



Standardized MedDRA Queries for statistical programmers

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Agenda

- **What are SMQs – where to get them ?**
- **SMQ Structure**
- **Merge of SMQs to MedDRA coded data**
- **Concept of Narrow and Broad SMQs**
- **SMQ Versioning**
- **Output examples**

SMQs - Standardized MedDRA Queries

■ What are SMQs ?

SMQs are groupings of relevant MedDRA terms to represent a particular area of interest. for data retrieval & analysis.

- Groupings at the MedDRA Preferred Term (PT) level terms, which represent unique medical concepts.
- SMQ include terms for signs, symptoms, diagnoses, syndromes, physical findings, laboratory and other physiologic data, etc.

■ Where can they be downloaded – more information?

- <http://www.meddramsso.com> SMQ FAQ (you need to subscribe)

SMQs - Standardized MedDRA Queries – Acronym - considerations

- **QUERY** = **Question**, often expressing doubt/suspicion about something, looking for an answer. (Cambridge Dictionary)
 - **QUESTIONS:**
 - » Is someone harmed during the course of a clinical trial ?
 - » If yes, how ? And why ? Who ?
 - » How ? Various possibilities → Use a **common, worldwide** accepted terminology
- Technically: **Grouping** of terms
- Terminology = **MedDRA**: Medical Dictionary for Regulatory Activities
- Worldwide accepted = **Standardized**

MedDRA - Dictionary for all medical data

Included

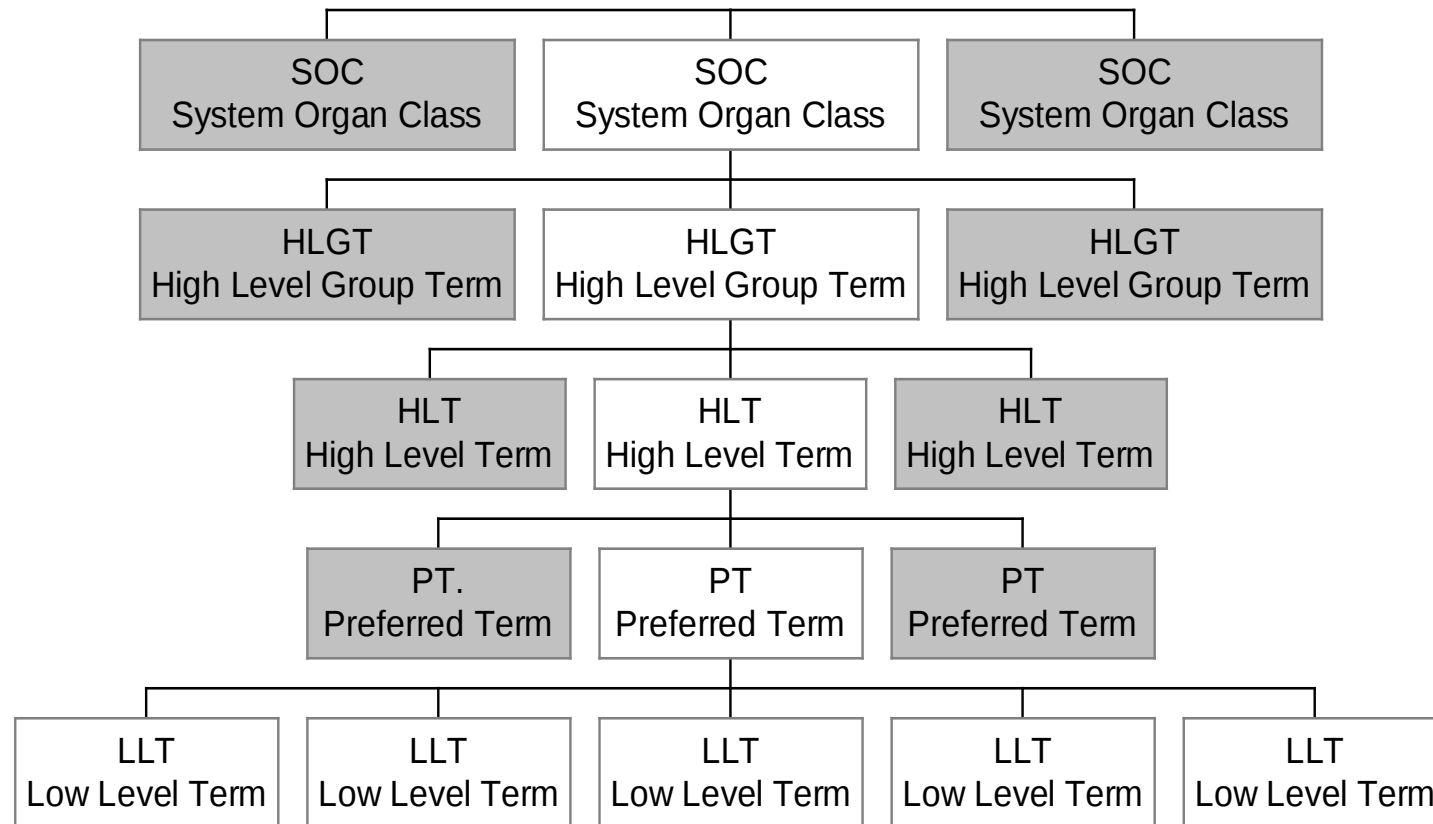
- Diseases, Diagnoses, Indications, Symptoms, Signs
- Medical Investigations and qualitative results
- Medical and surgical procedures
- Device related complications
- Drug monitoring related terms
- Social circumstances
- Terms of older Dictionaries (but many inactive)

Excluded

- Drug and product names
- Study design related terms
- Equipment and Device Terms
- Numerical values
- Demographic terms (age, gender etc)
- Descriptors of severity
- Descriptors of frequencies (rare, occasional etc.)

