Canadian Clinical Drug Data Set

Editorial Guidelines

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About the Editorial Guidelines

The Canadian Clinical Drug Data Set (CCDD) 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 that it will evolve based on user requirements and feedback.

The Editorial Guidelines will not be updated with each release. They will be updated when there is significant change to the guidelines.

Acknowledgements

Particular thanks go to the members of the initial Advisory Group that supported the development of these Guidelines and the French Advisory Group that supported the development of French Descriptions; names and organizations are listed in Appendix A of the Editorial Guidelines themselves.

Terms of Use

Introduction

Canada Health Infoway (Infoway) and Health Canada have partnered in the development of the Canadian Clinical Drug Data Set Editorial Guidelines and content. The Canadian Clinical Drug Data Set provides a consistent approach to the identification and naming of medications and a limited number of medical devices and is freely available for use in digital health solutions and design applications.

For the Canadian Clinical Drug Data Set to 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

Purpose of this Document

The Editorial Guidelines for the Canadian Clinical Drug Data Set 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. Changes to these Editorial Guidelines will be referenced in Release Notes that accompany each release of this document.

Intended Audience

This document is intended to provide health sector managers, terminology analysts, knowledge base 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 among 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 utilize 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.

Scope

The intended scope for the Canadian Clinical Drug Data Set (CCDD) 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) file contains brand independent and clinically oriented representations of manufactured (therapeutic) products. This includes combination products, which for the purpose of CCDD means products with more than one component, such as kits.
2. The Device Non-proprietary Therapeutic Product (Device-NTP) file contains brand independent and clinically oriented representations of manufactured devices. This includes only a small number of devices (such as lancets, glucose meters and blood glucose strips) that are prescribed by a community clinician and dispensed in a pharmacy.
3. The Therapeutic Moiety (TM) 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.
4. The file containing Manufactured Product (MP) contains descriptions of the brand specific drug that are available for clinical use in Canada.
5. Relationship files that describe the associations between the NTP concepts, MP concepts and TM concepts:
    a. One relationship file with the English formal name and codes and a separate relationship file with French descriptions and codes.
6. The Special Groupings file identifies specific concepts in the Canadian Clinical Drug Data Set and provides relationships between those concepts and policies (such as controlled substances) that apply to those products.
7. The Coded Attributes file provides the coded values used in an attribute field within the Canadian Clinical Drug Data Set.

The current scope of content within CCDD, driven by relevance to e-prescribing and to some extent medication profiles, has been modified from the intended scope as follows:

- Immunizing agents are currently under development for inclusion in the data set, and therefore not currently in CCDD
- Products present in the Licensed Natural Health Products Database (LNHPD) are out of scope for now
- Currently the following types of products are out of scope with the expectation that a stakeholder use case would be required prior to considering addition to CCDD:
    - Highly specialized hospital use products that might not be prescribed in the usual manner for medications and/or are unlikely to be included on a Patient Profile, including:
        - dialysis and hemofiltration fluids
        - large volume intravenous fluids
        - parenteral nutrition products
        - antidotes for poisoning

        - allergens for sensitivity testing
        - imaging products (x-ray contrast media, etc.)
        - antiseptics used for skin cleansing
    - General care products
        - Sunscreens
        - Disinfectants
        - Products whose primary use is cosmetic

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]. It will have the capacity to be used by knowledge base vendors, clinicians, researchers, statistical users, government agencies, healthcare organizations 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, Cerner Multum, DrugBank) and existing user interfaces. The knowledge base vendors (e.g. First Databank (FDB), Vigilance Santé and Cerner Multum, DrugBank) 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 Canadian Clinical Drug Data Set MP code (for manufactured products) or
- the Canadian Clinical Drug Data Set NTP code (as a generic, non-manufacturer-specific drug product) or
- the Canadian Clinical Drug Data Set Device-NTP code (non-manufacturer-specific device product) or
- the Canadian Clinical Drug Data Set TM code. If the TM is shared in a e-prescribe message additional information such as the strength, dosage form and possibly the route of administration must be sent (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

[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 interchange 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.

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 the 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 Canadian Clinical Drug Data Set is accessible via the Infoway Gateway (registration required) and through the Government of Canada Open Government portal.

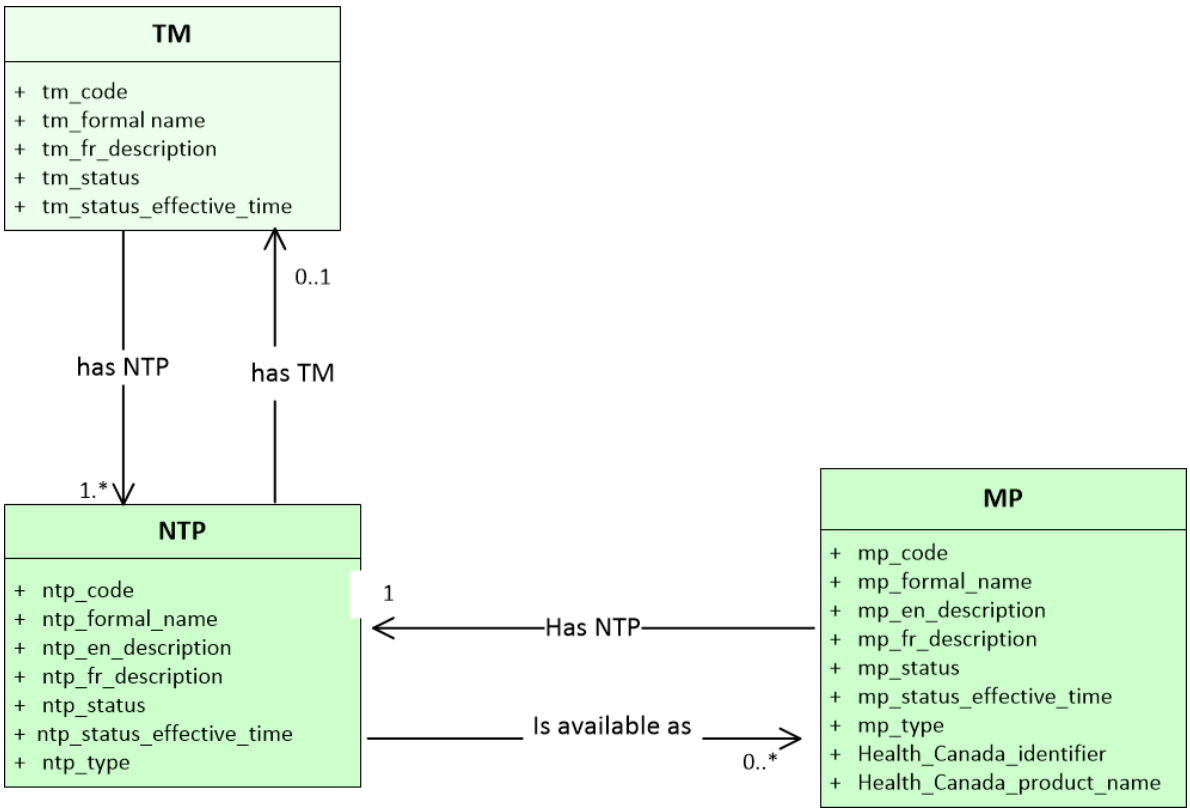
Canadian Clinical Drug Data Set Data Model

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 defining properties are:

- For the TM concepts: the set of active ingredient substance(s)
- For the NTP concepts: the set of active ingredient substance(s)and their strength(s), the dosage form, and for some products, their unit of presentation
- For the MP concepts: the set of active ingredient substance(s)and their strength(s), the dosage form, and for some products, their unit of presentation plus the product name and manufacturer company as published in the DPD.

These three types of concepts that make up the Canadian Clinical Drug Data Set can be described in a relational model that associates these medicinal product concepts with their different levels of granularity together. Note that this model may evolve over time to support new use cases (e.g., for immunization).

Figure 1: Canadian Clinical Drug Data Set Model



A TM will have one or more NTPs associated with it, but an NTP is not required to be associated to a TM (for example, devices will not be associated with a TM). The technical attributes associated with it include tm code, tm formal name, tm fr description, tm status and tm status effective time.

A normal NTP has at least one MP associated with it; however, for NTPs with the status of "deprec"(deprecated), there will not be an associated MP. An NTP has the following attributes: ntp

code, ntp formal name, ntp English description, ntp French description, ntp status, ntp status effective time and ntp type. For device NTPs, there are currently no associated MP products.

An MP will be associated with one and only one NTP. The attributes associated with an MP are mp code, mp formal name, mp en description, mp fr description, mp status, mp status effective time, mp type, Health Canada identifier and Health Canada product name.

Table 1 provides the definition and an example for each of the core classes in the Canadian Clinical Drug Data Set model.

Table 1: The Canadian Clinical Drug Data Set Model Classes

Model Class	Definition and Description	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. An NTP is described by the set of active ingredient substance(s) (both precise active ingredient substance and basis of strength substance, if different) and their strength(s), the dosage form, and for some products, their unit of presentation	amlodipine (amlodipine besylate) 2.5 mg oral tablet
Manufactured Product (MP)	A brand specific drug that is or, within the lifetime of the CCDD, has been available for prescribing and dispensing in Canada.	ACT AMLODIPINE (amlodipine (amlodipine besylate) 2.5 mg oral tablets) ACTAVIS PHARMA COMPANY

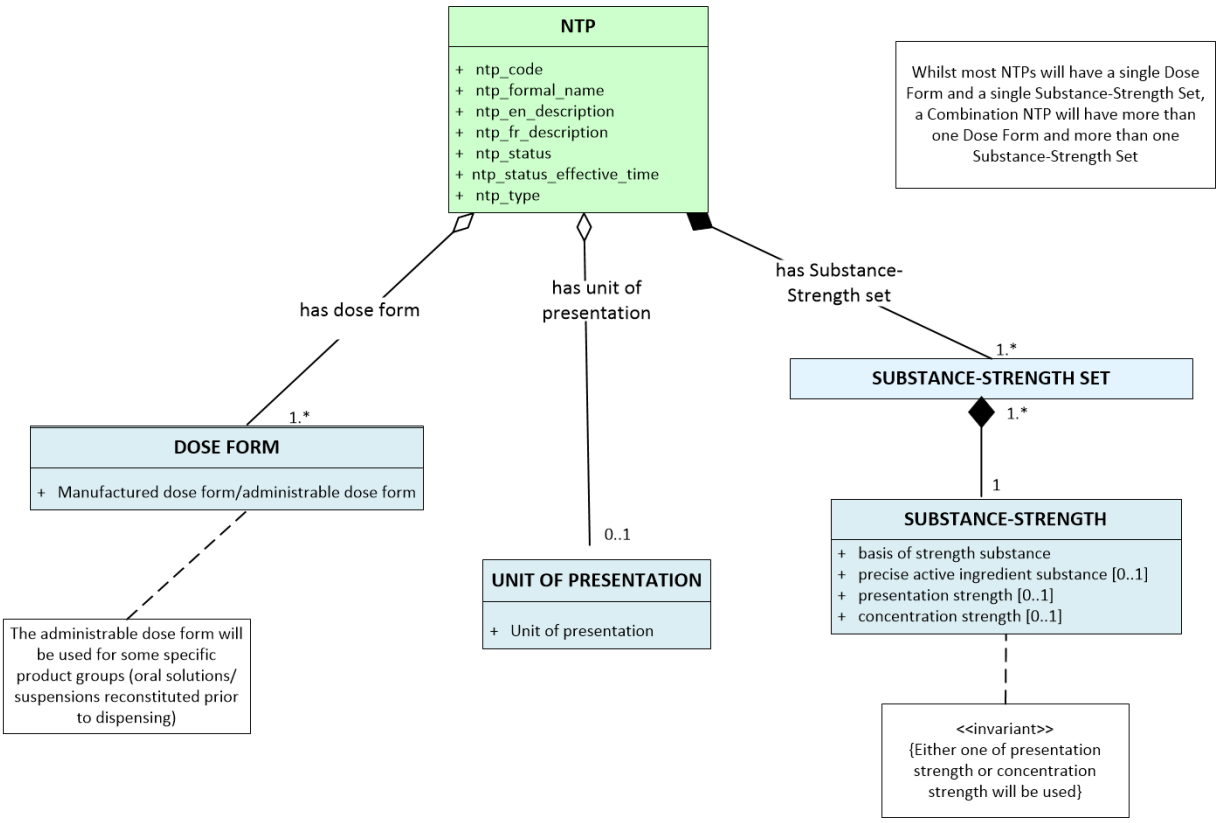
Technical Specification

The detailed technical specification for the content of the Canadian Clinical Drug Data Set which defines the attributes used for each class is provided in a separate Technical Specification (or Data Dictionary) document.

