Model for the representation of Medicinal Products in SNOMED CT

Use cases for the SNOMED CT Medicinal Product hierarchy

The main use cases for the SNOMED CT Medicinal Product hierarchy are as follows:

1. To provide a consistent and usable set of international medications concepts for member nations to use as a foundation for national medicinal product terminology
    a. For those member nations with an existing terminology, the improved model underpinning the concepts will facilitate both direct use or mapping
    b. For those member nations without an existing terminology, the concepts provide a consistent starting set of concepts and a model to develop from, reducing resource (especially set up costs) and risk in development
2. To provide compatibility with the IDMP model, where possible, for identification of medicinal products. Having compatibility between the patterns used to describe medicinal products in the regulatory environment and those used in clinical care will facilitate the information flow between the two domains of use. For all licensed medicinal products, the prime source of information for their description is their regulatory data; compatibility therefore streamlines the flow of information for maintenance of the clinical terminology. Similarly, for example in pharmacovigilance, the flow of information from clinical records into regulatory reporting, both for suspect and concomitant medications involved in safety events is streamlined. Describing the relationship between the SNOMED CT Medicinal Product hierarchy and the IDMP model also shows how some SNOMED CT medicinal product concepts complement and add value to IDMP-based concepts, particularly for patient care
3. To facilitate international interoperability of medication concepts for (for example) patient summaries and cross-border care; this is supported most efficiently when the medication concepts themselves are from national extensions built upon or mapped to the international core
4. To facilitate development of international medication decision support, such as allergy checking and duplicate therapy checking, thereby reducing costs of maintenance and implementation
5. To support the use of a classifier on both international and national medicinal product concepts, to facilitate maintenance of the hierarchy
6. To support analysis of medication information in healthcare data for various research purposes
7. To provide medication concepts to support sufficiently defining concepts in other hierarchies within SNOMED CT

Model: General Comments

Open and closed world views: the existential and universal restrictions in the Medicinal Product model

SNOMED CT as an ontology is constructed on the principle of an open world view (the existential restriction) with each concept having a distinct fully specified name. The implication of the open world view for the medicinal product hierarchy is that a concept represents the set of (real world) medicinal products that contains "(at least) some substance X as an active ingredient", but may contain other unspecified active ingredient substances. This 'open world' view is useful for analysis and in some types of decision support. However, the regulation of medicinal products for sale/supply is based on the 'closed world' view (the universal restriction), where **all** active ingredient substances must be explicitly described. This is also the premise for description of medicinal products in the medication process (prescribing, dispensing and administration). Therefore the Medicinal Product hierarchy differs from other concept hierarchies within SNOMED CT in that some classes of concepts within it are modelled using this 'closed world' view which states that a concept represents a medicinal product that contains "only substance X" as an active ingredient"; no other active ingredient substances are present within it. To implement that "closed world view" with the existing tools and systems of SNOMED CT, the "ingredient count" proxy has been developed; some description of this is given below, with further detailed information being available in the machine-readable concept model. For further details on the open and closed world views, please refer to the relevant SNOMED documentation and training materials, e.g. Description Logic: Advanced Features.

IDMP Compatibility

IDMP, being a suite of standards developed in and for the regulatory domain, uses a "closed world" view. The active ingredient substance(s) present in a product **must** be listed in full, with no exceptions, so IDMP exists is the "closed world" view and therefore would be compatible with the "universal restriction" only; the existential restriction is not compatible with the concepts in the IDMP suite of standards, which is particularly important to note for the abstract concepts within IDMP in ISO 11616 (PhPIDs, especially L1, L3 and L4).

Stated and inferred views in the medicinal product model

For further details on the meaning of stated and inferred views, please refer to the relevant SNOMED documentation and training materials for example at 2.3.1 Stated and Inferred Concept Definitions and 8 Alternative Views of Concept Definitions

Medicinal Product model diagrams

The diagrams below show the overall Medicinal Product model. Note that in each diagram, no role or disposition grouper concepts are shown. Definitions and detailed descriptions are given in the sections below this overall model introduction. This first diagram is a UML (Unified Modeling Language) class model illustrating the five classes of concepts in the model and the relationships between them, in their three groups (MP, MPF and CD) plus an additional optional sixth sub-class to be populated in limited cases and likely in national extensions only (MP Precise Only). Two classes use the existential restriction (MP and MPF) and four use the (proxy for the) universal restriction (MP only, MPF only, CD and MP Precise Only); MP Precise Only is the optional sub-class that represents a product described explicitly and only by its *precise* active ingredient substances i.e. including clinically significant modification such as "dexamethasone *sodium phosphate*". MP classes are shown in shades of blue, MPF classes in shades of yellow and the CD class in green.

