Introduction to MedDRA: Coding and Data Analysis

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ICH
harmonisation for better health

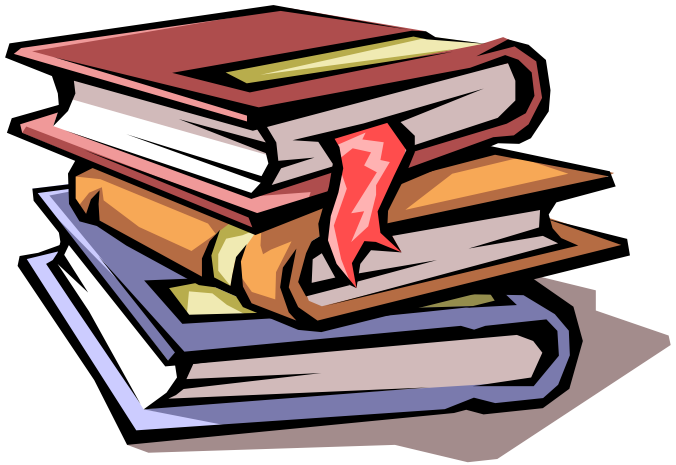
What is MedDRA?

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.

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 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

Regulatory Authority and Industry Databases

Individual Case Safety Reports and Safety Summaries

Clinical Study Reports

Investigators' Brochures

Core Company Safety Information

Marketing Applications

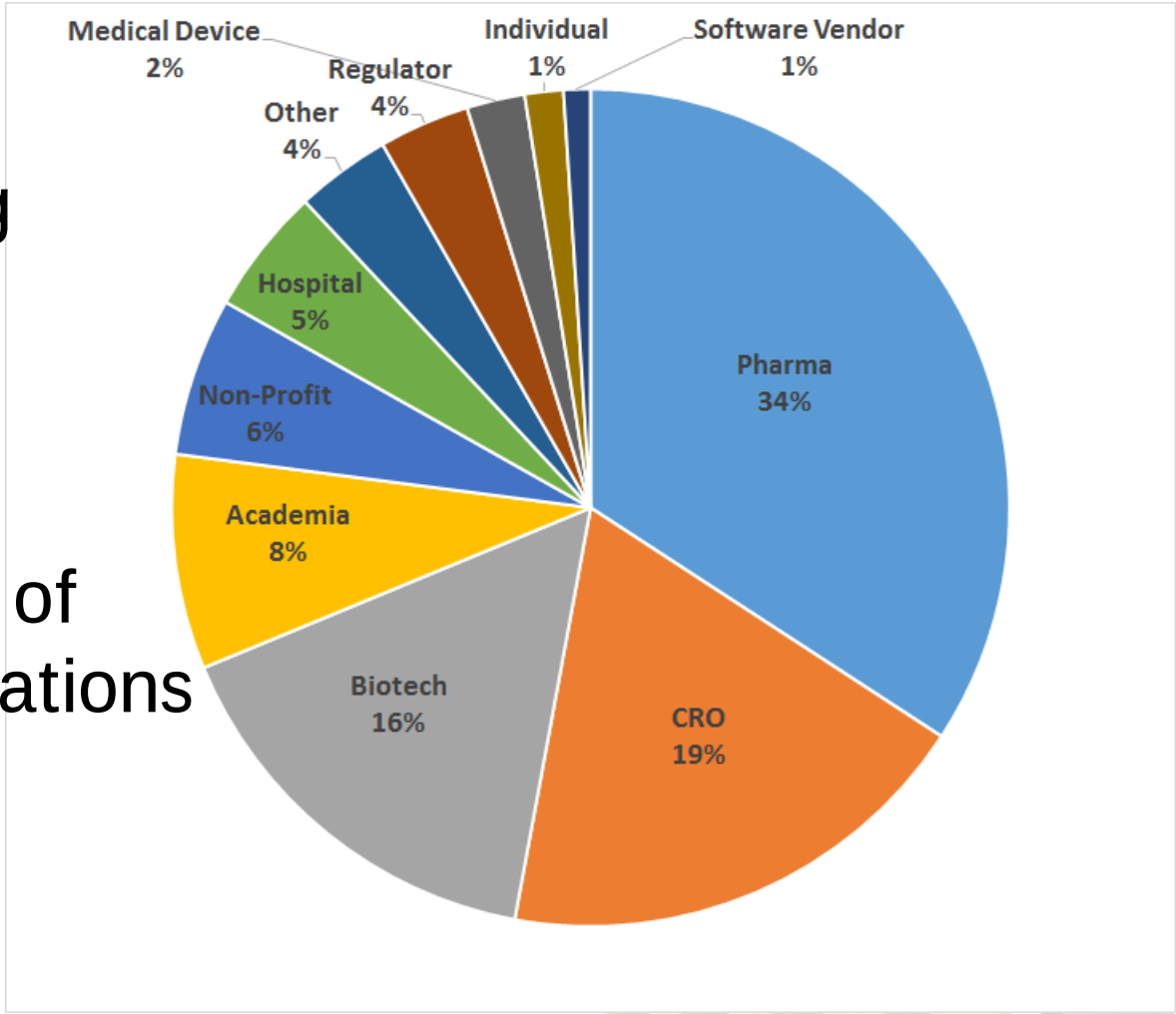
Publications

Prescribing Information

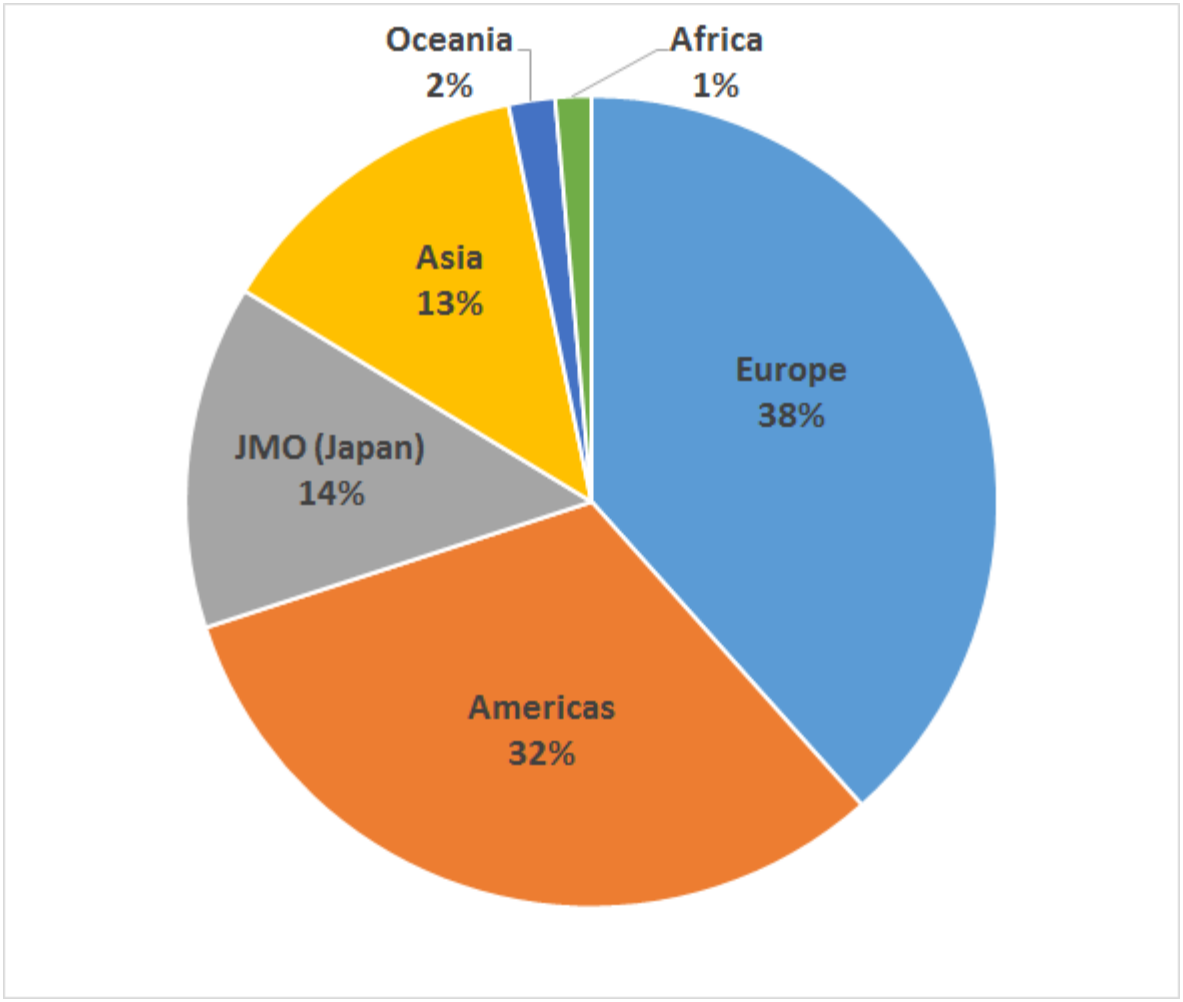
Advertising

MedDRA Users Profile

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

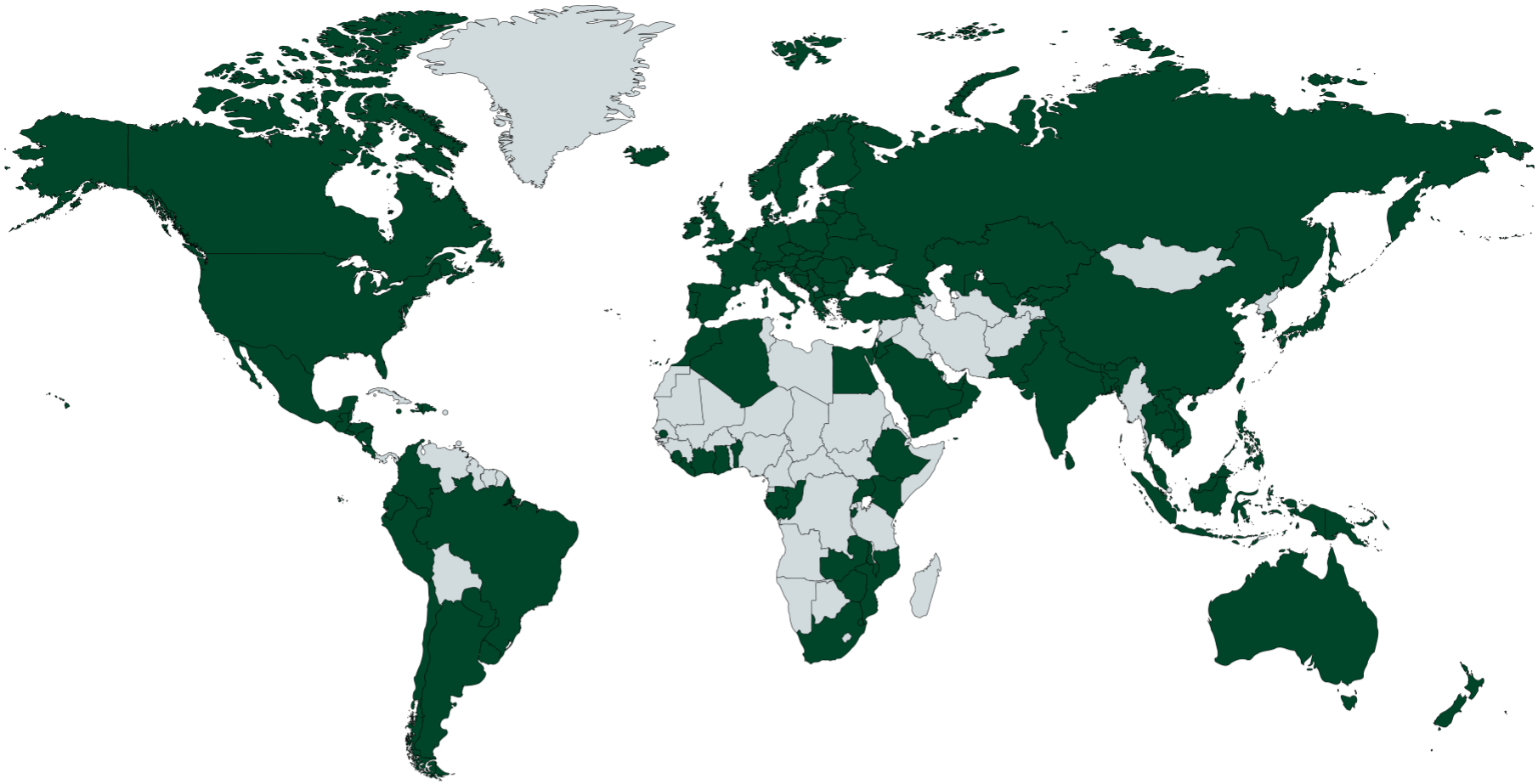


MedDRA Users by Region



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

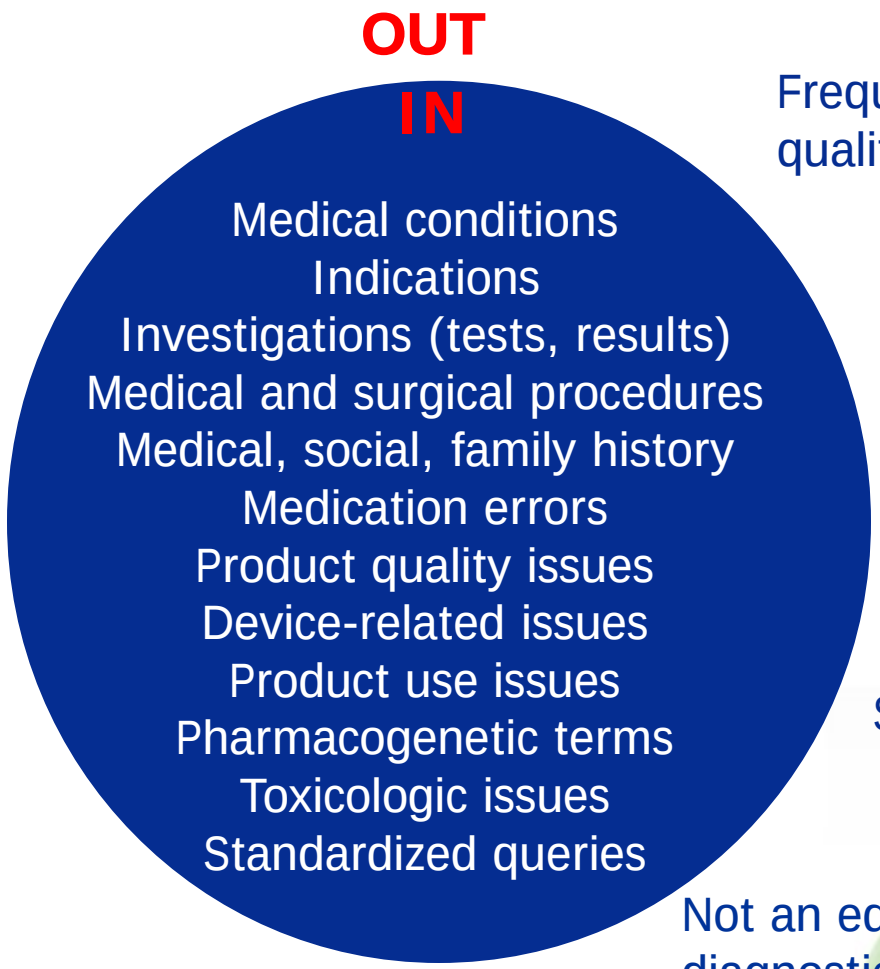
MedDRA Users By Country



MedDRA Data Sharing

- Subscription grants access to MedDRA for one year
- Subscriber cannot grant any sublicense, publish or otherwise distribute MedDRA to a third party
- Data may be freely exchanged between current MedDRA subscribers
  - Sponsor-sponsor, sponsor-CRO, vendor-user, etc.
  - Use Self-Service Application to check organization's subscription status
- Sharing MedDRA with a non-subscribing organization is a violation of the MedDRA license

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)

High Level Group Term (HLGT) (337)

High Level Term (HLT) (1,737)

Preferred Term (PT) (23,708)

Lowest Level Term (LLT) (80,262)

MedDRA in Use