MedDRA - Hierarchical Structure

The five levels of the MedDRA hierarchy





MedDRA History - Standardization

- Originally developed by British Health Authority
- Later adopted by ICH
- Present version 12.1
Updated every 6 months
- Maintained by MedDRA MSSO on behalf of ICH
Maintenance Support & Service Organization



SMQs - Rationale

■ Rationale behind development of SMQs*

The size (~ 18 000 PTs) and complexity of MedDRA terminology carries the risk that

- different users may select differing sets of terms while trying to retrieve cases relative to the same drug safety problem
- globally standardized search queries / analysis will give broader acceptance

* “Development and Rational Use of Standardised MedDRA Queries (SMQs)”, - CIOMS Working Group

SMQ structure – basic technical principles

MSSO provides **2 files** - **SMQ list** and **SMQ contents** in flat ascii format (see file description for variables)

- **List** contains **one observation per SMQ** (175 rows in Version 12.1)
- **Contents** contains **multiple observations per SMQ**, containing PT codes, LLT codes and information on child = subordinate SMQ's (54543 rows in Version 12.1)
- Bring the 2 SMQ dictionary files together with clinical **trial adverse event data**
→ get all smq information on a patient level ?

SMQ structure – basic principles - 2 merges

- 1) **Bring together List and Contents**
via SMQCODE and clarify hierarchy data information

- 2) **Bring the result together with „Patient Adverse/other Event“ data**
via PT / LLT TERMCODE / TERM TEXT

SMQ structure – example - MSSO browser

MedDRA Browser - SMQ View : MedDRA 12.1 - English

File View Tools About <Select MedDRA Data> Action

MedDRA 12.1 - English

- SMQ Biliary neoplasms (SMQ)
 - SMQ Biliary neoplasms malignant and unspecified (SMQ)
- + SMQ Angioedema (SMQ)
- + SMQ Anticholinergic syndrome (SMQ)
- + SMQ Asthma/bronchospasm (SMQ)
- SMQ Biliary disorders (SMQ)
 - SMQ Biliary neoplasms (SMQ)
 - + SMQ Biliary neoplasms benign (incl cysts and polyps) (SMQ)
 - SMQ Biliary neoplasms malignant and unspecified (SMQ)
 - + PT Bile duct cancer
 - + PT Bile duct cancer non-resectable
 - + PT Bile duct cancer recurrent
 - + PT Bile duct cancer resectable
 - + PT Bile duct cancer stage 0
 - + PT Bile duct cancer stage I

- + SMQ Acute renal failure (SMQ)
- + SMQ Adverse pregnancy outcome/repr...
- SMQ Agranulocytosis (SMQ)
 - + PT Agranulocytosis
 - + PT Aplastic anaemia
 - + PT Bone marrow failure
 - + PT Febrile bone marrow aplasia
 - + PT Febrile neutropenia
 - + PT Neutropenic colitis
 - + PT Neutropenic infection
 - + PT Neutropenic sepsis
 - + PT Pancytopenia
 - + PT Panmyelopathy
 - + PT Pure white cell aplasia
 - + PT Abdominal sepsis
 - + PT Acute tonsillitis
 - + PT Bacterial sepsis
- + SMQ Agranulocytosis (SMQ)
- SMQ Anaphylactic reaction (SMQ)
 - + PT Anaphylactic reaction
 - + PT Anaphylactic shock
 - + PT Anaphylactic transfusion reaction
 - + PT Anaphylactoid reaction
 - + PT Anaphylactoid shock
 - + PT Circulatory collapse
 - + PT First use syndrome
 - + PT Kounis syndrome
 - + PT Shock
 - + PT Type I hypersensitivity
 - + PT Acute respiratory failure
 - + PT Asthma
 - + PT Bronchial oedema

SMQ structure – MSSO browser details - list

- Accidents and injuries (SMQ)
- Acute central respiratory depression
- Acute pancreatitis (SMQ)
- Acute renal failure (SMQ)
- Adverse pregnancy outcome/reprod
- Agranulocytosis (SMQ)
- Anaphylactic reaction (SMQ)
- Angioedema (SMQ)
- Anticholinergic syndrome (SMQ)
- Asthma/bronchospasm (SMQ)
- Biliary disorders (SMQ)
- SMQ Biliary neoplasms (SMQ)**
 - SMQ Biliary neoplasms benign (incl**
 - PT Benign biliary neoplasm**
 - PT Biliary adenoma**
 - PT Biliary cyst**
 - PT Biliary polyp**
 - PT Cholangioadenoma**
 - PT Choledochal cyst**
 - PT Gallbladder polyp**
 - SMQ Biliary neoplasms malignant a**
- SMQ Congenital biliary disorders (SMQ**
- SMQ Functional, inflammatory and galls**
- SMQ Infectious biliary disorders (SMQ)**
- Breast neoplasms, malignant and un:
- Cardiac arrhythmias (SMQ)
- Cardiac failure (SMQ)
- Cardiomyopathy (SMQ)
- Cerebrovascular disorders (SMQ)
- Conjunctival disorders (SMQ)
- Convulsions (SMQ)
- Corneal disorders (SMQ)
- Dementia (SMQ)
- Demyelination (SMQ)
- Depression and suicide/self-injury (S
- Drug abuse, dependence and withdr
- Dyslipidaemia (SMQ)

