MedDRA Overview

MedDRA was developed under the auspices of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). The activities of the MedDRA Maintenance and Support Services Organization (MSSO) are overseen by an ICH MedDRA Management Committee, which is composed of the ICH parties, the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK, Health Canada, and the WHO (as Observer).
 AppleWebKit/537.36 (KHTML, like Gecko) Chrome/51.0.2704.103 Safari/537.36

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Course Overview

• Present background information about MedDRA
• Review MedDRA’s, scope, structure, and characteristics
• Describe the maintenance of MedDRA
• Describe MedDRA tools (browsers, MVAT)
• Discuss coding with MedDRA
• Introduce the MedDRA Points to Consider documents
• Describe Standardised MedDRA Queries (SMQs)
• Conclude with a question and answer session
MedDRA Background

What is MedDRA?

Med = Medical
D = Dictionary for
R = Regulatory
A = Activities
MedDRA’s Purpose

• Facilitate the exchange of clinical information through standardization
• Important tool for product evaluation, monitoring, communication, electronic records exchange, and oversight
• Supports coding (data entry) and retrieval and analysis of clinical information about human medical products including pharmaceuticals, biologics, vaccines, and drug-device combination products

MedDRA Definition

MedDRA is a clinically-validated international medical terminology used by regulatory authorities and the regulated biopharmaceutical industry. The terminology is used through the entire regulatory process, from pre-marketing to post-marketing, and for data entry, retrieval, evaluation, and presentation.
Governance Structure for MedDRA

• ICH MedDRA Management Committee appointed by the ICH Assembly to provide oversight of MedDRA related activities and the Maintenance and Support Services Organization (MSSO)

Management Committee/MSSO Relationship

• ICH owns MedDRA
• ICH MedDRA Management Committee
  – Contracts with MSSO to maintain it
  – Has oversight of all operations of the MSSO
    • Meets regularly with MSSO
    • Sets subscription rates
    • Approves developmental plans and services
  – Membership includes ICH regulatory authorities and industry associations
MedDRA and the MSSO

- International support and development of terminology
- Foster use of MedDRA through communications and educational offerings
- “Custodians”, not owners, of the terminology
- JMO (partner organization for Japanese-language MedDRA)
- Governed by a Management Committee (industry, regulators, multi-national, other interested parties)

Where MedDRA is Used

- Preclinical Testing
- Clinical Phase I
- Clinical Phase II
- Clinical Phase III
- Marketed Product Phase IV

Regulatory Authority and Industry Databases
- Individual Case Safety Reports and Safety Summaries
- Clinical Study Reports
- Investigators’ Brochures
- Core Company Safety Information
- Marketing Applications
- Publications
- Prescribing Information
- Advertising
MedDRA's Scope, Structure, and Characteristics

Scope of MedDRA

- Not a drug dictionary
- Patient demographic terms
- Clinical trial study design terms

Frequency qualifiers
- Medical conditions
- Indications
- Investigations (tests, results)
- Medical and surgical procedures
- Medical, social, family history
- Medication errors
- Product quality issues
- Device-related issues
- Product use issues
- Pharmacogenetic terms
- Toxicologic issues
- Standardized queries

Numerical values for results
- Severity descriptors
- Not an equipment, device, diagnostic product dictionary
MedDRA Structure

System Organ Class (SOC) (27)
High Level Group Term (HLGT) (337)
High Level Term (HLT) (1,737)
Preferred Term (PT) (24,289)
Lowest Level Term (LLT) (81,812)

MedDRA Version 23.0

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
- Product issues
- 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 Term**

- Synonyms, lexical variants, sub-elements

  - **SOC** = Cardiac disorders
  - **HLGT** = Cardiac arrhythmias
  - **HLT** = Rate and rhythm disorders NEC

  - **PT** = Arrhythmia

**LLT**

- Arrhythmia
- Arrhythmia NOS

**LLT**

- Dysrhythmias
  - LLT (Non-current) Other specified cardiac dysrhythmias

Not all LLTs shown

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**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, outdated, truncated, or misspelled
- Terms derived from other terminologies that do not fit MedDRA rules
MedDRA Codes

- Each MedDRA term assigned an 8-digit numeric code starting with “1”
- The code is non-expressive
- Codes can fulfill a data field in various electronic submission types (e.g., E2B)
- New terms are assigned sequentially

Codes and Languages
A Multi-Axial Terminology

- Multi-axial = the representation of a medical concept in multiple SOCs
  - Allows grouping by different classifications
  - Allows retrieval and presentation via different data sets
- All PTs assigned a primary SOC
  - Determines which SOC will represent a PT during cumulative data outputs
  - Prevents “double counting”
  - Supports standardized data presentation
  - Pre-defined allocations should not be changed by users

SOC = Respiratory, thoracic and mediastinal disorders (Secondary SOC)
HLGT = Respiratory tract infections
HLT = Viral upper respiratory tract infections
PT = Influenza

