IMDRF International Medical Device Regulators Forum

FINAL DOCUMENT

Title:	IMDRF terminologies for categorized Adverse Event Reporting (AER): terms, terminology structure and codes
Authoring Group:	IMDRF Adverse Event Terminology Working Group
Date:	16 March 2017

Kimby M Barton

Kimby Barton, IMDRF Chair

Table of Contents

The table of contents should be created on this page. See "IMDRF Document Format & Style

Preface

This guidance document was produced by the International Medical Device Regulators Forum (IMDRF), a voluntary group of medical device regulators from around the world. The document has been subject to consultation throughout its development.

There are no restrictions on the reproduction, distribution or use of this document; however, incorporation of this document, in part or in whole, into any other document, or its translation into languages other than English, does not convey or represent an endorsement of any kind by the International Medical Device Regulators Forum.

1.   Introduction

This document has been prepared by the IMDRF Adverse Event Working Group, charged with developing a harmonized terminology for reporting adverse events related to medical devices including in-vitro diagnostics (IVDs).

Widespread use of a single, appropriate adverse event terminology and coding system is expected to improve signal detection by adverse event management systems enabling a faster response by both industry and regulatory agencies.

Use of defined **terms** as well as associated **codes** to describe problems encountered with medical devices provides several benefits:

(1) it improves the accuracy of capturing and reporting of medical device related adverse events;

(2) it reduces ambiguity and hence increases effectiveness of the evaluation process; and

(3) it is readily usable, in contrast to narrative text, for more sophisticated approaches to signal detection (i.e. the identification of potential novel risks) and trending analysis by incident management systems including advanced querying functions and data visualization. Thus enabling a faster response by both regulatory agencies and device manufacturers.

A globally harmonized terminology and associated codes also has the following benefits:

- **For manufacturers (including local distributors/authorized representatives):** it provides **consistency for manufacturers** reporting to multiple jurisdictions, reducing the burden of managing multiple coding systems when preparing medical device adverse event reports for multiple jurisdictions;

- **For regulatory authorities:** by providing common terms and definitions, it supports analysis of safety, quality and performance information in a manner that can readily be shared globally: common terms will increase accuracy and reliability of information exchanged about medical device adverse events between regulatory agencies, and may facilitate more rapid detection of potential safety signals when pooled at inter-regional levels;

- **For patients:** it protects patients by **enabling faster local and international response** to medical device adverse events including those related to medical device malfunctions/deteriorations;

- **For healthcare providers:** the use of common terms with manufacturers and regulators may enhance accuracy, reliability and utility of the reports, especially when larger datasets can be pooled and analyzed. It may also, provide terms and definitions, some of which are within a hierarchical form, to be used for adverse event reporting within or between healthcare facilities.

2.   Scope

2.1   Use of the adverse event reporting terminology

This document provides the IMDRF terms, definitions and IMDRF alpha-numerical codes to be used for Adverse Event (AE) reporting concerning medical devices and in vitro diagnostics both pre and post market as described in section 5.

Notably, the precise criteria for reporting adverse events are defined by each regulatory jurisdiction and are not subject to this guidance document. Reference is made to the relevant guidance documents of each jurisdiction and the GHTF document on Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices (GHTF, 2006).

2.2   Intended end-users of the adverse event reporting terminology

The set of terminologies outlined in this document are intended for use by:
  (1) *reporters* of adverse events which are obligated to be reported to the authorities in accordance with the relevant regulations of each jurisdiction;
  (2) *regulatory authorities*, collecting and processing such information and related data in databases and other electronic systems to monitor and analyze adverse events to improve the protection of patients and public health. Regulatory authorities may be national competent authorities (NCAs) or supranational bodies charged with these tasks.

3.   References

The following documents were used in the development of this document.

