# Canadian Clinical Drug Dataset

Work Instructions

|  |  |
| --- | --- |
| Version | 01 – Initial launch |
| Date | 22 June 2018 |
| Previous Version/Date | NA |
| Changes this version | NA |

## Purpose

This Work Instructions document is a supporting document to the Editorial Guidelines for the CCDD. It contains more detail and more explanation for the population of the CCDD, based on different types of products and different therapeutic areas. It should be used to describe patterns of information for various types of products and elaborate on decision processes, particularly for challenging areas where the Team has discussed options and made decisions on which option to follow. Decisions about individual concepts should not be documented in Work Instructions; these should be described in the work relating to those products (e.g. monthly spreadsheets or customer queries).

The Work Instructions also contains directions on how to maintain the various supporting data (in addition to the DPD) that goes into the generation of the CCDD on a monthly basis.

## Audience

This document is for use by the CCDD Authoring and Quality Assurance Team: the medicinal product and terminology subject matter experts that manage the TM, NTP and MP concepts and their descriptors in the CCDD.

It may also be used as a reference by the CCDD Technical Team who undertake the concept generation for the CCDD.

## Relationship to Editorial Guidelines

Sometimes it can be difficult to decide whether to put information into Editorial Guidelines or into Work Instructions. The Editorial Guidelines describe the overall model of the CCDD and the general principles for its population. Work Instructions give more detail on how to apply those general principles in specific product patterns to promote clarity and consistency. They also document when less than ideal solutions must be adopted and have notes for future work to improve those resolutions.

## How to use and maintain these Work Instructions

This is a living document and will grow and develop as the CCDD grows and develops. All those responsible for the authoring and maintenance of the concepts that make up the CCDD are encouraged to use the Work Instructions regularly and to make additions to the document as new situations arise. However, there should be regular review of additions and changes by the whole Team, to increase shared knowledge and understanding.

Additions should be made in red text with the author’s initials and date following the entry. Team review on a monthly or bimonthly basis should discuss and confirm additions, at which point they are changed to the normal text colour and the document up-versioned. [JMJ 19June2018]

It is acceptable to add a placeholder for a topic into the Work Instructions, with or without brief notes and to return to complete the entry at a later point.

# Ingredient Stem Table

The Ingredient Stem Table is maintained in GitHub [location here]. It is a comma separated file (.csv) but can be opened through the GitHub tooling using Excel. There are six columns, as shown below:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ccdd** | **top250name** | **dpd\_ingredient** | **ing\_stem** | **hydrate** | **ntp\_ing** |
| Y |  | ABACAVIR (ABACAVIR SULFATE) | abacavir | FALSE | abacavir (abacavir sulfate) |
|  |  | ABATACEPT | abatacept | FALSE | abatacept |
|  |  | ABCIXIMAB | abciximab | FALSE | abciximab |
|  |  | Abiraterone acetate | abiraterone acetate | FALSE | abiraterone acetate |
|  |  | AbobotulinumtoxinA | abobotulinumtoxina | FALSE | abobotulinumtoxina |
|  |  | ACAMPROSATE CALCIUM | acamprosate calcium | FALSE | acamprosate calcium |
|  |  | ACARBOSE | acarbose | FALSE | acarbose |
| Y | ACEBUTOLOL | ACEBUTOLOL (ACEBUTOLOL HYDROCHLORIDE) | acebutolol | FALSE | acebutolol (acebutolol hydrochloride) |
|  |  | ACENOCOUMAROL | acenocoumarol | FALSE | acenocoumarol |
| Y | ACETAMINOPHEN | ACETAMINOPHEN | acetaminophen | FALSE | acetaminophen |
|  |  | ACETAZOLAMIDE | acetazolamide | FALSE | acetazolamide |
|  |  | ACETAZOLAMIDE (ACETAZOLAMIDE SODIUM) | acetazolamide | FALSE | acetazolamide (acetazolamide sodium) |
|  |  | ACETIC ACID | acetic acid | FALSE | acetic acid |
|  |  | ACETYLCHOLINE CHLORIDE | acetylcholine chloride | FALSE | acetylcholine chloride |
|  |  | ACETYLCYSTEINE | acetylcysteine | FALSE | acetylcysteine |
| Y |  | ACETYLSALICYLIC ACID | acetylsalicylic acid | FALSE | acetylsalicylic acid |
| Y | ACLIDINIUM | Aclidinium bromide | aclidinium | FALSE | aclidinium bromide |
| Y | ACYCLOVIR | ACYCLOVIR | acyclovir | FALSE | acyclovir |
| Y | ACYCLOVIR | ACYCLOVIR (ACYCLOVIR SODIUM) | acyclovir | FALSE | acyclovir (acyclovir sodium) |

# **CCDD** is a flag that is used to identify which TMs will be included in the generation of QA Release files.

**top250name** is the name of the ingredient from the IMS top 250 ingredients that was used for the initial releases of the CCDD. This is not used in the generation of CCDD files

# **dpd\_ingredient** is the name of the ingredient as found in the DPD. When generating the CCDD files, they do a string match to extract ingredients from the DPD so it is important that the name appear exactly as it is captured in the DPD with respect to case sensitivity.