SOC = Infections and infestations (Primary SOC)
HLGT = Viral infectious disorders
HLT = Influenza viral infections
• Users can send change requests (CRs) to MSSO for consideration
  – Organizations allowed 100 CRs/month
  – For simple changes (PT and LLT levels), response within 7-10 working days
  – Complex changes (above PT level) posted for comments mid-year
• Two MedDRA updates/year
  – 1 March X.0 (Complex release)
  – 1 September X.1 (Simple release)
WebCR

- Web-based tool for Change Requests (CR)
  - URL: https://mssotools.com/webcr/
  - Via the Change Request Information page
- Ability to submit CRs online
  - Requests must be in English
- Immediate confirmation
- Review unsubmitted CRs online
- Ability to query CR history back to v5.1

Submitting Changes

- Online change request submission tool
- Guides the user to enter all needed information
Submitting Changes (cont)

- Sample entry for a new PT in WebCR
- Justification and supporting documentation is important to help MSSO understand the need

Add a New PT

- Proposed PT (Required)
- Second degree chemical burns of skin
- Primary HLT (Optional)
- Chemical injuries
- Primary SOC (Optional)
- Injury, poisoning, and procedural complications
- Secondary HLT (Optional)
- Dermatologic condition of specific agent
- Secondary SOC (Optional)
- Skin and subcutaneous tissue disorders

Justification statement is required

Justification

Please consider including the gradation of chemical burns. Similar to the gradation of thermal burns under skin thermal burns to assist with coding and analysis.

Attach supporting document (Optional)

Proactive MedDRA Maintenance

- What is the proactive approach?
  - Corrections/improvements made internally by the MSSO
  - General changes suggested by users
- Submitting ideas
  - Send to MSSO Help Desk. Justification is helpful.
  - Example: Review placement of bruise and contusion terms to facilitate coding and analysis
- Evaluation of proposals
  - Final disposition is not time limited; MSSO may take time to review
  - Proactive approach does not replace usual CR process
MedDRA Tools

MSSO’s MedDRA Browsers

- MedDRA Desktop Browser (MDB)
  - Download MDB and release files from MedDRA website
- MedDRA Web-Based Browser (WBB)
  - [https://tools.meddra.org/wbb/](https://tools.meddra.org/wbb/)
- Mobile MedDRA Browser (MMB)
  - [https://mmb.meddra.org](https://mmb.meddra.org)

Features

- Each require MedDRA ID and password
- View/search MedDRA and SMQs
- Support for all MedDRA languages
- Language specific interface
- Ability to export search results and Research Bin to local file system (MDB and WBB only)
MDB and WBB Special Features

• Preview upcoming (supplemental) changes in next release*
• View primary and secondary link information
• Upload terms to run against SMQs
• Advanced search options (e.g., NOT, OR)

*Supplemental view not available on MDB

MedDRA Version Analysis Tool (MVAT)

• Web-based (https://tools.meddra.org/mvat)
• Free to all users
• Features
  – Version Report Generator (produces exportable report comparing any two versions)
  – Data Impact Report (identifies changes to a specific set of MedDRA terms or codes uploaded to MVAT)
  – Search Term Change (identifies changes to a single MedDRA term or code)
MedDRA Version Analysis Tool (MVAT) (cont)

- User interface and report output available in all MedDRA languages
- Ability to run reports on supplemental changes
- Option to run reports on secondary SOC changes
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
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

MedDRA Browser SOC View
MedDRA Points to Consider Documents

ICH M1 Points to Consider Working Group (PtC WG)

- Regulators and industry from EU, US, and Japan
- Health Canada, Canada
- MFDS, Republic of Korea
- ANVISA, Brazil
- NMPA, China
- MSSO
- JMO
- WHO (Observer)

November 2017, Geneva, Switzerland
<table>
<thead>
<tr>
<th>PtC Category</th>
<th>PtC Document</th>
<th>Purpose</th>
<th>Languages</th>
<th>Release Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term Selection</td>
<td>MedDRA Term Selection: Points to Consider</td>
<td>Promote accurate and consistent coding with MedDRA</td>
<td>English, Japanese, and other selected languages</td>
<td>Updated annually with the March release of MedDRA (starting with MedDRA Version 23.0)</td>
</tr>
<tr>
<td>Data Retrieval and Presentation</td>
<td>MedDRA Data Retrieval and Presentation: Points to Consider Condensed Version</td>
<td>Shorter version focusing on general coding principles to promote accurate and consistent use of MedDRA worldwide</td>
<td>All MedDRA languages (except English, Japanese, and other languages with an available translation of the full MTS:PTC document)</td>
<td>Update as needed</td>
</tr>
<tr>
<td>General</td>
<td>MedDRA Points to Consider Companion Document</td>
<td>More detailed information, examples, and guidance on specific topics of regulatory importance. Intended as a &quot;living&quot; document with frequent updates based on users' needs. First edition covers data quality and medication errors. New section on product quality is being drafted.</td>
<td>English and Japanese</td>
<td>Updated as needed</td>
</tr>
</tbody>
</table>
MedDRA Data Retrieval and Presentation: Points to Consider (DRP:PTC)

- Provides data retrieval and presentation options for industry or regulatory purposes
- Most effective when used in conjunction with MedDRA Term Selection: PTC document
- Recommended to be used as basis for individual organization’s own data retrieval conventions

MedDRA Data Retrieval and Presentation: PTC (cont)

- Developed by a working group of the ICH Management Committee
- Updated annually in step with the March release of MedDRA (starting with MedDRA Version 23.0)
- Available on MedDRA and JMO websites
  - English, Japanese, and other selected languages
  - Word (“clean” and “redlined”), PDF, HTML formats
  - “Redlined” document identifies changes made from previous to current release of document
What are Coding Conventions?

