MedDRA Blue Ribbon Panel on Extent of Versioning and Feasibility of Annual Release

13 May 2009
Schering-Plough Corporation, Kenilworth, NJ, USA

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Acknowledgments

The MSSO is grateful to

for hosting this Blue Ribbon Panel meeting
Blue Ribbon Panel Process

• Goal is to gather input from all interested parties to develop recommendations on an issue
• Panel members represent the ICH regions
• Observers play an important role
• MSSO will present recommendations to the MedDRA Management Board for approval
Panel Members

- Barry Hammond (GlaxoSmithKline)
- JoAnn Medbery (Johnson & Johnson)
- Tom Paternoster (European Medicines Agency)
- Toni Piazza-Hepp (US Food and Drug Administration)
- Yasuo Sakurai (Japanese Maintenance Organization)
Agenda

0900 – Introduction
0915 – Extent of versioning
  - Discussion of MSSO’s draft paper
  - Discussion by Panel
1045 – Refreshment break
1100 – Extent of versioning (cont)
  - Questions
  - Panel recommendations
1230 – Lunch break
Agenda (cont)

1330 – Feasibility of annual release
   - Background
   - Potential impacts to users, MSSO
   - Discussion by Panel
1430 – Refreshment break
1445 – Feasibility of annual release (cont)
   - Questions
   - Panel recommendations
1600 – Wrap up/meeting ends
Extent of Versioning
Background

- "Versioning" = process of updating to new MedDRA release
- An issue to be addressed since MedDRA was first available
- MedDRA is released twice a year
MedDRA Maintenance

- MedDRA is a user responsive terminology
- Subscribers may submit change requests
  - 100 change requests maximum
- Twice yearly official updates
  - 1 March X.0 release (all levels)
  - 1 September X.1 release (LLT and PT levels only)
MedDRA Maintenance (cont)

• Changes that can occur:
  – New terms added
  – Terms can change position in hierarchy
  – Primary SOC allocations can change
  – LLT currency can change
  – SMQ maintenance

• Many subscribers have processes in place to deal with version updates
Goals of Version Updates

- Implement current version of MedDRA
- Stay current with regulatory authorities and partners
- Harmonize use of MedDRA to optimize communication of data
Extent of Update

• What does it mean to implement latest version of MedDRA?
  – Since coding terms in MedDRA (LLTs) are not deleted, an organization could simply apply latest version with no data changes
  – What does your organization do?
    • Data coded to LLTs that become non-current
    • Data that have direct matches to new terms
    • Medically “better” terms available in new version
Extent of Update (cont)

- Many approaches to versioning by industry and regulators
- No real regulatory mandate
- MSSO has drafted a versioning “Best Practice” document
Versioning “Best Practice” (cont)

- Proposed implementation levels

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
</table>
| A     | Identify verbatim terms linked to non-current LLTs and recode existing data  
       | Recode verbatim terms to new LLTs that are direct or lexical matches  
       | Recode verbatim terms to new LLTs that are medically better matches |
| B     | Identify verbatim terms linked to non-current LLTs and recode existing data  
       | Recode verbatim terms to new LLTs that are direct or lexical matches |
| C     | Identify verbatim terms linked to non-current LLTs and recode existing data |
| D     | Begin to use new version for coding new data; no recoding of existing data |
### Version Change – LLT Non-Current

- **Automated approach**

**Example:**

<table>
<thead>
<tr>
<th>Verbatim Term</th>
<th>Previous Version LLT</th>
<th>Version Change</th>
<th>New Version LLT (Re-coded)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swelling (extensive) of arm that was vaccinated</td>
<td>Extensive limb swelling</td>
<td>LLT <em>Extensive limb swelling</em> became non-current in new version</td>
<td>Extensive swelling of vaccinated limb</td>
</tr>
</tbody>
</table>
Version Change – New LLTs Direct/Lexical Match

- Automated approach

Example:

<table>
<thead>
<tr>
<th>Verbatim Term</th>
<th>Previous Version LLT</th>
<th>Previous Version PT</th>
<th>Version Change</th>
<th>New Version LLT (Re-coded)</th>
<th>New Version PT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary calculus, migrating</td>
<td>Urinary calculus</td>
<td>Calculus urinary</td>
<td>LLT <em>Migrating urinary calculus was added to the new version</em></td>
<td>Migrating urinary calculus</td>
<td>Calculus urinary</td>
</tr>
</tbody>
</table>
Version Change – New LLTs Better Medical Match

