Use of MSSO tools during MedDRA Reversioning at CSL Behring

Martin A.O.H. Menke | Global Medical Coding Lead, Safety Risk Management

Outline

About CSL and PV
MedDRA Groupings
Data Impact Report (MVAT)
Supplemental Terms (WBB)
Version Report
Questions
CSC Behring Portfolio

5th Largest Global Biotech

- Global #1 in plasma therapies
  - $30 billion industry
- Global #2 in influenza vaccines
  - $6 billion industry

Strong Market Position

- Revenues ~$8.5bn into 100+ countries
- 8 major manufacturing sites in 6 countries
- Major capacity expansion underway
- Deep R&D pipeline fueling future growth

Solid Financial Position

- Net debt/EBITDA 1.4x
- A3 / A- credit rating (stable / stable)

CSC Today

Innovation for Future Growth

- Sickle Cell Anaemia – CSL200 (lentiviral stem cell gene therapy), CSL889 (Hemopexin)
- Contact-Mediated Thrombosis – CSL312 Garadacimab (Anti-Factor XIIa)
- Respiratory Disease – CSL311 (Anti-Beta common)
- Diabetic Nephropathy – CSL346 (Anti-VEGF-B)
- Neutrophilic Dermatoses – CSL324 (Anti-GCSF)
- Systemic Lupus Erythematosus – CSL362 (Anti-IL-3Ra)
- Scleroderma – PRIVIGEN® and HIZENTRA®
- Dermatomyositis – HIZENTRA®
- Hereditary Angioedema – CSL312 Garadacimab (Anti-Factor XIIa)
High-level Overview of CSL’s Pharmacovigilance System

Global Safety Governance System
Issue Escalation
Decision Making Process and Bodies

Case Processing
- Safety data collection
- Triage
- Database entry/coding
- Evaluation/assessment
- Report distribution
- Submission to regulatory authorities

Ongoing Benefit / Risk Assessment
- Signal Management System
  - Signal detection
  - Signal management (validation, analysis and prioritization, assessment, recommendation for action)
  - Signal escalation and communication

Risk Management System
- Risk management planning
- Decision making
- Implementation of risk minimisation measures
- Safety communications (including CCSI updates)

Quality Management System for Pharmacovigilance System

Resource Management
- Structure, people training

Procedures and Processes
- Policies, SOPs, etc.

Tools & IT Systems
- Global safety database etc.

Compliance Management
- Audits, inspections
- CAPAs & deviations

Communication
Risk minimisation
Transparency

Thanks to: Gudrun Dechert, CSLB EU QPPV Office Lead

MedDRA Groupings

- Signal Detection (e.g. CMQs)
- Quality Checks / Support
  - Assessment – Listedness / Seriousness
  - Coding Quality
  - Data Entry
- Reporting Rules

CMQ: Company / Custom MedDRA Query
MedDRA Groupings – How to Create:

• Purpose
• Medical Concept Definition
• (Signs and Symptoms)
• (Mono-axial SOCs)
• (Alternative reported Terms)
• MedDRA Term Search Strategy
• Inclusion / Exclusion Criteria
• (Detailed Term/Term Analysis)

• MedDRA® DATA RETRIEVAL AND PRESENTATION: POINTS TO CONSIDER

MedDRA Groupings in Pharmacovigilance at CSL

• Signal Detection / Risk Management:
  • Company MedDRA Query (CMQ)
    e.g. high-lighting a Case of potential or identified Risk

• Case Processing
  • Autolistedness
  • Company Important Medical Events (C_IME) > Seriousness
  • Coding Quality (Warnings/Errors, e.g. unqualified lab test terms as AEs)
  • Reporting Rules (e.g. Reporting Requirement for AEs of Special Interest beyond Seriousness/Listedness)

List is non-exhaustive!
Reversioning of MedDRA Groupings

• Impact on existing Terms:
  • MedDRA Version Analysis Tool (MVAT)

• New Terms matching the Concept behind the Grouping:
  • Supplemental Terms (in Web Based Browser – WBB)
  • MedDRA Version Report (in Release Info Package / MVAT for secondary SOCs)

• Changes to MedDRA inherent Groupings (Hierarchical / SMQs):
  • MedDRA Version Report

