

# Change request / New concept proposal

## Drug / Drug Administration Event / Drug Prescription / Drug Article

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<b>Dataset release</b>	2024.1	Consulted expert	Amanda Ramirez Ramos, Josip Matic

### Index:

1 Change request input / rationale.....	2
1.1 Ambiguities of 'quantity'-attributes of Drug Administration Event and Drug Prescription.....	2
1.2 Request to distinguish context-dependent quantity and unit quantity.....	3
1.3 Attribute name 'product code' vs. 'article code'.....	4
1.4 Description of 'active ingredient'.....	4
1.5 time-attribute for Drug Prescription.....	4
2 Comparison to other standards/data models.....	4
3 Change content.....	6
3.1 Drug.....	6
3.2 Drug Prescription.....	14
3.3 Drug Administration Event.....	19
4 Pros and cons.....	26
4.1 Advantages.....	26
4.2 Disadvantages.....	27
5 Impact on SPHN Dataset.....	28
6 Discussion.....	28
6.1 Definitions.....	28
6.2 Quantity.....	28
6.3 Total quantities.....	29
6.4 Drug metainformation ("Drug Article").....	30
6.5 Limitations.....	30
6.6 Removal of meaning bindings of composedOfs.....	31
7 Example.....	32
7.1 Proposal A.....	32
7.2 Proposal B.....	33
7.3 Proposal C.....	34

## 1 Change request input / rationale

The concepts Drug, Drug Administration Event, and Drug Prescription are of significant importance for the representation of clinical data and processes concerning medication and treatment. The design of these three concepts has been the subject of discussions repeatedly, in particular with regards to whether and how appropriate drug quantities and ingredient content can be represented.

This document contains change requests and concept proposals that have been discussed during concept development:

- change request for 'Drug Administration Event' (one proposal)
- change request for 'Drug Prescription' (one proposal)
- change requests for 'Drug' (three proposals A, B, and C)
- new concept proposal 'Drug Article' (two variants in line with 'Drug'-proposal B and C)

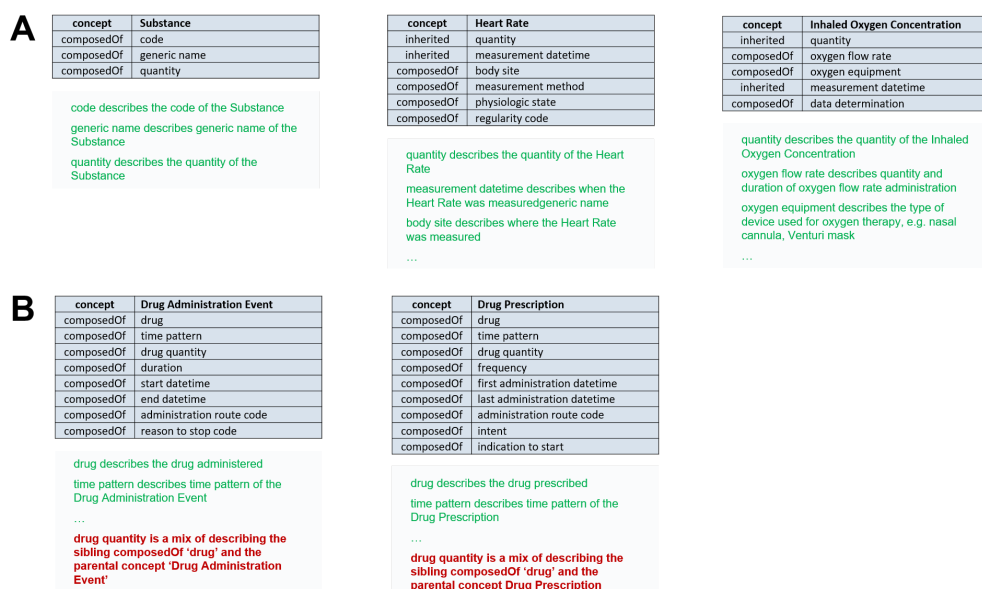
The change requests for 'Drug Administration Event' and 'Drug Prescription' have been integrated into the SPHN Dataset release 2024.1.