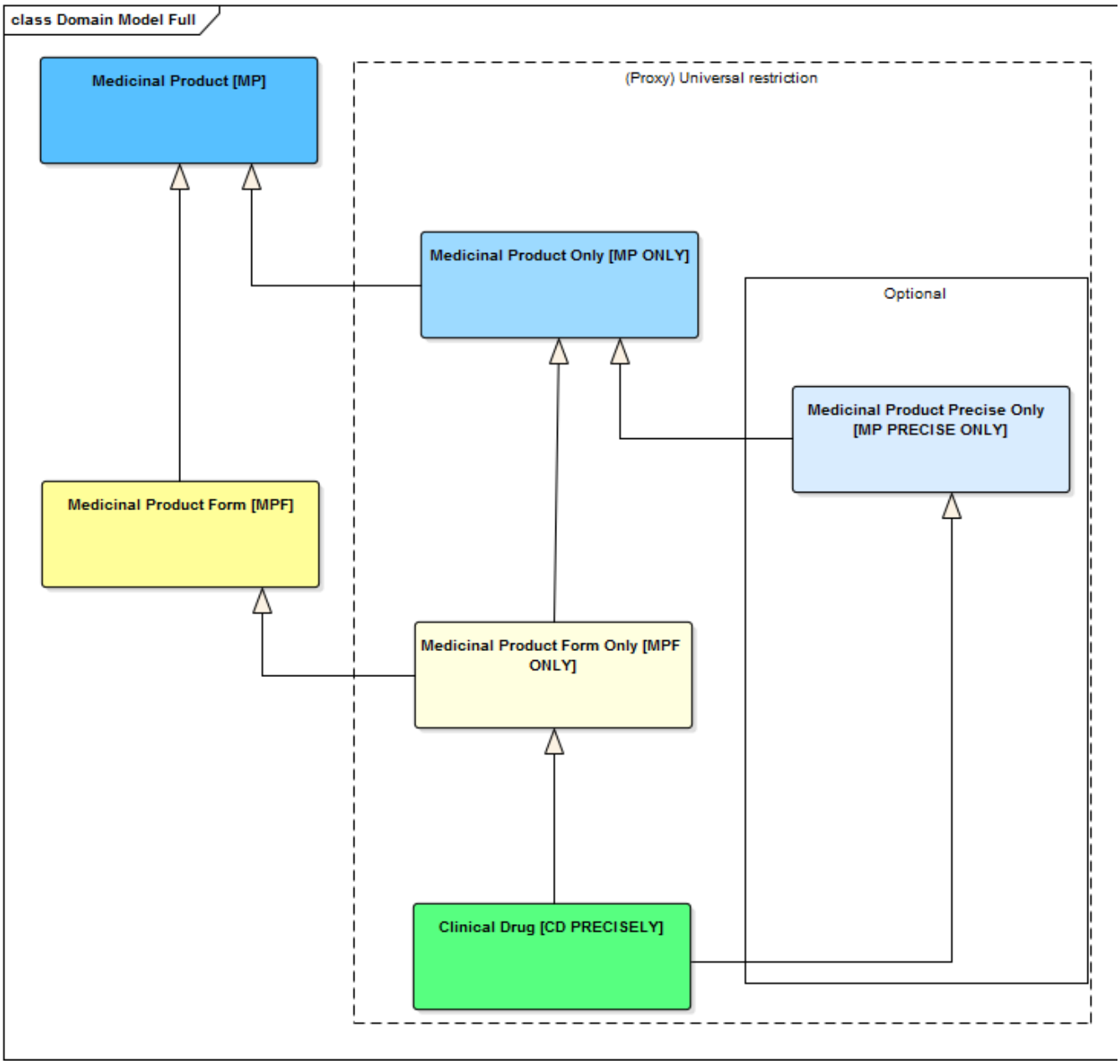

Figure 1: Medicinal Product concept model - International

The second diagram, below, is in SNOMED notation (inferred view), and shows only the five classes that will be populated in the international release, at least for the foreseeable future.
The Medicinal Product model is parented by the 763158003 |Medicinal product (product)| concept, an abstract concept representing an item that has been formulated and manufactured for administration to humans (or animals) for treatment or prevention of disease, for diagnosis of illness or to restore, correct or modify physiological function and which contains an active ingredient substance or combination of substances. This parent concept acts both to scope the domain and, in the future, will separate medicinal products from other products in a larger Products hierarchy, which may include medical devices and certain other products such as foods and cosmetics.