MedDRA Browser - Standardised MedDRA Query Details : 12.1 - English

SMQ - Standardised MedDRA Query

SMQ Code

SMQ Level

MedDRA Version

Status

SMQ Term

SMQ Description

Developed to detect all types of disorders related to the biliary tract (treatment-associated or as medical history). Concerns all types of gallbladder and bile duct disorders. SMQ Biliary neoplasms covers biliary neoplasms irrespective of malignancy. SMQ Biliary neoplasms benign covers benign biliary neoplasms.

SMQ Source

Harrison's Principles of Internal Medicine 16th ed, Mc Graw Hill, 2005, pp 1660-1236

SMQ Note

NOTE: If the user requires a complete search of all biliary tract and liver-related investigation terms, use of SMQ Liver related investigations, signs and symptoms (sub-search SMQ of SMQ Hepatic disorders) together with SMQ Biliary system related investigations, signs and symptoms is recommended. NOTE: LLT Pancreatitis due to gallstones links to PT Pancreatitis which is not included in SMQ Biliary disorders. Inclusion of this LLT in a search may, however, be considered by the user. NOTE: Sub-search SMQ Biliary system related investigations, signs and symptoms is called SMQ Bile system related investigations, signs and symptoms in the CIOMS WG original documentation.

Algorithm

N

SMQ structure – MSSO browser details - contents

...acute central respiratory depression (SMQ)
...acute pancreatitis (SMQ)
...acute renal failure (SMQ)
...adverse pregnancy outcome/reproductive failure (SMQ)
...agranulocytosis (SMQ)
...anaphylactic reaction (SMQ)
...angioedema (SMQ)
...anticholinergic syndrome (SMQ)
...asthma/bronchospasm (SMQ)
...biliary disorders (SMQ)
...Biliary neoplasms (SMQ)
SMQ Biliary neoplasms benign (incl cysts and polyps) (SMQ)
+ PT Benign biliary neoplasm
+ PT Biliary adenoma
+ PT Biliary cyst
+ PT Biliary polyp
+ PT Cholangioadenoma
+ PT Choledochal cyst
+ PT Gallbladder polyp
SMQ Biliary neoplasms malignant (incl cysts and polyps) (SMQ)
...Congenital biliary disorders (SMQ)
...Functional, inflammatory and gallstone related biliary disorders (SMQ)
...Infectious biliary disorders (SMQ)
...Liver neoplasms, malignant and unspecified (SMQ)

PT - Preferred Term (SMQ Details) : 12.1 - English

PT - Preferred Term (SMQ Details)

MedDRA Code	10056514		
MedDRA Term	Benign biliary neoplasm		
Term Level	PT	Term Status	Active
Term Scope	Narrow	Term Addition Version	10.1
Term Category	A	Term Last Modified Version	10.1
Term Weight	0		

	SMQ Code	SMQ Name
SMQ	20000129	Biliary neoplasms benign (incl cysts and polyps) (SMQ)

SMQ provided data structure – List and content - list

Table Name	Field Name	Description
1_smq_list	SMQ_code	Eight-digit numeric code assigned to the SMQ, which starts with “2”
	SMQ_name	Name for the SMQ, each SMQ carries “(SMQ)” at the end of the name
	SMQ_level	Value between 1 and 5 identifying the level of the SMQ within the hierarchy of SMQs; 1 is the most general, 5 is the most narrow
	SMQ_description	Description of the SMQ including inclusion and exclusion
	SMQ_source	Source for the development of the SMQ (e.g., medical references)
	SMQ_note	Note for users to better understand the scope and development process for the SMQ. The description of the algorithm used is included (if applicable), as well as the definition of categories
	MedDRA_version	MedDRA version to use in conjunction with this SMQ
	Status	Status of the SMQ. “A” = An active SMQ; “I” = An inactive SMQ
	SMQ_Algorithm	If the SMQ was developed for use with an algorithm, the Boolean expression of the algorithm is included. “N” if the SMQ does not utilize an algorithm

SMQ structure - content

1_smq_content	SMQ_code	Eight-digit code assigned to the SMQ
	Term_code	Subordinate term code; it could be a code for MedDRA PT, LLT, or child SMQ
	Term_level	MedDRA hierarchy level of the term (4=PT, 5=LLT) or 0 (zero) for a child SMQ
	Term_scope	Defines the MedDRA term as a member of the broad scope (1), narrow scope (2) of the SMQ search, or a child SMQ (0) (zero)
	Term_category	The category is assigned a single alphabetical letter depending upon the algorithm applied. If the SMQ does not use algorithms, then all Term_category values are assigned "A." For a child SMQ, this field is assigned "S."
	Term_weight	Term weight is used for some SMQ algorithms. "0" is used as default
	Term_status	Identifies a term as active within this SMQ or inactive within this SMQ. When a term is added to an SMQ, the value is set to "A" for Active. The term can be flagged as "I" for inactive if the term is no longer used in the SMQ.
	Term_addition_version	Identifies the version of MedDRA in which this term was added to the SMQ
	Term_last_modified_version	Identifies the version of MedDRA in which this term was last modified in this SMQ

Approach: Combine List and Content file

List:

Information about level for all smqs captured in list file, however no information about smq parent child relationship (indirectly level is captured in contents as well)

Content:

information about smq parent child relationship (where termlvl=0)

→ combine the 2 files to get the hierarchy information in a format, better to use for reporting, and have all information in one file.

