Uppsala Monitoring Centre

How to use the WHODrug C3 format for drug coding

Version 2.0

Content

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Version history

Date	Version	Summary of revisions
January 2023	**2.0**	General updates: Sections numbered; Illustrative tables for coding scenarios examples added to several sections Section 1.1 (Scope of the guidelines) Updated and clarified text Section 1.2 (About WHODrug Global) Title updated Section 2.1 (Code as accurately as possible) Example 3 added Section 2.2 (Code to the most detailed level) Updated and clarified text; Example 1 added Section 2.4 (Quality review of the coded data) New section added Section 2.5 (Drug coding decision flow) Some text transferred to section 2.2; Example 6 changed. Section 2.6.2 (Use of country as a differentiator) Updated and clarified text Section 2.8 (Missing drug in WHODrug) Updated and clarified text; Example 9 added Section 3.1 (Generic medicinal products) Example 11 added Section 3.2 (Company codes) New section added Section 3.3 (Combinations of active ingredients) New section added Section 3.4 (An active ingredient is reported in a language not captured in WHODrug) Updated and clarified text Section 3.5 (Medicinal products no longer on the market) New section added Section 3.6 (Trade names with special characters) New section added

Disclaimer

This document is intended to illustrate the best practices for coding drug information to WHODrug C3 format in the context of pharmacovigilance obligations and/or recommendations. Ultimately regulators will decide on the extent of implementation of such guidance within their jurisdiction. Uppsala Monitoring Centre (UMC) acknowledges that regulatory needs may vary depending on the region. This document alone does not stipulate any regulatory reporting requirements; these are determined by the national regulatory authority.

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Introduction

Scope of the guideline

The scope of this document is to recommend best practices when coding drug information with WHODrug Global C3 format, to achieve accurate and consistent medicinal product selection. Best practices in this document can be applied when coding suspect, interacting, concomitant, drug not administered, and historical medications.

This document does not constitute an in-depth description of WHODrug Global structure and content, and users are therefore recommended to undertake WHODrug training and to read the WHODrug User guide, both available via the UMC website.

About WHODrug Global

WHODrug is a comprehensive and actively used drug reference dictionary with a unique hierarchical system and standardised data. Once drug information is coded to WHODrug, a common and standardized language is enabled that allows data exchange with regulatory entities, promoting meaningful and effective aggregation of reported terms to facilitate analysis of safety data. The WHODrug structure enables aggregation on different levels which includes, but is not limited to, the following: active moieties, trade names, strengths, pharmaceutical forms, and ATC classes.

WHODrug is distributed in two formats, the B3 format and the C3 format. The C3 format contains Drug codes, drug names, ingredients (excluding excipients), ATC classifications, countries in which the drugs are marketed, Marketing Authorisation Holders (MAH), pharmaceutical forms, and strengths. The unique identifier for the C3 format is the alphanumeric WHODrug Medicinal Product Identifier (WHODrug MPID), while the Drug code can be used for data aggregation. More information about the content and structure of WHODrug can be found in the WHODrug User guide, available via the UMC website.

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General Coding principles

Code as accurately as possible

UMC recommends selecting the WHODrug record that corresponds most closely to the reported drug verbatim term.

Example 1. If the brand name Artrenac is reported as the verbatim, it should be coded to the brand name Artrenac in WHODrug.

Reported	Selected WHODrug record (MPID)
Artrenac Reporting Country unknown	Artrenac (103243)

Example 2. If the active ingredient Diclofenac sodium is reported as the verbatim, it should be coded to the active ingredient Diclofenac sodium in WHODrug.

Reported	Selected WHODrug record
Diclofenac sodium	Diclofenac sodium (24858)

Code to the most detailed level

Drugs in the WHODrug C3 format are presented in an information system with different levels of precision. Each information level is uniquely identified by the WHODrug MPID.

The information levels follow a hierarchy as shown in the tables below. All records represent the same medicinal product but with different levels of information. The least specific represents the active ingredients, whereas the most specific record also includes information about the country in which the drug is marketed, Market Authorisation Holder (MAH), pharmaceutical form, and strength. For an example of the different information levels, see Table 1.