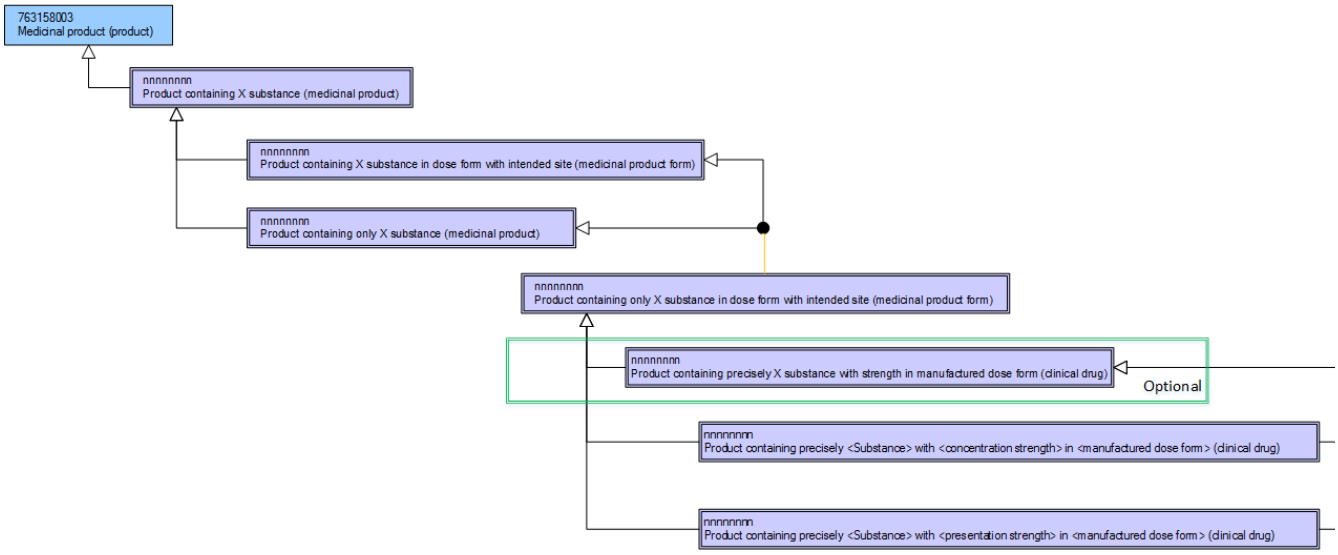

Figure 2: Medicinal Product concept model - International - SNOMED notation

The third model diagram below includes multi-ingredient medicinal products, and therefore has increased complexity. It again shows the three groups (MP, MPF and CD) with MP classes shown in shades of blue, MPF classes in shades of yellow and the CD class in green; each with two single active ingredient representations (X and Y) and one multi-ingredient representation (X + Y) and then the relationships between these. It shows how the single ingredient "containing" classes (the open world classes) subsume the appropriate multi-ingredient class, whereas the single ingredient "containing only" classes (the closed world classes) do not subsume the multi-ingredient class. The optional MP Precise Only class is present but is not shown with any multi-ingredient products, to limit complexity. MP Precise Only multi-ingredient products are discussed below in the Ingredient Count section.

