Understanding MedDRA

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MedDRA MSSO

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).

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Topics

- What is MedDRA?
- History and governance of MedDRA
- Recent worldwide trends on MedDRA use
- Purpose, scope, structure, and characteristics of MedDRA
- Where and how is MedDRA used?
- Medical Device terms in MedDRA

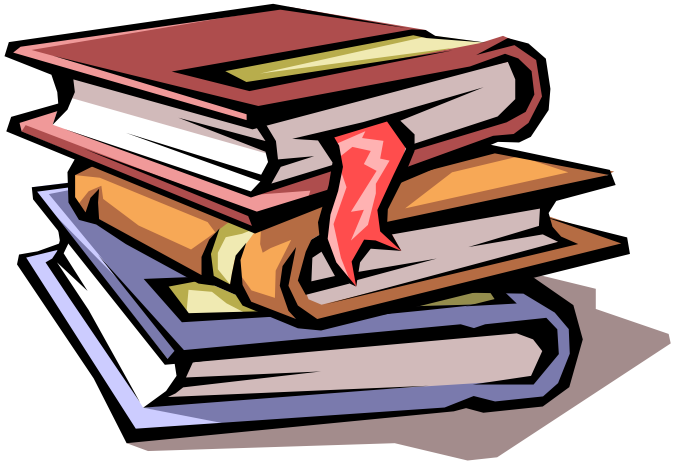
What is MedDRA?

Med = Medical

D = Dictionary for

R = Regulatory

A = Activities



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.

ICH Development of MedDRA

- 1990s – No standard international medical terminology
- 1993 – Working party : Industry and EU regulators amend UK Medicines Control Agency terminology
- October 1994 – ICH adopted MedDRA as basis for international terminology and established ICH M1 Expert Working Group
- March 1999 - MSSO (Maintenance & Support Services Organization) and JMO (Japanese Maintenance Organization) distribute first release of MedDRA (v2.1)

ICH Members

MEMBERS
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- MHLW/PMDA, Japan

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- JPMA
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- Swissmedic, Switzerland

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- CECMED, Cuba
- COFEPRIS, Mexico
- INVIMA, Colombia
- MMDA, Moldova
- National Center, Kazakhstan
- NPRA, Malaysia
- NRA, Iran
- Roszdravnadzor, Russia
- SAHPRA, South Africa
- SCDMTE, Armenia
- TGA, Australia
- TITCK, Turkey

Regional Harmonisation Initiatives (RHIs)
- APEC
- ASEAN
- EAC
- GHC
- PANDRH
- SADC

International Pharmaceutical Industry Organisation
- APIC

International Organisation regulated or affected by ICH Guideline(s)
- Bill & Melinda Gates Foundation
- CIOMS
- EDQM
- IPEC
- PIC/S
- USP

ICH and MedDRA

- ICH Role
  - Developed MedDRA as an ICH standard
  - ICH owns MedDRA
  - ICH has oversight of the MSSO through the MedDRA Management Committee

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)