Non-proprietary Therapeutic Product (NTP)

This section provides explanation on each of the key components of the NTP: the set of active ingredient substance(s) and their strength(s), the unit of presentation and dose form as well as how each of those components can be used to uniquely describe the NTP in the formal name.

Figure 2: The NTP Model



An NTP is defined by a unique combination of Substance-Strength Set(s), Unit of presentation and Dose Form(s).These entities will build the ntp_formal name but not be separate attributes within the ntp file. The attributes of an NTP will include the following: ntp code, ntp formal name, ntp en description, ntp fr description, ntp status, and ntp status effective time. The NTP formal name is built using the substance-strength set, a dose form and a unit of presentation.

The substance strength set is composed of the basis of strength substance, precise ingredient substance, and the strength, which may be represented as either presentation strength or concentration strength.

The dose form may be a manufactured dose form or an administrable dose form. The administrable dose form will be used for some specific product groups such as, oral solutions or suspensions reconstituted prior to dispensing.

An NTP has a unit of presentation, although in some cases it may be implicit in the dose form and not presented in the formal name. This will be explained further under Unit of Presentation for the NTP.

While most NTPs will have a single dose form and a single substance strength set, a Combination NTP will have more than one dose form and more than one single substance strength set.

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 an NTP: the substance and strength set and the dosage form, and additionally in some cases, the unit of presentation. The format, pattern or order in which these are presented are 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.

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 different components of the Substance-Strength Set, the precise active ingredient substance(s), basis of strength substance(s) and strength(s) have been documented in this section separately.

Describing and Naming Substances

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). When describing the active ingredient substance(s), the description used by Health Canada’s DPD will be used, with some exceptions.

Table 2: Canadian Substance Naming Examples

INN	USAN	DPD (BDPP)
glyceryl trinitrate	nitroglycerin	nitroglycerin (nitroglycérine)
orciprenaline	metaproterenol	orciprenaline (orciprénaline)
paracetamol	acetaminophen	acetaminophen (acétaminophène)
salbutamol	albuterol	salbutamol (salbutamol)

Modifiers, such as salts and esters will also be described in the NTP formal name using INN or USAN as appropriate (e.g., “mesylate” rather than the full chemical name for the modifier “methanesulfonate”). In French, salt names often occur at the beginning of the drug name. These will be expressed without modification in CCDD French; alphabetical order of ingredients will follow the order of ingredients in English, so that corresponding ingredient names are in the same order within the NTP in both languages.

Example:

- **English MP**
  - CLINDOXYL ADV GEL (benzoyl peroxide 3 % and clindamycin (clindamycin phosphate) 1 % cutaneous gel) GLAXOSMITHKLINE INC
- **French MP (note order of ingredients matches English alpha order, for consistency)**
  - CLINDOXYL ADV GEL (peroxyde de benzoyle 3 % et clindamycine (phosphate de clindamycine) 1 % gel cutané) GLAXOSMITHKLINE INC

Precise ingredient substances that include waters of hydration will not be described in the NTP formal names but will be described in the MP formal names: see Appendix C, Hydration and Solvation for detailed information.

Active ingredient substances are described using lower case, with upper case being used for letters within substance names if present in the official (INN) name, for example in ‘polymyxin B’ or ‘abobotulinumtoxinA’.

Products supplied with carrier fluids

Some products, usually but not always infusion products, are supplied with a “carrier fluid” – the fluid that adds volume to the product without contributing to its therapeutic effect. In the DPD, there are examples (such as some lidocaine infusions) where the carrier fluid is listed as an active ingredient substance (e.g., lidocaine and dextrose). The CCDD will not describe the carrier fluid as an active ingredient substance in the NTP, although it may be described in the MP if the DPD product (brand) name includes it.

Vitamin substance naming

Vitamin terminology in Canada reflects a variety of naming patterns. Vitamins B12, C, D, E and K tend to be referred to by their alphanumeric “vitamin” names in practice; in contrast, folic acid (vitamin B9), niacin/nicotinic acid (vitamin B3), pantothenic acid (vitamin B5), pyridoxine (vitamin B6), riboflavin (vitamin B2), thiamine (vitamin B1), and vitamin D analogues such as alfacalcidol, calcifediol, calcipotriol and calcitriol tend to be known by their INNs or other common names.

The term “vitamin” is defined as a group of nutritionally essential organic molecules with similar structures (known as “vitamers”), which share the activity of the parent group (A,B,C,D,E or K); ingredient substances in pharmaceutical products are actually vitamers, with names that reflect internationally standardized terms such as INN (most common), USAN, or other common name. Therefore, it is these vitamer names that will be used to describe vitamin ingredient substances in the products in the CCDD; the alphanumeric names will not be used.

Precise Active Ingredient Substance(s)

The precise active ingredient substance is an accurate and granular description of the substance as it is used in the product (as it is presented by the manufacturer, before any dilution or transformation) but without any description of waters of hydration or solvates in the NTP, since these have no little clinical significance. The precise active ingredient is usually described in terms of the modified INN/USAN. If no modifier is stated, the precise ingredient substance is the base substance moiety (see Table 3).

Table 3: Precise Active Ingredient Examples

English Precise Ingredient	**French Precise Ingredient**
phenytoin sodium (in Pfizer’s Dilantin capsule)	phénytoïne sodique
phenytoin (in Pfizer’s Dilantin Suspension) [example of the base moiety being the precise ingredient substance]	phénytoïne
beclomethasone dipropionate (in Valeant’s Qvar products)	dipropionate de béclométhasone
sumatriptan succinate (in GSK’s Imitrex DF tablet)	succinate de sumatriptan
sumatriptan hemisulfate (in GSK’s Imitrex Nasal spray)	hémisulfate de sumatriptan
potassium chloride (in Biomed’s Slo-Pot)	chlorure de potassium

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. See Table 4.

Table 4: Basis of Strength Substance

English BoSS	French BoSS
Coversyl: 4 mg of perindopril erbumine per tablet	périndopril erbumine 4 mg par comprimé
Dilantin: 50 mg of phenytoin sodium per capsule	phénytoïne sodique 50 mg par capsule
Dilantin: 125 mg of phenytoin per 5 mL	phénytoïne 125 mg par 5 mL
Qvar: 50 mcg of beclomethasone dipropionate per actuation	dipropionate de béclométhasone 50 mcg par actionnement
Imitrex DF: 50 mg of sumatriptan per tablet	sumatriptan 50 mg par comprimé
Imitrex Nasal spray: 5 mg of sumatriptan per actuation	sumatriptan 5 mg par actionnement
Norvasc: 10 mg of amlodipine per tablet	amlodipine 10 mg par comprimé

Describing the NTP using Precise Ingredient Substance and BoSS

- 1) Where the precise active ingredient substance is the basis of strength substance, only the precise active ingredient substance is required for the NTP (Table 5).

Table 5: NTP Where Precise Ingredient Substance Equals BoSS

NTP Formal Name (with precise ingredient and BoSS)	FR Description (with precise ingredient and BoSS)
Coversyl: perindopril erbumine 4 mg oral tablet	périndopril erbumine 4 mg comprimé oral
Dilantin: phenytoin sodium 50 mg oral capsule	phénytoïne sodique 50 mg capsule orale
Dilantin: phenytoin 125 mg per 5 mL oral suspension	phénytoïne 125 mg par 5 mL suspension orale

NTP Formal Name (with precise ingredient and BoSS)	FR Description (with precise ingredient and BoSS)
Qvar: beclomethasone dipropionate 50 mcg per actuation pressurized inhalation	dipropionate de béclométhasone 50 mcg par actionnement inhalation en flacon pressurisé

- 2) 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). See Table 6.

Table 6: NTP Where Precise Ingredient Substance is Not the BoSS

English Precise Ingredient Substance	French Description of Precise Ingredient Substance
Norvasc: amlodipine (amlodipine besylate) 10 mg per tablet	amlodipine (bésylate d'amlodipine) 10 mg par comprimé
Imitrex DF: sumatriptan (sumatriptan succinate) 50 mg per tablet	sumatriptan (succinate de sumatriptan) 5 mg par comprimé
Imitrex Nasal spray: sumatriptan (sumatriptan hemisulfate) 5 mg per actuation	sumatriptan (hémisulfate de sumatriptan) 5 mg par actionnement

Absence of specific excipient substances

The absence of a specific excipient substance 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 or FR description. However, for the MP, if the DPD product (brand) name contains information regarding “freeness”, then this will be included in the MP formal name and MP FR description. See Table 7 (where the “freeness is “sugar-reduced”).

Table 7: Absence of Excipient Substance MP Example

MP Formal Name	MP French Description
AMOXICILLIN **SUGAR-REDUCED** GRANULES FOR ORAL SUSPENSION (amoxicillin (amoxicillin trihydrate) 250 mg per 5 mL oral suspension) SIVEM PHARMACEUTICALS ULC	AMOXICILLIN **SUGAR-REDUCED** GRANULES FOR ORAL SUSPENSION (amoxicilline (trihydrate d’amoxicilline) 250 mg par 5 mL suspension orale) SIVEM PHARMACEUTICALS ULC

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

The strength of a therapeutic product is the amount (quantity) of (each) active ingredient substance per presentation unit (see section Presentation Strength and Concentration Strength (See also Unit of Presentation section)). 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 per unit of presentation).

Presentation Strength and Concentration Strength (See also Unit of Presentation section)

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 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 25000 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 10000 units per 0.4 mL.[2]

Using presentation strength is particularly helpful when there are several different product sizes available. For example, a pre-filled syringe product containing 10000 units per 0.4 mL and a different pre-filled syringe product containing 12500 units per 0.5 mL both have the same concentration strength (25000 units per (1) mL).

The Canadian Clinical Drug Data Set will use presentation strength for most product descriptions, with the exception of:

- insulin and related products, where a concentration strength is given (to allow the patient easy calculation of the amount to administer as this may change very frequently); similarly, products supplied in a "pen" with variable dosage
- bulk fluids: those expected to be used by healthcare professionals and which undergo further preparation prior to patient administration (e.g., bulk vials of nebuliser solutions or cytotoxics). However, please note that a bulk vial pattern NTP does not imply specific product characteristics, such as the presence or absence of a preservative
- large volume parenteral infusions (e.g., saline or dextrose) where it is the concentration and the volume that is clinically important

[2] Note that in CCDD NTPs, the term "unit" (and all strength units) will be in the singular form.

- liquids administered by "drops" or measured by a syringe (ophthalmic drops, nasal drops, oral drops, otic drops)
- semi-solid preparations (usually used topically) where a concentration strength expressed as a percentage shall be used

There may be other circumstances not listed above where concentration strength may be appropriate.

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 the case for solid 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).

