



MESSENGER

Published quarterly by MedDRA MSSO for our subscribers

How is J-Currency Determined in MedDRA/J (Japanese)?

By Dr. Anna Zhao-Wong
Manager, Terminology Development
and
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Senior MedDRA MSSO
International Medical Officer

MSSO subscribers have expressed confusion about the structure of the Japanese language version of MedDRA (MedDRA/J) especially regarding the J-currency of Lowest Level Terms (LLTs). The MSSO and its counterpart in Japan — the Japanese Maintenance Organization (JMO) — met to address these concerns by explaining the MedDRA/J J-currency flag maintenance principles.

First, MSSO subscribers should be reassured that MedDRA/J does not differ conceptually from the English and European-language versions of MedDRA; the concepts in all language versions of MedDRA are exactly the same. However, due to language, culture, and medical practice differences between regions, some modifications - especially at the LLT level - have been necessary.

PURPOSE OF MEDDRA/J J-CURRENCY

In MedDRA/J, there is an additional currency flag (located in a specific MedDRA/J ASCII file) for LLTs to address instances when two or more English LLTs are translated to the same Japanese term. Examples of these cases are British and American variant spellings, word order differences, singular vs. plural terms in English, word origin in Greek or Latin, etc.

MedDRA/J J-currency ensures the

uniqueness of Japanese MedDRA terms by flagging only one of the duplicated translations as current for use. The Japanese MedDRA users believe that it is difficult to use the terminology without its 'uniqueness' and that lack of uniqueness could lead to misunderstanding or confusion by the user. Just as users of English MedDRA require term 'uniqueness,' so too do MedDRA/J users for Japanese terms.

Japanese regulations recommend (but do not mandate) use of Japanese current MedDRA terms for Japanese domestic cases. For foreign cases, only English current terms are required.

CONVENTIONS FOR JAPANESE CURRENCY FLAG MAINTENANCE

The JMO has a set of conventions that are followed to apply and maintain the J-currency flag. These conventions are as follows:

- All non-current terms in English MedDRA are flagged as non-current in MedDRA/J.

- LLTs that are identical to their parent PT are flagged as **current** in MedDRA/J. Any other LLTs that have an identical Japanese translation are flagged as **non-current** in MedDRA/J.

- When the same Japanese translation is given to several LLTs, and if none of those is identical to its PT, only one LLT which seems to be 'most appropriate' among them is flagged as **current** in MedDRA/J; all other LLTs are flagged as non-current. To determine the 'most appropriate' term, the JMO applies the following criteria:

- British spelling LLTs have priority of being flagged current in MedDRA/J.

- When several English descriptions share the same Japanese translation at the LLT level, the first term that is listed in the Japan Medical Terminology (compiled by Japanese Association of Medical Sciences Committee of Medical Terminology) is flagged as current in MedDRA/J. If none of them are listed in the Terminology, then descriptions in the main entries of Dorland's Illustrated Medical Dictionary and Stedman's Medical Dictionary receive preference for flagging as current in MedDRA/J.

- The English description, which is most commonly used as medical terms in western countries, is flagged as current in MedDRA/J.

- The term that is expressed in natural word order is flagged as current in MedDRA/J. For example, a term that is expressed as 'adjective + noun' has preference over that of 'noun + adjective.'

IMPORTANT DATES

Freeze Date for Version 9.1

14 June, 2006

42nd Annual US DIA
 Philadelphia, PA

18-21 June, 2006

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Upcoming BRPs for 2006

Dr. Anna Zhao-Wong
Manager, Terminology Development

The MSSO plans to hold two Blue Ribbon Panels in 2006. The BRP is a one-day meeting of industry and regulatory experts from the ICH regions to provide insight and guidance to the MSSO on a specific topic. The 2006 BRPs will focus on CTCAE Grade/MedDRA Mapping and HLT/HLGT Feasibility Study proposals.

