Terminologies for coding of adverse reactions and drug information

Uppsala PV training course

Wednesday May 22nd 2013

Cecilia Biriell, Malin Jakobsson

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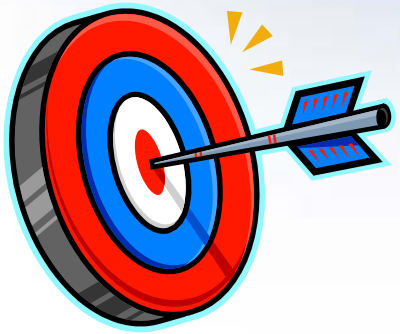
Aims & Goals

- To get enough knowledge about terminologies so that you can use them when coding in VigiFlow (or any other system) and searching in VigiLyze.
- What to do when you can't find a term you are looking for.



Outline

- Understand the need for terminologies
- What main terminologies are used in UMC tools
- WHO Drug Dictionaries
- Medical terminologies (WHO-ART, MedDRA)

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Definition of Pharmacovigilance

The science and activities relating to the...

- detection
- assessment
- understanding
- prevention

...of adverse effects or any other drug-related problem

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Why do we need terminologies?

- To be able to retrieve data in a consistent way from a database
- To be able to store data in a consistent way in a database

Freedom versus structure

Free text	Coded data
 Complete representation of complex data Flexible, expressive, familiar	 Computerised retrieval and analysis easy and efficient Language independence
 Computerised retrieval and analysis difficult Language dependent	 Data entry requires transformation of the information → risk of loss/distortion

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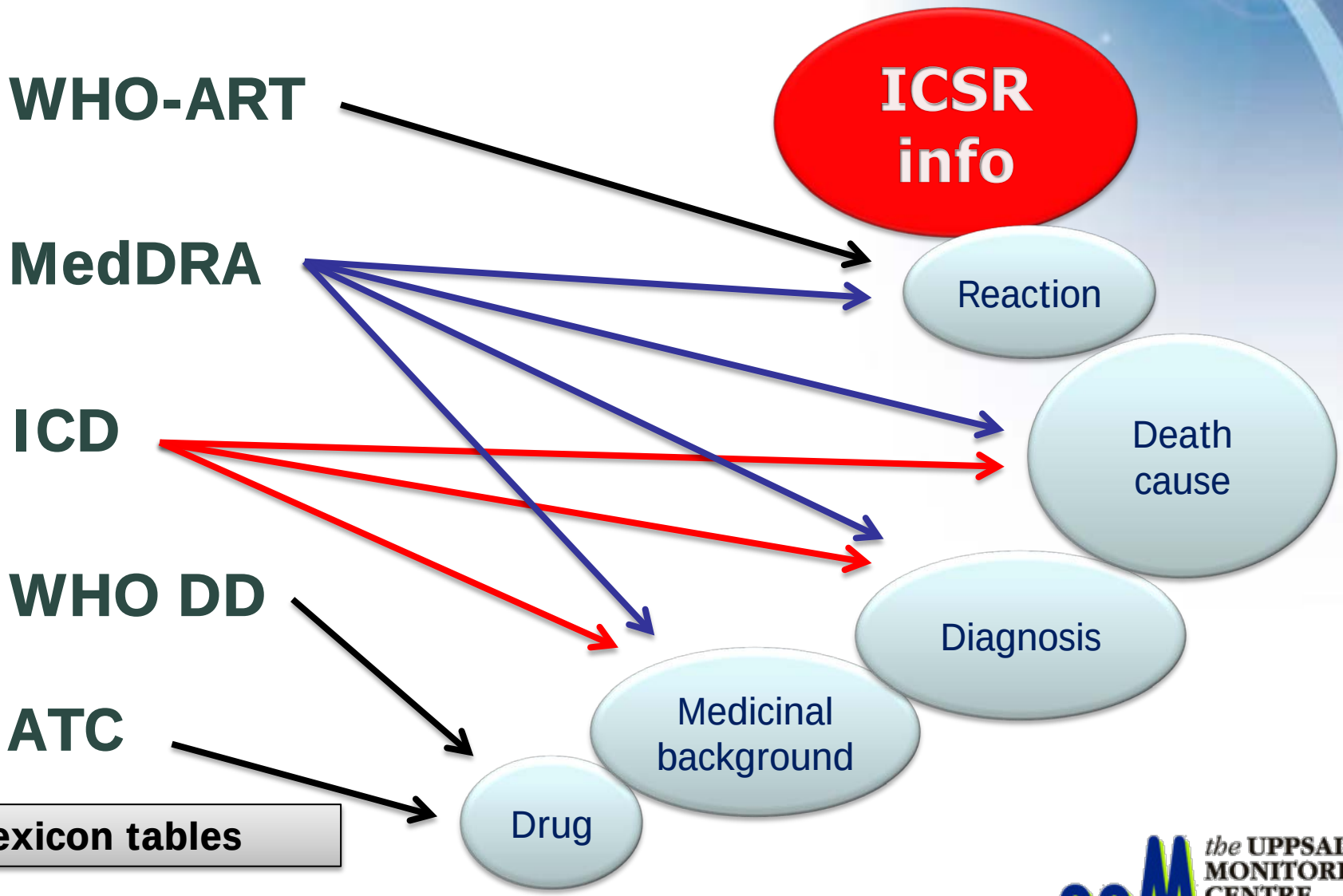
Terminologies in the WHO ICSR database



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WHO Drug Dictionaries

Malin Jakobsson, MSc Pharm

Product Manager

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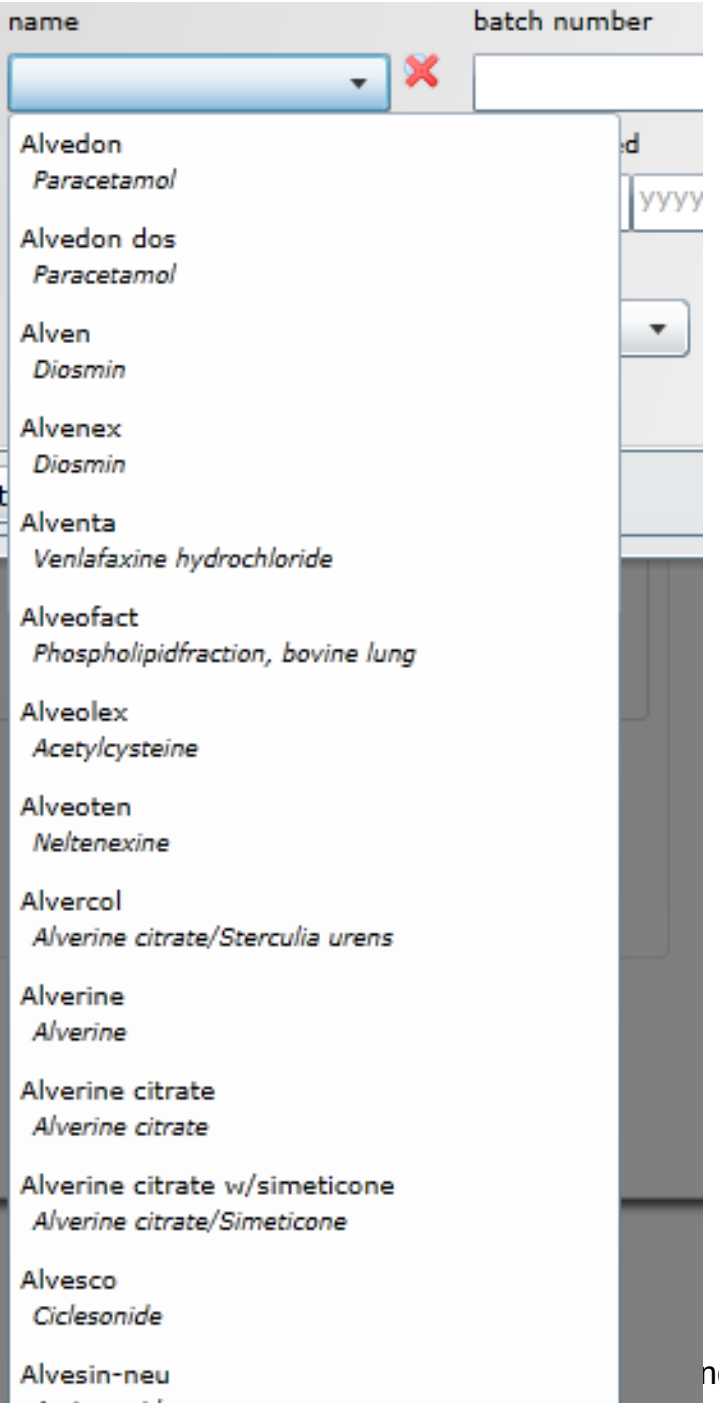
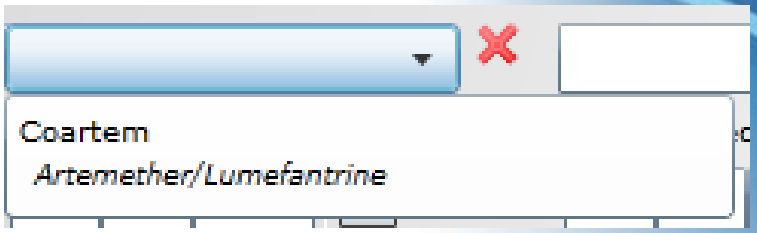
Outline

- What is coding?
- WHO Drug Dictionaries
- Drug analysis
- WHO Drug Dictionary users