In CCDD 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. See Table 8.

Table 8: Example of Strength Where Denominator is Not Stated

Strength	NTP Formal Name	NTP French Description
10 mg	clobazam 10 mg oral tablet	clobazam 10 mg comprimé oral
100 mcg	levothyroxine sodium 100 mcg oral tablet	lévothyroxine sodique 100 mcg comprimé oral

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. See Table 9.

Table 9: Example of Strength Where Denominator is Stated

Strength	NTP Formal Name	NTP French Description
250 mg per 5 mL	clarithromycin 250 mg per 5 mL oral suspension	clarithromycine 250 mg par 5 mL suspension orale
100 mg per 4 mL	morphine sulfate 100 mg per 4 mL solution for injection ampoule	sulphate de morphine 100 mg par 4 mL solution injectable ampoule

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 as in Table 10.

Table 10: Example of Product with Multiple Active Ingredient Substances

Strength	NTP Formal Name	NTP French Description
250 mg per 5 mL and 125 mg per 5 mL	amoxicillin 250 mg per 5 mL and clavulanic acid (clavulanate potassium) 62.5 mg per 5 mL oral suspension	amoxicilline 250 mg par 5 mL et acide clavulanique (clavulanate de potassium) 62,5 mg par 5 mL suspension orale

For those products where the denominator is correctly unitary:

1. for parenteral products the “1” denominator value will be explicitly stated when the total volume (for continuous liquids) of the presentation is 1 mL; the presentation strength is therefore clearly stated and cannot misinterpreted as a concentration strength, as in the first example in Table 11.
2. for metered dose presentations (where the strength is per 1 actuation) and for oral liquids (administered as drops or with an oral syringe) described using a concentration strength, the “1” does not need to be explicitly stated, as in the second and third examples in Table 11.

Table 11: Products Where the Denominator is Correctly Unitary

Strength	NTP Formal Name	NTP French Description
1 mg per 1 mL	vincristine sulfate 1 mg per 1 mL solution for injection vial	sulfate de vincristine 1 mg par 1 mL solution injectable fiole
100 mg per actuation	fluticasone propionate 100 mcg per actuation pressurized inhalation	propionate de fluticasone 100 mcg par actionnement inhalation en flacon pressurisé
0.05 mg per mL	digoxin 0.05 mg per mL oral solution	digoxine 0,05 mg par mL solution orale

Representing Strength Values

The value of the strength will be represented using a whole number or a decimal number.

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).

If the value is a decimal, there will be a leading zero, avoiding naked decimals (e.g., 0.75 mg not .75 mg). In CCDD French, the decimal will be represented by a comma.

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, 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. In order to enhance readability of larger numbers, any strength value greater than or equal to 1×10^9 will be expressed using scientific notation in the following format, 1e9. See also the guidance "Good Label and Package Practices Guide for Non-prescription Drugs and Natural Health Products" published by Health Canada, which can also be applied to prescription medicinal products.

Representing Units of Measure

The unit of measure should be in the metric system whenever possible.

The unit of measure should be stated in the singular.

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. One exception is that micrograms should be abbreviated to mcg not µg or ug. Although the SI system supports both ml and mL (and indeed l and L for litres) 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.

For those products whose strength is stated as "international units", the term "unit" 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 unit per 1 mL).

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 dipropionate 50 mcg per actuation nasal spray).

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 is described with 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 %".

Consistency of Strength Units and Alternative Strength Descriptions

Consistency of representation of strength units is also an important safety issue.

Some products have more than one type of units 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 unit per 0.5 mL of epoetin alfa) whereas Roche's Mircera product uses mass (e.g. 600 mcg per 0.6 mL). Lidocaine local anaesthetic products may be described using a percentage strength (e.g., 2 %) or as 20 mg per 1 mL. Sometimes, a product or monograph will reference both strength descriptions. For those products with alternative

strength descriptions, the NTP formal name will use mass in SI units 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.

Where products from different manufacturers use different representations of SI units (e.g. 0.02 mg vs 20 mcg) the NTP formal name will use one standard unit. The choice of representation for the unit will consider the following:

- any recommendation by ISMP Canada
- the unit which avoids using a decimal in the strength value
- the unit most commonly used for describing the dosage of the product in the monograph
- the unit most commonly used for describing the strength on the product label and packaging
- the unit used for the product in other national and international terminologies.

For example: combined oral contraceptives as described in DPD have a mix of milligram strengths (with decimals) and microgram strengths; to bring consistency, the estrogenic component will always be described using micrograms and the progestogen component will be described using micrograms or milligrams as appropriate to give whole numbers (e.g., norgestimate will use micrograms and norethindrone acetate will use milligrams). Digoxin products and clonidine products are described and dosed using decimals of milligrams; the NTPs for these products will continue to use milligrams for CCDD representations.

Unit of Presentation for the NTP

The unit of presentation is one of the definitional components of an NTP, although it is not mandatory for all types of concepts as will be described later. It is a qualitative component of the concept that describes how the NTP is "presented" by the manufacturer, in units that can be counted into a package (although note that CCDD does not represent pack sizes for medicinal products). The unit of presentation also supports expression of strength; it provides the denominator for the strength ratio for the majority of products (the quantity of active substance per unit of presentation).

As stated in the Substance Strength Set Section, the expression of strength in the Canadian Clinical Drug Data Set (CCDD) is primarily presentation strength.

1. For the majority of products, particularly used in primary care, the unit of presentation is in effect the basic discrete solid dose form - "tablet", "suppository", and the expression of strength does not require the unit of presentation to be explicitly stated (e.g., "amoxicillin 250 mg *per capsule* oral capsule" - the "per capsule" does not need to be described in the NTP or MP formal name and French description.
2. For some products, the unit of presentation needs to be stated explicitly. These include:
    - products whose dose form is powder or granules which may (or may not) be dissolved or suspended before administration and where the unit of presentation holds (or "bounds") the amount of dosage form. In this case the expression of strength requires the unit of presentation to be explicitly stated in the strength description:

    - cefotaxime sodium 2 g *per* ***vial*** powder for solution for injection
    - colestipol hydrochloride 5g *per* ***sachet*** granules for oral suspension
- products "presented" by the manufacturer with a metered dosing valve, such that the strength is the amount of active ingredient substance "per actuation", where the actuation is the unit of presentation and is stated in the strength description:
    - beclomethasone dipropionate 50 mcg per actuation pressurized inhalation
    - testosterone 12.5 mg per actuation cutaneous gel
- products that have a “continuous phase” dosage form (liquids and semi-solids) where the unit of presentation is an intimate container that holds (or "bounds") the dosage form. The presentation strength is the amount present in the unit of presentation, expressed as a ratio of quantity of active ingredient substance in the volume held in the unit of presentation, which is stated explicitly at the end of the NTP description.
    - Example:
        - metoclopramide hydrochloride 10 mg per 2 mL solution for injection **ampoule**
    - where two or more products with the same presentation strength have different units of presentation (usually syringes, ampoules and vials) it is important to describe these in the formal name to allow prescribers to select the correct presentation and to allow systems to track individual products correctly. For example, the NTPs for LIDOCAINE HYDROCHLORIDE INJECTION 100 mg per 5 mL products separate (as shown in bold):
        - lidocaine hydrochloride 100 mg per 5 mL solution for injection **ampoule**
        - lidocaine hydrochloride 100 mg per 5 mL solution for injection **syringe**
        - lidocaine hydrochloride 100 mg per 5 mL solution for injection **vial**
    - when the product strength is exceptionally expressed as concentration strength (see Substance Strength Set for exceptions), the amount held (bound) in the unit of presentation (the denominator when expressed as presentation strength) is entered at the end of the NTP description with the unit of presentation:
        - insulin glargine 100 unit per mL solution for injection **3 mL cartridge**
        - insulin glargine 100 unit per mL solution for injection **3 mL pen**
        - insulin glargine 100 unit per mL solution for injection **10 mL vial**

Some products do not have a unit of presentation; there is no intimate container or metered dosing valve. These products are supplied directly in a package (which is not described in CCDD), for example cutaneous semi-solids administered as "some" and liquids administered as "drops". Therefore, strength must be expressed as a concentration, for example:

- hydrocortisone 1% cutaneous cream
- timolol hydrochloride 0.5% ophthalmic drops

Dose Form for the NTP

The dose form is one of the definitional components of an NTP and therefore its correct description is an essential part of the human readable Formal Name and French Description for the NTP. The dose form (sometimes also known as the pharmaceutical dosage 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.

Dose Form Types

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

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

For the majority of products, the manufactured dose form and the administrable dose form are the same, but for products that undergo transformation prior to administration, they are different (e.g. "powder for suspension for injection" is a manufactured dose form, which after the transformation of addition of a liquid to reconstitute the powder, becomes "suspension for injection" as the administrable dose form).

The dose form for the NTP (and MP) will normally be the manufactured 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. 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 preparations that are reconstituted at the time of dispensing are an exception and have the administrable dose form for the NTP because the strength of these products is described in terms of the clinically useful strength (e.g., 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 12 provides examples of manufactured and administrable dose forms and, if required, the corresponding transformation needed to achieve the administrable dose form.

Table 12: 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 Formal Name and French Descriptions

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

The dose form description for the NTP should 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) and the clotrimazole cream product intended to treat tinea pedis (athlete's foot), there should be a specific dose form explicitly stating the dose form with its intended site of administration. For example, "vaginal cream" for the product for vaginal use (even if a difference in strength already differentiates the products).

Similarly, for products (usually solid dose oral products) that have undergone modification to change their release characteristics (e.g., prolonged release, extended release); this change needs to be explicitly stated in the dose form description. See Release Characteristics for further discussion.

The European Directorate for the Quality of Medicines & Healthcare (EDQM),[3] publishes a database of standard terms for dose forms, routes of administration and various other key concepts within the domain. This 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 description of medicines in both regulatory processes and in healthcare generally[4]. 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 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.

See also the EDQM Standard Terms Database (free registration required) and the accompanying document, EDQM Standard Terms: Introduction and guidance for use.

Release Characteristics

For dose forms that have modified release characteristics, the granularity of description of the modification in the EDQM concepts may not be sufficient for the NTP for documentation and interoperability. For example, for oral solid dosage forms such as tablet and capsule, 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

[3] https://www.edqm.eu/en/standard-terms-database

[4] 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.

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 (with examples provided in Table 13):

- 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;
- Gastro-resistant: Solid single-dose coated preparation obtained by compressing uniform volumes of particulate solids or by other means such as extrusion or moulding; preparations are intended for oral use to release active substance(s) in the gastrointestinal fluids by a rate depending essentially on the intrinsic properties of active substance(s) (conventional release);
- 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 13: Examples of Dose Forms with Release Characteristics in the Canadian Clinical Drug Data Set

DPD Term	EDQM	Canadian Clinical Drug Data Set (Formal Name)	Canadian clinical Drug Data Set (French dose form)
Tablet (Combined release)	Modified-release tablet	Modified-release oral tablet	comprimé oral à libération modifiée
Tablet (Delayed and extended-release)	Modified-release tablet	Modified-release oral tablet	comprimé oral à libération modifiée
Tablet (Enteric-coated)	Gastro-resistant tablet	Gastro-resistant tablet	comprimé gastrorésistant
Tablet (Delayed release)	Gastro-resistant tablet	Gastro-resistant tablet	comprimé gastrorésistant
Tablet (Extended-release)	Prolonged-release tablet	Prolonged-release oral tablet	comprimé oral à libération prolongée
Tablet (Immediate and delayed release)	Modified-release tablet	Modified-release oral tablet	comprimé oral à libération modifiée

DPD Term	EDQM	Canadian Clinical Drug Data Set (Formal Name)	Canadian clinical Drug Data Set (French dose form)
Tablet (Immediate release)	Tablet	Oral tablet	comprimé oral
Tablet (orally disintegrating)	Orodispersible tablet	Orodispersible tablet	comprimé orodispersible
Tablet (Chewable)	Chewable tablet	Chewable tablet	comprimé à croquer

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 may not be 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 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.

