Processes and Approaches for Using the ATC Classification Systems and Non-Unique Drug Names for Classifying Drugs

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Agenda

- The ATC classification system
  - How to utilize ATC classification in Drug Safety and Clinical Trials

- Non-Unique Drug Names
  - Challenges for coding, autocoding, dictionary versioning
  - How to select the best match from the multiple non-unique drug names

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Background

- The WHO Collaboration Centre for international Drug Monitoring, the Uppsala Monitoring Centre (UMC) has been responsible for the WHO Programme since 1978

- The WHO Drug Dictionary was developed for coding medicinal products within the WHO International Programme for Drug Monitoring in 1968.

- The WHO Drug Dictionary incorporates other international standards:
  - WHO INN for substance names
  - WHO ATC for classification of drug use
  - WHO Herbal ATC and nomenclature for herbal products and substances

ATC Classification Main Groups

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

Principal for ATC classifications

- Basic principle: Medicinal products are classified according to **the main therapeutic use** of **main active ingredient**

ATC Structure

- LEVEL 1: Main Group
  A ALIMENTARY TRACT AND METABOLISM
- LEVEL 2: Therapeutic Subgroup
  A02 DRUGS FOR ACID RELATED DISORDERS
- LEVEL 3: Chemical/Pharmacological/Therapeutic subgroups
  A02B DRUGS FOR PEPTIC ULCER AND GORD
- LEVEL 4: Chemical/Pharmacological/Therapeutic subgroups
  A02BC Proton pump inhibitors
- LEVEL 5: Chemical Substance
  A02BC01 Omeprazole

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Use of the ATC system in the WHO Drug Dictionaries

- Purpose of introducing ATC into WHO Drug is to automatically provide high level information about the drug name. Analysis, aggregation of statistics
  - To identify interactions
- Understanding of the use of a product
  - E.g. compare with indication when coding concomitant medication with non-unique names.

More than One ATC Code Per Drug

- Each drug has a minimum of ATC codes, often only one

- Drugs can be used for several indications and it's sometimes difficult to know why a drug was prescribed or used

- There is no "Primary ATC code"

ATC Structure - Multiaxiality

- LEVEL 1: Main Group
  C **CARDIOVASCULAR SYSTEM**
  N **NERVOUS SYSTEM**

- LEVEL 2: Therapeutic Subgroup
  C02 **ANTIHYPERTENSIVES**
  N02 **ANALGESICS**

- LEVEL 3: Chemical/Pharmacological/Therapeutic subgroups
  C02A **ANTIADRENERGIC AGENTS, CENTRALLY ACTING**
  N02C **ANTIMIGRAINE PREPARATIONS**

- LEVEL 4: Chemical/Pharmacological/Therapeutic subgroups
  C02AC **Imidazoline receptor agonists**
  N02CX **Other antimigraine preparations**

- LEVEL 5: Chemical Substance
  C02AC01 **Clonidine**
  N02CX02 **Clonidine**

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Non-Unique Drug Names Background

- Currently there are ~200,000 entries total in WHODDE B-2
  - ~160,000 of the entries are unique drug names that correspond to the same ingredient(s)
  - ~37,000 entries are non-unique names or same name entries
    - The drug code is added to the name in order to make the name field unique
    - 16,000 drugs with non-unique drug names

      ~8% of the drugs, but many very common drugs

- This does not optimize the use of TMS for coding and presents problems for autocoding and dictionary versioning

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TMS WHODrug Forum

- Members and Co-Chairs from the TMS focus group, representatives from the WHO-UMC and DBMS Consulting

- Our objective is to provide TMS users who have implemented the WHODrug dictionary with options to better manage the issue of non-unique drug names when:
  - Installing and versioning the WHODrug dictionary
  - Autocoding
  - Classifying
  - Searching for and selecting the best match

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Drug Names That Can Autocode

- TROMBYL: ‘Normal entries’
- A preferred name that also appears in trade names with variations of the ingredients and salts:

  AMPICILLIN
  AMPICILLIN /00000502/
  AMPICILLIN /00000503/

- A verbatim like ‘Ampicillin’ should autocode to the preferred name entry, not to a trade name.

- There are approximately 800 drugs with preferred name entries that fall into this category.

Trade Names That Cannot Autocode

ACTRON	/00020001/
ACTRON	/00109201/
ACTRON	/00321701/
ACTRON	/00391201/
ACTRON	/00727101/

Trade Names That Cannot Autocode

Drug Name	Name Specifier	Drug Code	MaHolder	Country	Ingredients
Actron		003912 01 026	Bayer	France	Acetylsalicylic acid Caffeine Paracetamol
Actron		001092 01 461	Bayer	Mexico	Ibuprofen
Actron		003217 01 053	Bayer	United States	Ketoprofen
Actron		000200 01 158	Bayer	Spain	Paracetamol
Actron	/Old form/	007271 01 001	Miles Martin	Spain	Acetylsalicylic acid Caffeine Citric acid Paracetamol Sodium bicarbonate

