Editorial Guidelines for the Canadian   
Clinical Drug Data Set

March 20, 2017

The Canadian Clinical Drug Data Set is licensed through the Open Government Licence (<http://open.canada.ca/en/open-government-licence-canada>).  
  
Within the Open Government Licence is the following disclaimer:  
  
No Warranty  
The Information is licensed “as is”, and the Information Provider excludes all representations, warranties, obligations, and liabilities, whether express or implied, to the maximum extent permitted by law.  
  
The Information Provider is not liable for any errors or omissions in the Information, and will not under any circumstances be liable for any direct, indirect, special, incidental, consequential, or other loss, injury or damage caused by its use or otherwise arising in connection with this licence or the Information, even if specifically advised of the possibility of such loss, injury or damage.

##### Document Control

|  |  |  |
| --- | --- | --- |
| **Date Issued** | **Canadian Clinical Drug Data Set Editorial Guidelines Release** | **Details** |
| December 15, 2016 | Draft content only | First draft Canadian Clinical Drug Data Set Editorial Guidelines for public review |
| March 20, 2017 | Version 1 (Draft) | Edits applied from public review and addition of combination product and therapeutic moieties (TM) sections |
|  |  |  |

Table of Contents

[1 Introduction to the Canadian Clinical Drug Data Set 6](#_Toc476299287)

[1.1 Purpose of this Document 6](#_Toc476299288)

[1.2 Intended Audience 6](#_Toc476299289)

[1.3 Background 6](#_Toc476299290)

[2 Scope 7](#_Toc476299291)

[3 Intended Use of the Canadian Clinical Drug Data Set 8](#_Toc476299292)

[3.1 Relationship between the Health Canada Drug Product Database (DPD) and Canadian Clinical Drug Data Set 8](#_Toc476299293)

[3.1 Access to the Canadian Clinical Drug Data Set 8](#_Toc476299294)

[4 Canadian Clinical Drug Data Set Data Model 9](#_Toc476299295)

[4.1 The NTP Class 12](#_Toc476299296)

[4.2 Technical Specification 13](#_Toc476299297)

[5 Status 13](#_Toc476299298)

[5.1 Manufactured Product Status 14](#_Toc476299299)

[5.2 Non-Proprietary Therapeutic Product and Therapeutic Moiety Product Status 15](#_Toc476299300)

[6 Substance-Strength Set for the NTP 16](#_Toc476299301)

[6.1 Substance Naming 16](#_Toc476299302)

[6.2 Precise Active Ingredient Substance(s) 16](#_Toc476299303)

[6.3 Basis of Strength Substance 17](#_Toc476299304)

[6.4 Substance in the NTP Formal Name 17](#_Toc476299305)

[6.5 Description of Strength (as part of the Strength-Set) in the NTP Formal Name 18](#_Toc476299306)

[6.5.1 Presentation Strength or Concentration Strength 19](#_Toc476299307)

[6.5.2 Representing Values 20](#_Toc476299308)

[6.5.3 Representing Units of Measure 20](#_Toc476299309)

[6.5.4 Alternative Strength Descriptions 20](#_Toc476299310)

[7 Dose Form for the NTP 21](#_Toc476299311)

[7.1 Dose Form Types 21](#_Toc476299312)

[7.2 Dose Form Description 22](#_Toc476299313)

[7.2.1 Release Characteristics 22](#_Toc476299314)

[7.2.2 DPD Dose Form Transformations 23](#_Toc476299315)

[8 Non-Proprietary Therapeutic Product (NTP) Formal Name Pattern 25](#_Toc476299316)

[8.1 Single Active Ingredient Substance NTPs: 26](#_Toc476299317)

[8.2 Multiple Active Ingredient Substance NTPs (up to 5) 26](#_Toc476299318)

[8.3 Compounded Methadone 27](#_Toc476299319)

[9 Manufactured Product (MP) Formal Name Pattern 27](#_Toc476299320)

[9.1 Single Ingredient MP 28](#_Toc476299321)

[9.2 Multiple Ingredient MP 28](#_Toc476299322)

[10 Therapeutic Moiety 29](#_Toc476299323)

[10.1 Introduction and Requirement 29](#_Toc476299324)

[10.2 Scope of TM in the Canadian Clinical Drug Data Set 29](#_Toc476299325)

[10.3 Therapeutic Moiety Formal Name 30](#_Toc476299326)

[10.4 Problematic Medicines 30](#_Toc476299327)

[10.4.1 Therapeutic Moiety for “Elemental Medicines” 30](#_Toc476299328)

[10.4.2 Therapeutic Moiety for Medicines with significant salts/modifiers 31](#_Toc476299329)

[11 Combination Products 32](#_Toc476299330)

[11.1 Introduction and Requirement 32](#_Toc476299331)

[11.2 Definition and Description 33](#_Toc476299332)

[11.2.1 Limitations 33](#_Toc476299333)

[11.3 Type code 34](#_Toc476299334)

[11.4 Combination Product NTP Formal Name 34](#_Toc476299335)

[11.5 Combination Product MP Formal Name 35](#_Toc476299336)

[Appendix A, Advisory Group Members 36](#_Toc476299337)

[Appendix B, Product Status Storyboard Example 37](#_Toc476299338)

[Appendix C: Diagrammatic Representation of Formal Naming 39](#_Toc476299339)

[NTP: Single active ingredient substance products 39](#_Toc476299340)

[NTP: Multiple active ingredient substance products 40](#_Toc476299341)

[Appendix D: International Units 41](#_Toc476299342)

[Appendix E: Glossary 43](#_Toc476299343)

# Introduction to the Canadian Clinical Drug Data Set

The Canadian Clinical Drug Data Set provides a consistent approach to the identification and naming of medications and medical devices, and is freely available for use in digital health solutions and design applications and is available in English and French.

For the Canadian Clinical Drug Data Set achieve this, the following objectives were set for these Editorial Guidelines:

* To provide a basic model to support identification of manufactured products and therapeutically equivalent (i.e. generic) medications and devices
* To provide standardized naming conventions and terminology used to describe medications and devices

Canada Health Infoway (Infoway) and Health Canada have partnered to work with an Advisory Group made up of Canadian industry experts (see Appendix A, Advisory Group Members) to develop the Editorial Guidelines, the standard terminology and infrastructure necessary to achieve these aims.

## Purpose of this Document

The Canadian Clinical Drug Data Set and its Editorial Guidelines have been designed and developed to reflect current clinical practice and safety advice. This document provides the detailed Editorial Guidelines that are used to build and maintain the drug terminology content going forward. It is expected this document will be a living document and evolve based on user requirements and feedback. A process will be defined to support this evolution.

Changes to these Editorial Guidelines will be referenced in release notes that accompany each release of this document. Future requirements for and enhancements to the Canadian Clinical Drug Data Set will be made available separately and referenced in the release notes.

## Intended Audience

This document is intended to provide health sector managers, terminology analysts, knowledgebase vendors and software vendors with a practical understanding of the editorial rules applied in the creation of the Canadian Clinical Drug Data Set.

The document is designed for use by those who wish to understand the process and rules necessary for the creation and maintenance of Canadian Clinical Drug Data Set concepts and descriptions, both from a technical and practical point of view. It may also be of interest to end users who wish to see the principles of how medicinal product concepts are authored.

## Background

Challenges with safe and reliable information exchange between different healthcare providers and the systems that they use, such as primary care electronic medical records systems (EMR) and pharmacy information systems, is in part due to the use of different terminologies and local identifiers (codes). As part of the evolution of digital health, it is essential that Canadian clinical systems utilise a freely accessible standard terminology to uniquely identify and describe medications and devices available in Canada.

Infoway and Health Canada are addressing the problem by focusing on the electronic prescribing (e-prescribing) use case, to fill the current gaps and develop a drug and device terminology to meet prescribing needs. These needs include the ability to prescribe a medicinal product without specifying a brand name, and to support interoperability between prescribers and pharmacy systems. The diagram below identifies the drug terminology that currently is available for use in e-prescribing, where the gap is and how the Canadian Clinical Drug Data Set will address this gap.

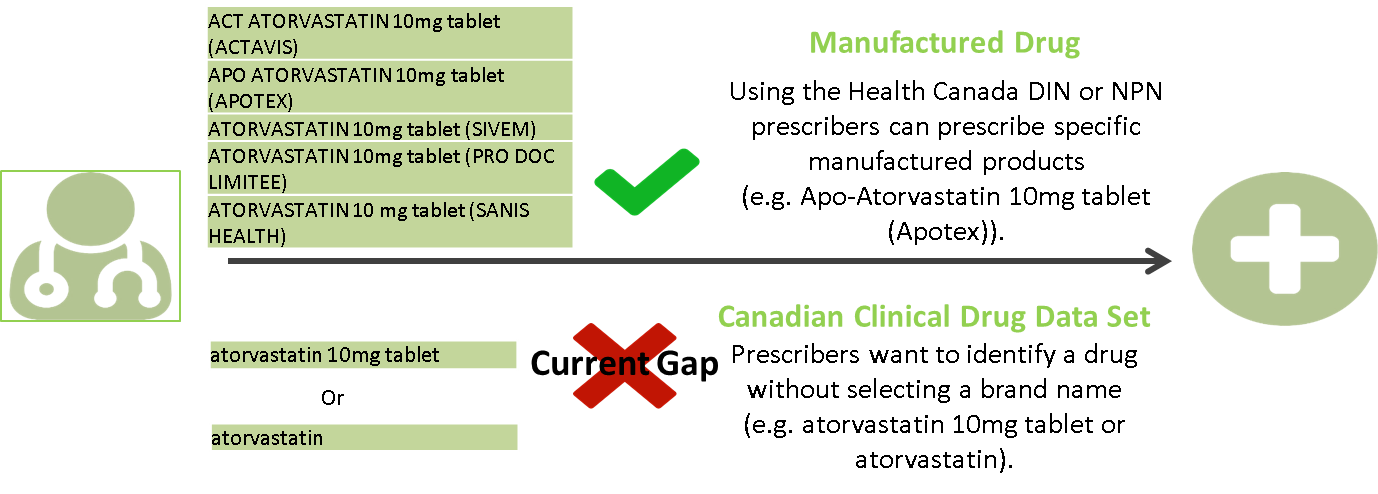


Figure : Current state of Canadian Drug Terminology

# Scope

The intended scope for the Canadian Clinical Drug Data Set is to include medicinal products (including immunizing agents), over the counter products, natural health products and a limited number of medical devices for human use within Canada in the following files:

1. The [Non-proprietary Therapeutic Product (NTP)](#_Non-Proprietary_Therapeutic_Product) file contains brand independent and clinically oriented representations of manufactured (therapeutic) products. This includes combination products (further discussed in [section 11](#_Combination_Products), some compounded products such as methadone and a very small number of devices (such as lancets, glucose meters and blood glucose strips):
2. The [Therapeutic Moiety (TM)](#_Therapeutic_Moiety) file, contains concepts that describe the functional and clinically significant part of the active ingredient substance(s) present in a medicinal product without reference to strength and dose form:
3. The file containing [Manufactured Product (MP)](#_Manufactured_Product_(MP)) contains descriptions of the brand specific drug that are available for clinical use in Canada. The content will include Health Canada assigned Drug Identification Numbers (DINs) and Natural Product Numbers (NPNs) with descriptions:
4. Relationship file(s) that describe the associations between the NTP concepts, MP concepts and TM concepts:

The current scope of the Canadian Clinical Drug Data Set is determined by the products required for e-prescribing in a community setting (i.e. community care prescribers and pharmacies). This scope will be extended and new content released in phases, driven by high frequency usage and user input first. Future requirements will be identified, prioritized and shared.

The first “beta” release of the Canadian Clinical Drug Data Set will include only the code and formal name for the NTP, TM and MP concepts in the files. The content will cover the top 250 dispensed medications that have been approved for market by Health Canada for human use within Canada (i.e. have a DIN and devices (as provided by the Institute of Clinical Evaluative Sciences (ICES)) and the editorial rules that apply. This represents 90% of the medications dispensed in community practice.