Liquid dose forms

For most liquid dose forms, the NTP dose form will use the most granular concepts, as found in the EDQM standard, distinguishing between solutions, suspensions, emulsions and pure liquids; for example: "oral suspension", "emulsion for injection", "cutaneous solution". For "drops" and "spray" dose forms, the NTP dose form will use a less granular dose form concept than those found in the EDQM standard (e.g. "ophthalmic drops" [rather than "ophthalmic drops, suspension"], "nasal spray" rather than "nasal spray, solution"), with the *exception of oral drops*, where the more granular concepts will be used (e.g. "oral drops, solution") when DPD has the data to support this. Oral and parenteral liquids may need to be mixed or administered through narrow tubing (such as a nasogastric tube) so having the formulation information (and therefore a sense of the risk of blocking) can be clinically useful in the NTP. The formulation of cutaneous liquids can also change their patient acceptability, so again, this information is clinically useful in the NTP.

The "drops" dose forms is used for all products presented with a dropper mechanism, either intrinsic to the container (e.g. an eye dropper bottle) or supplied separately. Strength for drops dose forms should be expressed as a concentration, either as a percentage or as "per 1 mL" (refer to the Substance Strength section).

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.

Example 1: Simple Mapping

DPD dose form = CAPSULE (ENTERIC COATED)

NTP dose form (formal name) = gastro-resistant 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 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 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 solution”

NTP Formal Name Pattern

- No part of the NTP description will be capitalized (with the exception of the “L” as a symbol/abbreviation for “litre” and as in “mL” for millilitre, and for capitalization of single letters as appropriate in a substance name (e.g., penicillin G, abobotulinumtoxinA);
- TALLman lettering will not be used;
- Waters of hydration will not be described in NTP substance names (see Appendix C, Hydration and Solvation)

Formal Naming Pattern for Single Active Ingredient Substance NTPs

The following pattern will be used for products with a single active ingredient substance:

<<Basis of Strength Substance (Precise ingredient substance*)>> <<Strength value and unit of measure>> <<Dose Form>> <<Unit of presentation*>>

*included only if required

Table 14 gives the components required to build a single ingredient NTP formal name, as well as the corresponding NTP formal name.

Table 14: Components Required to Build a Single Ingredient NTP Formal Name

Basis of Strength Substance (BoSS)	Precise Ingredient Substance	Strength	Dose form	Unit of presentation	NTP_Formal_Name
levothyroxine sodium	same as BoSS	25 mcg	oral tablet	not explicitly stated	levothyroxine sodium 25 mcg oral tablet
levothyroxine sodium	same as BoSS	500 mcg per vial	powder for solution for injection	not required – stated as part of strength (vial)	levothyroxine sodium 500 mcg per vial powder for solution for injection
atorvastatin	(atorvastatin calcium)	20 mg	oral tablet	not explicitly stated	atorvastatin (atorvastatin calcium) 20 mg oral tablet

Basis of Strength Substance (BoSS)	Precise Ingredient Substance	Strength	Dose form	Unit of presentation	NTP_Formal_Name
naproxen	(naproxen, naproxen sodium)†	200 mg	oral capsule	not explicitly stated	naproxen (naproxen, naproxen sodium) 200 mg oral capsule
metoclopramide hydrochloride	same as BoSS	10 mg per 2 mL	solution for injection	vial	metoclopramide hydrochloride 10 mg per 2 mL solution for injection vial

†If two forms of an active ingredient constitute the precise active ingredient, they will be in alpha-order separated by a comma within a single set of brackets

Formal Naming Pattern for Multiple Active Ingredient Substance NTPs

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 products with multiple ingredient substances:

<<Basis of Strength Substance A (Precise ingredient substance A)*>> <<Strength value and unit of measure>> <<and>> <<Basis of Strength Substance B (Precise ingredient substance B*) >> <<Strength value and unit of measure>> <<Dose Form>> <<Unit of presentation*>>

*included only if required

Table 15 gives the components required to build a multi-ingredient NTP formal name, as well as the corresponding NTP formal name:

Table 15: Components Required to Build a Multiple Ingredient NTP Formal Name

Basis of Strength Substance (BoSS)	Precise Ingredient Substance	Strength	Dose form	Unit of presentation	NTP_Formal_Name
amlodipine and atorvastatin	(amlodipine besylate) (atorvastatin calcium)	10 mg 20 mg	oral tablet	not explicitly stated	amlodipine (amlodipine besylate) 10 mg and atorvastatin (atorvastatin calcium) 20 mg oral tablet

Basis of Strength Substance (BoSS)	Precise Ingredient Substance	Strength	Dose form	Unit of presentation	NTP_Formal_Name
formoterol fumarate and mometasone furoate	same as BoSS	5 mcg per actuation 200 mcg per actuation	pressurised inhalation	not required – stated as part of strength (actuation)	formoterol fumarate 5 mcg per actuation and mometasone furoate 200 mcg per actuation pressurised inhalation
piperacillin and tazobactam	(piperacillin sodium) (tazobactam sodium)	4 g per vial 0.5 g per vial	powder for solution for injection	not required – stated as part of strength (vial)	piperacillin (piperacillin sodium) 4 g per vial and tazobactam (tazobactam sodium) 0.5 g per vial powder for solution for injection
sulfamethoxazole and trimethoprim	same as BoSS same as BoSS	400 mg per 5 mL 80 mg per 5 mL	solution for injection	ampoule	sulfamethoxazole 400 mg per 5 mL and trimethoprim 80 mg per 5 mL solution for injection ampoule

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

- “and” will be used as the conjunction between active ingredient substances/strengths;
- The order of active ingredient substances in a multi-ingredient NTP will be alphabetical for the formal name; the order of active substances in the French description will follow the order for the corresponding English ingredient names, and therefore ingredients might not appear in alphabetical order in French within multi-ingredient NTPs.

Therapeutic Moiety (TM)

Definition and Description

The 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).

As an abstraction of the NTP class, the TM acts as a grouping concept and the TM itself is often the basis of strength substance for the group of related NTPs. For multi-ingredient products, the TM describes all of the individual active moieties, as an NTP can be associated with only one TM. For example, an NTP containing ipratropium and salbutamol will be associated with the "ipratropium and salbutamol" TM, and will not be associated with the individual TM for "ipratropium" or the TM for "salbutamol". Not all NTPs have to be associated with a TM, although currently all medicinal product NTPs do (the device NTPs do not). NTPs for combination products associate to a multi-ingredient TM describing the active ingredient substance(s) present in all their components.

Therapeutic Moiety Naming Pattern

The Formal Name and the French Description of the TM shall describe the functional part of the active ingredient substance(s) present in a medicinal product (i.e., usually without salt or modifier description – but see dexamethasone example) 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 with a specific letter in the name (e.g., penicillin G).

For example:

- INN
    - sumatriptan
    - amoxicillin
    - amlodipine
    - salbutamol
- USAN
    - nitroglycerin
    - acetaminophen

When a single active moiety has more than one TM, because of clinically significant modifications, then the TM Formal Name and the French Description of the TM shall include the modification, and when necessary indicate the base moiety as TM so as to avoid any ambiguity.
For example:

- dexamethasone (base)
- dexamethasone phosphate

The dexamethasone (base) TM groups only those NTPs that have dexamethasone base as their basis of strength substance, whereas the dexamethasone phosphate TM groups those NTPs that have this substance as their basis of strength substance. If the "(base)" designation were not present, a TM described just as "dexamethasone" could be interpreted to represent all dexamethasone NTPs regardless of their basis of strength substance (a sort of grandparent concept), making it ambiguous to use.

Therapeutic Moiety Challenges

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.

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 which is also 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", so the therapeutic moiety should reflect this. This pattern is also seen in other national medicinal product terminologies that have a concept class similar to the TM.

Examples:

- potassium chloride
- ferrous sulfate
- ferrous gluconate
- aluminum hydroxide
- sodium phosphate

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 and many of the corticosteroids such as dexamethasone, liposomal products and pegylated products.

The following examples illustrate how the authoring of TM concepts requires editorial judgement both to determine clinical significance and the safe description of TM concepts.

1) 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 oral tablet
- diclofenac potassium 50 mg powder for oral solution

As there are three different basis of strength substances, there could possibly be three TMs as sibling concepts based on including the salt/modifier), such as:

- 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 a single concept based on the moiety itself:

- diclofenac

2) Phenytoin:

Phenytoin products are available with different precise ingredient substances:

- phenytoin sodium (e.g., Dilantin 30 mg oral capsules)
- phenytoin base (e.g., Dilantin 30 mg per 5 mL oral suspension)

Not only is the basis of strength substance different, 100 mg of phenytoin sodium is equivalent to 92 mg phenytoin (base) and dosage of phenytoin products may be safety critical

There should therefore be two TMs (as sibling concepts):

- Phenytoin (base)
- 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.

3) Doxorubicin:

Doxorubicin products are available in both a conventional form and encapsulated in liposomes.

- doxorubicin hydrochloride 10 mg per 5 mL solution for injection vial
- doxorubicin hydrochloride (doxorubicin hydrochloride pegylated liposomal) 20 mg per 10 mL suspension for injection vial

Currently within medicinal product terminology, there is no specific practice for describing liposomal products using, for example, a separate attribute. Despite being acknowledged as less than ideal, the pattern most often adopted is to include the liposomal content as a modification of the active ingredient substance.

The dose quantity used for liposomal products is usually significantly different from the conventional formulation and the side effect profile is also usually different, so it is important to differentiate these at all levels of the terminology. There should therefore be two TMs (as sibling concepts):

- doxorubicin (pegylated liposomal)
- doxorubicin (conventional)

Manufactured Product (MP)

This section describes the rules that govern the description of a unique Manufactured Product and the naming pattern used for Manufactured Products.

Describing MPs

A CCDD Manufactured Product concept is a brand specific medicinal product that is, or within the lifetime of the CCDD has been, available for prescribing and dispensing in Canada. Most have been or are currently licensed for use in Canada. Some authorizations granted by Health Canada and assigned a DIN cover what should be, according to the Canadian Clinical Drug Data Set (CCDD) Model and Editorial Guidelines, more than one Manufactured Product (MP) and associated Non-proprietary Therapeutic Product (NTP). The products involved are those that are primarily differentiated by using presentation strength (and/or proxy for unit of presentation) whereas the authorization is made at “concentration strength”.

For example:

The authorized DIN ((Drug Identification Number) [02300435] for MYLAN-IPRATROPIUM SOLUTION manufactured by MYLAN PHARMACEUTICALS ULC covers three presentations of “ipratropium bromide 250 mcg per mL inhalation solution:

- 250 mcg per 1 mL unit dose vial
- 500 mcg per 2 mL unit dose vial
- 250 mcg per mL bulk bottle

The CCDD creates three separate MPs as illustrated in Table 16.