Issues

- **Coding Issues:** ~15,000 of the WHODD names are non-unique
- **Autocoding Issues:** Non-unique names cannot autocode and require further investigation
- **Dictionary Versioning Issues:** More terms are requiring reclassification during the versioning process
- **Additional Issues:** TMS “learning” feature enables the system to automatically code VTAs

Constraints

- Need to balance the accuracy with the coder-friendliness of the WHODrug dictionary
- Coders must code all of the data before study lock; they cannot leave terms uncoded
- WHODrug does not provide the Country or drug form in the B2 format

Assumptions

- Trade names will continue to be added to WHODrug when drugs are developed for different countries
- Drug names are not deleted that are no longer used; if a product is withdrawn, it will still need to remain in the dictionary.
- Non-unique drugs are differentiated by Country and/or drug form and/or ingredients and/or ATC
- Majority of companies using TMS use the WHODrug B2 format, which does not include country or drug form

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Reduce Number of Non-Unique Drugs

- How can we reduce the number of terms requiring classification to the non-unique drug names?

- What guidelines and rules can be established to best load/update WHODrug, to code, and manage the terminology in TMS?

Establish Coding Rules

- Code/Autocode to the preferred name entry like ‘Ampicillin’, if a PN is available
- Code/Autocode to the base substance
- Collect the Generic name
- Code/Autocode to the term without salt in the case of drug names that are non-unique due to the salt variation like ‘Prilosec – Omeprazole’, which is a single substance with chemical variation with Minor therapeutic difference
    - Omeprazole (without salt)
    - Omeprazole magnesium (salt)

Coding When the Coding Rules Do Not Apply

- How do we select the best match?
- What data would help us classify the non-unique drug name to the correct dictionary term?
- What is the least common denominator?
- How can we provide the additional information when:
  - Collecting the VT?
  - Autocoding the VT?
  - Manually coding?
- Can additional data be included in or with the VT?

Differentiators

- **Ingredients:** If you have ingredients, don't need to go further.
- **Country:** If you have a drug name in several forms, identify what country they come from.
- **Drug Form:** There are cases where you have multiple drug forms in one country
- **Indication:** If you have the indication information, it can be used to identify ATC terms and can be used to identify some better matches.

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Coding Using Country

- **Questions:**
  - Can the country or form be captured on the CRF?
  - Can you accurately use the country of the site to establish the country where the drug is produced?
- **Advantage:**
  - Allows you to select the best match by geographic region
- **Disadvantage:**
  - Additional information may not be available or limited.
  - Need multiple domains if the country is not part of the VT
  - WHODrug does not include country information in the B2 Format

Coding Using Ingredient

- **Questions:**
  - Can you collect the active ingredients?
- **Advantage:**
  - Allows you to select the best match by ingredient without having to look further
- **Disadvantage:**
  - Data managers need to limit the number of queries to sites
  - The patient does not usually know the ingredients
  - The investigator may not have this information either

Coding Using Drug Form & Indication

Drug Form

- **Advantage:**
  - Allows you to select the best match by drug form alone or in combination with country
- **Disadvantage:**
  - WHODrug does not include drug form information in the B2 Format

Indication

- **Advantage:**
  - If you have the indication information, it can be used to identify ATC and can be used to identify some better matches
- **Disadvantage:**
  - VTs don't normally include the indication, although some TMS user combine this with the VT in a derivation procedure for coding (VT + Route + Indication)

Possible Options

- Use a similar algorithm for WHODrug Format C format loading for B2.
  - Requires establishing domain VTA rules for each of the multiple sets of Drug Recnums
  - Drug Names could be defaulted based on country or Preferred Name derivation
  - Create Global VTAs where a single drug exists with a Drug Code appended if the WHODD Type is being used.

- If the goal of coding is ONLY to derive Preferred Names and NOT ATCs, then it is possible to create a Global VTA if all the Preferred Names are the same, even if the Drug Recnums are different

- Possible enhancements to TMS to allow “single” VTA coding (formerly called VTI functionality), which is similar to HLC at the VT coding level instead

- Derive a specific match based on Site/Investigator/Patient location or country, and use this in a derived question or Search Object.

TMS WHODrug Users' Needs

- Be able to identify which non-unique drug name is the most recent and current entry
- Identify what distinguishes the non-unique drug names from each other on a drug name basis
- Collect the country, formulation, ingredients, or indication with the source VT
- Use the country, formulation, ingredients, or indication combined with the VT during classification
- Be able to view the country, formulation, ingredients, or indication information in the classification and approval screens when selecting the correct non-unique drug name
- Flag a preferred match for drug names with salt variations
- Avoid using multiple domains
- Increase the autocoding hit rate
- Reduce the number of terms that require re-coding after dictionary versioning

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Wednesday, 10 October
10:30am – noon
Session 26 – TMS WHODrug Forum

- Discuss optimized processes to manually code, autocode, and version the dictionary for non-unique drug names
- Analyze how we can:
  - Implement technical or terminology changes
  - Work together on acceptable work-around alternatives

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