The new WHODrug Dictionary

Details to be considered in SDTM

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Agenda

- Some background about the WHODrug Dictionary
- What will change with the new WHODrug version
- How this will impact SDTM

This presentation is based on the paper "How to use WHODrug for compliance with CM domain in the CDISC SDTM standard" from the Uppsala Monitoring Centre (UMC), released at 19-OCT-2016.

The original link doesn't work anymore but the document may be found at the German Speaking CDISC portal (link)

Some background about the WHODrug Dictionary

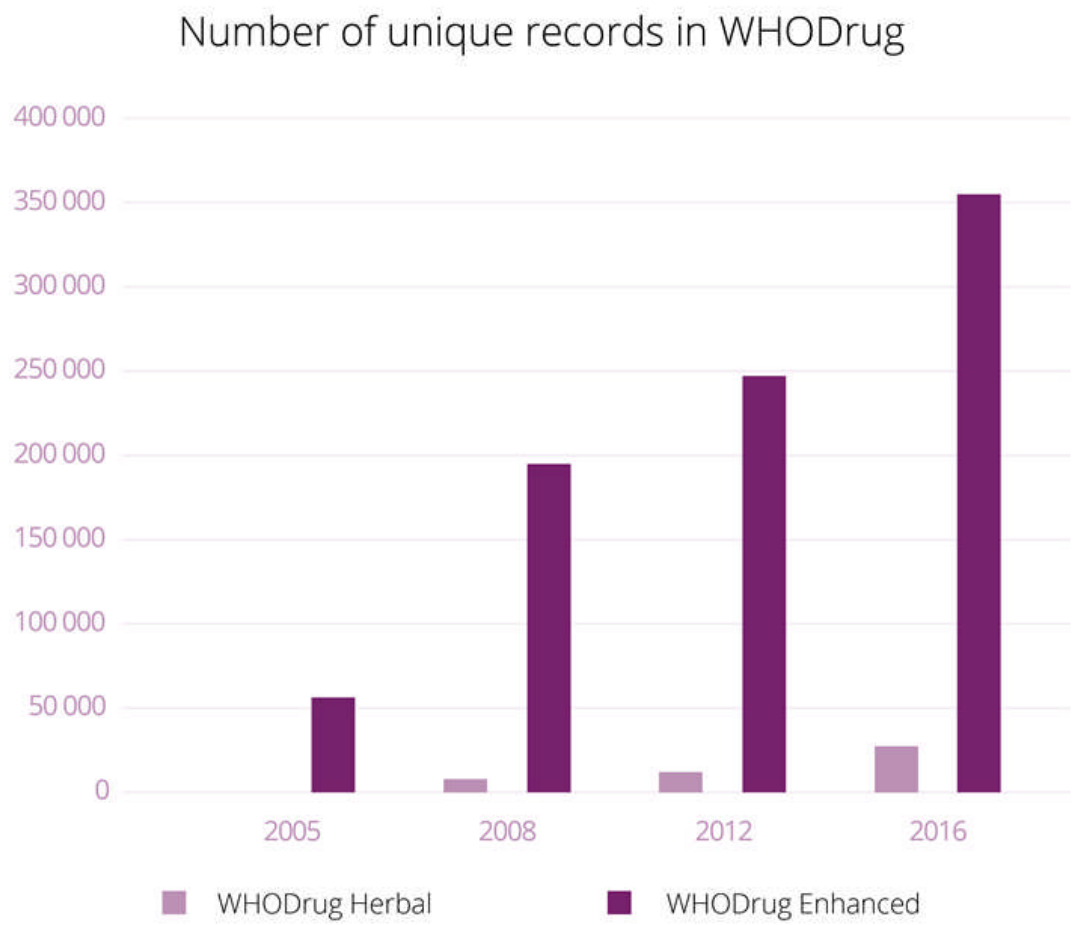
Some background about the WHODrug Dictionary (1)