Table 16: Example of Three MPs generated from One Authorized Product

MP Code	MP Formal Name	MP French Description
77700360	MYLAN-IPRATROPIUM SOLUTION (ipratropium bromide 250 mcg per 1 mL nebulizer solution unit dose vial) MYLAN PHARMACEUTICALS ULC	MYLAN-IPRATROPIUM SOLUTION (bromure d’ipratropium 250 mcg par 1 mL solution pour inhalation par nébuliseur fiole unidose) MYLAN PHARMACEUTICALS ULC
77700362	MYLAN-IPRATROPIUM SOLUTION (ipratropium bromide 500 mcg per 2 mL nebulizer solution unit dose vial) MYLAN PHARMACEUTICALS ULC	MYLAN-IPRATROPIUM SOLUTION (bromure d’ipratropium 500 mcg par 2 mL solution pour inhalation par nébuliseur fiole unidose) MYLAN PHARMACEUTICALS ULC
77700361	MYLAN-IPRATROPIUM SOLUTION (ipratropium bromide 250 mcg per mL nebulizer solution 20 mL bottle) MYLAN PHARMACEUTICALS ULC	MYLAN-IPRATROPIUM SOLUTION (bromure d’ipratropium 250 mcg par mL solution pour inhalation par nébuliseur 20 mL bouteille) MYLAN PHARMACEUTICALS ULC

and their associated NTPs:

- ipratropium bromide 250 mcg per 1 mL nebulizer solution unit dose vial
- ipratropium bromide 500 mcg per 2 mL nebulizer solution unit dose vial
- ipratropium bromide 250 mcg per mL nebulizer inhalation solution 20 mL bottle

In the MP_file, the single Health Canada DIN for the more granular MPs is also provided; please refer to the Technical Specification (Data Dictionary) for more information.

Waters of Hydration

See also Appendix C, Hydration and Solvation

Water of hydration information is present for the precise ingredient substance in a small number of Manufactured Products. The Canadian Clinical Drug Data Set describes the rules for how waters of hydration will be represented (see Appendix C). In MP concepts, in order to correctly identify (for mapping purposes) those Manufactured Products where waters of hydration are included in the precise active ingredient substance, this information will be included in the MP formal name pattern.

Table 17 provides an example of how waters of hydration will be applied to the MP.

Table 17: Waters of Hydration

NTP_code	NTP formal name	MP_code	MP formal name	DPD precise active ingredient
9002921	esomeprazole (esomeprazole magnesium) 20 mg gastro-resistant tablet	02339099	APO-ESOMEPRAZOLE (esomeprazole (esomeprazole magnesium) 20 mg gastro-resistant tablet) APOTEX INC	esomeprazole magnesium
		02423855	ACT ESOMEPRAZOLE (esomeprazole (esomeprazole magnesium **dihydrate**) 20 mg gastro-resistant tablet) ACTAVIS PHARMA COMPANY	esomeprazole magnesium **dihydrate**

MP Naming Pattern

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

MP names use the DPD Product Name and the DPD Company Name, with the associated NTP name placed in brackets between these two, with the addition of any solvate/hydrate description included for the substance(s) in the NTP part of the name. In the small number of cases where this produces duplicate MP names, the DPD Descriptor (if one exists) is added after the DPD Product Name.

The DPD Company name, as used in the Health Canada DPD, indicates the organization (company) that holds the authorization to place the product on the market in Canada, i.e., the market authorization holder. This may not be the company that has manufactured the product, but it is the company that holds the legal responsibility for the use of the product in Canada and should be the same as the company named on the product label/packaging.

The DPD Product Name, DPD Descriptor and DPD Company Name will use the letter case as it is in the DPD, which is usually upper case, whereas the NTP name in brackets will be all lower case.

This can be summarized as:

<<DPD PRODUCT NAME>> <<(ntp name)>> <<DPD COMPANY NAME>>

when de-duplicating MPs names, this pattern will be:

<<DPD PRODUCT NAME>> <<DPD DESCRIPTOR>> <<(ntp name)>> <<COMPANY NAME>>

and occasionally, when solvation is present in a precise ingredient substance:

<<DPD PRODUCT NAME>> <<(ntp name including waters of hydration)>> <<COMPANY NAME>>

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

MP Formal Name and French Description for Single Ingredient

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

<<Product name>> <<(ntp name)>> << Company Name>>

Table 18 provides examples of this naming pattern.

Table 18: Examples of MP Formal Name for Single Ingredient Products

MP Code	MP Formal Name	MP French Description
00878928	NORVASC (amlodipine (amlodipine besylate) 5 mg oral tablet) PFIZER CANADA INC	NORVASC (amlodipine (bésylate d'amlodipine) 5 mg comprimé oral) PFIZER CANADA INC
02297485	ACT AMLODIPINE (amlodipine (amlodipine besylate) 5 mg oral tablet) ACTAVIS PHARMA COMPANY	ACT AMLODIPINE (amlodipine (bésylate d'amlodipine) 5 mg comprimé oral) ACTAVIS PHARMA COMPANY

MP Formal Name and French Description for Multiple Ingredient

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

<<Product name>> << (ntp name)>> << Company Name>>

Table 19 provides examples of MP formal names for multiple ingredient products.

Table 19: Examples of MP Formal Name for Multiple Ingredient Products

MP Code	MP Formal Name	MP French Description
02382822	CLINDOXYL ADV GEL (benzoyl peroxide 3 % and clindamycin (clindamycin phosphate) 1 % cutaneous gel) GLAXOSMITHKLINE INC.	CLINDOXYL ADV GEL (peroxyde de benzoyle 3 % et clindamycine (phosphate de clindamycine) 1 % gel cutané) GLAXOSMITHKLINE INC
02411318	APO-AMLODIPINE-ATORVASTATIN (amlodipine (amlodipine besylate) 10 mg and atorvastatin (atorvastatin calcium propylene glycol solvate) 10 mg oral tablet) APOTEX INC	APO-AMLODIPINE-ATORVASTATIN (amlodipine (bésylate d'amlodipine) 10 mg et atorvastatine (solvate de propylène glycol d'atorvastatine calcique) 10 mg comprimé oral) APOTEX INC

MP Considerations and Exceptions

Duplicate information in MP formal name and French description pattern

When a DPD Product Name includes information that is also part of the naming 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, although when these go through their periodic review, it is usually being removed. Table 20 provides examples of Product Names that include strength, dose form and/or other information.

Table 20: MP Examples that Include Duplicate Information

MP Code	Existing DPD Product Name	Example MP Formal Name	Example MP French Description
02243826	PRAVASTATIN-40	PRAVASTATIN-40 (pravastatin sodium 40 mg oral tablet) PRO DOC LIMITEE	PRAVASTATIN-40 (pravastatine sodique 40 mg comprimé oral) PRO DOC LIMITEE
02167786	APO-METFORMIN - TAB 500MG	APO-METFORMIN - TAB 500MG (metformin hydrochloride 500 mg oral tablet) APOTEX INC	APO-METFORMIN - TAB 500MG (chlorhydrate de metformine 500 mg comprimé oral) APOTEX INC

Where multiple MPs have different MP codes (and different DINs) but a non-unique MP Formal Name:

For MP concepts where the basic naming pattern (<<DPD PRODUCT NAME>> <<(ntp name)>> <<DPD COMPANY NAME>>) produces a formal name description that is **not unique**, the DPD descriptor (or a portion thereof) is added to the MP pattern following the DPD Product Name, giving the pattern <<DPD PRODUCT NAME>> <<DPD DESCRIPTOR>> <<(ntp name)>> << COMPANY NAME>>.

Table 21 illustrates examples of how the DPD descriptor will be used to modify an MP formal name pattern.

Table 21: MPs with or without the DPD Descriptor

DIN	DPD Product name	DPD Descriptor	Modified MP Formal Name	Modified MP French Description
01934163	NOVAMOXIN	SUGAR REDUCED	NOVAMOXIN SUGAR REDUCED (amoxicillin (amoxicillin trihydrate) 250 mg per 5 mL oral suspension) TEVA CANADA LIMITED	NOVAMOXIN SUGAR REDUCED (amoxicilline (trihydrate d'amoxicilline) 250 mg par 5 mL suspension orale) TEVA CANADA LIMITED
00452130	NOVAMOXIN	none	NOVAMOXIN (amoxicillin (amoxicillin trihydrate) 250 mg per 5 mL oral suspension) TEVA CANADA LIMITED	NOVAMOXIN (amoxicilline (trihydrate d'amoxicilline) 250 mg par 5 mL suspension orale) TEVA CANADA LIMITED
02352761	AMOXICILLIN	SUGAR-REDUCED	AMOXICILLIN SUGAR-REDUCED (amoxicillin (amoxicillin trihydrate) 125 mg per 5 mL oral suspension) SANIS HEALTH INC	AMOXICILLIN SUGAR-REDUCED (amoxicilline (trihydrate d'amoxicilline) 125 mg par 5 mL suspension orale) SANIS HEALTH INC
02352745	AMOXICILLIN	none	AMOXICILLIN (amoxicillin (amoxicillin trihydrate) 125 mg per 5 mL oral suspension) SANIS HEALTH INC	AMOXICILLIN (amoxicilline (trihydrate d'amoxicilline) 125 mg par 5 mL suspension orale) SANIS HEALTH INC

DIN	DPD Product name	DPD Descriptor	Modified MP Formal Name	Modified MP French Description
02243861	FUCITHALMIC	WITHOUT PRESERVATIVE	FUCITHALMIC WITHOUT PRESERVATIVE (fusidic acid 1 % ophthalmic drops) AMDIPHARM LIMITED	FUCITHALMIC WITHOUT PRESERVATIVE (acide fusidique 1 % gouttes ophtalmiques) AMDIPHARM LIMITED
02243862	FUCITHALMIC	WITH PRESERVATIVE	FUCITHALMIC WITH PRESERVATIVE (fusidic acid 1 % ophthalmic drops) AMDIPHARM LIMITED	FUCITHALMIC WITH PRESERVATIVE (acide fusidique 1 % gouttes ophtalmiques) AMDIPHARM LIMITED

In rare cases, the DPD descriptor will be too long or not suitable for use as a modifier of the DPD Product Name. In such cases, only a portion of the DPD descriptor will be used. In the Adynovate example in Table 22, the reconstituted strength, as seen in the DPD descriptor, is excluded from the modified MP formal name to reduce the risk that it be confused with the product strength.

Table 22 provides examples of MP concepts with a modified MP formal name pattern where only a portion of the DPD descriptor is added.

Table 22: MPs with Only a Portion of the DPD Descriptor Added

DIN	DPD Product name	DPD Descriptor	Modified MP Formal Name	Modified MP French Description
02498588	ADYNOVATE	**500 UNITS/ML** (2 ML DILUENT) - SINGLE USE VIAL	ADYNOVATE (2 ML DILUENT) - SINGLE USE VIAL (rurioctocog alfa pegol **1000 unit per vial** powder for solution for injection with diluent solution) TAKEDA CANADA INC	ADYNOVATE (2 ML DILUENT) - SINGLE USE VIAL (rurioctocog alfa pégol **1000 unité par fiole** poudre pour solution injectable avec solution diluante) TAKEDA CANADA INC
02459051	ADYNOVATE	**200 UNITS/ML** (5 ML DILUENT) - SINGLE-USE VIAL	ADYNOVATE (5 ML DILUENT) - SINGLE-USE VIAL (rurioctocog alfa pegol **1000 unit per vial** powder for solution for injection with diluent solution) TAKEDA CANADA INC	ADYNOVATE (5 ML DILUENT) - SINGLE-USE VIAL (rurioctocog alfa pégol **1000 unité par fiole** poudre pour solution injectable avec solution diluante) TAKEDA CANADA INC

