Global Language for Pharmaceutical Regulation

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by Vera Rulon, RHIT, CCS

What will facilitate medical product regulation and related electronic data interchange worldwide? For some regulatory authorities, the answer is the Medical Dictionary for Drug Regulatory Affairs—also known as MedDRA.

MedDRA (the name is a trademark of the International Federation of Pharmaceutical Manufacturers Associations) is an international standardized medical terminology developed for use in pharmaceutical regulation.[1] Its advent presents an opportunity for HIM professionals to apply their unique knowledge of terminologies to an area that has global impact.

A Terminology Is Born

The need for a terminology like MedDRA is born from regulations that require pharmaceutical companies to report adverse events related to their products. Coding systems used for this purpose are literally an "alphabet soup" of classifications: WHO-ART (World Health Organization-Adverse Reaction Terminology), COSTART (Coding Symbols for a Thesaurus of Adverse Reaction Terms), ICD-9 (International Classification of Diseases, 9th Revision), ICD-9-CM (International Classification of Diseases, 9th Revision, Clinical Modification), J-ART (Japanese Adverse Reaction Terminology), and HARTS (Hoechst Adverse Reaction Terminology System).

As for the many clinical trials performed outside the United States, their results may be included in a New Drug Application (NDA) or other regulatory submission to the US Food and Drug Administration (FDA), or to a regulatory authority in another country. In the past, the industry was forced to duplicate expensive clinical trials in order to market new products internationally, although national regulatory systems were based on similar requirements to evaluate the quality, safety, and efficacy of drugs.[2]

To improve the regulation process, the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) was created in 1990. Charter members included regulatory and industry representatives from three regions: the European Community, the United States, and Japan.

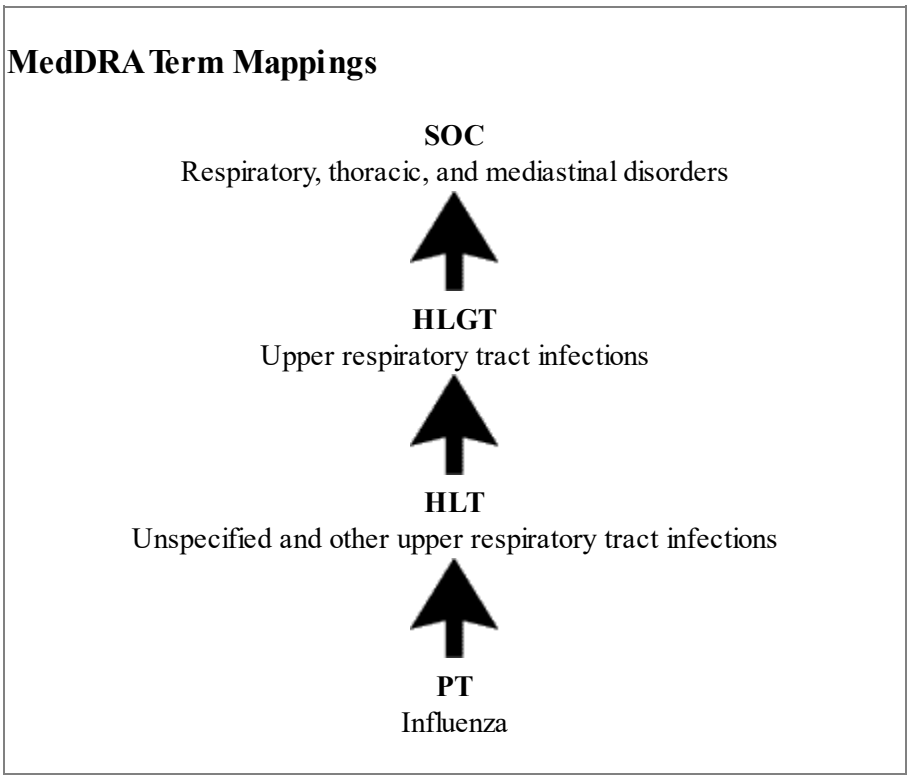
In the early 1990s, the ICH developed consensus guidelines for good clinical practice acceptable for use in the three ICH regions and continues to develop various standards for international use. One of these was in the area of medical terminology for regulatory communication. The ICH has adopted MedDRA as a new international medical terminology for regulatory purposes[3] and established the MedDRA Maintenance and Support Services Organization (MSSO) to facilitate the adoption of the system by regulatory authorities, the pharmaceutical industry, and many other users.[4, 5]

Several iterations of the terminology were reviewed and modified by clinicians and epidemiologists in their area of expertise during the system's development. For example, the psychiatry section follows DSM-IV, and the oncology section is based on National Cancer Institute-validated hierarchies showing that current medical practice and pathophysiology principles were considered in development.