Table 1. Information level hierarchy for the medicinal product with drug name: Alvedon and active ingredient: Paracetamol

WHODrug MPID	Drug name	Active ingredient	Country	MAH	Pharmaceutical form	Strength	Generic
87552	Alvedon	Paracetamol					No
1224867	Alvedon	Paracetamol	Sweden				No
1156072	Alvedon	Paracetamol	Sweden	AstraZeneca			No
1156071	Alvedon	Paracetamol	Sweden	AstraZeneca	Tablets		No
1156070	Alvedon	Paracetamol	Sweden	AstraZeneca	Tablets	500 mg	No

Active ingredient records are flagged as generic and do not include information about country, MAH, pharmaceutical form and strength (Table 2).

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Table 2. Information level hierarchy for the active ingredient with drug name: Paracetamol

WHODrug MPID	Drug name	Active ingredient	Country	MAH	Pharmaceutical form	Strength	Generic
4762	Paracetamol	Paracetamol					Yes

UMC recommends to code to the most detailed level possible by using all the reported information available at the time of coding. The contextual drug information provided, along with the reported drug name, could be used to select the most accurate and detailed record available in WHODrug.

Information available may for example include country, MAH, indication of use, route of administration, pharmaceutical form, strength, or intended site of administration. See section "How to utilize contextual information".

Example 3. Examples of reported drug information and selected WHODrug records.

Reported Information	Selected WHODrug record					
	WHODrug MPID	Drug Name	Active Ingredient	Country	MAH	Generic
Diclofenac sodium	24858	Diclofenac sodium	Diclofenac sodium			Yes
Diclofenac sodium, reported from Country Latvia, marketed by Kalcex Latvia	247041	Diclofenac sodium	Diclofenac sodium	Latvia	Kalcex Latvia	No
Artrenac, reported from Country Mexico	1259696	Artrenac	Diclofenac sodium	Mexico		No

Code to the most recent version of WHODrug

For WHODrug coding, it is recommended to use either WHODrug's upcoming data or the most recent version of WHODrug to ensure the most up-to-date coding. WHODrug upcoming data reflects how the dictionary would look like if released today. This data is updated on a daily basis and may be subject to change at any time until the data lock point prior to next release. Using the most recent version is especially important in safety coding since post-marketing cases often concern drugs that are new to the market.

Quality review of the coded data

Drug coded data, either manually or by automation, should be reviewed by a qualified individual, i.e., a person with medical and/or pharmaceutical background or training who has also received WHODrug training.

Drug coding decision flow

The WHODrug C3 format hierarchy enables the selection of records with different levels of information, depending on the amount of information reported. Detailed information about the reported drug is not always entered. If only the trade name and ingredient are available, a less specific record can be selected. When more detailed information, such as country and pharmaceutical form are available, the information levels make it possible to select a record with higher precision (Figure 1).

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- *Are medicinal product name, country, MAH, pharmaceutical form, and strength reported?* Code to the most detailed level record that specifies drug name, country, MAH, pharmaceutical form and strength.
- *Are medicinal product name, country, MAH, and pharmaceutical form reported?* Code to the record that specifies drug name, country, MAH and pharmaceutical form.
- *Are medicinal product name, country, and MAH reported?* Code to the record that specifies drug name, country, and MAH.
- *Are medicinal product name and country reported?* Code to the record that specifies drug name and country.
- *Is medicinal product name reported?* Code to the least specific record drug name.
- *Is active ingredient reported?* Code to the active ingredient record.