DIN	DPD Product name	DPD Descriptor	Modified MP Formal Name	Modified MP French Description
02498545	ADYNOVATE	**250 UNITS/ML** (2 ML DILUENT) - SINGLE USE VIAL	ADYNOVATE (2 ML DILUENT) - SINGLE USE VIAL (rurioctocog alfa pegol **500 unit per vial** powder for solution for injection with diluent solution) TAKEDA CANADA INC	ADYNOVATE (2 ML DILUENT) - SINGLE USE VIAL (rurioctocog alfa pégol **500 unité par fiole** poudre pour solution injectable avec solution diluante) TAKEDA CANADA INC
02459043	ADYNOVATE	**100 UNITS/ML** (5 ML DILUENT) - SINGLE-USE VIAL	ADYNOVATE (5 ML DILUENT) - SINGLE-USE VIAL (rurioctocog alfa pegol **500 unit per vial** powder for solution for injection with diluent solution) TAKEDA CANADA INC	ADYNOVATE (5 ML DILUENT) - SINGLE-USE VIAL (rurioctocog alfa pégol **500 unité par fiole** poudre pour solution injectable avec solution diluante) TAKEDA CANADA INC
02498537	ADYNOVATE	**125 UNITS/M**L (2 ML DILUENT) - SINGLE USE VIAL	ADYNOVATE (2 ML DILUENT) - SINGLE USE VIAL (rurioctocog alfa pegol **250 unit per vial** powder for solution for injection with diluent solution) TAKEDA CANADA INC	ADYNOVATE (2 ML DILUENT) - SINGLE USE VIAL (rurioctocog alfa pégol **250 unité par fiole** poudre pour solution injectable avec solution diluante) TAKEDA CANADA INC
02459035	ADYNOVATE	**50 UNITS/ML** (5 ML DILUENT) - SINGLE-USE VIAL	ADYNOVATE (5 ML DILUENT) - SINGLE-USE VIAL (rurioctocog alfa pegol **250 unit per vial** powder for solution for injection with diluent solution) TAKEDA CANADA INC	ADYNOVATE (5 ML DILUENT) - SINGLE-USE VIAL (rurioctocog alfa pégol **250 unité par fiole** poudre pour solution injectable avec solution diluante) TAKEDA CANADA INC

Note that there are some products that even with this additional rule, still generate non-unique MP Formal Names; however, this is acceptable if only one of the products has a status of Active. In the event the DPD descriptor does not provide useful differentiating information, the DPD PRODUCT NAME in the CCDD will be modified to create a meaningful distinction between the products.

Manufactured Product Name Changes

Current Health Canada policy allows pharmaceutical companies to transfer ownership of a product while retaining the same DIN. This means that the Company Name component of a CCDD

Manufactured Product may change although the mp_code remains the same. Similarly, product names may undergo minor changes, usually to remove strength or dose form information, but also to remove a prefix from a generic manufactured product name. SeeTable 23 for examples.

Table 23: Examples of MP Name Changes

CCDD Release	DIN	MP Formal Name	MP French Description	Comment
February 2018	02225964	APO-TEMAZEPAM (temazepam 15 mg oral capsule) APOTEX INC	APO-TEMAZEPAM (témazépam 15 mg capsule orale) APOTEX INC	Company change and Name change – prefix removed
March 2018	02225964	TEMAZEPAM (temazepam 15 mg oral capsule) AA PHARMA INC	TEMAZEPAM (témazépam 15 mg capsule orale) AA PHARMA INC	
February 2018	02302063	RASILEZ (aliskiren (aliskiren fumarate) 150 mg oral tablet) NOVARTIS PHARMACEUTICALS CANADA INC	RASILEZ (aliskirène (fumarate d'aliskirène) 150 mg comprimé oral) NOVARTIS PHARMACEUTICALS CANADA INC	Company change
March 2018	02302063	RASILEZ (aliskiren (aliskiren fumarate) 150 mg oral tablet) NODEN PHARMA DAC	RASILEZ (aliskirène (fumarate d'aliskirène) 150 mg comprimé oral) NODEN PHARMA DAC	
March 2019	02243961	DITROPAN XL -(10MG) (oxybutynin chloride 10 mg prolonged-release oral tablet) JANSSEN INC	DITROPAN XL -(10MG) (chlorure d'oxybutynine 10 mg comprimé oral à libération prolongée) JANSSEN INC	Strength removed from brand name
April 2019	02243961	DITROPAN XL (oxybutynin chloride 10 mg prolonged-release oral tablet) JANSSEN INC	DITROPAN XL (chlorure d'oxybutynine 10 mg comprimé oral à libération prolongée) JANSSEN INC	

For a medicinal product terminology such as CCDD, this level of change in the formal name of a concept is not ideal. The situation is under active review.

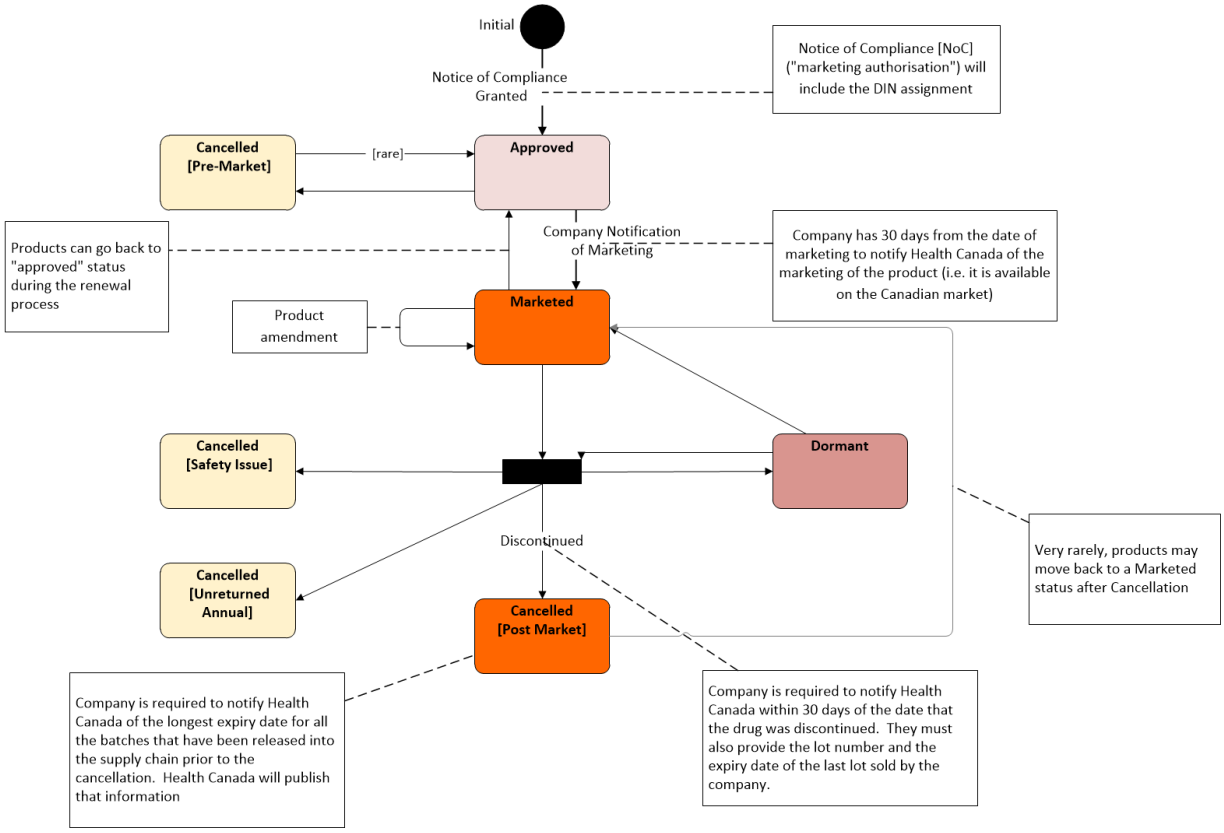
Status

The Non-Proprietary Therapeutic Product (NTP), Therapeutic Moiety (TM) and the Manufactured Product (MP) have a status attribute. The status attribute reflects the lifecycle of availability of the medicinal product 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 but it is derived from the information available in the DPD.

(Note: NoC stands for Notice of Compliance)

Status in the Drug Product Database

Figure 3: The Status Lifecycle for Products in the DPD



Once a product is granted a Notice of Compliance, it is assigned a DIN and its status is set as Approved. A product's status may be Cancelled Pre-market if it is cancelled without ever being marketed. The product's status is Marketed once it is available on the Canadian market; the company has 30 days to notify Health Canada of its marketing. Once a product is no longer available on the Canadian market, the following statuses are possible: Approved, Dormant, Cancelled (Safety-Issue), Cancelled (Unreturned Annual), Cancelled (Post-market). If a product is cancelled post-market, the company has 30 days to provide Health Canada with the date the product was discontinued as well as the lot number and the expiry date of the last lot sold by the company, which will be published. Very rarely, a product may move back to a Marketed status after cancellation.

Status in the Clinical Drug Data Set

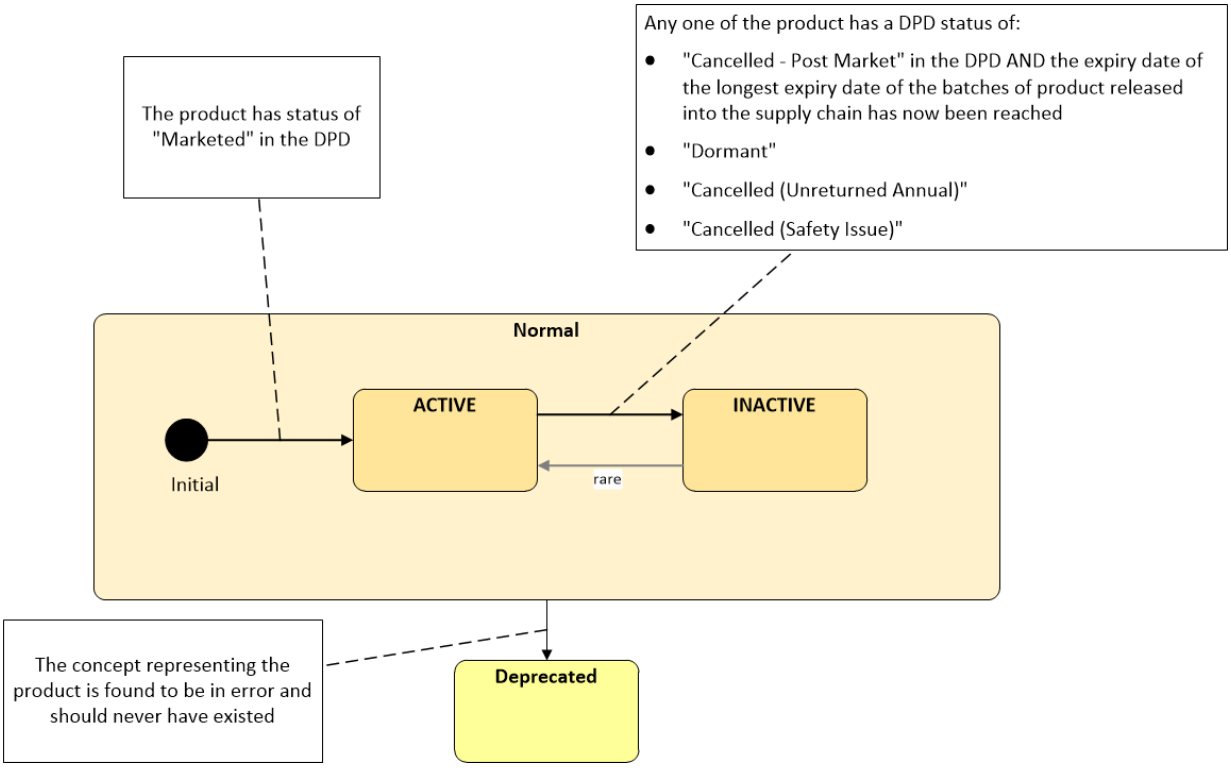
The allowable status strings for all concept classes in the Canadian Clinical Drug Data Set will be “Active”, “Inactive” and "Deprec" and the format for the status (change) date will be YYYYMMDD.