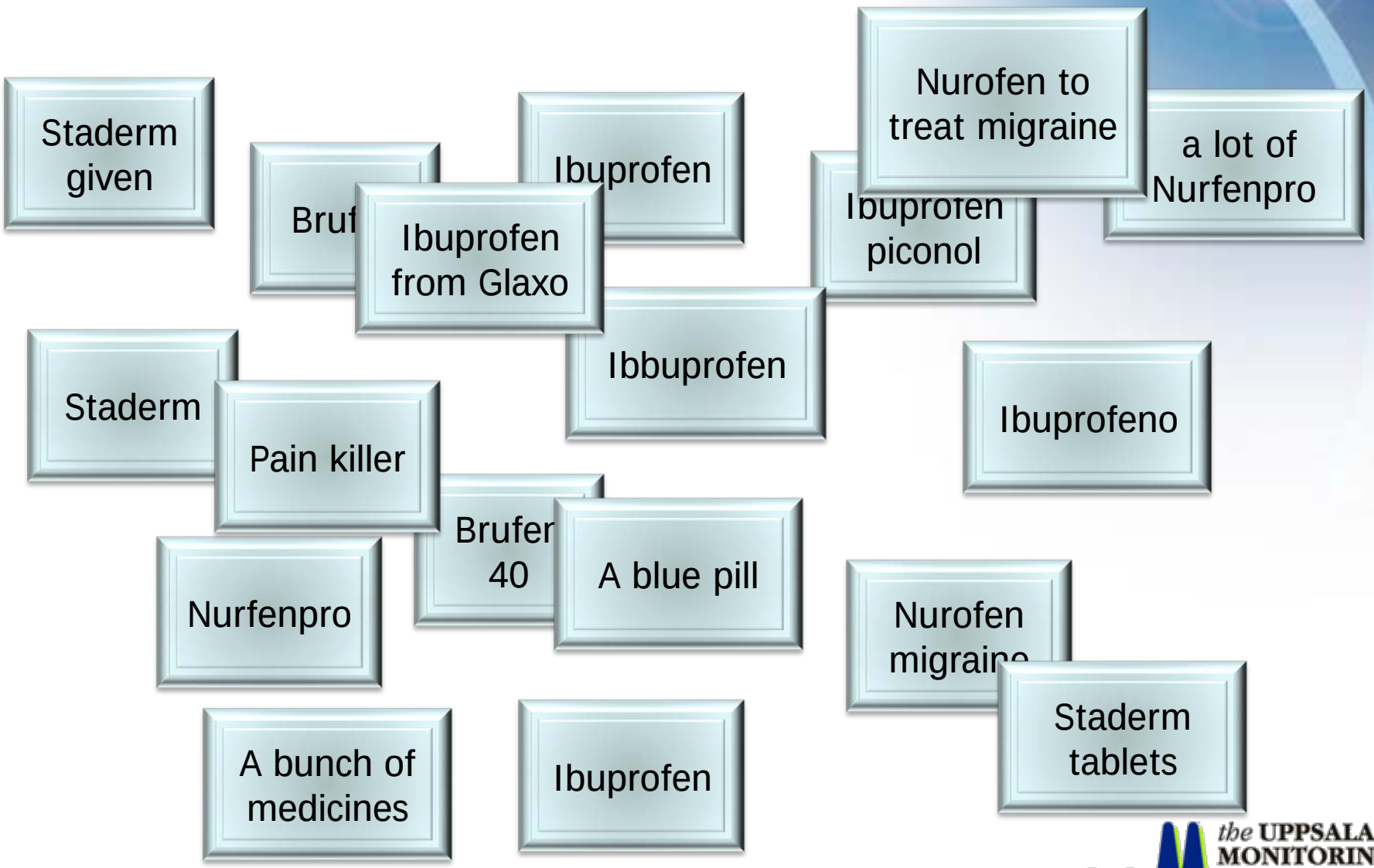


Results from search

	drug name	substance		
− add	**Arinate**	***Artesunate***		
− add	**Arinate**	Efra S.A	Tanzania, United Republic of	
add	**Arinate** - TABLETS, Unspecified			
− add	**Arinate**	Not specified	Tanzania, United Republic of	
no form or strength information available				
+ add	**Arsucam**	***Artesunate***		
+ add	**Arsumax**	***Artesunate***		
+ add	**Artemax**	***Artesunate***		
+ add	**Artenex**	***Artesunate***		
+ add	**Artesunate**	***Artesunate***		
+ add	**Askasunate**	***Artesunate***		
+ add	**Falcigo**	***Artesunate***		
+ add	**Gsunate**	***Artesunate***		
+ add	**Plasmotrim**	***Artesunate***		

1 to 10 of 10

What is coding?



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What is drug coding?

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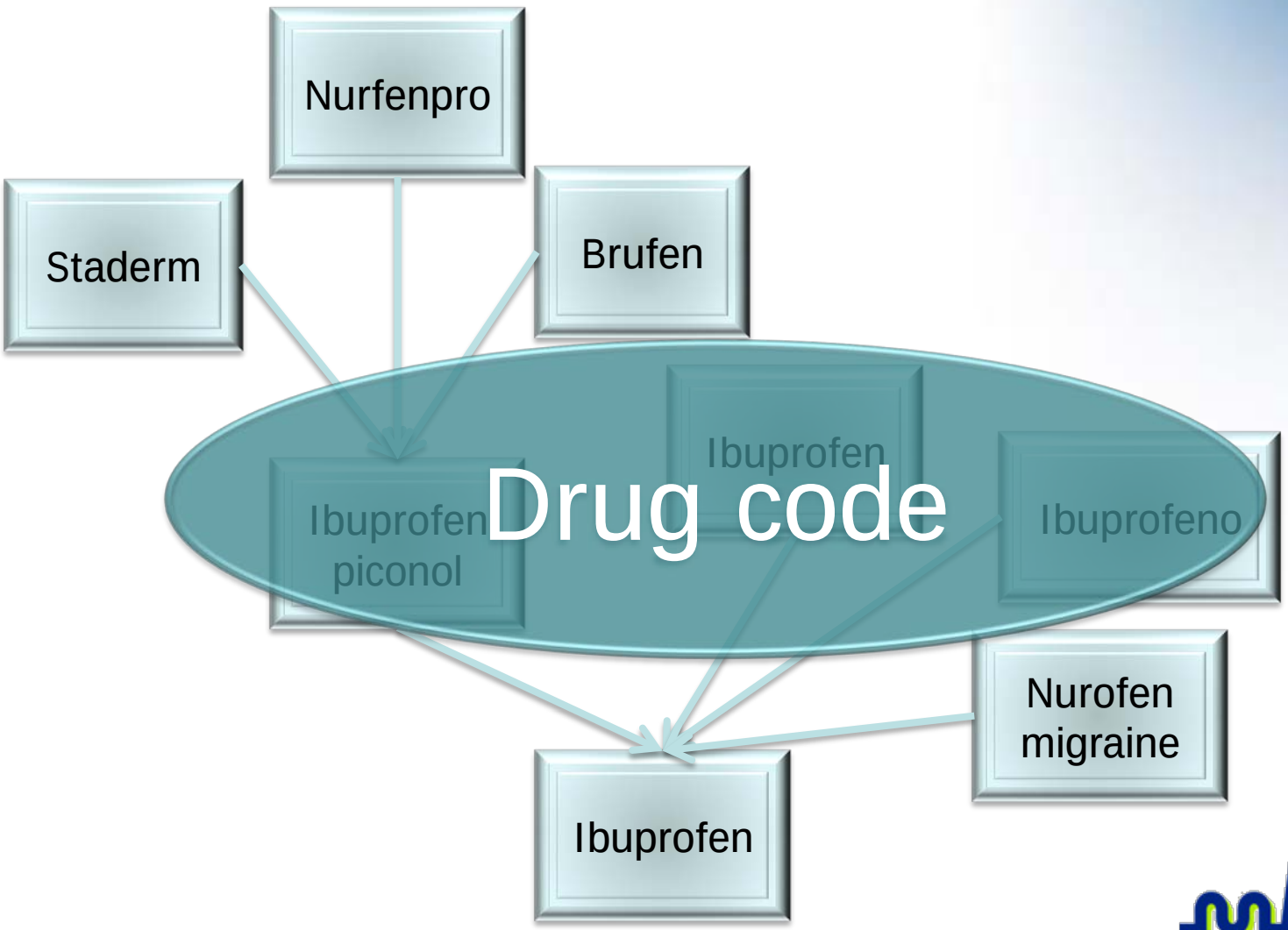
The added value of WHO Drug Dictionaries



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The WHO Drug Dictionaries

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The WHO Drug Dictionaries

Holds **standardised** medicinal information on:

- Trade name
- Active ingredient(s)
- MAHolder
- Strength
- Country of sales

Released	Quarterly (text files) Weekly (VigiFlow, CEM Flow) Monthly (VigiSearch/VigiLyze)

