MedDRA: Coding Fundamentals and New Developments

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Topics

• Coding with MedDRA
  – MedDRA basics
  – Key principles in the MedDRA Term Selection: Points to Consider document

• New (27th) SOC *Product issues*
  – Timeline
  – Contents
  – Impact on systems, processes, documentation
Coding with MedDRA

What is MedDRA?

Med = Medical
  D = Dictionary for
  R = Regulatory
  A = Activities
Where MedDRA is Used

- Clinical Study Reports
- Investigators’ Brochures
- Core Company Safety Information
- Marketing Applications
- Publications
- Prescribing Information
- Advertising

Regulatory Authority and Industry Databases
- Individual Case Safety Reports and Safety Summaries

MedDRA: Data entry (coding)
- Data Retrieval
- Data Evaluation
- Data Presentation

Scope of MedDRA

- Not a drug dictionary
- Patient demographic terms
- Clinical trial study design terms
- Medical conditions
- Indications
- Investigations (tests, results)
- Medical and surgical procedures
- Medical, social, family history
- Medication errors
- Product quality issues
- Device-related issues
- Pharmacogenetic terms
- Toxicologic issues
- Standardized queries
- Frequency qualifiers
- Numerical values for results
- Severity descriptors
- Not an equipment, device, diagnostic product dictionary
MedDRA Structure

System Organ Class (SOC) (26)
High Level Group Term (HLGT) (335)
High Level Term (HLT) (1,721)
Preferred Term (PT) (21,345)
Lowest Level Term (LLT) (74,229)

MedDRA System Organ Classes

- Blood and lymphatic system disorders
- Cardiac disorders
- Congenital, familial and genetic disorders
- Ear and labyrinth disorders
- Endocrine disorders
- Eye disorders
- Gastrointestinal disorders
- General disorders and administration site conditions
- Hepatobiliary disorders
- Immune system disorders
- Infections and infestations
- Injury, poisoning and procedural complications
- Investigations
- Metabolism and nutrition disorders
- Musculoskeletal and connective tissue disorders
- Neoplasms benign, malignant and unspecified (incl cysts and polyps)
- Nervous system disorders
- Pregnancy, puerperium and perinatal conditions
- Psychiatric disorders
- Renal and urinary disorders
- Reproductive system and breast disorders
- Respiratory, thoracic and mediastinal disorders
- Skin and subcutaneous tissue disorders
- Social circumstances
- Surgical and medical procedures
- Vascular disorders
Lowest Level Terms (Coding Level)

Synonyms, lexical variants, sub-elements

SOC = Cardiac disorders

HLGT = Cardiac arrhythmias

HLT = Rate and rhythm disorders NEC

PT = Arrhythmia

LLT = Arrhythmia NOS

LLT = Other specified cardiac dysrhythmias

LLT (Non-current) Other specified cardiac dysrhythmias

Not all LLTs shown

Non-Current Terms

- Flagged at the LLT level in MedDRA
- Not recommended for continued use
- Retained to preserve historical data for retrieval and analysis
- Terms that are vague, ambiguous, out-dated, truncated, or misspelled
- Terms derived from other terminologies that do not fit MedDRA rules
### Codes and Languages

- **Hoofdpijn** (Dutch)
- **Headache** (English)
- **Céphalée** (French)
- **Bolest hlavy** (Czech)
- **Cefaleia** (Portuguese)
- **Kopfschmerz** (German)
- **Fefjádas** (Hungarian)
- **Cefalea** (Italian)
- **頭痛** (Japanese)
- **Cefalea** (Spanish)

### Coding: Translating into MedDRA

<table>
<thead>
<tr>
<th>Reported Information</th>
<th>LLT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Throbbing above temple</td>
<td>Headache</td>
</tr>
<tr>
<td>Aching all over head</td>
<td></td>
</tr>
<tr>
<td>Pulsing pain in head</td>
<td></td>
</tr>
<tr>
<td>Really bad headache</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td>Infection in lungs</td>
<td>Lung infection</td>
</tr>
<tr>
<td>Patient took Drug A instead of Drug B and experienced hypertension</td>
<td>Wrong drug administered Hypertension</td>
</tr>
</tbody>
</table>
MedDRA Term Selection: Points to Consider (MTS:PTC)