- “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 to dispense to patients
- "Deprec": the concept is Deprecated. Concepts with this status indicate a concept that was created in error or is now an orphan concept (no longer linked to any MP due to a change in formal name) and should not be used in systems; it is an exceptional status. This status type applies to all of the file types with a status attribute EXCEPT the Special Groupings file.

Manufactured Product Status

Figure 4 shows how statuses for the Manufactured Product will be represented.

Figure 4: Manufactured Product Status Lifecycle in the Canadian Clinical Drug Data Set



The MP will not appear in the Canadian Clinical Drug Data Set until its status in the DPD has been set to “marketed” (from “approved”), at which point it will have an “Active” status in CCDD. The accompanying status date will usually be the first marketing date in the DPD.

The MP status will be set to “Inactive” when the product status in the DPD has been set to one of:

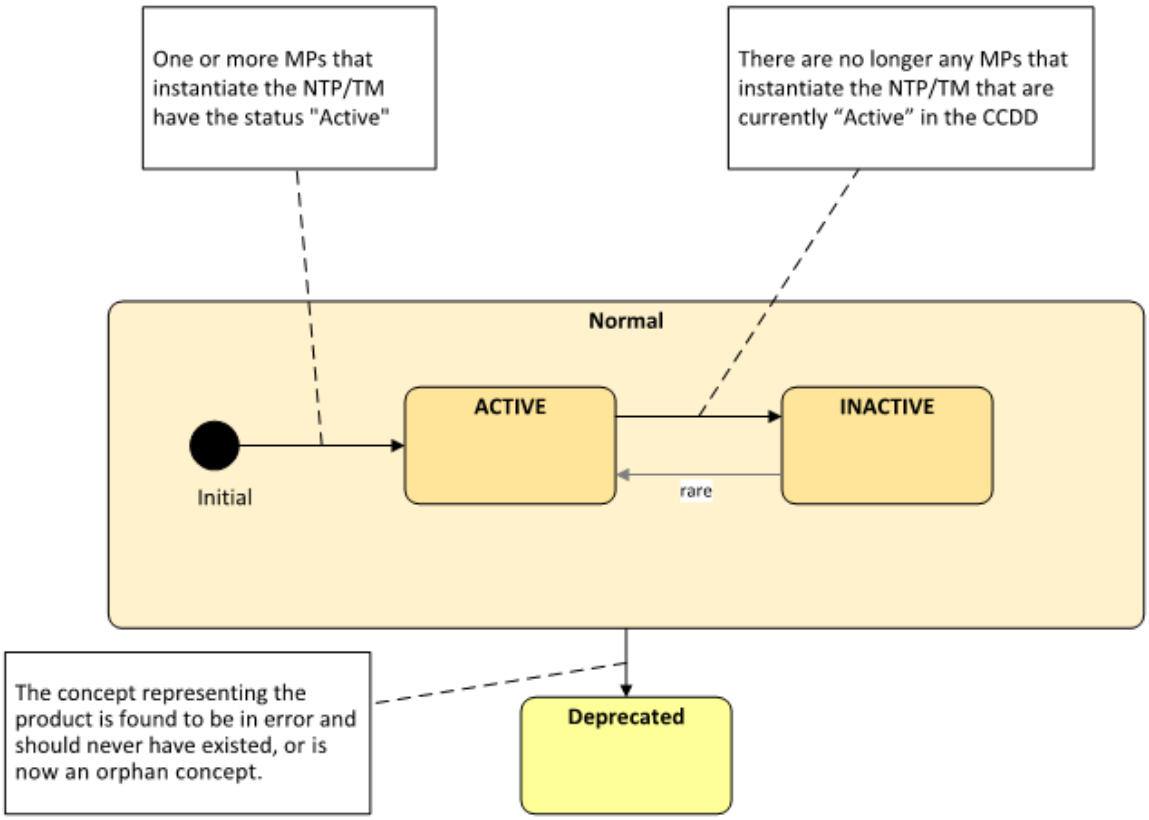
- “cancelled-post market”; the status date corresponds to the date of that change in the DPD, or if the expiry date of the last batch released into the supply chain is provided, then the later of the two dates
- “cancelled (unreturned annual)”; the status date corresponds to the date of that change in the DPD
- “cancelled (safety issue)”; the status date corresponds to the date of that change in the DPD
- or "dormant"; the status date corresponds to the date of that change in the DPD.

Conversely, an MP (and possibly therefore the associated NTP and TM) status may revert from “Inactive” back to “Active”, if the relevant product(s) is/are returned to the market unchanged, for example if a “dormant” product returns to “marketed”. MPs may have the exceptional status of "Deprec" (deprecated) if they are found to have been created in error; no product that corresponds to that concept has existed; the status date corresponds to the date of the deprecation.

Non-Proprietary Therapeutic Product and Therapeutic Moiety Product Status

Figure 5 shows how statuses for the NTP and TM will be represented.

Figure 5: NTP (and TM) Status Lifecycle in the Canadian Clinical Drug Data Set



An NTP and TM do not appear in the Canadian Clinical Drug Data Set until one or more of their related 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. An NTP and TM status may also revert from “Inactive” back to “Active” if one or more of their associated MP(s) is/are returned to the market unchanged. NTPs and TMs may have the exceptional status of "Deprec" (deprecated) if they are found to have been created in error (no product that corresponds to that concept representation has existed) or if it is now an orphan concept (no longer associated with any MP due to a change in DPD). In either case, the status date corresponds to the date of the deprecation.

Combination Products

Introduction and Requirement

A Combination Product is one that consists of more than one component part, commonly known as a “kit product”. It is presented as a single product and is licensed for a single set of indications.

There are two types of Combination Products within the CCDD:

1. Products where each component contains at least one active ingredient:
   Combination Product with multiple active components, each described by a unique combination of substance-strength set, single dose form and (if not continuous) a unit of presentation (whether explicitly stated or implicit); for example:
   - CANESTEN COMBI 1 DAY COMFORTAB + EXTERNAL CREAM BAYER INC
     - clotrimazole 1 % cutaneous cream
       - substance-strength set = clotrimazole 1%
       - dose form = cutaneous cream
       - unit of presentation = N/A (continuous)
     - clotrimazole 500 mg vaginal tablet
       - substance-strength set = clotrimazole 500 mg
       - dose form = vaginal tablet
       - unit of presentation = implicit – “per tablet”
   - HP-PAC TAKEDA PHARMACEUTICALS AMERICA INC
     - amoxicillin 500 mg oral capsule
       - substance-strength set = amoxicillin 500 mg
       - dose form = oral capsule
       - unit of presentation = implicit – “per capsule”
     - clarithromycin 500 mg oral tablet
       - substance-strength set = clarithromycin 500 mg
       - dose form = oral tablet
       - unit of presentation = implicit – “per tablet”
     - lansoprazole 30 mg gastro-resistant capsule
       - substance-strength set = lansoprazole 30 mg
       - dose form = gastro-resistant capsule
       - unit of presentation = implicit – “per capsule”
2. Products where one or more components may be inactive and act as a diluent or placebo:
   Combination Product with an active and an inactive component, where the component containing active ingredient substance is described by a substance-strength set, a single dose form and a unit of presentation (whether explicitly stated or implicit) but the inactive presentation is described minimally; for example:
   - BREVICON 0.5/35 TABLETS (28-DAY PACK) PFIZER CANADA ULC
     - ethinyl estradiol 35 mcg and norethindrone 0.5 mg oral tablet with lactose oral tablet

        - substance-strength set = ethinyl estradiol 35 mcg and norethindrone 0.5 mg
        - dose form = oral tablet
        - unit of presentation = implicit – “per tablet”
    - lactose oral tablet
- GLUCAGEN HYPOKIT NOVO NORDISK CANADA INC
    - glucagon (glucagon hydrochloride) 1 mg per vial powder for solution for injection with diluent solution syringe
        - substance-strength set = glucagon (glucagon hydrochloride) 1 mg per vial
        - dose form = powder for solution for injection
        - unit of presentation = explicit – “per vial”
    - diluent solution syringe

Why Combination Products are Needed in the CCDD

In order to generate the CCDD from the Health Canada Drug Product Database, a mechanism is required to describe combination products that differentiates them from multi-ingredient products and makes them easier for stakeholders to identify.

Limitations

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

NTP_type Attribute

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

The COMB ntp_type attribute will be used to indicate only those combination products that contain two or more components that contain active ingredient substance(s), even if a therapeutically inactive component is also present (as for example 9009392 in Table 24). The COMB ntp_type attribute 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)

Table 24 provides examples of combination products explicitly identified by having "COMB" in the ntp_type attribute.

Table 24: Combination Product Examples with an ntp_type Attribute Equal to “COMB”

NTP Code	NTP Formal Name	NTP French Description
9006481	clotrimazole 1 % cutaneous cream with clotrimazole 500 mg vaginal tablet	clotrimazole 1 % crème cutanée avec clotrimazole 500 mg comprimé vaginal
9009392	ethinyl estradiol 35 mcg and norethindrone 0.5 mg oral tablet with ethinyl estradiol 35 mcg and norethindrone 0.75 mg oral tablet with ethinyl estradiol 35 mcg and norethindrone 1 mg oral tablet with lactose oral tablet	éthinylestradiol 35 mcg et noréthindrone 0.5 mg comprimé oral avec éthinylestradiol 35 mcg et noréthindrone 0.75 mg comprimé oral avec éthinylestradiol 35 mcg et noréthindrone 1 mg comprimé oral avec lactose comprimé oral
9012653	amoxicillin 500 mg oral capsule with clarithromycin 500 mg oral tablet with lansoprazole 30 mg gastro-resistant capsule	amoxicilline 500 mg capsule orale avec clarithromycine 500 mg comprimé oral avec lansoprazole 30 mg capsule gastrorésistante

Table 25 provides examples of the combination products that would NOT have the "Comb" type but would have the usual “NA” attribute.

Table 25: Combination Product Examples with an ntp_type Attribute Equal to “NA"

NTP Code	NTP Formal Name	NTP French Description
9009393	ethinyl estradiol 35 mcg and norethindrone 0.5 mg oral tablet with lactose oral tablet	éthinylestradiol 35 mcg et noréthindrone 0.5 mg comprimé oral avec lactose comprimé oral
9012981	glucagon 1 mg per vial powder for solution for injection with diluent solution	glucagon 1 mg par fiole poudre pour solution injectable avec solution diluante

Combination Product NTP Formal Name Pattern

The Formal Name pattern to describe a combination NTP will respect that the product is described by either:

- Multiple sets of unique “substance-strength set, dose form and, when required, unit of presentation”.
- One or more sets of unique “substance-strength set, dose form and, when required, unit of presentation” PLUS a minimal description of an inactive component (diluent or placebo).

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 within each substance-strength set and between the different components, with the exception of inactive components such as lactose tablets, which will be described at the end of the formal name. For those components that have the same active ingredient substances (the clotrimazole example) the alphabetic order of dose form will be used. If the active ingredient substance(s) and dose forms are both the same, the components will be in ascending order of strength (as in some benzoyl peroxide products). See Table 26 for examples.