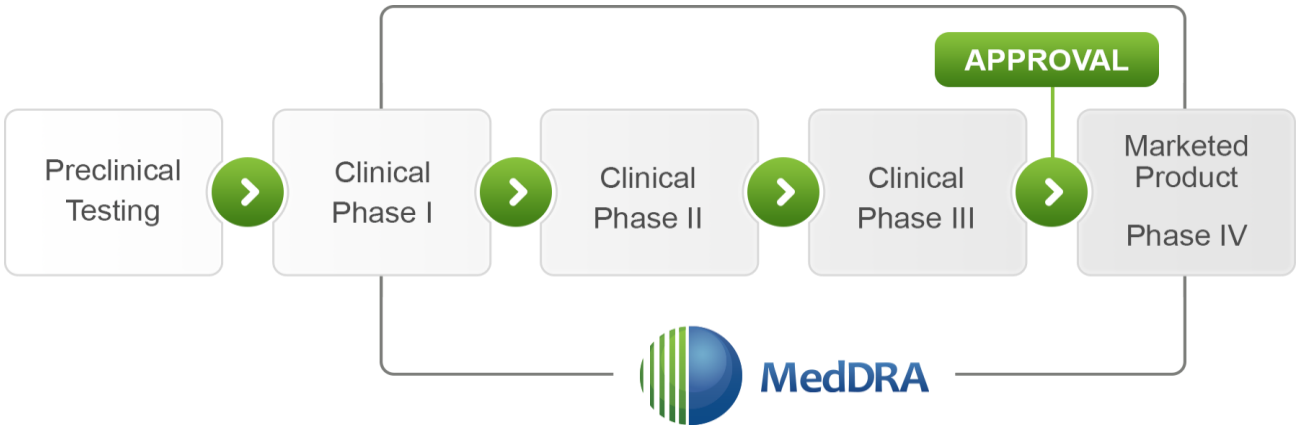
MedDRA's Purpose

- 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 Subscriptions

- MedDRA is free to all regulatory authorities and non-commercial users
- Commercial users pay an annual fee based on the organization's annual revenue
  - Commercial subscriptions start at $154 USD annually
- All users get the same access to MedDRA and MSSO services
  - MedDRA tools, training, User Groups, ability to submit changes

Where MedDRA is Used



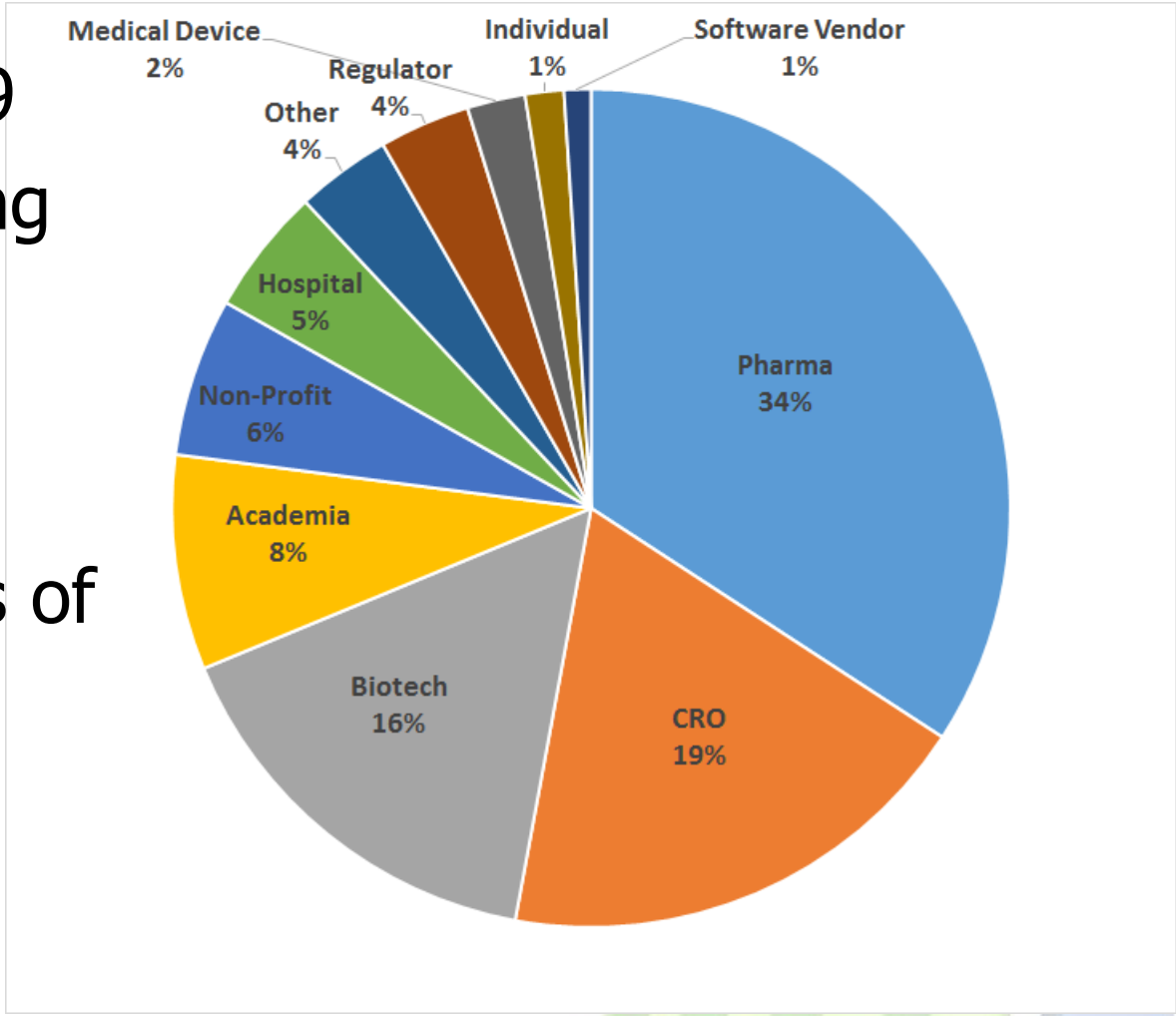
Regulatory Authority and Industry Databases
Individual Case Safety Reports and Safety Summaries
Clinical Study Reports
Investigators' Brochures
Core Company Safety Information
Marketing Applications
Publications
Prescribing Information
Advertising