**ing stem** is the name of the TM as it will appear in the CCDD files. It excludes the salts or other modifiers of the ingredient.

**hydrate** is the field that that is used by the generation team to exclude waters of hydration from the ntp formal name. There are two possible values:

TRUE – the DPD name includes waters of hydration and should be excluded from the NTP formal name

FALSE – the DPD name does not include waters of hydration

The waters of hydration will be include in the MP formal name.

ntp\_ing – the name of the ingredient as it will appear in the NTP formal name. The name should include the salts and modifiers but not the waters of hydration.

# NTP Strength Patterns

## Pattern 1: Presentation Strength is the clinically significant strength;

### Variation A:

The unit of presentation is bounded by the basic solid dose form (and draws its name from it). A single (1) unit of presentation is the denominator for the strength of the product, but is not stated explicitly in the strength expression (as it would be repeating the basic dose form part of the dose form concept).

**Used for:** tablets, capsules, pessaries, suppositories…

|  |  |  |
| --- | --- | --- |
| **Example** | **Bendroflumethiazide 5mg oral tablet** | |
| **Unit of Presentation** | The basic solid dose form | e.g. tablet |
| **Presentation strength (logical)** | Mass amount per 1 unit of presentation | 5 mg per tablet |
| **Presentation strength (usual description)** | Mass amount only; the “per” is implicit | mg |
| **Concentration strength (for information only)** | The weight of one finished dose form (including excipients) is rarely known so concentration strength is not usually available  Not deemed of any clinical significance | |

### Variation B:

The unit of presentation contains the solid dose form and is therefore the “intimate container” for it. A single (1) unit of presentation is the denominator for the strength of the product, and **is** stated explicitly in the strength expression as it is not elsewhere present in the formal name.

**Used for:** sachets, ampoules or vials ***containing*** powders or granules (which may or may not undergo transformation before administration)

|  |  |  |
| --- | --- | --- |
| **Example** | **Cefotaxime 2g per vial powder for solution for injection** | |
| **Unit of Presentation** | The “intimate container” | e.g. vial |
| **Presentation strength (logical)** | Mass amount per 1 unit of presentation | 2 g per vial |
| **Presentation strength (usual description)** | Mass amount, with the “per” or explicit | 2 g per vial |
| **Concentration strength (for information only)** | The concentration strength is not usually available (total amount of solid in the intimate container, including excipients not known)  Not deemed of any clinical significance | |

### Variation C:

The unit of presentation is a metered actuation; the volume delivery device effectively “bounds” the dose form that is presented. A single (1) unit of presentation is the denominator for the strength of the product, and **is** stated explicitly in the strength expression as it is not elsewhere present in the formal name.

**Used for:** any NTP product that is presented using a metering delivery system: pressurised inhalers, cutaneous sprays, nasal sprays etc.

|  |  |  |
| --- | --- | --- |
| **Example** | **Beclometasone dipropionate 100 mcg per actuation pressurised inhalation** | |
| **Unit of Presentation** | Actuation | Actuation |
| **Presentation strength (logical)** | Mass amount per 1 unit of presentation | 100 mcg per actuation |
| **Presentation strength (usual description)** | Mass amount, with the “per” or explicit | 100 mcg per actuation |
| **Concentration strength (for information only)** | The concentration of product (usually liquid) inside the metered delivery system may be known (to the regulatory agency) but is  Not deemed of any clinical significance | |

## Pattern 2: Presentation Strength and Concentration Strength are both clinically useful

### Variation A:

Using the unit of presentation describes a clinically useful volume of liquid dose form; the unit of presentation is the “intimate container” for that volume; concentration strength is also known/calculatable. For the presentation strength, the volume of the unit of presentation provides the strength denominator, and the unit of presentation is explicitly described at the end of the product name.

**Used for:** most small volume parenteral liquids, unit dose nebuliser solutions etc.…

|  |  |  |
| --- | --- | --- |
| **Example** | **Metoclopramine hydrochloride 100 mg per 20 mL solution for injection ampoule** | |
| **Unit of Presentation** | The “intimate container” | e.g. ampoule |
| **Presentation strength (logical)** | Mass amount per volume contained in the unit of presentation | 100 mg per 20 mL |
| **Presentation strength (usual description)** | Mass amount per volume the “per” is explicitly stated | 100 mg per 20 mL |
| **Concentration strength** | Mass amount per unitary volume | 5 mg per 1 mL |

**Variation B:** Using the unit of presentation describes a clinically useful volume of liquid dose form; the unit of presentation is the “volume delivery device” for that volume; concentration strength is also known/calculatable. For the presentation strength, the volume of the unit of presentation provides the strength denominator; no further description of the unit of presentation is provided (i.e. “spoon” or “spoonful” is not described).

**Used for:** oral liquids presented specifically for use with a medicine (tea)spoon (5 ml)

|  |  |  |
| --- | --- | --- |
| **Example** | **Aciclovir 200 mg per 5 mL oral suspension** | |
| **Unit of Presentation** | per 5 mL | 5 mL (tea)spoon |
| **Presentation strength (logical)** | Mass amount per volume of 1 unit of presentation | 200 mg per 5 mL |
| **Presentation strength (usual description)** | Mass amount per volume the “per” is explicitly stated | 200 mg per 5 mL |
| **Concentration strength** | Mass amount per unitary volume | 4 mg per 1 mL |

## Pattern 3: Concentration Strength is the clinically significant strength

### Variation A:

The unit of presentation exists but concentration strength is the clinically significant strength; expressing unit of presentation and its size is also clinically useful and is described at the end of the name. It is particularly suitable for presentations where a variable dose quantity likely so the concentration strength is more appropriate to support safe calculation.