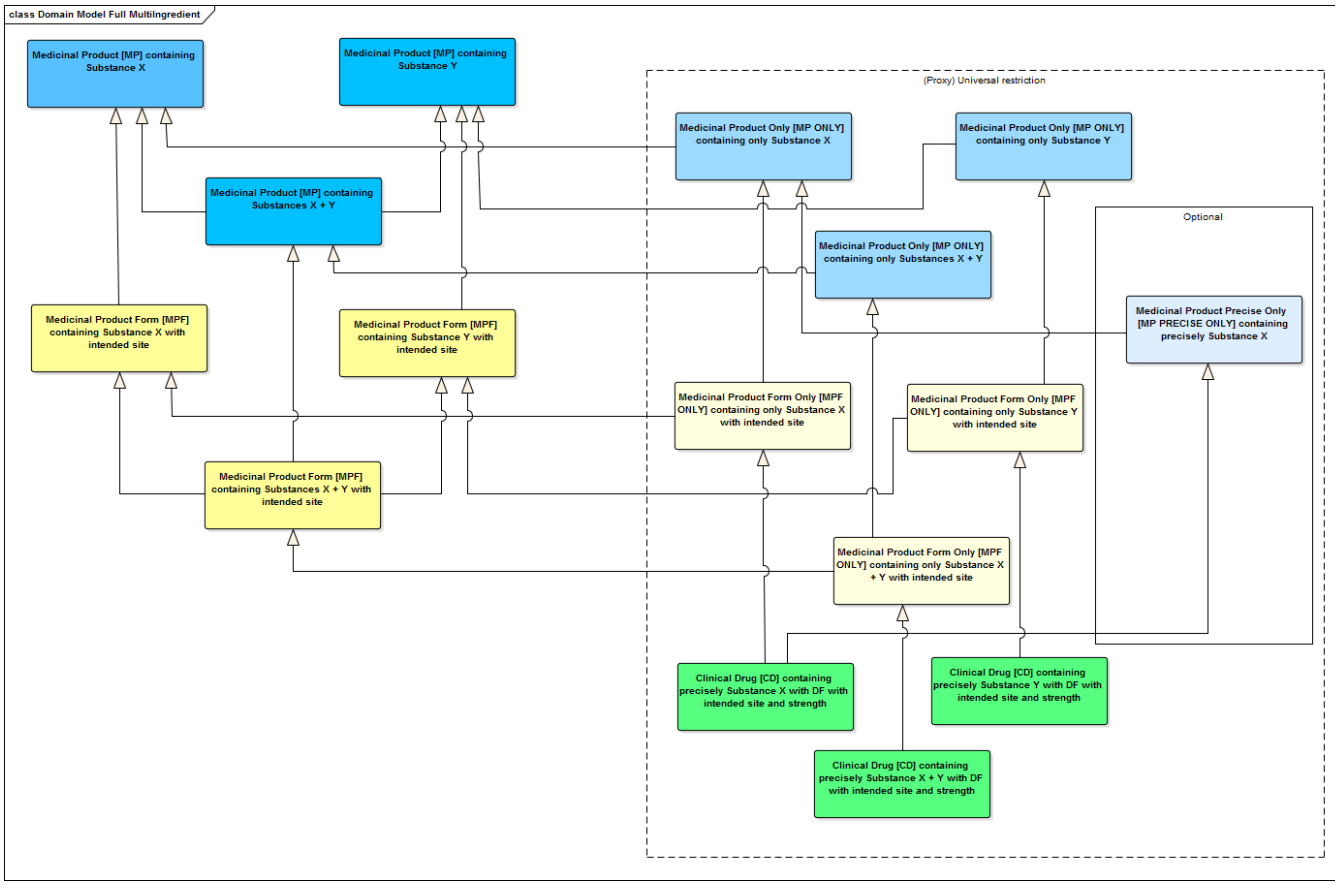

Figure 3: Medicinal Product concept model - International - showing multi-ingredient concepts

In the sections below, each group of classes and its members are defined and described in detail, with their attributes. Detailed definition and discussion of the attributes themselves follows on in a separate section.

Model population

The population of the international release is currently limited to description of those products for which there was already available content within SNOMED CT and for which verification has been obtained by reference to concepts in a small number of national medicinal product terminologies. There is nothing in the specification that deals with availability of medicinal products for use; neither the presence of a concept nor an absence of a concept gives any sense of its availability in the supply chain globally. Indeed, even when a medicinal product ceases to be available anywhere in the global supply chain, its representation will remain as a valid concept for use in historic records and Medication History and Medication Profiles. The rules and principles for ongoing maintenance of concepts within this model are part of the Editorial Guidelines for Modeling and Terming (see above).

In maintaining a medicinal product terminology, concepts are authored to describe those things that exist and can be used in clinical care and/or clinical research. This means that it is the more granular concepts that are usually recognised first, then the less concrete concepts are abstracted from these. In many medicinal product terminologies, this results in their being lowest level child concepts for every parent concept within the model classes. Due to the historic nature of some of the content in the SNOMED CT international release Medicinal Product hierarchy, there will be higher level parent concepts (i.e. MP and MPF concepts) that do not have clinical drug concepts associated with them. These MP and MPF concepts may have had clinical drug type concepts associated with them in the past, but the veracity and provenance of the detailed information to support these CD concepts could not be confirmed, so they have been inactivated whereas the more abstract MP and MPF concepts remain in the international release to support historic data use cases such as analysis and Medication Profiles.

New medicinal products, both from newly authorised therapeutic substances and in new formulations of existing therapeutic substances, are constantly appearing globally. The principles and process for the ongoing maintenance of and addition of new content to the Medicinal Product hierarchy are being developed.

IDMP Compatibility

The definition of the 763158003 |Medicinal product (product)| concept as providing the scope of the hierarchy is in agreement with the *scope* of the concept of a medicinal product in IDMP. This is a positive position generally and particularly for any future mapping exercise that might be undertaken, since there should be few concepts that cannot be mapped at some level of granularity. However, in IDMP, and specifically in ISO 11615, the Medicinal Product class represents an authorised medicinal product that consists of one or more Manufactured Items as authorised and available; in this sense it is much more concrete concept than the SNOMED parent concept. This difference is not of great significance other than to understand that the same term ("medicinal product") has a different and more specific meaning in IDMP than in the SNOMED CT Medicinal Product model. Also, the IDMP ISO 11615 model explicitly describes and includes "combination medicinal products" (also known as 'kit' products, 'component' products, 'multi-component packaged products' etc.) where the package placed into the supply chain contains more than one type of component element (clinical drug) within it; since these are correctly packaged products, and packaged products are out of scope of the Medicinal Product hierarchy for the international release of SNOMED CT, these combination products are not represented in this SNOMED model.