For 'Drug' and 'Drug Article', Proposal C has been selected and integrated into the SPHN Dataset release 2024.1.

### 1.1 Ambiguities of 'quantity'-attributes of Drug Administration Event and Drug Prescription

The concept Drug currently does not feature an attribute describing its quantity (SPHN dataset release 2023.2). Quantities can only be provided for the substances contained in a drug (via composedOfs 'active ingredient' and 'inactive ingredient').

This lack of a quantity-attribute of the Drug concept can result in misunderstandings in the context of the concepts Drug Administration Event and Drug Prescription: Each of them holds a composedOf 'drug quantity'. It is ambiguous whether the attribute refers to its parent concept (in line with semantic modeling) or the sibling composedOf 'drug' (as the descriptions of the composedOf suggest) (Figure 1A).



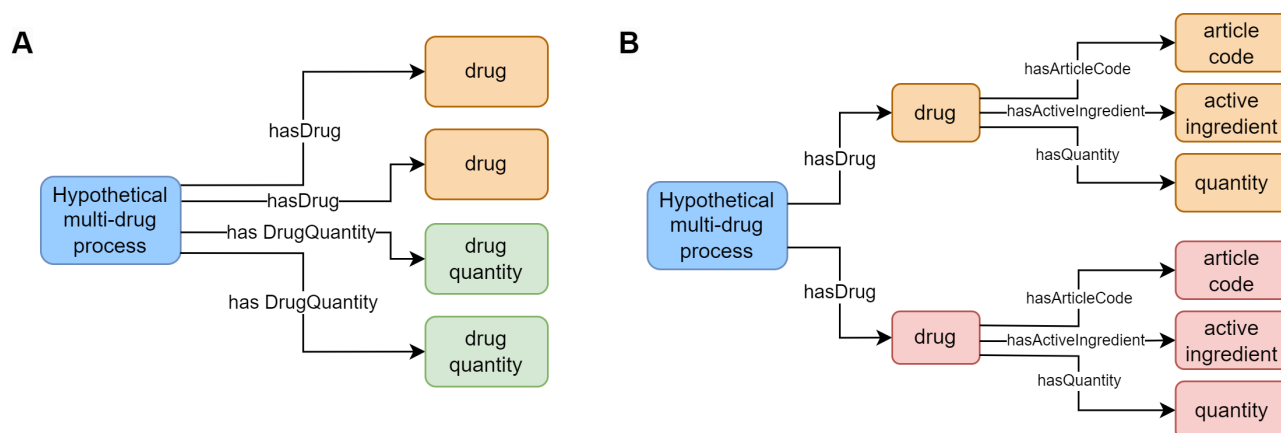
**Figure 1: General usage of attributes**

(A) composedOfs describe properties of the parent concept, not of each other. (B) The concepts 'Drug Administration Event' and 'Drug Prescription' create ambiguity by deviating from this rule.

Semantically, attributes on the same level (sibling attributes) always refer to the parent concept holding them but cannot describe each other, i.e., currently there is no link between ‘drug’ and ‘drug quantity’ in Drug Administration Event and Drug Prescription.

Attributes are context-dependent and describe the instance of the concept they refer to. The property ‘drug quantity’ of type Quantity of the concept Drug Administration Event therefore describes the number of Drug Administration Events rather than the quantity of the drug administered, despite the name of the composedOf suggesting otherwise (Figure 1B).

Bearing in mind expandability of the SPHN dataset, the concept design of Drug also does not allow unambiguous linkage of multiple amounts to multiple drugs in new concepts – it would not be clear which quantity belongs to which drug (Figure 2).