	Lowest Level Term	Preferred Term	High Level Term	High Level Group Term	System Organ Class
English	Asthmatic wheezing	Wheezing	Bronchospasm and obstruction	Bronchial disorders (excl neoplasms)	Respiratory, thoracic and mediastinal disorders
Russian	Астматическое свистящее дыхание	Свистящее дыхание	Бронхоспазм и обструкция	Бронхиальные нарушения (искл. новообразования)	Нарушения со стороны дыхательной системы, органов грудной клетки и средостения

Coding – Applied to individual events

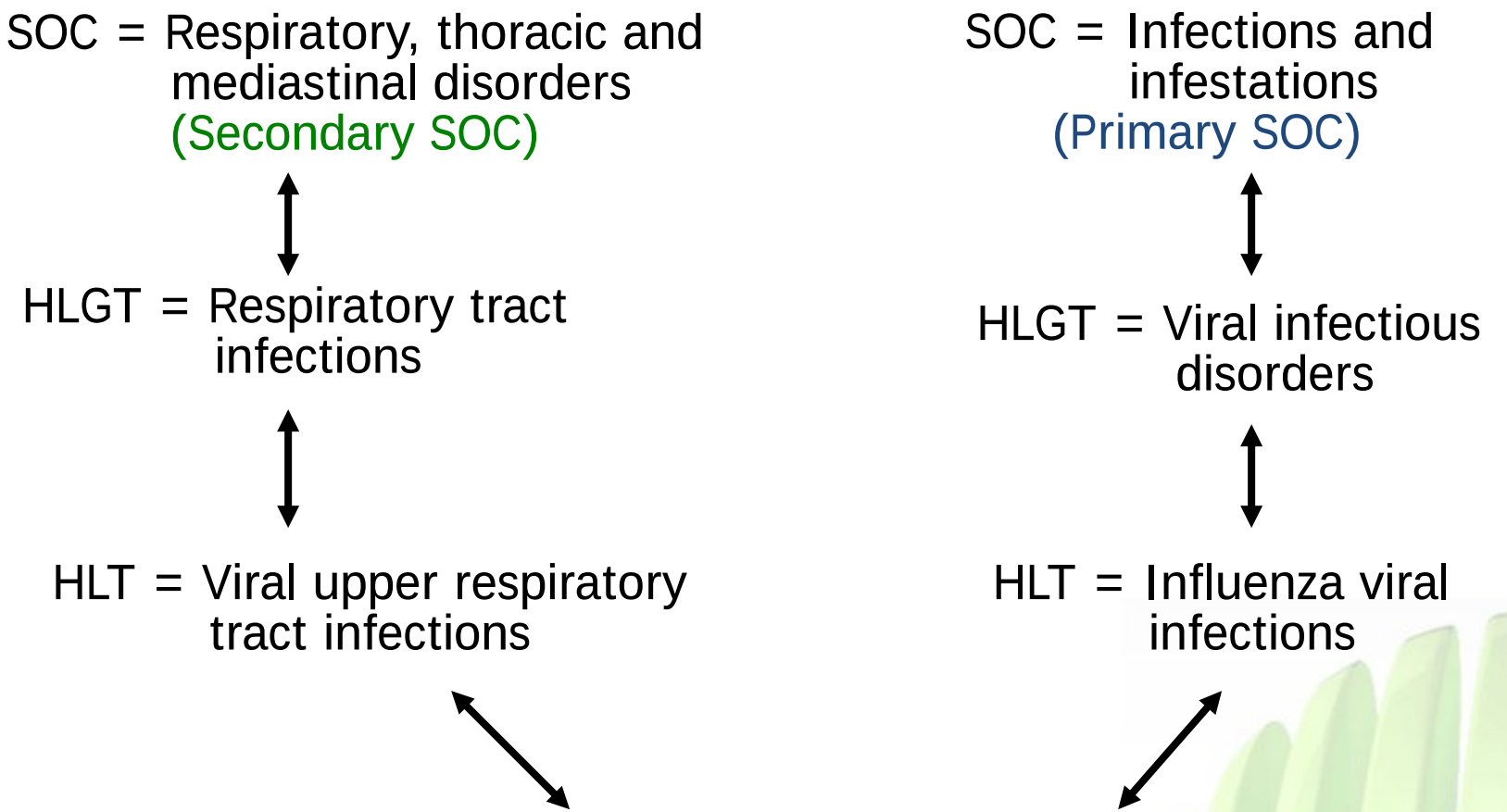
Analysis – Grouping of multiple events for signal detection

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)



Rules for Primary SOC Allocation

- PTs represented in only one SOC are automatically assigned that SOC as primary
- PTs for diseases, signs and symptoms are assigned to prime manifestation site SOC
- Congenital and hereditary anomalies terms have SOC *Congenital, familial and genetic disorders* as Primary SOC
- Neoplasms terms have SOC *Neoplasms benign, malignant and unspecified (incl cysts and polyps)* as Primary SOC
  - **Exception:** Cysts and polyps have prime manifestation site SOC as Primary SOC
- Infections and infestations terms have SOC *Infections and infestations* as Primary SOC

Primary SOC Priority

If a PT links to more than one of the exceptions, the following priority will be used to determine primary SOC:

- *1st: Congenital, familial and genetic disorders*
- *2nd: Neoplasms benign, malignant and unspecified (incl cysts and polyps)*
- *3rd: Infections and infestations*

A Multi-Axial Terminology (cont)

PTs in the following SOCs only appear in that particular SOC and not in others, i.e., they are not multi-axial