BRP – CTCAE GRADE/MEDDRA MAPPING (6 APRIL 2006, FAIRFAX, VA, USA)

Recently, in collaboration with the Cancer Therapy Evaluation Program (CTEP) at NCI (National Cancer Institute), the MSSO has updated the existing mapping to the newest version of MedDRA (9.0), using Lowest Level

Terms (LLTs) instead of PTs in order to obtain a more accurate representation of CTCAE term concepts.

Additionally, the MSSO has also mapped all the previously unmapped terms to MedDRA Version 9.0 LLTs.

Together with the updated mapping, a mapping convention document will be provided. This document will provide rules and conventions used in the mapping and will include examples so that the correct usage of the mapping is assured.

This updated complete mapping provides a one-to-one mapping of each CTCAE3.0 base term to one MedDRA Version 9.0 LLT; however, it does not incorporate any mechanism for mapping the different grades of CTCAE terms.

In the future, it is proposed that the MSSO and CTEP assume joint responsibility for updating the mapping with each new version of MedDRA.

The mapping will continue to be posted for download on the CTEP web site, and the MSSO web site will include a link to the mapping on the CTEP web site.

The purpose of this BRP is to discuss and come up with recommendations on the following:

- Does the updated mapping of CTCAE **base terms** with the proposed six month maintenance schedule meet the needs of MedDRA users?
- Is there a need for a standardized mapping of CTCAE grades to MedDRA?
 - If yes, what are the options for mapping?
 - If no, what guidance should be provided for users?

Representatives from both regulators and industry will be invited as panelists. MedDRA subscribers and subject experts will be invited as observers.

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J-Currency

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– Acronyms, abbreviations, and terms containing conjunctions have a lower priority for designation of currency in MedDRA/J.

– Terms containing conjunctions have a lower priority. For example, LLT

Aortic aneurysm is flagged as current in MedDRA/J while LLT *Aneurysm of aorta* is non-current.

The MSSO and JMO hope this explanation serves to address questions that MSSO subscribers have had regarding MedDRA/J. We welcome your feedback and comments. In addition, the JMO is

currently developing English language pages on their web site and will post these explanations there. For those of you who are interested, the JMO Web site is www.sjp.jp/~jmo2/index.shtml. Further explanation is available by contacting the JMO help desk at helpdesk.jmo@sjp.or.jp.

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IF YOU WANT TO BE ADDED TO THE MAILING LIST, PLEASE VISIT THE WEBSITE WWW.MEDDRAMSSO.COM OR E-MAIL US.

ACKNOWLEDGEMENTS

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Special Search Category Retirement: Possible Impact on Software Tools & Processes

In response to a frequent subscriber question and the ongoing releases of Standardised MedDRA Queries (SMQs), the MSSO is pleased to announce a timetable for the 'retirement' of MedDRA Special Search Categories (SSCs).

SSCs have been a component of MedDRA since the initial release of MedDRA Version 2.1 in March 1999.

In general, feedback from subscribers on the utility of SSCs has been that they are 'too broad' and that the topics represented are not very useful. With the development and implementation of SMQs, the utility of SSCs has been further diminished.

As a result, the MSSO will discontinue the maintenance and distribution of SSCs in March 2007 (MedDRA Version 10.0).

The MSSO anticipates that the most significant impact to subscribers will be on new version loading software tools. We intend to archive the existing SSC files on the subscriber section of the

MSSO Web site, and we will no longer include the SSC ASCII files (spec.asc and spec_pt.asc) in the set of MedDRA distribution files (Internet file download or CD-ROM).

For MedDRA Versions 9.0 and 9.1, SSCs will receive minimal maintenance (e.g., new Preferred Terms (PTs) will be considered for inclusion in existing SSCs), and no new SSCs will be developed.

This information is intended to provide subscribers more than one year to make the necessary changes to version loading software tools and processes. As mentioned above, if the SSC ASCII files are needed by any subscriber, archived versions will be available on the MSSO web site.

Eudravigilance and the MedDRA Subscription

Did you know? If you are a small organization headquartered in the EU and sponsoring non-commercial clinical trials in the EEA, your organization may be eligible for the Eudravigilance Fee Waiver MedDRA Subscription.

