



Review

Reporting adverse drug reactions: a view on ADR Dictionaries

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Abstract:

Adverse drug reaction (ADR) reporting constitutes most important reporting in clinical exploratory studies. There are defined terminologies by different bodies across the world which the clinical research professional must be aware of. These terminologies are provided in different ADR dictionaries such as WHOART, COSTART System, MedDRA, ICD9, SNOMED, etc. Some companies have developed their own dictionaries for reporting or defining adverse drug reactions. This review provides a glance through these dictionaries that provide detailing about adverse drug reactions terminologies.

Introduction

International Conference on Harmonization of technical requirements for registration of pharmaceuticals for human use (ICH) defines “Clinical investigation or clinical trial as any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s) and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.”¹

Whereas adverse drug reactions are defined as all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase responses to a

medicinal product means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out.¹

Identifying and reporting adverse reactions is of paramount importance in clinical research process. To identify events and indications associated with different diseases, it is important to define them. This can be achieved through dictionaries. These include COSTART System, WHO-ART, Japanese adverse reaction terminology (J-ART), International Classification of diseases 9th Revision (ICD9), Hoechst adverse reaction terminology (HARTS), MedDRA, Systematized nomenclature of medicine- clinical terms (SNOMED). This review provides brief information about these dictionaries.



Purpose of Adverse Drug reaction dictionaries²

ADR Dictionaries serve the same purpose as common vocabulary dictionaries. These provide investigators in clinical trials to identify and code the same diagnostic symptom all over the world. This system thus standardizes ADR reporting and eases work in clinical operations.

Adverse drug reactions reporting dictionaries

1. COSTART System^{2,3}

Coding Symbols for Thesaurus of Adverse Reaction Terms (COSTART) was developed by United States Food and Drug Administration (US FDA). It is used for coding, filing, retrieving adverse drug and biologics experience reports. It has anatomical hierarchical arrangement of terms from broad to narrow criteria. There are four indexes in COSTART: Index A provides list of search categories (body system and special); Index B provides alphabetical list of all coding symbols; Index C provides listing of coding symbols by body system categories; Index D provides listing of commonly used terms by physicians to report ADRs. COSTART was superseded by MedDRA. COSTART was last updated in metathesaurus in 1999.

2. Medical dictionary for regulatory activities (MedDRA)^{4,5}

It was developed by the International Conference on Harmonization (ICH). It is owned by the International Federation of Pharmaceutical Manufacturers and

Associations (IFPMA) that acts as trustee for the ICH steering committee. Maintenance and Support Services Organization (MSSO) serves as the repository, maintainer, and distributor of MedDRA as well as the source for the most up-to-date information regarding MedDRA and its application within the biopharmaceutical industry and regulators. The revised versions are released twice a year in the months of March and September. MedDRA is organized by System Organ Class (SOC), divided into High-Level Group Terms (HLGT), High-Level Terms (HLT), Preferred Terms (PT) and finally into Lower-Level Terms (LLT). In addition, it includes Standardized MedDRA Queries (SMQs). SMQs are groupings of terms that relate to a defined medical condition or area of interest.

3. World health organization – Adverse reaction terminology (WHOART)⁶

It is dictionary that means to serve basis for rational coding of adverse drug reactions. It consists of four level hierarchical structures such as system organ class, high level terms, preferred terms, and included terms. It is open ended dictionary i.e. new terms can be added as necessary and is updated once in three months. As it is developed by WHO, many pharmaceutical companies across the world follow this dictionary.

4. Japanese adverse reaction terminology (J-ART)

It was developed on basis of WHOART and is product of Japanese Ministry of Health, Labor and Welfare (MHLW). It consists of



30 system organ classes 1576 preferred terms and 2668 included terms.

5. International Classification of diseases 9th Revision (ICD9)⁷

ICD coding system provides alphanumeric codes to diagnosis, description of symptoms and cause of death related to human beings. ICD codes are used internationally, used by health authorities to track certain diseases. ICD was firstly developed by Jacques Bertillion in 1893 in France. In 1898, it was adopted in USA and considered ICD 1. Current version in use is ICD 9th Revision. But after 1 October, 2013; ICD 10 will become effective. ICD9 and ICD 10 are freely available on websites <http://www.icd9data.com/> and <http://www.icd10data.com/>

6. Hoechst adverse reaction terminology (HARTS)

Hoechst Company (now called Aventis) modified the currently available ADR dictionaries to create their own for certain purposes or regional use.

7. Systematized nomenclature of medicine- clinical terms (SNOMED)⁸

SNOMED was developed by College of American Pathologists in 1977. It is clinical healthcare terminology providing comprehensive resource of scientifically validated content. It contains more than 3 Lakh concepts with meanings. It is based on “concept” with unique meaning and unique identifier number. SNOMED can be searched online

via <http://www.snomedbrowser.com/> or through access provided by International health terminology standards development organization.

Using ADR Dictionaries

Many of the ADR dictionaries enlisted above are electronically compliant and various translations in different languages across the globe are available. Therefore, investigator at clinical trial site must be keen in reporting the ADR. Consistency in the use of same dictionary at all time points in clinical trial should be followed. Certain confusing terms must be clearly defined and coded. Care should be taken while reporting these types of data.

Conclusion

Adverse reactions’ reporting is key aspect in conducting clinical trial. Dictionaries like MedDRA and ICD 9 are the most commonly used dictionaries around the world. These allow investigators and clinical trial monitors to report the same ADR at all sites. Definitely, it causes streamlining of the process of clinical trials.

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