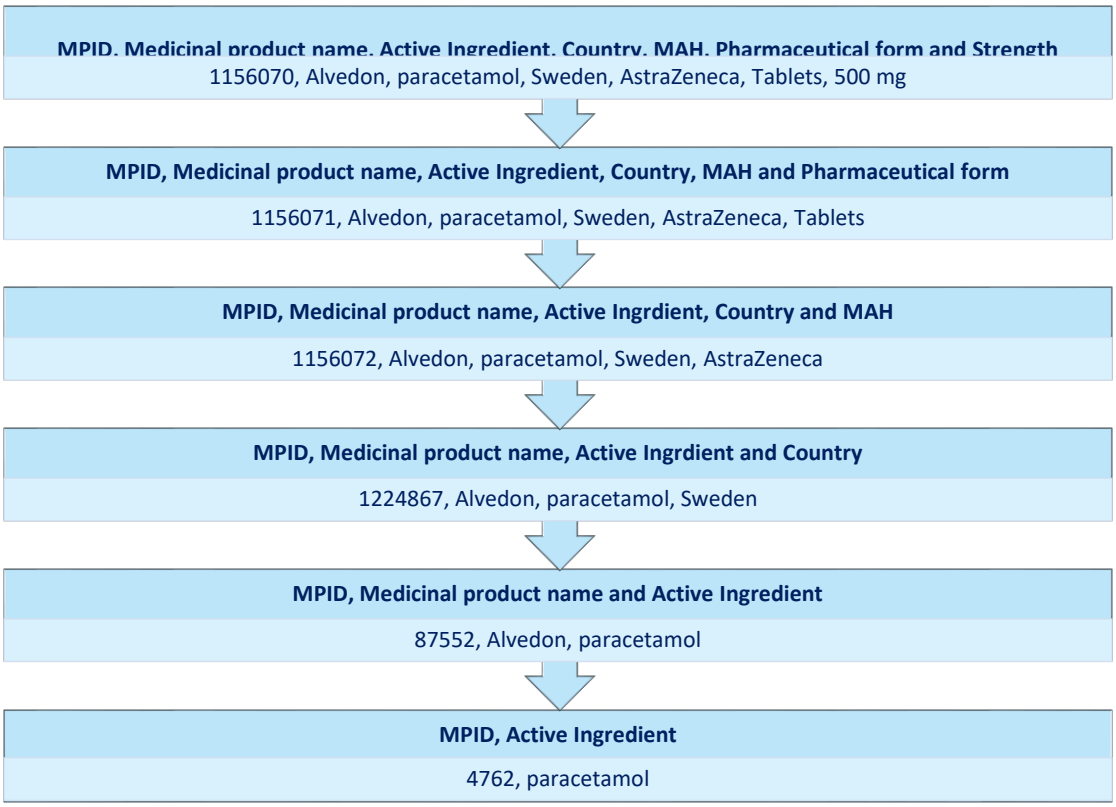

Figure 1. Example of a drug coding decision flow.

Strengths and pharmaceutical forms are information that are connected in the C3 format to a specific medicinal product marketed by a specific MAH. For this reason, it is not possible to code to a level that captures a drug name and a strength, or a drug name and pharmaceutical form, without knowing the MAH, or to code to a level that captures a drug name and MAH, without knowing the country. In these instances, a WHODrug MPID can be selected for the less specific medicinal product name while using the other information to populate available structured data fields.

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Example 4. If Alvedon tablets 500 mg is reported but information about the MAH is missing, the less specific record Alvedon (87552) should be chosen in WHODrug.

Reported	Selected WHODrug record (MPID)
Alvedon 500 mg tablet	Alvedon (87552)

Example 5. If Alvedon tablets from AstraZeneca are reported but information about the country is missing, the less specific record Alvedon (87552) should be chosen in WHODrug.

Reported	Selected WHODrug record (MPID)
Alvedon AstraZeneca	Alvedon (87552)

Example 6. If Paracetamol 500 mg tablet is reported, it should be coded to the active ingredient Paracetamol (4762), flagged as generic in WHODrug, and reported 500 mg separately, unless information about trade name and MAH can be retrieved.

Reported	Selected WHODrug record (MPID)
Paracetamol 500 mg tablet	Paracetamol (4762)

How to use contextual information

The most detailed medicinal product level should be selected when coding by using all the reported information available. The information needed to choose a more precise drug level in WHODrug may be taken from the drug verbatim or based on contextual information. Contextual information provided in the report, such as indication of use, route of administration, pharmaceutical form, dose or strength, could be used to select the most accurate and detailed record as possible in WHODrug (Table 3).

Table 3. Example of contextual information available that can be used to select a more detailed record in WHODrug

Contextual information	Information in WHODrug
Route of administration/dose form	Pharmaceutical form
Additional information in the Drug name	Strength, Pharmaceutical form, etc.

