

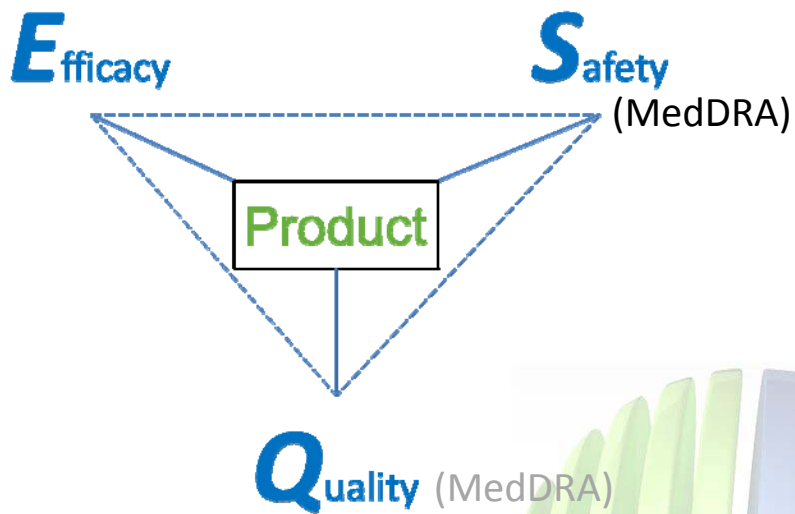


Medical Dictionary for Regulatory Activities (MedDRA)

Global Summit on Regulatory Science (GSRSS)
Brasilia, Brazil
19 September 2017
Anna Zhao-Wong, MD, PhD @ MedDRA MSSO



The Golden Triangle





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

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MedDRA

Topics

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

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MedDRA and MSSO Introduction



What is MedDRA?

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

An ICH Standard Medical Terminology





MedDRA

MedDRA Governance

ICH

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

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MedDRA


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

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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

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Codes and Languages



10019211

Electronic Submission

000024

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MedDRA

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

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MedDRA

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

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ICSR Data Elements Coded with MedDRA

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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)

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ICH E2B (R3) Data Elements in MedDRA

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


Element id	Element Name
D.7.1.r.1b	Medical History (disease / surgical procedure / etc.) (MedDRA code)
D.8.r.6b	Indication (MedDRA code)
D.8.r.7b	Reaction (MedDRA code)
D.9.2.r.1b	Reported Cause(s) of Death (MedDRA code)
D.9.4.r.1b	Autopsy-determined Cause(s) of Death (MedDRA code)
D.10.7.1.r.1b	Medical History (disease / surgical procedure / etc.) (MedDRA code)
D.10.8.r.6b	Indication (MedDRA code)
D.10.8.r.7b	Reactions (MedDRA code)
E.i.2.1b	Reactions / Event (MedDRA code)
F.r.2.2b	Test Name (MedDRA code)
G.k.7.r.2b	Indication (MedDRA code)
H.3.r.1b	Sender's Diagnosis / Syndrome and / or Reclassification of Reaction / Event (MedDRA code)

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Visualization of Safety Data Using MedDRA


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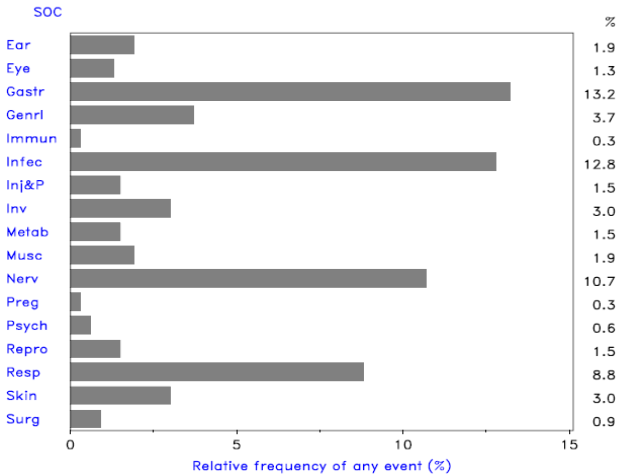
MedDRA System Organ Classes