**Figure 2: Reusability issues in a hypothetical concept using multiple drugs**

(A) Drugs and their respective quantities are not linked unambiguously using the current concept Drug. (B) Linking ‘quantity’ to Drug directly resolves the issue. *Note: Properties of the Drug concept such as article code, (in)active ingredient etc. are not shown in panel (A) for clarity.*

It is therefore suggested to add a composedOf ‘quantity’ to the concept Drug and remove the misleading composedOfs ‘drug quantity’ from Drug Administration Event and Drug Prescription (see 3. Change content).

## 1.2 Request to distinguish context-dependent quantity and unit quantity

Currently, there is no way to represent the “drug strength” (“pharmaceutical strength”) of a drug with the Drug concept. “Pharmaceutical strength” is defined by NCIT ([C53294](#)) as “The content of an active ingredient expressed quantitatively per dosage unit, per unit of volume, or per unit of weight, according to the pharmaceutical dose form.”. The lack of possibility to represent this property has probably been one of the causes for continued discussions revolving around “quantity” in the context of Drug and related concepts. One of the proposals outlined in this change request therefore introduces another concept (Drug Article) which can hold relevant meta-information of a medication, e.g., an article code (e.g., coded using a GTIN-identifier), the manufacturer, active and inactive ingredients, and the manufactured dose form (of type ‘Pharmaceutical Dose Form’). Active and inactive ingredients are of type Substance and feature a quantity-attribute which can hold the substance quantity per drug dosage unit.

### 1.3 Attribute name 'product code' vs. 'article code'

It has been noted that the current attribute 'product code' does in fact not describe a product but rather an article. Unfortunately, there is no freely available standard for describing a drug on product level at the moment (11/2023).

GTIN is the standard currently used for the composedOf 'product code'. GTIN codes vary with package size of the same drug, for example, "Aspirin C Brausetabletten" (Aspirin C effervescent tablets) with 400 mg acetylsalicylic acid and 240 mg Vitamin C, have the GTIN codes 7680336700282 and 7680336700367 for packages with 10 and 20 tablets, respectively.

It is therefore proposed to rename the composedOf 'product code' to 'article code'. It should use GTIN as an international standard wherever possible.

### 1.4 Description of 'active ingredient'

The definition of "active ingredient" in the SPHN dataset release 2023.2 ("pharmaceutically active component of the concept" (general definition) or "pharmaceutically active component of a drug" (contextualized definition)) excludes components which do not have a pharmacological effect but are used in diagnosis, for example contrast agents. Moreover, this description is in contrast to the one used in the Drug-concept: "any substance with the intent to prevent, **diagnose**, treat, or relieve symptoms of a disease or abnormal condition". An adaptation of the definition of "active ingredient" can solve this issue (compare 2.5).

### 1.5 time-attribute for Drug Prescription

The concept 'Drug Prescription' currently does not hold any information when the prescription of the medication occurred (release 2023.2). While this information is useful it may not be available in all cases. It was therefore proposed by the Semantic Working Group (30.08.2023) to add a composedOf 'record time' to 'Drug Prescription' as a datetime-attribute which is readily available and in most cases closely correlated with the actual occurrence of the prescription.

## 2 Comparison to other standards/data models

### 2.1 FHIR

FHIR features the concept 'Medication' (<https://build.fhir.org/medication.html>) which is intended to be "primarily used for the identification and definition of a medication, including ingredients, for the purposes of prescribing, dispensing, and administering a medication as well as for making statements about medication use."

### 2.2 OMOP

OMOP uses the drug\_concept\_id in the table DRUG\_STRENGTH, DRUG\_ERA, and DRUG\_EXPOSURE to "...[represent] a drug product or molecule otherwise introduced to the body."  
(<https://ohdsi.github.io/CommonDataModel/cdm60.html>).

## 2.3 SNOMED CT

The concept 'drug' is covered in SNOMED CT by code 410942007 (Drug or medicament (substance)) (<https://browser.ihtsdo.org/?perspective=full&conceptId1=410942007&edition=MAIN/SNOMEDCT-CH/2023-06-07&release=&languages=en>). It has 147 direct children representing various drugs and itself is a descendant of code 105590001 (Substance (substance)).