- *Investigations*
- *Surgical and medical procedures*
- *Social circumstances*

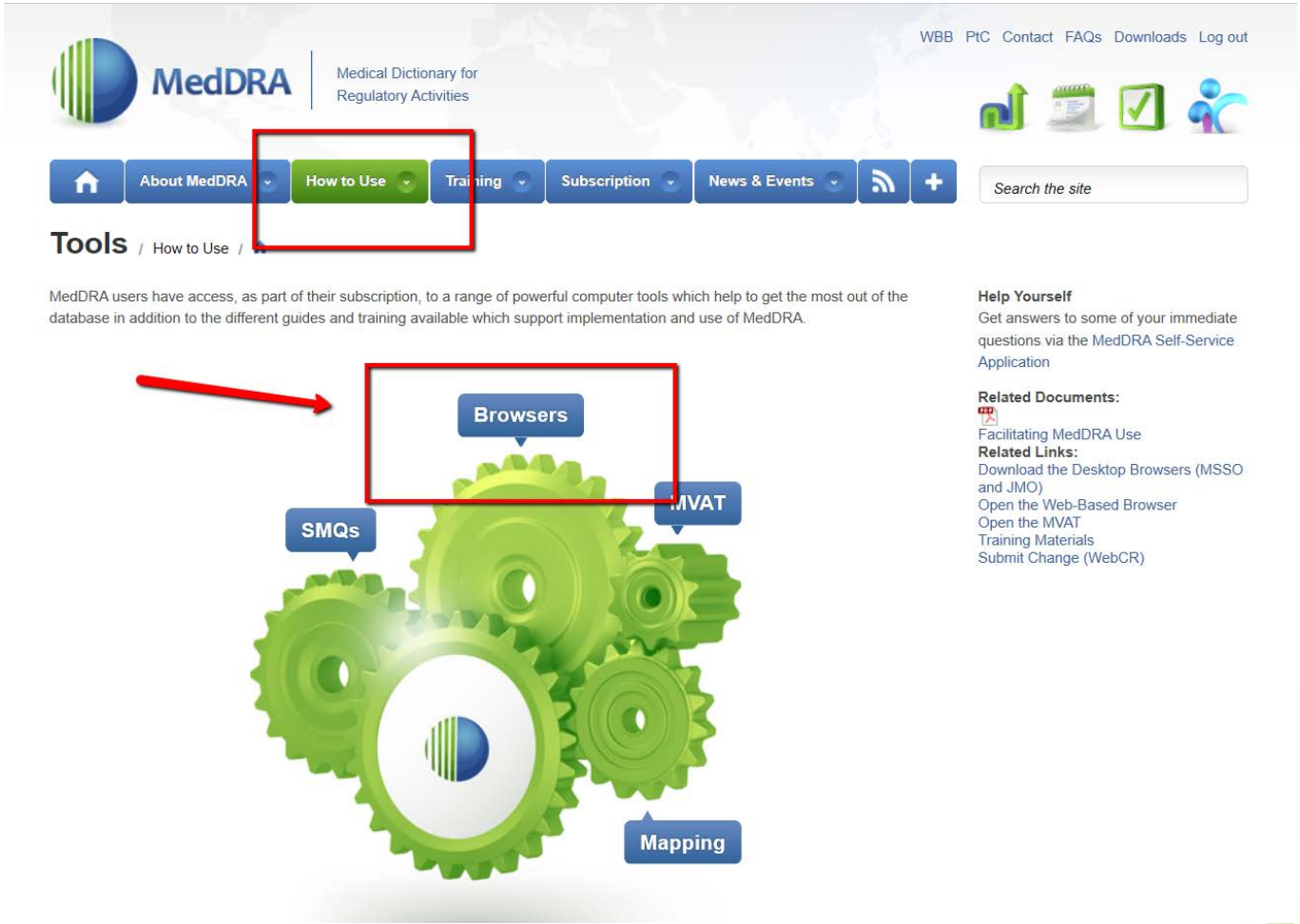
Can You Select the Primary SOC for This PT?

PT	HLT	HLGT	SOC
Congenital HIV infection	Viral infections congenital	Infections and infestations congenital	Congenital, familial and genetic disorders
	Congenital neonatal infections	Neonatal and perinatal conditions	Pregnancy, puerperium and perinatal conditions
	Retroviral infections	Viral infectious disorders	Infections and infestations
	Acquired immunodeficiency syndromes	Immunodeficiency syndromes	Immune system disorders

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

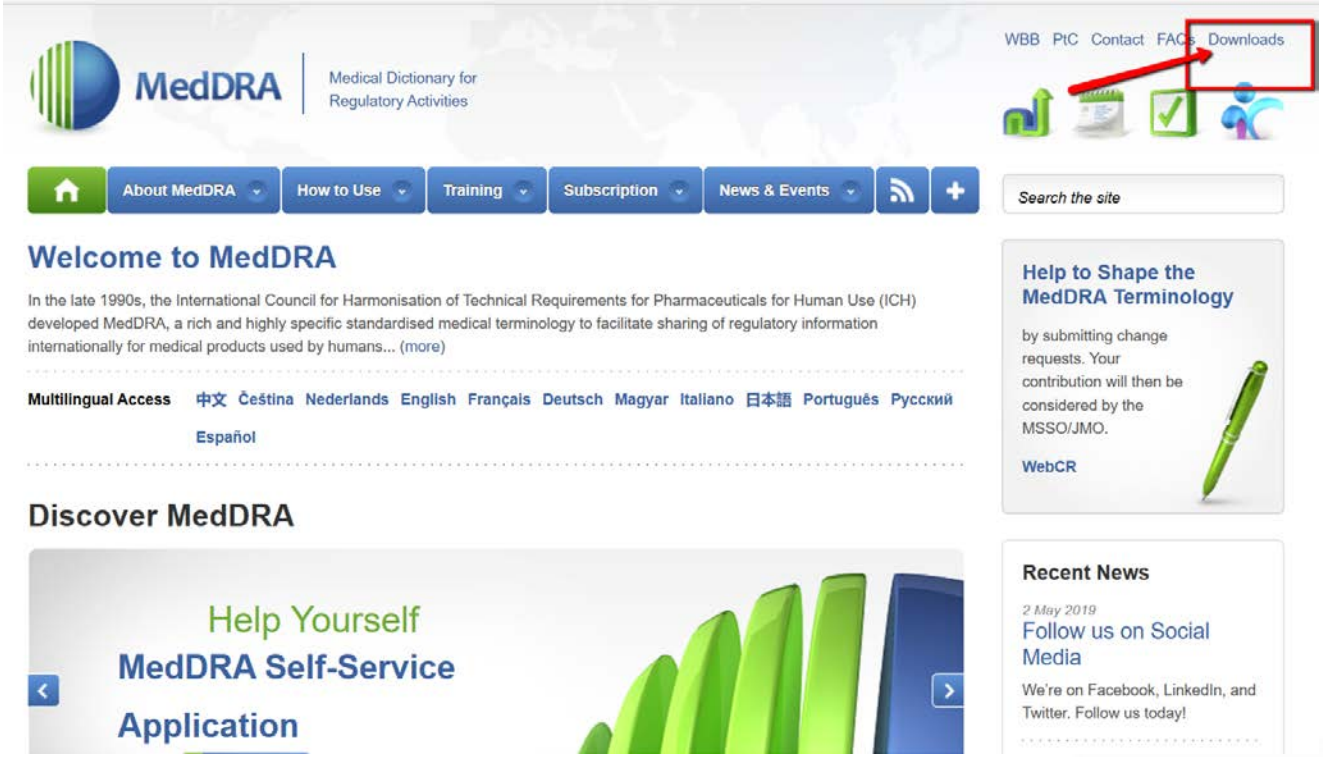
MedDRA Browsers



MedDRA Mobile Browser

- MedDRA Mobile Browser for use on phones and tablets
- Accessed at: mmb.meddra.org
- Requires your organisation's MedDRA ID and Password

Downloading MedDRA



- Requires MedDRA ID and Password

Select Version and Language

MedDRA Version Releases:

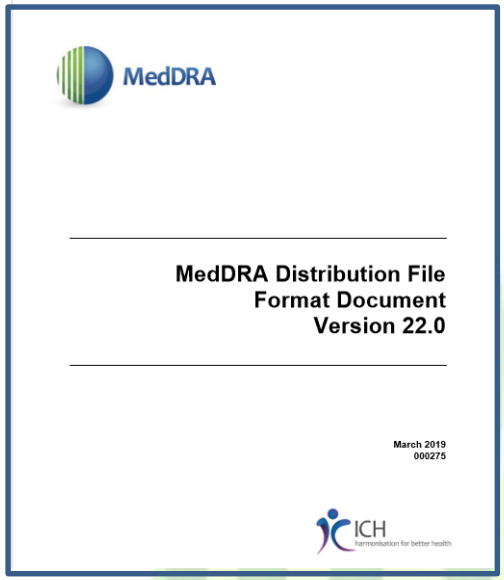
MedDRA Version 22.0 March 2019

Release package	Language	Size
MedDRA 22.0 版 中文	Chinese	7.18 MB
MedDRA verze 22.0 Čeština	Czech	7.1 MB
MedDRA Versie 22.0 Nederlands	Dutch	6.17 MB
MedDRA Version 22.0 English	English	8.66 MB
MedDRA Version 22.0 Français	French	6.5 MB
MedDRA Version 22.0 Deutsch	German	6.96 MB
MedDRA 22.0 változat Magyar	Hungarian	7.93 MB
MedDRA versione 22.0 Italiano	Italian	7.07 MB
日本語シノニム バージョン22.0対応版	Japanese	1.19 MB
MedDRA バージョン 22.0 日本語	Japanese	14.6 MB
MedDRA Versão 22.0 Português	Portuguese	7 MB
MedDRA Версия 22.0 Русский Март 2019 г.	Russian	8.53 MB
Versión 22.0 de MedDRA Español	Spanish	7.3 MB

Accessing MedDRA Content

- MedDRA content files are a series of ASCII files
- Folder is unzipped by a version-specific unzip password
- Files can be imported into the MedDRA Desktop Browser
- Files may also be incorporated into company database

- Release package contains documents, including:
  - MedDRA Introductory Guides
  - MedDRA Distribution File Format Document
  - Other support documents all available in Russian



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)