# Intended Use of the Canadian Clinical Drug Data Set

Although the focus of the content is to support e prescribing in Canada, it is recognized that the Canadian Clinical Drug Data Set (or parts of it) will support other use cases such as medication records, medication reconciliation and analytics. In most cases, the Canadian Clinical Drug Data Set will be used as an interchange terminology[[1]](#footnote-1). It will have the capacity to be used by knowledge base vendors, clinicians, researchers, statistical users, government agencies, healthcare organisations and consumers.

Clinical systems will continue to use their existing drug terminology (often a combination of Health Canada Drug Identification Number (DIN) or Natural Product Number (NPN) and proprietary terminology e.g. First Databank (FDB), Vigilance Santé) and existing user interfaces. The knowledge base vendors (e.g. FDB, Vigilance Santé) will include a mapping between their proprietary codes and the Canadian Clinical Drug Data Set in their products, thus enabling the interoperability of medicinal product names/descriptions.

When these systems share drug information, e.g. an e-prescription, they will share either:

* the Health Canada DIN or NPN (for manufactured products) or
* the Canadian Clinical Drug Data Set NTP code and description (as a generic, non-manufacturer specific product description) or
* the Canadian Clinical Drug Data Set TM code and description plus the required dose quantity and possibly the route of administration (each in separate fields in their system and in the message); this is in contrast to selecting a more fully defined product (as the NTP provides)

## Relationship between the Health Canada Drug Product Database (DPD) and Canadian Clinical Drug Data Set

The Canadian Clinical Drug Data Set will not replace the Health Canada Drug Product Database (DPD), but it will be published in addition to the DPD.

The purpose of the DPD is to provide the product specific information made available by the federal regulator of therapeutic drugs (Health Canada) for products approved for use in Canada. The DPD is managed by Health Canada and includes human pharmaceutical and biological drugs, veterinary drugs, radiopharmaceutical drugs and disinfectant products.

The purpose of the Canadian Clinical Drug Data Set is to provide a consistent representation of medications and medical devices including the identification and naming for use in digital health solutions.

The DPD provides source data for Canadian Clinical Drug Data Set. The content in the DPD will not be the same as the Canadian Clinical Drug Data Set. Each set of files have their own policy and editorial guidelines that make the content “fit for purpose”.

## Access to the Canadian Clinical Drug Data Set

Health Canada will be the owner of the product with the responsibility for publication and ongoing maintenance. The initial target is to publish the content monthly.

The first “beta” release of the Canadian Clinical Drug Data Set will be via the [Infoway Gateway](https://ic.infoway-inforoute.ca/en/tools/standards-tools/terminology-gateway). The Canadian Clinical Drug Data Set will also be released at some point in the future through the data.gc.ca portal: <http://open.canada.ca/data/en/dataset/bf55e42a-63cb-4556-bfd8-44f26e5a36fe>

# Canadian Clinical Drug Data Set Data Model

The Canadian Clinical Drug Data Set uniquely identifies and accurately describes medicines and a limited number of devices in a standardized format using a set of defining properties. These properties are the active ingredient substance(s), their strength and their dosage form, and for manufactured products, their product name and manufacturer company.

The Canadian Clinical Drug Data Set embodies a relational model that associates various medicinal and manufactured product at different levels of granularity. This model may evolve to support new use cases.



Figure : Canadian Clinical Drug Data Set Model

Table 1 below provides the definition and an example for each of the core classes in the Canadian Clinical Drug Data Set model and Table 2 below provides a description of the attributes of each class.

Table : The Canadian Clinical Drug Data Set Model Classes

|  |  |  |
| --- | --- | --- |
| **Model Class** | **Definition** | **Example (formal name)** |
| Therapeutic Moiety (TM) | The functional and clinically significant part of the active ingredient substance(s) present in a medicinal product, and as such the TM class is an abstract representation of a medicinal product without reference to strength and dose form, focusing only on active ingredient substance(s). | amlodipine |
| Non-proprietary Therapeutic Product (NTP) | A brand independent and clinically oriented representation of a manufactured (therapeutic) product. | amlodipine (amlodipine besylate) 2.5 mg oral tablet |
| Manufactured Product (MP) | A brand specific drug or device, that is available for prescribing and dispensing in Canada. | ACT AMLODIPINE [amlodipine (amlodipine besylate) 2.5 mg oral tablets] ACTAVIS PHARMA COMPANY |

Table : The Canadian Clinical Drug Data Set Model Attributes

|  |  |
| --- | --- |
| **Manufactured Product (MP) class attributes** | |
| **Attribute** | **Description** |
| MP code | The Health Canada assigned DIN or NPN that is currently published as part of the DPD. It is intended to be used as the unique code to represent a Manufactured Product.  There are leading zeros. |
| MP formal name | The unambiguous description of the Manufactured Product that includes details necessary to distinguish it from other similar products as defined in [Section 9](#_Toc476136047) of this document. |
| MP description EN | Not defined for this release of Editorial Guidelines.  The user-friendly English description that may be used for web applications or the user interface for any system. |
| MP description FR | Not defined for this release of Editorial Guidelines.  The user-friendly French description that may be used for web applications or the user interface for any system. |
| MP status | The lifecycle state for the product (i.e. not the terminology concept status). Allowable values for status include Active and Inactive. See Section 4 for more detail. |
| MP status date | This is the date of the product status as it appears in the file; in the format YYYYMMDD. |

|  |  |
| --- | --- |
| **Therapeutic Moiety (TM) class attributes** | |
| **Attribute** | **Description** |
| TM code | The code that is assigned by Health Canada. It is intended to be used as the unique meaningless identifier to represent a TM.  There are no leading zeros. |
| TM formal name | The unambiguous description of the TM that includes details necessary to distinguish it from other similar products. This will be defined in a future release of this document. |
| TM status | The lifecycle state for the product (i.e. not the terminology concept status). Allowable values for status include Active and Inactive. See Section 4 for more detail. |
| TM status date | This is the date of the product status as it appears in the file, in the format YYYYMMDD. |

|  |  |
| --- | --- |
| **Non-proprietary Therapeutic Product (NTP) class attributes** | |
| **Attribute** | **Description** |
| NTP code | The code that is assigned by Health Canada. It is intended to be used as the unique meaningless identifier to represent a NTP.  There are no leading zeros. |
| NTP formal name | The unambiguous description of the Non-proprietary Therapeutic Product that includes details necessary to distinguish it from other similar products as defined in [Section 8](#_Non-Proprietary_Therapeutic_Product) of this document. |
| NTP description EN | Not defined for this release of Editorial Guidelines.  The user-friendly English description that may be used for web applications or the user interface for any system. |
| NTP description FR | Not defined for this release of Editorial Guidelines.  The user-friendly French description that may be used for web applications or the user interface for any system. |
| NTP status | The lifecycle state for the product (i.e. not the terminology concept status). Allowable values for status include Active and Inactive. See Section 4 for more detail. |
| NTP status date | This is the date of the product status as it appears in the file, in the format YYYYMMDD. |
| NTP type | Indicates combination products that contain two or more manufactured items that contain active ingredient substance(s). |

## The NTP Class

An NTP is defined by a unique combination of Substance-Strength Set(s) (as described in Section 5 of this document) and Dose Form(s) (as described in Section 6 of this document). See Figure 3 below. The information in the blue boxes in Figure 3 is not provided as part of the Canadian Clinical Drug Data Set, but it is necessary for the maintenance of the Canadian Clinical Drug Data Set, as well as building the content represented in the formal name of each NTP.



Figure : The NTP Model

## Technical Specification

The detailed technical specification for the content of the Canadian Clinical Drug Data Set is provided in a separate Technical Specification document (with the files at publication time).

# Substance-Strength Set for the NTP

The set of active ingredient substance(s), when combined with an expression of their strength, is one of the definitional components of an NTP and therefore its correct description is an essential part of the human readable Formal Name for the NTP. The precise active ingredient substance(s), basis of strength substance and strength has been documented in this section separately.

## Substance Naming

To identify pharmaceutical substances that are acting as active pharmaceutical ingredients, Health Canada naming follows the International Non-proprietary Names (INN) or the United States Accepted Names (USAN.) In rare cases, Health Canada naming follows a Canadian specific practice (Canadian Standard Drugs – CSD). Therefore, when describing the active ingredient substance(s), the type of description used by Health Canada’s DPD will be used.

Table : Canadian Substance Naming Example

|  |  |  |
| --- | --- | --- |
| **INN** | **USAN** | **DPD** |
| paracetamol | acetaminophen | acetaminophen |
| salbutamol | albuterol | salbutamol |
| glyceryl trinitrate | nitroglycerin | nitroglycerin |
| orciprenaline | metaproterenol | orciprenaline |

Although not available in the first release, future considerations include provision of a table specifying which active ingredient-naming format is used.

Modifiers, such as salts and esters will also be described using INN/USAN as appropriate (e.g. “mesylate” rather than the full chemical name for the modifier “methanesulfonate”).

For vitamin substances, the specific naming rules apply to give a consistent approach for all vitamins; these rules are described in the table below:

Table : Vitamin Naming Rules

|  |  |
| --- | --- |
| **Vitamin Related Rules** | **Examples** |
| For vitamins, the alphanumeric names will be used. | vitamin B1  vitamin B6 |
| Vitamins such as Vitamin B12 and Vitamin D: the specific analogues will be part of the description when it impacts dispensing decisions. | vitamin B12 (cyanocobalamin) vitamin B12 (hydroxocobalamin) |

## Precise Active Ingredient Substance(s)

The rules to describe the precise active ingredient substances for NTPs and MPs are defined in this section.

The precise active ingredient substance is the fullest and most accurate description of the substance as it is used in the product (as it is presented by the manufacturer, before any dilution or transformation). It is usually described in terms of the modified INN/USAN. If no modifier is stated, the precise ingredient substance is the base substance moiety.

Examples:

*perindopril arginine* (in Servier’s Arcosyl products)

*perindopril erbumine* (in Servier’s Coversyl products)

*phenytoin sodium* (in Pfizer’s Dilantin capsule)

*phenytoin* (in Pfizer’s Dilantin Suspension) [example of the base moiety being the precise ingredient substance]

*beclomethasone dipropionate* (in Valeant’s Qvar products)

*sumatriptan succinate* (in GSK’s Imitrex DF tablet)

*sumatriptan hemisulfate* (in GSK’s Imitrex Nasal spray)

*potassium chloride* (in Biomed’s Slo-Pot)

*pegylated doxorubicin hydrochloride* (in Janssen’s Caelyx)

## Basis of Strength Substance

The basis of strength substance (often referred to as the BoSS) is the substance against which the strength quantity(s) of the product is measured. It is usually described in terms of the INN or the modified INN, as appropriate.

Examples:

Arcosyl: 5 mg of *perindopril arginine* per tablet

Coversyl: 4 mg of *perindopril erbumine* per tablet

Dilantin: 50 mg of *phenytoin sodium* per capsule

Dilantin: 125 mg of *phenytoin* per 5 mL (teaspoon)

Qvar: 50 mcg of *beclomethasone dipropionate* per actuation

Imitrex DF: 50 mg of *sumatriptan* per tablet

Imitrex Nasal spray: 5 mg of *sumatriptan* per actuation

Norvasc: 10 mg of *amlodipine* per tablet

Slo-Pot:600 mg of *potassium chloride* per tablet

Caelyx: 2 mg of *doxorubicin hydrochloride* per 1 mL

## Substance in the NTP

Where the precise active ingredient substance is the basis of strength substance, only the precise active ingredient substance is required for the NTP:

Examples:

Arcosyl: perindopril arginine 5 mg oral tablet

Coversyl: perindopril erbumine 4 mg oral tablet

Ascor L: vitamin C 500 mg per 50 mL solution for injection

Dilantin: phenytoin sodium 50 mg oral capsule

Dilantin: phenytoin 125 mg of per 5ml oral suspension

Qvar: beclomethasone dipropionate 50 mcg per actuation pressurised inhalation

Where the precise active ingredient substance is not the basis of strength substance, both the precise active ingredient substance and basis of strength substance are required to define the NTP. In the formal name, the basis of strength substance will be stated first, outside the brackets and the precise active ingredient substance will be stated second within brackets (parentheses). Reading the formal name without the brackets therefore gives the strength correctly (e.g. “sumatriptan 50 mg per oro-dispersible tablet”) as in the examples below:

Examples:

Norvasc: *amlodipine (amlodipine besylate)* 10mg per tablet

Imitrex DF: *sumatriptan (sumatriptan succinate)* 50 mg per oro-dispersible tablet

Imitrex Nasal spray: *sumatriptan (sumatriptan hemisulfate)* 5 mg per actuation nasal solution

Where the basis of strength substance is a different precise substance from the precise active ingredient substance, the basis of strength substance is given in square brackets using the phrase “equivalent to”:

Examples:

Slo-Pot: *potassium chloride* 600 mg [equivalent to 8 mEq potassium] modified release oral tablet

Caelyx: *pegylated doxorubicin hydrochloride* 2 mg per 1 mL *[equivalent to doxorubicin hydrochloride]* liposomal suspension for injection

Note: with the exception of units of measure, where the L of mL is upper case, and the alphabetic vitamin name, all text in the NTP formal name should be lower case.