## 2.4 NCIT

The NCIT code [C459](#) defines the term "Medication" as "A drug product that contains one or more active and/or inactive ingredients; it is intended to treat, prevent or alleviate the symptoms of disease. This term does not refer to the individual ingredients that make up the product."

"Pharmaceutical strength" (NCIT code [C53294](#)) is defined as "The content of an active ingredient expressed quantitatively per dosage unit, per unit of volume, or per unit of weight, according to the pharmaceutical dose form."

## 2.5 FDA glossary

The term "active ingredient" in context of a drug or pharmaceutical product is defined as follows in the FDA glossary: "An active ingredient is any component that provides pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or animals." ([link to definition](#)). This definition is broader than the current definition of "active ingredient" in the SPHN dataset ("pharmaceutically active component of the concept" (general definition) or "pharmaceutically active component of a drug" (contextualized definition)) and includes components which do not have a pharmacological effect, e.g. contrast agents.

### 3 Change content

#### 3.1 Drug

##### 3.1.1 Currently released concept

Concept or concept compositions or inherited	General concept name	General description	Contextualized concept name	Contextualized description	Type	Standard	Value set or subset	Meaning binding	Cardinality for composedOf
<b>concept</b>	Drug	any substance with the intent to prevent, diagnose, treat, or relieve symptoms of a disease or abnormal condition	Drug	any substance with the intent to prevent, diagnose, treat, or relieve symptoms of a disease or abnormal condition				SNOMED CT: 410942007 [Drug or medicament (substance)]	
<b>composedOf</b>	product code	code, name, coding system and version describing the product of the concept	product code	code, name, coding system and version representing the drug, e.g. GTIN	Code	GTIN			0:1
<b>composedOf</b>	active ingredient	pharmaceutically active component of the concept	active ingredient	pharmaceutically active component of a drug	Substance				0:n
<b>composedOf</b>	inactive ingredient	inert ingredients or excipients, and generally have no pharmacological effect of the concept	inactive ingredient	inert ingredients or excipients, and generally have no pharmacological effect	Substance				0:n

<b>composedOf</b>	manufactured dose form	dose form presented in the manufactured item, e.g. powder	manufactured dose form	dose form presented in the manufactured item, e.g. powder	Pharmaceutical Dose Form				0:1
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General concept name	Cardinality for concept to Administrative Case	Cardinality for concept to Data Provider Institute	Cardinality for concept to Subject Pseudo Identifier
Drug	-	-	-

- = not applicable

### 3.1.2 Proposed new concept

#### 3.1.2.1 Proposal A

##### 3.1.2.1.1 Drug

Concept or concept compositions or inherited	General concept name	General description	Contextualized concept name	Contextualized description	Type	Standard	Value set or subset	Meaning binding	Cardinality for composedOf
<b>concept</b>	Drug	any substance with the intent to prevent, diagnose, treat, or relieve symptoms of a disease or abnormal condition	Drug	any substance with the intent to prevent, diagnose, treat, or relieve symptoms of a disease or abnormal condition				SNOMED CT: 410942007  Drug or medicament (substance)	
<b>composedOf</b>	article code	coded information specifying the concept	article code	coded information specifying the drug on the level of the commercial article, possibly specific for package sizes	Code	GTIN			0:1
<b>composedOf</b>	quantity	an amount or a number of the concept	drug amount	amount of the drug itself in the relevant context (e.g., administered or prescribed), such as 5 pills, 2 puffs, or 3 mL	Quantity				0:1
<b>composedOf</b>	active ingredient	active component of the concept	active ingredient	active component of a drug	Substance				0:n



<b>composedOf</b>	inactive ingredient	inert ingredients or excipients, and generally have no pharmacological effect of the concept	inactive ingredient	inert ingredients or excipients, and generally have no pharmacological effect	Substance				0:n
<b>composedOf</b>	manufactured dose form	dose form presented in the manufactured item	manufactured dose form	dose form presented in the manufactured item, e.g. powder	Pharmaceutical Dose Form				0:1