- 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

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MedDRA Safety Profile




SOC	Relative frequency of any event (%)
Ear	1.9
Eye	1.3
Gastr	13.2
Genrl	3.7
Immun	0.3
Infec	12.8
Inj&P	1.5
Inv	3.0
Metab	1.5
Musc	1.9
Nerv	10.7
Preg	0.3
Psych	0.6
Repro	1.5
Resp	8.8
Skin	3.0
Surg	0.9


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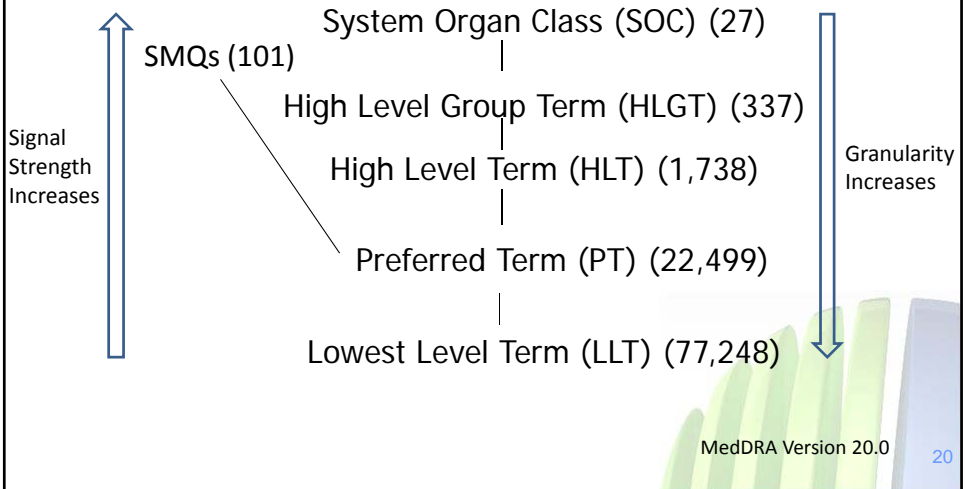
Signal Detection and MedDRA



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MedDRA Structure & Size



System Organ Class (SOC) (27)

SMQs (101)

High Level Group Term (HLGT) (337)

High Level Term (HLT) (1,738)

Preferred Term (PT) (22,499)

Lowest Level Term (LLT) (77,248)

