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Coding in Pharmacovigilance Using MedDRA: A Review

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Abstract: *This review explain process what is used for medical coding in Pharmacovigilance and, in brief, most commonly used medical dictionary MedDRA. The purpose of this paper is a modest contribution to easier and more successful understanding of the encoding process in clinical data management in the field of Pharmacovigilance. There may be severe result if there is miscategorise of adverse events in clinical trials. For the purpose of decreasing the scope for interpretation several steps are involved such as from subject adverse event experience to presentation in tablets should be possibly standardised. MedDRA is a predefined dictionary where adverse events, signs, symptoms, diseases and diagnosis and statistical analysis are categorized. Coding is a process in which the universal dictionary is which is required for translating the event which is reported by the investigator into a standard term. For the hunt for safety signal frequencies and incidences of adverse events can be scrutinized once the adverse events have been accurately coded[5].*

Keywords: *Adverse events, MedDRA MSSO, MSSO, System Organ Class (SOC), High Level Group Term (HLGT), High Level Term (HLT), Preferred Term (PT), Lowest Level Term (LLT), Scope, Languages, Maintenance of MedDRA*

I. INTRODUCTION

Pharmacovigilance is an important part of clinical research[4]. Both clinical trials safety and post marketing pharmacovigilance are critical throughout the product lifecycle. Pharmacovigilance is "defined as the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects, particularly long term and short term adverse effects of medicines." Pharmacovigilance is still in its infancy in India and there exist very limited knowledge about the discipline. Pharmacovigilance has received different adverse event reports and this report is classified in four methods in Pharmacovigilance such as,

- Passive surveillance
- Active surveillance
- Cohort event monitoring
- Targeted Clinical Investigations

Medical Dictionary for Regulatory Activities (MedDRA) is an internationally used set of terms relating to medical conditions, medicines and medical devices. It was created to assist regulators with sharing information. It is also used by industry, academics, health professionals and other organisations that communicate medical information. The Pharmacovigilance are received safety reports in mail, mobile phone, via fax or through any social media also reporter of safety report could be healthcare professionals and non-healthcare professionals. MedDRA Coding is process of converting investigators "verbatim" terms to standardized "Preferred Term" (PT). Standardization allows sorting of adverse event (AE) and grouping of like events. Preferred Term is used to calculate incidence of AEs in signalling, PSUR/ DSUR document preparation.

1.1 Medical Coding

Medical coding is the conversion of procedures, healthcare diagnoses, medical services, and equipment into medical alphanumeric codes. These codes act as the communicating language between doctors, insurance companies, insurance clearinghouses, hospitals, government agencies, and other health-specific organizations. ICD codes (International Classification of Diseases) to a patient's injury or sickness.

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Hence medical coding is required by using standardize medical dictionaries. Data listed above like AEs, SAEs, MH , CM and any other category generally are coded. However coding AEs, SAEs and CM is mandate in any given clinical trial. There are five standardized medical coding dictionaries in the market;