Global View

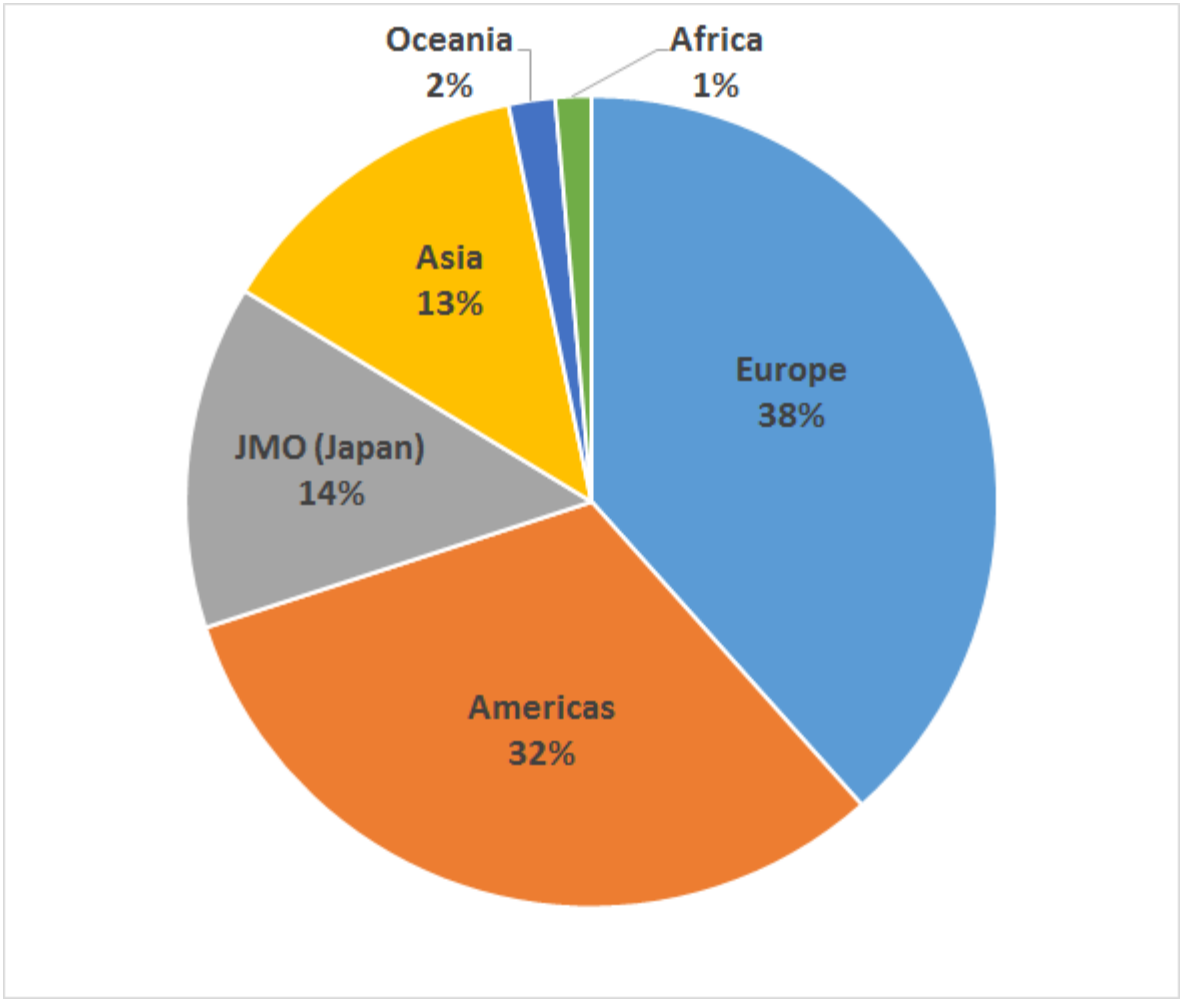
MedDRA is in 125 countries

MedDRA Users Profile

- As of January 2019
  - 5,700 Subscribing organizations (MSSO+JMO)
  - 122 Countries
- Graph shows types of subscribing organizations



