# Canadian Clinical Drug Dataset

Work Instructions

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| --- | --- |
| Version | 03 (Working) |
| Date | 27 March 2019 ongoing |
| Previous Version/Date | 02 / 20180823 |
| Accepted Changes into this version: | Multi-use pen example in Strength 1c  New section on Overrage  New section on the Black List |

## 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** | **CCDD.status** | **Comments** |
| Y |  | ABACAVIR (ABACAVIR SULFATE) | abacavir | FALSE | abacavir (abacavir sulfate) | Released | Single and multi-ingredient TMs |
|  |  | ABATACEPT | abatacept | FALSE | abatacept | Released |  |
|  |  | 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 | No products in scope |  |
|  |  | 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** is 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 (except in special cases – see below).

**CCDD.Status** is a field used to track whether all, some or none of the products that have this substance as an active ingredient substance are released into CCDD for tracking and maintenance purposes. Uses “Standard Text for CCDD.Status in the Ingredient Stem Table” to aid sorting and analysis.

**Comments** is a field that can be used for additional information about the ingredient substance and its use in CCDD for tracking and maintenance purposes. It also uses “Standard Text for CCDD.Status in the Ingredient Stem Table” but free text may also be appropriate.

## Further Notes on Solvates and Hydrates in the NTP

The Editorial Guidelines state that “when generating the NTP, the hydration/solvation information would be disregarded in the precise ingredient substance.  This provides a smaller, more clinically acceptable set of NTPs for prescribing but continues to maintain the granular detail of actual manufactured products in the MP”.

The ntp\_ing field in the Ingredient Stem table described above will have the substance name for the NTP which should not have *any* solvation/hydration information. Some substances have both a solvate and a hydrate; both should be removed for the NTP precise ingredient substance (which usually means that the NTP precise ingredient substance is equivalent to the basis of strength substance.

**For example:**

DIN 02278499 DOM-AZITHROMYCIN (azithromycin (azithromycin monohydrate hemiethanolate) 250 mg oral tablet) DOMINION PHARMACAL

The precise ingredient substance is both a monohydrate and a hemiethanolate – for every two azithromycin moieties there are two water molecules and one ethanol molecule acting as solvates. However, the NTP will disregard both of these as they have no clinical significance, meaning that the ntp\_ing should be (just) “azithromycin” as shown below:



This will give an NTP of “azithromycin 250 mg oral tablet” to be associated with the DOM-AZITHROMYCIN product.

Very occasionally, knowledge of the hydrated substance is important, for example if it is the BoSS, or where it forms part of the name of the substance itself. Currently there are at least two examples where the hydration information remains in the substance name in the NTP as well as in the MP. These are:

* Chloral hydrate
  + with an NTP of “chloral hydrate 500 mg per 5 mL syrup” (and indeed a TM of “chloral hydrate)
* The sacubitril-valsartan complex, with NTPs of pattern
  + sacubitril (sacubitril valsartan sodium hydrate complex) 24 mg and valsartan (sacubitril valsartan sodium hydrate complex) 26 mg oral tablet

# 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 |

Some multi-use pen products also use Pattern 1C as the pen has the equivalent to a metered dose delivery that “bounds” the presentation of the product to the patient. For these products, the addition of the container (pre-filled pen) is added to the NTP formal name.

|  |  |
| --- | --- |
| **Example** | **Exenatide 5 mcg per actuation solution for injection pen** |
| **Unit of Presentation** | Actuation | Actuation |
| **Presentation strength (logical)** | Mass amount per 1 unit of presentation | 5 mcg per actuation |
| **Presentation strength (usual description)** | Mass amount, with the “per” or explicit | 5 mcg per actuation |
| **Concentration strength (for information only)** | The concentration of product (usually liquid) is often known (for exenatide, this is 250 mcg per ml) but does not have the same clinical usefulness as the amount delivered per actuation of the pen device |

## 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 |

Some multi-use pen or cartridge products also use Pattern 2A, such as when they are labelled as such and widely known in the clinical world as the presentation strength. The calculated concentration strength may not produce nice round numbers.

|  |  |  |
| --- | --- | --- |
| **Example** | **somatropin 5 mg per 1.5 mL solution for injection cartridge** |  |
| **Unit of Presentation** | The “intimate container” | e.g. cartridge |
| **Presentation strength (logical)** | Mass amount per volume contained in the unit of presentation | 5 mg per 1.5 mL |
| **Presentation strength (usual description)** | Mass amount per volume the “per” is explicitly stated | 5 mg per 1.5 mL |
| **Concentration strength** | Mass amount per unitary volume | 3.33 mg per 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. For exceptions, see multi-use pens in Pattern 2A above.

