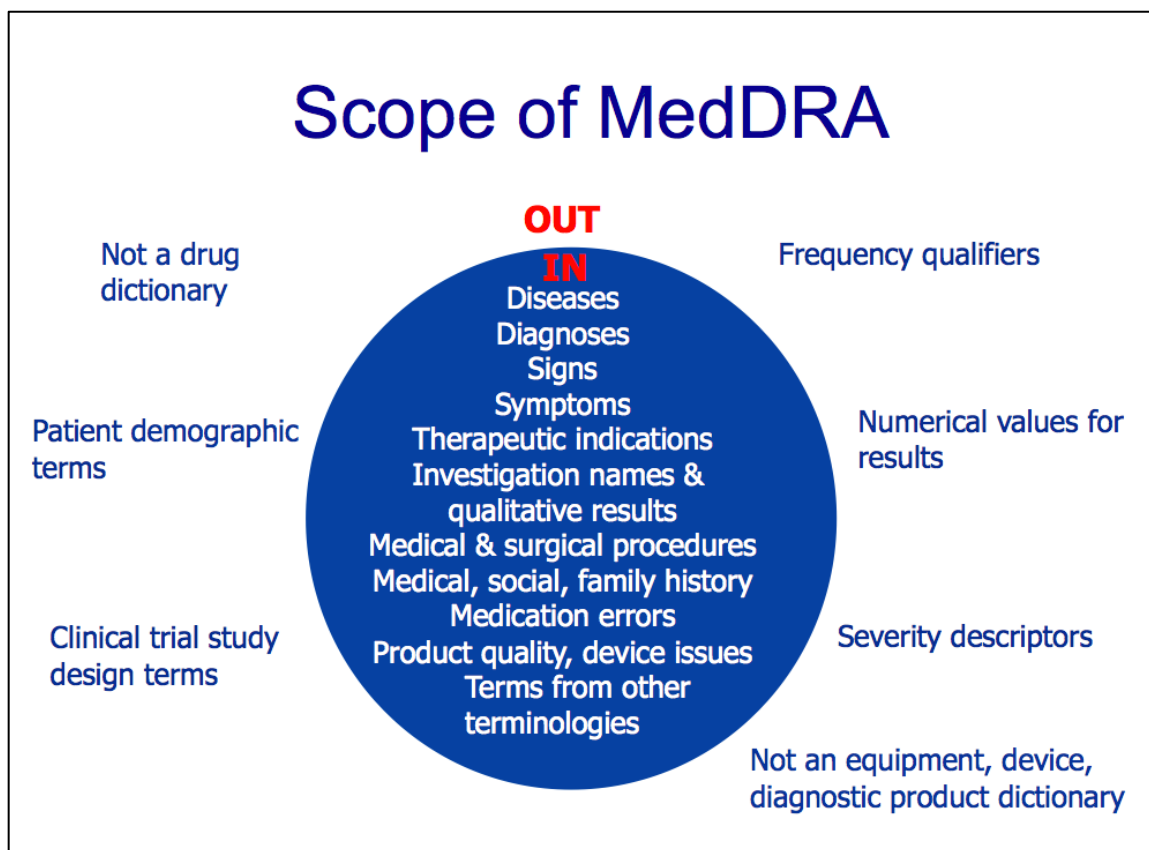


Blue Ribbon Panel 8 - Scope of MedDRA

Background



MedDRA was developed by ICH as a standardized medical terminology to facilitate sharing of regulatory information internationally for medical products used by humans. The terminology is available to all for use in the registration, documentation and safety monitoring of medical products both before and after a product has been authorized for sale.

Medical products covered by the scope of MedDRA include pharmaceuticals, biologics, vaccines, and drug-device combination products. The ICH M1 "Points to Consider" Working Group and the MSSO recently developed a concept description for "product" to clarify the types of medical products that are covered by MedDRA. This concept description is included in the MedDRA Introductory Guide for version 17.0 as follows: "In the context of MedDRA, "product" can refer to various types of products intended for human use such as drugs (prescription and over the counter), biologics, vaccines, combination products, devices, nutraceuticals, dietary supplements, etc."