One possibility to combine:

→ Get “level 1 only SMQ’s” from **list**

→ For transposing get the level information from list for smqcode variable in **contents**. The termcode variable contains (for termlvl=0) the child code information of smqcode ie.

smqcode = parent = (I1-I3 on next slide)

termcode = child = (I2-I4 on next slide)

where child can be parent for level 2 and 3 codes ! (eg. 20000006, 20000007)

Combine information from List and Content file – illustration1

smqcode termcode T1 - t2 - t3 - 3 obs become one

TABLE: Work.T1

	I1-I3	I2-I4	I1-I3 level
	20000001	.	1
	20000002	.	1
	20000003	.	1
	20000004	.	1
L1	20000005	20000006	1
	20000005	20000014	1
	20000005	20000016	1
	20000005	20000017	1
	20000005	20000018	1
L2	20000006	20000007	2
	20000006	20000008	2
	20000006	20000009	2
	20000006	20000015	2
L3	20000007	20000010	3
	20000007	20000011	3
	20000007	20000012	3
	20000007	20000013	3
	20000019	.	1

VIEWTABLE: Work.T2

	I1,I3	I2,I4	I3	I1,I3 level
1	20000001	.	.	1
2	20000002	.	.	1
3	20000003	.	.	1
4	20000004	.	.	1
L1	20000005	20000006	20000007	1
6	20000005	20000006	20000008	1
7	20000005	20000006	20000009	1
8	20000005	20000006	20000015	1
9	20000005	20000014	.	1
10	20000005	20000016	.	1
11	20000005	20000017	.	1
12	20000005	20000018	.	1
L3	20000007	20000010	.	3
14	20000007	20000011	.	3
15	20000007	20000012	.	3
16	20000007	20000013	.	3
17	20000019	.	.	1
18	20000020	.	.	1
19	20000021	.	.	1

VIEWTABLE: Work.T3

	I1	I2	I3	I4	I1 level
1	20000001	.	.	.	1
2	20000002	.	.	.	1
3	20000003	.	.	.	1
4	20000004	.	.	.	1
5	20000005	20000006	20000007	20000010	1
6	20000005	20000006	20000007	20000011	1
7	20000005	20000006	20000007	20000012	1
8	20000005	20000006	20000007	20000013	1
9	20000005	20000006	20000008	.	1
10	20000005	20000006	20000009	.	1
11	20000005	20000006	20000015	.	1
12	20000005	20000014	.	.	1
13	20000005	20000016	.	.	1
14	20000005	20000017	.	.	1
15	20000005	20000018	.	.	1
16	20000019	.	.	.	1

Combine information from List and Content file – illustration2

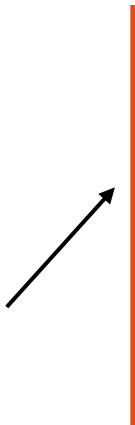
Merging process

TABLE: Work.T1			
SMQ_CODE	I2	SMQ_LEVEL	
20000001	.	1	
20000002	.	1	
20000003	.	1	
20000004	.		20000000
20000005	20000006		20000000
			20000000
			20000000
20000005	20000014	1	
20000005	20000016	1	
20000005	20000017	2	
20000005	20000018	2	
		2	
		2	
		3	
		3	
		3	
		3	
20000019	.	1	

20000007	20000010
20000007	20000011
20000007	20000012
20000007	20000013

Final merged content and list dataset including PT's

Merge hierarchy via lowest SMQ level onto Content SMQcode (where termlvl=4) → get PT's



MedDRA preferred term	SMQ level1 name	SMQ level2 name	SMQ level3 name
Hepatic congestion	Cardiac failure (SMQ)		
Hepatic congestion	Hepatic disorders (SMQ)	Drug related hepatic disorders - comprehensive search (SMQ)	Liver related investigations, signs and symptoms (SMQ)
Hepatic congestion	Shock (SMQ)	Anaphylactic/anaphylactoid shock conditions (SMQ)	
Hepatic congestion	Shock (SMQ)	Hypoglycaemic and neurogenic shock conditions (SMQ)	
Hepatic congestion	Shock (SMQ)	Hypovolaemic shock conditions (SMQ)	
Hepatic congestion	Shock (SMQ)	Shock-associated circulatory or cardiac conditions (excl torsade de pointes) (SMQ)	
Hepatic congestion	Shock (SMQ)	Torsade de pointes, shock-associated conditions (SMQ)	
Hepatic congestion	Shock (SMQ)	Toxic-septic shock conditions (SMQ)	
Jugular vein distension	Cardiac failure (SMQ)		
Jugular vein distension	Pulmonary hypertension (SMQ)		
Jugular vein distension	Shock (SMQ)	Anaphylactic/anaphylactoid shock conditions (SMQ)	

Example: PT „Hepatic congestion” in different smqs (hierarchy level 1-3)

Each patient event needs to be assigned to every SMQ it is contained in.