**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.

## Overage (or Shortfall) and description of Strength

Some products, usually injectable products, are supplied with an “overage”, a surplus amount of medication to account for it being almost impossible to withdraw the total volume of liquid from a vial or ampoule, either when supplied as a liquid or after reconstitution to a liquid. When describing strength, particularly presentation strength, any overage should not be taken into account. Mostly, the DPD description of strength disregards overage, but occasionally an overage strength has been described; for example (at the time of writing) for

DIN 02215187, CAVERJECT sterile powder where the strength is described as 23.2 mcg per vial, rather than as the clinically relevant strength of 20 mcg per vial, as the monograph states.

In cases such as this, a request should be made to the DPD team to alter the strength to the clinically relevant strength, which is usually as stated on the monograph and relates directly to the dose quantities that are used for the medication. This will allow the NTP to be generated using the clinically relevant presentation strength, without consideration of the overage volume.

Very rarely, a product is described as having a shortfall in its volume – for example (at the time of writing) ENBREL (DIN 02274728), in both the DPD and the monograph, is stated to have a presentation strength of 50 mg per 1 mL, but the syringe is stated to contain only 0.98 mL of liquid. Dosing is based on a 50 mcg dose quantity. In this case, the stated ‘shortfall’ should be disregarded and the clinically relevant strength be used in the NTP. The DPD strength is 50 mg per 1 mL, so no change is required.  
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

**Also used as the Override Table – see below**

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.

## Combination Product Table being used as the Override Table

The content of the Combination Product Table is applied at the end of the CCDD generation process and therefore “overrides” the generated content for the concepts generated from the drug\_code entered. Therefore, it can be used in exceptional circumstances as a way of manually entering NTP and therefore MP concepts that will not generate correctly based on current DPD data. This can be helpful if, for example, there is an entry in DPD that is generating an NTP that does not conform to the Editorial Guidelines and it is difficult for the DPD to make the necessary data change.  
Example: TM “desmopressin”

In the generation originally there is@

|  |  |  |  |
| --- | --- | --- | --- |
| **mp\_code** | **mp\_formal\_name** | **ntp\_code** | **ntp\_formal\_name** |
| 00402516 | DDAVP RHINYLE (desmopressin acetate 0.1 mg per mL nasal spray) FERRING INC | 9002446 | desmopressin acetate **0.1 mg per mL nasal spray** |

But the product is actually ‘nasal drops’, so by using the Override for DIN 00402516, the generated NTP and MP can be overridden to give the correct NTP and MP:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **drug\_code** | **DIN** | **mp\_formal\_name** | **ntp\_formal\_name** | **ntp\_type** |
| 14413 | 00402516 | DDAVP RHINYLE (desmopressin acetate 0.1 mg per mL nasal drops) FERRING INC | desmopressin acetate 0.1 mg per mL nasal drops | NA |

For any concepts that produce a duplicate MP formal name and for which there is a DPD Descriptor that could be used to give unique MP names, these must be added manually. This is because the generation process that looks for duplicate MP formal names and then checks for DPD Descriptors occurs before the Combination Product/Override Table. An example of the use of DPD Descriptor is for two cholestyramine products:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **drug\_code** | **DIN** | **mp\_formal\_name** | **ntp\_formal\_name** | **ntp\_type** |
| 14332 | 00890960 | OLESTYR **LIGHT POWDER SUGAR FREE** (cholestyramine 4 g per sachet powder for oral suspension) PHARMASCIENCE INC | cholestyramine 4 g per sachet powder for oral suspension | NA |
| 19757 | 02210320 | OLESTYR **REGULAR POWDER** (cholestyramine 4 g per sachet powder for oral suspension) PHARMASCIENCE INC | cholestyramine 4 g per sachet powder for oral suspension | NA |

No commas can be used in names in the Combination Product/Override table, so in the above example, where in the DPD the descriptor is ‘LIGHT POWDER, SUGAR FREE’ the comma is removed in the Override Table.