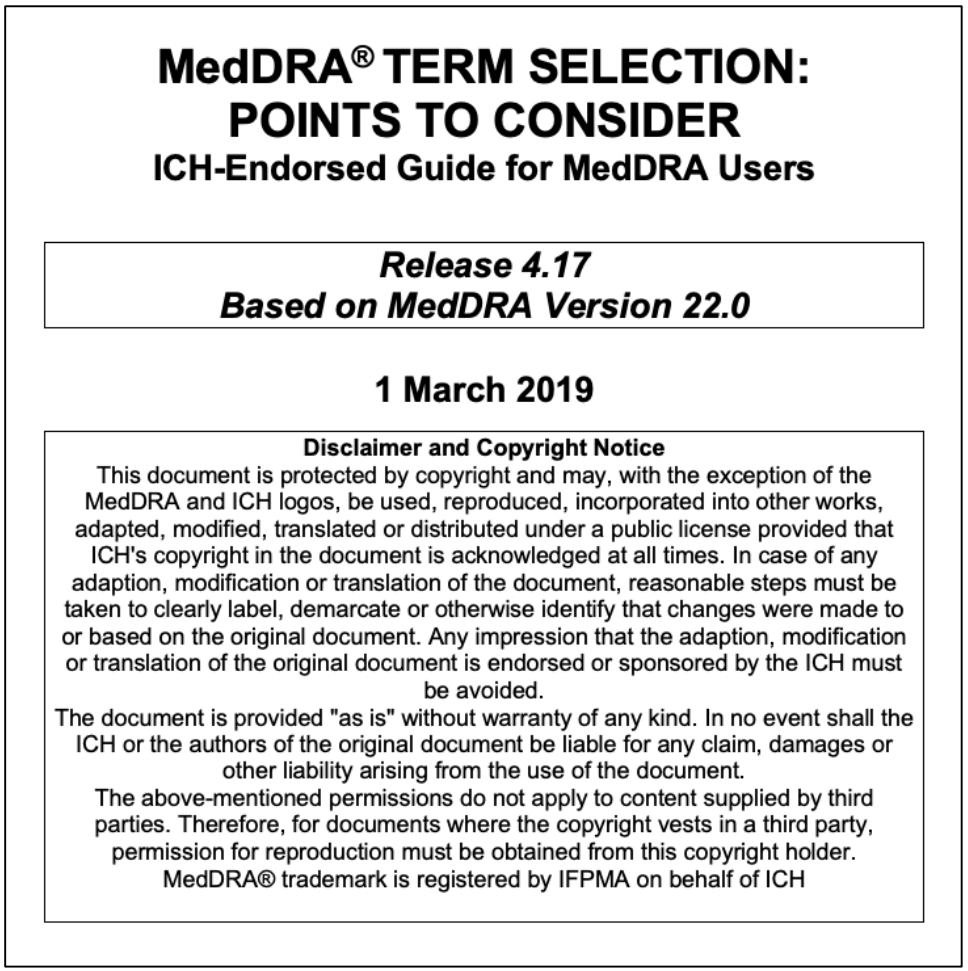
MedDRA Version Analysis Tool (MVAT)

- 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

PtC Documents

PtC Category	PtC Document	Purpose	Languages	Release Cycle
Term Selection	MedDRA Term Selection: Points to Consider	Promote accurate and consistent coding with MedDRA	English and Japanese	Updated with each MedDRA release
	MedDRA Term Selection: Points to Consider Condensed Version	Shorter version focusing on general coding principles to promote accurate and consistent use of MedDRA worldwide	All MedDRA languages (except English and Japanese)	Update as needed
Data Retrieval and Presentation	MedDRA Data Retrieval and Presentation: Points to Consider	Demonstrate how data retrieval options impact the accuracy and consistency of data output	English and Japanese	Updated with each MedDRA release
	MedDRA Data Retrieval and Presentation: Points to Consider Condensed Version	Shorter version focusing on general retrieval and analysis principles to promote accurate and consistent use of MedDRA worldwide	All MedDRA languages (except English and Japanese)	Update as needed
General	MedDRA Points to Consider Companion Document	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.	English and Japanese	Updated as needed

MedDRA Term Selection: Points to Consider (MTS:PTC)



MedDRA® TERM SELECTION: POINTS TO CONSIDER

ICH-Endorsed Guide for MedDRA Users

Release 4.17
Based on MedDRA Version 22.0

1 March 2019

- 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

MTS:PTC Points of Note

- In some cases with more than one option for selecting terms, a “preferred option” is identified but this does not limit MedDRA users to applying that option. Organizations should be consistent in their choice of option.
- Section 4.1 – Versioning (Appendix)
  - 4.1.1 Versioning methodologies
  - 4.1.2 Timing of version implementation

General Term Selection Principles

- Quality of Source Data
- Quality Assurance
- Do Not Alter MedDRA
- Always Select a Lowest Level Term
- Select Only Current Lowest Level Terms
- When to Request a Term
- Use of Medical Judgment in Term Selection
- Selecting More than One Term
- Check the Hierarchy
- Select Terms for All Reported Information, Do Not Add Information

Quality of Source Data Quality Assurance

- Quality of original information impacts quality of output
- Obtain clarification of data
- Can be optimized by careful design of data collection forms and proper training of staff
- Organizations' coding guidelines should be consistent with MTS:PTC
- Review of term selection by qualified individuals
- Human oversight of automated coding results

Do Not Alter MedDRA

- MedDRA is a standardized terminology with a pre-defined term hierarchy
- Users must not make *ad hoc* structural alterations, including changing the primary SOC allocation
- If terms are incorrectly placed, submit a change request to the MSSO

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

When to Request a Term Use of Medical Judgment

- Avoid company-specific “work-arounds” for MedDRA deficiencies. If concept not adequately represented in MedDRA, submit Change Request to MSSO.
- If no exact match in MedDRA, use medical judgment to match to an existing term that adequately represents the concept

Selecting More than One Term Check the Hierarchy

- Can select more than one LLT to represent reported information. Document procedures.
  - Selecting one term may lead to loss of specificity
  - Selecting more than one term may lead to redundant counts
- Check the hierarchy above a selected LLT (PT, HLT, HLGT, SOC) to ensure placement accurately reflects meaning of reported term

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

Do Not Add Information

- Do not make diagnosis if only signs/symptoms reported

Reported	LLT Selected	Comment
Abdominal pain, increased serum amylase, and increased serum lipase	Abdominal pain	It is inappropriate to assign an LLT for diagnosis of "pancreatitis"
	Serum amylase increased	
	Lipase increased	

Important Coding Errors

- Missed Concepts
  - All medical concepts described after the product is taken should be coded
  - Example: "*The patient took drug X and developed alopecia, increased LFTs and pancreatitis*". Manufacturer only codes alopecia and increased LFTs (missed concept of pancreatitis)
  - Example: "*The patient took drug X and developed interstitial nephritis which later deteriorated into renal failure*". Manufacturer only codes interstitial nephritis (missed renal failure concept)

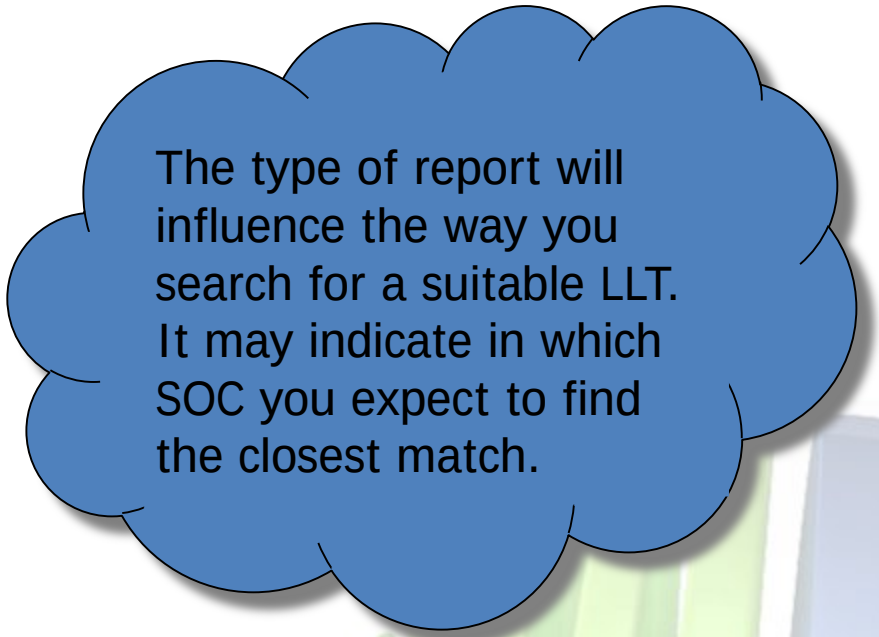
Important Coding Errors (cont)

- "Soft Coding"
  - Selecting a term which is both less specific and less severe than another MedDRA term is "soft coding"
  - Example: "*Liver failure*" coded as hepatotoxicity or increased LFTs
  - Example: "*Aplastic anemia*" coded as unspecified anemia
  - Example: "*Rash subsequently diagnosed as Stevens Johnson syndrome*" coded as rash

Assessing the Reported Information

- Consider what is being reported. Is it a:
  - Clinical condition - Diagnosis, sign or symptom?
  - Indication?
  - Test result?
  - Injury?
  - Procedure?
  - Medication error?
  - Product use issue?
  - Product quality issue?
  - Social circumstance?
  - Device issue?
  - Procedural complication?

  - **Is it a combination of these?**



Coding Example - Narrative

Narrative vignette

A 75-year-old male receiving Drug X for rheumatoid arthritis developed symptomatic aortic valve stenosis. The patient's medical history is significant for colon cancer and cigarette smoking. He underwent an aortic valve replacement and developed a sternal wound infection three days post-surgery.

Coding Example 1

Specificity

The patient suffered from an allergic reaction to an antibiotic

Coding Example 2

Symptoms

The patient states she has been experiencing cold sweats

Coding Example 3

Investigations

Lab results indicate the patient has increased troponin and increased CPK-MB

Coding Example 4

Medication errors

Patient accidentally took drug Y instead of drug X and became short of breath

Coding Example 5

Patient demographics

A 2 day old baby was noted to have a mild fever

Coding Example 6

Indications

A 35 year old woman was taking Drug X to prevent relapses of multiple sclerosis

Coding Example 8

Specificity

Following the procedure, the patient experienced several days of constipation

Coding Example 9

Death and other patient outcomes

The 66 year old man died from a ruptured aortic aneurysm

Coding Example 10

Product quality issues

It was determined that the product was counterfeit

Coding Example 11

Social circumstances

The patient was confined to a wheelchair

Coding Example 12

Medication errors/Product use errors and issues

The pharmacist made a mistake in compounding the medication

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

Diagnoses and Provisional Diagnoses

SINGLE DIAGNOSIS	
DEFINITIVE DIAGNOSIS	**PROVISIONAL DIAGNOSIS**
Single diagnosis without signs and symptoms •Diagnosis (only possible option)	Single provisional diagnosis without signs and symptoms •Provisional diagnosis (only possible option)
Example: *"Myocardial infarction"* → select *"Myocardial infarction"*	Example: *"Possible myocardial infarction"* → select *"Myocardial infarction"* (select term as if definitive diagnosis)

Similar principles apply for multiple diagnoses

Diagnoses and Provisional Diagnoses (cont)

