Medical Dictionary for Regulatory Activities (MedDRA)

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The Golden Triangle

Efficacy

Safety (MedDRA)

Product

Quality (MedDRA)
Examples of Regulatory Safety Databases Coded in MedDRA

- US FDA
  - FAERS: drugs and biologics
  - VAERS: vaccines
  - CAERS: foods, dietary supplements, cosmetics
- EMA
  - EudraVigilance Database
- Health Canada
  - Canada Vigilance Database
- MHLW/PMDA
  - Safety database

Topics

- MedDRA and MSSO Introduction
- Safety data elements coded with MedDRA
- Signal detection and MedDRA
MedDRA and MSSO Introduction

What is MedDRA?

Med = Medical
D = Dictionary for
R = Regulatory
A = Activities

An ICH Standard Medical Terminology
MedDRA Governance

ICH
INTERNATIONAL COUNCIL for HARMONISATION of Technical Requirements for Pharmaceuticals for Human Use
www.ich.org

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
Where MedDRA is Used

- Regulatory Authority and Industry Databases
- Individual Case Safety Reports and Safety Summaries
- Pharmacovigilance and Signal Detection
- Clinical Study Reports
- Investigators' Brochures
- Core Company Safety Information
- Marketing Applications
- Publications
- Prescribing Information
- Advertising

Codes and Languages

- Hoofdpijn Dutch
- Headache English
- Céphalée French
- Bolesť hlavy Czech
- Céntro Chinese
- Kopfschmerz German
- Felftélés Hungarian
- Céfalea Italian
- Célfu Japanese
- Célfio Spanish

Electronic Submission
MSSO

- MedDRA Maintenance and Support Services Organization (MSSO)
  - Maintain MedDRA
  - Support MedDRA
  - Distribute MedDRA
- Headquartered in Washington, DC, USA
  - Staff also in France, Germany, Spain, UK

MedDRA Maintenance

- MedDRA is a user-responsive terminology
- Users may submit change requests (CRs) to the MSSO for consideration
  - Electronic change request submission tool
- MSSO review and implement approved changes
- Twice yearly official updates
  - 1 March X.0 release
  - 1 September X.1 release
ICSR Data Elements Coded with MedDRA

Electronic Transmission of Data

- MedDRA is a standard terminology used in
  - ICH E2B Electronic Transmission of Individual Case Safety Reports (ICSRs)
  - ICH M4E Electronic Common Technical Document (eCTD)
ICH E2B (R3) Data Elements in MedDRA

- E2B (R3) – ICSR
- Clinical Trials
- Post market

Visualization of Safety Data Using 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
- 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

Safety Profile

![Graph showing relative frequency of events in various system organ classes]
Signal Detection and MedDRA

MedDRA Structure & Size

- System Organ Class (SOC) (27)
- High Level Group Term (HLGT) (337)
- High Level Term (HLT) (1,738)
- Preferred Term (PT) (22,499)
- Lowest Level Term (LLT) (77,248)

SMQs (101)

Granularity Increases

Signal Strength Increases

MedDRA Version 20.0
MedDRA Hierarchy Example

- SOC = Cardiac disorders
- HLGT = Cardiac arrhythmias
- HLT = Rate and rhythm disorders NEC
  - PT = Tachycardia
    - LLT = Tachycardia
      - Reflex tachycardia
  - PT = Arrhythmia
    - LLT = Arrhythmia
  - PT = Bradycardia
    - LLT = Dysrhythmias

Use of MedDRA at FDA

Acknowledgement: Dr. Chuck Cooper, Office of Translational Sciences, CDER, FDA
Standardised MedDRA Queries (SMQs)

- Groupings of terms from one or more MedDRA System Organ Classes related to defined medical condition or area of interest
- Included terms may relate to signs, symptoms, diagnoses, syndromes, physical findings, laboratory and other physiologic test data, etc., related to medical condition or area of interest
- Intended to aid in case identification and signal detection

SMQs in Production - Examples

- As of Version 20.0, a total of 101 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
Signal Detection at EMA

- MedDRA supports signal detection and management in EU
  - Early detection of possible safety signals associated with medicinal products
  - Continuous monitoring and evaluation of potential safety issues in relation to reported adverse reactions
  - Decision making process based on a broader knowledge of the adverse reaction profile of medicinal products especially in the frame of the continuous benefit risk assessment of medicines
Signal Detection in EudraVigilance (cont)

- 43 signals were validated, prioritised and analysed in 2013
- 21 of the 43 signals led to a recommendation for changes to the product information
  - Directly (n=7)
  - Cumulative review (n=14)
  - DHPCs to increase awareness about the new safety information (n=4)
- One signal led to a formal evaluation of the benefit-risk balance via an Article 31 referral

Access MedDRA and User Support
**MedDRA Subscription**

- Users access MedDRA through subscription
- Regulators, Non-Profits, Academics, Healthcare providers have free subscription
- Commercial users pay a subscription fee
  - Funds MSSO
  - Rates reviewed and approved by ICH MedDRA Management Board
  - Sliding scale fee based on organization’s annual revenue, starting at $171
  - MedDRA rates flat or decreased for 12 years
- All subscribers receive the same quality services from the MSSO

**MedDRA Users**

- ~5000 organizations in 106 countries using MedDRA
  - MedDRA provided as an enterprise wide license, e.g., J&J
- Coordinating with WHO to support transition of countries to MedDRA
User Support

• Training
  – Free training to subscribers (F2F, webinars)
    • Over 4,400 users trained in 2016
  – Training videocasts on MedDRA.org public page

• Support
  – Help Desk (European and US)
  – MedDRA documentation: ICH MedDRA Guides, MSSO
    Best Practice documents
  – User Groups (China, Europe, US)
  – Software tools
    • Browsers, Versioning tools, Self-Service tool

Questions?