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).
Disclaimer and Copyright Notice

• This presentation is protected by copyright and may, with the exception of the MedDRA and ICH logos, 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.

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

- 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
MedDRA Structure

System Organ Class (SOC) (27)
High Level Group Term (HLGT) (337)
High Level Term (HLT) (1,737)
Preferred Term (PT) (23,708)
Lowest Level Term (LLT) (80,262)

MedDRA Structure

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

LLT = 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, 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
**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
(SOCC = Respiratory tract infections
**HLGT** = Viral upper respiratory tract infections
**HLT** = Influenza viral infections
**PT** = Influenza

**SOC** = Infections and infestations
(Primary SOC)
**HLGT** = Viral infectious disorders
**HLT** = Influenza viral infections

**A Multi-Axial Terminology (cont)**
MedDRA Maintenance

• 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

<table>
<thead>
<tr>
<th>Proposed PT (Required)</th>
<th>Secondary HLT (Optional)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Controlled Text]</td>
<td>[Controlled Text]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary HLT (Optional)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Controlled Text]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary SOC (Optional)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Controlled Text]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary SOC (Optional)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Controlled Text]</td>
</tr>
</tbody>
</table>

Justification statement is required

Justification

Please consider including the gradation of chemical burns similar to the gradation of thermal burns under skin and subcutaneous tissue disorders 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
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/)

Features
- Both 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
MedDRA Desktop Browser (MDB) and Web-Based Browser (WBB) Update

• New functionality for users
  – 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](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)
• User interface and report output available in all MedDRA languages
MedDRA Version Analysis Tool

Coding with MedDRA
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

PtC Documents

<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 and Japanese</td>
<td>Updated with each MedDRA release</td>
</tr>
<tr>
<td></td>
<td>MedDRA Term Selection: 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 and Japanese)</td>
<td>Update as needed</td>
</tr>
<tr>
<td>Data Retrieval and Presentation</td>
<td>MedDRA Data Retrieval and Presentation: Points to Consider</td>
<td>Demonstrate how data retrieval options impact the accuracy and consistency of data output</td>
<td>English and Japanese</td>
<td>Updated with each MedDRA release</td>
</tr>
<tr>
<td></td>
<td>MedDRA Data Retrieval and Presentation: Points to Consider Condensed Version</td>
<td>Shorter version focusing on general retrieval and analysis principles to promote accurate and consistent use of MedDRA worldwide</td>
<td>All MedDRA languages (except English and Japanese)</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 “living” document with frequent updates based on users’ needs. First edition covers data quality and medication errors.</td>
<td>English and Japanese</td>
<td>Updated as needed</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 Management Committee
- Updated twice yearly with each MedDRA release
- Available on MedDRA and JMO websites
  - English and Japanese
  - 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
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:
POINTS TO CONSIDER
ICH-Endorsed Guide for MedDRA Users on Data Output

Release 3.17
Based on MedDRA Version 22.0

I March 2019

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

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

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.

MedDRA® trademark is registered by IPPMA on behalf of ICH

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

- Collaboration between CIOMS (Council for International Organizations of Medical Sciences) and ICH (MSSO)
- 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)

Clinical Trial Database
Safety Database

Query

Case
LLT1
LLT2
LLT3

"Hit"
SMQs in Production - Examples

• As of Version 22.0, a total of 104 level 1 SMQs in production
  • Agranulocytosis
  • Anaphylactic reaction
  • Cerebrovascular 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
• Reviewed MedDRA’s scope, structure, and characteristics
• Described the maintenance of MedDRA
• Described MedDRA tools (browsers, MVAT)
• 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
Question and Answer Session