Example:

The adverse event „**Hepatic congestion**” PTCODE = 10019645 of a patient falls in the **SMQ's** described above (ie. **8 SMQ's**). The superordinated level information is used to count higher levels (see example table).

Final merged content and list dataset

Example: PT “Hepatic congestion” – more variables

TABLE: Work.Exmore2

MedDRA preferred term	I1	I2	I3	I4	lowest	TERM_LEVEL	TERM_SCOPE
Hepatic congestion	20000004	.	.	.	20000004	4	2
Hepatic congestion	20000005	20000006	20000008	.	20000008	4	2
Hepatic congestion	20000066	20000071	.	.	20000071	4	1
Hepatic congestion	20000066	20000072	.	.	20000072	4	1
Hepatic congestion	20000066	20000069	.	.	20000069	4	1
Hepatic congestion	20000066	20000067	.	.	20000067	4	1
Hepatic congestion	20000066	20000068	.	.	20000068	4	1
Hepatic congestion	20000066	20000070	.	.	20000070	4	1
Jugular vein distension	20000004	.	.	.	20000004	4	1
Jugular vein distension	20000130	.	.	.	20000130	4	1

MedDRA preferred term	MedDRA term code
Hepatic congestion	10019645
Hepatic congestion	10019645
Hepatic congestion	10019645
Hepatic congestion	10019645
Hepatic congestion	10019645
Hepatic congestion	10019645
Hepatic congestion	10019645
Hepatic congestion	10019645
Hepatic congestion	10019645
Jugular vein distension	10059865
Jugular vein distension	10059865

MedDRA preferred term	TERM_CATEGORY	TERM_WEIGHT	TERM_STATUS	TERM_ADDITION_VERSION	TERM_LAST_MODIFIED_VERSION
Hepatic congestion	A	0	A	10.0	10.0
Hepatic congestion	A	0	A	8.0	12.1
Hepatic congestion	A	0	A	9.1	9.1
Hepatic congestion	A	0	A	9.1	9.1
Hepatic congestion	A	0	A	9.1	9.1
Hepatic congestion	A	0	A	9.1	9.1
Hepatic congestion	A	0	A	9.1	9.1
Hepatic congestion	A	0	A	9.1	9.1
Jugular vein distension	A	0	A	12.0	12.0
Jugular vein distension	A	0	A	10.1	10.1

SMQs – Concept of narrow and broad search

SMQs may have a mixture of very specific and less specific terms that are consistent with a description of the overall clinical syndrome associated with a particular adverse event and drug exposure

Narrow search: To identify cases likely representing the condition

Broad search: To identify all possible cases, including some that may prove to be of little or no interest

SMQs – Narrow and broad search example

SMQ Acute Renal Failure

Terms of the “Narrow search”:

Acute prerenal failure, Anuria, Azotaemia, Continuous haemodiafiltration, Dialysis, Haemodialysis, Neonatal anuria, Nephropathy toxic, Oliguria, Peritoneal dialysis, Renal failure acute, Renal failure neonatal, Renal impairment, Renal impairment neonatal

Additional terms of the “Broad search”:

Albuminuria, Blood creatinine abnormal, Blood creatinine increased, Blood urea abnormal, Blood urea increased, Blood urea nitrogen/creatinine ratio increased, Creatinine renal clearance decreased, Glomerular filtration rate abnormal, Glomerular filtration rate decreased, Hypercreatininaemia, Nephritic syndrome, Nephritis, Nephritis interstitial, Oedema due to renal disease, Protein urine present, Proteinuria, Renal function test abnormal, Renal transplant, Renal tubular disorder, Renal tubular necrosis, Tubulointerstitial nephritis, Urea renal clearance decreased, Urine output decreased

SMQs – Source and version

■ Who updates SMQs?

- ❖ Standardised MedDRA Queries (SMQs) are a joint effort of the Council for International Organizations of Medical Sciences (CIOMS) SMQ Working Group and ICH (MSSO/JMO).
- ❖ All SMQs updated to MedDRA versions by MSSO
- ❖ SMQs accessible as SAS views from MedDRA version 10.0 upwards

Impact of Version Management for SMQ analysis

- Concept for version management should be documented before programming activity starts.

Novartis approach: Apply latest available (MedDRA) SMQ version for analyses (i.e. for MedDRA and SMQ table generation) as agreed with drug safety / clinical, apply the same MedDRA version as used for all other MedDRA data presentations (e.g. SOC-HLT-PT)

- Storage as LLT codes together with version number enables reproduction of analyses.
- (MedDRA) SMQ version and hierarchy is likely to change during drug development.
- Results of any re-analysis may look different.