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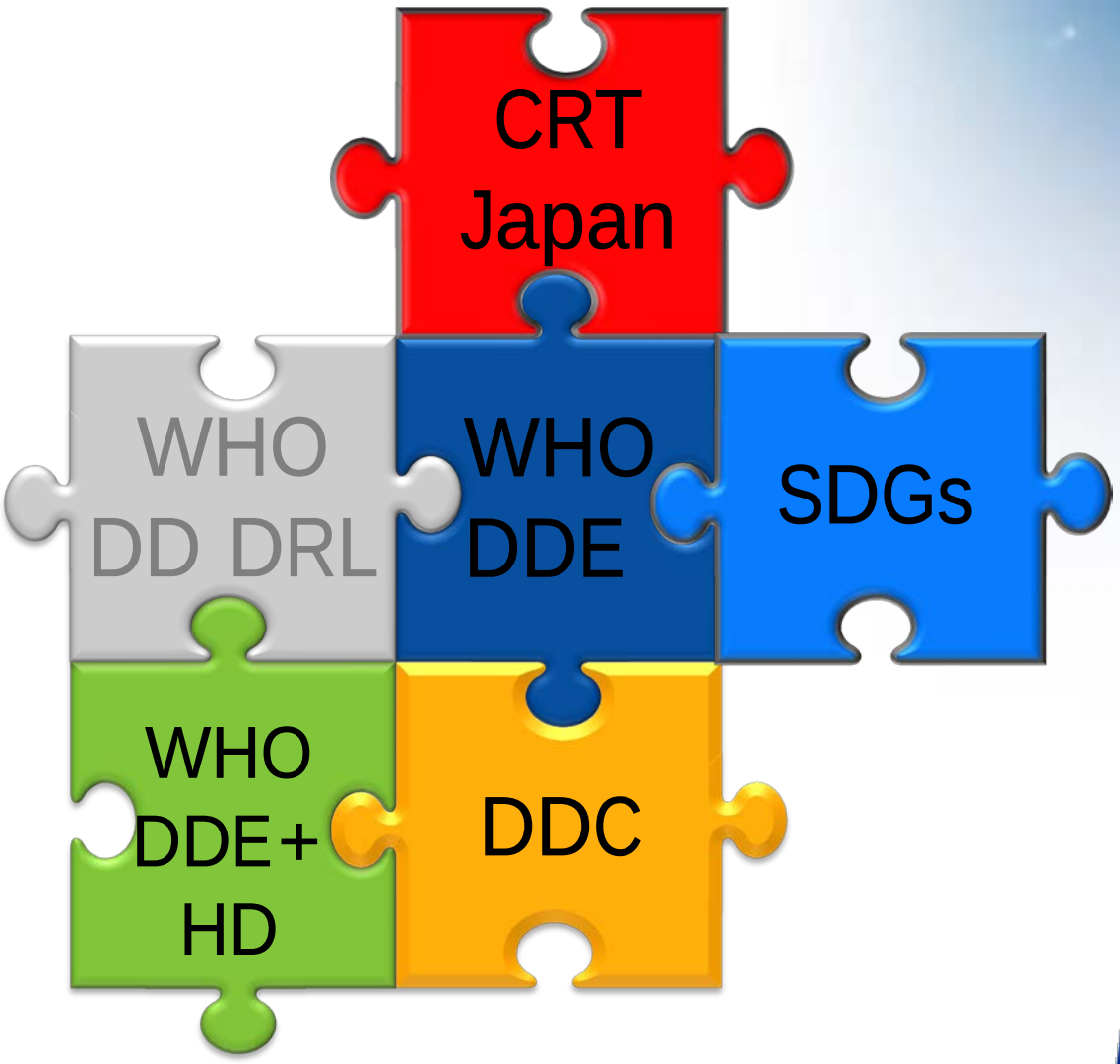
The WHO Drug Dictionaries



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Product types in the WHO Drug Dictionaries

- Conventional drugs (Arinate, Cetamol)
- Biologicals (vaccines, biosimilars, heparins etc)
- Umbrella entries (antibiotics,
- Blood products
- Radiopharmaceutical diagnostics
- Herbal products
- Generic products
- Substance and substance synonyms

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ATC classification

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What is ATC?

- Anatomical Therapeutic Chemical (ATC)
- Originally created for drug utilization statistics
- Maintained by WHO Collaborating Centre for Drug Statistics Methodology
- Each product in the WHO Drug Dictionaries is assigned at least one ATC code
- More information: www.whocc.no

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5 ATC levels

A	Alimentary tract and metabolism (1st level, anatomical main group)
A10	Drugs used in diabetes (2nd level, therapeutic subgroup)
A10B	Oral blood glucose lowering drugs (3rd level, pharmacological subgroup)
A10B A	Biguanides (4th level, chemical subgroup)
A10B A02	Metformin (5th level, chemical substance)

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SDG classification

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Standardised Drug Groupings (SDG)

Definition

"An SDG is any grouping of medicines having one or several properties in common.

The individual grouping can be based on indication, chemical properties, pharmacodynamic properties and/or pharmacokinetic properties as well as any other property of interest. "

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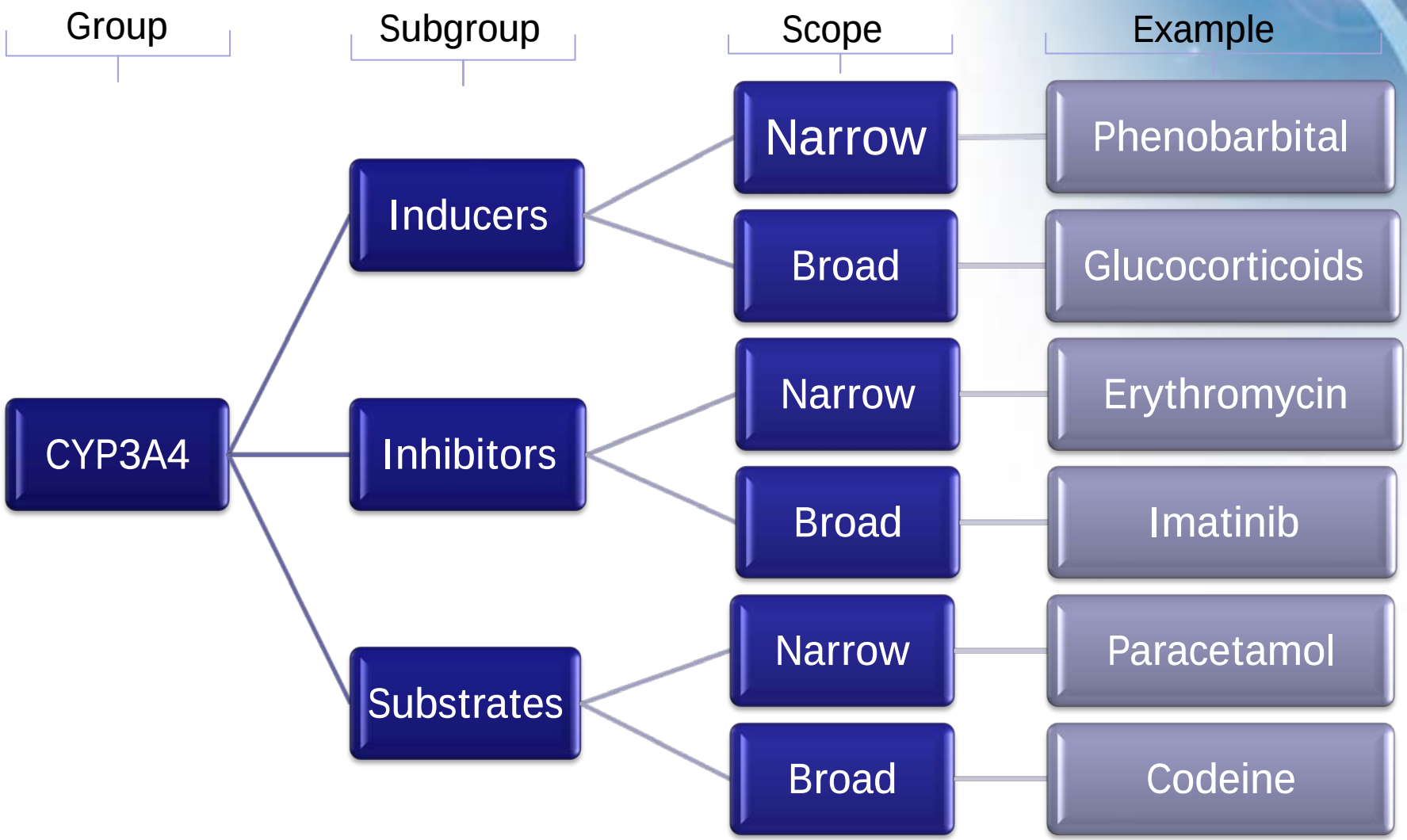
SDG Hierarchy



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The importance of using a standardised dictionary

- Facilitates data analysis
- All data in the dictionary handled the same way → standardised analysis
- No logic gaps in data extraction
- Facilitates communication and data exchange among different organisations
- Quality assured data
- Consistent workflow