- **COSTART:** The Coding Symbols for a Thesaurus of Adverse Reaction Terms (COSTART) was developed by the United States Food and Drug Administration (FDA) for the coding, filing and retrieving of post-marketing adverse reaction reports. COSTART provides a method to deal with the variation in vocabulary used by those who submit adverse event reports to the FDA. Use of this dictionary allowed for standardization of adverse reaction reporting towards the FDA in a consistent way.
- **ICD9CM & ICD10CM:** The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) is based on the World Health Organization's Ninth Revision, International Classification of Diseases (ICD-9). ICD-9-CM is the official system of assigning codes to diagnoses and procedures associated with hospital utilization in the United States. The ICD-9 was used to code and classify mortality data from death certificates until 1999, when use of ICD-10 for mortality coding started.
- **MedDRA:** Medical Dictionary for Regulatory Activities (MedDRA®) is a medical coding dictionary developed by Maintenance and Support Services Organization (MSSO). MedDRA is supported by International Conference on Harmonization (ICH) on Technical Requirements for Registration of Pharmaceuticals for Human use. Prior to development of MedDRA, there was no internationally accepted medical terminology for biopharmaceutical regulatory purposes.
- **WHO-ART:** The WHO Adverse Reactions Terminology (WHOART) is a dictionary meant to serve as a basis for rational coding of adverse reaction terms. The system is maintained by the Uppsala Monitoring Centre (UMC), the World Health Organization Collaborating Centre for International Drug Monitoring. The system is no longer actively maintained.
- **WHO-DDE:** The Uppsala Monitoring Centre (UMC) WHO Drug Dictionary Enhanced. (WHO DDE) is the most comprehensive and actively used drug coding reference work in the world. The information it contains helps ensure that clinical trial data as well as safety data is accurately coded, analysed, interpreted and reported.
- MedDRA is widely used medical coding dictionaries used for coding medical terms generated in clinical trials. To maintain uniformity in reporting a term is next to impossible in any given clinical trial. However for a coder it is a challenging task to ensure that the term recorded/reported on data collection instrument (CRF/eCRF) is coded appropriately.

II. MedDRA

MedDRA is a rich and highly specific standardised medical terminology developed by ICH to facilitate sharing of regulatory information internationally for medical products used by humans. It is used for registration, documentation and safety monitoring of medical products both before and after a product has been authorised for sale. Products covered by the scope of MedDRA include pharmaceuticals, vaccines and drug-device combination products. MedDRA is open to anyone who would like to use it, although on its initial implementation in 1999, most users were based in Europe, Japan and USA. Today, its growing use worldwide by regulatory authorities, global pharmaceutical companies, clinical research organisations and health care professionals, allows better global protection of patient health. In the entire regulatory process starting from premarketing to post-marketing and also for data entry, retrieval evaluation and presentation, the terminology is used. In extension, it is the classification of Adverse Events approved by International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.3 It is updated biannually, once in March which is a complex release and other update is on September which is a simple release. MedDRA is used extensively including in United States, European Unions and Japan. Its use is presently authorized in European and Japan for the purpose of safety reporting. ICH MedDRA management board inspects the activities of MedDRA MSSO. The management board consists of six ICH parties, Medicines and Health Care Products Regulatory Agency (MHRA) of UK, Health Canada and WHO (as an observer). MedDRA is used for coding in medical terms generated during all phases of clinical trial, excluding animal toxicology, therapeutic indications which include signs, symptoms, diseases, diagnosis, or prophylaxis of disease, and modi-fication of functions, coding names and quantitative results of investigations, surgical procedures and medical/social/family history.

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2.1 Purpose of MedDRA

- Facilitate the exchange of clinical information through standardization.
- Important tool for product evaluation, monitoring, communication, electronic records exchange, and oversight.
- Supports coding (data entry) and retrieval and analysis of clinical information about human medical products including pharmaceuticals, biologics, vaccines, and drug-device combination products.

2.2 Structure of MedDRA

The MedDRA dictionary contains 5 hierarchial levels of medical terms coding in (Fig.1)