### Absence of specific excipient substances

The absence of a specific excipient substances that may have some clinical considerations such as sugar, dye, preservatives etc. (i.e. “freeness”) will not be part of the consideration for an NTP and will not be included in the NTP formal name. However, for the MP, if the "product name" explicitly contains information regarding “freeness”, then this will be included in the MP formal name.

Example: (where the “freeness” is highlighted for illustration in italics):

DPD Product name:

AMOXICILLIN *SUGAR-REDUCED GRANULES* FOR ORAL SUSPENSION SIVEM PHARMACEUTICALS ULC

MP formal name:

AMOXICILLIN *SUGAR-REDUCED GRANULES* FOR ORAL SUSPENSION [amoxicillin (amoxicillin trihydrate) 250 mg per 5 mL oral suspension] SIVEM PHARMACEUTICALS ULC

Related NTP:

amoxicillin (amoxicillin trihydrate) 250 mg per 5 mL oral suspension

## Description of Strength (as part of the Strength-Set) in the NTP

The strength of a therapeutic product is the amount of (each) active ingredient substance per presentation unit (see below). Representation of strength is a safety issue, and the Institute for Safe Medication Practices Canada (ISMP Canada) has made several recommendations that have been considered.

An amount is a physical quantity – it is expressed as a value and the unit of measure for that value, but for a therapeutic product, the strength is actually a “ratio concept” – a numerator quantity and denominator quantity (an amount **per** unit – where the unit is also a physical quantity or unit of presentation).

Often the “per” or “denominator” part of the strength description is implicit rather than explicit, especially when the unit of presentation uses the same term as the dose form, as is often the case of solid phase dose forms. For example, the concept “amoxicillin 250mg capsule” is fully “amoxicillin 250 mg **per 1 capsule** oral capsule” where the unit of presentation is “capsule” and the dose form is “oral capsule”.

In other products, particularly those that are presented in a continuous phase, the “per amount” is stated explicitly (e.g. amoxicillin 250 mg **per 5 mL** oral solution) or almost explicitly (e.g. clotrimazole 1% topical cream, where the 1% represents 10 mg of clotrimazole per 1 g of the cream base).

For those strengths that do not require explicit statement of the denominator, the strength is expressed as a value then its unit, separated by a space.

|  |  |
| --- | --- |
| * 10 mg | e.g. clobazam 10 mg oral tablet |
| * 100 mcg | e.g. levothyroxine sodium 100 mcg oral tablet |

For those strengths where the denominator is stated explicitly, the numerator and denominator will ***each*** be expressed as a value then its unit, separated by a space and the numerator and denominator will themselves be separated by the word “per” with a space on either side.

|  |  |
| --- | --- |
| * 250 mg per 5 mL | e.g. clarithromycin 250 mg per 5 mL oral suspension |
| * 500 mcg per 2 mL | e.g. digoxin 500 mcg per 2 mL oral solution |

For products with multiple active ingredient substances, the strength will be stated with the active ingredient it relates to, and therefore if the numerator and denominator must both be explicitly present, the denominator will be stated in each case:

|  |  |
| --- | --- |
| * 250 mg per 5 mL and 125 mg per 5 mL | e.g. amoxicillin 250 mg per 5 mL and clavulanic acid 125 mg per 5 mL oral suspension |

In circumstances where the denominator is correctly unitary, the “1” value will be explicitly stated so that the total volume (for continuous liquids) is clearly stated, as in the first example below. Where the unitary amount is for a metered dose presentation, the “1” does not need to be explicitly stated, as in the second example:

|  |  |
| --- | --- |
| * 1 mg per 1 mL | e.g. vincristine sulfate 1 mg per 1 mL solution for injection |
| * 100 mcg per [1] actuation | fluticasone propionate 100 mcg per actuation pressurised inhalation |

### Presentation Strength or Concentration Strength

For certain types of products, particularly continuous liquids, there are two options to describe the product strength: concentration strength, which describes strength with a standard (unitary) denominator (e.g. per 1 mL); and presentation strength, which explicitly describes the amount of (each), active ingredient substance **per presentation unit**.

For example: dalteparin injection is a solution of dalteparin sodium whose unitary concentration is 25,000 units per (1) mL. However, the product is “presented” for use in various volumes within a pre-filled syringe, such as 0.4 mL pre-filled syringes. These are the “presentation units” for the product. The presentation strength for the pre-filled syringe product is therefore 10,000 units per 0.4 mL.

Using presentation strength is particularly helpful when there are several different product sizes available. For example, a pre-filled syringe product containing 10,000 units per 0.4 mL and a different pre-filled syringe product containing 12,500 units per 0.5 mL both have the same concentration strength (25,000 units per 1 mL).

The Canadian Clinical Drug Data Set will use only the presentation strength in most cases, with the exception being for insulin and related products, where a concentration strength is given (to allow the patient easy calculation of the volume to administer as this may change very frequently).

### Representing Strength Values

1. The value of the strength will be represented using a whole number or a decimal number.
2. If the value is a whole number, (integer) there will be no decimal point or trailing zeros (e.g. **10 mg** not 10.0 mg).
3. If the value is a decimal, there will be a leading zero, avoiding naked decimals (e.g. **0.75 mg** not .75 mg)
4. If the value is greater than a thousand, commas or spaces will not be used to separate the thousands (e.g. 1000 rather than 1,000 or 1 000). Although the ISMP recommends the use of commas[[2]](#footnote-2), the DPD does not use spaces or commas in strength description, due to the subtle differences in what these represent between English and French and the risks that this introduces. See also the guidance “Good Label and Package Practices Guide for Non-prescription Drugs and Natural Health Products” published by Health Canada in June 2016, which can also be applied to prescription medicinal products.

### Representing Units of Measure

1. The unit of measure should be in the metric system whenever possible.
2. The unit of measure should be stated in the singular, with the exception of “units” (see 4 below).
3. The Standard International (SI) abbreviations are to be used, without a terminal period (e.g. 1 mg not 1 mg.). Volume should be expressed using litres (L) or millilitres (mL) not cubic centimetres[[3]](#footnote-3).
   1. One exception is that micrograms should be abbreviated to mcg not µg or ug.
4. For those products whose strength is stated as “international units”, the term “units” will be used and must be stated in full, not as the abbreviation “u” or “U” or “iu” or “IU”. (E.g. insulin lispro 100 units per 1 mL). See Appendix D, International Units for more information.
5. For those products that are supplied in some form of metered-dose packaging, the unit of measure (for the denominator) should be “actuation” (e.g. beclomethasone propionate 50 mcg per actuation nasal spray).
6. For those products whose strength is presented as a percentage (where the denominator is in the unit of measure), the type of percentage (weight in weight (w/w), weight in volume (w/v) or volume in volume (v/v)) will **not** be stated. For example, Spectro Eczemacare Medicated Cream could be described as having a strength of 0.05 % **w/w**, meaning that there is 5 mg of clobetasone butyrate per 10 g of cream base; however, the NTP or MP strength description will be just “0.05 %”.

### Alternative Strength Descriptions

Some products have more than one way to describe their strength; for example, Epinephrine 1 mg per 1 mL solution for injection may also be described as Epinephrine 1:1000 (as in the Efra Adrenalin product). Similarly, epoetin products may be described either using mass or using units: Janssen’s Eprex product uses units (e.g. 1,000 units per 0.5 mL of epoetin alfa) whereas Roche’s Mircera product uses mass (e.g. 600 mcg per 0.6 mL). Sometimes, a product or monograph will reference both strength descriptions.

For those products with alternative strength descriptions, the formal name will use mass in SI units (e.g. 1 mg per 1 mL for epinephrine products) wherever possible. Units (international units) should only be used if the manufacturer consistently describes both the product and the dosage schedule using units (as is the case for Eprex or dalteparin products) and no mass strength is provided.

# Dose Form for the NTP

The dose form is one of the definitional components of a NTP. Its correct description is an essential part of the human readable formal name for the NTP and the MP descriptions. The rules to represent dose form for NTPs and MPs are provided in this section.

## Dose Form Types

The ***dose form*** (sometimes also known as the pharmaceutical dose form) is the physical manifestation (formulation) of a medicinal product that contains the active (and inactive) ingredient substance(s) that are intended to be delivered to the patient.

The ***manufactured dose form*** of the product is its manufactured form (as it is supplied by the manufacturer) and may require transformation into an administrable dose form.

The ***administrable dose form*** of the product is to be used for administration to the patient.

In many cases, the manufactured dose form and the administrable dose form are the same, but for products that undergo transformation prior to administration, they are different.

The dose form for the NTP and MP will normally be the manufactured dose form. For the majority of products, the manufactured dose form is the same as the administrable dose form.

For those products where the manufactured dose form and administrable dose form are different, it is the manufactured dose form that most closely co-ordinates with the description of strength (with one exception, see below). For example, for injectable Cefotaxime products, the dose form is the manufactured dose form of “powder for solution for injection” because the product strength is described as the mass amount of powder per vial (e.g. 500 mg per vial).

Oral liquids that are reconstituted for dispensing are one group of products where the administrable dose form will be used for the NTP because the strength of these products is described in terms of the administered dose quantity – the “5 mL teaspoon” (for example amoxicillin 125 mg per 5 mL). The administrable dose form reflects this liquid preparation: oral suspension, oral solution etc. (rather than the manufactured dose form of powder for oral suspension, powder for oral solution).

Table : Dose Form Examples

|  |  |  |
| --- | --- | --- |
| Manufactured Dose Form | Administrable Dose Form | Transformation |
| Vaginal cream | Vaginal cream | None |
| Powder for oral suspension | Oral suspension | Reconstitution |
| Modified release tablet | Modified release tablet | None |
| Powder for solution for injection | Solution for injection | Reconstitution |

## Dose Form Description

Unit dose forms such as tablet, capsule, pessary etc. will be stated using the singular form and not the plural.

The dose form description for the NTP and MP needs to be granular and explicit enough to allow a prescriber to clearly identify the product to be supplied to the patient. For example: to differentiate between the clotrimazole cream product intended to treat vaginal candidiasis (yeast infection) from the clotrimazole cream product intended to treat tinea pedis (athlete’s foot), as well as there being a strength difference, there should also be a dose form difference – explicitly stating the dose form as “vaginal cream” for the product for vaginal use.

Similarly, for products (usually solid dose oral products) that have undergone modification to change their release characteristics (prolonged release, extended release); this change needs to be explicitly stated in the dose form description (see below).

EDQM[[4]](#footnote-4), the European Directorate for the Quality of Medicines & Healthcare, publishes a database of standard terms, for dose forms, routes of administration and various other key concepts within the domain. This database was originally created in response to a request from the European Commission, but now is available for wider global use to support the Identification of Medicinal Products (IDMP) initiative and to support healthcare generally[[5]](#footnote-5). A relevant subset of the EDQM dose forms (based on the product scope of the Canadian Clinical Drug Data Set), with their definitions, forms the basis of the NTP-CA dose form terminology. Some specific adjustment of individual concepts within the subset has been undertaken; for example, for prescribing use cases, there is no requirement to differentiate between hard and soft gelatin capsules, therefore a single “oral capsule” concept is used in the Canadian Clinical Drug Data Set.