No ingredient reported

In WHODrug, identical drug names may be available with different sets of ingredients, this is what is referred to as non-unique names.

If a drug name is non-unique in WHODrug and no information about an ingredient is available in the report, the drug name alone may not be sufficient to identify the reported term. In this case, there are two possible ways to find the correct record, and achieve the most precise coding:

1. Seek clarification of the ingredient. See section “When to seek clarification”.
2. Make use of the additional information available such as country, MAH, strength, and pharmaceutical form to differentiate between non-unique names.

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Use of country as a differentiator

The country where the patient is located purchased the drug, or other information that gives the coder a suggestion as to where the drug was obtained, is information that can be used to select a more detailed level of information in the dictionary.

One challenge in recent years has been that drugs are sometimes purchased over the internet or in a neighbouring country. In this eventuality, it can be helpful to use other reported drug related information, such as indication of use, MAH, pharmaceutical form, or strength in order to determine whether the drug was bought over the internet or in another country.

When to seek clarification

There may be instances where the drug information reported is either imprecise, ambiguous, or conflicts with other drug related information available in the report. UMC generally recommends seeking clarification in these instances, to achieve the most precise coding.

Example 7. The verbatim term corticosteroid is reported, but a specific corticosteroid could not be selected from WHODrug. In this case it is recommended to seek clarification with the reporter to achieve more precise coding. If it is not possible to retrieve more information, the imprecise record Corticosteroid nos may be selected.

Example 8. The verbatim term Movibon is reported with the indication hypertension. Movibon is marketed in India and contains ibuprofen. In this case it is recommended to seek clarification with the reporter to confirm the drug name and the indication of use.

Missing drug in WHODrug

WHODrug is a standardised medicinal product names dictionary with active moiety-based hierarchies and drug classes. Its content is strictly and solely maintained by Uppsala Monitoring Centre. A WHODrug user with a valid licence can at any time submit a request for a new drug name (a brand name, a company code, etc.) to be added to the dictionary. This can be done in the WHODrug Change Request application.

Some users may be coding to WHODrug's upcoming data, which is updated on a daily basis, while others may be using the most recent released version of WHODrug Global. In the latter case, it is recommended to verify that the drug name does not already exist in the upcoming WHODrug version before submitting a change request.

While waiting for a response about the change request the reported term can either be left uncoded until the approval response has been received or coded to a placeholder.

Example 9. The Medicinal Product Ebvallo has been granted marketing authorization and it will first be included in version of March 1, 2023, of WHODrug Global. If coding the reported verbatim Ebvallo while waiting for the new version to be released, the verbatim may be coded to the active substance as a placeholder.

Reported	Selected WHODrug record (MPID)
Ebvallo	Tabelecleucel (4108787)

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Other points to consider

Generic medicinal products

Generic products are included in WHODrug C3 format in the same way as products with proprietary trade names. Information such as country, MAH, pharmaceutical form and strength is available for these generic products (Tables 4 and 5) and should be coded to the most detailed level possible by using all the reported information available at the time of coding.

Table 4. Information level hierarchy for the medicinal product with drug name: Amlodipino and active ingredient: Amlodipine maleate.

WHODrug MPID	Drug name	Active ingredient	Country	MAH	Pharmaceutical form	Strength	Generic
683126	Amlodipino	Amlodipine maleate					No
2292537	Amlodipino	Amlodipine maleate	Mexico				No
2765813	Amlodipine	Amlodipine maleate	Mexico	Pfizer			No
2765812	Amlodipine	Amlodipine maleate	Mexico	Pfizer	Tablets		No
2765811	Amlodipine	Amlodipine maleate	Mexico	Pfizer	Tablets	5 mg	No

Example 10. If the product Amlodipino marketed by Pfizer is reported from Mexico, it should be coded to the record that specifies drug name, country, and MAH, i.e. Amlodipino (2765813) in WHODrug. In this case, Pfizer is not included in the drug name.