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Creation of a drug standard

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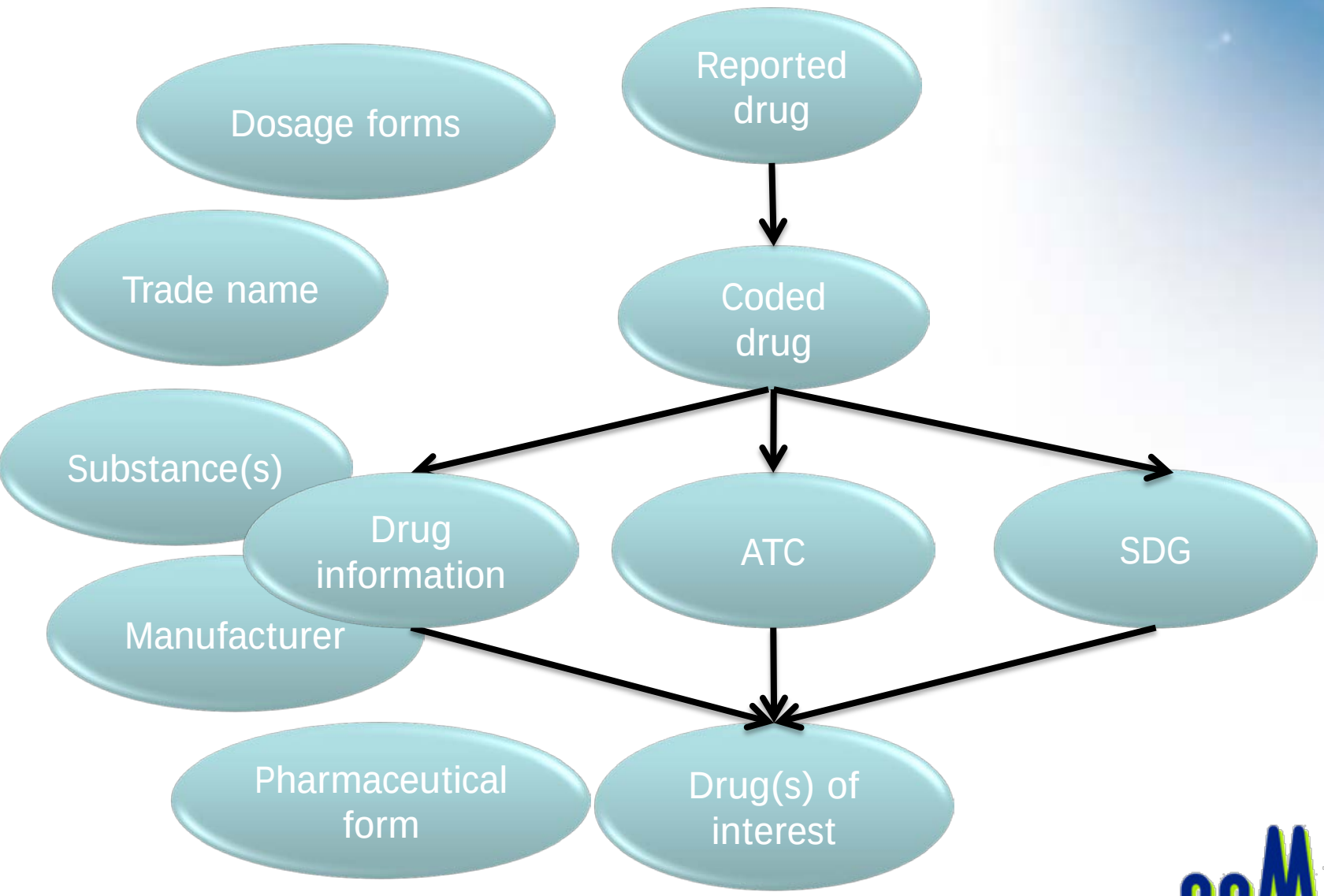
WHO DDs production team

WHO DDs: to be used in analysis



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Suspected / interacting / concomitant

- Trend: moving towards analyzing all medications on a report, not just the reactions.
- It is not always the medications stated as being suspected or interacting that truly was the cause of the reaction.
- Concomitant medications give information about underlying diseases, they might be interacting with the suspected drug and they contribute to give the whole picture of the patient.

Choice of specificity of drug information matters!

- What kind of analysis do you want to be able do?
- How much information do you need for suspected vs concomitant medication?
- Instruct reporters how to report

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Choice of specificity of drug information matters!

Example: generics products

Omeprazole (Sweden)

- Sandoz, Stada, Teva, Arrow, Evolan, Ranbaxy, Qdoxx, Altavis, Apofri, Alternova, Bluefish, BMM pharma, Evolan, Mylan, Pensa, Ratiopharm

Choice of specificity of drug information matters!

Ibuprofen suppositories

- One of the generic drugs melts to fast
  → no effect for patients
- What would happen if Ibuprofen + lack of effect was reported

  compared to Ibuprofen + **manufacturer** + lack of effect?

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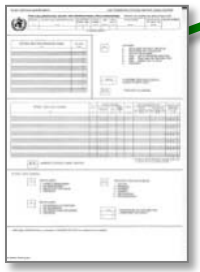
Users of the WHO Drug Dictionaries

Doctors & Patients



National Centre

VigiBase™

VigiLyze*

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WHO Drug Dictionary User Group

- Yearly meetings
  - USA
  - Europe
  - Japan
  - India
- User group portal
  - News, information, documentation
- Working groups
  - SDG, best practices, new developments

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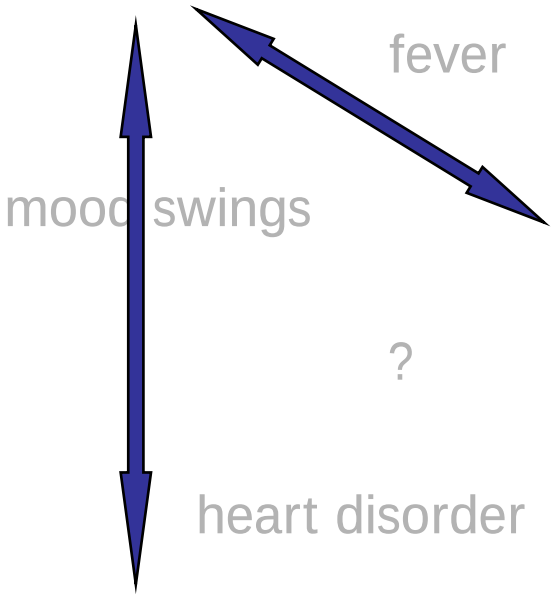
Summary

- You are all users of WHO Drug Dictionaries
- The WHO Drug Dictionaries are de facto standard for drug coding within the industry and within many national auhtorities
- Plan, decide and inform about the desired level of specificty of the drug information in order to be able to do the analysis in the best way

The need for a medical terminology



dyspnoea ? tinnitus

fever feeling high

mood swings breath shortness local reaction

? unconsciousness

heart disorder headache ALTE

SOB somnolence rash

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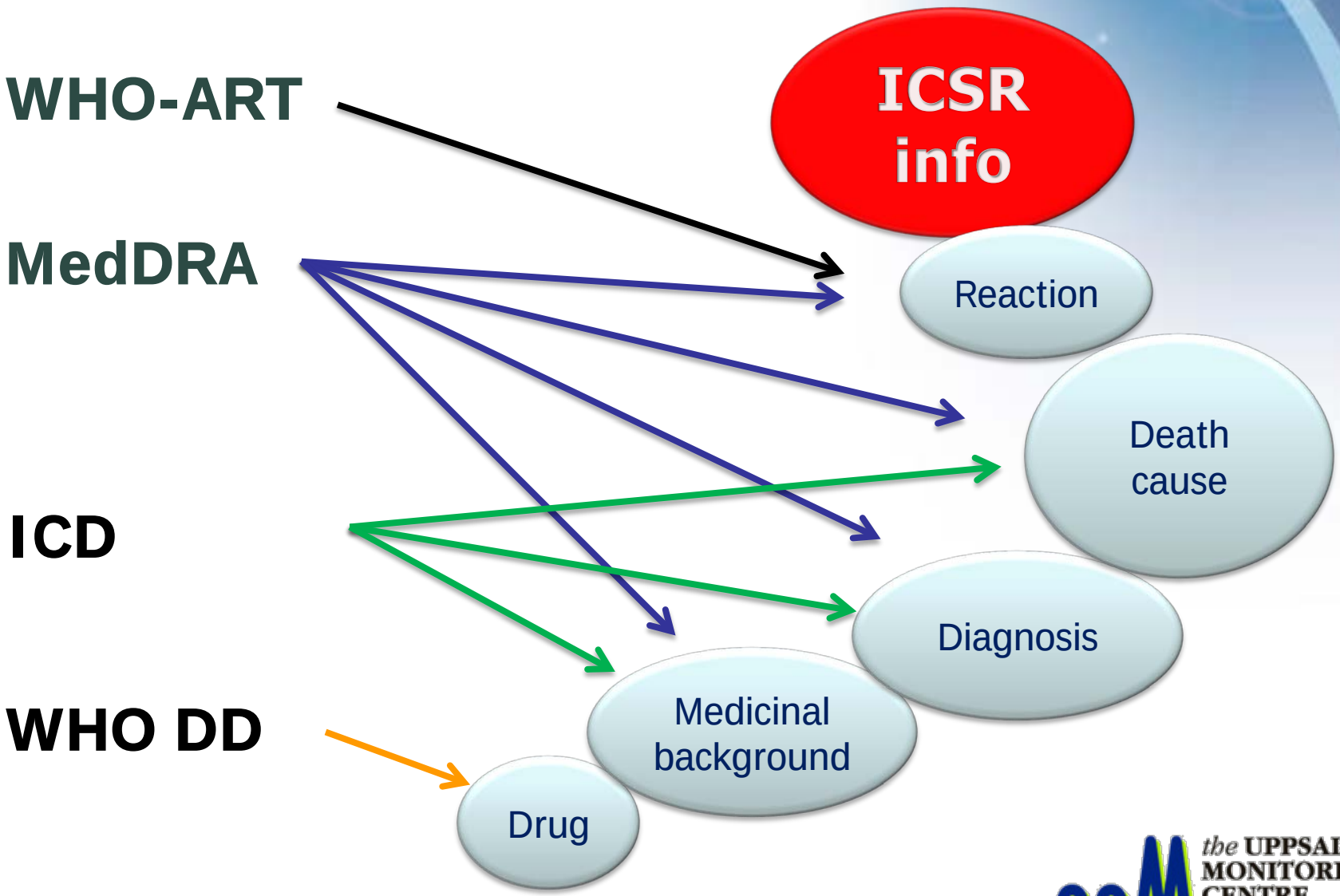
Terminologies in the WHO ICSR database



