MedDRA was developed under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The activities of the MedDRA Maintenance and Support Services Organization (MSSO) are overseen by an ICH MedDRA Management Board, which is composed of the six ICH parties (EU, EFPIA, MHLW, JPMA, FDA, PhRMA), the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK, Health Canada, and the WHO (as Observer).
Disclaimer and Copyright Notice

This presentation is protected by copyright and may be used, reproduced, incorporated into other works, adapted, modified, translated or distributed under a public license provided that ICH's copyright in the presentation is acknowledged at all times. In case of any adaption, modification or translation of the presentation, reasonable steps must be taken to clearly label, demarcate or otherwise identify that changes were made to or based on the original presentation. Any impression that the adaption, modification or translation of the original presentation is endorsed or sponsored by the ICH must be avoided.

The presentation is provided "as is" without warranty of any kind. In no event shall the ICH or the authors of the original presentation be liable for any claim, damages or other liability arising from the use of the presentation.

The above-mentioned permissions do not apply to content supplied by third parties. Therefore, for documents where the copyright vests in a third party, permission for reproduction must be obtained from this copyright holder.

Developer Webinar

• Goals
  – MSSO to provide information about a new MedDRA System Organ Class (SOC)
  – Provide information about what is available to developers
  – MSSO to share feedback from users on systems that incorporate MedDRA
  – Obtain your feedback on MedDRA from an IT perspective

• Intended audience
  – Software developers (commercial and internal tools), IT staff, data managers
Topics

– Implementation of new *Product issues* SOC
– What’s Available with each Release
– Feedback from MedDRA users related to IT
  • Secondary SOC views
  • Supporting “split coding”
  • International Order of SOCs
  • SMQ support
– Future Plans
  • Cloud distribution of MedDRA

Implementation of new SOC

*Product issues*
General

• Introduction of new Product issues SOC is a content change, not a structural change
  – File structure is the same
  – Changes in content
    • References to new SOC appear in the following tables and fields
      – MdHierarchy (SOC_Code, SOC_Name, SOC_abbrev, PT_SOC_code)
      – PT (PT_SOC_Code)
      – History* (Term_Code, Term_Name)
      – SOC (SOC_Code, SOC_Name, SOC_abbrev)
      – International Order of SOCs (SOC_Code)
      – SOC-HLGT (SOC_Code)

*For use with the MedDRA Desktop Browser

Basic Information

• New (27th) SOC implemented in MedDRA Version 19.0
  – First new SOC since the launch of MedDRA
  – Released 1 March 2016
  – Accommodates non-clinical/non-patient related concepts pertaining to products
• Important concepts as they may affect patient safety
• Includes terms relevant for issues with
  – Product quality
  – Devices
  – Manufacturing and quality systems
  – Supply and distribution
  – Counterfeit products
MedDRA Files

<table>
<thead>
<tr>
<th>Code</th>
<th>SOC Name</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>10005229</td>
<td>Blood and lymphatic system disorders</td>
<td>Blood</td>
</tr>
<tr>
<td>10007541</td>
<td>Cardiac disorders</td>
<td>Card</td>
</tr>
<tr>
<td>10010331</td>
<td>Congenital, familial and genetic disorders</td>
<td>Cong</td>
</tr>
<tr>
<td>10013993</td>
<td>Ear and labyrinth disorders</td>
<td>Ear</td>
</tr>
<tr>
<td>10014609</td>
<td>Endocrine disorders</td>
<td>Endo</td>
</tr>
<tr>
<td>10015019</td>
<td>Eye disorders</td>
<td>Eye</td>
</tr>
<tr>
<td>10017047</td>
<td>Gastrointestinal disorders</td>
<td>Gastro</td>
</tr>
<tr>
<td>10018065</td>
<td>General disorders and administration site conditions</td>
<td>Genri</td>
</tr>
<tr>
<td>10019805</td>
<td>Hepatobiliary disorders</td>
<td>Hepat</td>
</tr>
<tr>
<td>10021428</td>
<td>Immune system disorders</td>
<td>Immun</td>
</tr>
<tr>
<td>10021881</td>
<td>Infections and infestations</td>
<td>Infec</td>
</tr>
<tr>
<td>10022117</td>
<td>Injury, poisoning and procedural complications</td>
<td>InjP</td>
</tr>
<tr>
<td>10022891</td>
<td>Investigations</td>
<td>Inv</td>
</tr>
<tr>
<td>10027433</td>
<td>Metabolism and nutrition disorders</td>
<td>Metab</td>
</tr>
<tr>
<td>10028085</td>
<td>Musculoskeletal and connective tissue disorders</td>
<td>Musc</td>
</tr>
<tr>
<td>10029104</td>
<td>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</td>
<td>Neopl</td>
</tr>
<tr>
<td>10029205</td>
<td>Nervous system disorders</td>
<td>Nerv</td>
</tr>
<tr>
<td>10036585</td>
<td>Pregnancy, puerperium and perinatal conditions</td>
<td>Preg</td>
</tr>
<tr>
<td>10037715</td>
<td>Psychiatric disorders</td>
<td>Psych</td>
</tr>
<tr>
<td>10039039</td>
<td>Renal and urinary disorders</td>
<td>Renal</td>
</tr>
<tr>
<td>10039040</td>
<td>Reproductive system and breast disorders</td>
<td>Repro</td>
</tr>
<tr>
<td>10038738</td>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Resp</td>
</tr>
<tr>
<td>10040765</td>
<td>Skin and subcutaneous tissue disorders</td>
<td>Skin</td>
</tr>
<tr>
<td>10041214</td>
<td>Social circumstances</td>
<td>SocCi</td>
</tr>
<tr>
<td>10042813</td>
<td>Surgical and medical procedures</td>
<td>Surg</td>
</tr>
<tr>
<td>10047065</td>
<td>Vascular disorders</td>
<td>Vasc</td>
</tr>
<tr>
<td>10077536</td>
<td>Product issues</td>
<td>Prod</td>
</tr>
</tbody>
</table>