SMQ: Standardised MedDRA Query

Impact on existing Terms – The MVAT

• Autolistedness

  • Set of Terms set up in Adverse Event Database to assist Listedness Assessment / Data Entry
  • Transition of Terms from Reference Safety Information to MedDRA Term Lists need to follow the Rules of Listedness Assessment

  • Export from Data Base
  • Upload to MVAT > “Data Impact Report”
  • Review Results
  • Update Autolistedness
The MVAT

- [https://tools.meddra.org/mvat/](https://tools.meddra.org/mvat/)

Demo MVAT - Autolistedness

Amend as needed!
### Data Impact Report

**MedDRA Version** | **Import Data** | **Data Validation**
---|---|---

**Data Impact Report Description**

- **Language**: English
- **Starting Version**: MedDRA 22.0 English
- **Ending Version**: MedDRA 22.1 English

Include Secondary SOC Information: **O**

**Note:** The starting MedDRA version must be older than the ending MedDRA version.

---

**The MVAT**

**Search** … your path

**Load Your Data**

Your data must be in Microsoft Office Excel format. The first row must contain a column header; data must begin from the second row. The required column sequence is Row ID, LL1PT Term, LL1PT Code. For the English language, supply either the LL1PT Term information, LL1PT Codes, or both. For other languages, supply either the LL1PT Term information and LL1PT Codes together, or LL1PT Codes only. Row ID information is optional. The following is an example:

<table>
<thead>
<tr>
<th>Row ID</th>
<th>LL1PT Term</th>
<th>LL1PT Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC/123 (optional)</td>
<td>Adenoma benign NOS</td>
<td>10001234</td>
</tr>
</tbody>
</table>

**Notes:**

- The MedDRA version of the imported data should match the MedDRA starting version.
- MVAT does not store your data. Your data will be erased after generating the data impact report.
- The maximum number of records accepted is 100,000.
- The data impact report assumes the uploaded data are existing MedDRA terms, therefore new term information is not included. Also, Complex Change and SW2 changes are not included.

Select data file (* .xls, * .xls) ortsuchen...
Source list is in 22.1, hence the validation errors as these terms hadn’t existed in 22.0.

Details can be visualised online and exported
Re-versioning of Auto-listedness

• Critical for Auto-listedness are Demotions i.e. a PT becomes an LLT.

Checking for new Terms – The Supplemental Terms

• Risk for Preparations containing Heparin (as Excipient)
  • Heparin-induced thrombocytopenia (HIT)
    • Definition: Type 1 HIT is a nonimmune disorder that results from the direct effect of heparin on platelet activation. Type 2 HIT is an immune-mediated disorder that typically occurs 4-10 days after exposure to heparin and has life- and limb-threatening thrombotic complications. Both types cause a pro-thrombotic condition in the setting of lowering platelets approximately 1-2 weeks after exposure to heparin.
    • Algorithm: Selection from HLT Thrombocytopenias and HLT Platelet analyses. Double check via LLT string search “heparin”.
    • Inclusion criteria: Terms specifying heparin as causative or not referring to a specific cause.
Checking for new terms – The Supplemental Terms

The Supplemental Terms, how to get there …

• https://tools.meddra.org/wbb/
The Version Report

### MedDRA Version Releases:

<table>
<thead>
<tr>
<th>Release package</th>
<th>Language</th>
<th>Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>MedDRA version 21.1.0.0D-CH 2019</td>
<td>Czech</td>
<td>8.54 MB</td>
</tr>
<tr>
<td>MedDRA Version 21.1 Nederland September 2019</td>
<td>Dutch</td>
<td>9.01 MB</td>
</tr>
</tbody>
</table>

Related Documents:
- Earlier Terminologies Legacy Codes
- MedDRA Support Documentation
- MedDRA Self Service Application