Versioning - Challenges

- if MedDRA version in AE dataset differs from SMQ version, **use LLT codes for merge of SMQ dictionary** (default in SMQ merge macro **and not PT codes**
 - LLT's, unlike PT's, will not disappear over time and matching LLT's are always available
Counts will at least be displayed under another PT.
(reason for storage of LLT codes in datasets)

SMQ Reporting

• SMQ Hierarchy Example – Table Shell

L	Adverse events, by Standardized MedDRA Query and treatment		
	Analysis Population		
	Treat A N=xx n (%)	Treat. B N=xx n (%)	Total N=xx n (%)
SMQ level 1 to 4			
Acute pancreatitis	x (xx.x)	x (xx.x)	x (xx.x)
Acute renal failure	x (xx.x)	x (xx.x)	x (xx.x)
Adverse pregnancy outcome/reproductive toxicity (incl neonatal disorders)	x (xx.x)	x (xx.x)	x (xx.x)
Reproductive toxicity	x (xx.x)	x (xx.x)	x (xx.x)
Agranulocytosis	x (xx.x)	x (xx.x)	x (xx.x)
Anaphylactic reaction	x (xx.x)	x (xx.x)	x (xx.x)
Angioedema	x (xx.x)	x (xx.x)	x (xx.x)
Anticholinergic syndrome	x (xx.x)	x (xx.x)	x (xx.x)
Cardiac arrhythmias	x (xx.x)	x (xx.x)	x (xx.x)
Cardiac arrhythmia terms (incl bradyarrhythmias and tachyarrhythmias)	x (xx.x)	x (xx.x)	x (xx.x)
Bradyarrhythmias (incl conduction defects and disorders of sinus node function)	x (xx.x)	x (xx.x)	x (xx.x)

SMQ Reporting

- SMQ: SMQ – PT Table Example – Table Shell

Adverse events, by Standardized MedDRA Query, preferred term and treatment
Analysis Set

SMQ Preferred Term	Treat. A N=XXX	Treat. B N=XXX	Total N=XXX
Acute pancreatitis (SMQ)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Abdominal distension	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Abdominal pain	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Abdominal pain upper	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Nausea	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Vomiting	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)



Backup slides



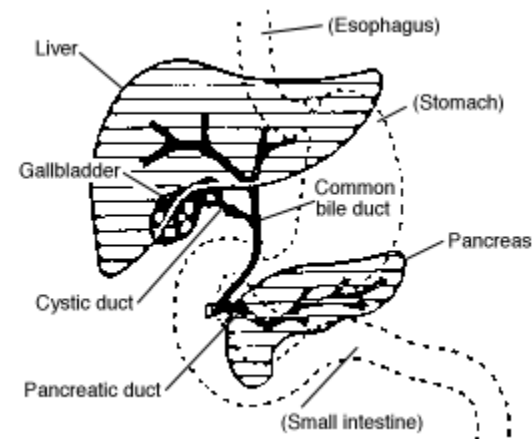
Example of MedDRA hierarchical structure

- LLT Adynamic ileus*
- PT Ileus paralytic
- HLT Non-mechanical ileus
- HLGT Gastrointestinal motility and defaecation conditions
- SOC Gastrointestinal disorders

** Ileus: or gastro(stomach)intestinal(gut) atony is a disruption of the normal propulsive gastrointestinal motor activity.*

Biliary disorder – clinical background

- **Bile** (or gall), required for the digestion of food, is excreted by the liver into passages that carry bile toward the hepatic duct, which joins with the cystic duct (carrying bile to and from the gallbladder) to form the common bile duct, which opens into the intestine.
- A bile duct is any of a number of long tube-like structures that carry bile.
- The biliary tree (see below) is the whole network of various sized ducts branching through the liver.
- **Biliary:** Of bile or of the gallbladder and bile ducts that transport bile and make up the biliary system or tract. (dictionary the free med)



SMQ structure – goal - final merged data

- The final merged dataset would have the following structure per Adverse event ie. PT/LLT code/text (currently at Novartis for standard program).

Note: One event (PT/LLT) can fall into multiple SMQ's (smqcode) !

Variable Name	Label	Type	Code	Format
ALL AE input dataset variable +				
LVL1CODE	SMQ level 1 code	Num		12.
LVL1NAME	SMQ level 1 name	Char 100		\$100.
LVL2CODE	SMQ level 2 code	Num		12.
LVL2NAME	SMQ level 2 name	Char 100		\$100.
LVL3CODE	SMQ level 3 code	Num		12.
LVL3NAME	SMQ level 3 name	Char 100		\$100.
LVL4CODE	SMQ level 4 code	Num		12.
LVL4NAME	SMQ level 4 name	Char 100		\$100.
SMQCODE	SMQ code lowest level	Num		12
SMQNAME	SMQ name lowest name	Char 100		\$100.
TERMSCP	Narrow and broad search	Num	1 = 'Broad' 2 = 'Narrow'	SCOPE.

