



MESSENGER

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MedDRA Release 5.1

By **Marvin Meinders,**
Manager
Terminology Maintenance

The MedDRA release version 5.1 is a simple change release which means that all changes to the terminology only occurred at the Preferred Term (PT) or Lowest Level Term (LLT) levels.

The focus of the MedDRA 5.1 release was threefold. The first area was the review of "-itis" terms for consistency of placement. The general rule applied for this review was to link to SOC *Infections and Infestations* only those "-itis" terms that were most frequently associated with infections, e.g., PT *Tonsillitis*. Those terms that were most frequently considered non-infectious inflammation, e.g., PT *Bursitis*, were only linked to their corresponding sites of manifestation SOC.

CONSISTENCY

The second focus area was ensuring that "metastatic" terms were consistently placed within the terminology. Metastatic terms (e.g., PT *Ovarian cancer metastatic*) are presently at the PT level in MedDRA and are distinct from other PT terms that indicate a "stage IV" of malignancy. This has been done

because metastases can occur at different stages of disease and are not exclusively associated with stage IV; thus, a linkage of "metastatic" terms to "stage IV" terms would not always be appropriate.

STABILIZATION

The final initiative was the stabilization of the terminology. The MSSO requested, and has been given permis-

sion from the MedDRA Management Board, to enact measures to stabilize the terminology by reducing the number of changes relative to the degree that has taken place over the past few releases. Another purpose for stabilizing the terminology was to prevent MedDRA from becoming too academic in nature and thus lessen its usefulness as a reporting tool. The number of change requests (CRs) processed has decreased from approximately 7,000 during the MedDRA release version 5.0 to just over 4,000 for MedDRA version 5.1. The stabilization initiative did not take effect until the last few months of preparation of the MedDRA release 5.1. A larger reduction in changes should be seen in the future.

IMPROVED TERMINOLOGY

With each release of MedDRA, the MSSO attempts to improve the terminology with changes that are consistent with overall subscriber needs. The updates are based on subscriber change requests, subscriber web posting responses, and user group participation. We certainly hope that you find the MedDRA 5.1 version is improved and better serves your needs.

The MedDRA International User Group Meeting

15 November
 2002

Keidanran Hall
 Tokyo, Japan

Time: To Be Determined

Check website for details



MAGs: a new — and improved — way of thinking

By Patricia Mozzicato, M.D.
Medical Officer USA

Many organizations are well on their way to converting to MedDRA, and now several organizations are MedDRA "veterans."

Having dealt with the immediate issues of MedDRA implementation (such as legacy data conversion, revised coding conventions, etc.), more and more organizations are turning their attention to data analysis issues.

As most subscribers to MedDRA know, there are some aspects of the current configuration of MedDRA that are intended to assist in understanding and organizing MedDRA-coded data. The MedDRA hierarchy itself groups terms into logical partitions at the High Level Group Term (HLGT) and High Level Term (HLT) levels. In addition, the MedDRA Special Search Categories (SSCs) were developed to link terms that are neither equivalent nor hierarchically related, but may be related symptoms, signs, or diseases relevant to a diagnosis.

Through informal discussions with the user community, the MSSO has come to realize that more might be done to assist users in understanding their MedDRA-coded data. The MSSO is highly interested in developing new ways for the user community to employ MedDRA's structure in ways that are relevant to their concerns. It is apparent from our discussions with users that the current MedDRA SSCs are not widely used. Hence, the concept of MedDRA Analytical Groupings (MAGs) has been proposed.

There are several reasons for developing MAGs: 1) MedDRA is a large and complex terminology, and "navigating" it takes some degree of acquired skill as well as fairly sophisticated medical knowledge. Providing users with "pre-packaged" relevant analytical groupings will relieve the average user of the time and trouble it takes to organize MedDRA terms into relevant groupings; 2) because organizations have been developing their own ad hoc search categories, there is the potential to drift

from the concept of standardization for which MedDRA had been developed; and 3) veteran users of the terminology have indicated to us that the current SSCs do not address the significant issues, particularly safety issues, that organizations face in drug development and regulatory processes. MAGs were envisioned to address these issues.

So, what's in a MAG?