Table 26: Examples of NTP Formal Name Patterns of Combination Products

NTP Code	NTP Formal Name	NTP French Description
9006481	clotrimazole 1 % cutaneous cream with clotrimazole 500 mg vaginal tablet	clotrimazole 1 % crème cutanée avec clotrimazole 500 mg comprimé vaginal
9009397	ethinyl estradiol 35 mcg and norethindrone 1 mg oral tablet with lactose oral tablet	éthinylestradiol 35 mcg et noréthindrone 1 mg comprimé oral avec lactose comprimé oral
9012653	amoxicillin 500 mg oral capsule with clarithromycin 500 mg oral tablet with lansoprazole 30 mg gastro-resistant capsule	amoxicilline 500 mg capsule orale avec clarithromycine 500 mg comprimé oral avec lansoprazole 30 mg capsule gastrorésistante
9012981	glucagon 1 mg per vial powder for solution for injection with diluent solution	glucagon (chlorhydrate de glucagon) 1 mg par fiole poudre pour solution injectable avec solution diluante seringue

For products that are supplied with a diluent (often referred to as “kits”) the diluent should be only briefly described (e.g., as “diluent solution”) rather than in detail (e.g., “bacteriostatic water for injection”), and no volume stated. Similarly, for products with an effectively inert component (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 oral tablet”).

Special Groupings

There is a requirement in Canada for a nationally consistent way to identify opioid products and other controlled substances to enable digital health solutions and medication processes in the implementation of appropriate (additional) actions in the medication process to assist in the opioid crisis and the monitoring of controlled substances. The Canadian Clinical Drug Data Set (CCDD) will identify opioid products and controlled substances at the following levels of granularity; Manufactured Product (MP), Non-proprietary Therapeutic Product (NTP) and Therapeutic Moiety (TM). The solution to identify these concepts is extensible to support other future requirements (hence the term "Special Groupings").

Currently, the scope of this information is constrained to the scope of the CCDD, which is medicinal products authorized for supply in Canada. As such, any information about unlicensed substances and the recording of any substance used “recreationally” is out of scope. Compounded products containing an opioid active ingredient substance are also currently out of scope.

The approach to provide the information is via a relationship table to associate the desired "special grouping" to any/all appropriate concepts in the CCDD. This approach has the advantage of being very flexible, allowing each concept, of whatever class within the CCDD, to be associated to its correct information directly.

The delivery of the Special Groupings information is provided in a separate table, as shown in Table 27. The first two columns provide the relevant CCDD concept, the next column provides the CCDD file type the concept can be found in, the next two columns provide the policy information (please note the policy type is encoded and a separate file provides the details for the coded information in the coded_attribute file), and the final two columns provide the status and date of the association between the product and the policy. Any one concept could be part of multiple policy types (see examples in Table 27). For more information, please refer to the Technical Specification (Data Dictionary).

Table 27: Example of the Special Groupings File

ccdd code	ccdd formal name	ccdd type	policy type	policy reference	special groupings status	special groupings status effective time
9000195	acetylsalicylic acid 325 mg and oxycodone hydrochloride 5 mg oral tablet	NTP	500002	http://laws-lois.justice.gc.ca/eng/acts/C-38.8/FullText.html	active	20170919

ccdd code	ccdd formal name	ccdd type	policy type	policy reference	special groupings status	special groupings status effective time
9000195	acetylsalicylic acid 325 mg and oxycodone hydrochloride 5 mg oral tablet	NTP	500001	http://www.gazette.gc.ca/rp-pr/p1/2017/2017-06-17/html/reg8-eng.php	active	20170919
8000774	acetylsalicylic acid and oxycodone	TM	500002	http://laws-lois.justice.gc.ca/eng/acts/C-38.8/FullText.html	active	20170919
8000774	acetylsalicylic acid and oxycodone	TM	500001	http://www.gazette.gc.ca/rp-pr/p1/2017/2017-06-17/html/reg8-eng.php	active	20170919
0608157	RATIO-OXYCODAN (acetylsalicylic acid 325 mg and oxycodone hydrochloride 5 mg oral tablet) TEVA CANADA LIMITED	MP	500002	http://laws-lois.justice.gc.ca/eng/acts/C-38.8/FullText.html	active	20170919
0608157	RATIO-OXYCODAN (acetylsalicylic acid 325 mg and oxycodone hydrochloride 5 mg oral tablet) TEVA CANADA LIMITED	MP	500001	http://www.gazette.gc.ca/rp-pr/p1/2017/2017-06-17/html/reg8-eng.php	active	20170919

Appendix A, Advisory Group Members

Advisory Group Members

Name	Organization
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Name	Organization
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Barbara Jovaisas	Canada Health Infoway
Beverly Knight	Canada Health Infoway

Appendix B, Glossary and Acronyms

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) 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

Term used in this document	Definition of Term
	• camsilate for rac-(7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methanesulfonate)
Manufactured item	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

Acronyms

Acronym	English Description	French Acronym	French Description
CCDD	Canadian Clinical Drug Data Set	RCM	Répertoire canadien des médicaments
TM	Therapeutic Moiety	FT	Fraction thérapeutique
NTP	Non-proprietary Therapeutic Product	PTC	Produit thérapeutique commun
MP	Manufactured Product	PM	Produit manufacturé
DIN	Drug Identification Number	DIN	Numéro d'identification d'un médicament
DPD	Drug Product Database	BDPP	Base de données sur les produits pharmaceutiques
LNHPD	Licensed Natural Health Products Database	BDPSNH	Base de données des produits de santé naturels homologués
NPN	Natural Product Number	NPN	Numéro de produit naturel
INN	International Nonproprietary Name	DCI	Dénomination commune internationale
USAN	United States Adopted Names	USAN	dénomination commune américaine

Acronym	English Description	French Acronym	French Description
EDQM	European Directorate for the Quality of Medicines	DEQM	Direction européenne de la qualité du médicament
IDMP	Identification of Medicinal Products	IDMP	Identification des produits médicaux
EMR	electronic medical record	DSE	dossier de santé électronique

Appendix C, Hydration and Solvation

Introduction

Water of hydration (also called “water of crystallization” and sometimes “lattice water”) describes the water molecules that exist within the molecules of (usually) complex substances. "Solvate" is the term used to describe small molecules other than water (such as acetone) that similarly exist within large molecules.

Water of hydration is described chemically using a dot or period after the main formula (e.g. $CuSO_4.5H_2O$ – copper sulfate with 5 molecules of water hydrating it). In text, which is where we find it in substance names in medicinal products, the term is “hydrate” with the Greek numeric descriptions – monohydrate, dihydrate, trihydrate, quadrahydrate, pentahydrate, hexahydrate etc.

Water of hydration or solvate information is present for precise ingredient substance in approximately 10% of the moieties currently in scope for the CCDD, and approximately 5% of the eventual total scope of the CCDD.

Hydrates and Solvates for Medicinal Product Terminology

Medicinal product terminology needs to accurately describe products both in their pharmaceutical description (and pharmaceutical equivalence) – which IDMP does – and in their clinical description and clinical equivalence. For most situations, these two descriptions are the same; in the case of substances with waters of hydration, they may not be. Medicinal product terminology needs to accommodate the situation when there is difference because prescribers need the clinical description (for which hydration/solvation information is irrelevant) and dispensers (usually pharmacists) must deal with the pharmaceutical description of the licensed products, where hydration/solvation information may have relevance.

Hydrates and Solvates for the CCDD

The requirement is to reflect both what clinicians wish to see in the NTP and what pharmacists actually see on the MP and its attendant information.

For Manufactured Products, where hydration/solvation information is currently provided for the precise active ingredient substance, this should be included in the MP formal name and French Description following the standard pattern.

But, when generating the NTP, the hydration/solvation information should be disregarded in the precise ingredient substance. This provides a smaller, more clinically acceptable set of NTPs for prescribing but continues to maintain the granular detail of actual manufactured products in the MP. It also allows a prescription written as the NTP to be fulfilled using any of the associated MPs; the dispenser is not inappropriately constrained by hydration/solvation information (or lack of it) in the

description of the NTP precise ingredient substance. See Table 28 for examples of products with a single NTP yet different precise ingredient substances because of hydration states.

Table 28: Example of MPs with Different Hydration/Solvation States and a Single NTP

NTP Code	NTP Formal Name	MP Code	MP Formal Name	MP French Description	DPD Precise Active Ingredient
9002921	esomeprazole (esomeprazole magnesium) 20 mg gastro-resistant tablet	02339099	APO-ESOMEPRAZOLE (esomeprazole (esomeprazole magnesium) 20 mg gastro-resistant tablet) APOTEX INC	APO-ESOMEPRAZOLE (ésoméprazole (ésoméprazole magnésien) 20 mg comprimé gastrorésistant) APOTEX INC	EN: esomeprazole magnesium FR : ésoméprazole magnésien
		02423855	ACT ESOMEPRAZOLE (esomeprazole (esomeprazole magnesium dihydrate) 20 mg gastro-resistant tablet) ACTAVIS PHARMA COMPANY	APO-ESOMEPRAZOLE (ésoméprazole (ésoméprazole magnésien dihydraté) 20 mg comprimé gastrorésistant) APOTEX INC	EN: esomeprazole magnesium dihydrate FR : ésoméprazole magnésien dihydraté

The precise ingredient substance will not be stated in the NTP for those products where the precise ingredient substance is the hydrated/solvated form of the basis of strength substance with no other modification as it is redundant information without the hydrate; this gives a clinically correct and recognizable NTP.

For example:

- MP: PRO-AZITHROMYCINE (azithromycin (azithromycin monohydrate hemiethanolate) 250 mg oral tablet) PRO DOC LIMITEE
    - Precise Active Ingredient: azithromycin monohydrate hemiethanolate
    - NTP Formal Name without hydrate/solvate information but including precise ingredient substance field: azithromycin (azithromycin) 250 mg oral tablet
    - NTP Formal Name without precise ingredient substance: azithromycin 250 mg oral tablet

It is important that when hydration/solvation information is removed from the ingredient substance as described in the NTP, a recognizable substance is still described. Each substance that is manipulated in this way should be checked to ensure that the resulting information is reasonable both chemically and clinically.

There are one or two very rare cases where the basis of strength substance is the same as the precise ingredient substance and includes the water of hydration information that is required for correct expression of strength; for example, the dopamine agonist used in Parkinson's disease: pramipexole dihydrochloride monohydrate. In some healthcare cultures (particularly in Europe), the clinically used description of strength of pramipexole products (and dosage quantity for administration) refers to the base substance; but in Canada the description of strength refers to the full hydrated precise ingredient substance. In the US, the strength also refers to the full hydrated precise ingredient substance, but it is clinically described using only the salt (pramipexole dihydrochloride). The CCDD will follow that pattern, acknowledging that it is not, for this product, a strictly correct basis of strength.

Table 29: Product Where the Basis of Strength Substance is the Precise Ingredient

NTP Code	NTP Formal Name	MP Code	MP Formal Name	MP French Description	DPD Precise Active Ingredient
9000783	pramipexole dihydrochloride 0.25 mg oral tablet	02237145	MIRAPEX (pramipexole dihydrochloride monohydrate 0.25 mg oral tablet) BOEHRINGER INGELHEIM (CANADA) LTD LTEE	MIRAPEX (dichlorhydrate de pramipexole monohydraté 0,25 mg comprimé oral) BOEHRINGER INGELHEIM (CANADA) LTD LTEE	EN: pramipexole dihydrochloride monohydrate FR: dichlorhydrate de pramipexole monohydraté

Note on DPD Information:

It is likely, particularly for older products, that the granularity of description of ingredient substances in the DPD may not be as complete as for more recently authorized products. For example, recent investigation has confirmed that all solid dose oral presentations of amoxicillin contain amoxicillin trihydrate, although the DPD information does not reflect this at present.

Regulatory agencies and medicinal product manufacturers are now moving towards implementation of IDMP with its increased level of precision and consistency. This is also being seen in more regular and updated descriptions of CMC (Chemistry and Manufacturing Controls) data with a particular focus on active ingredient substances. Therefore, this pattern of including hydration/solvation information in the MP but not in the NTP is likely to be the most pragmatic for all concerned, particularly as data are made more consistent over time, and will minimize change in the NTP description, which is important for clinical use.