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Why two terminologies for the same purpose

- MedDRA can also be used to describe e.g death causes, medicinal background, diagnosis
- MedDRA is the standard in ICH* countries
- WHO-ART is especially designed as a reaction vocabulary for spontaneous reporting
- WHO-ART is less complex and contains fewer term - less training is needed to use it

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WHO-ART and MedDRA are medical dictionaries and it takes some **training** and **medical knowledge** to use them

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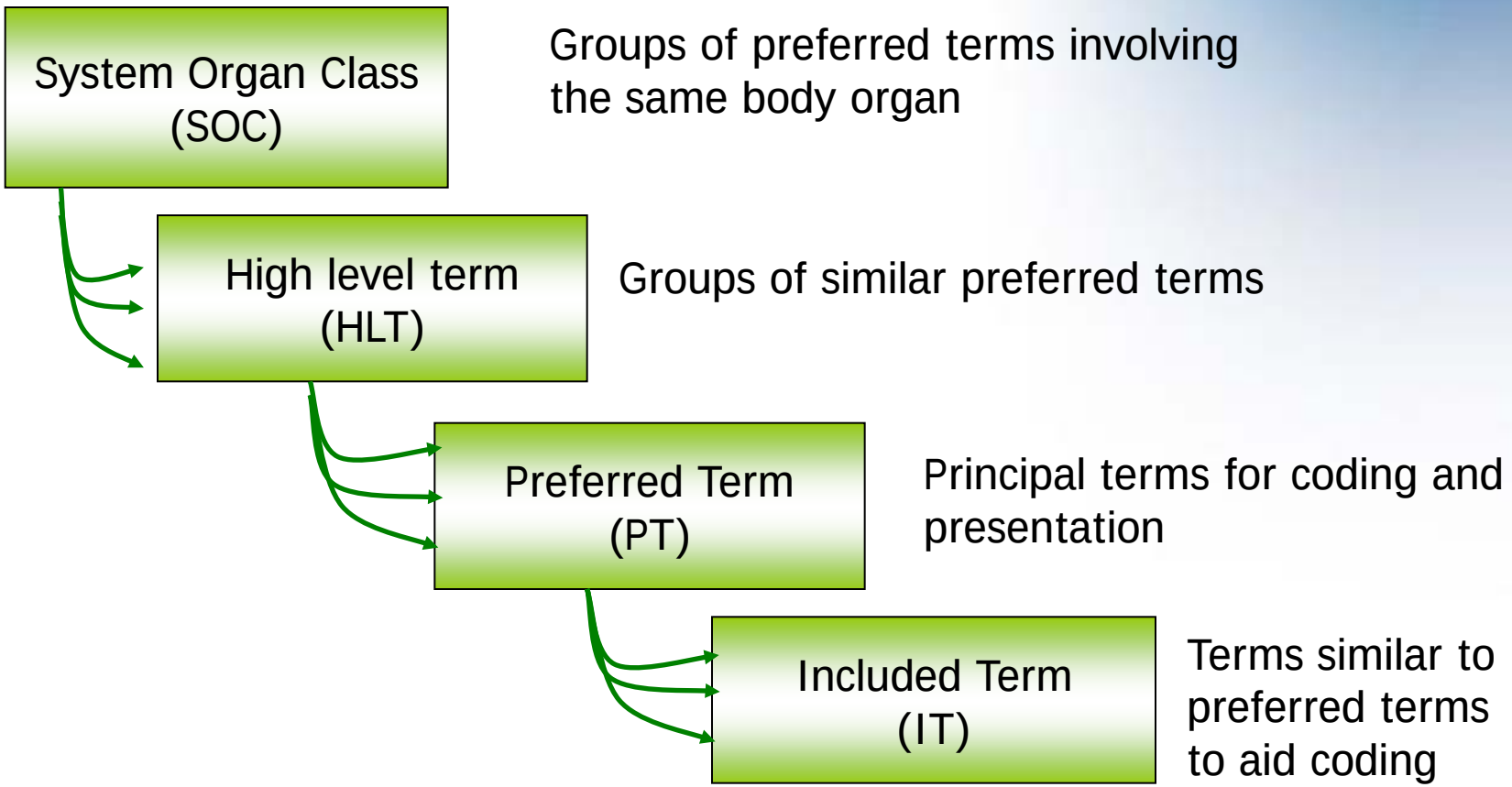
WHO-ART hierarchy



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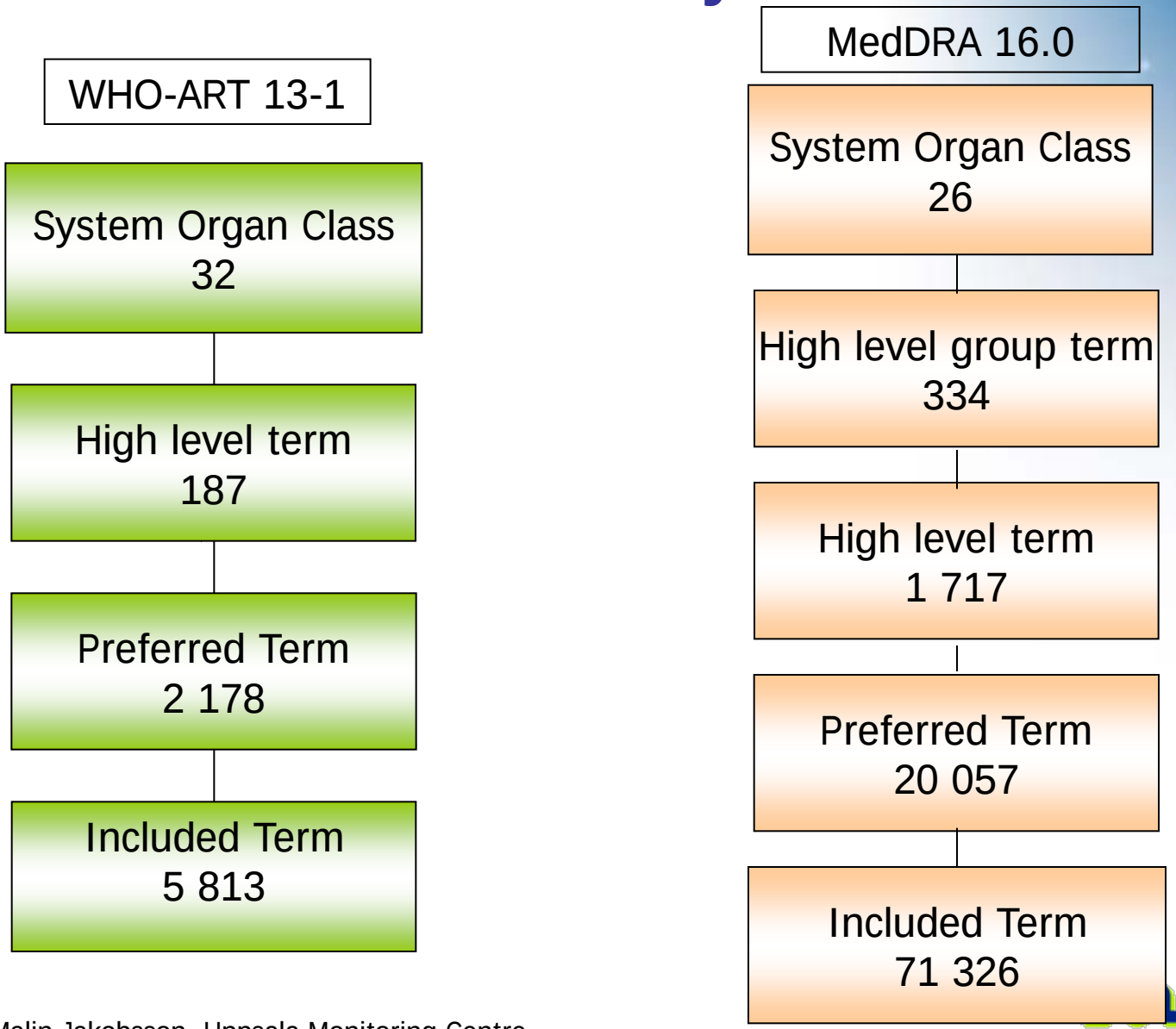
WHO-ART compared to MedDRA hierarchy



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Scope of MedDRA

All aspects of drug safety:

- signs & symptoms
- diseases & indications for use
- investigations
- surgical and medical procedures
- medical / social / family history

Not all SOCs e.g. Investigations, intended for adverse event reporting

Some difficulties e.g. Hypertension vs. Blood pressure increased

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WHO-ART System Organ Classes

Skin and appendages disorders	0100
Musculo-skeletal system disorders	0200
Collagen disorders	0300
Central & peripheral nervous system disorders	**0410**
Autonomic nervous system disorders	**0420**
Vision disorders	**0431**
Hearin	
Specia	
Psychia	
Gastro-	
Liver ar	
Metabo	
Endocrine disorders	0900
Cardiovascular disorders, general	**1010**
Myo-, endo-, pericardial & valve disorders	**1020**
Heart rate and rhythm disorders	**1030**
Vascular (extracardiac) disorders	**1040**