### Release Characteristics

For various dose forms that can have modified release characteristics, the granularity of description of the modification in the EDQM concepts may not be sufficient for the NTP for e-prescribing. For example, for oral solid dosage forms such as tablet and capsule, the EDQM does not differentiate between different release rates as there are no pharmacopoeial standards to support this differentiation. There are concepts for “modified release tablet” (tablet with a rate, a place and/or a time of release different from that of a conventional-release tablet and “prolonged release tablet” (a tablet with a slower release of the active substance(s) than that of a conventional-release tablet).

The following release characteristic types will be used for NTPs:

* Modified release: a rate, a place and/or a time of release different from that of a conventional-release. Modified-release is used only when the more specific terms 'gastro-resistant tablet' or 'prolonged-release tablet' do not apply;
* Prolonged release, (a type of modified release): Solid single-dose preparation showing a slower release of the active substance(s) than that of a conventional-release preparation. Prolonged release is achieved by a special formulation design and/or manufacturing method. Prolonged-release preparations are intended for oral use;
* Orodispersible: Solid single-dose preparation consisting of an uncoated tablet intended to be placed in the mouth where it disperses rapidly in saliva before being swallowed;
* Chewable: Solid single-dose preparation consisting of an uncoated tablet intended to be chewed before being swallowed. Chewable tablets are intended for oral administration

Table : Examples of Dose Forms with Release Characteristics in the Canadian Clinical Drug Data Set

|  |  |  |
| --- | --- | --- |
| **DPD Term** | **EDQM** | **Canadian Clinical Drug Data Set  (Formal Name)** |
| Tablet (Combined release) | Modified-release tablet | Modified-release oral tablet |
| Tablet (Delayed and extended-release) | Modified-release tablet | Modified-release oral tablet |
| Tablet (Enteric-coated) | Gastro-resistant tablet | Gastro-resistant tablet |
| Tablet (Delayed release) | Gastro-resistant tablet | Gastro-resistant tablet |
| Tablet (Extended-release) | Prolonged-release tablet | Prolonged-release oral tablet |
| Tablet (Immediate and delayed release) | Modified-release tablet | Modified-release oral tablet |
| Tablet (Immediate release) | Tablet | Oral tablet |
| Tablet (orally disintegrating) | Orodispersible tablet | Orodispersible tablet |
| Tablet (Chewable) | Chewable tablet | Chewable tablet |

Some groups of products with the same active ingredient substance are available with more than one “duration” of prolonged release: morphine prolonged release capsules are available for both a twice-daily dosage (e.g. M-Eslon) and a once daily dosage (e.g. Kadian). These could not be safely differentiated by the dose form “prolonged release capsule”. Similar considerations apply to transdermal patches whose strength is stated as a rate (amount administered over 24 hours, usually) but whose dosing may be “one patch per 4 days” or “one patch per 7 days”. Note that the 4-day patch may actually contain more total active ingredient substance than the 7-day patch, but because of the matrix of the patch, release it reliably only over 4 days. As there is no pharmacopoeial or pharmacokinetic standard for dose forms with specific durations and no standardised source from which to obtain such information, development of any additional granularity of prolonged-release dose forms based on dosage schedule (e.g. **prolonged release** (xx-hour recommended)) cannot be supported currently. This position will be actively reviewed based on user feedback.

### DPD Dose Form Transformations

In order to undertake generation of the more granular dose forms for the NTP from the DPD dose forms, a set of rules is used, mapping the existing DPD dose form for a product to the NTP dose form. These rules are described in detail in separate Dose Form document. Please see examples below (Sections 6.2.2.1-4) in this version of the document.

Each mapping will have a dose form term to be used in the NTP formal name, which may be very explicit (for example stating “oral tablet”) and a dose form term to be used in the NTP Description, which may be less explicit, but which must still be granular enough to support safe electronic prescribing.

#### Example 1: Simple Mapping

DPD dose form = CAPSULE (ENTERIC COATED)

NTP dose form (formal name) = gastro-resistant oral capsule

Definition: “Solid single-dose, delayed-release preparation contained in a hard or soft shell. The preparation is intended to resist the gastric fluid and to release the active substance(s) in the intestinal fluid. Hard gastro-resistant capsules are usually made by filling capsules with gastro-resistant granules or solid particles made gastro-resistant by coating or, in certain cases, by providing capsules with a gastro-resistant shell. They are intended for oral use.”

**Transform**:

*All products with DPD Dose form = CAPSULE (ENTERIC COATED) (code =14) transform to have the NTP dose form as “gastro-resistant oral capsule”*

#### Example 2: Simple Change

DPD dose form = TABLET (CHEWABLE)

NTP dose form (formal name) = chewable tablet

Definition: “Solid single-dose preparation consisting of an uncoated tablet intended to be chewed before being swallowed. Chewable tablets are intended for oral administration.”  
Note: “oral” is not explicitly in the formal name dose form because chewable implies an oral site.

**Transform**:

*All products with DPD Dose form =* TABLET (CHEWABLE) (code = 151*) transform to have the NTP-CA formal name dose form as “chewable tablet”*

#### Example 3: Transform Using Route of Administration

DPD dose form = CREAM

An NTP with a dose form of “cream” would not be granular enough to identify the correct set of products for prescribing.

EDQM “cream” dose forms include the intended site of use; for example:

* vaginal cream
  + Definition: “Semi-solid preparation consisting of a cream usually presented in a single-dose container provided with a suitable applicator, intended for vaginal use to obtain a local effect” or
* ophthalmic cream
  + Definition: “Semi-solid sterile single-dose or multi-dose preparation consisting of a cream intended for ocular use. Eye creams may be presented in collapsible tubes fitted with a cannula and having a content of not more than 5 g of the preparation. Eye creams may also be presented in suitably designed single-dose containers. The containers or nozzles of tubes are of a shape that facilitates administration without contamination”
* cutaneous cream
  + Definition: Semi-solid single-dose or multidose preparation of homogeneous appearance consisting of a lipophilic phase and an aqueous phase, one of which is finely dispersed in the other. Active substance(s) are dissolved or dispersed in the basis, which may be hydrophilic or hydrophobic. Creams are intended for cutaneous use. In certain cases, transdermal delivery may be obtained

Use the route of administration information present in the DPD to transform to the more granular dose form:

*Where DPD Dose form = CREAM (code =9) and DPD Route of administration = VAGINAL (code = 74)* *transform to have the NTP dose form (formal name) as “vaginal cream”*

*Where DPD Dose form = CREAM (code =9) and DPD Route of administration = OPHTHALMIC (code = 55)* *transform to have the NTP dose form (formal name) as “ophthalmic cream”*

*Where DPD Dose form = CREAM (code =9) and DPD Route of administration = TOPICAL (code = 70)* *transform to have the NTP dose form (formal name) as “cutaneous cream”*

Note: "Cutaneous" (defined as "administration of a medicinal product to the skin and/or cutaneous wounds and/or nails and/or hair in order to obtain a local effect") is used in preference to "topical" in the formal description of dose forms for the NTP formal name. This is because there is no good definition of "topical" - it tends to be defined as "not systemic" and definition by exclusion is not recommended.

#### Example 4: Product Based Transform

DPD Dose form = TINCTURE

Not an EDQM dose form (or anything similar.)

Used by two products:

* DIN = 00873195; Product = CETRIMIDE TINCTURE 0.5%
* DIN= 00545279; Product =  FRIAR'S BALSAM BENZOIN TINCTURE

Select an NTP formal dose form appropriate for each product:

*Transform DIN = 00873195 to have the dose form of “cutaneous solution”  
Transform DIN= 00545279 to have the dose form of “inhalation vapour, solution”*

# Status

The Non-Proprietary Therapeutic Product (NTP), Therapeutic Moiety (TM) and the Manufactured Product (MP) have a status attribute that needs to be populated. The requirement for the lifecycle is that the status reflects is the availability of that concept in the supply chain and therefore by implication its availability for use in e-prescribing and dispensing to patients. The concepts in the Canadian Clinical Drug Data Set have a different status lifecycle from the products in the DPD to avoid confusion. The derivation of the Canadian Clinical Drug Data Set statuses is described below, and is based on the information available in the DPD. For a storyboard example, please see [Appendix B, Status Example](#_Appendix_B,_Product).

(Note: NoC stands for Notice of Compliance)



Figure : The Status Lifecycle for Products in the DPD

The allowable status for all concept classes in the Canadian Clinical Drug Data Set will be “Active” and “Inactive” and the format for the status (change) date will be YYYYMMDD.

* “Active”: the product that the concept describes is available on the Canadian market
* “Inactive”: the product that the concept describes is no longer marketed; it was “Active” but is no longer so. It should not be prescribed as it would not be possible to find the product for it to be dispensed to patients

## Manufactured Product Status

The MP will not appear in the Canadian Clinical Drug Data Set until its status in the DPD has been set to “marketed”, at which point it will have an “Active” status.

The MP status will be set to “inactive” when the product status in the DPD has been set to “cancelled”. The date of that state transition to inactive will be determined using the furthest expiry date of all the batches released into the supply chain. Note that this may well be a future date, but it is likely that the product will have been used up and therefore will not be in the supply chain prior to that time. The figure below shows how statuses for the Manufactured Product will be represented.



Figure : Manufactured Product Status Lifecycle in the Canadian Clinical Drug Data Set

## Non-Proprietary Therapeutic Product and Therapeutic Moiety Product Status

An NTP and TM do not appear in the Canadian Clinical Drug Data Set until one or more MPs have a status of “marketed” in the Health Canada DPD. The product status date for “Active” will be the earliest date the NTP was instantiated by an active Manufactured Product, and the status date for “Inactive” will be the date that the last related Manufactured Product was set to inactive. The figure below shows how statuses for the NTP and TM will be represented.



Figure : NTP and TM Product Status Lifecycle in the Canadian Clinical Drug Data Set

Although it occurs infrequently, an MP and possibly an NTP and TM may have their status changed back from “Inactive” to “Active”, if the relevant product(s) is/are returned to the market unchanged.

# Non-Proprietary Therapeutic Product (NTP) Formal Name Pattern

Formal naming rules will be consistent with the rules documented for the following components (as shown in [Figure 3](#_The_NTP_Class) above):

* Active ingredient substance(s) and strength
* Dose form

Correct identification of therapeutic products is a major safety issue. Vendors who need to map Canadian Clinical Drug Data Set content to their local content must have accurate information to map correctly, prescribers must accurately identify the correct product that they wish the patient to receive, and pharmacists must be able to accurately interpret the prescribed product to dispense a correct actual product for the patient.

If no formal pattern for naming was provided, here is an example of how this might look if a prescriber or pharmacist searched for “hydrocortisone”:

* Hydrocortisone 1% topical cream
* HYDROCORTISONE tablet 10mg
* Hydrocortisone 25mg tablet
* 1mg/g hydrocortisone Eye Ointment
* Solution for Injection 100mg/1ml HYDROCORTISONE (as sodium phosphate)
* Hydrocortisone 500mg/5ml (as Na2 PO4) injection solution

As the supporting classes for the Canadian Clinical Drug Data Set show, there are two things that will always be required to identify a NTP: the substance and strength set and the dose form. The format, pattern or order in which these are presented should be controlled so that the information can be well ordered and presented to minimize mapping errors or (if used directly) the accidental selection of an incorrect product.

## Single Active Ingredient Substance NTPs:

The following pattern will be used for single ingredient substances:

**<<Substance name(s) (both BoSS and precise ingredient substance if required)**>> <<**Strength>>** <<**Dose Form>>**

* No part of the NTP description will be capitalized (with the exception of the “L” as a symbol/abbreviation for “liter” and as in “mL” for millilitre, and for capitalization of the alphabetic symbol for vitamin substances);
* TALL MAN lettering will not be used.