Example: Biliary disorders (SMQ)

- + SMQ Accidents and injuries (SMQ)
- + SMQ Acute central respiratory depression (SMQ)
- + SMQ Acute pancreatitis (SMQ)
- + SMQ Acute renal failure (SMQ)
- + SMQ Adverse pregnancy outcome/reproductive toxicity (incl r
- + SMQ Agranulocytosis (SMQ)
- + SMQ Anaphylactic reaction (SMQ)
- + SMQ Angioedema (SMQ)
- + SMQ Anticholinergic syndrome (SMQ)
- + SMQ Asthma/bronchospasm (SMQ)
- + SMQ Biliary disorders (SMQ)
- + SMQ Breast neoplasms, malignant and unspecified (SMQ)
- + SMQ Cardiac arrhythmias (SMQ)
- + SMQ Cardiac failure (SMQ)
- + SMQ Cardiomyopathy (SMQ)
- + SMQ Cerebrovascular disorders (SMQ)
- + SMQ Conjunctival disorders (SMQ)
- + SMQ Convulsions (SMQ)
- + SMQ Corneal disorders (SMQ)
- + SMQ Dementia (SMQ)
- + SMQ Demyelination (SMQ)
- + SMQ Depression and suicide/self-injury (SMQ)
- + SMQ Drug abuse, dependence and withdrawal (SMQ)
- + SMQ Dyslipidaemia (SMQ)
- + SMQ Embolic and thrombotic events (SMQ)
- + SMQ Eosinophilic pneumonia (SMQ)
- + SMQ Extrapyrimalidal syndrome (SMQ)
- + SMQ Extravasation events (injections, infusions and implants)

- + SMQ Agranulocytosis (SMQ)
- + SMQ Anaphylactic reaction (SMQ)
- + SMQ Angioedema (SMQ)
- + SMQ Anticholinergic syndrome (SMQ)
- + SMQ Asthma/bronchospasm (SMQ)
- SMQ Biliary disorders (SMQ)
 - + SMQ Biliary neoplasms (SMQ)
 - SMQ Congenital biliary disorders (SMQ)
 - + PT Choledochal cyst
 - + PT Congenital hepatobiliary anomaly
 - + PT Gallbladder anomaly congenital
 - + PT Hyperbilirubinaemia neonatal
 - + PT Jaundice neonatal
 - + PT Malformation biliary
 - + PT Neonatal cholestasis
 - + SMQ Functional, inflammatory and gallstone relat
 - + SMQ Infectious biliary disorders (SMQ)
- + SMQ Breast neoplasms, malignant and unspecified
- + SMQ Cardiac arrhythmias (SMQ)
- + SMQ Cardiac failure (SMQ)
- + SMQ Cardiomyopathy (SMQ)

Screenshots : MSSO MedDRA browser – SMQ view

SMQ structure – List –var 1-5

TABLE: Work.List

SMQ_CODE	SMQ_NAME	SMQ_LEVEL	SMQ_DESCRIPTION	SMQ_SOURCE
20000004	Cardiac failure (SMQ)	1	A condition in which the heart is unable to pump an adequate amount of blood to meet metabolic and physiological needs of body. Classified (classes I - IV) on basis of severity according to criteria set by New York Heart Association (NYHA) starting from no limitation of physical activity to slight or marked limitation, up to the inability to carry out any physical activity without discomfort. Clinical findings vary but include: dependent oedema, raised jugular venous pressure, hepatomegaly, pulmonary congestion/oedema, tachycardia, cardiomegaly, and dyspnoea. Ejection fraction is less than 35%.	Council for International Organisations of Medical Sciences (CIOMS). Reporting Adverse Drug Reactions. Definition of terms and criteria for their use. 1999: p 64-65
20000005	Hepatic disorders (SMQ)	1	Disorders of the liver, including signs, symptoms, radiologic and laboratory findings. Sub-searches address cholestatic conditions, neoplasms, non-infectious hepatitis, alcohol-associated, and pregnancy associated conditions involving the liver. Possible drug-related events are also addressed in the sub-searches. Note that biliary disorders (e.g., cholelithiasis) are excluded from this SMQ	
20000006	Drug related hepatic disorders - comprehensive search (SMQ)	2	This SMQ is a sub-SMQ of Hepatic disorder (SMQ). For detailed description, please refer to the one in Hepatic disorder (SMQ).	
20000007	Drug related hepatic disorders - severe events only (SMQ)	3	This SMQ is a sub-SMQ of Possible drug related hepatic disorders - comprehensive search (SMQ), which is itself a sub-SMQ of Hepatic disorder (SMQ). For detailed description, please refer to the one in Hepatic disorder (SMQ).	

Each term above represents one SMQ – There are 4 SMQ hierarchy levels.

In MedDRA Version 10.0 there were **96 SMQs**, in Version 10.1 **135 SMQ's**, and in Version 11.1 there were **151 SMQ's** across all 4 hierarchy levels, in Version 12.1 it is **175 SMQ's**

SMQ structure – List –var 1,2, 6-9

TABLE: Work.List					
SMQ_CODE	SMQ_NAME	SMQ_NOTE	MEDDRA_VERSION	STATUS	SMQ_ALGORITHM
20000004	Cardiac failure (SMQ)	The CIOMS Working Group discussed in detail whether an algorithm could be applied to this SMQ based on the definition of cardiac failure provided. Such an algorithm, however, has not been tested by the CIOMS Working Group, therefore, the Working Group is requesting users to comment on the practical relevance of an algorithm approach. Such an algorithm could involve broad terms as follows: one oedema term, one dyspnoea term plus one clinical/sign/symptom or investigation making up 3 terms in total	12.1	A	N
20000005	Hepatic disorders (SMQ)		12.1	A	N
20000006	Drug related hepatic disorders - comprehensive search (SMQ)		12.1	A	N
20000007	Drug related hepatic disorders - severe events only (SMQ)		12.1	A	N
20000008	Liver related investigations, signs and symptoms (SMQ)		12.1	A	N