Gastro-intestinal system disorders	0600
Liver and biliary system disorders	0700
Metabolic and nutritional disorders	0800

Respiratory system disorders	1100
Red blood cell disorders	**1210**
White cell and RES* disorders	**1220**
Platelet, bleeding & clotting disorders	**1230**
Urinary system disorders	1300
Reproductive disorders, male	1410
	1420
	1500
	1600
	1700
rs	1810
	1820
Resistance mechanism disorders	1830
Secondary terms - events	2000
Poison specific terms	2100

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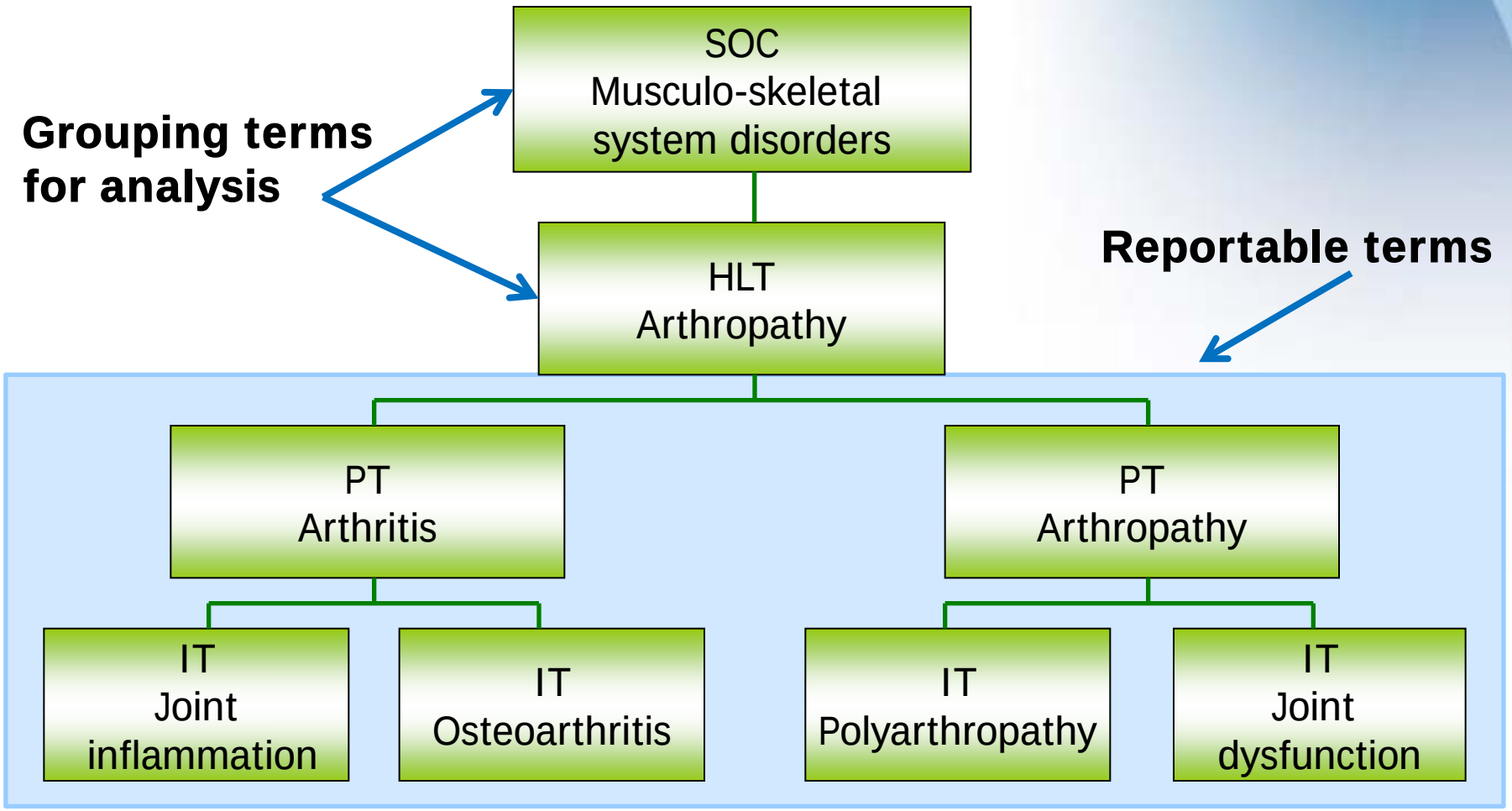
WHO-ART hierarchy

- an example



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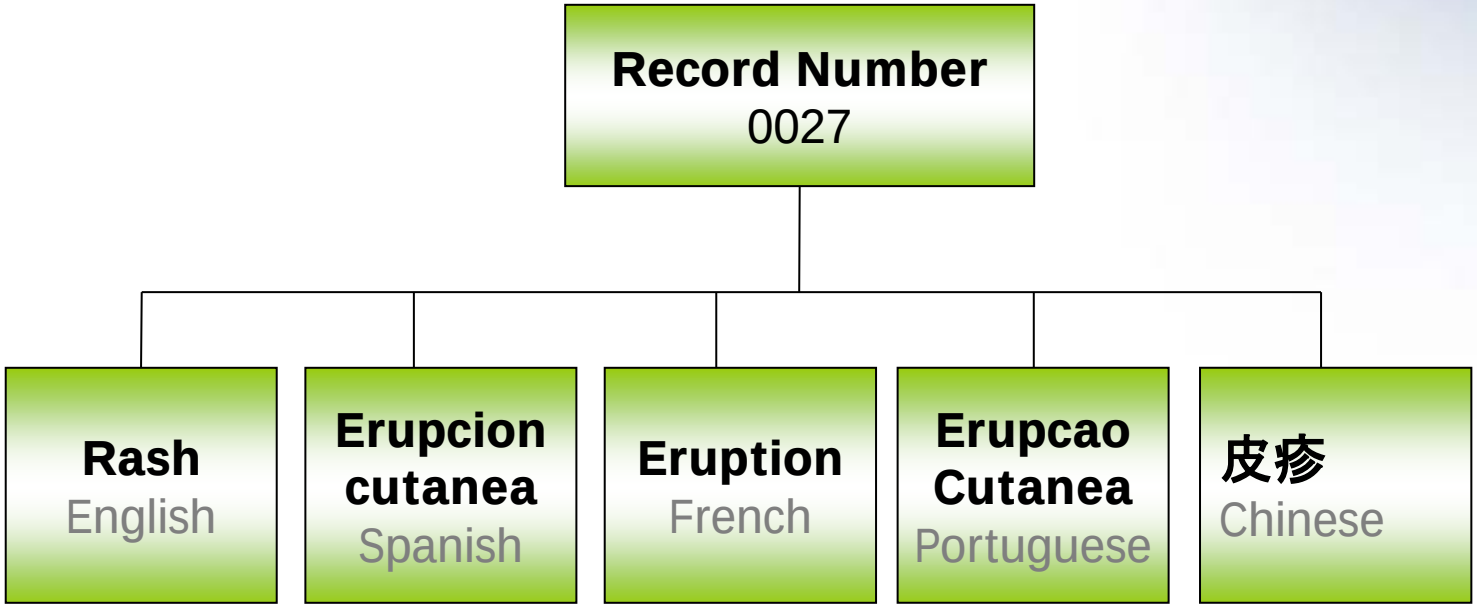
WHO-ART

Different languages linked through the Record Number System

Only record numbers are stored with case reports in the database



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WHO-ART - Critical terms

A subset of adverse reaction terms referring to, or possibly being indicative of, serious disease states, which have been regarded as particularly important to monitor