The scope of MedDRA, as defined in the MedDRA Introductory Guide, has not changed appreciably since the first version of MedDRA. The terminology

applies to all phases of drug development, excluding animal toxicology. It also applies to the health effects and malfunction of devices (e.g., *PT Device related infection* and *PT Device failure*).

MedDRA is a medical terminology and the categories of terms classified as “medical” for the purpose of inclusion are as follows:

- signs, symptoms, diseases, diagnoses
- therapeutic indications
- names and qualitative results of investigations
- medication errors and product quality terms
- surgical and medical procedures
- medical/social/family history

Social circumstances falling within the “medical” scope are also included if they are relevant to the evaluation of regulatory data (e.g., in the assessment of clinical outcome of treatment in the light of exposure to risk factors).

The inclusion of terms from other terminologies such as WHO-ART and COSTART in the initial release of MedDRA (v2.1 in March 1999) was restricted to those within the scope of MedDRA as defined above.

As noted in the MedDRA Introductory Guide, the exclusion criteria used in the development of the terminology do not necessarily limit its expansion. Since it is a medical terminology, the following terms used in regulatory affairs are out of scope:

- drug/product terminology
- equipment/device/diagnostic products terminology
- study design
- demographics

As its focus is on health effects in individual patients, the following are also excluded:

- qualifiers referring to populations (e.g., rare, frequent)
- numerical values for investigations
- severity descriptors

Through its Terminology Maintenance Change Request process, the MSSO has a mechanism for ensuring that new terms added to the terminology meet the inclusion criteria as defined in the MedDRA Introductory Guide and other supporting documentation. Internal and external audits of this process also ensure that new terms fall within the currently defined scope of MedDRA.

Over the years, the growing use of MedDRA by a worldwide community of users from regulatory authorities, the biopharmaceutical industry, academic institutions, clinical research organizations, and other organizations dedicated to public health has resulted in an expansion of the types of included

medically relevant terms, e.g., toxicology terms related to chemical health threats and pharmacogenetic terms.

More recently, the MSSO has received requests from MedDRA users to add terms in certain categories that could be considered to be “pushing the boundaries” of the scope of the terminology as originally conceived and described above. However, this said, MedDRA, by its very name “Medical Dictionary for Regulatory Activities” suggests the possibility for expanding the dictionary scope within the regulatory realm, beyond the exclusive use for adverse event reporting. There is now a need to reexamine the scope of MedDRA as a medical regulatory terminology in the light of new developments in medicine and in the global regulatory environment, and to provide a framework for its evolution.

The MSSO will convene a Blue Ribbon Panel on 29 April 2014 to provide specific guidance and recommendations to the MSSO, JMO, and the MedDRA Management Board on the scope of MedDRA as it relates to the needs of its users.

Blue Ribbon Panel (BRP) to discuss and provide recommendations on:

- What should be defined as the scope of MedDRA, taking into account its function as an international medical and regulatory terminology?
- What are the general criteria to be applied when considering new topic areas for expansion in the future? For example, what would be considered to have no medical or regulatory relevance and be entirely out of scope? For example, are food and tobacco, which are regulated in certain countries, within the scope of MedDRA?
- What are the criteria for accepting terms that include human use factors or causality related concepts? Should liability issues be considered as an acceptance criterion?
- Where should new concepts/topics be placed in MedDRA? Can they be accommodated within the existing structure or, for “product related” topics, should they be placed within a separate area of the terminology?
- For certain types of information, can the use of MedDRA be expanded in combination with maintained lists? Should this expansion be based on an extended structure instead of MedDRA’s five level hierarchy or used in conjunction with MedDRA terms?

Potential topic areas for expansion:

The following are examples of topic areas that illustrate how users are requesting new types of terms at the moment that fall within a “gray area” according to the currently defined scope of MedDRA. The intent is not to have the BRP discuss these individual topics in detail but rather to use them as examples for formulating general criteria and principles for the inclusion of these types of topics in the future.