TABLE: Work.List					
SMQ_CODE	SMQ_NAME	SMQ_NOTE	MEDDRA_VERSION	STATUS	SMQ_ALGORITHM
20000017	Events specifically reported as alcohol-related (SMQ)		12.1	A	N
20000018	Pregnancy-related hepatic disorders (SMQ)		12.1	A	N
20000019	Haemolytic disorders (SMQ)		12.1	A	N
20000020	Severe cutaneous adverse reactions (SMQ)		12.1	A	N
20000021	Anaphylactic reaction (SMQ)	The following algorithm is used: All narrow search terms as well as: If one term from category B and one term from category C is present, or If one term from (category B or category C) plus one term from category D.	12.1	A	A or (B and C) or (D and (B or C))

SMQ structure – Content – var1-7

TABLE: Work.Cont						
SMQ_CODE	TERM_CODE	TERM_LEVEL	TERM_SCOPE	TERM_CATEGORY	TERM_WEIGHT	TERM_STATUS
20000001	10048352	5	1	A	0	A
20000001	10048916	5	1	A	0	A
20000001	10049418	4	1	A	0	A
20000001	10049993	4	1	A	0	A
20000001	10051888	5	1	A	0	A
20000001	10052464	4	1	A	0	A
20000001	10052509	5	1	A	0	A
20000001	10052810	5	1	A	0	A
20000001	10053604	5	2	A	0	A
20000001	10053698	5	2	A	0	A
20000001	10054581	5	2	A	0	A
20000001	10055032	4	1	A	0	A
20000001	10055068	4	1	A	0	A
20000001	10057926	4	2	A	0	A
20000001	10057936	5	2	A	0	A
20000001	10058185	5	2	A	0	A
20000006	20000007	0	0	S	0	A
20000006	20000008	0	0	S	0	A
20000006	20000009	0	0	S	0	A
20000006	20000015	0	0	S	0	A
20000007	20000010	0	0	S	0	A
20000007	20000011	0	0	S	0	A
20000007	20000012	0	0	S	0	A
20000007	20000013	0	0	S	0	A
20000008	10000028	4	1	A	0	A
20000008	10000156	5	2	A	0	A
20000008	10000158	5	2	A	0	A

SMQ structure – Content – var1-3 8,9

TABLE: Work.Cont				
SMQ_CODE	TERM_CODE	TERM_LEVEL	TERM_ADDITION_VERSION	TERM_LAST_MODIFIED_VERSION
20000004	10067025	5	10.0	10.0
20000004	10067051	5	10.0	10.0
20000005	20000006	0	8.0	8.0
20000005	20000014	0	8.0	8.0
20000005	20000016	0	8.0	8.0
20000005	20000017	0	8.0	8.0
20000005	20000018	0	8.0	8.0
20000006	20000007	0	8.0	8.0
20000006	20000008	0	8.0	8.0
20000006	20000009	0	8.0	8.0
20000006	20000015	0	8.0	8.0
20000007	20000010	0	8.0	8.0
20000007	20000011	0	8.0	8.0
20000007	20000012	0	8.0	8.0
20000007	20000013	0	8.0	8.0
20000008	10000028	4	8.0	8.0
20000008	10000156	5	8.0	12.1
20000008	10000158	5	8.0	12.1

Final merged content and list dataset

Hierarchy – without PT's or LLT's

SMQ level1	SMQ level2	SMQ level3	SMQ level4
Accidents and injuries (SMQ)			
Acute central respiratory depression (SMQ)			
Acute pancreatitis (SMQ)			
Acute renal failure (SMQ)			
Adverse pregnancy outcome reproductive toxicity (incl neonatal disorders) (SMQ)	Congenital, familial and genetic disorders (SMQ)		
	Disorders of the offspring (SMQ)		
	Pregnancy complications (SMQ)		
	Reproductive toxicity (SMQ)		
Agranulocytosis (SMQ)			
Anaphylactic reaction (SMQ)			
Angioedema (SMQ)			

Final merged dataset – merge patient data

- Combine information from combined List and Content with Adverse or other event dataset.
- Merge by PT or LLT code / term
- In example of event „Hepatic congestion“ in the final merged dataset there will be 8 rows ie. for each SMQ the event falls into one row. In a corresponding table the subject would be counted for each SMQ category once, depending on selection criteria (eg. narrow or broad scope etc.) .

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Adverse events, by Standardized MedDRA Query and treatment			
	Analysis Population		
	Treat A	Treat. B	Total
	N=xx	N=xx	N=xx
SMQ level 1 to 4	n (%)	n (%)	n (%)
Acute pancreatitis	x{xx.x}	x{xx.x}	x{xx.x}
Acute renal failure	x{xx.x}	x{xx.x}	x{xx.x}
Adverse pregnancy outcome/reproductive toxicity (incl neonatal disorders)	x{xx.x}	x{xx.x}	x{xx.x}
Reproductive toxicity	x{xx.x}	x{xx.x}	x{xx.x}
Cardiac arrhythmias	x{xx.x}	x{xx.x}	x{xx.x}
Cardiac arrhythmia terms (incl bradyarrhythmias and tachyarrhythmias)	x{xx.x}	x{xx.x}	x{xx.x}
Bradyarrhythmias (incl conduction defects and disorders of sinus node function)	x{xx.x}	x{xx.x}	x{xx.x}