e.g. Death, anaphylactic shock, convulsions, erythema multiforme

How to enter information

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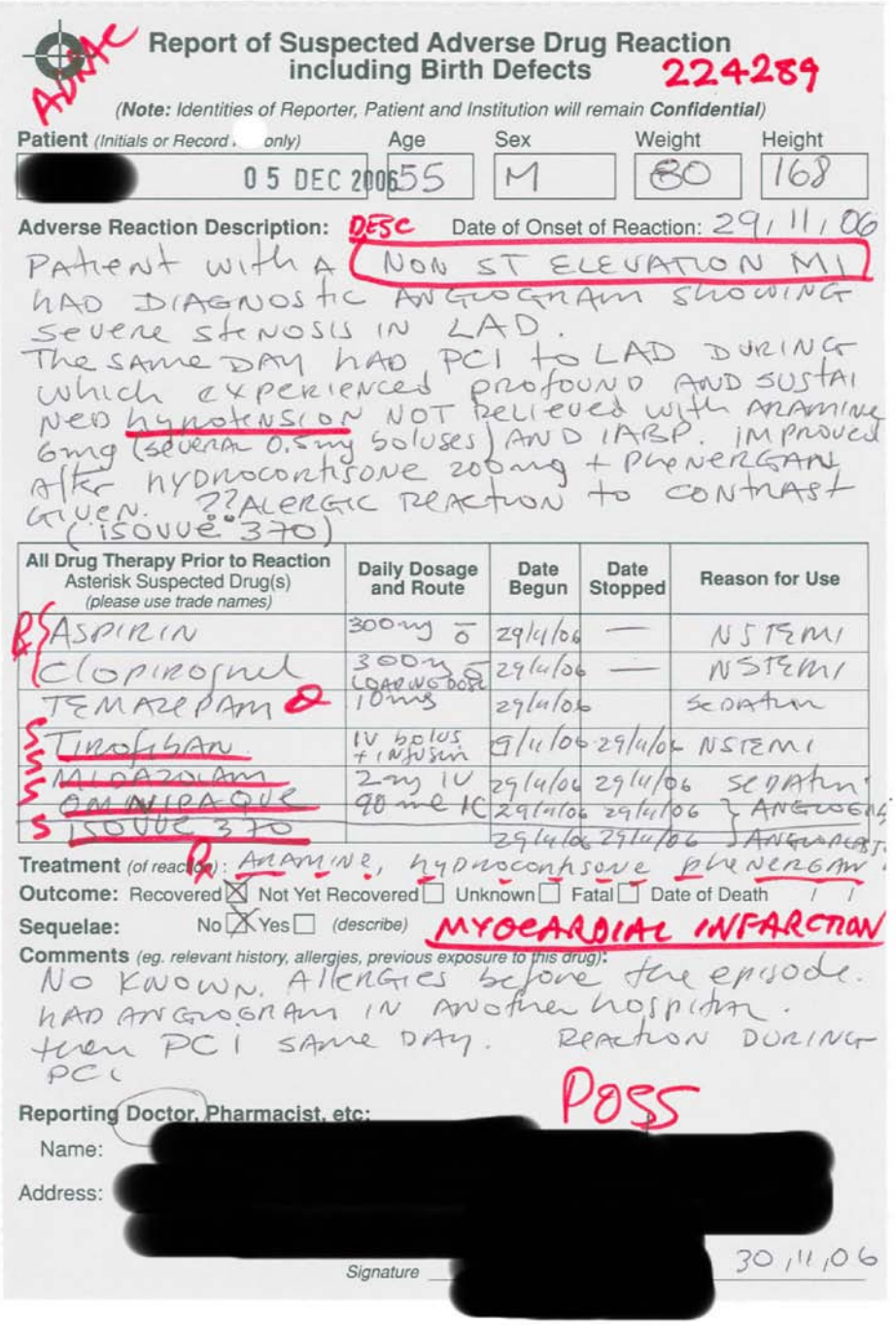

Report of Suspected Adverse Drug Reaction including Birth Defects 224289

(Note: Identities of Reporter, Patient and Institution will remain Confidential)

Patient (Initials or Record No. only)	Age	Sex	Weight	Height
[redacted] 05 DEC 2006	55	M	80	168

Adverse Reaction Description: DESC Date of Onset of Reaction: 29/11/06

PATIENT WITH A NON ST ELEVATION MI HAD DIAGNOSTIC ANGIOGRAM SHOWING SEVERE STENOSIS IN LAD. THE SAME DAY HAD PCI to LAD DURING WHICH EXPERIENCED PROFOUND AND SUSTAINED hypotension NOT RELIEVED WITH ARAMINE 6mg (SEVERAL 0.5mg boluses) AND IABP. IMPROVED A/fr HYDROCORTISONE 200mg + PHENERGAN GIVEN. ??ALERGIC REACTION to CONTRAST (ISOVUE 370)

All Drug Therapy Prior to Reaction Asterisk Suspected Drug(s) (please use trade names)	Daily Dosage and Route	Date Begun	Date Stopped	Reason for Use
ASPIRIN	300mg O	29/11/06	—	NSTEMI
Clopidogrel	300mg LOADING DOSE	29/11/06	—	NSTEMI
TEMAZEPAM	10mg	29/11/06		SEDATION
Tirofiban	IV bolus + INFUSION	29/11/06	29/11/06	NSTEMI
MIDAZOLAM	2mg IV	29/11/06	29/11/06	SEDATION
ARAMINE	90 mg IV	29/11/06	29/11/06	} ANGIOGRAM
ISOVUE 370		29/11/06	29/11/06	} ANGIOPLASTY

Treatment (of reaction): ARAMINE, HYDROCORTISONE PHENERGAN

Outcome: Recovered ☒ Not Yet Recovered ☐ Unknown ☐ Fatal ☐ Date of Death / /

Sequelae: No ☒ Yes ☐ (describe) MYOCARDIAL INFARCTION

Comments (eg. relevant history, allergies, previous exposure to this drug):

NO KNOWN ALLERGIES before the episode. HAD ANGIOGRAM IN another hospital. then PCI SAME DAY. REACTION DURING PCI

Reporting Doctor, Pharmacist, etc: POSS

Name: [redacted]

Address: [redacted]

Signature [redacted] 30/11/06

An authentic ADR reporting form

A mix between structured fields and free text boxes

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Case report in free text

An 86-year-old female with bipolar disorder was admitted with anxiety, insomnia, fatigue, and acute renal failure. Although lithium levels were normal, lithium had been discontinued and replaced with carbamazepine 100 mg daily 2 days prior to admission.

She was also taking hydralazine 100 mg three times daily for hypertension for 2 years with no dosage change in 8 months. On hospital day 8, she developed fever and conjunctivitis followed by oral erosions and painful lesions on her nose, ears, back, and fingers.

Extracted case information

Original information	Closest WHO-ART terms
...anxiety...	Anxiety
...insomnia...	Insomnia
...fatigue...	Fatigue
...acute renal failure...	Renal failure acute
...fever...	Fever
...conjunctivitis...	Conjunctivitis
...oral erosions...	Erosion gingival
...painful lesions on her nose, ears, back, and fingers...	Skin ulceration

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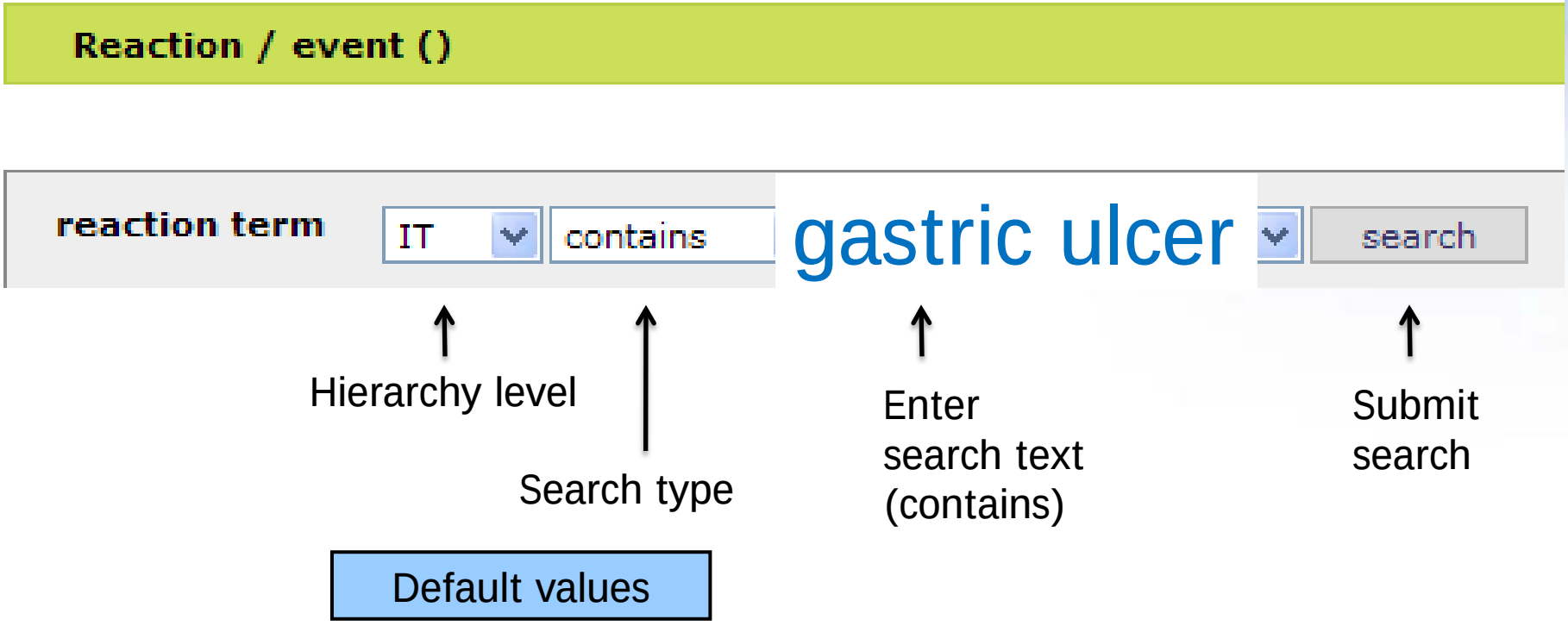
Reactions → Entering

Reaction coding interface (VF)