- The WHODrug Dictionary is an international classification of medicines created by the WHO program for International Drug Monitoring and managed by the Uppsala Monitoring Centre (UMC)
- Created in 1968 and regularly updated
- Since 2005 there have been major developments in the forms of
  - WHO Drug Dictionary Enhanced
  - WHO Herbal Dictionary (covers traditional and herbal medicines)
- From 2017, WHODrug Enhanced will also include all records previously found in WHODrug Herbal

Some background about the WHODrug Dictionary (2)

- Regulators around the world (FDA, PMDA, EMA) recommend using WHODrug Enhanced Dictionary
- WHODrug Enhanced…
  - …is an unique hierarchical drug-code system
  - …contains exact terminology
  - …helps to identify product names
  - …lists active ingredients
- WHODrug delivers the preferred term/name for a medication
- WHODrug uses the Anatomical Therapeutic Chemical (ATC) classification system

Some background about the WHODrug Dictionary (3)



ATC Classification System (1)

- ATC is used for the classification of active ingredients of drugs according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties

- ATC contains 5 level:
  - First level indicates the anatomical main group (there are 14 groups)
  - Second level of the code indicates the therapeutic main group
  - Third level indicates the therapeutic/pharmacological subgroup
  - Fourth level indicates the chemical/therapeutic/pharmacological subgroup
  - Fifth level of the code indicates the chemical substance

ATC Classification System (2)

- Structure of an ATC code:
  - first level consists of one letter, e.g. “C” for Cardiovascular system
  - second level consists of two digits, e.g. “C03” for Diuretics
  - third level consists of one letter, e.g. “C03C” for High-ceiling diuretics
  - fourth level consists of one letter, e.g. “C03CA” for Sulfonamides
  - fifth level consists of two digits, e.g. “C03CA01” for Furosemide
- But: there may be different codes for the same drug available when it is used for a different purpose, route or dosing:
  - Acetylsalicylic acid code is “B01AC06” as platelet aggregation inhibitor
  - …and “A01AD05” as a drug for local oral treatment (stomatology)
  - …and “N02BA01” being used as pain killer

ATC Classification System (3)

- List of first level codes:

Code	Contents
A	Alimentary tract and metabolism
B	Blood and blood forming organs
C	Cardiovascular system
D	Dermatologicals
G	Genito-urinary system and sex hormones
H	Systemic hormonal preparations, excluding sex hormones and insulins
J	Antiinfectives for systemic use
L	Antineoplastic and immunomodulating agents
M	Musculo-skeletal system
N	Nervous system
P	Antiparasitic products, insecticides and repellents
R	Respiratory system
S	Sensory organs
V	Various

ATC Classification System (4)

- In the coding process these levels are known as ATC 1 to 5, where in clinical studies normally for coding only ATC level 1 to 4 is used

- Typically only one ATC level is used for the analysis of a clinical study – mostly ATC 4 information

What will change with the new WHODrug version

What will change with the new WHODrug version (1)

- Due to regulatory updates the UMC will update the standard
  - There is an updated guideline from the WHO Collaboration Centre for Drug Statistics Methodology
  - This complies with EMA regulatory requirements about the "Data submission on medicines (Article 57)" which will change from "Eudra Vigilance Product Report Message" (XEVPRM) format to the "Substance, Product, Organisation and Referential" (SPOR) data format
- Update is planned to be implemented in second half of 2017
- Therefore the ATC 5 level is now in place - to be on the most specified level as requested by the EMA

What will change with the new WHODrug version (2)

- The most important concomitant medication information that can be retrieved from WHODrug is CMDECOD, CMCLAS and CMCLASCD
- WHODrug comes in different formats
  - B2-format has a character limitation of 45 for the preferred term
  - C-format has a character limitation of 80 for the preferred term
- Adding the ingredient list of ATC 5 into the preferred term might cause truncation
- The new B3- and C3-formats will resolve this problem by using a character limitation of 1500
  - New formats are going to be released in March 2017

What will change with the new WHODrug version (3)

- To obtain the generic names without truncation a workaround is needed:

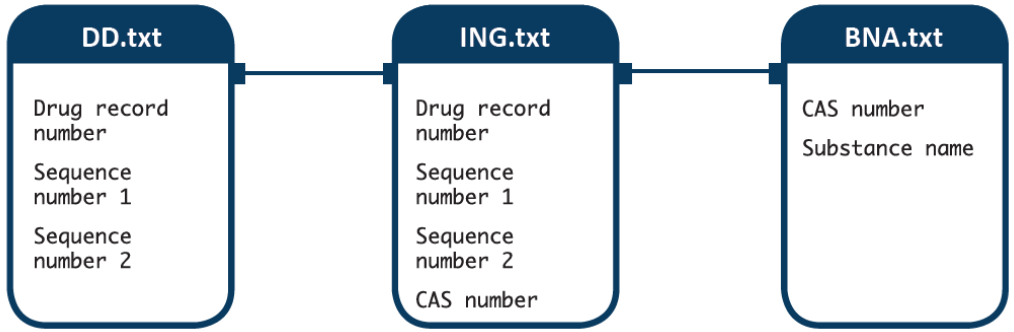


Figure 2. The linkage between drug name and generic name in WHODrug B2-format.

Drug Record Number, Sequence Number 1 and Sequence Number 2 together constitute the drug code.

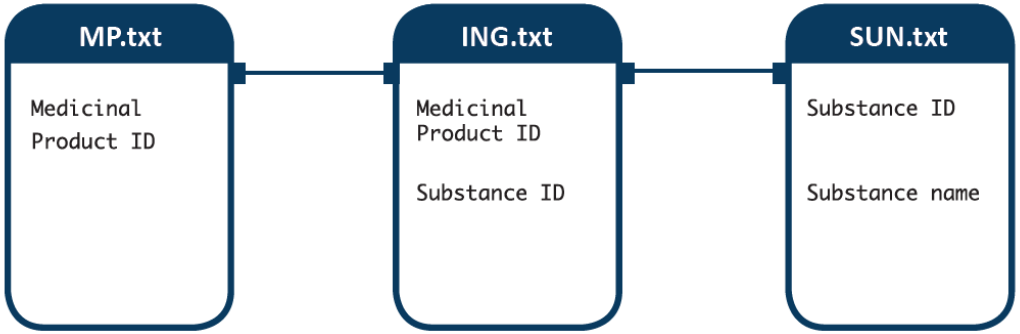


Figure 4. The linkage between drug name and generic name in WHODrug C-format.

Drug Record Number, Sequence Number 1 and Sequence Number 2 together constitute the drug code.

What will change with the new WHODrug version (4)

- The B3- and C3-formats are designed to remove the workaround
- To obtain the generic name in the B3- and C3-formats, simply use the preferred drug name from drug name field in DD.txt or MP.txt, depending on format used

How this will impact SDTM

How this will impact SDTM (1)

- In SDTM there exists several variables to store CM information:

CMTRT	Verbatim medication name that is either pre-printed or collected on a CRF.
CMMODIFY	If CMTRT is modified to facilitate coding, then CMMODIFY will contain the modified text.
CMDECOD	Standardized or dictionary-derived text description of CMTRT or CMMODIFY. Equivalent to the generic medication name in WHO Drug. The sponsor is expected to provide the dictionary name and version used to map the terms utilizing the define.xml external code list attributes. If an intervention term does not have a decode value in the dictionary then CMDECOD will be left blank.
CMCLAS	Drug class. May be obtained from coding. When coding to a single class, populate with class value. If using a dictionary and coding to multiple classes, then follow assumption 4.1.2.8.3 or omit CMCLAS.
CMCLASCD	Class code corresponding to CMCLAS. Drug class. May be obtained from coding. When coding to a single class, populate with class code. If using a dictionary and coding to multiple classes, then follow assumption 4.1.2.8.3 or omit CMCLAS.