**Providing “NTP\_type” for Overrides**

\*\*This guidance may change if the generation process changes\*\*

For concepts that go into the Override Table because they need to be made to match with an existing NTP, the NTP\_type should be left blank rather than have the “NA” put in. This is because of some logic in the generation that assumes that the presence of the NA means that the NTP is different from one already in the generation with the same text. For example:

|  |  |  |  |
| --- | --- | --- | --- |
| **mp\_code** | **mp\_formal\_name** | **ntp\_code** | **ntp\_formal\_name** |
| 02440911 | HEAD & SHOULDERS NOURISHING HAIR & SCALP CARE CONDITIONER (pyrithione zinc 0.5 % shampoo) PROCTER & GAMBLE INC | 9005596 | pyrithione zinc 0.5 % shampoo |
| 02429292 | HEAD & SHOULDERS INSTANT COOLING RELIEF CONDITIONER (pyrithione zinc 0.5 % shampoo) PROCTER & GAMBLE INC | 9005596 | pyrithione zinc 0.5 % shampoo |
| 02244286 | HEAD & SHOULDERS DANDRUFF CONDITIONER (pyrithione zinc 0.5 % lotion) PROCTER & GAMBLE INC | 9004380 | pyrithione zinc 0.5 % **lotion** |

The Override table is used to “correct” the dose form for the HEAD & SHOULDERS DANDRUFF CONDITIONER product thus:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **drug\_code** | **DIN** | **mp\_formal\_name** | **ntp\_formal\_name** | **ntp\_type** |
| 68253 | 02244286 | HEAD & SHOULDERS DANDRUFF CONDITIONER (pyrithione zinc 0.5 % shampoo) PROCTER & GAMBLE INC | pyrithione zinc 0.5 % shampoo |  |

But since the NTP for pyrithione zinc 0.5 % shampoo already exists (9005596) the ntp\_type should be left blank in the Override Table; it will be carried through into the delivery from the generated NTP for the other two products.

# “Black List” File

### Purpose

The Black List File is used to exclude a product (an MP and its associated NTP) from a publication dataset. It is used in the generation of the Release Candidate; it is not applied for the QA generation(s) so that all data can be checked, including any changed data.

When a new product is added to the DPD and therefore becomes eligible for inclusion in the CCDD, the data in the DPD is not always authored so that the NTP that is generated conforms to the CCDD Editorial Guidelines. It may even be that an NTP is created that should not exist.