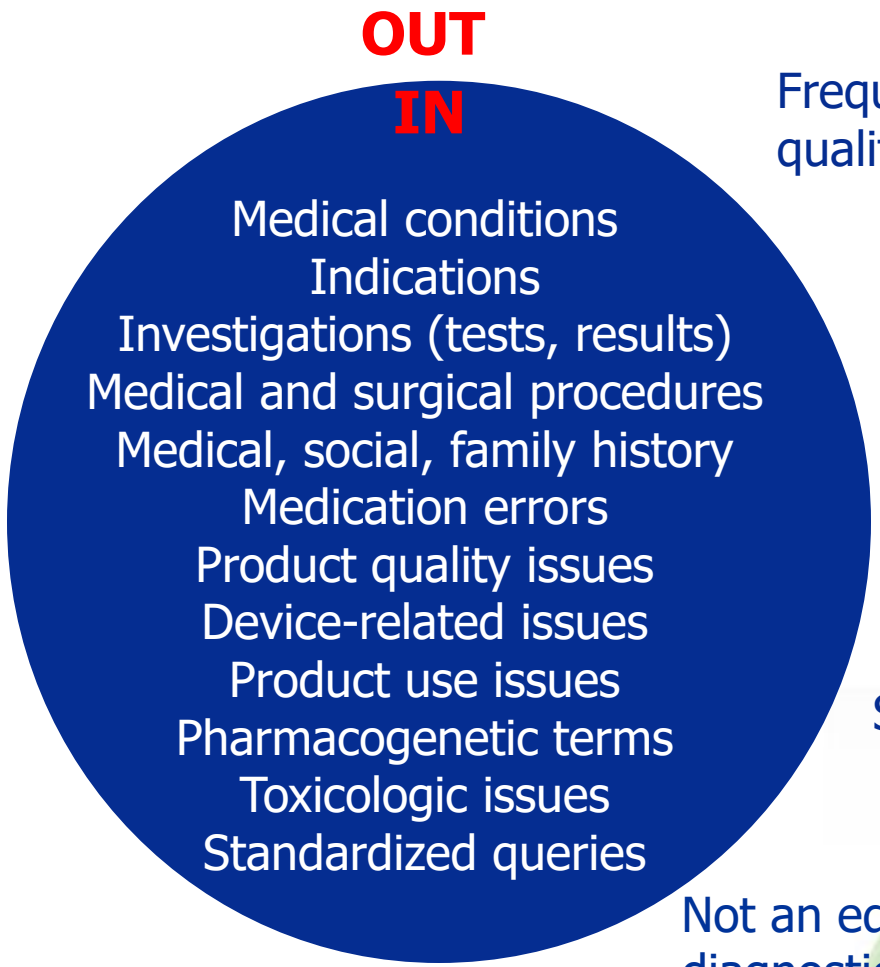
MedDRA Users by Region



Country	Count
United States	1571
Japan	785
UK	336
Germany	325
China	299
France	245
Italy	207
Spain	150
Canada	127
Republic of Korea	111
Sweden	96
Australia	95
Netherlands	92
India	90
Switzerland	84
Poland	71
Belgium	61
Chinese Taipei	60
Israel	57
Greece	56
Portugal	52
Denmark	50
Austria	43
Russian Federation	37
Czechia	36

Overview of MedDRA Scope, Structure, and Characteristics

Scope of MedDRA



Not a drug dictionary

Frequency qualifiers