**Used for:** bulk parenteral fluids, insulins, transdermal patches (sized UoP not needed but may be quoted in the monograph), bulk (pharmacy) vials of nebuliser solutions or parenteral injections

|  |  |  |
| --- | --- | --- |
| **Example** | **Insulin human soluble 100 unit / mL solution for injection 1.5 mL cartridge** | |
| **Unit of Presentation** | The “intimate container” | Cartridge |
| **Unit of Presentation size** |  | 1.5 mL |
| ***Presentation strength (logical)*** | *Mass amount contained in the unit of presentation* | *150 unit per cartridge* |
| **Presentation strength (usual description)** |  |  |
| **Concentration strength** | Mass amount per unitary volume/time | 100 unit per (1) mL |

|  |  |  |
| --- | --- | --- |
| **Example** | **Estradiol 0.1% transdermal gel 0.5 mg sachet** | |
| **Unit of Presentation** | The “intimate container” | Sachet |
| **Unit of Presentation size** |  | 0.5 mg |
| ***Presentation strength (logical)*** | *Mass amount contained in the unit of presentation* | *0.5 mg per sachet* |
| **Presentation strength (usual description)** |  |  |
| **Concentration strength** | Mass amount per unitary volume/time | 1 mg per 1 g  *Expressed as: 0.1%* |

|  |  |  |
| --- | --- | --- |
| **Example** | **Sodium chloride 0.9% solution for infusion 500 mL bag** | |
| **Unit of Presentation** | The “intimate container” | Bag |
| **Unit of Presentation size** |  | 500 mL |
| ***Presentation strength (logical)*** | *Mass amount contained in the unit of presentation* | *450 mg per 500 mL* |
| **Presentation strength (usual description)** |  |  |
| **Concentration strength** | Mass amount per unitary volume/time | 9 mg per 1 mL  *Expressed as: 0.9% w/v* |

|  |  |  |
| --- | --- | --- |
| **Example** | **salbutamol (salbutamol sulfate) 1 mg per mL nebuliser solution 10 mL bottle** | |
| **Unit of Presentation** | The “intimate container” | Bottle |
| **Unit of Presentation size** |  | 10 mL |
| ***Presentation strength (logical)*** | *Mass amount contained in the unit of presentation* | *10 mg per 10 mL* |
| **Presentation strength (usual description)** |  |  |
| **Concentration strength** | Mass amount per unitary volume/time | 1 mg per 1 mL |

### Variation B:

The unit of presentation exists but concentration strength is the clinically significant strength; expressing unit of presentation is not required as it is implicit from the dose form.

**Used for:** transdermal patches

|  |  |  |
| --- | --- | --- |
| **Example** | **Fentanyl 100 mcg per hour transdermal patch** | |
| **Unit of Presentation** | The “intimate container” | Patch |
| ***Unit of Presentation size*** |  | *32 cm2* |
| ***Presentation strength (logical)*** | *Mass amount contained in the unit of presentation* | *20.4 mg per patch* |
| **Presentation strength (usual description)** |  |  |
| **Concentration strength** | Mass amount per unitary volume/time | 100 mcg per (1) hour |

### Variation C:

No unit of presentation exists, the dose form is “unbounded” (also known as “continuous”)

**Used for:** Used for: “bulk” powders and granules, semi-solids (not metered actuation), liquids not presented with a fixed volume delivery device (i.e. those expected to be measured in drops or in different volumes based on patient need; 0.5mL, 0.8mL etc.)

The bottle or tube or carton that contains the unbounded dose form, even though it could be considered an “intimate container” as it is in direct contact with the dose form, it is in fact the package that the medicinal product is supplied in. The package has no relationship to the amount administered to a patient; it will contain many administrations-worth of medication. It may have no additional packaging with it, although a bottle or tube can be placed inside a carton as further packaging. Information about packaged medicinal products is not within scope of the CCDD.

|  |  |  |
| --- | --- | --- |
| **Example** | **Hydrocortisone 1% cutaneous cream** | |
| **Unit of Presentation** | Does not exist |  |
| ***Presentation strength (logical)*** |  |  |
| ***Presentation strength (usual description)*** |  |  |
| **Concentration strength** | Mass amount per unitary volume/mass | 10 mg per 1 g  *Expressed as: 1 % [w/w]* |

|  |  |  |
| --- | --- | --- |
| **Example** | **Chloramphenicol 0.5% eye drops** | |
| **Unit of Presentation** | Does not exist |  |
| ***Presentation strength (logical)*** |  |  |
| ***Presentation strength (usual description)*** |  |  |
| **Concentration strength** | Mass amount per unitary volume/mass | 5 mg per 1 mL  *Expressed as: 0.5 % [w/v]* |

|  |  |  |
| --- | --- | --- |
| **Example** | **Sterculia 62% oral granules** | |
| **Unit of Presentation** | Does not exist |  |
| ***Presentation strength (logical)*** |  |  |
| ***Presentation strength (usual description)*** |  |  |
| **Concentration strength** | Mass amount per unitary volume/mass | 620 mg per 1 g  *Expressed as: 62 % [w/w]* |

|  |  |  |
| --- | --- | --- |
| **Example** | **Digoxin 50 mcg per 1 mL oral solution** | |
| **Unit of Presentation** | Does not exist |  |
| ***Presentation strength (logical)*** |  |  |
| ***Presentation strength (usual description)*** |  |  |
| **Concentration strength** | Mass amount per unitary volume/mass | 50 mcg per 1 mL |