Grouper concepts

Medicinal products and their representations in a terminology can be put into groups in many ways, both in terms of abstraction and aggregation of product descriptions. In the SNOMED CT Medicinal Product model, the following grouping concepts will be used:

- groupings based on the pharmaceutical characteristics of manufactured medicinal products, and the primary subject of this model and documentation: in each of the sections below, these various model classes and their attributes are defined, described in detail and diagrams provided. In addition, their relationship to IDMP is described and a note as to their population status within the upcoming releases of SNOMED CT is provided.
    - Medicinal product - grouping based on active ingredient substance(s)
    - Medicinal product form - grouping based on active ingredient substance(s) combined with a grouping of the site of administration of manufactured dose form (parenteral dose forms, oral dose forms etc.)
        - These concepts are also grouped using the site of administration of manufactured dose form as a grouping concept
    - Clinical drug - a grouping based on active ingredient substance(s), with their strength, combined with manufactured dose form
- groupings based on the chemical or behavioural characteristics that the products exhibit:
    - Disposition - grouping based on mechanism of action of the active ingredient substance(s) in the product
    - Structure - grouping based on structural patterns of the active ingredient substance(s) in the product
    - Structure and Disposition - combination of the above

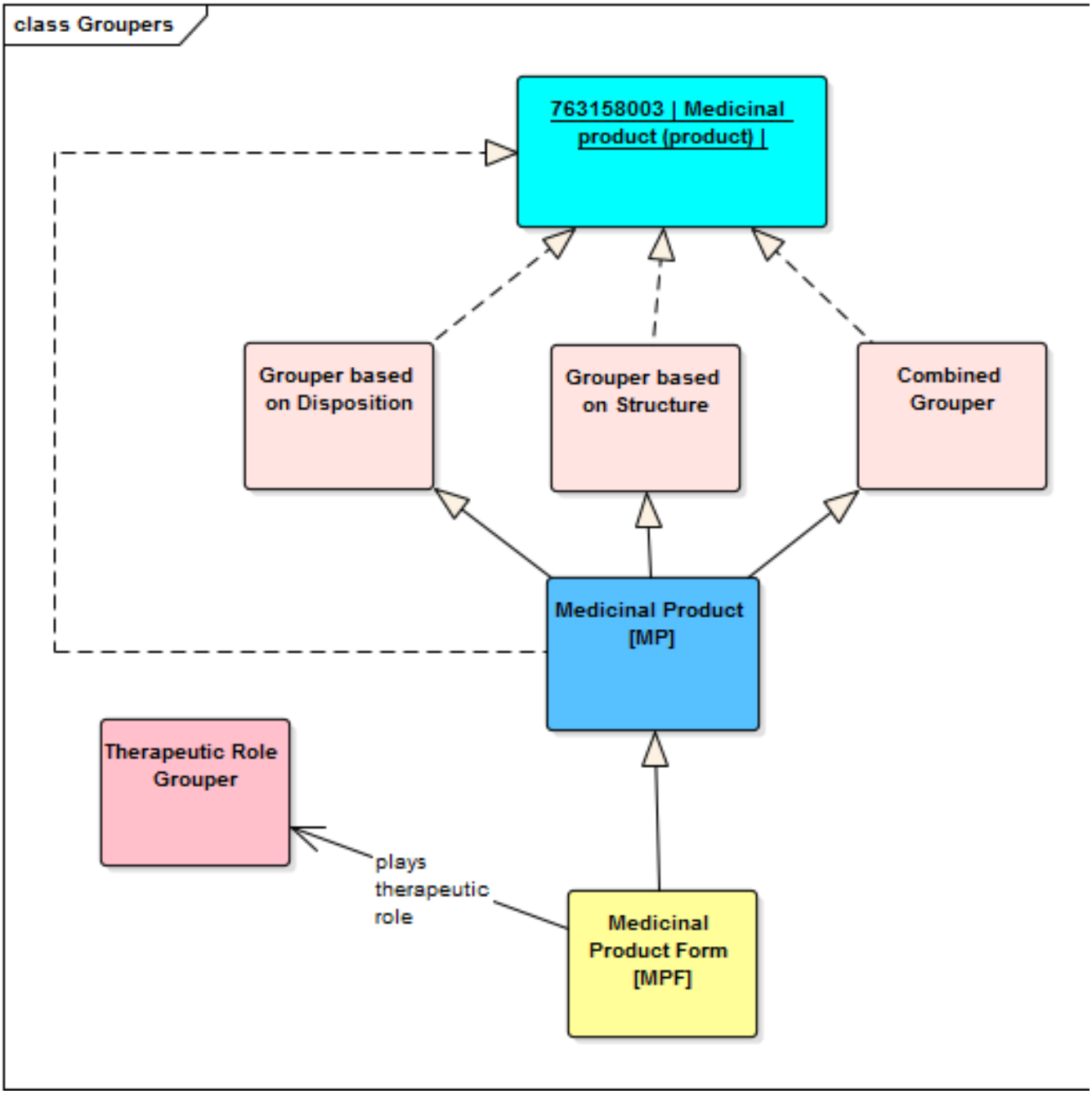

Figure 4: Medicinal Product grouping concepts

Groups of Products based on Disposition