Like SSCs, MAGs cross over SOC hierarchies and group terms found in disparate places, but in contrast to SSCs which, by definition, consist only of Preferred Terms (PTs), MAGs are not subject to such a restriction. In many cases, an HLT or sometimes even an HLGT, could consist in whole as a concept to be included in a MAG; in other cases, a whole HLT might be used with exclusion of only one or two of its linked PTs deemed not relevant.

MAGs also include signs, symptoms and conditions as well as relevant investigations and other supporting concepts. MAGs exclude Lowest Level Terms (LLTs) which were never intended to be terms on which analyses should be made or based, given their relationship to their parent PTs.

What kind of MAGs will be developed and how will they be maintained?

In response to the challenge that the current SSCs do not address relevant safety issues, the MSSO has completely re-evaluated what topics/issues should be included in the list of available MAGs. The decision of what to include will initially be drawn from the internal expertise of the MSSO staff as well as some pertinent research, but MAGs are intended to be responsive to the needs of the user community. As such, user feedback and suggestions for new and expanded MAGs will be taken into account.

Whereas "pain" and "oedema" (current SSCs) may have some academic interest, they have little relevance to the type of safety issues that organizations are faced with on a daily basis. Instead, look for the MSSO to develop analytical groupings for issues such as QT prolongation, rhabdomyolysis, pan-

creatitis, hepatotoxicity, and other important events that require special consideration during drug development and in the post-marketing milieu.

MAGs will be maintained as a separate function of the MSSO with the same medical rigor as the terminology itself. Our proposal is to establish a secondary offering consisting of MAGs which will be a complement to the official MedDRA terminology. Please note that the structure of MedDRA will be unaffected by the presence of MAGs.

Next Steps

MAGs are early in their development at the MSSO, and further refinements to our proposal will likely occur, especially as we analyze user feedback. It is possible, for example, that the MAGs themselves could have their own independent hierarchy, but it is still too early to know exactly how that concept will evolve. In the spirit of making the MedDRA a better, smarter terminology, the MSSO is committed to move forward swiftly to develop MAGs. Please check our website or attend our User Group meetings as we will communicate our progress on this important new concept. Please feel free to contact the MSSO (our email address is mssohelp@trw.com) with thoughts on MAGs.

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MedDRA translations issues

By **Jim Mundell**
Director
MedDRA MSSO

As of the first public release of MedDRA 2.1, the JMO has provided a Japanese version of MedDRA to MSSO subscribers for an additional fee.

More recently, the MSSO has received additional translations of MedDRA from the EMEA, and the MSSO has announced the availability of the Spanish and Portuguese versions of MedDRA.

Unlike the Japanese version, the Spanish and Portuguese versions are not complete through the LLT level at this time. The LLT level terms are currently provided in English. The MSSO is working to prepare the Spanish LLT terms for release, but the MSSO does not have the Portuguese LLT terms.

TRANSLATED VERSIONS

The MSSO is also in possession of the German and French versions of MedDRA, but these versions, like the Portuguese version, do not yet include the LLT level terms. In addition the MSSO has not been given permission to distribute these last two translations.

In response to questions as to why it is taking so long to provide translated versions of MedDRA, the MSSO would like to explain some of the issues involved in trying to complete each translation version.

First, there is the obvious issue that the LLT level has the largest number of terms in MedDRA. There are 56,981 terms at the LLT level in MedDRA release 5.1. Even if you remove the PT terms that are repeated at the LLT level and discount all the non-current terms, you are still dealing with 32,174 terms that need to be translated.

Second, there is the issue of finding the right translation. To translate each MedDRA term, the translated term must also be verified against the English definition of the MedDRA term for correctness of meaning.

For example, in several cases during our change request process when the MSSO medical reviewers translate pro-

posed terms, there have been issues, for example the literally translated term does not completely match the definition provided with the English term.

In such cases, a non-literal translation is used that provides the translation that would be used in the specific country, Spain or France for example, to communicate the same concept as the English MedDRA term.

EXPERT GROUP

Third, there is the issue that originally the PT level terms were targeted for reporting/communicating.

The Expert Working Group, in developing MedDRA, looked upon the LLT level with less rigor. The end result is a series of issues that complicate translating this level.

For instance the LLTs are generally synonyms for the PT terms. It is often the case that where English has five or six synonyms at the LLT level, a translation can only be provided once or twice. (It should be mentioned that there are cases where the English MedDRA sometimes only provides one or two LLT terms for a PT, but another language may have five or six commonly used variants that currently cannot be added to MedDRA.)