Table : The components required to build a single ingredient NTP

|  |  |  |
| --- | --- | --- |
| **Substance** | **Strength** | **Dose form** |
| levothyroxine sodium | 25 mcg | oral tablet |
| levothyroxine sodium | 500 mcg | powder for solution for injection |
| atorvastatin (atorvastatin calcium) | 20 mg | oral tablet |
| salbutamol (salbutamol sulfate) | 2 mg | oral tablet |

Here are the applicable NTPs for the above examples:

* levothyroxine sodium 25 mcg oral tablet
* levothyroxine 500 mcg powder for solution for injection
* atorvastatin (atorvastatin calcium) 20 mg oral tablet
* salbutamol (salbutamol sulfate) 2 mg oral tablet

## Multiple Active Ingredient Substance NTPs (up to 5)

The early versions of the Canadian Clinical Drug Data Set will exclude products with greater than 5 active ingredients. The following pattern will be used for multiple ingredient substances (up to 5):

**<< Substance A name(s) (both BoSS and precise ingredient substance if required) and Strength A**>> **<<and>>** **<< Substance B name(s) (both BoSS and precise ingredient substance if required) and Strength B**>> <<**Dose Form>>**

Table : The components required to build a multi-ingredient NTP

|  |  |
| --- | --- |
| **Substance and Strength** | **Dose form** |
| amoxicillin (amoxicillin trihydrate) 250 mg and clavulanic acid 125 mg | oral tablet |
| amoxicillin (amoxicillin trihydrate) 250 mg per 5 mL and clavulanic acid 125 mg per 5 mL | oral solution |
| amlodipine (amlodipine besylate) 10 mg and atorvastatin (atorvastatin calcium) 20 mg | oral tablet |

Here are the applicable NTPs for the above examples:

* amoxicillin (amoxicillin trihydrate) 250 mg and clavulanic acid 125 mg oral tablet
* amoxicillin (amoxicillin trihydrate) 250 mg per 5 mL and clavulanic acid 125 mg per 5 mL oral solution
* amlodipine (amlodipine besylate) 10 mg and atorvastatin (atorvastatin calcium) 20 mg oral tablet

The following rules will be applied to all multi-ingredient NTPs:

* “and” will be used as the conjunction between each active ingredient substance and strength;
* The order of active ingredient substances in a multi-ingredient NTP will be alphabetical

## Compounded Methadone

Due to the complex prescribing and dispensing requirements surrounding compounded methadone, special care has been taken to ensure the guidelines align. An environmental scan was conducted of Canadian methadone prescribing and dispensing standards, provincial and territorial formularies, as well as ISMP recommendations.

Methadone oral solution is available as manufactured products or it can be compounded from methadone powder. The form in which methadone oral solution is dispensed varies across jurisdictions based on prescribing and dispensing standards, as well as product coverage on provincial/territorial formularies. The prescriber may or may not be aware when the pharmacy is required to dispense a compounded methadone product.

In all Canadian jurisdictions, prescribers are not required to specify if a methadone oral solution needs to be compounded. Only the methadone ingredient with the dose (e.g. methadone solution, 50 mg daily) needs to be indicated. The Therapeutic Moiety level can be used for specifying compounded methadone at this time.

**NTP**

methadone example

**Therapeutic Moiety**

methadone example

code: 923456987

Formal name: methadone

Status: available

code: 123456987

Formal name: methadone hydrochloride 10 mg per 1 mL oral solution

Status: available

Figure : An Example for Methadone products

# Manufactured Product (MP) Formal Name Pattern

A correct and unambiguous formal name for the MP will enable vendor mapping to their local content.

Formal naming rules will be consistent with the rules documented for the NTP for the active ingredient substance(s) and strength(s) and dose form components:

In addition, for each MP, the DPD Product Name and DPD Company Name will be part of the formal name, in the pattern described below. The case used for the Product Name and Company Name with be as it is in the DPD, which is usually upper case for both components.

The following table identifies the components of the MP formal name.

Table : MP Formal Name Components and Examples

|  |  |  |
| --- | --- | --- |
| **Components** | **Branded Example Component** | **Generic Example Component** |
| **Active ingredient substance (BoSS and/or precise ingredient substance)** | amlodipine (amlodipine besylate) | amlodipine (amlodipine besylate) |
| **Strength** | 5 mg | 5 mg |
| **Product name (from the DPD)** | NORVASC | ACT AMLODIPINE |
| **Dose form (as transformed by the rules for dose form)** | oral tablet | oral tablet |
| **Company Name – (from the DPD and as provided by the medication supplier)** | PFIZER CANADA INC | [ACTAVIS PHARMA COMPANY](https://health-products.canada.ca/dpd-bdpp/search-fast-recherche-rapide.do?code=15772&lang=en) |

The next sections describe how the components will be used in the MP pattern.

## Single Ingredient MP

For single ingredient products, the pattern will be as follows:

**<<Product name>> <<[NTP Name]>> << Company Name>>**

Formal Name Branded Example:

NORVASC [amlodipine (amlodipine besylate) 5 mg oral tablet] PFIZER CANADA INC

Formal Name Generic Manufactured Example:

ACT AMLODIPINE [amlodipine (amlodipine besylate) 5 mg oral tablet] [ACTAVIS PHARMA COMPANY](https://health-products.canada.ca/dpd-bdpp/search-fast-recherche-rapide.do?code=15772&lang=en)

## Multiple Ingredient MP

For multiple ingredient products, the pattern will be as follows:

**<<Product name>> << [NTP Name]>> << Company Name>>**

Formal Name Branded Example:

CLINDOXYL ADV GEL [benzoyl peroxide 3 % and clindamycin (clindamycin phosphate) 1 % topical gel] GLAXOSMITHKLINE INC.

Formal Name Generic Manufactured Example:

APO-AMLODIPINE-ATORVASTATIN [amlodipine (amlodipine besylate) 5 mg and atorvastatin (atorvastatin calcium) 10 mg oral tablet] APOTEX INC.

When a Product Name includes information that is also part of the pattern there will be duplicate information in the MP formal name. The current Health Canada practice with confirming product names is to exclude this information but it is present in the older products. The following are examples of Product Names that include strength, dose form and/or other information.

Table : MP Examples that include duplicate information

|  |  |
| --- | --- |
| **Existing DPD Product Name** | **Example MP** |
| AMOX 250 CAP 250MG | AMOX 250 CAP 250MG [amoxicillin (amoxicillin trihydrate) 250 mg oral capsule] JAAPHARM CANADA INC. |
| AMOX S 125 SUS 125MG/5ML | AMOX S 125 SUS 125MG/5ML [amoxicillin (amoxicillin trihydrate) 125 mg per 5 mL oral suspension] JAAPHARM CANADA INC. |
| AMOXICILLIN SUGAR-REDUCED GRANULES FOR ORAL SUSPENSION | AMOXICILLIN SUGAR-REDUCED GRANULES FOR ORAL SUSPENSION [amoxicillin (amoxicillin trihydrate) 250 mg per 5 mL granules for oral suspension] SIVEM PHARMACEUTICALS ULC |
| ACYCLOVIR SODIUM INJECTION | ACYCLOVIR SODIUM INJECTION [acyclovir (acyclovir sodium) 500 mg per 20 mL solution for injection] HOSPIRA HEALTHCARE CORPORATION |
| CARDIZEM CD | CARDIZEM CD [diltiazem hydrochloride 180 mg prolonged-release capsule] VALEANT CANADA LP/VALEANT CANADA S.E.C. |
| EES 400 | EES 400 [erythromycin ethylsuccinate 400 mg per 5 mL powder for oral suspension] AMDIPHARM LIMITED |
| APO-AMLODIPINE-ATORVASTATIN | APO-AMLODIPINE-ATORVASTATIN [amlodipine (amlodipine besylate) 5 mg and atorvastatin (atorvastatin calcium) 10 mg oral tablet] APOTEX INC. |
| CLINDOXYL ADV GEL | CLINDOXYL ADV GEL [benzoyl peroxide 3 % and clindamycin (clindamycin phosphate) 1 % topical gel] GLAXOSMITHKLINE INC |

# Therapeutic Moiety

## Introduction and Requirement

To support electronic prescribing, a requirement for an entity in addition to the NTP emerged. Prescribers wish to select the “therapeutic moiety” (without specifying dose form and product strength) and then to specify the dose quantity and possibly the route of administration; this is in contrast to selecting a more fully defined product (as the NTP provides).

The Therapeutic Moiety (TM) is the functional and clinically significant part of the active ingredient substance(s) present in a medicinal product, and as such, the TM class is an abstract representation of a medicinal product without reference to strength and dose form, focusing only on active ingredient substance(s).

The Therapeutic Moiety (TM) is an abstraction of the NTP class, and is therefore a grouping concept. Each NTP will belong to only one TM; however not all NTPs will require a TM (devices will not, nor will combination NTPs).

## Scope of TM in the Canadian Clinical Drug Data Set

Not all NTPs will have a TM, since it is not clinically sensible or clinically safe to have a TM concept for some types of products.

Types of products that will not have a TM include:

* Devices (at least initially)
* Combination products – since these, by definition, are explicitly “products” and require more than just their moieties to correctly describe them
* Multi-ingredient products with more than 5 active ingredient substances (for which there is not a fully specified NTP, so a TM would be meaningless)
* Initially “problematic medicines” (see below)

## Therapeutic Moiety Formal Name

The Formal Name of the TM shall describe the functional part of the active ingredient substance(s) present in a medicinal product (i.e. without salt or modifier description) using the INN, USAN or occasionally CSD name, as reflected in the related NTP concepts, and respecting the Canadian Clinical Drug Data Set guidance for naming substances such as vitamins.

For example:

* INN
  + sumatriptan
  + amoxicillin
  + amlodipine
  + salbutamol
* USAN
  + nitroglycerin
  + acetaminophen

However, there are exceptions to this: see the “Problematic medicines” section below.

## Problematic Medicines

### Therapeutic Moiety for “Elemental Medicines”

Because the TM is “the functional part of the active ingredient substance(s) present in a medicinal product”, it can be difficult to describe TMs for elemental substances, for example potassium and iron; the TM could be “potassium chloride” or just “potassium”; it could be “ferrous sulfate” and “ferric chloride” or just iron. Note that the NHS dm+d includes the salt for elemental TMs (potassium chloride, ferrous sulfate etc.).

In almost all cases, the salt/modifier has a significant effect on the clinical use of elemental substances (e.g. it usually dictates the dose quantity that must be prescribed) and therefore prescribers are familiar with and wish to describe both the element and its salt/modifier (usually the basis of strength substance). Therefore the “functional part of the active ingredient substance(s) present in a medicinal product” for these medicinal products is “the element **with** its salt/modifier”, the therapeutic moiety should reflect this.

Examples:

* potassium chloride
* ferrous sulfate
* ferrous gluconate
* aluminum hydroxide
* aluminum chloride

### Therapeutic Moiety for Medicines with significant salts/modifiers

For some medicines, more than one salt/modifier is used as the precise ingredient substance in various manufactured products AND the salt/modifier has clinical significance, usually affecting the description of the strength. Examples include phenytoin, doxorubicin (indeed anything that can be supplied in liposomes), dexamethasone and diclofenac, two of which are shown below and which illustrate how the approach to the authoring of TM concepts requires editorial intervention to determine clinical significance (and therefore is not completely auto-generate-able):

**Diclofenac:**

* Diclofenac is available with a variety of NTPs with different precise ingredient substances:
  + diclofenac sodium 25 mg gastro-resistant tablet
  + diclofenac sodium 50 mg gastro-resistant tablet
  + diclofenac sodium 75 mg prolonged-release oral tablet
  + diclofenac sodium 100 mg prolonged-release oral tablet
  + diclofenac sodium 50 mg suppository
  + diclofenac sodium 100 mg suppository
  + diclofenac sodium 0.1% ophthalmic drops, solution
  + diclofenac sodium 1.5% cutaneous solution
  + diclofenac diethylamine 2.32% cutaneous gel
  + diclofenac potassium 50 mg film coated oral tablet
  + diclofenac potassium 50 mg powder for oral solution

There could possibly be three TMs (as sibling concepts) based on including the salt/modifier (from the basis of strength substance), as shown here:

* + diclofenac sodium
  + diclofenac potassium
  + diclofenac diethylamine

However, in this case, non-pharmacist users are rarely familiar with these different modifiers and their effects, particularly for the modifier(s) used in some of the topical products, and the differences between the salts for the oral form are not considered to be so clinically significant in Canadian healthcare culture and practice that they must be described in a prescription. Pharmacists have the ability to choose the appropriate salt (for example for a prescription written as “diclofenac [TM] 50 mg oral”) based on their discretion and the patient’s requirements.