Disposition is a behaviour that something can exhibit (or participate in) given the appropriate context in which to do this. For example, a person may be "disposed" (or pre-disposed) to fidget in their seat when in a stressful situation such as an interview. For medicinal products, disposition behaviour can be thought of as "mechanism of action" of its active ingredient substance(s): the behaviour that the active ingredient substance(s) in the product exhibit when used clinically. Disposition (mechanism of action) is distinguishable from therapeutic role, which is context dependent: for example the mechanism of action of timolol is as a beta-adrenoceptor antagonist; this action can be used therapeutically to reduce hypertension when administered in a product given orally or to treat glaucoma when administered in a product intended to be given ophthalmically. Medicinal products can be collected together into groups based on the disposition of their active ingredient substance(s).

Disposition is a characteristic of the active ingredient substance(s) present in the Medicinal Product, therefore disposition grouping concepts are assigned (inferred) by the classifier to Medicinal Products and include all their child concepts.

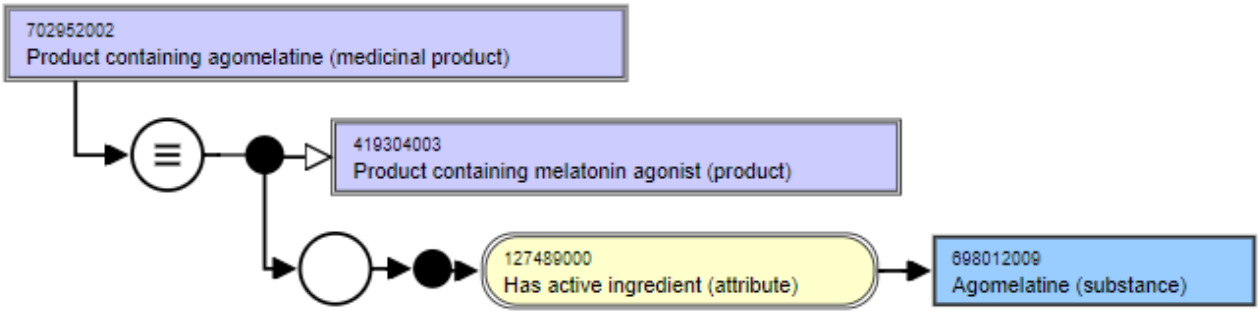

Figure 5: Medicinal Product showing membership of a disposition grouping (melatonin agonist)

Groups of Products based on (Chemical) Structure

All substances have spatial arrangement of the atoms and molecules and bonds that they are constituted from and which therefore govern the final shape that the substance takes; this arrangement is their "structure". Substance structures often follow patterns so that similar structures are grouped together and are often particular name patterns. Medicinal products can be collected together into groups based on the structural pattern(s) of their active ingredient substance(s).

Structure-based grouping is a characteristic of the active ingredient substance(s) present in the Medicinal Product, therefore structure-based grouping concepts are assigned (inferred) by the classifier to Medicinal Products and include all their child concepts.

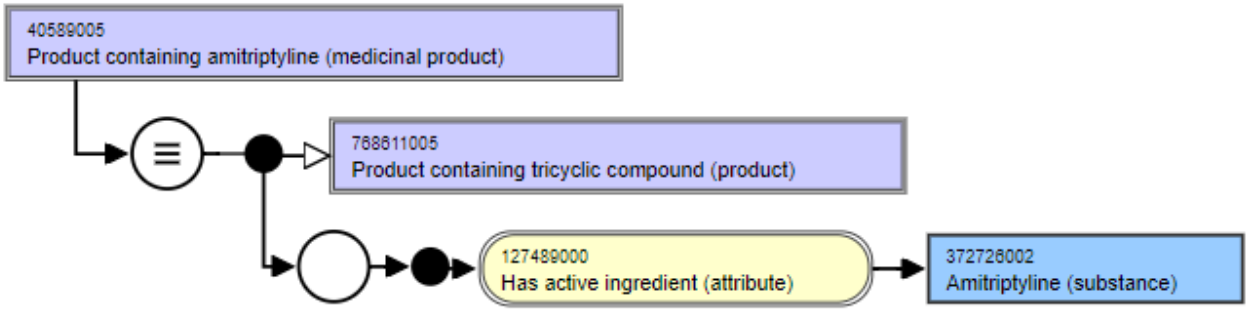

Figure 6: Medicinal Product showing membership of a structural grouping (tricyclic compound)