A variation on this problem is that MedDRA was developed with both British English and American English at the LLT level. This condition automatically violates MedDRA's own rule for unique terms. "Oedema" and "Edema" are the same term and can only be translated once.

Related to this issue are all the lexical variants that were included into MedDRA by the Expert Working Group some to create an appearance of uniqueness such as "Congenital eye disorder" and "Eye disorder congenital." (The MSSO has tried over time to reduce some of these types of issues, but many remain.)

There are also the variants introduced by the inclusion of legacy terminologies, for example "Back pain" and "Pain back," that generally can only be translated once.

In an attempt to solve some of the translation issues at the LLT level, the

MSSO has proposed a solution to EMEA that is based in part on the Japanese translation of MedDRA, which is referred to as MedDRA/J.

The Japanese version deals with all the problems mentioned above in the following manner. First it should be pointed out that MedDRA/J uses additional files. The Japanese version uses all the English files and provides five translation files — SOC/J, HLG/J, HLT/J, PT/J, and LLT/J. Some people have looked at these files, especially the LLT/J file and have assumed it had the same structure as the English LLT file. It does not. It is a completely unique file. In this file, MedDRA/J deals with non-translatable LLT terms with a flag similar to the English non-current flag, but do not confuse the two issues.

In order to maintain the MedDRA guideline of unique terms, the MSSO has proposed a variation on the MedDRA/J concept for solving translation issues at the LLT level.

DISTRIBUTION

The MSSO, unlike the JMO, is not providing translation through a different file format. Instead the MSSO is distributing translations in the same file format as the English MedDRA. In this way, the subscribers that already have created load scripts or tools that use MedDRA can still load the translation version of MedDRA. For example, you can load the Portuguese version of MedDRA into the MSSO MedDRA browser in the same way you load the English version.

The MSSO proposal for LLT terms that cannot be translated or would require the use of duplicate translations is as follows: instead of leaving a term blank and using a flag as in the MedDRA/J, the non-translatable LLT's MedDRA Code is copied into the term field. This avoids blank data fields, duplication rule violations, and confusion over the use of multiple flags.

It will also become clearly apparent when looking at a report that the LLT is untranslatable. Systems and processes can be defined for this condition, and when it occurs, the PT level term should be used in place of the LLT term.



We want your feedback! Please contact us:

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MedDRA MSSO update

By **Jim Mundell**
Director
MedDRA MSSO Healthcare Solutions
TRW Systems

The MedDRA MSSO has two initiatives that are being implemented. The first is the stabilization of the MedDRA terminology. Now that the follow-on work that was identified during the MedDRA 4.0 SOC review has been completed, the MSSO is scaling back the amount of internal maintenance changes to MedDRA.

The MSSO, with the approval of the MedDRA MSSO Management Board, will also be enforcing the MedDRA change request requirement that all change requests must include a justification for making the requested change. This means that change requests without accompanying justifications, or insufficient justifications, such as "term currently does not exist in MedDRA," will be rejected and sent back to the subscriber for more information.

This initiative is being taken by the MSSO in response to subscribers' concerns over the number of changes taking place in MedDRA, and that MedDRA changes were becoming too academic

in nature. Subscribers fear that this latter issue would impact MedDRA's usability.

The impact of this stabilization will not be completely noticed until MedDRA release 6.0 (March 2003) as it was not initiated until over midway through the preparation for the release of MedDRA release 5.1.

The second MSSO initiative is to stimulate public debate in the area of MedDRA data analysis.

Members of the MSSO have been using speaking engagements and MedDRA user group breakout sessions to encourage general consideration of this topic. The MSSO has also met with representatives from WHO and the Uppsala Monitoring Center in regard to this issue.

The MSSO and some of the MedDRA

subscribers believe that the basic structure of MedDRA, although suitable for data placement and coding, is not necessarily optimal for data analysis, such as signal detection or specific health issue monitoring.

The MSSO intends to work toward the development of useful term grouping, provisionally designated MedDRA Analysis Groupings (MAGs). The MAGs will not overlie the existing MedDRA structure, but will be a separate structure designed as an external related product to MedDRA.

The MAGs will be made available to those who want to use them, but they will not impact the use of MedDRA for those who do not want to use them.