This type of subscription is obtained through the EMEA (not the MSSO) and allows use of the web-based EVWEB system to collect and store ICSRs for all drugs with adverse events in Europe.

To see if your organization is eligible, please contact the EMEA in relation to the Fee Waiver via email eudravigilance@emea.eu.int or web site at eudravigilance.emea.eu.int.

Upcoming BRPs

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BRP - HLT/HLGT FEASIBILITY STUDY PROPOSALS (TBD)

The MSSO developed a series of proposed hierarchical changes (HLT and HLGT) for consideration by subscribers. The proposed changes were aimed at improving the utility of MedDRA hierarchy groupings in supporting statistical analysis and reporting.

There were seven proposals posted on the MSSO web site in June 2005. They are:

1. Review 'NEC' HLTs (including 'NEC' HLGTs)
2. Group congenital PTs and their acquired counterparts under the same HLT where applicable
3. Multi-axiality of SOC *Investigations*
4. Multi-axiality of SOC *Social circumstances*

5. Multi-axial HLTs in Cumulative Data Output

6. Primary SOC for Post Procedural Terms

7. Consider whether hyper- and hypo- metabolic disorders should be under the same HLT in SOC *Metabolism and nutrition disorders*

For detailed rationale and a list of terms involved, please go to the Open for Comment section of the MSSO web site www.meddrasso/MssoWeb/comments/index.htm.

Based on subscriber feedback and discussions with the MedDRA Management Board, the MSSO plans the following actions:

1. Implement the proposal to group congenital PTs and their acquired counterparts under the same HLT where applicable in MedDRA Version 9.0
2. Implement the proposal to group hyper- and hypo- metabolic disorders

under the same HLT in SOC *Metabolism and nutrition disorders* in MedDRA Version 9.0

3. Reject the proposal to assign primary SOC of post procedural term to its site of manifestation

4. Conduct a Blue Ribbon Panel in 2006 to consider the following topics:

- a. Review 'NEC' HLTs (including 'NEC' HLGTs)
- b. Multi-axial HLTs in Cumulative Data Output
- c. Multi-axiality of SOC *Investigations*
- d. Multi-axiality of SOC *Social circumstances*

Detailed information on this meeting will be posted on the web site as soon as it is available. The HLT/HLGT BRP has not been scheduled as yet. Please continue to monitor the MSSO web site for further information.



MedDRA OPEN TRAINING

JANUARY – JUNE 2006

The training schedule is periodically updated. Please access www.meddramsso.com for updates.

EUROPE

	FULL SCOPE	CODING WITH MedDRA	ADVANCED CODING	MEDDRA FOR DRUG SAFETY PROFESSIONALS
MARCH		Madrid, Spain Mar 23	Madrid, Spain Mar 24	
APRIL	London, England Apr 25-26		London, England Apr 26	London, England Apr 27
MAY		Paris, France May 31		
JUNE	Frankfurt, Germany Jun 6-7		Paris, France Jun 1 Frankfurt, Germany Jun 7	Frankfurt, Germany Jun 8

NORTH AMERICA

MARCH		Iselin, NJ Mar 14	Iselin, NJ Mar 15	Iselin, NJ Mar 16
APRIL	Chicago, IL Apr 4-5		Chicago, IL Apr 5	Chicago, IL Apr 6
MAY	Reston, VA May 9-10	Seattle, WA May 16	Reston, VA May 10 Seattle, WA May 17	Reston, VA May 11 Seattle, WA May 17-18

WEBINARS

What's New in MedDRA 9.0 Date TBD	MedDRA for the IT Professional Date TBD
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Registration for all open sessions can be accomplished through the MSSO web site
www.meddramsso.com AT&T toll free number: (877) 258-8280



MedDRA Course Descriptions

ADVANCED CODING: CODING CONVENTIONS AND THE MEDDRA "POINTS TO CONSIDER" DOCUMENT (1/2 DAY SESSION)

This half-day course provides experienced MedDRA users with a basis for understanding the importance and utility of coding conventions as they pertain to the conversion of legacy data to MedDRA and for new data received post-conversion. Participants will be given a thorough overview of the MedDRA Term Selection: Points to Consider document and will see examples of challenging verbatim terms to code by applying the principles described in the document. Finally, participants will take a final 'test' to assess their knowledge and understanding of what had been presented in the course.