## Strength Units of Measure

Unfortunately, there is currently no consistency on when to use which unit of measure to describe strength in the DPD (e.g. no rule that “if product strengths less than or equal to 1 mg use microgram strengths”). This means that for any one TM, the related products may use a mixture of strength units. This was clearly evident in the combined oral contraceptives, where one product or group of products might describe the estrogen component as “ethinyl estradiol 0.035 mg” and another as “ethinyl estradiol 35 mcg” [see detail in CCDD Issue document 18].

However, as an interchange terminology, promoting interoperability for ePrescribing, medication profiles and medication reconciliation etc., the CCDD, particularly for the NTP Formal Name, requires consistency of representation of strength within product groups for safety and usability.

The decision for the combined oral contraceptive product group was for “the CCDD NTP Formal Name representation of strength for oral contraceptives to use whole numbers of micrograms rather than the decimal representation of milligrams when appropriate”. But for other products (notably digoxin, clonidine, dutasteride, nitroglycerin, naloxone and tamsulosin) there was consistency within the product group and therefore the “CCDD will continue to use decimals of milligrams to represent the strength of these products until such time as this is changed across the healthcare culture, either by regulatory changes to the product description or by recommendation from safety bodies”.

* The pattern is therefore, if all the products in the product group (i.e. all the products associated to a particular TM) use a single strength representation (gram, milligram, or microgram) in the DPD, the NTPs should also use that strength representation.

Example: TM = exotocillin

|  |  |
| --- | --- |
| **Manufactured Product (in DPD)** | **NTP** |
| EXOCIN 500mg capsule FREDS PHARMA | exotocillin 500 mg oral capsule |
| EXOCIN 250mg capsule FREDS PHARMA | exotocillin 250 mg oral capsule |
| EXOCIN 500mg IV FREDS PHARMA | exotocillin 500 mg per vial powder for solution for injection |
| XCILLIN 250mg Capos DONS DRUGS | exotocillin 250 mg oral capsule |
| XCILLIN 250mg IV INJ DONS DRUGS | exotocillin 250 mg per vial powder for solution for injection |
| XCILLIN 1000mg IV INJ DONS DRUGS | exotocillin 1000 mg per vial powder for solution for injection |
| EXOTOCILLIN 250mg CAPS JOES GENERICS INC | exotocillin 500 mg oral capsule |
| EXOTOCILLIN 500mg CAPS JOES GENERICS INC | exotocillin 250 mg oral capsule |
| EXOTOCILLIN 250mg IV INJ JOES GENERICS INC | exotocillin 250 mg per vial powder for solution for injection |
| EXOTOCILLIN 500mg IV INJ JOES GENERICS INC | exotocillin 500 mg per vial powder for solution for injection |
| EXOTOCILLIN 1000mg IV INJ JOES GENERICS INC | exotocillin 1000 mg per vial powder for solution for injection |

* And, if there is a mixture of strength representations in the DPD, if all the NTPs generate without **duplication**, this is also acceptable.

Example: TM = exotocillin

|  |  |
| --- | --- |
| **Manufactured Product (in DPD)** | **NTP** |
| EXOCIN 500mg capsule FREDS PHARMA | exotocillin 500 mg oral capsule |
| EXOCIN 250mg capsule FREDS PHARMA | exotocillin 250 mg oral capsule |
| EXOCIN 500mg IV FREDS PHARMA | exotocillin 500 mg per vial powder for solution for injection |
| XCILLIN 250mg Capos DONS DRUGS | exotocillin 250 mg oral capsule |
| XCILLIN 250mg IV INJ DONS DRUGS | exotocillin 250 mg per vial powder for solution for injection |
| XCILLIN 1G IV INJ DONS DRUGS | exotocillin 1 g per vial powder for solution for injection |
| EXOTOCILLIN 250mg CAPS JOES GENERICS INC | exotocillin 500 mg oral capsule |
| EXOTOCILLIN 500mg CAPS JOES GENERICS INC | exotocillin 250 mg oral capsule |
| EXOTOCILLIN 250mg IV INJ JOES GENERICS INC | exotocillin 250 mg per vial powder for solution for injection |
| EXOTOCILLIN 500mg IV INJ JOES GENERICS INC | exotocillin 500 mg per vial powder for solution for injection |
| EXOTOCILLIN 1g IV INJ JOES GENERICS INC | exotocillin 1 g per vial powder for solution for injection |