  • ISO /TS 19218-1 Medical device- Hierarchical coding structure for adverse event – Part 1 Event –type codes

  • GHTF/SG1/N70:2011 Label and Instructions for Use for Medical Devices

  • GHTF/SG2/N54R8:2006 Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices

  • GHTF/SG2/N87:2012 Medical Devices: Post Market Surveillance: An XML Schema for the electronic transfer of adverse event data between manufacturers, authorized representatives and National Competent Authorities

  • GHTF/SG5/N5:2012 Reportable Events During Pre-Market Clinical Investigations

  • Event Problem Codes of the US FDA, which is available at:
    http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/EventProblemCodes/default.htm

4   Adverse event terminology

4.1   Adverse Event Reporting

GHTF/SG2/ N54R8:2006 outlines GHTF global guidance for **post-market adverse event reporting**. The GHTF guidance covers: what to report; to whom to report; when to report; and how to report (content, including dataset elements). While it does not provide a definition of an adverse event or an incident or a serious incident involving a medical device (and IVD) it does outline the types of adverse events that that should be reported to Regulatory agencies.

Notably, the term "**adverse event**" in the context of clinical trials (i.e. in the pre-market space) has a more restricted meaning (c.f. GHTF/SG5/N5:2012) than in the post-market space (see above and GHTF/SG2/ N54R8:2006).
Finally, it should also be noted that, depending on jurisdictions, the term **adverse event** (in its post-market meaning) and **incident** can typically be used interchangeably.

4.2   Adverse event terminology used in adverse event reporting

This adverse event terminology is intended to serve as a tool for addressing reporting needs identified in previous guidance (e.g. GHTF/SG2/N54R8:2006) and relating to the occurrence of adverse events in the post-marketing period. The terminology may also be used for events and incidents occurring during the pre-market period (e.g. during clinical trials GHTF/SG5/N5:2012).

The adverse event terminology outlined here consists of four sets of specific terminologies (see section 4.4 for more details) and is intended to facilitate the reporting of:
  • **observations** at the level of the *medical device*
  • its *components* including accessories,
  • **observations** (typically adverse effects on health) at the level of subjects, i.e. *patients, users or other persons,*
  • **investigations** into possible *causes* of the event as well as *causal links* between use of the device (independent of whether malfunctioning or not) and adverse health effects.

4.3   Basic considerations regarding terms, codes and hierarchical coding structure

To ease the use of these terminologies (in particular in databases) and to reduce possible ambiguities of meaning, each term is uniquely identified by an alphanumerical code and is further explained by a definition and, in some cases, examples. The set of terminologies is based on currently available terminologies which have been reviewed, improved, and as appropriate, either expanded or simplified.

The four keywords (term, terminology, code and hierarchical coding structure) are briefly explained in the following:

- **Term/Terminology:** The use of terminologies (i.e. a controlled set of well-defined terms) can aid in the description of events by reducing ambiguity of narrative text through categorization of events.
- **Code/coding:** Ambiguity can be further reduced by the use of alphanumerical *codes*, assigned to a predefined *term* from a given pre-defined and controlled *terminology*. The assignment of these codes is known as "*coding*".
- **Hierarchical coding structure** refers to the logical arrangement of such coded terms in branching structures comprising several levels, i.e. comparable to a logical decision tree.

Although the hierarchical arrangement has been referred to as a "coding structure" (e.g. 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, and are thus of secondary importance. In such a hierarchical term structure (coding structure), more general terms comprise the entry level (e.g. Level 1). From each level 1 term, second and in some cases third level terms (Level 2 and 3) branch-off which allow various more detailed options of 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 ("coding structure") is that a large variety of terms can be utilized by users in a relatively accessible way, i.e. without the need to know all terms before using the system. Developing an effective hierarchical coding structure however requires that;

(1) level 1 terms are kept to a small number so as to ease entry into the hierarchical coding structure;
(2) that the arrangement of second and third and any other levels follows intrinsically and/or maps logical options; and
(3) avoids duplication of terms / codes which would be confusing.

Inevitably, there is a trade-off between *resolution* (i.e. number of levels and number of terms/codes) and *practicability* of such systems for users, including health care workers, manufacturers and regulatory authorities.