Patient demographic terms

Numerical values for results

Clinical trial study design terms

Severity descriptors

Not an equipment, device, diagnostic product dictionary

MedDRA Structure

System Organ Class (SOC) (27)

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High Level Group Term (HLGT) (337)

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High Level Term (HLT) (1,737)

|

Preferred Term (PT) (23,708)

|

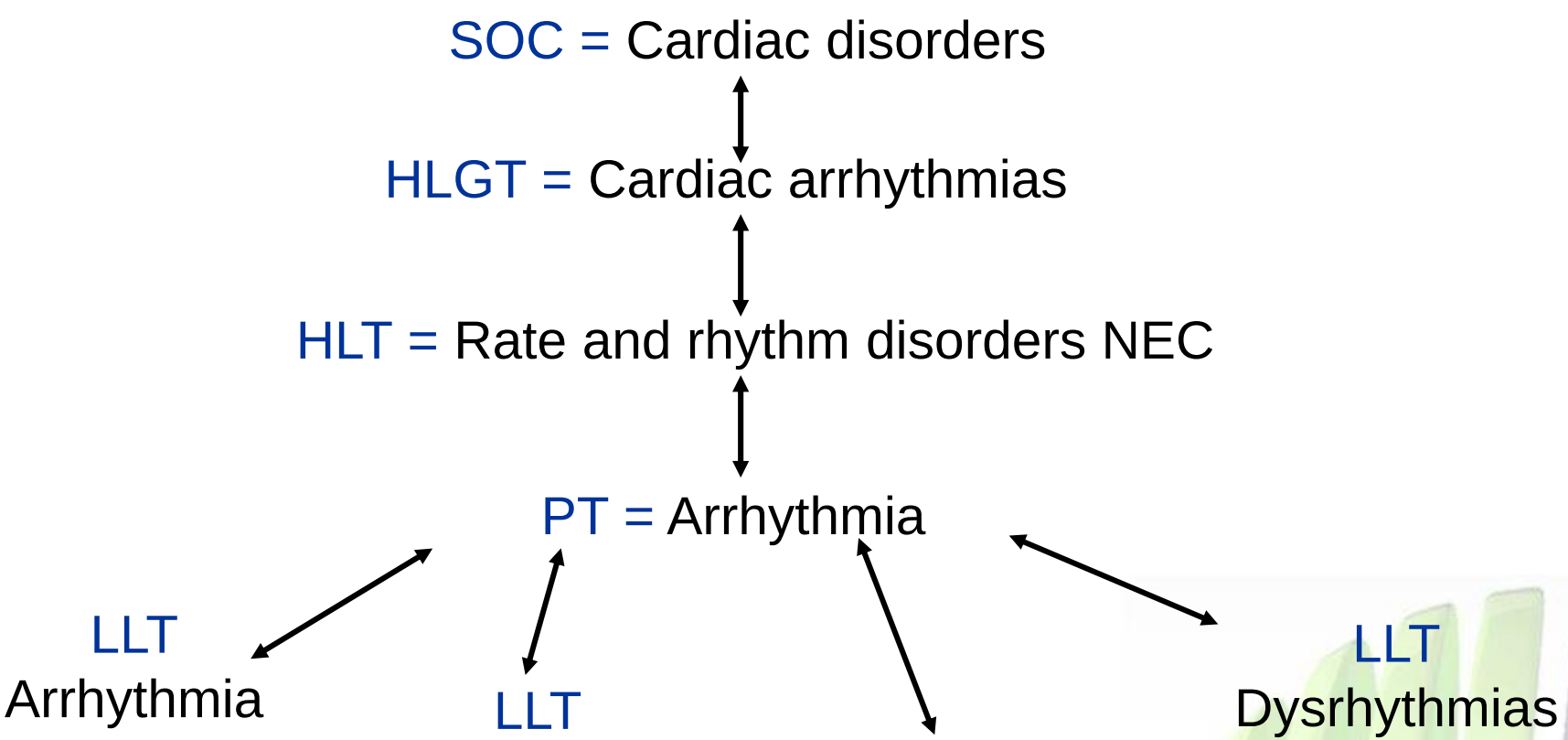
Lowest Level Term (LLT) (80,262)