The most useful Therapeutic Moiety concept would therefore be:

* + diclofenac

**Phenytoin:**

* Phenytoin products are available with different precise ingredient substances:
  + phenytoin sodium (e.g. Dilantin 30mg oral capsules)
  + phenytoin base (e.g. Dilantin 30 mg per 5 mL oral suspension)
* 100mg of phenytoin sodium is equivalent to 92mg phenytoin (base) and dosage of phenytoin products may be safety critical
* There could be two TMs (as sibling concepts):
  + Phenytoin (base) – *must include the “base” else would be any phenytoin product*
  + Phenytoin sodium

In this case, users **must** be cognisant of the clinically significant differences between the different precise ingredient substances and how they relate to the strength of the medicinal product, and therefore the dose quantity that a patient would receive. Consequently, most users would usually prescribe an NTP (or even an MP) although in hospital practice, especially when a patient is being newly stabilised, a TM might be used in the prescription. The two sibling TMs as shown above was considered appropriate for the Canadian Clinical Drug Data Set.

# Combination Products

## Introduction and Requirement

There is a type of medicinal products that are in scope of the Canadian Clinical Drug Data Set, that are different from “standard” medicinal products (which contains one or more identical manufactured items with the same active ingredient substance(s) in the same strength(s) and with the same dose form); this subtype is known as combination products.

A combination product may also be called a “component product” or a “multi-component product” as it contains more than one component element (manufactured item) within it; it may also be known as or a “kit product” (or just “kit”). Occasionally a combination product is may be known as a “compound product” but this risks being confused with products that are extemporaneously compounded by a pharmacist from a formula provided by the prescriber for an individual patient (sometimes known as “magistral products”).

Examples of combination products:

* Canesten Combi-pak Comfortab 1
  + clotrimazole 1 % cutaneous cream
  + clotrimazole 500 mg vaginal tablet
* Brevicon 0.5/35 Tablets (28 day pack)
  + ethinylestradiol 35 microgram and norethindrone 500 microgram oral tablet
  + lactose oral tablet
* Premplus 0.625MG-2.5MG Tablets
  + conjugated estrogen 625 microgram oral tablet
  + medroxyprogesterone acetate 2.5 mg oral tablet
* HP-PAC
  + amoxicillin (amoxicillin trihydrate) 500 mg oral capsule
  + clarithromycin 500 mg film coated oral tablet
  + lansoprazole prolonged release 30 mg oral capsule
* Entocort
  + budesonide 2 mg dispersible tablet for rectal solution
  + vehicle for rectal solution
* GlucaGen HypoKit
  + glucagon 1 mg powder for solution for injection
  + water for injection 1.5 mL
* GONAL-F
  + follitropin alfa 33 mcg powder for solution for injection
  + diluent solution

In some senses, a Combination Product should be described *only* as a Packaged Medicinal Product as only in the context of the complete package can all the component parts be fully described. This strict limitation is not helpful either in the regulatory context, where “the product” is licensed as a whole entity. It is also not helpful in the clinical environment, where prescribing clinicians wish to see combination products in the same pick list as other “standard” products, without having to search in any separate “package” lists, as packages are rarely of importance when prescribing. For dispensing, selection of a packaged product is often appropriate but is often reached by initial product selection.

Because combination products are licensed as a “whole entity” and are prescribed and dispensed as such, they will be included in the Canadian Clinical Drug Data Set and represented both as MPs and as a particular type of NTP (see below). Explicit and individual inclusion of their component manufactured items as concepts with the Canadian Clinical Drug Data Set will not be undertaken (see [Limitations](#_Limitations) below).

## Definition and Description

A combination product is a particular type of medicinal product that contains two (or more) “*manufactured items*”[[6]](#footnote-6) that are authorized as and presented in a single “packaged product” and licensed for a single (set of) indications.

A combination product may contain only a single active ingredient substance; presented in more than one manufactured item (as in the Canesten example) or each manufactured item in the combination may have a different active ingredient substance (as in the Premplus and HP-PAC examples). Note that in the Brevicon example, one of the manufactured items is itself a multi-ingredient item. In some component products, one of the components is provided purely to support reconstitution of another (active) component (e.g. a diluent).

The strength of each active ingredient substance must be stated uniquely, especially when both components contain the same one (as in the Canesten example).

The combination product will have two or more dose forms, even if they are the same (as in the Brevicon and Premplus examples, where oral tablet is the dose form for both components). Although these could be expressed using a combined dose form concept from the EDQM combined dose form terminology, because it is most helpful to prescribers to indicate which component has which dose form, formal “combined dose forms” will not be used in the naming.

### Limitations

It is possible to describe the dose form(s) and ingredient substance-strength set(s) information for a combination product, it is not currently possible in the available structures to describe the quantity (either explicitly or by proportion) of each manufactured item present in the combination product. For example: it is not possible to describe that there are **21** “ethinylestradiol 35 mcg and norethindrone 500 mcg oral tablets” with **7** “lactose oral tablets” in the Brevicon 28-day product.

Although rarely authorized for this, and sometimes explicitly prohibited in an authorization, a patient may be directed to use just one of the components in a combination product, if that is the only way to obtain the particular manufactured item. The Canadian Clinical Drug Data Set cannot currently support the description of one manufactured item from within the Combination Product for this type of prescribing.

It is acknowledged that the provision of decision support for combination products can be challenging, especially for dose range checking.

Some medicinal product terminologies (e.g. the UK’s NHS dm+d) do explicitly model the individual component concepts, for the reasons given above. However, this adds complexity to the terminology model and to its implementation, and for the e-prescribing/dispensing use cases (and for the EHR use case), this complexity is currently deemed unnecessary.

## NTP type code

To indicate that combination products are a different type of medicinal product, rather than use an additional qualifier (such as “combination product”) in the NTP description, combination products will be indicated using a “type” attribute in the NTP class.

The type code will be used to indicate only those combination products that contain two or more manufactured items that contain active ingredient substance(s). The type code will not be used on combination products where the second manufactured item is:

* a therapeutically inactive diluent
* a therapeutically inactive “placebo” (as in the Brevicon 28-day product)

**Examples**: the combination products shown in normal text below would have the type code applied; those shown in grey would not

* clotrimazole 1 % cutaneous cream **with** clotrimazole 500 mg vaginal tablet
* ethinylestradiol 35 microgram oral tablet ***and*** norethindrone 500 microgram **with** lactose oral tablet
* conjugated estrogen 625 microgram oral tablet **with** medroxyprogesterone acetate 2.5 mg oral tablet
* amoxicillin (amoxicillin trihydrate) 500 mg oral capsule **with** clarithromycin 500 mg film coated oral tablet **with** lansoprazole prolonged release 30 mg oral capsule
* budesonide 2 mg dispersible tablet for rectal solution **with** vehicle for rectal solution
* glucagon 1 mg powder for solution for injection **with** water for injection 1.5 mL
* follitropin alfa 33 mcg powder for solution for injection **with** diluent solution

## Combination Product NTP Formal Name Pattern

The Formal Name pattern to describe a combination NTP will respect that the product is not “an ingredient strength set” but a “set of ingredient strength sets” and that there will be a dose form associated with each set. The (EDQM) combined dose form will not be used as this would have the drawback of not identifying clearly, which ingredient strength set applies to which dose form.

The phraseology that will clearly differentiate a combination product from a multi-ingredient product will be to use “**with**” as the conjunction between each manufactured item component.

The order of active ingredient substances will be alphabetic, both for within the manufactured item, and between the different components. For those manufactured items that have the same active ingredient substances (the clotrimazole example) the alphabetic order of dose form will be used.

Examples:

* clotrimazole 1 % cutaneous cream **with** clotrimazole 500 mg vaginal tablet
* ethinylestradiol 35 microgram oral tablet **and** norethindrone 500 microgram **with** lactose oral tablet
* conjugated estrogen 625 microgram oral tablet **with** medroxyprogesterone acetate 2.5 mg oral tablet
* amoxicillin (amoxicillin trihydrate) 500 mg oral capsule **with** clarithromycin 500 mg film coated oral tablet **with** lansoprazole prolonged release 30 mg oral capsule
* budesonide 2 mg dispersible tablet for rectal solution **with** vehicle for rectal solution
* glucagon 1 mg powder for solution for injection **with** water for injection 1.5 mL
* follitropin alfa 33 mcg powder for solution for injection **with** diluent solution

For products that are supplied with a diluent (often referred to as “kits”) the diluent should be only briefly described (e.g. as “diluent”) rather than in detail (e.g. “bacteriostatic water for injections”). Similarly, for products with one of their component manufactured items that is effectively inert (as in the every-day oral contraceptive products) the inert component will also be minimally described without any requirement for strength information (e.g. “lactose tablets”).

## Combination Product MP Formal Name Pattern

The formal name pattern to describe a combination MP will follow the pattern for MP Formal Names; it is acknowledged that this will produce very long names, but since these are for “under the hood” use only, to date no issues have been raised against this.

Examples:

* CANESTEN COMBI-PAK COMFORTAB 1 [clotrimazole 1 % cutaneous creamwith clotrimazole 500 mg vaginal tablet] BAYER INC CONSUMER CARE
* BREVICON 0.5/35 TABLETS (28-DAY PACK) [ethinylestradiol 35 microgram oral tablet and norethindrone 500 microgram with lactose oral tablet] PFIZER CANADA INC
* PREMPLUS [conjugated estrogen 625 microgram oral tablet with medroxyprogesterone acetate 2.5 mg oral tablet] PFIZER CANADA INC
* HP-PAC [amoxicillin (amoxicillin trihydrate) 500 mg oral capsule **with** clarithromycin 500 mg film coated oral tablet **with** lansoprazole prolonged release 30 mg oral capsule] TAKEDA PHARMACEUTICALS AMERICA INC
* ENTOCORT ENEMA [budesonide 2 mg dispersible tablet for rectal solution **with** vehicle for rectal solution] TILLOTS PHARMA GMBH
* GLUCAGEN HYPOKIT [glucagon 1 mg powder for solution for injection **with** water for injection 1.5 mL] NOVO NORDISK CANADA INC
* GONAL-F [follitropin alfa 33 mcg powder for solution for injection **with** diluent solution] EMD SERONO A DIVISION OF EMD INC CANADA

# Appendix A, Advisory Group Members

|  |  |
| --- | --- |
| **Name** | **Organization** |
| Raymond Chevalier | Vigilance Santé |
| Isabelle Filion | Vigilance Santé |
| Shelita Dattani | Canadian Pharmacists Association (CPhA) |
| Barbara Jovaisas | Canadian Pharmacists Association (CPhA) |
| Natalie Borden | Nova Scotia Department of Health and Wellness |
| Jordan Hunt | Canadian Institute for Health Information (CIHI) |
| Marc L’Arrivee | Manitoba eHealth |
| Karen Hay | Ontario Ministry of Health |
| Melva Peters | Ontario Ministry of Health |
| Jim Kavanagh | Telus Health |
| Benjamin Yuen | Telus Health |
| John McBride | Institute for Safe Medication Practices Canada (ISMP Canada) |
| Doris Nessim | GS1 |
| Martin Darveau | Ministry of Health and Social Services Quebec (MSSS) |
| George Robinson | First DataBank |
| Joanne Luong | First DataBank |
| Dr. Rashaad Bhyat | Canada Health Infoway |
| Vikesh Srivastava | Health Canada |
| Louise Travill | Health Canada |
| Daniel Buijs | Health Canada |
| Kartik Goyal | Health Canada |
| Tanya Achilles | Canada Health Infoway |
| Seema Nayani | Canada Health Infoway |
| Julie James | Canada Health Infoway |
| Beverly Knight | Canada Health Infoway |

# Appendix B, Product Status Storyboard Example

Fred’s Pharmaceuticals gains a Notice of Compliance (NoC) from Health Canada for “Exotodrug 250mg and 500mg Capolets” (which contain exotocillin hydrochloride in a “proprietary” dose form for Fred’s Pharmaceuticals called “capolet”) on 12 Jan 2012 and these have a DIN of 40928121 and 40928122 respectively. They notify Health Canada that they are marketing both products in Canada on 25 Jan 2012. They continue to market those products on an ongoing basis.

