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In the next issue of ***EDC Today:***

Standards, Standards, and More Standards

About EDC Management:

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Fundamentals of MedDRA

EDC Today *is an independent publication on current information and issues in Electronic Clinical Systems (ECS) strategies and technologies for the Biotechnology and Pharmaceutical (Biopharma) industry. Each month we examine topics related to ECS theory, technology, practice, or implementation.*

EDC Management is pleased to see that after many years of numerous "do-it-yourself" medical terminology coding dictionaries in use by Biopharmas, the FDA has committed to a standard dictionary, and that this dictionary has become the standard for adverse event reporting in the USA. This fairly recent commitment is to the ***Med****ical* ***D****ictionary for* ***R****egulatory* ***A****ctivities, most commonly known as MedDRA. While for some the adoption of a new dictionary has meant a lot of turmoil in terms of reorganization of Biopharma dictionary group personnel and the "recoding" of data collected prior to the adoption, most have seen the change well worthwhile.*

In this issue, we explore the fundamentals of MedDRA, hoping to provide a primer in medical terminology coding for the uninitiated, non-dictionary group, persons otherwise involved in clinical trials. We begin by discussing the need for coding, and then delve into MedDRA, its structure, its use, and why we are pleased to see it after all these years.

Introduction

For many years Biopharmas performed medical terminology coding using their own private dictionaries developed totally "in-house" or modified in some way from one or more dictionary sources such as Coding Symbols for Thesaurus of Adverse Reaction Terms (COSTART), World Health Organization - Adverse Reactions Terminology (WHO-ART), International Classification of Diseases (ICD9), and World Health Organization – Drug (WHO-DRUG) resulting in a hodgepodge of dictionaries and coding schemas.

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In order to bring consistency and uniformity to the coded data being submitted to it, the FDA has recently committed to a standard coding dictionary, namely MedDRA. In addition to the FDA's selection of MedDRA, the International Conference on Harmonization (ICH) backs MedDRA and the European Union and Japanese regulatory bodies mandate the use of MedDRA for safety reporting.[1]

Biopharmas have dedicated entire organizations (often known as Dictionary Groups) to the task of maintaining their private clinical trial dictionaries, coding medical terminology and/or resolving autoencoding failures (i.e., terms that could not be "automatically coded" by a computer algorithm). Commonly coded clinical data includes adverse event verbatim descriptions, medical history, physical conditions and procedures, and medications.

While MedDRA brings consistency and uniformity to the situation, these dictionary groups are still needed. In fact, according to Coding Plus, "The MedDRA dictionary itself poses significant challenges. It is new, complex, and roughly 10 times larger than COSTART or WHO-ART."[2] MedDRA also brings its own challenges concerning the performing of autoencoding failure resolution, dictionary updates, and version control.

Incidentally, while the FDA and other regulatory agencies have selected MedDRA, the other dictionaries (and sources) previously mentioned still have their supporters and uses. Obviously the World Health Organization and the Center of Disease Control continue to support "their" dictionaries while the ICD9 dictionary is used extensively in the Health Care industry for insurance claims purposes.

Why Is Coding Necessary?

At one time, coding of data stored in a computer database was required due to technical limitation and cost. In the early days of computer usage, electronic storage space was very limited and extremely expensive. This is no longer the case, but it seems that the habits formed in the past (in computer terms, this could be as little as a year or two!) centered on storage space frugality lingered for far longer than necessary. The lingering impact of this legacy of the past has only been overcome fairly recently.

The need for coding however, continues and may always be necessary. The reason being that in order to perform statistical analysis, clinical trial data needs to be structured in such as way that a computer program or human being are able to count data items that are "identical" (in clinical terms) and to be able to group items that are "similar" (in categorical terms). One of the requirements for being able to do this is found in the labeling that must be provided for all prescription medications. The labeling provides the consumer with information concerning possible adverse reactions they might experience in terms of probabilities, that is, the percentage of people that have experienced a particular reaction. In order to calculate these percentages, it is necessary to be able to count "identical" experiences and divide them by the total number of subjects that were in the clinical trial(s) that collected this safety information.

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Counting these unintended reactions (i.e., experiences) is hard to do when data are collected in "free text" form. It is perhaps unfortunate that, by and large, the descriptions of unintended reactions or experiences incurred during a clinical trial need to be captured and entered into the clinical trial database in "free text" form. Adverse events such as "Slight headache", "Very bad headache", "Debilitating Migraine", "Sinus Headache", "Stress headache", "Earache", "Achy right knee" may not be a description of the same thing in clinical terms, but how does one report on the occurrence of headaches, infections, and muscle and/or joint pains (as in our example) given the wide variety and variations in reporting adverse events? The answer is to code the verbatim terminology using a medical terminology dictionary that gives synonymous terms the same code (known as "equivalence") and provides a mechanism whereby grouping and classification of terms can be performed.

Furthermore, it is necessary to provide a preferred wording for synonymous terms to use for reporting purposes, for example, "Headache" might be used for "Slight headache", "Very bad headache", and "Debilitating Migraine". At a higher level, one might want to classify these terms based on the body system (or organ class) that they impact. For "Headache", this might be the central nervous system.

Coding, of course, is not limited to adverse event verbatim terminology. It is desirable to code other medical terminology such as medication names, medical procedures such as surgeries, and physical conditions.

What Is MedDRA?