* **BUT**, if there is a mixture of strength representations in the DPD that creates essentially duplicate NTPs, this is not acceptable. There should be a request to the DPD to change the strength description of the outlier product(s) to match the majority; if there is no majority (as in the example below where there are just two products) the strength description should use what is deemed “safest” – which is usually to minimise the use of decimal places and/or the use of zeros (therefore to use “g” in this example rather than the three zeros needed if “mg” is used)

Example: TM = exotocillin

|  |  |
| --- | --- |
| **Manufactured Product (in DPD)** | **NTP** |
| EXOCIN 500mg capsule FREDS PHARMA | exotocillin 500 mg oral capsule |
| EXOCIN 250mg capsule FREDS PHARMA | exotocillin 250 mg oral capsule |
| EXOCIN 500mg IV FREDS PHARMA | exotocillin 500 mg per vial powder for solution for injection |
| XCILLIN 250mg Capos DONS DRUGS | exotocillin 250 mg oral capsule |
| XCILLIN 250mg IV INJ DONS DRUGS | exotocillin 250 mg per vial powder for solution for injection |
| XCILLIN 1G IV INJ DONS DRUGS | exotocillin 1 g per vial powder for solution for injection |
| EXOTOCILLIN 250mg CAPS JOES GENERICS INC | exotocillin 500 mg oral capsule |
| EXOTOCILLIN 500mg CAPS JOES GENERICS INC | exotocillin 250 mg oral capsule |
| EXOTOCILLIN 250mg IV INJ JOES GENERICS INC | exotocillin 250 mg per vial powder for solution for injection |
| EXOTOCILLIN 500mg IV INJ JOES GENERICS INC | exotocillin 500 mg per vial powder for solution for injection |
| EXOTOCILLIN 1000mg IV INJ JOES GENERICS INC | exotocillin 1000 mg per vial powder for solution for injection |

The DPD Team should be requested to change “EXOTOCILLIN 1000mg IV INJ JOES GENERICS INC” to a strength description of 1 g.

# Unit of Presentation Table (UoP Table)

## Purpose

The UoP Table provides a data input into the CCDD generation to add information about the intimate container into the NTP formal name in cases where that does not generate automatically from the data in the DPD. It is also used to support the calculation of presentation strength when that is required and the DPD uses concentration strength.

## Unit of Presentation Table Details

The UoP Table is maintained in GitHub [location here]. It is a comma separated file (.csv) but can be opened through the GitHub tooling using Excel. The UoP table does not have codes with leading zeros, so does not suffer from the Excel habit of trying to change text strings containing numbers into integers, thereby losing leading zeros.

There are six columns, as shown below:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **drug\_code** | **unit\_of\_presentation** | **uop\_size** | **uop\_unit\_of\_measure** | **calculation** | **uop\_size\_insert** |
| 69790 | vial | 10 | mL | N | Y |
| 73683 | cartridge | 3 | mL | N | Y |
| 93005 | cartridge | 3 | mL | N | Y |
| 77967 | pen | 3 | mL | N | Y |
| 93006 | pen | 3 | mL | N | Y |
| 71180 | vial | 3 | mL | Y | N |
| 66036 | vial | 3 | mL | Y | N |
| 86000 | syringe | 3 | mL | Y | N |
| 66036 | vial | 9 | mL | Y | N |
| 71180 | vial | 18 | mL | Y | N |
| 66036 | vial | 18 | mL | Y | N |
| 69271 | vial | 3 | mL | Y | N |
| 19798 | unit dose vial | 1 | mL | Y | N |
| 19798 | unit dose vial | 2 | mL | Y | N |
| 50443 | bottle | 20 | mL | N | Y |
| 50551 | unit dose vial | 1 | mL | Y | N |
| 50552 | unit dose vial | 2 | mL | Y | N |
| 43176 | unit dose vial | 1 | mL | Y | N |
| 43176 | unit dose vial | 2 | mL | Y | N |
| 62586 | bottle | 20 | mL | N | Y |

**drug\_code** is the DPD code for the DIN; it is the “primary key” for the product in the DPD database. The drug\_code for the product is usually available in the QA spreadsheets; if not it can be found using a DPD database query or obtained from the DPD Team (Louise).

**unit\_of\_presentation** is a text string for the unit of presentation for the product. Note: this is a text string for each row of data; it is not a coded data item so check carefully for typos (all lower case). Unit of presentation concepts are:

* ampoule
* bag
* bottle
* cartridge
* pen
* sachet
* syringe
* tube
* unit dose ampoule
* unit dose vial
* vial

**uop\_size** is the value of the size of the unit of presentation; this should always be entered in the table even if it is not used in calculation

**uop\_unit\_of\_measure** is the unit of measure for the uop\_size expressed using a formal abbreviation; usually mL, occasionally g or mg

**calculation** is a Boolean flag (Y or N); Y indicates that the CCDD generation process should take the strength as expressed in DPD and use the uop\_size value to as a multiplier for calculation of presentation strength and it will use the uop\_size and uop\_unit\_of\_measure to provide the denominator for the presentation strength. If no calculation is required, the flag should be set to N

**uop\_size\_insert** is a Boolean flag (Y or N); Y indicates that the CCDD generation process should take the uop\_size and insert this before the uop in the NTP formal name. If no uop\_size is needed in the formal name, the flag should be set to N

NOTE: all fields in this table are strings; all entries should be checked for spelling, typos and correct use of letter case.