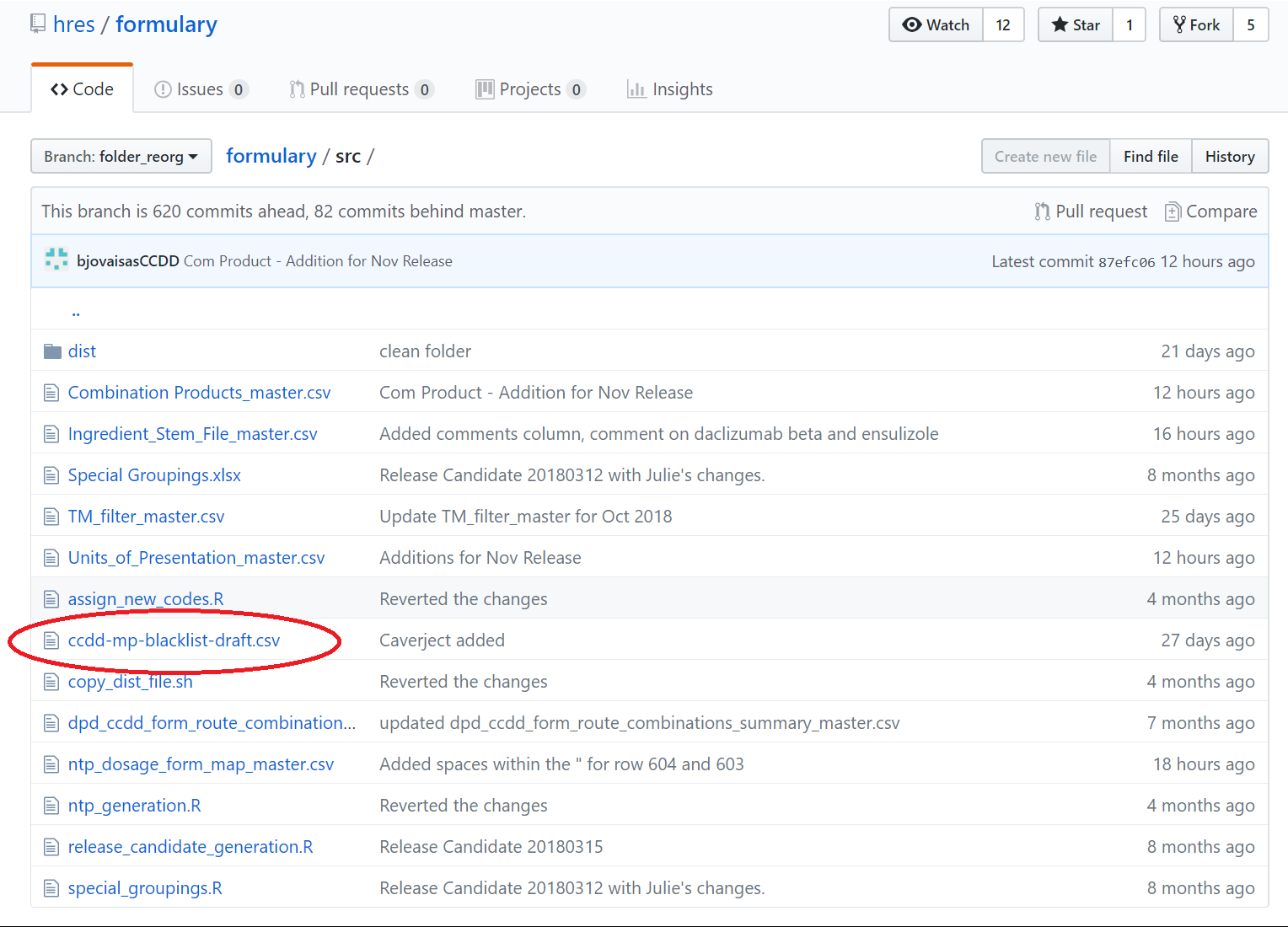
For TMs already released it is important not to release new related NTPs and MPs if the NTP has not generated correctly. The mechanism to do this is to exclude the “offending” MP(s) from the generation process that creates the Release Candidate, so that neither it nor the incorrect NTP that is associated with it are within the set of content for publication.

**For example:**   
MOSASPRAY (DIN 02455870) changed to a ‘marketed’ status in DPD some time after the main set of mometasone products were released. The Editorial Guidelines pattern for description of strength for metered dose nasal sprays is “per actuation” whereas MOSASPRAY had its strength data entered as “50MCG/SPRAY” generating an NTP of  
 mometasone furoate 50 mcg per spray nasal spray  
instead of   
 mometasone furoate 50 mcg per actuation nasal spray  
which matches with the three other existing MPs and the existing NTP (9006259).