MedDRA files distributed with each release
• Detail of SOC file displayed

Check your Tools

• Will the new SOC load?
• Awareness within organization for locally developed applications
• Version 19.0 adds a few device and product quality terms but most of the impacts are moves of existing terms
  – Primary and Secondary SOC assignments
• Impact on International Order of SOCs
  – Added as last entry on list
### Impact on Existing Data

**MedDRA Version 18.1**
- General disorders and administration site conditions
- Administration site reactions
- Body temperature conditions
- Complications associated with device
- Device issues
- Fetal outcomes
- General system disorders NEC
- Product quality issues
  - Product contamination and death issues
  - Exposure via contaminated device
  - Product cleaning inadequate
  - Product contamination
  - Product contamination chemical
  - Product contamination microbial
  - Product contamination physical
  - Product contamination with body fluid
  - Product integrity
  - Product strength
  - Product sterilization and disinfection
  - Transmission of an infectious agent via product
  - Product label issues
  - Product packaging issues
  - Product quality issues NEC
  - Therapeutic and nontherapeutic effects (exc/tox)
- Traumatic disorders NEC

**MedDRA Version 19.0**
- Product issues
  - Device issues
  - Product quality, supply, distribution, manufacturing and quality system issues
  - Counterfeit, falsified and substandard products
  - Manufacturing facilities and equipment issues
  - Manufacturing issues NEC
  - Manufacturing laboratory controls issues
  - Manufacturing materials issues
  - Manufacturing production issues
  - Manufacturing production issues
  - Medication administration and use issues
  - Exposure via contaminated device
  - Product cleaning inadequate
  - Product contamination
  - Product contamination chemical
  - Product contamination microbial
  - Product contamination physical
  - Product contamination with body fluid
  - Product identity lacking
  - Suspected transmission of an infectious agent via product
  - Transmission of an infectious agent via product
  - Product distribution and storage issues
  - Product label issues
  - Product packaging issues
  - Product physical issues
  - Product quality issues NEC
  - Product supply and availability issues

### Two Levels of IT Systems

**Commercial systems**
- Clinical, Safety, and Electronic Data Capture
- Validated by developer and end user organization
- MedDRA loading based on contents of MedDRA files

**Locally developed**
- Varying levels of validation
- MedDRA loading could be "hard coded"
- Some developers less familiar with MedDRA and not receiving MedDRA information
Two Levels of IT Systems – Next Steps

• Testing your system’s loading process with v19.0 files
• If successful, no problem
• If unsuccessful, check to see if the “26” SOCs was hard coded in the load script
  – System loading process may crash
  – Only 26 SOCs may be loaded

What’s Available with each Release
• MedDRA Distribution File Format Document
  – Provides the MedDRA schema
    • Current complete version (*.ASC files)
    • Differences between this version and last version (*.SEQ files)
  – Includes record counts for all tables updated with each release
  – Provides the necessary information to access and link MedDRA files accurately

• What’s New Document
  – Describes major changes to MedDRA (technical and medical) in this release
  – Relatively short (15 pages)
• Version Report
  – Spreadsheet format
  – Version impact reports (e.g., New LLTs, New PTs, Hierarchy changes)
  – Produced with MVAT
• SMQ Production Spreadsheet
  – Provides all SMQs and their relationships (i.e., hierarchical)
Free MedDRA Tools

- MedDRA Version Analysis Tool (MVAT)
  - Provides differences between any two versions of MedDRA
    - Added, moved, renamed, currency changes
  - Used to produce the Version Report spreadsheet
  - Provides impacts between selected versions of PT / LLTs you upload
  - History of terms

- Browsers
  - Desktop and Web-based versions available

- WebCR
  - Supports the entry of change requests
  - Provides a tool to search the history of previous change requests

- All accessible from MedDRA.org site

Feedback from MedDRA Users related to IT
Version Maintenance

• What should be stored in the database?
  – MSSO suggests LLT code and version number
  – All other parts of hierarchy can be derived from MedDRA hierarchy table
• Storing the hierarchy with the term creates maintenance of the hierarchy with each release of MedDRA
  – Terms move, change primary and secondary links

Migraine headache in MedDRA

• Data Available
  – Term Text
  – Code (10027602)
  – Currency (Y)
  – Version (19.0)
  – Hierarchy (PT-HLT-HLGT-SOC)

• Only the Code (10027602) and Version (19.0) needs to stored in a database
  • All other information can be derived from a MedDRA version repository
Migraine headache in MedDRA (cont)

With this approach, the AE database is less impacted by MedDRA changes (i.e., currency changes).