Reported	Selected WHODrug record (MPID)
Amlodipine; Reported from country Mexico; Marketed by Pfizer	Amlodipine (2765813)

Table 5. Information level hierarchy for the medicinal product with drug name: Amlodipine liomont and active ingredient: Amlodipine maleate

WHODrug MPID	Drug name	Active ingredient	Country	MAH	Pharmaceutical form	Strength	Generic
2043454	Amlodipine liomont	Amlodipine maleate					No
2043453	Amlodipine liomont	Amlodipine maleate	Mexico				No
2043452	Amlodipine liomont	Amlodipine maleate	Mexico	Liomont			No
2043451	Amlodipine liomont	Amlodipine maleate	Mexico	Liomont	Tablets		No
2043450	Amlodipine liomont	Amlodipine maleate	Mexico	Liomont	Tablets	5 mg	No

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Example 11. If the product Amlodipine Liomont is reported from Mexico, it should be coded to the record that specifies drug name, country, and MAH, i.e., Amlodipine Liomont (2043452) in WHODrug.

Reported	Selected WHODrug record (MPID)
Amlodipine Liomont; Reported from Country Mexico; Marketed by Liomont	Amlodipine Liomont (2043452)

Company codes

Sometimes an investigational active ingredient is given a company specific name called 'company code' before receiving an official International Non-proprietary Name for Pharmaceutical substances (INN), or similar. These company codes are included in WHODrug as regular active ingredients, with a generic flag, and not linked to a specific country. Company codes are coded as the generic active ingredient record. See Table 6 for an example of a company code drug name.

Table 6. Information level hierarchy for the company code drug name ABBV.

WHODrug MPID	Drug name	Active ingredient	Country	MAH	Pharmaceutical form	Strength	Generic
4874280	ABBV 184	ABBV 184					Yes

Example 12. If the company code ABBV184 is reported as the verbatim, it should be coded to the active ingredient ABBV 184 (4874280) and flagged as generic in WHODrug.

Reported	Selected WHODrug record (MPID)
ABBV-184	ABBV 184 (4874280)

Combinations of active ingredients

Combinations of two (or more) ingredients can be available in WHODrug, as a separate combination record, with a generic flag. The ingredients of the combination are always displayed in alphabetical order, separated by a semicolon. When available, a combination record should always be selected for coding. See Table 7 for the combination example of amoxicillin and clavulanic acid.

Table 7. Information level hierarchy for the active ingredient with drug names: Amoxicillin, Clavulanic acid and Amoxicillin; Clavulanic acid.

WHODrug MPID	Drug name	Active ingredient	Country	MAH	Pharmaceutical form	Strength	Generic
20493	Amoxicillin	Amoxicillin					Yes
33346	Clavulanic acid	Clavulanic acid					Yes
3815525	Amoxicillin; Clavulanic acid	Amoxicillin; Clavulanic acid					Yes

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Example 13. If Amoxicillin and Clavulanic acid is reported as the verbatim, it should be coded to the combination Amoxicillin; Clavulanic acid (3815525) in WHODrug.

Reported	Selected WHODrug record (MPID)
Amoxicillin and Clavulanic acid	Amoxicillin; Clavulanic acid (3815525)

Active ingredients reported in a language not captured in WHODrug

If an active ingredient is reported in a language not captured in WHODrug, a change request can be submitted to UMC. It is also acceptable to code to the closest English active ingredient available in WHODrug as long as the translation to English is not ambiguous.

Medicinal products no longer on the market

Drug names in the dictionary could be marked as old form when no longer marketed. Carefully investigate the reported information and/or utilize contextual information such as the active ingredient to confirm or exclude the selection of an old form WHODrug record.

Example 14. If the product Cortidex is reported from Mexico, it should be coded to Cortidex /old form/ (1316561) in WHODrug.

Reported information	Selected WHODrug record (MPID)
Cortidex Reported from Mexico	Cortidex /old form/ (1316561)

Trade names with special characters

Special characters such as hyphens, as well as trademark, registered trademark, copyright symbols etc. are not included in the trade names in WHODrug to enable drug name harmonization at a global level. When trade names with special characters are reported it is acceptable to code to the corresponding record in WHODrug without special characters.

Example 15. If the trade name ALVI-TEC® is reported, it should be coded to ALVI TEC in WHODrug.

Reported	Selected WHODrug record (MPID)
ALVI-TEC®	ALVI TEC (3820776)

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