- Provides term selection advice for industry and regulatory purposes
- Objective is to promote accurate and consistent term selection to facilitate a common understanding of shared data
- Recommended to be used as basis for individual organization’s own coding conventions

MedDRA Term Selection: PTC (cont)

- Developed by a working group of the ICH Steering Committee
  - Regulators and industry representatives from EU, Japan, and USA
  - Canadian and Korean regulatory authorities
  - WHO
  - MSSO and JMO
- Updated twice yearly with each MedDRA release
- Available on MedDRA and JMO websites
  - English and Japanese
  - Word (“clean” and “redlined”), PDF, HTML formats
    - “Redlined” documents identify changes made from previous to current release of documents
Quality of Source Data

Quality Assurance

- Quality of original information impacts quality of output
- Obtain clarification of data
- Can be optimized by careful design of data collection forms and proper training of staff
- Organizations’ coding guidelines should be consistent with MTS:PTC
- Review of term selection by qualified individuals
- Human oversight of automated coding results

Always Select a Lowest Level Term

Select Only Current LLTs

- Lowest Level Term that most accurately reflects the reported verbatim information should be selected
- Degree of specificity may be challenging
  - Example: “Abscess on face” → select “Facial abscess,” not simply “Abscess”
- Select current LLTs only
  - Non-current terms for legacy conversion/historical purposes
Which Term to Select?

- Man with decreased fertility
  Infertility?
  Decreased fertility male?
  Male infertility?
  Decreased fertility?

Which Term to Select?

- Infection after surgery
  Infection?
  Postoperative wound infection?
  Surgical wound infection?
  Postoperative infection?
Select Terms for All Reported Information

- Select terms for every AR/AE reported, regardless of causal association
- Select terms for device-related events, product quality issues, medication errors, medical and social history, investigations and indications as appropriate

Do Not Add Information

- Do not make diagnosis if only signs/symptoms reported

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain, increased serum amylase, and increased serum lipase</td>
<td>Abdominal pain</td>
<td>It is inappropriate to assign an LLT for diagnosis of “pancreatitis”</td>
</tr>
<tr>
<td></td>
<td>Serum amylase increased</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lipase increased</td>
<td></td>
</tr>
</tbody>
</table>
Combination Terms

• One condition is more specific than the other

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmia due to atrial fibrillation</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Hepatic function disorder (acute hepatitis)</td>
<td>Hepatitis acute</td>
</tr>
</tbody>
</table>

• A MedDRA combination term is available

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinopathy due to diabetes</td>
<td>Diabetic retinopathy</td>
</tr>
<tr>
<td>Rash with itching</td>
<td>Itchy rash</td>
</tr>
</tbody>
</table>

Combination Terms (cont)

• If splitting provides more clinical information, select more than one term
• In all cases of combination terms, apply medical judgment

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea and vomiting</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
</tr>
<tr>
<td>Wrist fracture due to fall</td>
<td>Wrist fracture</td>
</tr>
<tr>
<td></td>
<td>Fall</td>
</tr>
</tbody>
</table>
What Terms to Select?

- Retinal disease from HIV with near total blindness (R and L)
  Retinal damage?
  Retinal disorder?
  HIV disease?
  Blindness?
  HIV retinopathy?
  Blindness both eyes?

What Terms to Select?

- Sepsis leading to shock from bowel perforation due to stage III colon cancer
  Sepsis?
  Shock?
  Septic shock?
  Bowel perforation?
  Colon cancer?
  Colon cancer stage III?
Autoencoder Pitfalls

• Inappropriate terms may be selected by autoencoder
• Review all autoencoding carefully
  – “Allergic to CAT scan” autoencoded as:
    LLT Allergic to cats
  – “Myocardial infarction in the fall of 2000” autoencoded as:
    LLT Myocardial infarction
    LLT Fall

FDA-Defined Coding Errors

• Missed Concepts
  – All medical concepts described after the product is taken should be coded
  – Example: “The patient took drug X and developed alopecia, increased LFTs and pancreatitis”. Manufacturer only codes alopecia and increased LFTs (missed concept of pancreatitis)
  – Example: “The patient took drug X and developed interstitial nephritis which later deteriorated into renal failure”. Manufacturer only codes interstitial nephritis (missed renal failure concept)

Acknowledgement: Dr. Toni Piazza-Hepp, Office of Surveillance and Epidemiology, CDER
FDA-Defined Coding Errors (cont)