CODING WITH MEDDRA (1 DAY SESSION)

In addition to lecture instruction providing a basic understanding of the scope, structure, and rules of MedDRA, trainees receive 'hands-on' experience coding challenging verbatim terms to demonstrate their knowledge of MedDRA's structure and rules.

MEDDRA FOR DRUG SAFETY PROFESSIONALS: DATA RETRIEVAL, ANALYSIS & SMQs (1 DAY SESSION)

Combines the materials of two former MedDRA courses, "MedDRA: Interpreting Data and Query Development" and "Standardised MedDRA Queries (SMQs) Primer," into a full day class designed to provide an overview of the features of MedDRA that relate to the analysis and retrieval of MedDRA encoded data.

THE FULL SCOPE OF MEDDRA (11/2 DAY SESSION)

Provides a basic understanding of the scope, structure, and rules of MedDRA, reviews the System Organ Classes that are unique to MedDRA, and explains how MedDRA was developed. With electronic regulatory submissions now in place, it is imperative for your organization to understand the rules, usage, and practices of the only international, clinically validated, maintained medical terminology for biopharmaceutical regulatory purposes. The course illustrates coding examples as they pertain to the scope of MedDRA, the differences between older coding terminologies and MedDRA, tools that support coding, and a hands-on approach to coding verbatims and narratives with MedDRA.

Webinar Training Topics

MEDDRA FOR THE IT PROFESSIONAL (WEBINAR PRESENTATION IN TWO 2-HOUR SESSIONS)

MedDRA will soon become a regulatory requirement. Most organizations are taking advantage of the time now to develop a MedDRA implementation strategy. The IT systems provide the

infrastructure for this process. MedDRA for the IT Professional covers MedDRA implementation issues from the IT perspective and identifies the key points to consider for existing or new systems, data issues, MISO interaction, and electronic submissions.

WHAT'S NEW IN MEDDRA (WEBINAR PRESENTATION IN ONE 1.5 HOUR SESSION)

The MISO periodically schedules webinars to provide information on changes incorporated into new version releases.

On-Site MedDRA Training

All of the above listed topics are available for on-site presentation.

Training Modules Available for Download

DATA QUALITY, CODING AND MEDDRA TRAINING MODULE (FREE OF CHARGE — SUBSCRIBER LOG-IN REQUIRED)

This course provides a general discussion of the importance of collecting quality data and the role of MedDRA. The target audiences are investigators, study coordinators, and pharmaceutical company and CRO personnel including

physicians, CRAs, safety officers, statisticians, programmers, and data managers. The presentation has a 'place holder' slide for subscribers to customize the course with their own company-specific data collection and reporting conventions. This feature can be a very useful adjunct for investigator training.

Course descriptions may be found at www.meddramsso.com



Summarizing What's New in Version 9.0

By Dr. Maya Nair
Medical Officer, MedDRA MISO

MedDRA Version 9.0 brings some notable enhancements and updates since Version 8.1. As expected, being a complex change version, MedDRA 9.0 Version incorporates several

New Subscriber and Regulator Training Offered by MedDRA MISO

In order to continue to provide high levels of service to our subscribers, effective 1 January, 2006, the MISO is offering free MedDRA training for new subscribers at the Basic, Core 0, and Core 1 subscription levels.

Each qualifying subscription will receive two complimentary training credits for attendance in the Full Scope of MedDRA course (1 day). Course attendance must occur within the initial (12) months of the subscription period. For regulator training, the MISO will provide training classes in Europe and the United States. Two regulators per agency may attend one of the free training classes.

For more information on course content and schedules, please visit the Training portion of our web site at www.meddramsso.com/MssoWeb/training/training.htm.

changes at the higher grouping levels.

This article provides a brief overview of the salient developments in Version 9.0, to be elaborated on in the official *What's New* document coming out with the MedDRA Version 9.0 release.