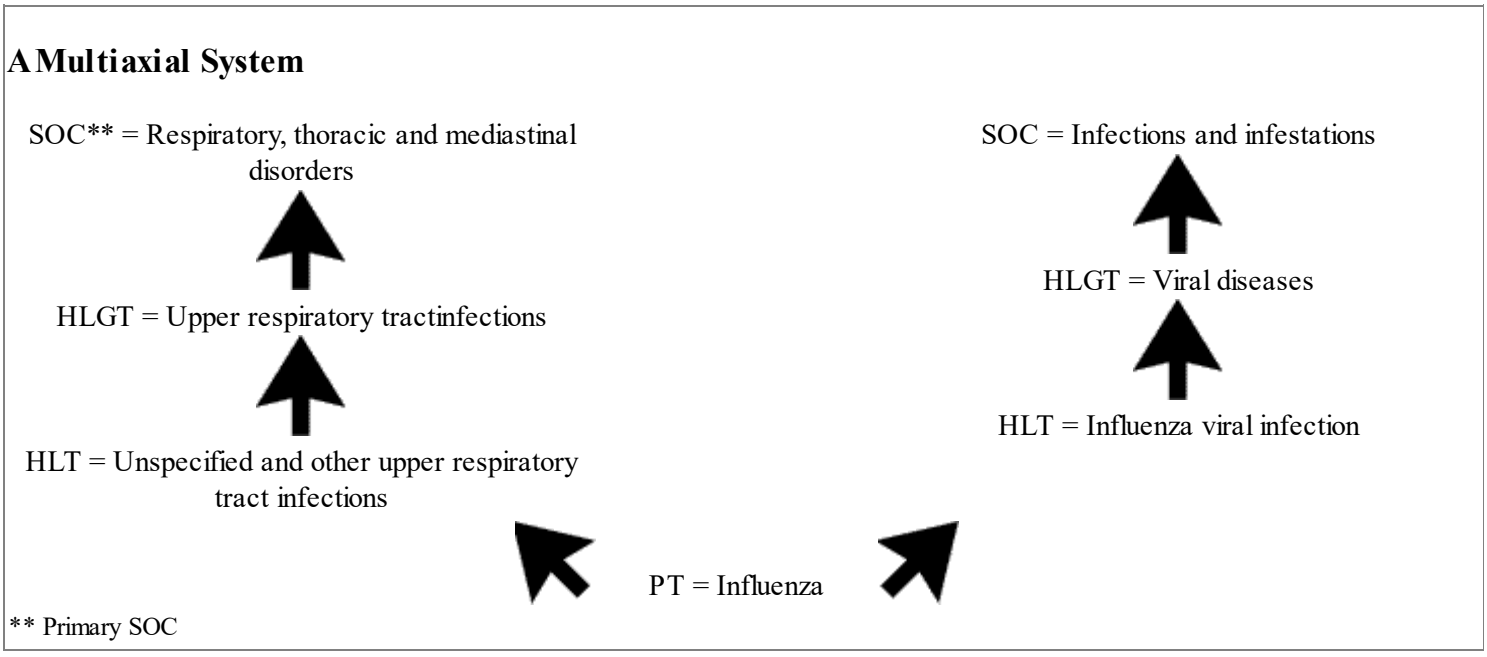
The scope of the system is broad by design. MedDRA's scope includes terms for symptoms, signs, diseases, diagnoses, therapeutic indications, names and qualitative results of investigations, surgical and medical procedures, and medical, social, and family history. In addition, previously existing systems (COSTART, WHO-ART, J-ART, HARTS, and ICD-9-CM) have all been built into MedDRA.[6] MedDRA does not, however, contain drug names.