SINGLE DIAGNOSIS	
DEFINITIVE DIAGNOSIS	**PROVISIONAL DIAGNOSIS**
Single diagnosis with signs/ symptoms •Preferred: Diagnosis only	Single provisional diagnosis with signs/symptoms •Preferred: Provisional diagnosis and signs/symptoms
Example: *"Anaphylactic reaction with rash, dyspnoea, hypotension, and laryngospasm"* → select "*Anaphylactic reaction*"	Example: "*Possible myocardial infarction with chest pain, dyspnoea, diaphoresis*" → select *"Myocardial infarction*" "*Chest pain"*, "*Dyspnoea*", and "*Diaphoresis*"

Similar principles apply for multiple diagnoses

Diagnoses and Provisional Diagnoses (cont)

SINGLE DIAGNOSIS	
DEFINITIVE DIAGNOSIS	**PROVISIONAL DIAGNOSIS**
Single diagnosis with signs/ symptoms •Alternate: Diagnosis and signs/symptoms	Single provisional diagnosis with signs/symptoms •Alternate: Signs/symptoms only (as provisional diagnosis may change
Example: *"Anaphylactic reaction with rash, dyspnoea, hypotension, and laryngospasm"* → select "*Anaphylactic reaction*", "*Rash*", "*Dyspnoea*", *Hypotension*", and "*Laryngospasm*"	Example: "*Possible myocardial infarction with chest pain, dyspnoea, diaphoresis*" → select "*Chest pain"*, "*Dyspnoea*", and "*Diaphoresis*"

Similar principles apply for multiple diagnoses

Diagnoses and Provisional Diagnoses (cont)

- Always include signs/symptoms not associated with diagnosis

Reported	LLT Selected
Myocardial infarction, chest pain, dyspnoea, diaphoresis, ECG changes and jaundice	Myocardial infarction Jaundice (note that jaundice is not typically associated with myocardial infarction)

Conflicting/Ambiguous Information

- First, try to obtain more specific information

Reported	LLT Selected	Comment
Hyperkalaemia with a serum potassium of 1.6 mEq/L	Serum potassium abnormal	LLT *Serum potassium abnormal* covers both of the reported concepts (note: serum potassium of 1.6 mEq/L is a low result, not high)
GU pain	Pain	"GU" could be either "genito-urinary" or "gastric ulcer". If additional information is not available, then select a term to reflect the information that is known, i.e., LLT *Pain*

Vague Information

- First, try to obtain more specific information

Reported	LLT Selected	Comment
Turned green	Unevaluable event	"Turned green" reported alone is vague; this could refer to a patient condition or even to a product (e.g., pills)
Patient had a medical problem of unclear type	Ill-defined disorder	Since it is known that there is some form of a medical disorder, LLT *Ill-defined disorder* can be selected

Combination Terms

- One condition is more specific than the other

Reported	LLT Selected
Arrhythmia due to atrial fibrillation	Atrial fibrillation
Hepatic function disorder (acute hepatitis)	Hepatitis acute

- A MedDRA combination term is available

Reported	LLT Selected
Retinopathy due to diabetes	Diabetic retinopathy
Rash with itching	Itchy rash

Combination Terms (cont)

- If splitting provides more clinical information, select more than one term
- In all cases of combination terms, apply medical judgment

Reported	LLT Selected
Diarrhoea and vomiting	Diarrhoea Vomiting
Wrist fracture due to fall	Wrist fracture Fall

Investigations

- Medical condition vs. investigation result

Reported	LLT Selected	Comment
Hypoglycaemia	Hypoglycaemia	LLT *Hypoglycaemia* links to SOC *Metabolism and nutrition disorders*
Decreased glucose	Glucose decreased	LLT *Glucose decreased* links to SOC *Investigations*

Investigations (cont)

- Unambiguous investigation result

Reported	LLT Selected	Comment
Glucose 40 mg/dL	Glucose low	Glucose is clearly below the reference range

- Ambiguous investigation result

Reported	LLT Selected	Comment
His glucose was 40	Glucose abnormal	No units have been reported. Select LLT *Glucose abnormal* if clarification cannot be obtained.

Investigations (cont)

- Investigation results consistent with diagnosis

Reported	LLT Selected	Comment
Elevated potassium, K 7.0 mmol/L, and hyperkalaemia	Hyperkalaemia	It is not necessary to select LLT *Potassium increased*

- Grouped investigation result terms

Reported	LLT Selected	Comment
Increased alkaline phosphatase, increased SGPT, increased SGOT and elevated LDH	Alkaline phosphatase increased SGPT increased SGOT increased LDH increased	Select four individual terms. A single term such as LLT *Liver function tests abnormal* should not be selected.

MedDRA Coding Exercise

Instructions

- Open the MedDRA Web-Based Browser (WBB)
  - https://tools.meddra.org/wbb/
- Open an excel workbook
- Look up the MedDRA dictionary and select the most suitable LLT match for each of the reported verbatims
- Note the LLT, PT and SOC of your selection in your excel workbook against each verbatim
- Observe the MedDRA dictionary hierarchy

Which LLT Would You Select for the following terms?

1. Mild skin itching
2. Prolapse L5 surgery
3. Feeling of numbness in throat
4. Mass in ear
5. COPD with shortness of breath
6. Warm feeling in face after infusion
7. Fractured femur from tripping over
8. Increased fatigue
9. Perinephric abscess due to Proteus
10. Recurring C.difficile infection with diarrhoea
11. Using 2 mg tablets thinking they were 0.5 mg
12. Pulled out her IUD so she could get pregnant

Which LLT Would You Select for the following terms?

	Verbatim	LLT	PT	SOC
1	Mild skin itching	Itchy skin	Pruritus	Skin and subcutaneous tissue disorders
2	Prolapse L5 surgery	Prolapsed disc repair	Intervertebral disc operation	Surgical and medical procedures
3	Feeling of numbness in throat	Numbness throat	Pharyngeal hypoaesthesia	Respiratory, thoracic and mediastinal disorders
4	Mass in ear	Mass	Mass	General disorders and administration site conditions
5	COPD with shortness of breath	COPD	Chronic obstructive pulmonary disease	Respiratory, thoracic and mediastinal disorders
6	Warm feeling in face after infusion	Feeling of warmth facial	Feeling hot	General disorders and administration site conditions
7	Fractured femur from tripping over	Fracture femur	Femur fracture	Injury, poisoning and procedural complications
		Fall	Fall	Injury, poisoning and procedural complications
8	Increased fatigue	Fatigue aggravated	Fatigue	General disorders and administration site conditions
9	Perinephric abscess due to Proteus	Perinephric abscess	Perinephric abscess	Infections and infestations
		Proteus infection	Proteus infection	Infections and infestations
10	Recurring C. difficile infection with diarrhoea	C.difficile diarrhoea	Clostridium difficile colitis	Infections and infestations
11	Using 2 mg tablets thinking they were 0.5 mg	Incorrect dose administered	Incorrect dose administered	Injury, poisoning and procedural complications
12	Pulled out her IUD so she could get pregnant	Intentional medical device removal by patient	Intentional medical device removal by patient	Injury, poisoning and procedural complications

Which LLT Would You Select?

Verbatim: “Man with decreased fertility.”

A. Infertility
B. Fertility decreased male
C. Infertility male
D. Fertility decreased

Which LLT Would You Select?

Verbatim: “Became color blind in adolescence”

A. Color blindness
B. Blindness color
C. Colour blindness acquired
D. Color blindness acquired

Which LLT Would You Select?

Verbatim: “Turned very greasy”

A. Ill-defined disorder
B. Unevaluable event
C. Skin greasy
D. Unevaluable reaction

Which LLT Would You Select?

Verbatim: "Deliberately took an overdose"

A. Intentional overdose
B. Overdose NOS
C. Deliberate overdose
D. Overdose

Which LLT Would You Select?

Verbatim: “Patient reported medical problem”

A. Adverse event
B. Unevaluable event
C. Unevaluable reaction
D. Ill-defined disorder

Which LLT Would You Select?

Verbatim: "Toddler accidentally took his mother's medication"

A. Accidental overdose
B. Accidental exposure to product by child
C. Accidental drug intake by child
D. Accidental ingestion

Which LLT Would You Select?

Verbatim: "Infection after surgery"

A. Infection
B. Postoperative wound infection
C. Surgical wound infection
D. Postoperative infection

Which LLT Would You Select?

Verbatim: "He sold his father's medication"

A. Drug diversion
B. Intentional product misuse
C. Drug use for unapproved indication
D. Intentional drug misuse

Which LLT Would You Select?

Verbatim: "Had MI"

A. Myocardial infarction
B. Ill-defined disorder
C. MI
D. Unevaluable event

Which LLT Would You Select?

Verbatim:

“Hypernatraemia (Serum sodium = 115 mEq/L)”

A. Serum sodium abnormal
B. Hypernatraemia
C. Hyponatraemia
D. Serum sodium decreased

Which LLT Would You Select?

Verbatim: "Took intramuscular drug by mouth"

A. Wrong route of administration
B. Drug administered via inappropriate route
C. Medication error
D. Intramuscular formulation administered by other route

Which LLT Would You Select?

Verbatim: “Death from cerebral haemorrhage”

A. Sudden death
B. Death
C. Cerebral haemorrhage
D. Brain death

Which LLT Would You Select?

Verbatim: "Patient was found dead"

A. Death from natural causes
B. Death
C. Died in sleep
D. Found dead

Which LLT Would You Select?

Verbatim: “The doctor mistakenly prescribed the wrong drug; the pharmacist noticed the error before dispensing the drug”

A. Wrong drug dispensed
B. Medication error
C. Intercepted drug prescribing error
D. Intercepted drug dispensing error

Which LLT Would You Select?

Verbatim: “Died as a result of a suicide attempt”

A. Suicide gesture
B. Attempted suicide
C. Completed suicide
D. Death

Which LLT Would You Select?

Verbatim: "Dose taken was below the minimum recommended dose in the product label"

A. Underdose
B. Drug administration error
C. Accidental underdose
D. Incorrect dosage administered

Which LLT Would You Select?

Verbatim: "Abused by her husband"

A. Physical abuse
B. Battered wife
C. Spousal abuse
D. Victim of spousal abuse

Which LLT Would You Select?

Verbatim: “After taking an antihistamine along with her prescribed proton pump inhibitor, a 53-year-old woman developed vertigo.”

A. Drug interaction NOS
B. Vertigo subjective
C. Vertigo
D. Drug interaction

Which LLT Would You Select?

Verbatim: "The medication was stored at room temperature instead of in the refrigerator where it belonged."

A. Incorrect storage of drug
B. Improper storage of unused product
C. Intercepted medication error
D. Product storage error temperature too high

Which LLTs Would You Select?

Verbatim: “Because the label on the package was missing the wording on dosing information, the patient took the drug twice daily instead of once daily, resulting in the administration of an overdose.”