## When to use the UoP Table

|  |  |  |
| --- | --- | --- |
| **Strength Pattern** | **UoP Table Use** | **Comment** |
| 1A | Not required | UoP not explicitly stated |
| 1B | Not required | UoP as strength denominator generates directly from DPD data |
| 1C | Not required | UoP as strength denominator generates directly from DPD data |
| 2A | Yes | See below |
| 2B | Not required | UoP not explicitly stated |
| 3A | Yes | See below |
| 3B | Not required | UoP not explicitly stated |
| 3C | Not required | UoP does not exist |

### UoP for Strength Pattern 2A

The objective is to generate the correct presentation strength and have the unit of presentation at the end of the formal name.

1. **If the DPD uses concentration strength**
   1. Fill in the UoP table for each presentation that is covered by the DIN; if several vial/ampoule/syringe presentations are included in a single DIN, this will require several rows of data. The generation process recognises when there are multiple entries for a single drug\_code and knows that therefore it must assign an mp\_code to each, which is then associated to the single DIN
      1. Enter the drug\_code for each presentation
      2. Enter the unit of presentation for each presentation
      3. Enter the UoP size for each presentation
      4. Enter the UoP unit of measure for each presentation (this will be mL as strength pattern 2A is for liquids)
      5. Set the calculation flag to “Y” to indicate that the DPD strength must undergo a calculation to give the presentation strength
      6. Set the uop\_size\_insert to “N” to indicate that the UoP size does not need to be added to the end of the NTP formal name; the generation will add only the UoP description to the end of the NTP formal name  
         Note: if the presentation strength of the product is “per 1 mL” this pattern above needs to be used so as to get the “per 1 mL” inserted into something that in the DPD is “per mL”.
2. **If the DPD uses presentation strength**
   1. Fill in the UoP table the presentation that is covered by the DIN (there can only be one as this is presentation strength)
      1. Enter the drug\_code for the presentation
      2. Enter the unit of presentation for the presentation
      3. Enter the UoP size for the presentation
      4. Enter the UoP unit of measure for the presentation (this will be mL as strength pattern 2A is for liquids)
      5. Set the calculation flag to “N” to indicate that the DPD strength should be used without further calculation as it is the presentation strength
      6. Set the uop\_size\_insert to “N” to indicate that the UoP size does not need to be added to the end of the NTP formal name; the generation will add only the UoP description to the end of the NTP formal name

### UoP for Strength Pattern 3A

The objective is to use the concentration strength as it is the clinically significant strength but also to have the unit of presentation and its size described at the end of the NTP formal name.

1. The DPD will be using concentration strength
   1. Fill in the UoP table for each presentation that is covered by the DIN; if several vial/ampoule/syringe presentations are included in a single DIN, this will require several rows of data. The generation process recognises when there are multiple entries for a single drug\_code and knows that therefore it must assign an mp\_code to each, which is then associated to the single DIN.
      1. Enter the drug\_code for the presentation
      2. Enter the unit of presentation for the presentation
      3. Enter the UoP size for the presentation
      4. Enter the UoP unit of measure for the presentation (this will probably be mL for liquids (maybe L) or g or mg for solids/semi-solids)
      5. Set the calculation flag to “N” to indicate that the DPD strength must undergo a calculation to give the presentation strength
      6. Set the uop\_size\_insert to “Y” to indicate that the UoP size does need to be added to the end of the NTP formal name; the generation will add both the UoP description and the UoP size to the end of the NTP formal name

# Dose Form Transform Table

The Dose Form Transform Table is used in the CCDD generation process to provide consistent and granular (and EDQM compatible) CCDD dose forms for NTPs from the less granular DPD dose forms and DPD route of administration information. It is also able to bring some consistency in cases where the DPD has used non-standard dose form concepts.

The generation process takes the DPD dose forms and DPD routes of administration for a product and uses the Dose Form Transform Table to find the appropriate NTP dose form for the product. This means that every combination of dose form and route of administration that is present in the DPD must be present in the Dose Form Transform Table. Occasionally new combinations of dose form and route of administration are used in the DPD; the generation process will detect this and provide a report; a new entry must then be made in the Dose Form Transform Table.

Note that a Dose Form Transform will apply to *every product* that has the particular combination of dose form and route of administration and this limits what can be done. For example: the Dose Form Transform cannot currently (June 2018) “correct” the dose form for nebuliser solutions, where the DPD nebuliser products have the dose form as “solution” and the route of administration as “inhalation” since other products (the Respimat inhalers) also use this combination and the correct dose form for these is “inhalation solution”.