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



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

MedDRA Codes

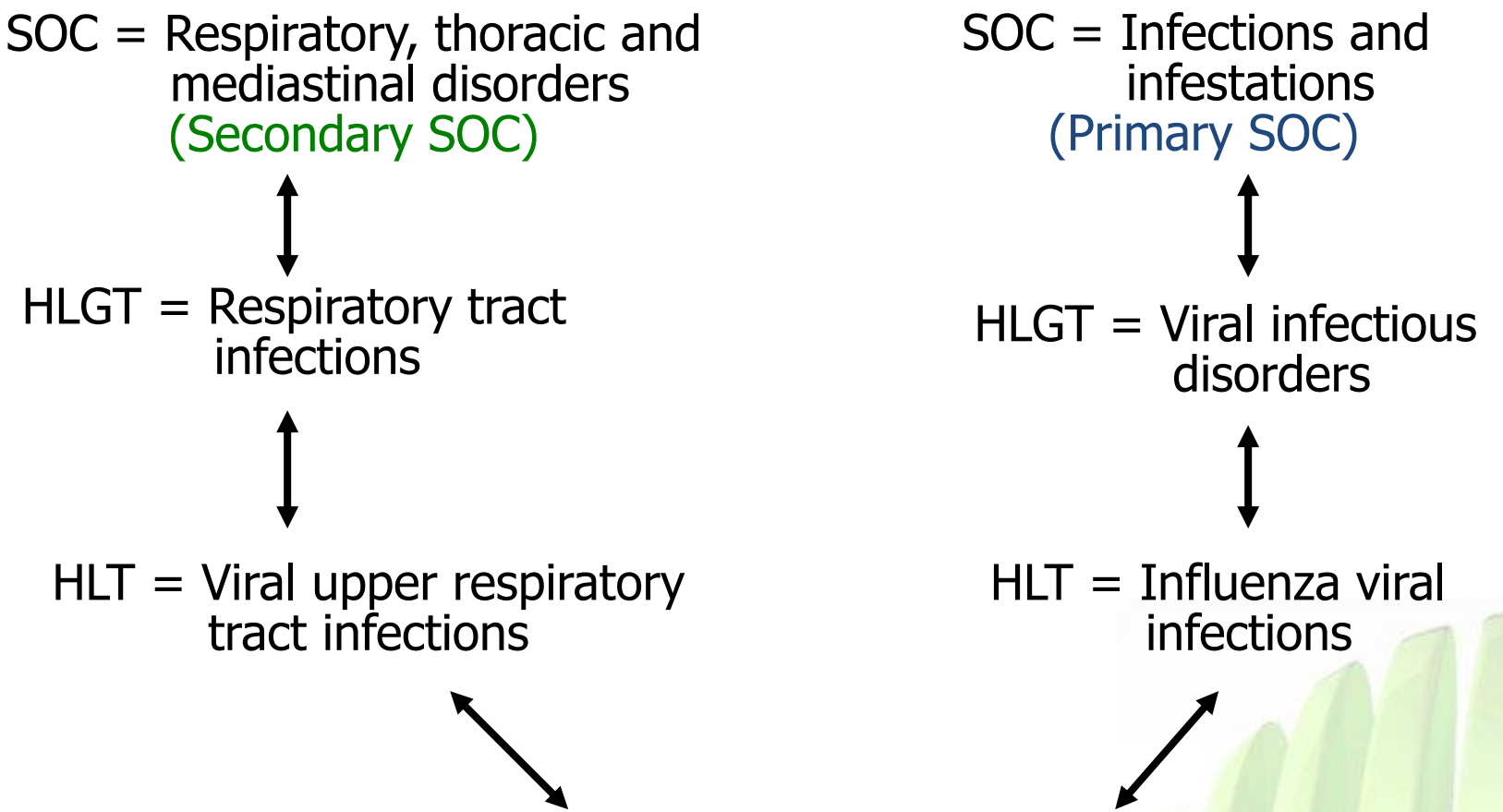
- Each MedDRA term assigned an 8-digit numeric code starting with "1"
- The code is non-expressive
- Codes can fulfill a data field in various electronic submission types (e.g., E2B)
- New terms are assigned sequentially