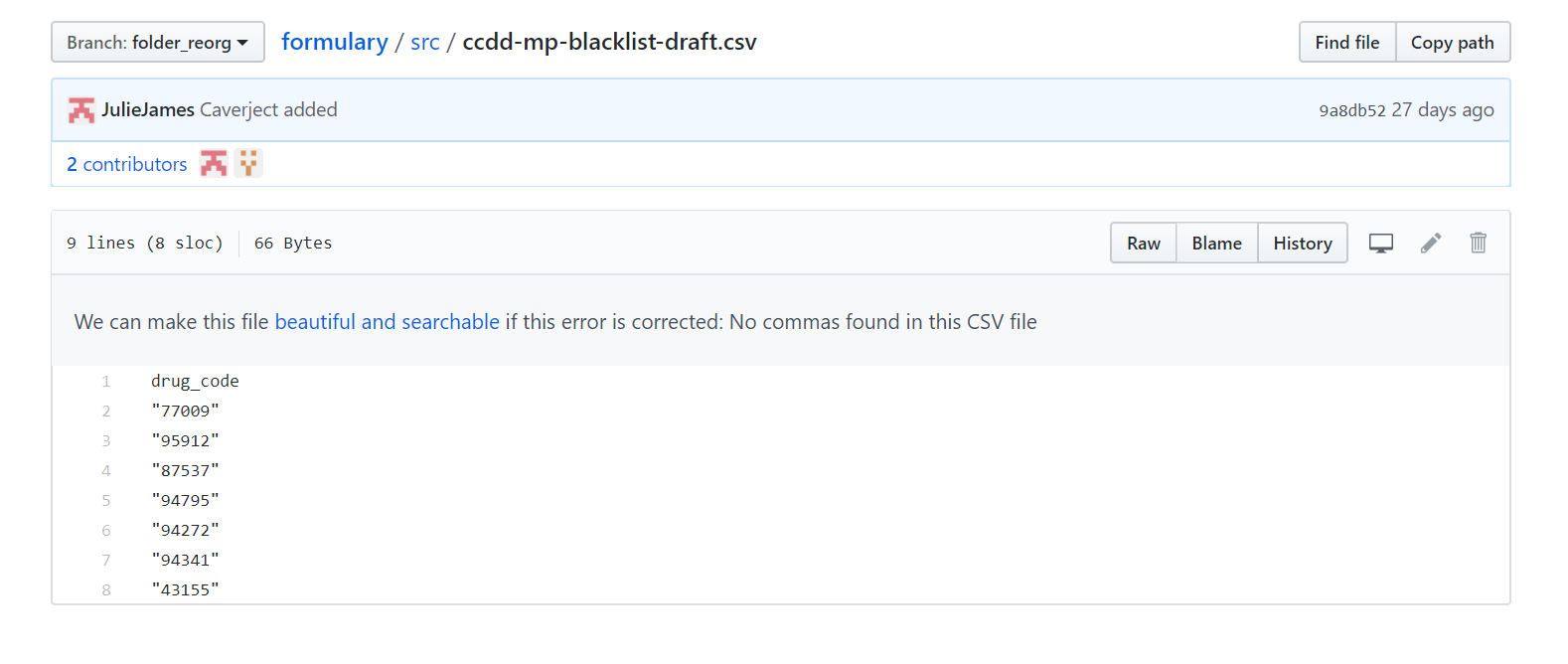
Therefore, the MOSASPRAY product needed to be suppressed so that neither it nor its incorrect NTP were released until the DPD data could be changed to give the correct NTP through the generation. To do this, the MOSASPRAY drug\_code was included on the Black List, using its drug\_code of 94272.

### Black List File Details

The Black List file [ccdd-mp-blacklist-draft.csv] is found in the src folder on GitHub:



The structure of the “Black List” is a flat list of DPD drug\_codes (NOT DINs) with each one on a separate line, enclosed in double quotes:



The drug\_code for any product to be added to the Black List must be obtained from the DPD, either by direct request of HC staff or by look-up in the DPD QRYM\_DRUG\_PRODUCT files.

Note: The Black List can be used for active (marketed) and inactive (cancelled post market or dormant) products; particularly for the latter products may stay on the Black List indefinitely as it is not always possible or sensible to ask for DPD data change for a product that is no longer available for clinical use.

# 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.

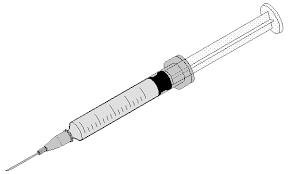
Note: it is also important to be consistent within a product group (see “[Strength Units of Measure](#_Strength_Units_of)” above).

## Pens and Syringes

As well as being presented in (standard) ampoules and vials, injectable products, especially liquid injectable (e.g. solutions for injection and suspensions for injection) may be presented in syringes and pens. Syringes and pens can therefore be units of presentation, as they are the intimate container that the medicinal product is delivered in from the manufacturer.