Signal Strength Increases

Granularity Increases

MedDRA Version 20.0

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MedDRA

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

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MedDRA

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

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MedDRA

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

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MedDRA

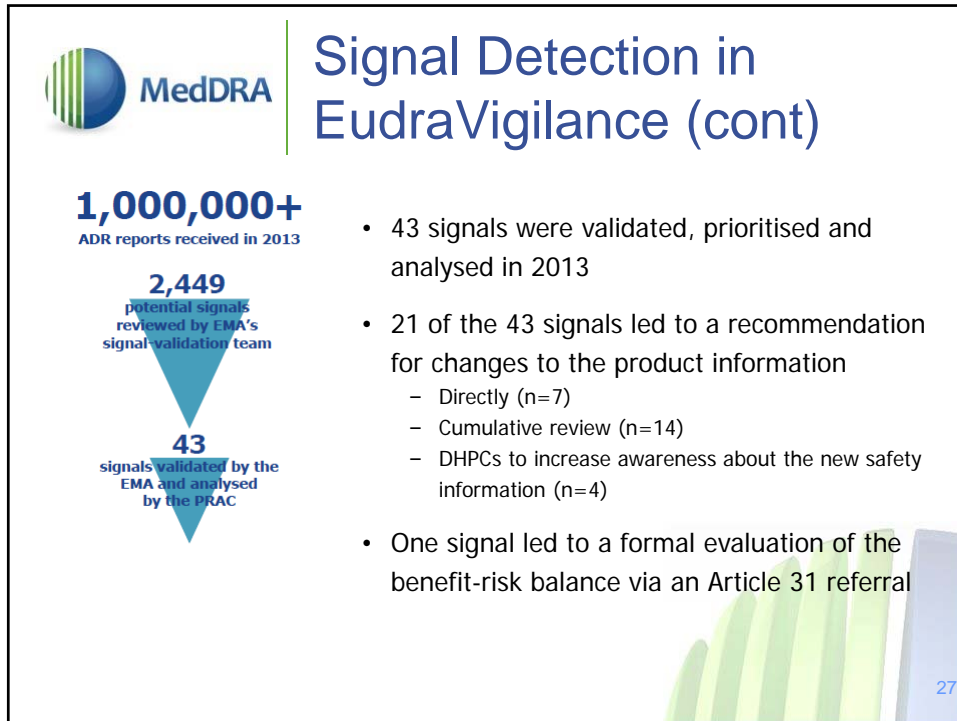
Signal Detection in EudraVigilance

Active Substance	SOCs	Higher levels of hierarchy		SMQs		Screening at PT level							
		HLGTs	HLTs	SMQ Broad	SMQ Narrow	PTs	IME / DME	New EV	Tot EV	New Fatal	PAR (1)	Priority	SDR
Drug A	Immun	Allergic Conditions	Anaphylactic Reactions	Anaphylactic Reaction -- Hypersensitivity -- Shock	Anaphylactic Reaction Hypersensitivity -- Shock	Anaphylactic Shock	Ime / Dme	1	2	0	0.03	Pr 1	
Drug A	Inv	Haematology Investigations (Incl Blood Groups)	Platelet Analyses	Haematopoietic Cytopenias		Platelet Count Abnormal		2	4	1	1.73	Pr 3	
Drug A	Inv	Haematology Investigations (Incl Blood Groups)	White Blood Cell Analyses	Haematopoietic Cytopenias -le	Haematopoietic Cytopenias	White Blood Cell Count Decreased		1	33	1	1.11	Pr 3	SDR (25)
Drug A	Neopl	Leukaemias	Myelodysplastic Syndromes	Haematopoietic Cytopenias Premalignant Disorders	Premalignant Disorders	Myelodysplastic Syndrome	Ime	1	37	0	11.21	Pr 2	SDR (25)
Drug A	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failure -- Retroperitoneal Fibrosis -- Iohdomyolysis/Myopathy	Acute Renal Failure	Renal Impairment	Ime	2	18	0	0.56	Pr 3	
Drug A	Skin	Angioedema And Urticaria	Angioedemas	Anaphylactic Reaction -- Angioedema -- Hypersensitivity -- Oropharynx Disorders	Angioedema -- Hypersensitivity -- Oropharynx Disorders	Angioedema	Ime / Dme	1	2	0	0.01	Pr 1	
Drug A	Vasc	Vascular Hypertensive Disorders	Accelerated And Malignant Hypertension	Hypertension	Hypertension	Malignant Hypertension	Ime	1	5	0	1.11	Pr 2	SDR (11)

MedDRA embedded

Disproportionality

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MedDRA

MedDRA Subscription

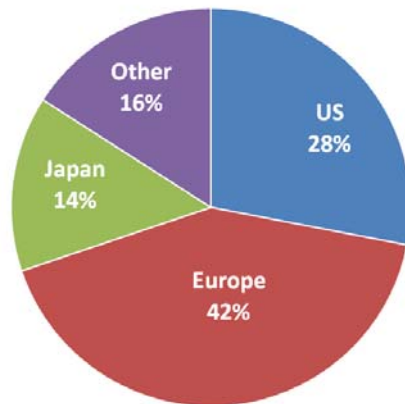
- Users access MedDRA through subscription
- Regulators, Non-Profits, Academics, Healthcare providers have free subscription
- Commercial users pay a subscription fee
 - Funds MSSO
 - Rates reviewed and approved by ICH MedDRA Management Board
 - Sliding scale fee based on organization's annual revenue,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

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MedDRA

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

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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

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MedDRA

Medical Dictionary
for Regulatory Activities

Questions?