In June 2016, the patent for exotocillin runs out and Joe’s Generics gains a NoC for a generic version of exotocillin using the “reference product” procedure.

As margins drop, Fred’s Pharmaceuticals decides it is no longer viable for them to continue to market their branded presentation, and in March 2017 sell it on to Mike’s MeToos who continue to market it as EXOTODRUG in Canada, but with new DINs.

Eventually, the antibiotic resistance to exotocillin is so widespread that it is no longer sensible to market any products containing exotocillin. Joe’s Generics notify HC of their decision to stop marketing in April 2019 and Mike’s MeToos do so in September 2020.

**In the Canadian Clinical Drug Data Set January 2012:**

**Two new MPs:**

* EXOTODRUG CAPOLETS [exotocillin (exotocillin hydrochloride) 250 mg oral capsule] FRED’S PHARMACEUTICALS INC
* EXOTODRUG CAPOLETS [exotocillin (exotocillin hydrochloride) 500 mg oral capsule] FRED’S PHARMACEUTICALS INC

Both have status “active”

**Two new NTPs:**

* exotocillin (exotocillin hydrochloride) 250 mg oral capsule
* exotocillin (exotocillin hydrochloride) 500 mg oral capsule

Both have status “active”

**In the Canadian Clinical Drug Data Set June 2016:**

The same two NTPs are present as “active”, but two new MPs join the existing EXOTODRUG concepts, all with the status “active”

* JG-EXOTOCILLIN [exotocillin (exotocillin hydrochloride) 250 mg oral capsule] JOE’S GENERICS INC
* JG-EXOTOCILLIN [exotocillin (exotocillin hydrochloride) 500 mg oral capsule] JOE’S GENERICS INC

**In the Canadian Clinical Drug Data Set March 2017:**

The same two NTPs are present as “active”, but the new MPs now look like this:

**Active:**

* JG-EXOTOCILLIN [exotocillin (exotocillin hydrochloride) 250 mg oral capsule] JOE’S GENERICS INC
* JG-EXOTOCILLIN [exotocillin (exotocillin hydrochloride) 500 mg oral capsule] JOE’S GENERICS INC
* EXOTODRUG CAPOLETS [exotocillin (exotocillin hydrochloride) 250 mg oral capsule] MIKE’S METOOS PHARMA
* EXOTODRUG CAPOLETS [exotocillin (exotocillin hydrochloride) 500 mg oral capsule] MIKE’S METOOS PHARMA

**Inactive:**

* EXOTODRUG CAPOLETS [exotocillin (exotocillin hydrochloride) 250 mg oral capsule] FRED’S PHARMACEUTICALS INC
* EXOTODRUG CAPOLETS [exotocillin (exotocillin hydrochloride) 500 mg oral capsule] FRED’S PHARMACEUTICALS INC

**In the Canadian Clinical Drug Data Set April 2019:**

The same two NTPs are present as “active”, but the new MPs now look like this:

**Active:**

* EXOTODRUG CAPOLETS [exotocillin (exotocillin hydrochloride) 250 mg oral capsule] MIKE’S METOOS PHARMA
* EXOTODRUG CAPOLETS [exotocillin (exotocillin hydrochloride) 500 mg oral capsule] MIKE’S METOOS PHARMA

**Inactive:**

* EXOTODRUG CAPOLETS [exotocillin (exotocillin hydrochloride) 250 mg oral capsule] FRED’S PHARMACEUTICALS INC
* EXOTODRUG CAPOLETS [exotocillin (exotocillin hydrochloride) 500 mg oral capsule] FRED’S PHARMACEUTICALS INC
* JG-EXOTOCILLIN [exotocillin (exotocillin hydrochloride) 250 mg oral capsule] JOE’S GENERICS INC
* JG-EXOTOCILLIN [exotocillin (exotocillin hydrochloride) 500 mg oral capsule] JOE’S GENERICS INC

**In the Canadian Clinical Drug Data Set September 2020:**

Both NTP concepts are marked as inactive and all 6 MP concepts are now marked as inactive.

# Appendix C: Diagrammatic Representation of Formal Naming

## NTP: Single active ingredient substance products

**Precise ingredient substance and basis of strength substance are the same**

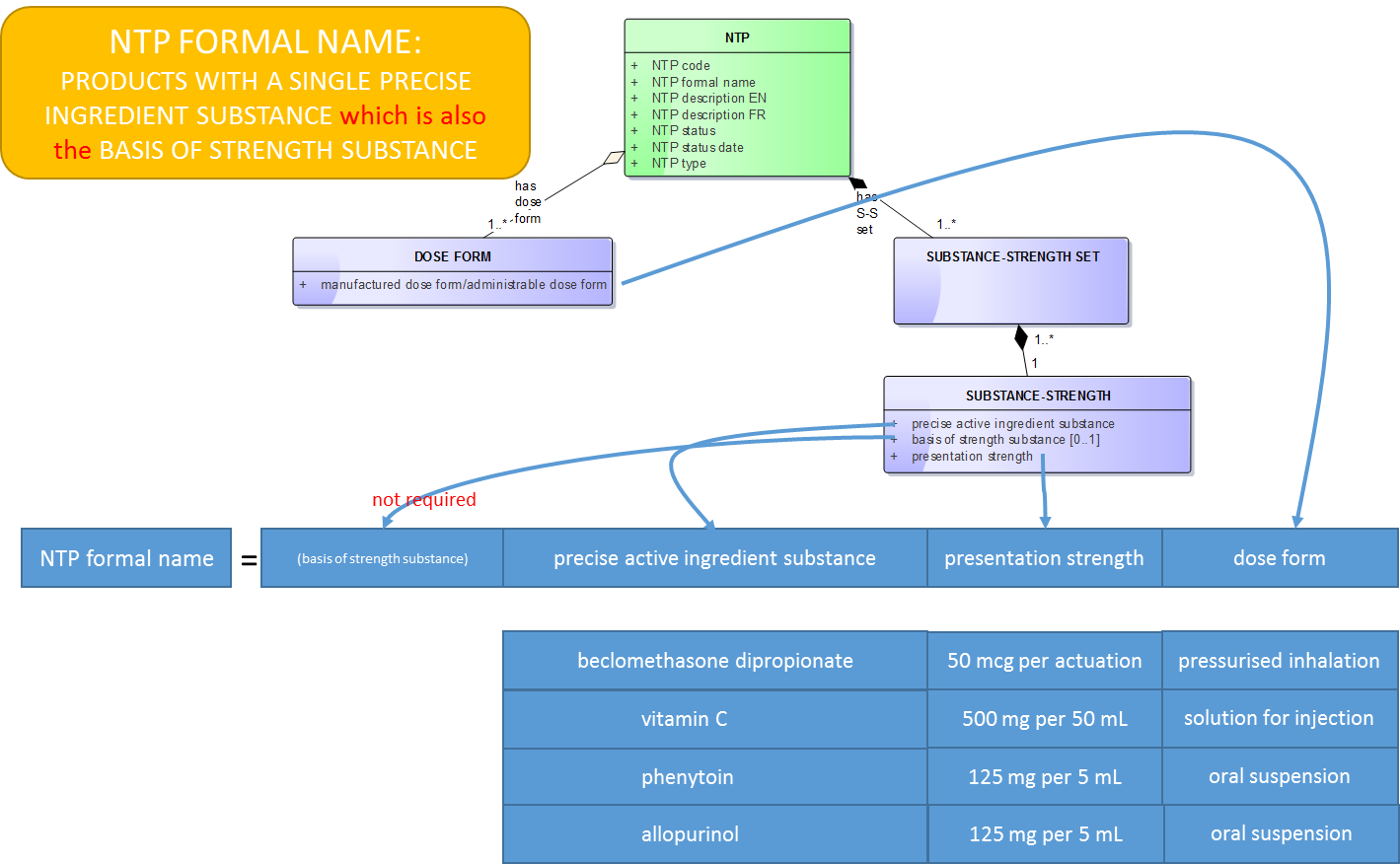


Figure : NTP formal name pattern for NTPs where basis of strength substance is the same as the precise ingredient substance

**Precise ingredient substance and basis of strength substance are different**

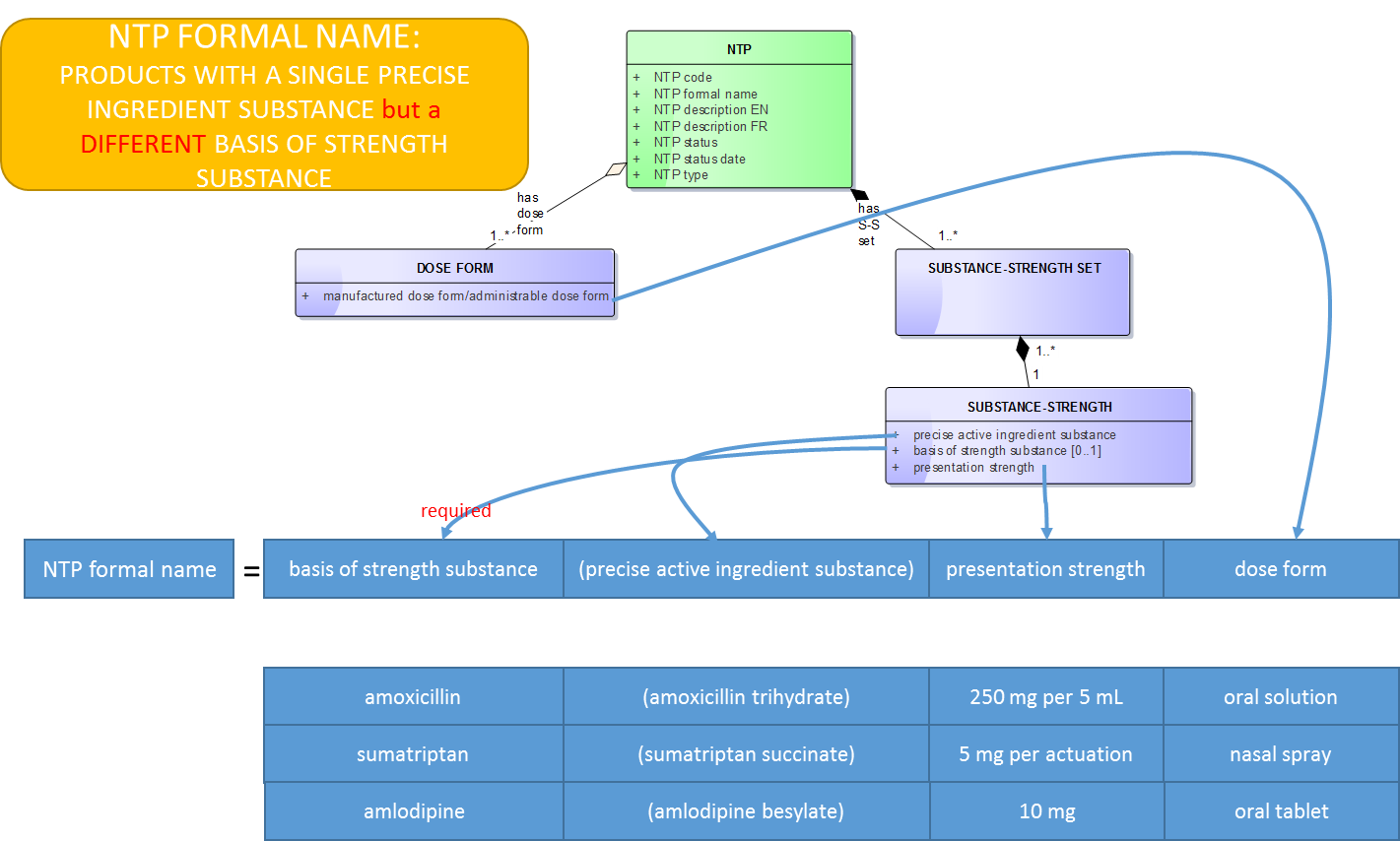


Figure : NTP formal name pattern for NTPs where basis of strength substance is different from the precise ingredient substance