The MSSO is in the process of formulating an article for Regulatory Affairs Journal on this subject.

ACKNOWLEDGEMENTS

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AutoCode CS™ is a trademark of TRW Inc.

MedDRA® is a registered trademark of the International Federation of Pharmaceutical Manufacturers Associations.

EMEA Requirements

The use of MedDRA in the EU will become mandatory for all regulatory adverse drug reaction reporting from January 2003.

Single case reports transmitted electronically should use MedDRA from January 2002. MedDRA terms should be provided as either text or code according to regional preferences until January 2003 when codes should be used in all regions.

With regard to the management of the backlog, i.e. the ICSRs received by the EMEA before the electronic submission of ICSRs is fully implemented (including the transition phase until 31 January 2003), retrospective data submission is required.

The practical arrangements including the timeframe for the retrospective data submission needs to be communicated by each stakeholder to the EMEA and should take place between 5 December 2001 and 31 January 2004.



SEPTEMBER-DECEMBER 2002 TRAINING SCHEDULE

Listed below are the currently scheduled MSSO classes. The training schedule is periodically updated. Please access www.meddramsso.com for updated information. For your convenience and quick reference, course descriptions are provided.

<u>CLASS</u>	<u>LOCATION</u>	<u>DATES</u>
Coding with MedDRA	Barcelona, Spain	4 September 2002
Full Scope of MedDRA	New York, NY, USA	17-18 September 2002
Coding with MedDRA	Amsterdam, Holland	9 October 2002
Full Scope of MedDRA	Orlando, FL USA	15-16 October 2002
Advanced Training for MedDRA	Orlando, FL USA	17 October 2002
MedDRA Information Technology Training	Orlando, FL USA	18 October 2002
Coding with MedDRA	Basel, Switzerland	6 November 2002
Full Scope of MedDRA	Durham, NC USA	12-13 November 2002
Advanced Training for MedDRA	Reston, Virginia, USA	13 November 2002
MedDRA Information Technology Training	Reston, Virginia, USA	14 November 2002
Full Scope of MedDRA	London, UK	3-4 December 2002
Advanced Training for MedDRA	London, UK	5 December 2002
MedDRA Information Technology Training	London, UK	6 December 2002
Full Scope of MedDRA	Las Vegas, NV USA	10-11 December 2002
Advanced Training for MedDRA	Las Vegas, NV USA	12 December 2002
MedDRA Information Technology Training	Las Vegas, NV USA	13 December 2002

Registration for all open sessions can be accomplished through the MSSO web site: www.meddramsso.com

MSSO Training Advantages

The MSSO provides expert MedDRA training to members of the pharmaceutical industry. MSSO instructors have an extensive industry and MedDRA background. In addition to this expertise, the MSSO offers continuing education credits to recipients of MedDRA training. Check out the MSSO website for specific information about CEUs for each course: www.meddramsso.com

Up-to-date MedDRA Training

MedDRA training materials are periodically updated to remain current with the latest version of MedDRA. Course materials will reflect MedDRA 5.1 updates starting in late fall 2002.

On-Site Training

In addition to the open enrollment training chart above, the MSSO provides enterprise-wide and individual training courses at your company's location. Percentage discounts apply. Please contact the MSSO for more information.

MedDRA course descriptions

MedDRA ESSENTIALS (1 DAY)

Scope, structure and rules of MedDRA; examination of the idiosyncrasies of each System Organ Class and how it was developed; provides insight into the rules, usage and practices of the medical terminology.

CODING WITH MedDRA (1 DAY)

Illustrates coding examples as they pertain to the scope of MedDRA; differences between current terminologies and MedDRA; tools that support coding, and a hands-on approach to coding verbatims and narratives with MedDRA.

THE FULL SCOPE OF MedDRA (2 DAYS)

MedDRA Essentials and Coding with MedDRA. Offered as a package (more hands-on than when offered separately).

ADVANCED TRAINING FOR MedDRA (1 DAY)

Designed for the participant to understand MedDRA's impact on analysis and how to use this impact to their benefit; understand why their data looks different in MedDRA; identify search strategies, and design queries using MedDRA.

MedDRA INFORMATION TECHNOLOGY TRAINING (1/2 DAY)

Covers MedDRA implementation issues from the IT perspective and identifies the key points to consider for existing or new systems data issues, and electronic submissions.