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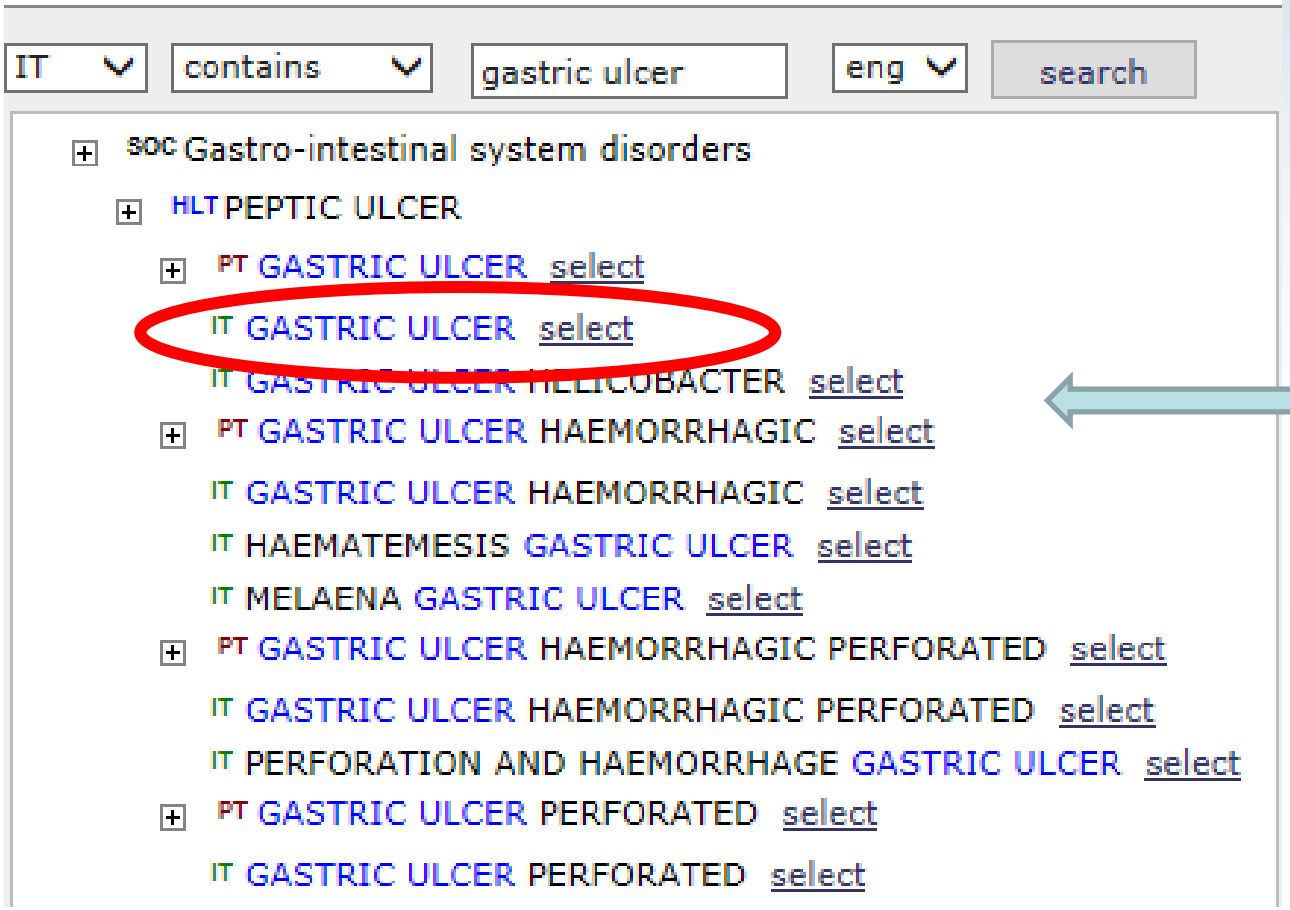
Reactions → Coding



Find term as exact as possible.
Search on IT level.
Don't make assumptions

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Entering data - example WHO-ART

Be clear about what information you are entering

What is a **local reaction**?

12 different terms in WHO-ART

If possible – go back to reporter and ask

Urticaria localized

Inflammation localized

Anaesthesia local

Osteoarthritis localised

Convulsions local

Numbness localized

Coldness local

Paralysis muscle local skeletal

Localised oedema

Infection localised

Skin exfoliation localised

Skin reaction localised

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Fever vs Febrile

HAY FEVER

FEVER

DRUG FEVER

Q FEVER

FEVER NEONATAL

FEVER

CONVULSIONS

METAL FUME FEVER

FEBRILE NEUTROPENIA

FEBRILE REACTION

FEBRILE SEIZURE

ACUTE FEBRILE

NEUTROPHILIC DERMATOSIS

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Reactions → Searching

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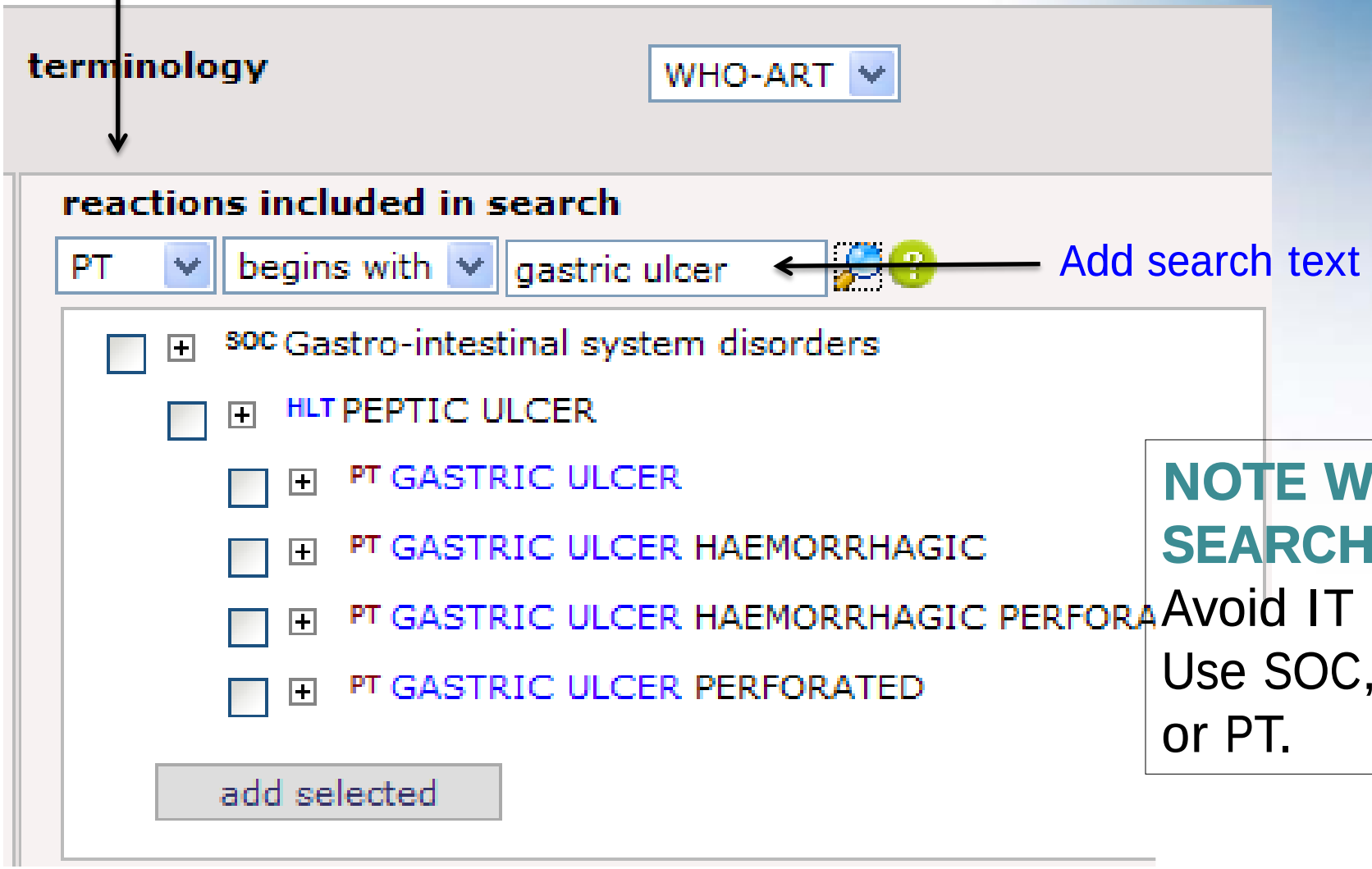
Reaction → Searching (VigiBase) → Quick find

Choose level



NOTE WHEN SEARCHING!
Avoid IT level
Use SOC, HLT or PT.

Reactions → Searching

When looking for cases with ‘Gastric Ulcer’;

- **Wide search**
  System Organ Class level – ‘G-I system disorders’ – all cases with GI related disorders
- **’Middle level’ search**
  High level term – ’Peptic ulcer’
- **Narrow search**
  Included term ’Gastric Ulcer’ – only cases with the exact term are retrieved.

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Variations of spelling Stevens Johnson syndrome

The problem of not using a controlled vocabulary

- all have been reported to UMC!
- enter only 'Steven'
- search with 'IT contains'

STEVENS - JOHNSON SYNDROME
STEVENS JOHSON SYNDROME
STEVENS-JOHNSON SYNDROMES
STEVENS-JHONSON SYNDROME
STEVENS-JONSON SYNDROME
STEVEN-JOHNSON LIKE SYNDROME
STEVEN´S JOHNSON, SINDROME
SINDROME DE STEVEN JOHNSON
STEVEN'S JOHNSON SYNDROME
STEVEN JOHNSON'S SYN
STEVEN JOHNSON SYNDROMS
STEVEN JOHNSON SYNDROME
STEVEN JOHNSON'S SYNDROME
STEVEN JOHNSON SYNDROM
SINDROME DE STEVEN JHONSON
STEVEN JOHNSON SYDROM

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New terms for WHO-ART or drugs for WHO DD

Suggestion for new terms or drugs can be done if needed:

- first check your spelling
- search for all possible variants using broad search - SOC

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Thank you!

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