How this will impact SDTM (2)

- CMDECOD can now be longer than 200 characters
  - For drugs with many ingredients, the generic name may be longer than 200 characters
  - Use the normal approach to store text that is longer as 200 characters in the SUPPCM
  - The text should be truncated between words, in the case of long generic names the text should be truncated after the semicolon closest to 200 characters

How this will impact SDTM (3)

Table 1. Illustration of SDTM dataset where CMDECOD is longer than 200 characters.

USUBJID	CMSEQ	CMTRT	CMMODIFY	CMDECOD	CMCLAS	CMCLASCD
AB-21-01	1	....	...	Ascorbic acid w;Biotin;Calcium;Carb ohydrates nos;Chloride;Choline;Chr mium;Colecalciferol;Copper;Cyanoco balamin;Docosahexaenoic acid;Fats nos;Folic acid;Fructooligosaccha rides;Iodine;Iron;Magnesium;	....	....

Table 2. Illustration of supplemental dataset for CM domain where CMDECOD is longer than 200 characters.

USUBJID	RDOMAIN	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
AB-21-01	CM	CMSEQ	1	Standardized Medication Name 1	Standardized Medication Name 1	nganese;Nicotinic acid;Panto thenic acid;Phosphorus;Phytom enadione;Potassium;Proteins nos;Pyridoxine;Retinol;Ribo flavin;Selenium;Sodium;Thi amine;Vitamin e nos;Zinc

How this will impact SDTM (4)

- CMCLAS and CMCLASCD are used to store the ATC classification
  - The ATC codes themselves shouldn't be a problem, but maybe for CMCLASCD having a term that is longer than 200 characters

- WHODrug suggests two different ways of submitting ATC information:
  - 1. One single class selected
  - 2. Multiple classes selected

How this will impact SDTM (5)

- Single class ATC code
  - This should be used when the single ATC code must be manually selected based on information available on the CRF from the investigator
  - It is not recommended to randomly select one ATC code, for example to choose the first or last of ATC codes in the list

Table 2. Illustration of SDTM dataset where single class ATC code is used.

USUBJID	CMTRT	CMMODIFY	CMDECOD	CMCLAS	CMCLASCD
AB-21-01	Asprina 03	Aspirina 03	Acetylsalicylic acid; Aluminium glycinate; Magnesium hydroxide	B01AC	Platelet aggregation inhibitors excl. heparin

How this will impact SDTM (6)

- Multiple classes ATC code
  - Using multiple classes is equivalent to submitting all ATC codes available for a specific drug name
  - Some drugs have one ATC code only and in these cases the single ATC code structure should be used

Table 3. Illustration of ordinary dataset where multiple classes ATC code is used. Aspirina 03 has several ATC codes in WHODrug and Tylenol has one ATC code.

USUBJID	CMSEQ	CMTRT	CMMODIFY	CMDECOD	CMCLAS	CMCLASCD
AB-21-01	1	Asprina 03		Acetylsalicylic acid; Aluminium glycinate; Magnesium hydroxide	MULTIPLE	MULTIPLE
AB-21-01	2	Tylenol (actaminophen)	Tylenol	Paracetamol	Anilides	N02BE

How this will impact SDTM (7)

Table 4. Illustration of supplemental dataset for CM domain where the decode for Aspirina 03 has several ATC codes.

USUBJID	RDOMAIN	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
AB-21-01	CM	CMSEQ	1	CMCLAS1	Medication Class 1	Platelet aggregation inhibitors excl. heparin
AB-21-01	CM	CMSEQ	1	CMCLSCD1	Medication Class Code 1	B01AC
AB-21-01	CM	CMSEQ	1	CMCLAS2	Medication Class 2	Salicylic acid and derivatives
AB-21-01	CM	CMSEQ	1	CMCLSCD2	Medication Class Code 2	N02BA
AB-21-01	CM	CMSEQ	1	CMCLAS3	Medication Class 3	Other agents for local oral treatment
AB-21-01	CM	CMSEQ	1	CMCLSCD3	Medication Class Code 3	A01AD

Thank you