Level 1	Level 2	Level 3

Term	Code
Term	Code
Term	Code
Term	Code
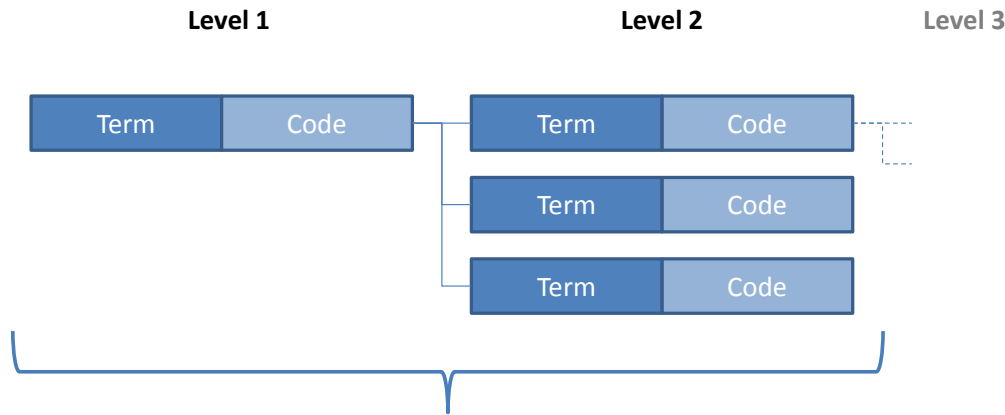
Coding =	The act of assigning a alphanumerical code to a term
Terminology =	Totality of terms used
Hierarchical Coding Structure =	Arrangement of terms in a hierarchical (logical tree-like) structure with various "levels"

Figure 3: Schematic summary of relevant keywords with respect to adverse event terms: "term", "terminology", "code", "coding", "hierarchical coding structure" and associated "levels".

4.4 The four terminologies comprising the complete adverse event reporting terminology

The complete adverse event terminology is comprised of four distinct sets of terminologies and their associated alphanumeric codes (***Table 1, Figure 3***). Reporters should be encouraged to code to the most detailed level possible in agreement with requirements of relevant jurisdictions.

1. **Medical Device Problem terms/codes (Annex A):** these terms allow capturing of the problems encountered at device(s) level through observational language without yet describing possible reasons or causes for the problems or failures observed. Annex A provides a comprehensive list of medical device problem terms and codes. It is recognized that not all jurisdictions may want to code to such detailed levels. The hierarchical structure will allow jurisdictions to choose the level of coding to use. These terms are largely based on FDA's device issue terms and are harmonized with ISO Technical Specifications 19218-1, where possible.
2. **Cause investigation terms/codes (Annex B – currently under development)**
3. **Patient problem terms/codes (Annex C – currently under development)**
4. **Component terms/codes (Annex D – currently under development)**
An overview of the four terminologies and associated codes is given in Table 1.

The code structure for the nomenclature is as follows and has been used for the medical device problem terminology (Annex A):

X|nn[nn][nn]

X is a placeholder for the annex in which the relevant nomenclature is reproduced (i.e. A to D):

Annex A: Medical Device Problem Terminology
Annex B: Cause Investigation Terminology
Annex C: Patient Problem Terminology
Annex D: Component Terminology

N are placeholders for Arabic numbers uniquely identifying the term with Level 1 terms populating digits 1-2 only, Level 2 terms populating digits 3 to 4 (maintaining the Level 1 parent term digits), Level 3 terms using digits 5 to 6 – again maintaining the level 1 and 2 parent term digits.

Each code thus reflects the relationship to the parent / child term and the body of nomenclature it belongs to. Having two digits per level allows for changes in the future (deletion of terms / introduction of terms), which requires assignment of *new* codes so as to allow *backward compatibility* with existing terms/codes from previous reporting and as compiled in data bases.

Table 1: Overview of the four terminologies comprising the complete terminology for adverse event reporting.