- Requires manual medical review

**Example:**

<table>
<thead>
<tr>
<th>Verbatim Term</th>
<th>Previous Version LLT</th>
<th>Previous Version PT</th>
<th>Version Change</th>
<th>New Version LLT (Re-coded)</th>
<th>New Version PT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darkened surface of tongue (new finding)</td>
<td>Tongue discoloration</td>
<td>Tongue discolouration</td>
<td>LLT/PT <em>Tongue pigmentation</em> was added to new version</td>
<td>Tongue pigmentation</td>
<td>Tongue pigmentation</td>
</tr>
</tbody>
</table>
JMO Survey

- All JMO subscribers have received a questionnaire from JMO
- Questions are based on “Questions to Panel” from MSSO
- JMO has received 30 answers to date
Extent of Versioning Issue

• Many answers agreed the proposed schema
• Level A to D are understandable, but there would be various modification levels
• Small size users mentioned that level D is the only way to implement
Extent of Versioning Issue (cont)

- Multiple users have a concern “Medically significant change” which include p-SOC change, LLT-PT link change and Japanese translation change. They record these cases when they judged “Medically significant”
PTC Working Group Comments

- The A-D classification scheme does not capture all currently used methods of versioning (e.g., FDA)
- State which version of MedDRA was used when implemented in pharmacovigilance database
- Is versioning undertaken on biannual or annual basis? (Simple vs. complex release?)
- If database underwent a terminology conversion, which legacy terminology was used?
PTC Working Group Comments (cont)

- Does the organization also update coding conventions/practices with new PTC release?
- A number of issues impact on level of coding, including:
  - Coding conventions
  - Stored searches
  - Labeling issues
  - PSURs
  - Seriousness lists
  - Database structure and characteristics
PTC Working Group Comments (cont)

- PTC WG suggestions:
  - Move A-D classification table to beginning section; add descriptions of how each scenario might work
  - Data should be exchanged at LLT level
  - User may want to recode terms for which they have submitted change requests

- One company noted that during period of a version change, company databases are shut down to prevent out-of-compliance submissions from being sent
Questions for Panel

1. Does the proposed system of versioning "levels" adequately address the needs of users?

2. If the answer to No. 1 is "no", or "partly", please provide specific recommendations to improve the system
Questions for Panel (cont)

3. Does the MSSO’s document address the following points adequately?:
   - The differences for versioning between safety reporting and clinical trials databases
   - The variations of versioning steps used the industry and regulatory authorities
Questions for Panel (cont)

4. What other improvements could be made to the document?
Discussion
Frequency of MedDRA Releases
Background

- MedDRA was originally released quarterly
- MSSO went to twice a year releases with MedDRA 4.0 (June 2001)
  - Based on user feedback
- Discussion of frequency of release of MedDRA has increased
  - Number of MedDRA changes decreased dramatically after MedDRA 6.1 (September 2003)
• **MSSO** averages approximately 1300 changes per release (since 7.0)
  - New terms, changes to existing terms
• Adding terms vs. changes to existing terms
  – 3 phases of maintenance

• SMQ maintenance started with MedDRA 8.0
  – Accounts for 34% of all changes after MedDRA 8.0
Background (cont)

• Supplemental terms
  – Approved changes between official releases of MedDRA
    • New terms
    • Changes to existing terms
  – Posted on MSSO website
### Supplemental Changes to MedDRA 12.1

#### Comprehensive:
- Comprehensive Supplemental Changes for MedDRA 12.1 (PDF format) *(8 May 2009)*
- Comprehensive Supplemental Changes for MedDRA 12.1 (SEQ Ascii format) *(Updated 8 May 2009)*