A. Product label issue
B. Product label missing
C. Product label missing text

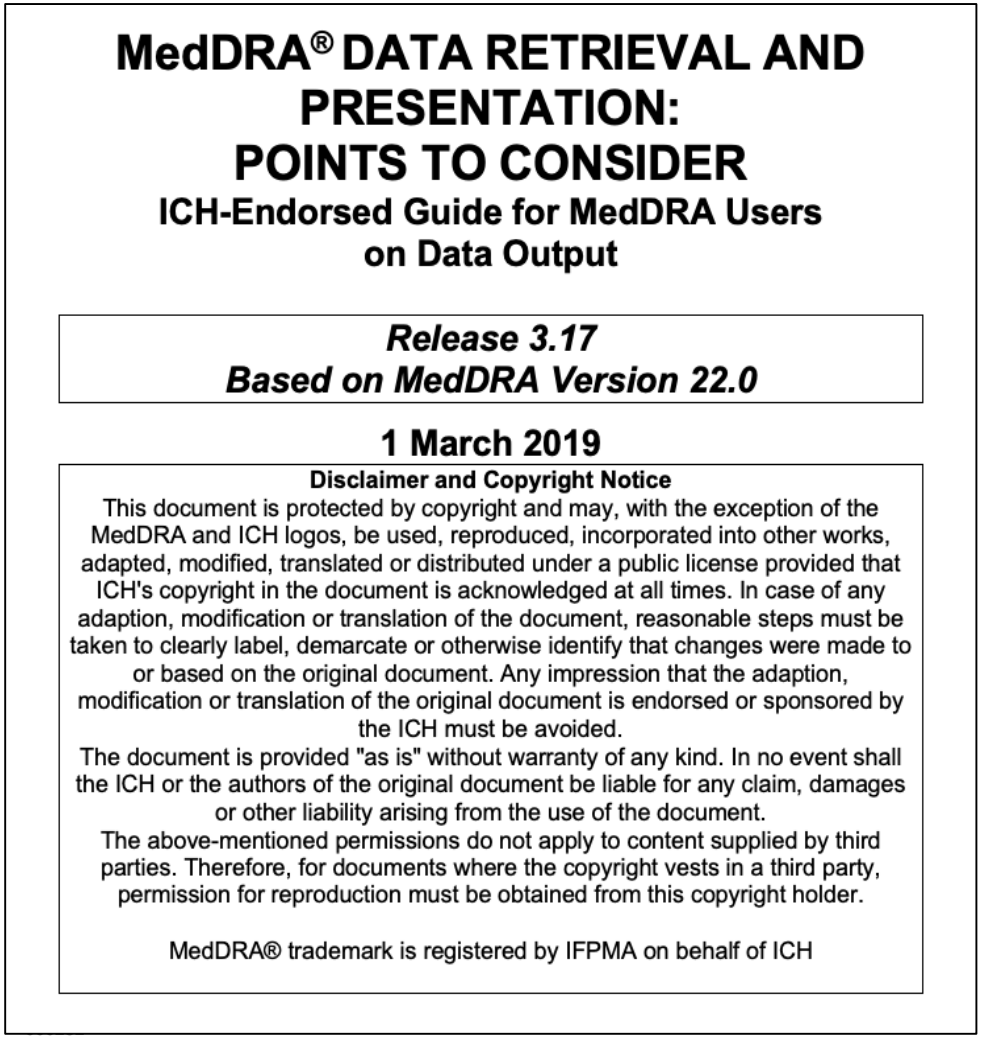
D. Wrong dose administered
E. Once daily dose taken more frequently
F. Inappropriate schedule of drug administration

G. Overdose
H. Accidental overdose

PtC Documents

PtC Category	PtC Document	Purpose	Languages	Release Cycle
Term Selection	MedDRA Term Selection: Points to Consider	Promote accurate and consistent coding with MedDRA	English and Japanese	Updated with each MedDRA release
	MedDRA Term Selection: Points to Consider Condensed Version	Shorter version focusing on general coding principles to promote accurate and consistent use of MedDRA worldwide	All MedDRA languages (except English and Japanese)	Update as needed
Data Retrieval and Presentation	MedDRA Data Retrieval and Presentation: Points to Consider	Demonstrate how data retrieval options impact the accuracy and consistency of data output	English and Japanese	Updated with each MedDRA release
	MedDRA Data Retrieval and Presentation: Points to Consider Condensed Version	Shorter version focusing on general retrieval and analysis principles to promote accurate and consistent use of MedDRA worldwide	All MedDRA languages (except English and Japanese)	Update as needed
General	MedDRA Points to Consider Companion Document	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.	English and Japanese	Updated as needed

MedDRA Data Retrieval and Presentation: Points to Consider (DRP:PTC)



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

1 March 2019

- 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

Data Retrieval PTC Points Addressed

- General Principles
  - Quality of Source Data
  - Documentation of Data Retrieval and Presentation Practices
  - Do Not Alter MedDRA
  - Organisation-Specific Data Characteristics
  - Characteristics of MedDRA that Impact Data Retrieval and Analysis
  - MedDRA Versioning
- General Queries and Retrieval
- Standardised MedDRA Queries
- Customised Searches

Legacy Data Conversion

- Method 1 - Data converted from legacy terminology terms to MedDRA

Reported	Legacy Term	MedDRA Term
Gastrointestinal ischaemia	Gastrointestinal disorder	Gastrointestinal disorder

-Results reflect specificity of legacy terminology
-Benefits of greater specificity of MedDRA not attained

Legacy Data Conversion (cont)

- Method 2 - Data converted from original reported terms (verbatim terms) to MedDRA

Reported	Legacy Term	MedDRA Term
Gastrointestinal ischaemia	Gastrointestinal disorder	Gastrointestinal ischaemia

-Specificity of reported term reflected by MedDRA term

MedDRA Versioning

- MedDRA is updated twice a year
  - 1 March X.0 release (all levels)
  - 1 September X.1 release (LLT and PT levels only)
- Version used in data retrieval and presentation should be documented
- Resources:
  - "What's New" document
  - Version report
  - MedDRA Version Analysis Tool (MVAT)
- Terms used for queries should be in same version as data being queried

MedDRA Versioning (cont): Effect of PT Demotion

MedDRA Version 18.1	Number of Events at PT Level
Metastatic pain (PT)	15
Cancer pain	5
MedDRA Version 19.0	**Number of Events at PT Level**
Metastatic pain (no longer a PT)	0
Cancer pain	20

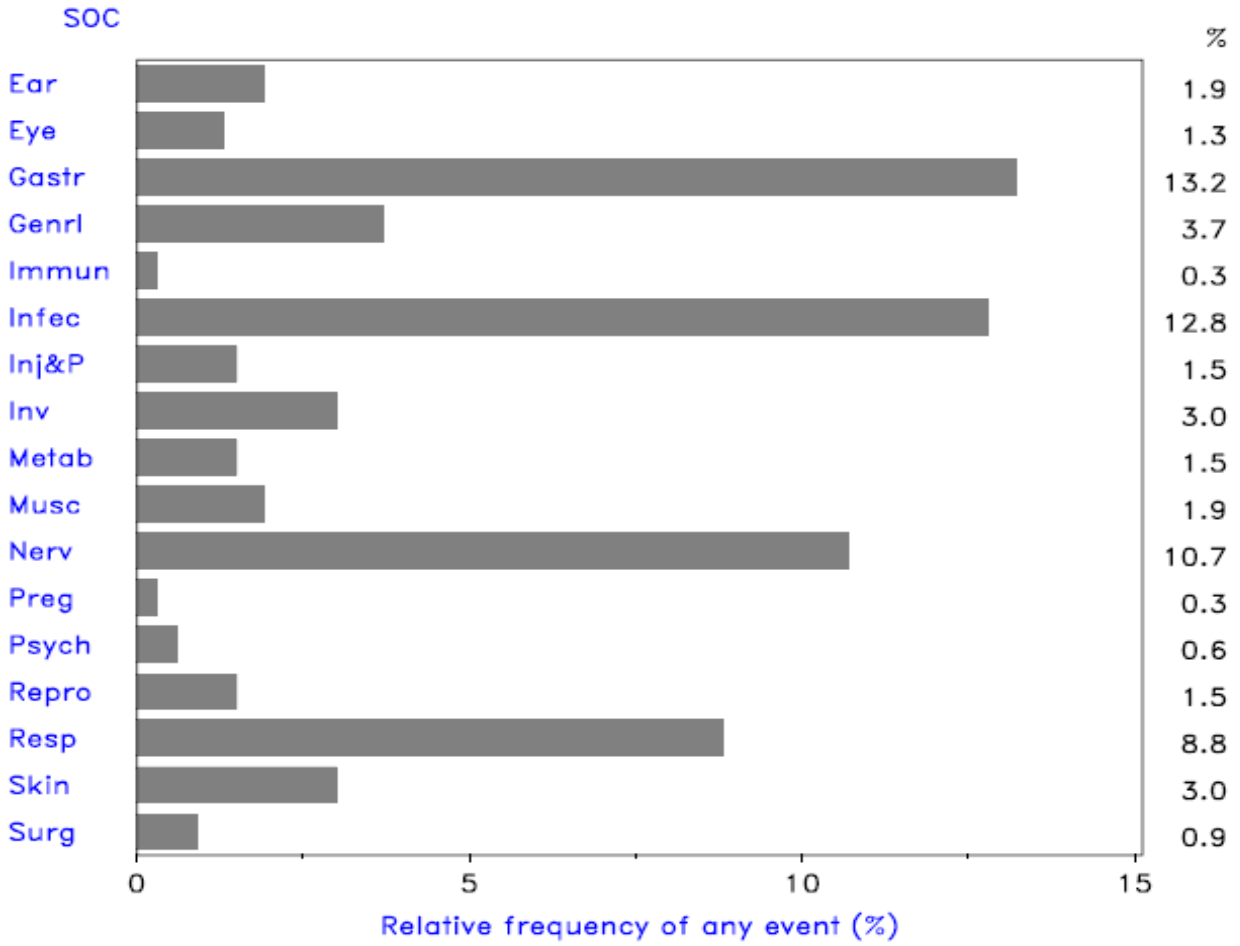
MedDRA Versioning (cont): Effect of Primary SOC Change

MedDRA Version 18.0	Number of Events
SOC *Vascular disorders* PT *Intra-abdominal haematoma*	20
MedDRA Version 18.1	**Number of Events**
SOC *Vascular disorders*	0
SOC *Gastrointestinal disorders* PT *Intra-abdominal haematoma*	20