MedDRA's Structure

MedDRA has a hierarchical structure. Lowest-level terms (LLT) are mapped to a preferred term (PT), further to a high-level term (HLT), to a high-level group term (HLGT), and finally to a system organ class (SOC). The SOC is akin to major diagnostic categories of Diagnosis Related Groups (DRGs). Here's an illustration of the progression of preferred term "influenza" through this hierarchy:[7]



Within a classification system such as ICD-9-CM, a code can represent one whole medical concept or a component of a diagnosis or procedure. In addition, the ICD-9-CM code maps to one and only one body system or disease entity as defined by the classification system. For example, code 486 (pneumonia, organism unspecified) would be found in the diseases of the respiratory section of ICD-9-CM and not in infectious and parasitic diseases. MedDRA, on the other hand, is multiaxial. This means that terms can roll up to more than one SOC (although one SOC is designated primary SOC for each preferred term). Using the preferred term influenza once again, we can see the multiaxial capabilities of MedDRA below:[8]



Depending on the data analysis perspective, MedDRA's multi-axial structure can be used in a variety of ways for data retrieval. In our influenza example, if you are analyzing data on respiratory, thoracic, and mediastinal disorders occurring during the use of a certain drug, or if you are analyzing infections and infestations, all instances of influenza will appear in both cases. In addition, there are special search categories (SSCs) that allow linkage of terms which are neither equivalent nor hierarchically related and group terms which are all relevant to an issue, usually a disease or syndrome. They also accommodate clinical concepts that cross SOC hierarchies.[9] The SSC listing includes (please note spelling of terms, as British English was adopted as the standard for MedDRA):

- anaphylaxis
- arrest (cardiac)
- blood dyscrasias/bone marrow depression
- cardiac ischaemia
- haemorrhage
- hypersensitivity reactions
- thrombosis
- upper GI bleeding/perforation
- vasculitis

Because a large number of terms (more than 40,000) are included in MedDRA, auto-encoders will be used to aid assignment of terms. Each MedDRA term is assigned an eight-digit code that does not confer taxonomic meaning. Initially, codes are assigned alphabetically by term starting with 10000001, with new terms assigned sequentially.[10]

Global Impact

Currently, MedDRA is available in English and Japanese, with French, German, Spanish, and Portuguese versions slated for future release. In the US, the FDA has been using MedDRA to code adverse event terms in post-marketing safety reports since November 1997. Further, pharmaceutical companies will soon be required to apply MedDRA terms in adverse event reporting.

Implementation of an international terminology like MedDRA raises many issues, such as language. Although British English is the official language, many countries' regulatory agencies may require reporting using their local language. Thus, a "translation effect" may affect the meaning of encoded information.

In addition, there's also a concern that while the FDA and the Japanese Ministry of Health and Welfare have endorsed the preferred term level as the currency of exchange, the European Union has announced the intention to require the reporting of lower-level terms for centrally approved products.

Furthermore, MedDRA, as a living terminology, is updated on a quarterly basis. Users will need to pay careful attention to version control as updates are released and implemented. In addition, safety data collected over several years during a clinical trial may show variation in assignment of terms and in interpretation of resulting data. And special algorithms may be needed when the results of several clinical trials conducted during a product development program need to be integrated. ICH is currently developing a "points to consider" document on these and other term selection issues.

As HIM professionals broaden their knowledge of terminologies and vocabularies in the future, MedDRA will be one to watch.

Notes

1. MedDRA MSSO Web site. "MedDRA Spoken Here." Available at www.meddramsso.com.

2. International Conference on Harmonisation Web site. "A Brief History of ICH." Available at www.ich.org/ich8.html.

3. White, Claudia A. "A Preliminary Assessment of the Impact of MEdDRA on Adverse Event Reports and Product Labeling." *Drug Information Journal* 32, no. 2 (1998): 348.

4. MedDRA MSSO Web site. "MedDRA Spoken Here."
5. White, Claudia A. "A Preliminary Assessment of the Impact of MEdDRA."
6. Green, Gary. "MedDRA—Essential Element in the Future of Electronic Submissions." Presented for Barnett International Conference Group, The Common Technical Document and Electronic Submissions, Philadelphia, PA, April 20, 1999.
7. TRW, Inc. "MedDRA Overview." Seminar presented in Boston, MA, 1999.
8. Ibid.
9. Ibid.
10. Ibid.

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