MedDRA FOR CRAs AND STUDY COORDINATORS (1/2 DAY)

Describes how MedDRA is organized and how it is used; impact of MedDRA on adverse event and clinical trial data reporting; how case report form data translates into MedDRA.

AUTOCODE CS™ (1 DAY)

Provides an overview of the AutoCode CS software program and is intended for users (extractors, classifiers, and reviewers). The course also provides an overall understanding of AutoCode functionality for those who need this perspective.

REGISTRATION FOR OPEN SESSIONS:

MSSO Web site: www.meddramsso.com
AT&T toll free number: (877) 258-8280



Version management with MUST

The MedDRA update software tool

By Eric Lindamood
Manager
MedDRA Products and Services

As more and more companies implement and begin to use MedDRA, the most asked question of the MSSO seems to be, "how do I handle version updates?"

The MSSO is currently developing a tool to help address this need. MUST — the MedDRA Update Software Tool — will assist companies in assessing the impact of MedDRA version changes and updating their coded data.

The MSSO is working with a group of companies to develop requirements and assist in the development and testing of the tool. While the requirements

definition process is in progress, enough initial requirements have met with agreement to give our user community a sneak preview of the potential capabilities.

A version update tool needs to help you in three areas — reviewing the changes in the new MedDRA version, assessing the impact of these changes on your coded data, and assisting in recoding those records that you identify. In addition, the tool should be able to help you compare any two versions of MedDRA, not just consecutive versions.

REVIEWING CHANGES IN THE NEW MEDDRA VERSION

Most of these changes are documented in the sequential ASCII files provided by the MSSO with each ver-

sion of MedDRA. MUST will present to you in an easy-to-read and review format those terms that have been made non-current, LLTs and PTs that have moved, and LLTs and PTs that have a different hierarchy above them. MUST will allow you to filter these results to look at just those parts of MedDRA that are of interest to you.

ASSESSING THE IMPACT OF CHANGES ON YOUR CODED DATA

MUST will compare the changes identified in the review step to your coded data. Your coded data may consist of coded verbatims or a synonym list that you use to facilitate coding. MUST will assist in the relatively easy step of identifying impacts based on the review in step one, as well as new direct matches to the terminology. However MUST will also assist in the much more difficult and subjective step of identifying potential areas where a better MedDRA term now exists. This could be due to a new term with slightly different, but still not exactly matching, wording. MUST will also identify those records in your coded data where a new term has been added in the same area of the terminology.

ASSISTING IN RECODING RECORDS

Finally MUST will assist in recoding records in your coded data. For each potentially affected term, MUST will provide one or more recommendations. If none of the recommended terms are appropriate, MUST will provide a link to a MedDRA browser so that you can search for the best term. MUST will be developed with all the necessary 21 CFR Part 11 requirements for audit trail and security that are appropriate.

For many companies, the next big challenge in implementing MedDRA is the handling of new MedDRA releases. The MSSO believes that MUST will be able to help companies tackle this problem. If the MUST tool is of interest to your company, please feel free to contact the MSSO at 703.345.7799 or mssohelp@trw.com.

Northrop Grumman acquires TRW

By Michele Kang
Vice President & Deputy General Manager
Global Information Technology Division
TRW Systems

On July 1, 2002, Northrop Grumman Corporation and TRW Inc. jointly announced that we have entered into a definitive merger agreement under which Northrop Grumman will acquire TRW.

In light of this announcement, I want to restate our commitment to the ongoing work that TRW provides to the MSSO and assure you that there will be no change in our support or commitment toward meeting your program needs.

The completion of the acquisition will take time, as the merger must be approved by antitrust regulators and by the shareholders of both companies. The companies have announced that we anticipate that the closing will occur in the fourth quarter of 2002.

We are currently undergoing the requisite reviews by the government and regulators. Northrop Grumman has publicly announced its intention to initially operate TRW Systems as a separate sector within the Northrop Grumman family, seamlessly transitioning TRW into the company over time. Consequently, we anticipate no changes that will materially affect our contractual relationships with the MSSO.

TRW's Director of MSSO, Jim Mundell, will continue to have the authority to obtain whatever resources are required to meet the needs of the MSSO and he has the full backing and support of executive management. He and I are available to discuss the Northrop Grumman acquisition of TRW or any matters of concern to you.

Thank you for your continued confidence in TRW.