Groups of Products based on Structure and Disposition

For some medicinal products, their clinical usefulness is related to the combination of both their structure and their disposition; it is the structure that produces the disposition; for example clemastine, a substance whose anti-histamine behaviour is based upon its structure being ethanolamine derived.

Since structure-based grouping and disposition are characteristics of the active ingredient substance(s) present in the Medicinal Product, combined 'structure and disposition grouping' concepts are assigned (inferred) by the classifier to Medicinal Products and include all their child concepts.

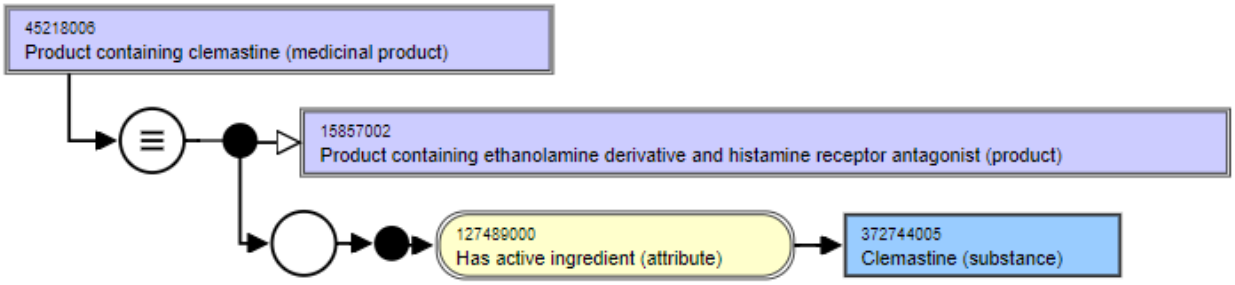

Figure 7: Medicinal Product showing membership of a structure-and-disposition grouping (ethanolamine derivative and histamine receptor antagonist)

Groups of Products based on Therapeutic Role

Medicinal products can be collected together into groups based on the therapeutic role that they are designed to fulfil. Roles are very context dependent and may change over time and with changing circumstances (including the culture and practice of healthcare). Roles are therefore not definitional for medicinal products. Therapeutic role is a broader concept than 'indication for use' of a medicine. Indication may describe information such as the disease(s) that the product may be used in, the intended effect (prophylaxis, cure, symptom relief etc.), the role within an overall treatment regimen (first line, adjunctive etc.) and specific populations for use (e.g. in adults, in children) whereas therapeutic role describes the general condition that the product may be used to treat (e.g. Product acting as antidementia agent) or describes the general treatment effect of the product (e.g. Product acting as haemostatic). Since therapeutic role is often closely associated with product formulation (targeting the therapeutic substance to the correct site of action), therapeutic roles may be assigned to Medicinal Product Form concepts and occasionally to Clinical Drug concepts; if all the products share a therapeutic role, it can be assigned at the higher MP level.