### Syringe as a Unit of Presentation

A **syringe** is a unit of presentation consisting of a barrel tube which contains the medication, and a plunger that is pushed to allow the contents to discharge through the end of the barrel. There is usually has a needle attached to allow direct administration (often subcutaneously). The barrel of the syringe typically has graduated marking to indicate volume (or quantity) of medication. For many products presented in a syringe unit of presentation, the entire contents of the syringe will be given in a single administration event.



A syringe unit of presentation is most likely to be single use only.

When used as a unit of presentation, the term should be “syringe”. When used as a container description, EDQM recommends the term “pre-filled syringe” to distinguish the two concepts.

Describing strength for products presented in a syringe

Since the entire contents of the syringe will usually be given in a single administration event, presentation strength should be used to describe the product strength. There is no requirement to provide the total volume contained, only the presentation strength.

For example:

dalteparin sodium 5000 unit per 0.2 mL solution for injection syringe

furosemide 40 mg per 4 mL solution for injection syringe

Auto-injectors

An autoinjector is a (north American) term that describes a medical device for medicine administration that is a variation of pre-filled syringe.  An autoinjector device contains a pre-filled syringe and a pre-loaded spring or similar that, when activated, depresses the plunger of the syringe so that, in combination with the needle, the medication is “automatically” injected to the required depth (usually subcutaneous).  This overcomes any hesitation that might be incurred by a patient or carer in administering the product through the skin’s barrier.  Newer devices may use compressed gas rather than a spring.

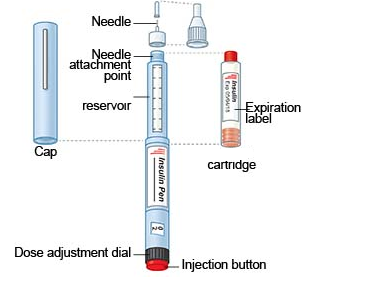
Since an autoinjector is an administration device, it is not included in an NTP formal name for CCDD concepts, although the term is likely to be present in the DPD Brand Name and therefore it will be present in the MP formal name.  Products that are described as having an autoinjector should have their unit of presentation as “syringe” as this is the intimate container that presents the medication inside the autoinjector device.  Prescribers that specifically wish a patient to receive an autoinjector product should prescribe by brand name.

For example:

sumatriptan (sumatriptan succinate) 6 mg per 0.5 mL solution for injection syringe

### Pen as a Unit of Presentation

A pen is a unit of presentation consisting of a barrel which houses the medication reservoir (usually a cartridge) and a cap which covers the (disposable) needle. Because most pen devices are designed specifically to support variable delivery amounts for the medication, there is usually a dose adjustment dial at the opposite end to the cap. This may be a completely variable dose adjustment, as in the insulin pens where any (reasonable) quantity of units can be selected, or there may be a small selection of dose amounts offered.



Almost all pens are re-usable, with the needles being replaced after each use although there are a small number of single use pen products, where the entire content of the reservoir is discharged in a single administration (in these cases there is no dose adjustment dial).

Some pen devices (e.g. for insulin) are re-fillable, with the cartridges being made available separately, in which case the unit of presentation for the medicinal product is “cartridge”. Other pen devices are not re-fillable; once the medication in the reservoir has been used up (or has exceeded its expiry date) then the entire pen must be discarded. These products have “pen” as their unit of presentation.

When used as a unit of presentation, the term should be “pen”. When used as a container description, EDQM recommends the term “pre-filled pen” to distinguish the two concepts.

Describing strength for products presented in a syringe

Pens with a variable dosage

Since pens are used primarily for medications that have a variable administration dose quantity and have some sort of dosage adjustment mechanism, it is more appropriate to describe their strength as a concentration strength rather than a presentation strength, but also to give the total volume of the medication present in the pen.