#### Segmented:
- Supplemental Changes for MedDRA 12.1 (PDF format) *(8 May 2009)*
- Supplemental Changes for MedDRA 12.1 (SEQ Ascii format) *(Updated 8 May 2009)*
- Supplemental Changes for MedDRA 12.1 (PDF format) *(1 May 2009)*
- Supplemental Changes for MedDRA 12.1 (SEQ Ascii format) *(Updated 1 May 2009)*
- Supplemental Changes for MedDRA 12.1 (PDF format) *(24 Apr 2009)*
- Supplemental Changes for MedDRA 12.1 (SEQ Ascii format) *(Updated 24 Apr 2009)*
- Supplemental Changes for MedDRA 12.1 (PDF format) *(17 Apr 2009)*
- Supplemental Changes for MedDRA 12.1 (SEQ Ascii format) *(Updated 17 Apr 2009)*
Background (cont)

• Supplemental terms (cont)
  – Most users do not implement until release
    • Not clear what version number to associate with the term
    • Using a supplemental term in an electronic message may produce a rejection from the recipient
    • Difficult to get the necessary resources available to review and implement small numbers of changes multiple times between official releases
  – Useful to know what will be in next release
Dates to Consider

• “Freeze” date
  – Last date to submit changes for the next release
• Release date for the English/Japanese version
• Release date for the translations of MedDRA
  – Currently two weeks after English/Japanese
Annual MedDRA release – JMO Survey

- All answers agreed to change MedDRA annual release
- Merits seem to be greater than demerits
Supplemental terms

- Change requests from JMO subscribers are very small
- Supplemental terms could be used for regulatory ICSR reporting in Japan, but it needs very complex method. This method was used very seldom.
Supplemental terms in Japanese ICSR reporting

• If there is not suitable existing MedDRA term and a supplemental term can be used
  – Supplemental term in B.2.i.0 (Reaction/Event as reported by the primary source)
  – Nearest existing MedDRA term (MedDRA LLT)
  – Nearest existing MedDRA term (MedDRA PT)

• Submit a follow-up report using implemented supplemental term when MedDRA new version available
What would be the most convenient release date for MedDRA annual release?

- March - Major version-up currently
- April - Beginning of fiscal year in many organizations in Japan
- To avoid March or April - busy business season
- JMO concluded June, September or January would be convenient for Japanese users
Modification of the Japanese Translation

• When a new MedDRA term seems be more appropriate for the existing Japanese translation, existing MedDRA would have a different Japanese translation

• When the link of a existing MedDRA term change, such as p-SOC from disorder SOC to Surgical SOC or Social SOC, there are many cases which different Japanese would be more appropriate
Other comments

• Each organization should have MedDRA up-versioning strategy
• Up-versioning process should be documented
• Recommendation for MedDRA versioning should be include either of the PTC documents
• If MedDRA move to annual release, it is better to have new SMQs release biannual
Questions to the Panel

1. If MedDRA is released once a year, a MedDRA user will have to wait as much as 19 months before a change is officially released in MedDRA. Is that scenario acceptable?
2. If users cannot wait 19 months to implement new terms, can the MedDRA user community (industry and regulatory authorities) revise current practices to incorporate supplemental terms?
Questions to the Panel (cont)

3. If a change is made to support supplemental terms, it will be necessary to define a version associated with supplemental changes? Could we simply use the next release number of MedDRA?
Questions to the Panel (cont)

4. If a single annual release of MedDRA were recommended, what would be the most convenient release date?
Questions to the Panel (cont)

5. If now is not the right time to go to an annual release, when should this question be revisited (i.e., if the number of changes in MedDRA falls below a certain threshold)?
Discussion
Back-up Slides
Annual Release – Maximum Wait

- MedDRA “Freeze” Date for version X
- Change Request Received by MSSO
- Released without change request received on 2 Dec
- MedDRA “Freeze” Date for version X+1
- Released with change request received on 2 Dec

2 Dec, 2009 - 1 Jun, 2011
Maximum wait time for a change request

1 Dec, 2009
MedDRA “Freeze” Date for version X

1 Jun, 2010
MedDRA X Released

1 Jun, 2011
MedDRA X+1 Released

15 Nov, 2009
Change Request Received by MSSO

2 Dec, 2009

1 Jun, 2010

1 Dec, 2010

1 Jul, 2011

Released with change request received on 2 Dec 2009
Uptake of Added Terms with an Industry User

As a Percentage of New LLTs available
(Overall percentage use of LLTs in Clinical Database is 31.3%)