PUT COPY OF DOSE FORM TRANSFORM TABLE HERE

# Combination Products Table

Combination products are products that contain more than one component element (in IDMP terms, more than one manufactured item); they are sometimes described as “kits”. Combination products are represented in the CCDD as MPs and NTPs, even though strictly speaking they can only be correctly represented as packaged medicinal products. Therefore, their representation cannot be generated directly from DPD information; they must be manually authored into the CCDD using the Combination Products table. For more information on Combination Products in the CCDD, including the formal name pattern to use for the authoring, see the Combination Products section in the Editorial Guidelines. See also below for details on a particular subtype of Combination Product, the dual-chamber products.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **drug\_code** | **drug\_identification\_number** | **mp\_formal\_name** | **ntp\_formal\_name** | **ntp\_type** |
| 74243 | 02257238 | LINESSA 28 (desogestrel 100 mcg and estradiol 25 mcg oral tablet with desogestrel 125 mcg and estradiol 25 mcg oral tablet with desogestrel 150 mcg and ethinyl estradiol 25 mcg oral tablet with lactose oral tablet) ASPEN PHARMA TRADING LIMITED | desogestrel 100 mcg and estradiol 25 mcg oral tablet with desogestrel 125 mcg and estradiol 25 mcg oral tablet with desogestrel 150 mcg and ethinyl estradiol 25 mcg oral tablet with lactose oral tablet | Comb |
| 75841 | 02272903 | LINESSA 21 (desogestrel 100 mcg and estradiol 25 mcg oral tablet with desogestrel 125 mcg and estradiol 25 mcg oral tablet with desogestrel 150 mcg and ethinyl estradiol 25 mcg oral tablet) ASPEN PHARMA TRADING LIMITED | desogestrel 100 mcg and estradiol 25 mcg oral tablet with desogestrel 125 mcg and estradiol 25 mcg oral tablet with desogestrel 150 mcg and ethinyl estradiol 25 mcg oral tablet | Comb |
| 92592 | 02441535 | XARELTO (rivaroxaban 15 mg oral tablet with rivaroxaban 20 mg oral tablet) BAYER INC | rivaroxaban 15 mg oral tablet with rivaroxaban 20 mg oral tablet | Comb |
| 78377 | 02298465 | RISPERDAL CONSTA (risperidone 12.5 mg per vial powder for prolonged-release suspension for injection with diluent solution) JANSSEN INC | risperidone 12.5 mg per vial powder for prolonged-release suspension for injection with diluent solution | NA |
| 49563 | 02230509 | CANESTEN COMBI-PAK CREAM 1 (clotrimazole 1 % cutaneous cream with clotrimazole 10 % vaginal cream) BAYER INC CONSUMER CARE | clotrimazole 1 % cutaneous cream with clotrimazole 10 % vaginal cream | Comb |
| 2219 | 00030600 | SOLU-CORTEF 100 MG ACT-O-VIAL (hydrocortisone (hydrocortisone sodium succinate) 100 mg powder for solution for injection with diluent solution per vial) PFIZER CANADA INC | hydrocortisone (hydrocortisone sodium succinate) 100 mg powder for solution for injection with diluent solution per vial | NA |

**drug\_code** is the DPD code for the DIN; it is the “primary key” for the product in the DPD database. The drug\_code for the product is usually available in the QA spreadsheets; if not it can be found using a DPD database query or obtained from the DPD Team (Louise).

**drug\_identification\_number** is the DIN for the product

**mp\_formal\_name** is the full string of text for the MP Formal Name that must be authored in, using the pattern as described in the Editorial Guidelines [<<Product name>> <<[NTP Name]>> << Company Name>>]

**ntp\_formal\_name** is the full string of text for the NTP Formal Name that must be authored in, using the pattern as described in the Editorial Guidelines [<<Component X NTP formal name>> **with** <<Component Y NTP formal name>>] where Component Y may not be fully specified (e.g. “diluent solution” or “lactose tablet”), and see below for the different semantic pattern for dual chamber products.

**ntp\_type** is either “Comb” for those products where all components contain an active ingredient substance, and “NA” for those products where the second component is an inactive substance (a diluent, vehicle or “placebo”). If there are more than two components that are active, then the ntp\_type is “Comb”.

NOTE: all fields in this table are strings; all entries should be checked for spelling, typos and correct use of letter case.

# Notes for Product Types

## Oral Liquid Products

Oral liquid products are presented using two general forms:

* those where the majority of use is expected to be “per 5 mL” and are supplied with an appropriate medicine spoon (e.g. most liquid antibiotics for oral use)
* those where the majority of use is expected to be either “per 1 mL” and are supplied with an appropriate oral syringe (e.g. nystatin oral suspension) or where the majority of use is where the exact amount to administer is expected to be calculated on a per patient basis and (probably) administered using an oral syringe (e.g. digoxin oral solution)

For the first of these forms, the strength is described using presentation strength using Strength Pattern 2B (“per 5 mL”). The dose form for the NTP should be either “oral solution”, “oral suspension” or “oral emulsion” as appropriate to the product’s formulation.

For the first of these forms, the strength is described using concentration strength using Strength Pattern 3C (“per mL”) and no unit of presentation is provided. The dose form for the NTP should be “oral drops, solution”, “oral drops, suspension”, or “oral drops, emulsion”, even if not administered by means of counting drops (see EDQM dose form definition, which states that “the preparation is administered in small volumes by means of a suitable measuring device such as a dropper, pipette or oral syringe capable of accurate dosing”). However, the DPD may not be able to provide the granularity of information to support these dose form descriptions, in which case the grouping concept of “oral drops” should be used.

Note: it is also important to be consistent within a product group (see “[Strength Units of Measure](#_Strength_Units_of)” above).