- Written guidelines for coding with MedDRA in your organization
- Support accuracy and consistency
- Common topics
  - Misspellings, abbreviations and acronyms
  - Combination terms and “due to” concepts
  - “Always query” terms, e.g., “Chest pain”
- Should be consistent with the MedDRA Term Selection: Points to Consider document

Why Do We Need Coding Conventions?

- Differences in medical aptitude of coders
- Consistency concerns (many more “choices” to manually code terms in MedDRA compared to older terminologies)
- Even with an autoencoder, may still need manual coding
Term Selection Points

- Diagnoses and Provisional Diagnoses with or without Signs and Symptoms
- Death and Other Patient Outcomes
- Suicide and Self-Harm
- Conflicting/Ambiguous/Vague Information
- Combination Terms
- Age vs. Event Specificity
- Body Site vs. Event Specificity
- Location-Specific vs. Microorganism-Specific Information
- Modification of Pre-existing Conditions
- Exposures During Pregnancy and Breast Feeding
- Congenital Terms
- Neoplasms
- Medical and Surgical Procedures
- Investigations

Term Selection Points (cont)

- Medication Errors, Accidental Exposures and Occupational Exposures
- Misuse, Abuse and Addiction
- Transmission of Infectious Agent via Product
- Overdose, Toxicity and Poisoning
- Device-related Terms
- Drug Interactions
- No Adverse Effect and “Normal” Terms
- Unexpected Therapeutic Effect
- Modification of Effect
- Social Circumstances
- Medical and Social History
- Indication for Product Use
- Off Label Use
- Product Quality Issues
• Provides data retrieval and presentation options for industry or regulatory purposes
• Most effective when used in conjunction with MedDRA Term Selection: PTC document
• Recommended to be used as basis for individual organization’s own data retrieval conventions

Standardised MedDRA Queries (SMQs)
Standardised MedDRA Queries (SMQs)

- Groupings of terms from one or more MedDRA SOCs related to medical condition or area of interest
- Terms relate to signs/symptoms, diagnoses, syndromes, physical findings, laboratory and other test data, etc.
- Intended to aid in case identification

How to “Run” SMQs (cont)
SMQs in Production - Examples

• As of Version 23.0, a total of 106 level 1 SMQs in production
  • Agranulocytosis
  • Anaphylactic reaction
  • Central nervous system vascular disorders
  • Convulsions
  • Depression and suicide/self-injury
  • Hepatic disorders
  • Hypersensitivity
  • Ischaemic heart disease
  • Lack of efficacy/effect
  • Medication errors
  • Osteonecrosis
  • Peripheral neuropathy
  • Pregnancy and neonatal topics
  • Pseudomembranous colitis
  • Rhabdomyolysis/myopathy
  • Severe cutaneous adverse reactions
  • Systemic lupus erythematosus

SMQ Benefits and Limitations

• Benefits
  – Application across multiple therapeutic areas
  – Validated reusable search logic
  – Standardized communication of safety information
  – Consistent data retrieval
  – Maintenance by MSSO/JMO

• Limitations
  – Do not cover all medical topics or safety issues
  – Will evolve and undergo further refinement even though they have been tested during development
SMQ Applications

- Clinical trials
  - Where safety profile is not fully established, use multiple SMQs on routine basis as screening tool
  - Selected SMQs to evaluate previously identified issue (pre-clinical data or class effect)

- Post-marketing
  - Selected SMQs to retrieve cases for suspected or known safety issue
  - Signal detection (multiple SMQs employed)
  - Single case alerts
  - Periodic reporting (aggregate cases for safety and other issues, e.g., lack of efficacy)

MedDRA Browser SMQ View
Summary

In this course, we:

- Presented background information about MedDRA
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- Discussed coding with MedDRA
- Discussed the MedDRA Points to Consider documents
- Described Standardised MedDRA Queries (SMQs)

MSSO Contacts

- Website
  - www.meddra.org
- Email
  - mssohelp@meddra.org
- Frequently Asked Questions
  - www.meddra.org/faq
- MedDRA Browsers
  - https://www.meddra.org/meddra-desktop-browsers (Desktop Browser)
  - https://tools.meddra.org/wbb/ (Web-Based Browser)
  - https://mmb.meddra.org (Mobile Browser)
MSSO Contacts (cont)

• Self-Service Application
  – https://www.meddra.org/meddra-self-service-application

• Training Schedule
  – https://www.meddra.org/training/schedule

• Change Request Submission
  – https://www.meddra.org/how-to-use/change-requests

• MedDRA Support Documentation
  – https://www.meddra.org/how-to-use/support-documentation

Question and Answer Session