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

A Multi-Axial Terminology (cont)



Medical Device Terms in MedDRA

Device Terms in MedDRA

- Device specific terms included from the inception of MedDRA
  - Currently over 700 device specific terms in MedDRA
  - Can be found in various SOCs
- The scope of MedDRA encompasses medical, health-related, and regulatory concepts pertaining to medical products for human use and these include the health effects and malfunction of devices
  - e.g., PT *Device related infection* and PT *Device failure*
- Device names/components are out of scope

Device Term Developments in MedDRA History

- March 2008(Version 11.0), Device Patient Terms
  - A series of device patient adverse event terms were added to support the use of MedDRA for combination products
  - These terms were taken from a list of patient problem terms that were provided by the FDA
- March 2010(Version 13.0), Device Hierarchy Change
  - Comprehensive device related term review with the help of industry volunteers
  - New device related HLGTs and HLTs were added to SOC General disorders and administration site conditions

Device Terms in MedDRA : Important Grouping Levels

- SOC General disorders and administration site conditions
  - HLGT Administration site reactions
  - HLGT Body temperature conditions
  - HLGT Complications associated with device
    - HLT Breast complications associated with device
    - HLT Cardiac complications associated with device
    - HLT Complications associated with device NEC
    - HLT Eye complications associated with device
    - HLT Reproductive complications associated with device
    - HLT Respiratory complications associated with device
    - HLT Vascular complications associated with device

- SOC Product issues
  - 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

- SOC Injury, poisoning and procedural complications
  - HLGT Administration site reactions
  - HLGT Bone and joint injuries
  - HLGT Exposures, chemical injuries and poisoning
  - HLGT Injuries by physical agents
  - HLGT Injuries NEC
  - HLGT Medication errors and other product use errors and issues
  - HLGT Off label uses and intentional product misuses/use issues
  - HLGT Overdoses and underdoses NEC
  - HLGT Procedural related injuries and complications NEC
    - HLT Anaesthetic and allied procedural complications
    - HLT Cardiac and vascular procedural complications
    - HLT Device site reactions
      - PT Medical device site abscess
      - PT Medical device site anaesthesia
      - PT Medical device site atrophy
      - PT Medical device site bruise
      - PT Medical device site burn
      - PT Medical device site calcification
      - PT Medical device site cellulitis