For example:

insulin lispro 100 unit per mL solution for injection 3 mL pen

insulin glargine 300 unit per mL solution for injection 1.5 mL pen

Pens with a single dosage

Single use pens

For those pens that are single use, presentation strength is appropriate; for example:

adalimumab 40 mg per 0.4 mL solution for injection pen

alirocumab 150 mg per 1 mL solution for injection pen

Multiple use pens

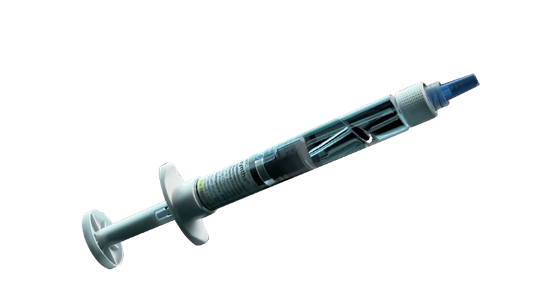
By having a fixed dosage amount, these pens are equivalent products that have a metered dose delivery that “bounds” the presentation of the product to the patient, and as such are best described using Strength pattern 1C, with the addition of “pre-filled pen” as this is truly a description of the container added to help the user.

For example:

exenatide 5 mcg per actuation solution for injection pre-filled pen

lixisenatide 20 mcg per actuation solution for injection pre-filled pen

### 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.

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

## Lotions

“Lotion” is not an EDQM standard dose form (although there is a concept called an “eye lotion”, defined as “Liquid sterile single-dose or multidose preparation consisting of an aqueous solution intended for washing or bathing the eye”; here the implication of the lotion appears to be the sense of “washing” the eye, which is explicitly stated in the administration method characteristic (bathing/rinsing/washing)).

The Merriam-Webster medical dictionary defines a lotion as “*a liquid usually aqueous medicinal preparation containing one or more insoluble substances and applied externally for skin disorders*”. This definition hints at the problem; products called “lotions” must be either:

* a **cutaneous solution**, where agents have been used to make an insoluble active substance (such as a corticosteroid) “soluble” in the liquid phase; the most common agents being some of the long chain alcohols (such as propylene glycol)
* a **cutaneous suspension**, where particles of the insoluble active substance are suspended in the liquid phase often with the help of a suspending agent; [example: calamine lotion]
* a **cutaneous emulsion**, where the active substance is dissolved in a hydrophobic liquid, small droplets of which are emulsified into the hydrophilic liquid [example: benzoyl peroxide]

Because of this variation and because the use of “lotion” as a dose form has been somewhat loosely applied in the past, it is not possible to do a “dose form transform” on products that have the DPD dose form.

It can be very difficult, even with full product monographs and lists of excipients, to know exactly how a particular “lotion” product is formulated, so even trying to make changes to individual products (or groups of products) is challenging.

For products already released with an NTP dose form of “lotion” unless there is a customer query (as there has been for one or two products), this dose form will continue to be used (e.g. betamethasone (betamethasone valerate) 0.1 % lotion) until or unless a more accurate dose form can be found. For all new NTPs, if at all possible, the DPD dose form should be one of cutaneous solution/ cutaneous suspension/ cutaneous emulsion and so the NTP will have the correct dose form on generation. If this is not possible, then new NTPs may also use the dose form of “lotion”.

## 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.

## Naming of Insulins in CCDD

Across jurisdictions there are various terms used to refer to natural or native insulin such as ‘soluble’, ‘regular’ or ‘Toronto’. In the CCDD, natural insulin is simply referred to as insulin, followed by its source (insulin human, insulin pork). When the insulin molecule or formulation has been modified in some way, the modifier will follow the term insulin (e.g., insulin isophane, insulin aspart, insulin lispro). Canadian marketed insulin isophane products may originate from human or pork and therefore the source will be specified after the modifier. As all recombinant analogues are derived from human insulin, human is implied and therefore “human” is not used in the name and the analogue name is given as ‘insulin [analogue]’ (e.g. ‘insulin lispro’).

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| --- |
| **Insulin Concepts in CCDD** |
| Insulin aspart  Insulin aspart and insulin aspart protamine  Insulin degludec  Insulin detemir  Insulin glargine  Insulin glulisine  Insulin human  insulin human and insulin isophane human  Insulin isophane human  Insulin isophane pork  Insulin lispro  Insulin lispro and insulin lispro protamine  Insulin pork |