SIMPLE CHANGE REQUEST TRENDS: The MISO continues to see a trend where requests are based on analysis requirements versus coding requirements.

We continue to receive a large number of simple change requests for general grouping terms in SOC *Infections and infestations*. Subscriber justification for these requests included the need for consistency in their analysis.

The MISO is also seeing an increase in vaccination-related terms.

COMPLEX CHANGE PROPOSALS: Of the 12 original proposals, 10 complex changes were implemented in this release. Complex change proposals considered for Version 9.0 include the results of the HLT/HLGT feasibility study.

Congenital PT concepts and their equivalent 'acquired' counterparts will now group under the same HLT as applicable in MedDRA Version 9.0.

Both Hyper- and Hypo- metabolic disorders will come under the same HLT in SOC *Metabolism and nutrition disorders*.

In addition, a Blue Ribbon Panel in 2006 will consider a review of the following hierarchy change proposals, 'NEC' HLTs (and 'NEC' HLGTs), multi-axial HLTs in cumulative data outputs as also a multi-axiality review of SOC *Investigations* and SOC *Social circumstances*.

STANDARDISED MEDDRA QUERIES (SMQs): Ten additional SMQs were added in the MedDRA since Version 8.1 bringing it to a total of (16) production SMQs, accessible at www.meddramsso.com/Translations/translationDownloads.htm.

They include Acute pancreatitis (SMQ), Agranulocytosis (SMQ), Anaphylactic reaction (SMQ), Angioedema

(SMQ), Asthma/bronchospasm (SMQ), Dyslipidaemia (SMQ), Haematopoietic cytopenias (SMQ), Lack of efficacy/effect (SMQ), Lactic acidosis (SMQ), and Peripheral neuropathy (SMQ).

COMMON TERMINOLOGY CRITERIA FOR ADVERSE EVENTS (CTCAE) AND MEDDRA MAPPING: Common Terminology Criteria for Adverse Events (CTCAE) is an adverse event dictionary used by the National Cancer Institute to report acute AEs in cancer clinical trials (ctep.cancer.gov/forms/aboutctcae.pdf). To facilitate data transfer to the FDA and other regulatory agencies, NCI has also mapped their CTCAE v3.0 terms to MedDRA V6.0, resulting in all mapping documents provided to the CTEP web sites to have MedDRA V6.0 codes, unless otherwise specified. The MedDRA- MISO and Cancer Therapy Evaluation Program (NCI/CTEP) jointly formed a task force to improve the utility of such mapping to all MedDRA and CTCAE users, and Version 9.0 reflects the latest updated mapping of such terms. More details will become available effective 1 March 2006 at the Cancer Therapy Evaluation Program website at ctep.cancer.gov.

MEDDRA AND MODIFIER TERMS: The Blue Ribbon Panel discussion on modifiers as an add-on to a MedDRA "base" term resulted in recommendations to add the modifier terms to MedDRA in a planned process. A list of proposed modifier terms is now available in early 2006 for subscriber comments and feedback. The MISO will accept all feedback until 31 March 2006. Based on feedback from MedDRA subscribers, the MISO will begin to process the terms for inclusion in MedDRA Version 9.1 (September 2006).



The MSSO and Industry Initiatives

By Mr. Eric Lindamood
MedDRA Terminology Development

As a MedDRA user, you are familiar with the MSSO's activities to maintain and distribute MedDRA. However you may not be as familiar with the MSSO's activities to promote the use of MedDRA in other areas.

MedDRA is listed in the Object Identifier (OID) Registry of the Health Level 7 (HL7) standard. The OID can be used to identify MedDRA as a vocabu-

lary used in an HL7 message. More information on HL7 can be found at www.hl7.org.

The MSSO is participating as a member in meetings of the Healthcare Information Technology Standards Panel (HITSP). HITSP will be identifying standards and vocabularies to be used in the Nationwide Health Information Network. More information on HITSP can be found at www.hitsp.org.