## Pens/Syringes

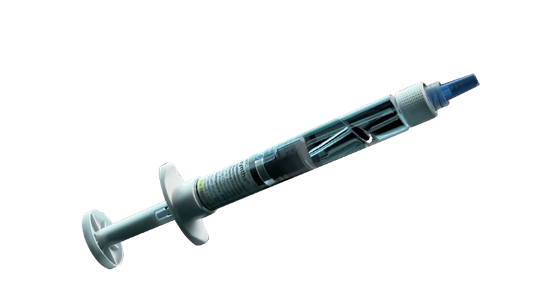
Pen and syringe are UoP

Pre-filled syringe and pre-filled pen are Container descriptions

When to use pen and when to use cartridge (e.g. Auto-Injector)

## Film coated tablets – not included in CCDD dose forms

## Dual Chamber Products

Some products, usually powders for solution or suspension for injection, are presented in an intimate container that contains two chambers, usually separated by some sort of bung or plug. The bung or plug barrier is removed (usually by being mechanically pushed though) just prior to administration, dissolving the powder that was held in one chamber in the diluent in the other chamber.

In CCDD, products specifically supplied with a diluent are considered combination products and are described using the following format:

<substance> <strength per vial> <dose form) with diluent solution

Example: risperidone 25 mg per vial powder for prolonged-release suspension for injection with diluent solution

Dual chamber products are also considered combination products, but are described using the following pattern:

<substance> <strength> <dose form) with diluent solution per vial

Example: hydrocortisone (hydrocortisone sodium succinate) 1 g powder for solution for injection with diluent solution per vial

This pattern differentiates dual chamber products from combination products, and by having the “per vial” (or per syringe) at the end, it indicates that both the active ingredient substance *and* the diluent are in the intimate container together.

All combination product information is authored manually and added into the CCDD generation process, so this change in pattern order can be maintained without needing any change to the generation process.

## Respiratory Product Patterns

### Inhalers

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Pattern** | **NTP Dose form** | **NTP Expression of strength** | **Container (not in scope)** | **Example products** | **Comment** |
| Metered dose inhalers (MDI) | pressurised inhalation | per actuation  (Pattern 1C) | metered dose inhaler | Airomir, Flovent, QVAR, Sprivia, Ventolin, Zenhale | Can be a solution, emulsion or suspension that is aerosolised |
| Dry powder inhalers (DPI) | inhalation powder | per actuation  (Pattern 1C) | metered dose inhaler | Advair Diskus, Incruse Ellipta, Asmanex Twisthaler, Pulmicort Turbuhaler, Duaklir Genuair | The powder is integral to the inhaler device and cannot be separated from it, and the dosage is metered by either a value or the disk inside the inhaler |
| Powder capsule inhalers | inhalation powder capsule | per capsule (implicit) (Pattern 1A) | various (box, carton etc.) | Foradil, Ultibro Breezhaler, Serevent Diskhaler | A system that delivers “dry powder to inhale” but the powder is supplied separately from the inhalation device |
| Mist inhalers | inhalation solution; (possibly inhalation suspension if will aerosolise) | per actuation  (Pattern 1C) | metered dose inhaler | Inspiolto Respimat, Spiriva Respimat | No propellant; a tensioned spring that draws medication into a chamber, then forces it out using jets and filter to get the aerosolisation |
| Nebuliser liquids | nebuliser solution;  nebuliser suspension (as appropriate) | per x mL (Pattern 2A or |  |  |  |

### Nebuliser solutions

Some medicinal products are designed to be administered using in a nebuliser: a device that aerosolises a liquid medication into a fine mist by various mechanisms (e.g. a jet nozzle or ultrasound) and then delivers the medication to the patient in a flow of air or air with added oxygen administered through a mask or mouthpiece.

NTPs for products that are designed to be administered using in a nebuliser should have a nebuliser-specific dose form which should be reflected in the NTP Formal Name. There are 2 of these dose forms:

|  |  |
| --- | --- |
| **nebuliser solution** | Liquid preparation consisting of a solution intended for inhalation use. The solution is converted into an aerosol by a continuously operating nebuliser or a metered-dose nebuliser |
| **nebuliser suspension** | Liquid preparation consisting of a suspension intended for inhalation use. The suspension is converted into an aerosol by a continuously operating nebuliser or a metered-dose nebuliser |

However, the DPD has not been using this dose form description, and it is currently (Summer 2018) not possible to use any transform to give the correct nebuliser dose form for the nebuliser products because other products use the DPD combination of a dosage form of “Solution” and a route of administration of “Inhalation” which is transformed to a dose form for “inhalation solution” for NTPs. This is the correct dose form for a percentage of the products with that “Solution” and “Inhalation” combination (e.g. all the Respimat inhaler products) so any change would negatively impact them.

The working position is therefore to accept that “inhalation solution” is a less than perfect dose form for the nebuliser products, as its definition explicitly excludes use on products for which nebuliser solution should be the correct dose form) but to release nebuliser NTPs with that dose form (e.g. “salbutamol (salbutamol sulfate) 2.5 mg per 2.5 mL inhalation solution unit dose vial”), with the plan that the DPD will work to address this directly by changing its dose form to nebuliser solution as and when they can.