Nr.	Name of terminology	Description	Annex	Coding system
1	Medical device problem	Terms/codes for describing problems (malfunction, deterioration of function, failure) of medical devices that have occurred in pre- or post-market contexts (e.g. clinical studies, clinical evaluation or post-market surveillance)	A	A|00[00][00]
2	Cause investigation	underdevelopment	B – to be developed	B|… (to be defined)
3	Patient Problem	underdevelopment	C – to be developed	C|… (to be defined)
4	Component	underdevelopment	D – to be developed	D|… (to be defined)
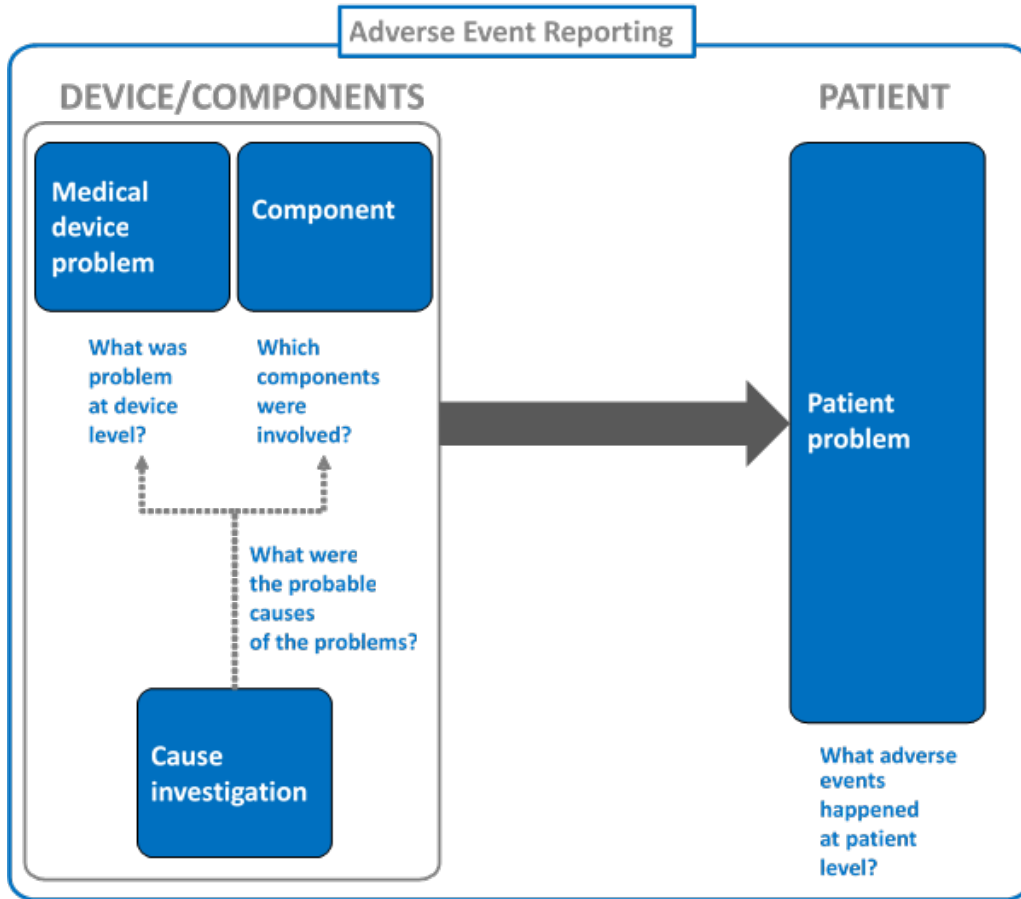
Figure 4: *The Adverse Event Reporting terminology is composed of four sets of terminologies: (1) Medical device problem terminology, (2) components terminology, (3) cause investigation terminology and (4) patient problem terminology. Note that for an effective monitoring of adverse events, means of effectively identifying devices as well as the category they belong to (e.g. GMDN) are important.*

5. Maintenance of adverse event terminology

Due to the nature of the medical device industry and the implementation of new technologies, materials, designs, procedures etc., the medical device problem terms, and its associated component terms are expected to require updating to adapt to technical progress. For this reason there is need for periodic review and maintenance of the constituting terminologies and codes in view of adding, modifying or removing terms as required.

However, it is important that changes to the AE terminology should be restricted to the absolute necessary, i.e. mainly reserved for adaptation to technical progress (new terms 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 alike so needs to be managed with this in mind.

The detailed maintenance plan adverse event terminology can be found in IMDRF/AE WG/N44FINAL:2017.

Annexes

Annex A: Medical Device Problem Terms and Codes