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 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).
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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 MedDRA Management Committee
  - Owns MedDRA
    - 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
- Clinical Phase IV
- 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
- 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

Frequency qualifiers
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) (23,088)
Lowest Level Term (LLT) (78,808)

MedDRA Structure

MedDRA Version 21.0

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
**MedDRA**

**Lowest Level Term**

- Synonyms, lexical variants, sub-elements
- **SOC** = Cardiac disorders
- **HLGT** = Cardiac arrhythmias
- **HLT** = Rate and rhythm disorders NEC
- **PT** = Arrhythmia
- **LLT** (Non-current) Other specified cardiac dysrhythmias

**MedDRA**

**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
• 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

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/

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 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)
- User interface and report output available in all MedDRA languages
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 Points to Consider Documents

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

ICH M1 Points to Consider Working Group (PtC WG)

- Regulators and industry from EU, US, and Japan
  - Health Canada
  - MSSO
  - JMO
  - WHO (Observer)

**New members 2017/2018**
- MFDS, Republic of Korea
- ANVISA, Brazil
- CFDA, China

Meeting 13-15 November 2017, Geneva, Switzerland
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

- 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)

- 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)
SMQs in Production - Examples

As of Version 21.0, a total of 103 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

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MSSO Contacts

• Website
  – www.meddra.org
• Email
  – mssohelp@meddra.org
• Frequently Asked Questions
  – www.meddra.org/faq
Question and Answer Session