1. Manufacturing product quality terms

- Terms for product manufacturing concepts such as testing, out of specification issues, process control issues, shipping and packaging issues
- Integration in MedDRA would enable a single system to be used for adverse events and pre- and post-distribution manufacturing product quality issues without medical concepts related to them

Term Example		
Existing MedDRA Term	Possible future terms if scope of MedDRA is expanded	Not suggested for scope expansion at the moment
PT Product raw material issue	a) Process controls incorrect temperature issue b) Testing stability performed incorrectly	HEPA filter

•Possible future terms if scope of MedDRA is expanded:

- a) Refers to manufacturing process quality control. Not directly related to patient but product quality issue may have impact on patient safety.
- b) Example of "Performed incorrectly" concept

•Not suggested for scope expansion: Equipment terminology

2. Additional device-related terms

- There is no current regulatory mandate for use of MedDRA for device reporting but device and biopharmaceutical companies are increasingly using MedDRA in internal databases to facilitate communication with other company divisions and external parties

Term Example		
Existing MedDRA Term	Possible future terms if scope of MedDRA is expanded	Not suggested for scope expansion at the moment
PT Wrong device used	a) No check of device prior to use b) Reckless use	Femoral component

• Possible future terms if scope of MedDRA is expanded:

- a) Example of "Negative" or "Not done" concept
- b) "Human use/causality" term with potential legal implications

•Not suggested for scope expansion: Device terminology

3. Drug Utilization Terms

- Terms for drug utilization issues such as stopping or changing medication and the reasons for which these occur (compliance, adverse events, patient decision)
- Important concepts for EU Risk Management Plans, Phase IV studies, and pharmacoeconomic analyses

Term Example		
Existing MedDRA Term	Possible future terms if scope of MedDRA is expanded	Not suggested for scope expansion at the moment
PT Refusal of treatment by patient	Drug withdrawn from market	Drug could not be prescribed on NHS

•Possible future terms if scope of MedDRA is expanded: “Product availability” concept

•Not suggested for scope expansion: Product availability concept specific to one particular country

4. Labeling qualifiers

- A review was conducted on the applicability of MedDRA for coding indications in the labeling of various products
- Many indications concepts are represented in MedDRA (disease, symptoms, treatment, prophylaxis) but there are certain categories of qualifiers that are not currently included, e.g., age groups, response to other therapies, low vs. high risk, stage of disease, first-, second-, third-line treatment, etc.
- Including additional qualifier and attribute concepts would facilitate the use of MedDRA in coding all relevant indications information in labeling

Term Example		
Existing MedDRA Term	Possible future terms if scope of MedDRA is expanded	Not suggested for scope expansion at the moment
PT Convulsion prophylaxis	Failed first-line treatment	15-17 years

•Possible future terms if scope of MedDRA is expanded: Example of “Response to previous therapy” concept

•Not suggested for scope expansion: Numerical values

Placement of topic areas in MedDRA

The BRP will be asked to provide recommendations on the placement of any potential new topics in MedDRA, taking into consideration the four topic examples presented above, as well as any other topics which may arise in the future. The specifics will depend in part on the nature of the topic being proposed and a variety of options can be considered, including:

- Within the existing MedDRA hierarchy with 26 SOCs
- An additional “27th SOC” for product related terms
 - Topic areas 1, 2, and 3 can be considered as examples of “product related” topics given that they relate to products rather than people. One option would be to place them in a new “SOC” or “Category” in MedDRA with the usual five level hierarchy and the appropriate multi-axial links to the existing SOCs to facilitate coding and data retrieval. Other groups of existing product related terms in MedDRA such as product quality issues and device terms could also be accommodated in this new SOC or Category.
- Maintained term lists
 - Labeling qualifiers can be considered to be a type of information that is quite distinct from the product and patient topics discussed previously and therefore, they cannot easily be accommodated in the typical hierarchical structure of MedDRA. Labeling qualifiers are data elements that could be used in conjunction with MedDRA terms capturing the main indications information (disease, etc.) and these qualifiers could be placed in a maintained list that is separate from the MedDRA terminology. The MSSO already maintains lists of pediatric and gender specific terms that are used for quality assurance purposes. Points to Consider on the use of maintained term lists in conjunction with MedDRA terminology could be developed by the ICH Points to Consider Working Group to provide guidance to users in relation to coding, retrieval, and data analysis.

Recommendations should be based on the following factors

- a) On the principle of MedDRA itself
- b) On the availability of other terminologies
- c) On the analyses and coding process of the data when using MedDRA for medical concepts vs. products, if the MedDRA structure is amended