Secondary SOC Views

Many users say their applications don’t support viewing a term in a Secondary SOC.

Using PT Influenza as an example:

- Influenza is an Infection and a Respiratory issue:
  - Primary to infection but still should be viewable in reports if a user wants to get a full picture of respiratory issues.
  - Regulatory authorities are capable of viewing your data in Secondary SOCs.
International Order of SOCs

- Not a standard alphabetic order of SOCs due to the multi-lingual nature of MedDRA
- International order of SOCs created to facilitate consistency irrespective of language

SMQ Support

- Standardised MedDRA Queries (SMQ)
  - Can be thought of as stored queries
  - SMQs relate to a defined medical condition
  - SMQs are intended to aid in the identification and retrieval of potentially relevant individual case safety reports
  - Included terms may relate to signs, symptoms, diagnoses, syndromes, physical findings, laboratory and other physiologic test data
- Users are looking for the ability to apply SMQs to specific data sets
- Does your tool support all features of SMQs?
  - Broad/Narrow, Algorithmic, and Hierarchical
Narrow and Broad Searches

- “Narrow” scope – specificity (cases highly likely to be condition of interest)
- “Broad” scope – sensitivity (all possible cases)
- “Broad search” = All broad + all narrow terms

Narrow Search → Narrow Terms

Broad Search → Broad Terms

Narrow vs. Broad Example

SMQ Lactic acidosis

**Definition**
Lactic acidosis is a form of high anion gap metabolic acidosis - Intrinsic cardiac contractility may be depressed, but inotropic function can be normal because of catecholamine release. Peripheral arterial vasodilatation and central vasoconstriction can be present - Central nervous system function is depressed, with headache, lethargy, stupor, and, in some cases, even coma - Glucose intolerance may occur - Characterized by an increase in plasma lactate. - Acidosis is seldom significant unless blood lactate exceeds 5 mmol/l. - Clinical presentation in type B lactic acidosis: a Symptoms: hyperventilation or dyspnea, stupor or coma, vomiting, dyspnoea, and abdominal pain. Onset of symptoms and signs is usually rapid accompanied by deterioration in the level of consciousness.

**Source**

**Note**
Testing in two regulatory databases confirmed that the term list is adequate, in one regulatory database, the term “acidosis” identified cases, but this may be a phenomenon of the database characteristics (coding of varbitans to terms of an older terminology or other coding conventions).

<table>
<thead>
<tr>
<th>Narrow Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood lactate acid increased</td>
</tr>
<tr>
<td>Hyperlactacidemia</td>
</tr>
<tr>
<td>Lactic acidosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Broad Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid base balance abnormal</td>
</tr>
<tr>
<td>Anion gap abnormal</td>
</tr>
<tr>
<td>Anion gap increased</td>
</tr>
<tr>
<td>Blood bicarbonate abnormal</td>
</tr>
<tr>
<td>Blood bicarbonate decreased</td>
</tr>
<tr>
<td>Blood gases abnormal</td>
</tr>
<tr>
<td>Blood lactate acid abnormal</td>
</tr>
<tr>
<td>Blood pH abnormal</td>
</tr>
<tr>
<td>Blood pH decreased</td>
</tr>
<tr>
<td>Coma acidotic</td>
</tr>
<tr>
<td>Kussmaul respiration</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
</tr>
<tr>
<td>pCO2 abnormal</td>
</tr>
<tr>
<td>pCO2 decreased</td>
</tr>
<tr>
<td>Urine lactate acid increased</td>
</tr>
</tbody>
</table>
Split Coding

• At times reports include terms with multiple concepts
  – “Wrist fracture due to fall”
• MedDRA terms are generally single concepts
• Causes an issue for the user if they are unable to split the reported term and code both events
  – Code to LLTs Wrist fracture and Fall
  – Otherwise user must choose one term and lose information in the coding process

Future Plans and Your Needs
Future Plans

• MedDRA in the Cloud
  – At some point we anticipate users will request a cloud based version of MedDRA
  – An informal set of discussions found that most organizations had plans to move to the cloud but few have gone to the implementation stage
  – MSSO will monitor this need

Your Needs

• What could the MSSO do from an IT perspective to make it easier to work with MedDRA?
Questions?