• “Soft Coding”
  – Selecting a term which is both less specific and less severe than another MedDRA term is “soft coding”
  – Example: “Liver failure” coded as hepatotoxicity or increased LFTs
  – Example: “Aplastic anemia” coded as unspecified anemia
  – Example: “Rash subsequently diagnosed as Stevens Johnson syndrome” coded as rash

Acknowledgement: Dr. Toni Piazza-Hepp, Office of Surveillance and Epidemiology, CDER

Challenging Verbatims

– Went to hell
– Recurrent fatal stroke
– Hears New Age music when the furnace turns on
  – LK RTCTL UNSP XTRNDL
– Charcoal-like, gritty granules in his underwear
– Can’t control patient during menses
– His nodule is sticking out
– Normally normal after drinking coffee
– Died of cancer of the placebo
– Superior members fornication
– Barely visible posterior
– Seeing people in room, seeing chickens at window
– Seeing stars and chicken farting
– Patient recently began new job where he works around chicken wings and barbecue sauce
ICH MedDRA Management Board endorsed creation of a new (27th) SOC for implementation in MedDRA Version 19.0

Includes terms relevant for issues with
- Product quality
- Devices
- Manufacturing and quality systems
- Supply and distribution
- Counterfeit products

Expert Working Group provided input on structure and contents
- Representatives from regulatory authorities, industry, MSSO, JMO
- Expertise in MedDRA and product quality
Concept Description - Product

• In the context of MedDRA, "product" can refer to various types of products intended for human use such as drugs (prescription and over the counter), biologics, vaccines, combination products, devices, nutraceuticals, dietary supplements, etc.

• Other products regulated in at least one region such as food or cosmetics

27th SOC Web Page

• Updates, presentations, information

• Communication Document
  – Purpose, timing, potential impact of new SOC
### Features

- **Same structure and characteristics of other SOCs**
  - Five level hierarchy (SOC, HLGT, HLT, PT, LLT)
  - 100 character limit for terms
  - 8 digit MedDRA codes
  - Multi-axial links to aid in retrieval and preserve links to patient safety
    - PT *Transmission of an infectious agent via product* (primary link to SOC *Infections and infestations*)
Complex Change Proposals

- HLGT Product quality, supply, distribution, manufacturing and quality system issues
  - HLT Counterfeit, falsified and substandard products
  - HLT Manufacturing facilities and equipment issues
  - HLT Manufacturing issues NEC
  - HLT Manufacturing laboratory controls issues
  - HLT Manufacturing materials issues
  - HLT Manufacturing production issues
  - HLT Product contamination and sterility issues
  - HLT Product distribution and storage issues
  - HLT Product label issues
  - HLT Product packaging issues
  - HLT Product physical issues
  - HLT Product quality issues NEC
  - HLT Product supply and availability issues

Complex Change Proposals (cont)

- HLGT Device issues
  - HLT Device computer issues
  - HLT Device electrical issues
  - HLT Device incompatibility issues
  - HLT Device information output issues
  - HLT Device issues NEC
  - HLT Device malfunction events NEC
  - HLT Device operational issues NEC
  - HLT Device physical property and chemical issues
Next Steps

- Populate HLGTs and HLTs
  - Move existing PTs/LLTs to more specific groupings
  - Add new PTs/LLTs through CR process
    - Manufacturing terms
    - Quality system terms
- Users encouraged to submit terms from own internal quality terminologies
- Terms must be unambiguous, fit MedDRA rules
- Create concept descriptions where necessary