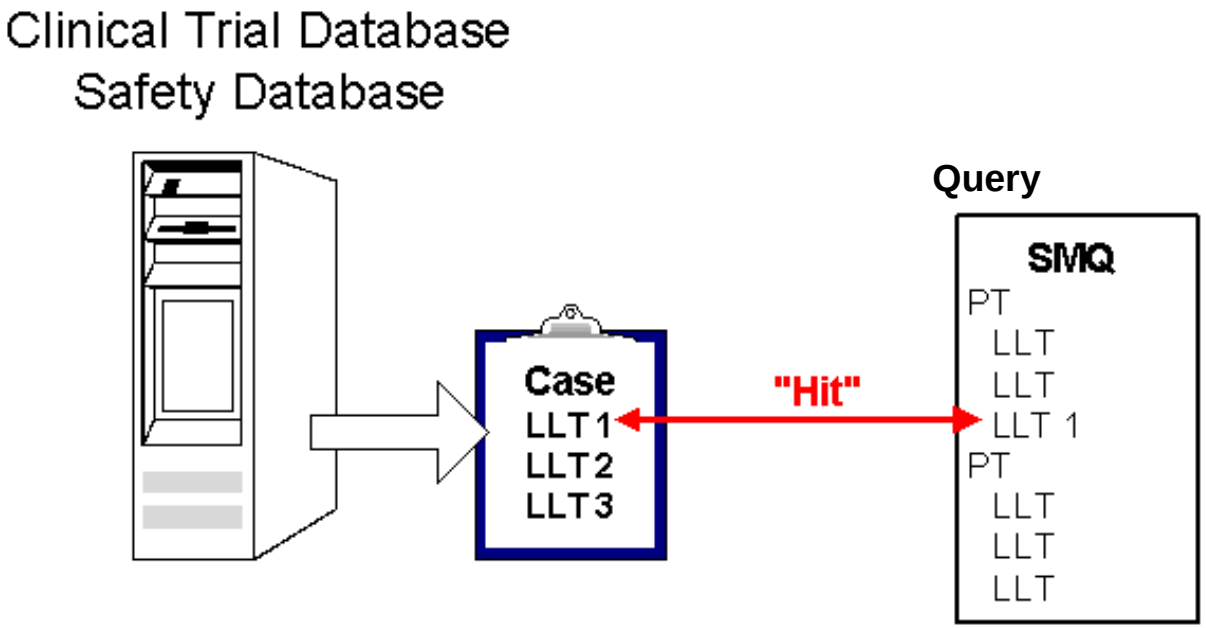
Overview by Primary SOC

- Use Internationally Agreed Order of SOCs when applicable, e.g., the EU SPC guideline
  - See MedDRA Introductory Guide, ASCII files
- Consider use of HLTs and HLGTs
- Line listings, tables, graphs
- Benefits - Broad overview, PTs displayed only once
- Limitations - Incomplete groupings due to SOC allocation rules, lengthy output

Primary SOC Graphical Display Example



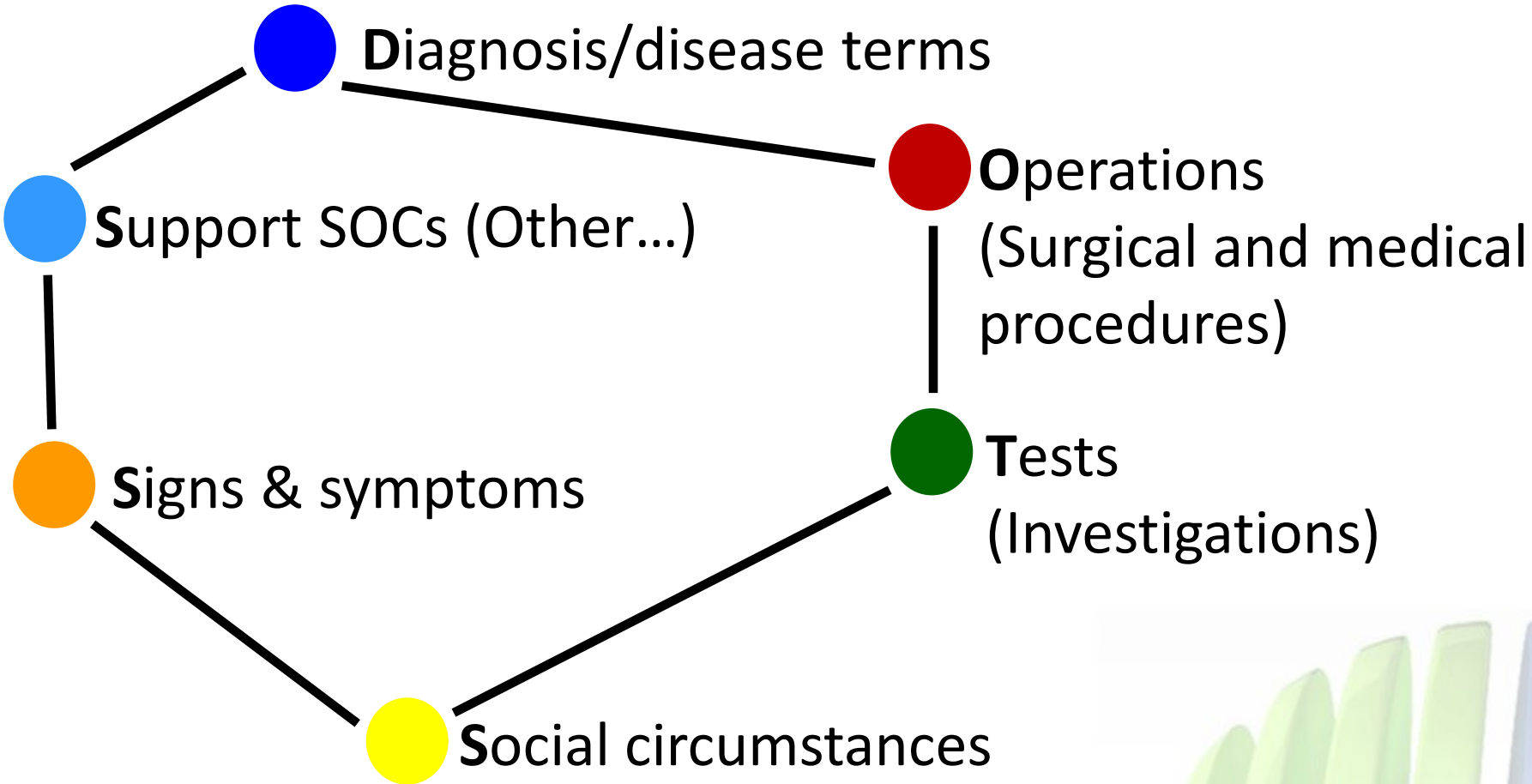
What is a Query?



Query Strategy Tips

- Define the condition
- Develop inclusion/exclusion criteria
- Good browser is key component
- Search “non multi-axial” and “other/support” SOCs
- Search a term’s “neighbors”, including secondary locations
- Use grouping terms where applicable
- Avoid using LLTs (Exception: species information at LLT level in SOC *Infections and infestations*)
- Store for future use
- Review for impact of new MedDRA versions

Complete the Circle (Connect the DOTSSS!)



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

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)

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 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

MedDRA Term Inclusion

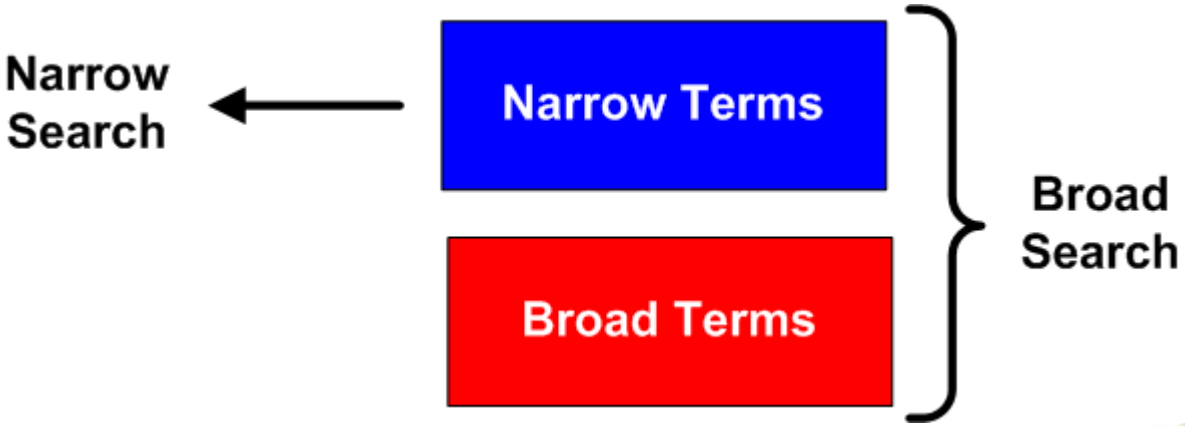
- SMQs are constructed at MedDRA PT level
- LLTs that are subordinate to an included PT are also included

SMQ Versioning

- It is recommended that organizations use the SMQs with data coded with the same version of MedDRA
  - Match the MedDRA version of the SMQ with the MedDRA version of the coded data
  - Mismatches of SMQ and MedDRA coded data could produce unexpected results

Narrow and Broad Searches

- "Narrow" scope – specificity (cases highly likely to be condition of interest)
- "Broad" scope – sensitivity (all possible cases)
- "Broad search" = All broad **+** all narrow terms



Narrow *vs.* Broad Example

SMQ *Lactic acidosis*

Definition

Lactic acidosis is a form of high anion gap metabolic acidosis - Intrinsic cardiac contractility may be depressed, but inotropic function can be normal because of catecholamine release- Peripheral arterial vasodilatation and central vasoconstriction can be present - Central nervous system function is depressed, with headache, lethargy, stupor, and, in some cases, even coma - Glucose intolerance may occur - Characterized by an increase in plasma L-lactate - Acidosis is seldom significant unless blood lactate exceeds 5 mmol/l - Clinical presentation in type B lactic acidosis: o Symptoms: hyperventilation or dyspnea, stupor or coma, vomiting, drowsiness, and abdominal pain o Onset of symptoms and signs is usually rapid accompanied by deterioration in the level of consciousness.

Source

1. Braunwald E, Fauci A, Kasper D. Harrison's Principles of Internal Medicine. 15th Edition, 2001 pp 285-9 2. Weatherall D, Ledingham J and Warrell D. Oxford Textbood of Medicine. Third edition, 1996; volume 2 pp 1541-44

Note

Testing in two regulatory databases confirmed that the term list is adequate; in one regulatory database, the term "acidosis" identified cases, but this may be a phenomenon of the database characteristics (coding of verbatims to terms of an older terminology or other coding conventions).

