

The component terms are grouped into sections to help the user to find an appropriate term. Each term appears in only one section, and some simple rules are applied in order to choose the appropriate section in cases where a term could logically fit into more than one section.

Components that have multiple attributes are allocated to a section in the following order of preference:

Safety > Measurement > Optical > Biological & Chemical > Electrical & Magnetic > Mechanical

There will be some devices and/or adverse events where it is not necessary or appropriate to select an individual component. The terminology includes a term and code to capture these cases, so it is possible for jurisdictions to make it mandatory that a report includes at least one term or code from each and every annex.

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Accessing the codes is very easy. They have been made freely available for download from the IMDRF website at the link provided.

The codes can be downloaded in either XLSX or JSON format and integrated into your systems for ease of use.

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Given the nature of the medical device industry and the constant introduction of new technologies, materials, designs, procedures etc., it is very important to ensure that the terminology remains up-to-date, accurate, and responds well to the growing needs of the intended users.

This is why annual maintenance is required. Adjustments may be needed because of new technologies, technical updates, and innovations. There may be a need to refine definitions and terminology, or to improve the clarity of meanings. As a result, the IMDRF has put in place a clear system for the annual maintenance of the terminology with a view to adding, modifying or removing terms as required.

The maintenance cycle for IMDRF runs from March to March. Organisations may submit change requests from March until 1 September every year.

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Stakeholder organisations, for example, industry, patient associations, and medical associations can make requests to add, modify, or delete an adverse event term between March and the end of August. Please note that individuals cannot submit a change request, only national competent authorities or stakeholder organisations can do so.

As noted, the maintenance cycle for IMDRF runs from March to March. Organisations may submit change requests from March until 1 September every year.

Between 1 September and the end of December, all change requests are reviewed by the AE Terminology Working Group who then submit a Change Log to the Management Committee for approval.

Following approval by the Management Committee, the updated terms and codes are then published in March of the following year.

It is important that changes to the AE terminology should be restricted to those that are absolutely necessary. They should mainly be reserved for adaptation to accommodate technical progress. There will be new terms required as new devices, designs and materials emerge.

Frequent changes to the terminology are not anticipated. Any change for involved parties and end users will require re-programming of existing coding systems at the level of industry, healthcare facilities, and regulators, so change requests need to be managed with this in mind.

Where terms become obsolete during the maintenance phase, these obsolete terms and their corresponding codes are not deleted but will be flagged as 'inactive'. These obsolete terms will be available for reference only but will not be available for selection.

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There is a designated webpage on the IMDRF website where the most current version of the terminology is published and where the Change Request Form (Appendix A) can be downloaded to submit change requests.

Users should remember to FIRST refer to previous IMDRF decisions to check whether the proposed changes have already been addressed.

The Working Group's response to reviewed change requests will also be published on this website using the Change Log .

The completed Change Request Form should be sent to the current IMDRF AE Terminology Working Group Maintenance Chair at the latest by 1 September each year.

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At the end of the maintenance cycle, the revised IMDRF adverse event terminology is posted on the IMDRF website.

The revised terminology annexes are then given an updated version number. A change log is kept for each terminology for Annexes A through G and published on the dedicated IMDRF web page.

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What are the main benefits of a globally harmonised terminology and codes for both regulators and manufacturers?

For regulators, the use of globally harmonised terminology and codes is critical to supporting the effective analysis of safety, quality, and performance information.

In addition, common terms make the exchange of information between regulators on medical device adverse events easier, more accurate and more reliable.

For manufacturers, such terminology and codes provide a comprehensive, easy-to-use coding system that can be used as part of a world-wide post-market surveillance system.

They facilitate ongoing global oversight and analysis of adverse events and the reporting of them.

Finally, they provide consistency for reporting to multiple jurisdictions. This reduces the burden of managing multiple coding systems when preparing medical device adverse event reports for several jurisdictions.

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The use of the IMDRF Adverse Event Terminology can play an important role in addressing AE reporting needs in the post-market period.

In particular, it can help in:

- assessing the frequency of reports;
- assessing the severity of the clinical and/or patient consequences;
- assessing the root cause;
- assessing patterns relating to specific devices;
- assessing patterns relating to specific manufacturers;
- assessing the compliance of manufacturers to the AER requirements;
- assessing and monitoring the introduction of new technologies.

In contrast to narrative text, the use of the IMDRF AE terminology allows for more sophisticated approaches to signal detection – the identification of potential novel risks and trending analysis by incident management systems including advanced querying functions and data visualisation.

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The IMDRF AE Terminology was developed with the global market in mind and the intention that it should be a global tool to facilitate and harmonise AE reporting worldwide. It was designed to complement and be used in conjunction with existing reporting systems and its use around the world is expanding every year.

It is a public resource, accessible to all, available for free on the IMDRF website. Its use is facilitated and maintained by the IMDRF regulators and specifically the IMDRF AE Terminology working group.

We strongly encourage manufacturers, regulators and healthcare establishments in all jurisdictions to integrate the use of these codes into their reporting systems in order to maximise the potential benefits of a harmonised global terminology for AE reporting systems.

Use of the IMDRF AE Terminology is already very widespread.

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We hope you found this training session helpful. Thank you for watching.