MedDRA Files

<table>
<thead>
<tr>
<th>Code</th>
<th>Name</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>10995329</td>
<td>Blood and lymphatic system disorders</td>
<td>Blood</td>
</tr>
<tr>
<td>10997541</td>
<td>Cardiologic disorders</td>
<td>Card</td>
</tr>
<tr>
<td>10991931</td>
<td>Congenital, familial and genetic disorders</td>
<td>Cong</td>
</tr>
<tr>
<td>10991933</td>
<td>Ear and labyrinth disorders</td>
<td>Ear</td>
</tr>
<tr>
<td>10991956</td>
<td>Endocrine disorders</td>
<td>Endo</td>
</tr>
<tr>
<td>10991919</td>
<td>Eye disorders</td>
<td>Eye</td>
</tr>
<tr>
<td>10991947</td>
<td>Gastrointestinal disorders</td>
<td>Gastro</td>
</tr>
<tr>
<td>10991905</td>
<td>General disorders and administration site conditions</td>
<td>Genral</td>
</tr>
<tr>
<td>10991805</td>
<td>Hepatobiliary disorders</td>
<td>Hepat</td>
</tr>
<tr>
<td>10991428</td>
<td>Immune system disorders</td>
<td>Immun</td>
</tr>
<tr>
<td>10991861</td>
<td>Infections and infestations</td>
<td>Infect</td>
</tr>
<tr>
<td>10992117</td>
<td>Injury, poisoning and procedural complications</td>
<td>Inj&amp;P</td>
</tr>
<tr>
<td>10992391</td>
<td>Investigations</td>
<td>Inv</td>
</tr>
<tr>
<td>10992433</td>
<td>Metabolism and nutrition disorders</td>
<td>Metab</td>
</tr>
<tr>
<td>10992355</td>
<td>Musculoskeletal and connective tissue disorders</td>
<td>Musc</td>
</tr>
<tr>
<td>10992910</td>
<td>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</td>
<td>Neopl</td>
</tr>
<tr>
<td>10992005</td>
<td>Nervous system disorders</td>
<td>Nerv</td>
</tr>
<tr>
<td>10995858</td>
<td>Pregnancy, puerperal and perinatal conditions</td>
<td>Preg</td>
</tr>
<tr>
<td>10997175</td>
<td>Psychiatric disorders</td>
<td>Psych</td>
</tr>
<tr>
<td>10993209</td>
<td>Renal and urinary disorders</td>
<td>Renal</td>
</tr>
<tr>
<td>10993804</td>
<td>Reproductive system and breast disorders</td>
<td>Repro</td>
</tr>
<tr>
<td>10993736</td>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Resp</td>
</tr>
<tr>
<td>10990785</td>
<td>Skin and subcutaneous tissue disorders</td>
<td>Skin</td>
</tr>
<tr>
<td>10991244</td>
<td>Social circumstances</td>
<td>SocDi</td>
</tr>
<tr>
<td>10992913</td>
<td>Surgical and medical procedures</td>
<td>Surg</td>
</tr>
<tr>
<td>10995005</td>
<td>Vascular disorders</td>
<td>Vasc</td>
</tr>
</tbody>
</table>

MedDRA files distributed with each release
- Detail of SOC file displayed
Impact on Data Summaries

- No major impact on AE data summaries or subsequent conclusions
  - If no terms are reported, SOC is not displayed, e.g., SOC Social circumstances
  - Versioning impact (pre- to post-27th SOC) similar to primary SOC changes
  - Programming of standard tables/listings
- Impact on International Order of SOCs
  - To be added as last on list
- Minimal impact on organizations not involved in product quality

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
- End-users will need to be made aware of new SOC
MSSO Tools

- No impact on Desktop Browser, Web-Based Browser, MVAT, WebCR
- Mock files successfully loaded and tested

Anticipated IT Impact

- Commercial systems
  - Very low (if any)
  - Initial discussions with vendors confirm
  - Loading based on content of files, not a fixed number
  - Revisions to IT SOPs and other documentation possible

- Local systems
  - Higher impact
  - Too many to reach individually

- No formal IT system
  - Low (using spreadsheets, simple databases, MSSO tools)

- Mitigation of impact
  - Communication in multiple forums
  - Developer webinar
Developer Webinar

- Objective
  - Information on new MedDRA initiatives impacting IT systems
  - Feedback on how to make MedDRA easier to use for developers
- Designed for system developers, IT staff
- Topics to include
  - Implementation of new SOC Product issues
  - Secondary SOC views
  - Supporting “split coding”
  - SMQ support
  - Application programming interfaces (APIs)
  - Cloud distribution of MedDRA
- Scheduled for Fall 2015

Impact on Documentation and Processes

- MSSO documents, e.g., Introductory Guide
- SOPs, procedures documentation
- In-house coding and retrieval guidelines
- Points to Consider documents
- Regulatory data standards, guidances, and rules
Communication and Collaboration

• Communication with users
  – Webinars, MedDRA website, broadcast emails, What’s New, User Group meetings, training sessions, videocasts, etc.

• Collaborative effort
  – MedDRA experts
  – Quality experts

Thank You

Questions?