- SOC Surgical and medical procedures
  - HLGT Bone and joint therapeutic procedures
  - HLGT Breast therapeutic procedures
  - HLGT Cardiac therapeutic procedures
    - HLT Cardiac device therapeutic procedures
      - PT Artificial heart implant
      - PT Cardiac contractility modulation therapy
      - PT Cardiac device reprogramming
      - PT Cardiac pacemaker adjustment
      - PT Cardiac pacemaker insertion
      - PT Cardiac pacemaker removal
      - PT Cardiac pacemaker replacement
      - PT Cardiac resynchronisation therapy
      - PT Implantable cardiac monitor insertion
      - PT Implantable cardiac monitor removal
      - PT Implantable cardiac monitor replacement

- These are not all device terms though!

IMDRF and MedDRA

IMDRF and MedDRA

- International Medical Device Regulatory Forum (IMDRF)
  - Developing set of harmonized terminologies for reporting adverse events for medical devices
  - One of the terminologies being developed to describe Patient Problems
  - IMDRF posted a draft term list and structure for comment

IMDRF Patient Problem Codes

- Annex E: Health Effects – Clinical Signs, Symptoms and Conditions Terms and Codes
  - Term list includes ~700 terms (Patient Problem Codes)
  - Provides terminology to describe the observed condition of the affected persons after the medical device adverse event occurs
  - Terms are largely based on a subset of MedDRA terms

IMDRF Patient Problem Codes Mapping

- MSSO mapped Annex E to MedDRA LLTs (v21.1) in December 2018
- IMDRF agreed to include the mapped MedDRA terms and codes in the distributed file
- IMDRF released the mapping in March 2019
- Mapping will help manufacturers who produce drugs, combination products, and devices since many are MedDRA users

IMDRF Patient Problem Codes Mapping (cont)

Annex E. Clinical signs, symptoms and conditions

Device (bold): For the purpose of this Annex, a device means a medical device including accessories and components
Wherever appropriate "patient" should be taken to include user, operator or any other person affected by the incident.

LEVEL 1	LEVEL 2							LEVEL 3						
Category	Term	Definition	IMDRF Code	MedDRA Code	MedDRA LLT	Primary Category	Secondary Category	Term	Definition	IMDRF Code	MedDRA Code	MedDRA LLT	Primary Category	Secondary Category
Nervous System	Balance Problems	A feeling of falling down which can occur whether the person is standing, sitting or lying down.	E0101	10049848	Balance disorder									
	Brain Injury	Damage to the brain.	E0102	10060690	Traumatic brain injury	Nervous System	Injury	Encephalocele	Hernia of brain substance and meninges through a congenital or traumatic opening of the skull.	E010201	10014617	Encephalocele	Nervous System	Injury
	Cerebral Edema	A swelling in the brain caused by the presence of excessive fluid.	E0103	10008107	Cerebral edema	Nervous System	Generalized Disorders							
	Cerebral Hyperperfusion Syndrome	Unexpected increase in cerebral blood flow after carotid endarterectomy (CEA) or carotid artery stenting (CAS).	E0104	10064730	Cerebral hyperperfusion syndrome	Nervous System	Vascular System							
	Cerebral Ventriculomeglia	Abnormal enlargement of the cerebral ventricles.	E0105	10068352	Cerebral ventriculomegaly									
	Cerebrospinal Fluid Leakage	The loss of cerebrospinal fluid into the surrounding tissues.	E0106	10008164	Cerebrospinal fluid leakage									
	Cognitive Changes	Changes in perception, thinking, or remembering.	E0107	10057668	Cognitive disorder			Confusion/ Disorientation	A mental state characterized by a lack of clear and orderly thought and behavior.	E010701	10010300	Confusion		

http://www.imdrf.org/documents/documents.asp

MedDRA | Medical Dictionary for Regulatory Activities

Thank you, Questions?

✉ mssohelp@meddra.org

ICH harmonisation for better health