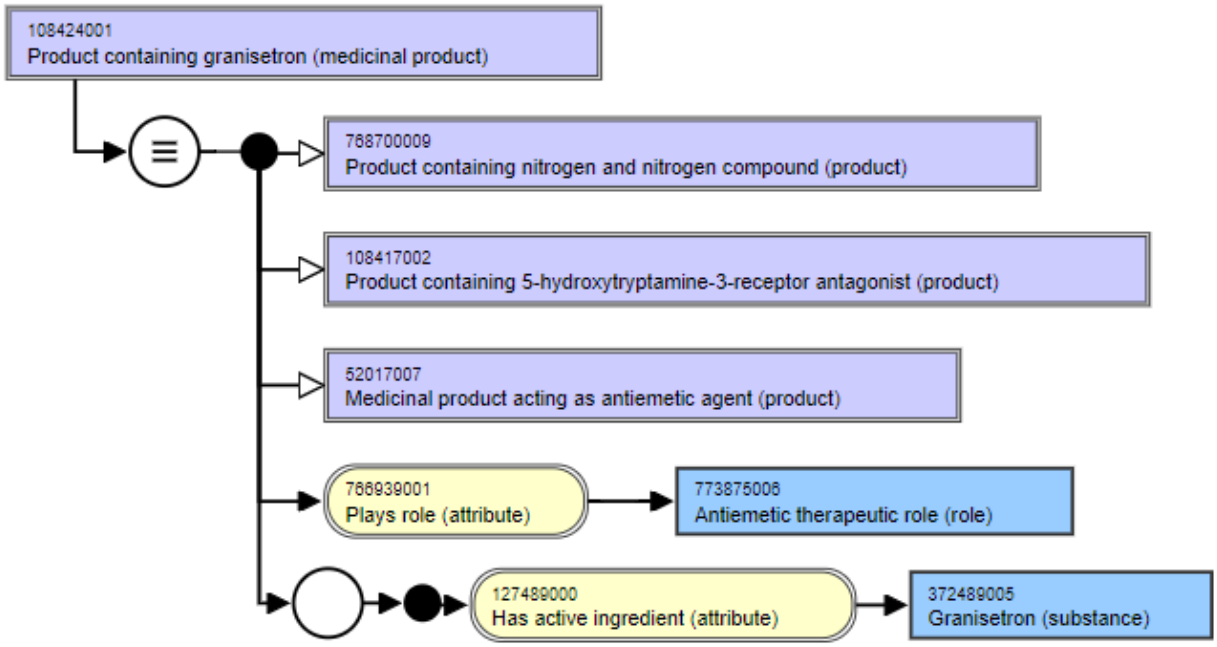

Figure 8: Anti-emetic agent therapeutic role, assigned at Medicinal Product

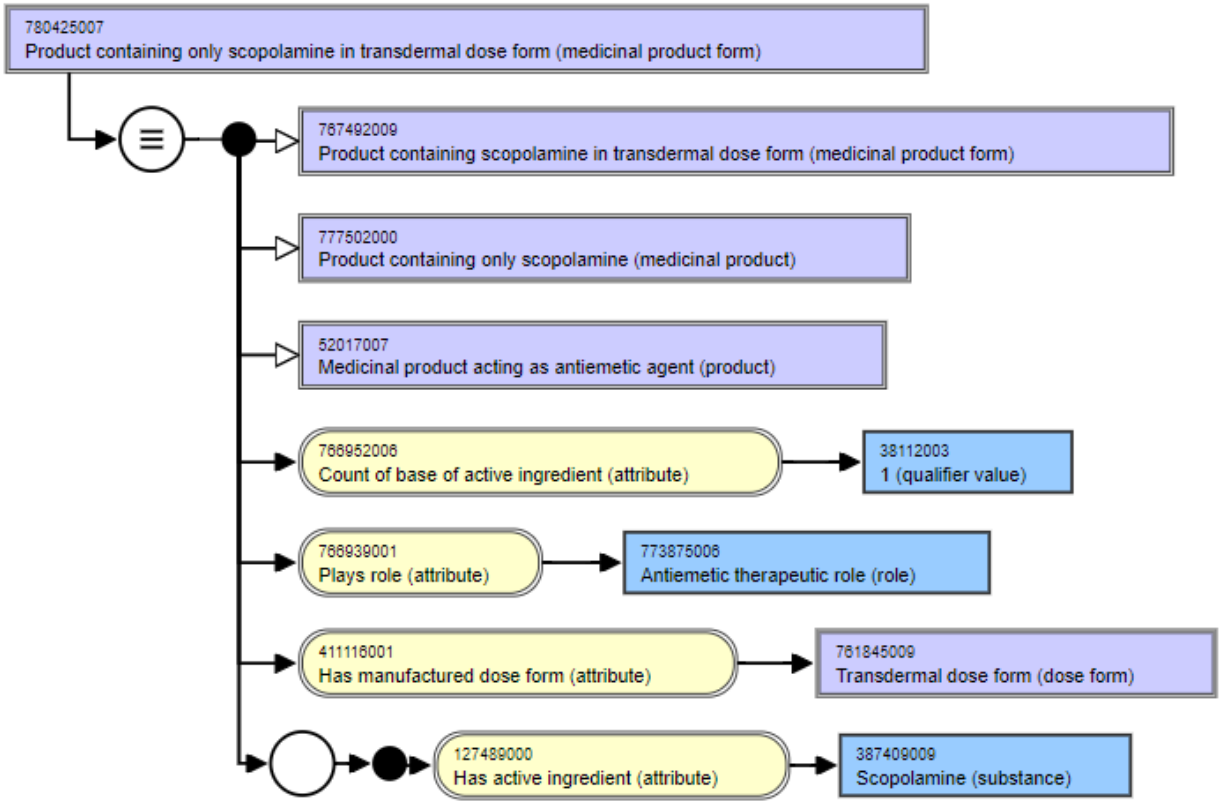

Figure 9: Anti-emetic agent therapeutic role, assigned at Medicinal Product Form (only)