If you have questions or comments about these or other initiatives, please contact the MSSO help desk at mssohelp@ngc.com or 877-258-8280 (Toll Free Worldwide)/703-345-7799 (US).

New Standardised MedDRA Queries Released for Version 9.0

Standardised MedDRA Queries (SMQ) are developed as a joint cooperative effort between the Council for International Organization of Medical Sciences (CIOMS) and the International Conference on Harmonization (ICH).

There are (10) SMQs that have completed Phase II testing since the release of Version 8.1 and will be available on the MedDRA Version 9.0*. With the release of Version 9.0, the current list of production SMQs includes the following (16 total):

1. Acute pancreatitis (SMQ)*
2. Acute renal failure (SMQ)
3. Agranulocytosis (SMQ)*
4. Anaphylactic reaction (SMQ)*
5. Angioedema (SMQ)*

6. Asthma/bronchospasm (SMQ)*
7. Dyslipidaemia (SMQ)*
8. Haematopoietic cytopenias (SMQ)*
9. Haemolytic disorders (SMQ)
10. Hepatic disorders (SMQ)
11. Lack of efficacy/effect (SMQ)*
12. Lactic acidosis (SMQ)*
13. Peripheral neuropathy (SMQ)*
14. Rhabdomyolysis/myopathy (SMQ)
15. Severe cutaneous adverse reactions (SMQ)
16. Torsade de pointes/QT prolongation (SMQ)

For updated information on SMQs, please visit www.meddramsso.com/MSSOWeb/SMQ/index.htm

THE MSSO IS FREQUENTLY ASKED HOW MANY TERMS ARE AT EACH LEVEL OF THE HIERARCHY FOR THE LATEST RELEASE. FOR CONVENIENCE WE HAVE PROVIDED THIS INFORMATION BELOW:

MedDRA Version 9.0 Contains

System Organ Classes (SOC)	26
High Level Group Terms (HLGT)	332
High Level Terms (HLT)	1,682
Preferred Terms (PT)	17,320
Lowest Level Terms (LLT) **	63,817
Special Search Categories (SSC)	13
Standardised MedDRA Queries (SMQ)	16

(** LLT total includes LLTs identical to their parent PTs, as well as non-current LLTs)



Visit MedDRA at the 18th Annual EuroMeeting (DIA)

The MedDRA MSSO will have a booth at the 18th Annual Drug Information Association (DIA) EuroMeeting & Exhibition being held 6-8 March, 2006. Please visit us in Booth #40. We will be available to answer inquiries from prospective and current subscribers and to provide valuable informational updates.

Please also join Patrick Revelle, Director MedDRA MSSO, for a joint session (Track 11) entitled MedDRA: From Investigator Term to Label. This session, which takes place on Wednesday, 8 March, 2006, 11:00am - 12:30pm, focuses on MedDRA's use for statistical analyses, coding adverse events in MedDRA, and building adequate groupings for labeling.

Join us: User Group Meeting, Paris 9 March, 2006

The MedDRA MSSO holds two International User Group meetings per year. Please join us in Paris, France, for our upcoming EU User Group meeting. User Group meetings are for current MedDRA subscribers and invited guests, and are usually held in proximity to the Annual DIA conference.

Various topics of interest including regulatory information, CTC-AE mapping to MedDRA, SSCs, and SMQs will be covered. Guest speakers from Roche and the EMEA will join members of the MSSO staff in presentations.

Date: 9 March 2006, 0900 - 1330

Place: Hôtel Concorde La Fayette — Champs-Elysees
3, place du Général Koenig
75017 Paris

Meeting Room: Arc en Ciel

Cost: No Charge (includes light fare buffet lunch)

Open to: Current registered MedDRA subscribers

Register: Please see the MSSO web site to register
www.meddrasso.com/MSSOweb/activities/usrmtg.htm

For directions, please visit the hotel web site at www.concorde-lafayette.com. The nearest metro station is "Porte Maillot" (Line 1).

Should you have additional inquiries in relation to this meeting, please contact the MSSO help desk at mssohelp@ngc.com or 877-258-8280 (Toll Free Worldwide) or 703-345-7799 (in the US).



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