The Version Report

```plaintext
meddra_22_1_english
```

<table>
<thead>
<tr>
<th>Name</th>
<th>Änderungsdatum</th>
<th>Typ</th>
<th>Größe</th>
</tr>
</thead>
<tbody>
<tr>
<td>MedAscii</td>
<td>02.09.2019 07:08</td>
<td>Dateiordner</td>
<td></td>
</tr>
<tr>
<td>SeqAscii</td>
<td>02.09.2019 07:09</td>
<td>Dateiordner</td>
<td></td>
</tr>
<tr>
<td>detail_report_22_1_English</td>
<td>02.09.2019 07:05</td>
<td>Adobe Acrobat Document</td>
<td>2.654 KB</td>
</tr>
<tr>
<td>dist_file_format_22_1_English</td>
<td>02.09.2019 07:05</td>
<td>Adobe Acrobat Document</td>
<td>253 KB</td>
</tr>
<tr>
<td>intguide_22_1_English</td>
<td>02.09.2019 07:05</td>
<td>Adobe Acrobat Document</td>
<td>426 KB</td>
</tr>
<tr>
<td>readme_22_1_English</td>
<td>02.09.2019 07:06</td>
<td>Textdokument</td>
<td>4 KB</td>
</tr>
<tr>
<td>SMQ_intguide_22_1_English</td>
<td>02.09.2019 07:05</td>
<td>Adobe Acrobat Document</td>
<td>1.480 KB</td>
</tr>
<tr>
<td>smq_spreadsheet_22_1_English</td>
<td>02.09.2019 07:06</td>
<td>Microsoft Excel-Arbeitsblumen</td>
<td>1.171 KB</td>
</tr>
<tr>
<td>version_report_22_1_English</td>
<td>02.09.2019 07:06</td>
<td>Microsoft Excel-Arbeitsblumen</td>
<td>245 KB</td>
</tr>
<tr>
<td>whatsnew_22_1_English</td>
<td>02.09.2019 07:09</td>
<td>Adobe Acrobat Document</td>
<td>278 KB</td>
</tr>
</tbody>
</table>
Identifying new Term for an SMQ based CMQ with the Version Report

- **Unknown Risk for home-based Self-Administration (Infusion)**

- Monitor errors specifically occurring during self-administered Infusions
  - Algorithm: Selection from Medication errors (SMQ).
  - Inclusion criteria: Errors which possibly may be due to or more likely in the uncontrolled environment during home-based self-administration.
  - Exclusion criteria: Error terms that refer to procedures outside the home-administration setting, e.g., prescription, titration, etc. as well as errors not relevant due to specific product characteristics (e.g., vaccine related errors) or errors excluded by the nature of self-administration (e.g., wrong patient receiving drug).

---

Identifying new Terms for an SMQ based CMQ with the Version Report

<table>
<thead>
<tr>
<th>Change Type</th>
<th>Term Id</th>
<th>Term</th>
<th>22.0 SMQ</th>
<th>22.1 SMQ</th>
<th>22.0 Term Level</th>
<th>22.1 Term Level</th>
<th>22.0 Stat</th>
<th>22.1 Stat</th>
<th>22.0 Scope</th>
<th>22.1 Scope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Removed</td>
<td>10079135</td>
<td>Device used for unapproved schedule</td>
<td>Medication errors (SMQ)</td>
<td>Medication errors (SMQ)</td>
<td>PT</td>
<td>LLT</td>
<td>Active</td>
<td>Active</td>
<td>Broad</td>
<td>Broad</td>
</tr>
<tr>
<td>Existing PT Added</td>
<td>10074861</td>
<td>Drug delivery system issue</td>
<td>Medication errors (SMQ)</td>
<td>Medication errors (SMQ)</td>
<td>LLT</td>
<td>PT</td>
<td>Active</td>
<td>Broad</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New PT Added</td>
<td>10063151</td>
<td>Device use confusion</td>
<td>Medication errors (SMQ)</td>
<td>Medication errors (SMQ)</td>
<td>PT</td>
<td>Active</td>
<td>Narrow</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New PT Added</td>
<td>10082712</td>
<td>Product confusion</td>
<td>Medication errors (SMQ)</td>
<td>Medication errors (SMQ)</td>
<td>PT</td>
<td>Active</td>
<td>Narrow</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Promoted</td>
<td>10008383</td>
<td>Drug delivery system malfunction</td>
<td>Medication errors (SMQ)</td>
<td>Medication errors (SMQ)</td>
<td>LLT</td>
<td>PT</td>
<td>Active</td>
<td>Active</td>
<td>Broad</td>
<td>Broad</td>
</tr>
</tbody>
</table>

**Action:** Remove duplicate as “Device use issue” is already in CMQ.
Summary

• MVAT allows you to quickly analyse any MedDRA version related impact on your data.

• The Supplemental Terms and the Version Report allows easy identification of new terms that may need to be added to your MedDRA Groupings

• Use of this tools do not require a high-tech environment or specific programming skills.

Questions?

Please use the question functionality of the webinar tool!

We will try to provide answers at the end.