## NTP: Multiple active ingredient substance products

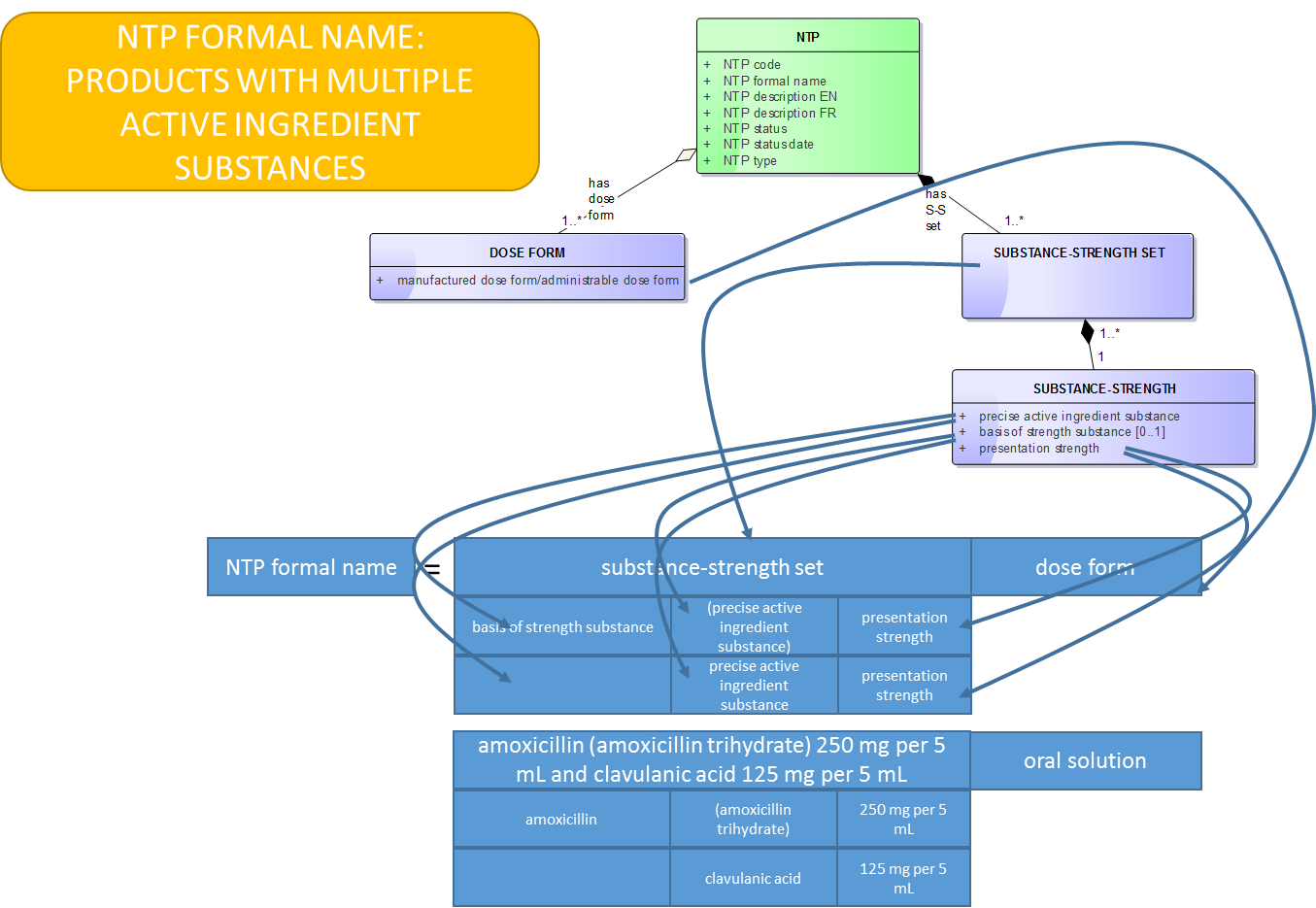


Figure : NTP formal name pattern for NTPs multiple active ingredient substances

# Appendix D: International Units

International units are a unit of measurement for the biological activity of a variety of substances, particularly vitamins, hormones, some vaccines and blood products and some biologically active medicinal substances.

Although International Units are widely used in laboratory test result reporting, there is no equivalence between IU measurements of different biological agents. For instance, one IU of vitamin E cannot be equated with one IU of vitamin A in any way, by [mass](https://en.wikipedia.org/wiki/Mass) or by biologic activity or therapeutic [efficacy](https://en.wikipedia.org/wiki/Efficacy).

Although produced by the [WHO](https://en.wikipedia.org/wiki/World_Health_Organization) [Expert Committee on Biological Standardization](https://en.wikipedia.org/wiki/WHO_Expert_Committee_on_Biological_Standardization), international units are NOT part of the International System of Units (also known as the SI units, Système international d'unités).

**Examples of International units**

**Vitamin A**

1 IU is the biological equivalent of

* 300 nanograms of retinal or
* 600 nanograms of beta-carotene

**Vitamin E**

1 IU is the biological equivalent of

* 667 micrograms of d-alpha-tocopherol
* 450 micrograms of dl-alpha-tocopherol acetate

**Insulin**

1 IU is the biological equivalent of

* 34.7 micrograms of human insulin (Ph Eur)

**Penicillin**

1 IU is the biological equivalent of

* 590 nanograms of phenoxymethylpenicillin (penicillin V)

**Rationale**

International units are used to compare different forms or different preparations of similarly acting biological agents; different presentations that will produce the same biological effect will contain the same number of IUs.

**Nomenclature**

The name **international unit** has often been capitalized (in English and other languages), although major English-language dictionaries treat it as a common noun and thus use lower case. In some other languages, the term is:

* unité internationale (French)
* unidad internacional (Spanish)
* unità internazionale (Italian)
* internationale Einheit (German)
* internationale eenheid (Dutch)
* mezhdunarodnaya jedinica (Russian) [международная единица]

Because the language terms vary, it is hard to have a standard abbreviation. The following are frequently used:

* IU – in Romance languages
* UI – in Germanic languages
* ME – in Russian

There is a risk of having the letter "I" confused with the digit "1". Many institutions and medicines safety bodies have a stated policy to omit the "I" and therefor to use only **U** or **E** when describing abbreviated strength using international units. Other institutions and medicines safety bodies require the word "units" (or words "international units") to be written out in full.

For the Canadian Clinical Drug Data Set, the word “units” will be used in full.

**Methodology**

To define the IU for a substance, an international collaborative study is organized by the [WHO](https://en.wikipedia.org/wiki/World_Health_Organization) [Expert Committee on Biological Standardization](https://en.wikipedia.org/wiki/WHO_Expert_Committee_on_Biological_Standardization) to reach a consensus on the methods of analysis and biological assay, and therefore to draw a baseline for standardization for the substance. This uses highly purified preparations of the [substance](https://en.wikipedia.org/wiki/Chemical_substance), typically in [lyophilized](https://en.wikipedia.org/wiki/Lyophilize) form, called "international reference preparations" or IRPs. Assays are performed and initially an arbitrarily set number of IUs contained in that IRP preparation. Similar substances are then calibrated against this initial IU standard.

All assay results can be quite variable; the final IU value for samples of a given IRP are determined by consensus.

The IRP that provides the best results and shows the best long-term stability is selected to define the next IU. This IRP is then referred to as the "international standard.

**Enzyme units (katals)**

International units should not be confused with enzyme units (international unit of enzyme activity: this is the amount of the enzyme that produces a certain amount of [enzymatic activity](https://en.wikipedia.org/wiki/Enzyme_assay#Enzyme_activity); the amount that [catalyzes](https://en.wikipedia.org/wiki/Catalysis) the conversion of 1 [micro](https://en.wikipedia.org/wiki/Micro-)[mol](https://en.wikipedia.org/wiki/Mole_(unit)) of [substrate](https://en.wikipedia.org/wiki/Substrate_(biochemistry)) per minute. The enzyme unit has been deprecated in favour of the SI unit of **katal** (the amount of enzyme that converts 1 mole of substrate per second)

# Appendix E: Glossary

|  |  |
| --- | --- |
| **Term used in this document** | Definition of Term |
| Identification of Medicinal Products (IDMP) | Identification of Medicinal Products (IDMP) is a set of five ISO norms, which has been developed in response to a worldwide demand for internationally harmonized specifications for medicinal products. |
| European Directorate for the Quality of Medicines and Healthcare (EDQM) | The European Directorate for the Quality of Medicines & Healthcare publishes a database of standard terms, for dose forms, routes of administration and various other key concepts within the domain. This was originally in response to a request from the European Commission, but now is available for wider global use to support the Identification of Medicinal Products (IDMP) initiative and to support healthcare generally. |
| Health Canada Drug Product Database (DPD) | The DPD contains product specific information on drugs approved for use in Canada. The database is managed by Health Canada and includes human pharmaceutical and biological drugs, veterinary drugs, radiopharmaceutical drugs and disinfectant products. |
| International Nonproprietary Names (INN) | International Nonproprietary Names (INN)[[7]](#footnote-7) are managed by the World Health Organization (WHO) and can be used to identify pharmaceutical substances that are acting as active pharmaceutical ingredients. Each INN is a unique name that is globally recognized and is public property, and therefore can be used freely.  The INN is also intended to be used as a basis for non-branded product names in healthcare, to provide clear identification of medicines, safe prescription and dispensing of medicines to patients, and for communication and exchange of information among health professionals and scientists worldwide. |
| Modified International Nonproprietary Names (INNm) | An INN is usually authored for the active part of the molecule only, to avoid the multiplication of entries in cases where several salts, esters, etc. are actually used in medicinal products. To describe active ingredient substances precisely, modified INNs (INNMs) must be created independently (e.g. within a terminology itself).  For example: mepyramine maleate (a salt of mepyramine with maleic acid) is an example of an INNM. However, when the creation of an INNM would require the use of a long or inconvenient name for the radical/modifier part of the INNM, the INN programme will author a short name for such a radical or modifier; for example:  mesilate for methanesulfonate and  camsilate for rac-(7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methanesulfonate) |

1. An interchange terminology is one that is primarily designed to be used *inside* systems to support the sharing of meaning when systems communicate between each other. An interface terminology is often only used to provide mappings. This is in contrast to an interface terminology whose purpose is to support clinicians’ entry of patient-related information into systems, and to facilitate display of computer-stored patient information to clinician users as simple human-readable text. [↑](#footnote-ref-1)
2. ISMP’s List of Error-Prone Abbreviations, Symbols, and Dose Designations (2015) [↑](#footnote-ref-2)
3. Although the SI system supports both ml and mL (and indeed l and L for liters) and both are used in science and in medicine. The convention in medicinal product terminology appears to be moving towards mL to try to avoid any possibility of confusion between lower case l and the numeric 1 [↑](#footnote-ref-3)
4. https://www.edqm.eu/en/Standard-Terms-590.html [↑](#footnote-ref-4)
5. The EDQM dose form terminology was developed on a model originally designed by a team including representatives from HL7, SNOMED CT and regulatory agencies. It has been adopted for use by a number of organizations around the globe for use in healthcare as well as in the regulatory domain. It was therefore felt to be a good choice to support the Canadian NTP development and helps Health Canada towards IDMP compliance. [↑](#footnote-ref-5)
6. A “manufactured item” (in ISO 11615) is the entity that describes the qualitative and quantitative composition of a product that is contained in the packaging of a Medicinal Product – so it is the entity that has the Substance-Strength Set and a Dose Form [↑](#footnote-ref-6)
7. <http://www.who.int/medicines/services/inn/en/> and <http://www.who.int/medicines/services/inn/innguidance/en/> [↑](#footnote-ref-7)