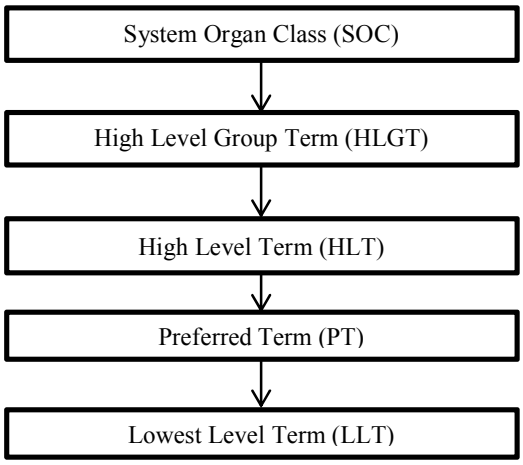

Fig.1 Five level of medical terms coding

1. **System Organ Class (SOC):** It can be defined as the maximal level of the MedDRA terminology which is notable by anatomical or physiological system, aetiology or purpose. It contains 27 System organ class.
2. **High Level Group Term:** HLGT is a miraculous caption for one or several HLT's which is associated with anatomy, physiology, pathology, aetiology or function.
3. **High Level Term (HLT):** HLT is superior to PT level. It is connected to PT by anatomy and physiology, pathologically, causes and its functions. For instance, HLT Broncho spasms and obstruction and HLT Mediastinal disorders. Here, the terms used are not based on classification so, there is no specific uniformity all over the phraseology.
4. **Preferred Term (PT):** It is well defined for signs and symptoms, disorders, identifying the disease, drug indications, examinations, surgery or any medical process, also history of family, medical history or social history. PT must be distinct and self-defined to achieve global standard conditions.
5. **Lowest Level Term (LLT):** LLT contains the least term. It is connected solely to single preferred term. It is the base level of terminology which is associated to a single PT as a synonym, lexical variant or quasi-synonym.

Common Problems Faced by Medical Coding Expert while Coding

- Illegible verbatim term
- Spelling errors
- Use of abbreviations
- Multiple signs and symptoms recorded as separate events which may lead to some diagnosis (for example: signs and symptoms recorded as running nose, cough and fe-very may lead to diagnosis of Pneumonia)
- Multiple medical concepts recorded together. To code we need to split the terms.
- Event is recorded without mentioning the site e.g. ulcer is recorded without additional information like moth ulcer, leg ulcer etc
- Multiple medical concepts recorded which had surgical procedure and reason for injury. However the reason or cause or site of injury is not clarified.
- A medication term reported however allergy due to the medication or outcome of the allergy is not specified[7].

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2.3 Languages of MedDRA

The users of MedDRA have found it to be such an important tool that, in addition to English, it has been translated into multiple languages. Multiple languages allow most users to operate in their native language which promotes accuracy and precision of assigning terms. This interoperability is very powerful and allows easy multinational sharing of data. Supporting documentation is maintained with each release of MedDRA for many of the languages.

1. English
2. Chinese
3. Czech
4. French
5. Dutch
6. Portuguese
7. German
8. Hungarian
9. Italian
10. Japanese
11. Spanish
12. Russian
13. Korean
14. Brazilian Portuguese

2.4 Maintenance of MedDRA

Maintenance and Support Services Organization (MSSO) governs MedDRA. The intellectual property rights of MedDRA are maintained by International Federation Pharmaceutical Manufacturers and Association (IFPMA) which is a trustee of International Conference on Harmonization (ICH) Steering Committee. As per the request2 of the subscriber, MedDRA is updated by MSSO

MSSO is the management board appointed by ICH steering committee.

- Maintain and upgrade MedDRA.
- Release Updated MedDRA versions twice a year (in March and September).
- MSSO activities are governed by ICH MedDRA Management Board.

2.5 ICH MedDRA Management Board

Six Parties: EU, EFPIA, FDA, MHLW, JPMA, PhRMA.

Three Observers: WHO, EFTA, Canada European.

1. Commission – European union (EU)
2. European Federation of Pharmaceutical Industries and Associations (EFPIA)
3. US Food and drug Administration (FDA)
4. Pharmaceutical Research and Manufactures of America (PhRMA)
5. Ministry of Health, Labor and Welfare, Japan (MHLW)
6. Japan Pharmaceutical Manufacturers Association (JPMA)

III. CONCLUSION

In Pharmacovigilance, medical coding is required by using standardize medical dictionaries. MedDRA is a rich and highly specific standardised medical terminology developed by ICH to facilitate sharing of regulatory information internationally for medical products used by humans. It is used for registration, documentation and safety monitoring of medical products both before and after a product has been authorised for sale. This is a continually evolving area, and we are just beginning the process of standardization in the pharmacovigilance field. If true standardization of dictionaries and their mode of use are ever achieved, then it will greatly facilitate the sharing of safety data and should improve the effectiveness of the pharmacovigilance process.

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