Narrow Terms
Blood lactic acid increased
Hyperlactacidaemia
Lactic acidosis

Broad Terms
Acid base balance abnormal
Acidosis
Anion gap abnormal
Anion gap increased
Blood alkalinisation therapy
Blood bicarbonate abnormal
Blood bicarbonate decreased
Blood gases abnormal
Blood lactic acid abnormal
Blood pH abnormal
Blood pH decreased
Coma acidotic
Kussmaul respiration
Metabolic acidosis
PCO2 abnormal
PCO2 decreased
Urine lactic acid increased

Algorithmic SMQs

- Some SMQs are designed to utilize algorithms
- Better case identification among broad search terms may result if cases are selected by a defined combination of selected terms

Algorithmic SMQ Example

- *Anaphylactic reaction (SMQ):*
  - A case with any of the following PTs:
    - *Anaphylactic reaction*
    - *Anaphylactic shock*
    - *Anaphylactic transfusion reaction*
    - *Anaphylactoid reaction*
    - *Anaphylactoid shock*
    - *Circulatory collapse*
    - *Dialysis membrane reaction*
    - *Kounis syndrome*
    - *Procedural shock*
    - *Shock*
    - *Shock symptom*
    - *Type I hypersensitivity*

(Narrow search terms = Category A)

Algorithmic SMQ Example (cont)

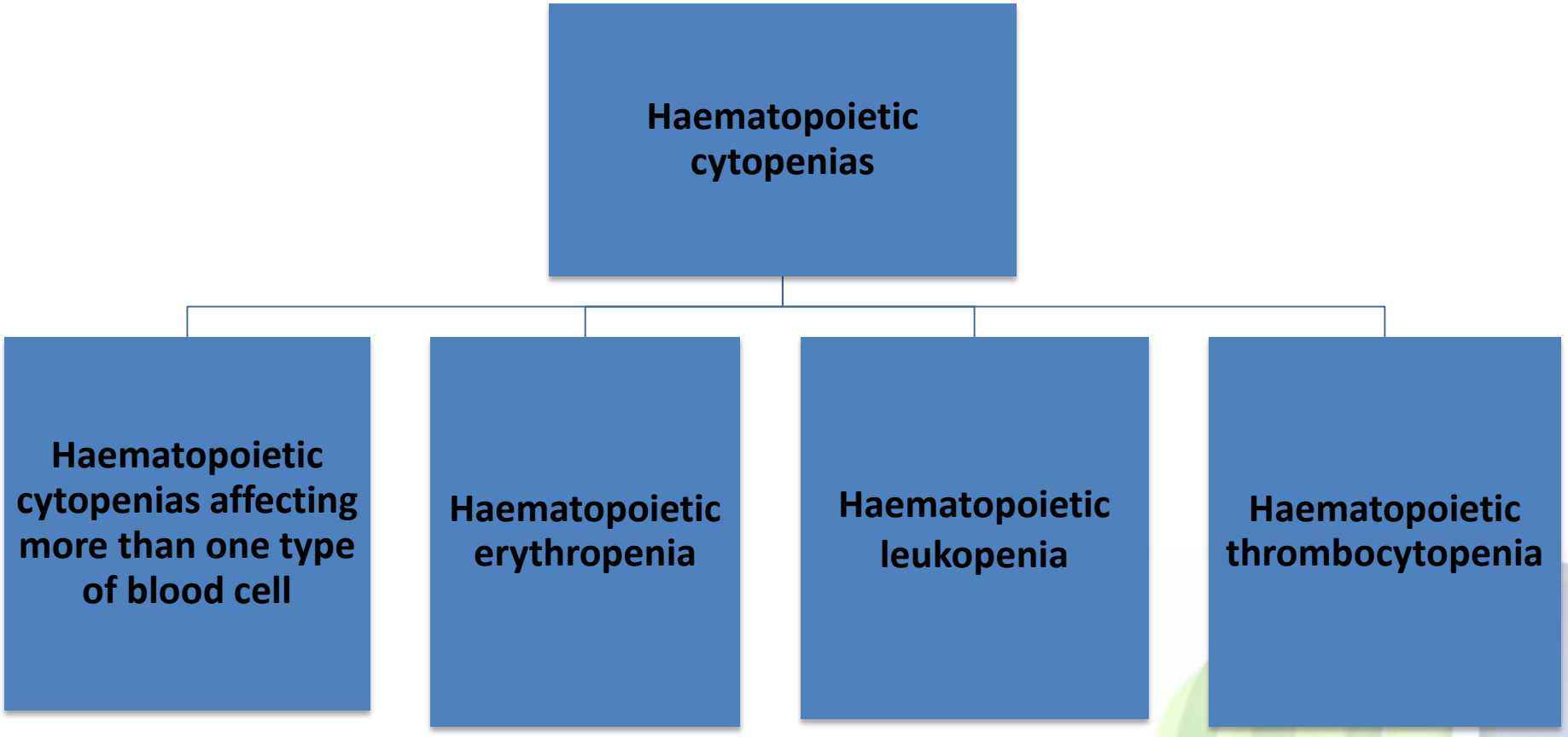
Category B – Upper airway / Respiratory	Category C – Angioedema / Urticaria, etc.	Category D – Cardiovascular / Hypotension
Acute respiratory failure	Allergic oedema	Blood pressure decreased
Asthma	Angioedema	Blood pressure diastolic decreased
Bronchial oedema	Erythema	Blood pressure systolic decreased

- Case = A (Narrow terms)
- Or Term from Category B **and** term from Category C
- Or Term from **either** Category B or Category C **plus** Term from Category D

Hierarchical SMQs

- Some SMQs may develop as set of queries related to one another in a hierarchical relationship
- Not related to MedDRA standard hierarchy
- One or more subordinate SMQs combined to create a superordinate, more inclusive SMQ

Hierarchical SMQ Example



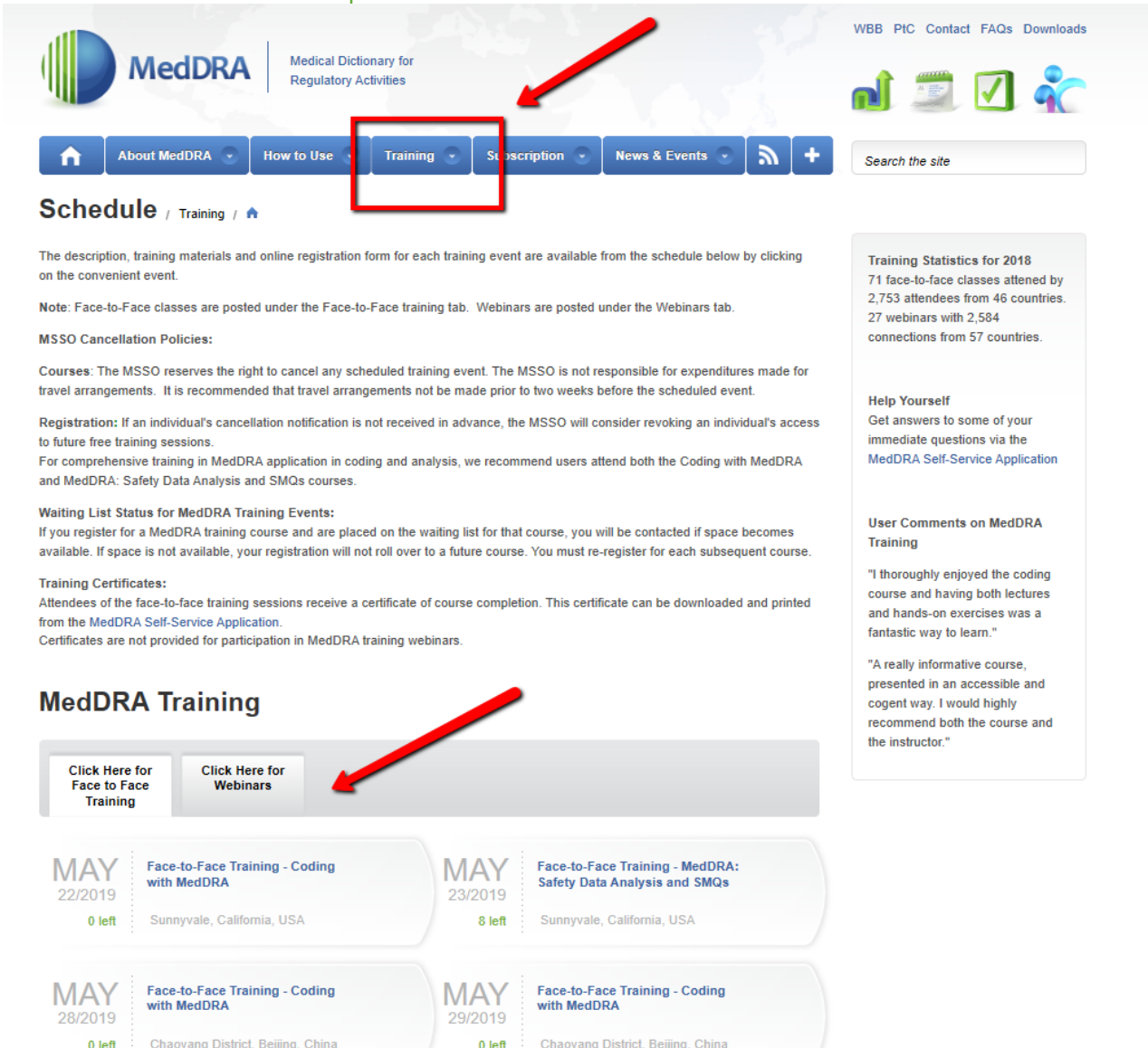
IT Considerations

- Software tools support the use of MedDRA
  - Several are free with MedDRA subscription
    - Two browsers (Desktop and Web-Based)
    - MedDRA Version Analysis Tool (MVAT)
  - Software tools need driven by the volume of data
    - With small amounts, users can use simple software tools (e.g., free MSSO browsers, spreadsheets)
    - Larger implementations may need commercial data management products
    - List of third-party software tools on MedDRA website

MedDRA Training Opportunities – Available for Users

- Free Face-to-Face (F2F) training
  - Coding with MedDRA
  - Safety Data Analysis and Standardised MedDRA Queries
  - Getting Started with MedDRA
- Free webinars
  - Getting Started with MedDRA
  - MedDRA Overview
  - MedDRA Coding Basics
  - Advanced MedDRA Coding
  - Data Analysis and Query Building with MedDRA
  - Standardised MedDRA Queries
  - What's New with MedDRA (with each MedDRA release)

Registration for Training



Training Scheduled in Moscow

September 24th 2019 – Coding with MedDRA

September 25th 2019 – MedDRA Data Analysis and SMQs

Marco Polo Presnja Hotel
Spiridonyevsky Pereulok 9
Presnensky
123104 Moscow
Russia

Марко Поло Пресня Отель
Спиридоньевский переулок 9
Пресненский, Москва, Россия

MedDRA Training Opportunities – Available to All

- Free resources on MedDRA website
  - Slides for all F2F courses and webinars
  - Short videocasts on MedDRA-related topics
    - Available in several languages
    - Can be downloaded or viewed directly on website
    - Help trainees prepare for F2F courses
- Webinars and videocasts available on new MedDRA MSSO YouTube Channel

More Resources for MedDRA Users

- MedDRA website
  - Help Desk
  - Subscriptions
  - News and Events
  - MedDRA Best Practices document
  - Points to Consider documents
  - Terminology downloads
  - Training
  - Tools
  - MedDRA publications
  - User group meetings
  - Expert meetings

MSSO Contacts

- Website
  - www.meddra.org
- Email
  - mssohelp@meddra.org
- Frequently Asked Questions
  - www.meddra.org/faq