According to Wikipedia, an on-line encyclopedia, MedDRA is a:

> "…clinically validated international medical terminology used by regulatory authorities and the regulated biopharmaceutical industry throughout the entire regulatory process, from pre-marketing to post-marketing activities, and for data entry, retrieval, evaluation, and presentation."[1]

MedDRA is free for regulators and priced according to company revenue for industry.

MedDRA is stratified across a five-level hierarchy ranging from the broadest grouping found in System Organ Classes (SOCs) to the maximum specificity found in Lowest Level Terms (LLTs). Each System Organ Class is divided into High-Level Group Terms (HLGT), which are further divided into High-Level Terms (HLT), which are in turn divided into Preferred Terms (PT) and finally into Lower-Level Terms (LLT).

Where Does MedDRA Come From And How Is It Updated?

The Maintenance and Support Services Organization (MSSO), an organization that reports to the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), manages MedDRA. The Japanese counterpart for MSSO is called JMO.[3]

The current version of MedDRA is version 9.0, which was released in March 2006. The dictionary is available in a number of languages (with terminology translated down to at least the preferred term level) including Dutch, French, German, Italian, Portuguese, Spanish, and Japanese.[3]

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MedDRA version updates are released twice a year (March and September).

> "MedDRA is updated continuously by subscriber change requests to add a new medical concept that is yet to be in MedDRA. The decisions are made by international medical officers on how to map the terminology within the grouping categories according to a general consensus based on language considerations internationally." [1]

The process of change requests is performed within 7 calendar days from initial receipt by the MSSO. Approved Change Requests are designated as supplemental changes to MedDRA and are posted on the MSSO Web site for review by all subscribers. It should be noted that supplemental releases are not considered "official" MedDRA releases. Supplemental terms, however, will be included in the "official", scheduled version release.

What Does All This Mean Insofar As EDC Is Concerned?

A consideration when it comes to selecting an EDC vendor is whether or not (and how well) its product(s) is integrated and/or supports the use of the MedDRA dictionary. How well the EDC product manages the twice-yearly updates to the dictionary, as well as supplemental releases, should also be a consideration.

An interesting functionality that might be offered is Version Impact Analysis. That is, a computerized process of determining what impact the changes between the current version of the dictionary and the new (as yet unimplemented) dictionary will have on the clinical trial data coded to-date. The potential exists that data previously coded will require coding changes and, in turn, this could impact previously performed statistical analysis and submitted reports. Determining the impact of upgrading to a new version of MedDRA beforehand could be a very useful feature.

Autoencoding of medical terminology and/or drug names is another functionality an EDC product might offer. Autoencoding systems typically use verbatim matching methods whereby a computer program attempts to assign a dictionary term (code) to the raw adverse event term based on matched spellings. In order to maximize the success rate of the autoencoding process (that is reduce autoencoding failures) many Biopharmas have implemented proprietary coding algorithms, many based on sophisticated speech recognition principles.[4] To what degree these proprietary-coding algorithms can be retained or modified to work with a specific EDC product and MedDRA is something that each Biopharma should investigate when selecting an EDC vendor.

In any event, the Biopharma will most likely investigate process improvement, SOP changes, and even reorganization of dictionary groups, when implementing either or both, EDC and MedDRA.

While MSSO offers a MedDRA dictionary browser, for use in searching for terms and manual coding, there are a growing number of vendors that offer coding products. A well-known example of one of these vendors is DZS Software Solutions, Inc., which offers ClinPlus, a SAS-based product.[5] DZS has also partnered with Coding Plus, offering a dictionary browser.[6]

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Conclusion

The FDA's selection of a medical terminology coding dictionary brings consistency and uniformity to what has been a hodgepodge of "do-it-yourself", Biopharma proprietary coding systems. While computer storage space is no longer expensive, the need for coding medical terminology for statistical analysis remains even with the increasing power and sophistication of computer technology.

The requirement to change to MedDRA offers Biopharmas both challenges and opportunity. The challenge will be to reorganize their existing dictionary groups and rearrange their existing coding processes. The opportunity exists to streamline their processes and more effectively share across the industry coding challenges and dilemmas.

At the same time, challenges and opportunities exist for EDC vendors to alter existing products to integrate with, and fully support the use of MedDRA. An opportunity also exists for third party vendors offering dictionary tools such as browsers and autoencoding software.

Resources

[1] http://en.wikipedia.org/wiki/MedDRA

[2] http://codingplus.com/focus.htm

[3] http://www.meddramsso.com/MSSOWeb/index.htm

[4] http://findarticles.com/p/articles/mi_qa3899/is_200210/ai_n9122481/print

[5] http://www.clinplus.com/

[6] http://codingplus.com/index.htm

Who's behind the research?

Our lead researcher, Kirk Mousley, PhD received BS and MS degrees in Electrical Engineering from MIT and a PhD in Computer Science from Lehigh University. He has been the President of Mousley Consulting, Inc. since its founding in 1993 and has directed the company's efforts in the areas of clinical database design, data editing/cleaning, document management, and submissions.

Karl Mousley received his BS in Mechanical Engineering from Rose-Hulman Institute of Technology and a MS in Computer Science from Villanova University. He has been a senior member of the technical staff at Mousley Consulting, Inc. since 1993. Among his significant accomplishments are the investigation, evaluation, and implementation of new computer technologies for clinical data management systems and developing strategic plans for integrating these technologies into current systems. He has extensive experience preparing Standard Operating Procedures (SOPs).