General concept name	Cardinality for concept to Administrative Case	Cardinality for concept to Data Provider	Cardinality for concept to Subject Pseudo Identifier	Cardinality for concept to Source System
Drug	-	-	-	1:1

- = not applicable

### 3.1.2.2 Proposal B

#### 3.1.2.2.1 Drug

Concept or concept compositions or inherited	General concept name	General description	Contextualized concept name	Contextualized description	Type	Standard	Value set or subset	Meaning binding	Cardinality for composedOf
<b>concept</b>	Drug	any substance with the intent to prevent, diagnose, treat, or relieve symptoms of a disease or abnormal condition	Drug	any substance with the intent to prevent, diagnose, treat, or relieve symptoms of a disease or abnormal condition				SNOMED CT: 410942007  Drug or medicament (substance)	
<b>composedOf</b>	article	commercial identifier of the concept	drug article	general properties identifying the drug on the level of the article	Drug Article				0:1
<b>composedOf</b>	quantity	an amount or a number of the concept	drug amount	amount of the drug itself in the relevant context (e.g., administered or prescribed), such as 5 pills, 2 puffs, or 3 mL	Quantity				0:1
<b>composedOf</b>	active ingredient	active component of the concept	active ingredient	active component of a drug	Substance				0:n
<b>composedOf</b>	inactive ingredient	inert ingredients or excipients, and generally have no pharmacological effect of the concept	inactive ingredient	inert ingredients or excipients, and generally have no pharmacological effect	Substance				0:n

General concept name	Cardinality for concept to Administrative Case	Cardinality for concept to Data Provider	Cardinality for concept to Subject Pseudo Identifier	Cardinality for concept to Source System
Drug	-	-	-	1:1

- = not applicable

### 3.1.2.2.2 Drug Article

Concept or concept compositions or inherited	General concept name	General description	Contextualized concept name	Contextualized description	Type	Standard	Value set or subset	Meaning binding	Cardinality for composedOf
concept	Drug Article	general details identifying a drug	Drug Properties	general details identifying a drug					
composedOf	code	coded information specifying the concept	article code	coded information specifying the drug on the level of the commercial article, possibly specific for package sizes	Code	GTIN			0:1
composedOf	name	name associated to the concept	article name	name associated to the drug article, possibly specific for package sizes	string				0:1
composedOf	manufacturer	producer of the concept	manufacturer	producer of the drug	string				0:1

<b>composedOf</b>	active ingredient	active component of the concept	active ingredient	active component of a drug	Substance				0:n
<b>composedOf</b>	inactive ingredient	inert ingredients or excipients, and generally have no pharmacological effect of the concept	inactive ingredient	inert ingredients or excipients, and generally have no pharmacological effect	Substance				0:n
<b>composedOf</b>	manufactured dose form	dose form presented in the manufactured item	manufactured dose form	dose form presented in the manufactured item, e.g. powder	Pharmaceutical Dose Form				0:1

General concept name	Cardinality for concept to Administrative Case	Cardinality for concept to Data Provider	Cardinality for concept to Subject Pseudo Identifier	Cardinality for concept to Source System
Drug Article	-	-	-	1:1

- = not applicable

### 3.1.2.3 Proposal C

#### 3.1.2.3.1 Drug

Proposal C for 'Drug' is the same as [Proposal B](#).

#### 3.1.2.3.2 Drug Article

Proposal C for 'Drug Article' is similar to the one of Proposal B, however, with fewer composedOfs.

Concept or concept compositions or inherited	General concept name	General description	Contextualized concept name	Contextualized description	Type	Standard	Value set or subset	Meaning binding	Cardinality for composedOf
<b>concept</b>	Drug Article	general details identifying a medication on the level of its commercial article	Drug Article	general details identifying a medication on the level of its commercial article					
<b>composedOf</b>	code	coded information specifying the concept	article code	coded information specifying the drug on the level of the commercial article, possibly specific for package sizes	Code	GTIN			0:1
<b>composedOf</b>	name	name associated to the concept	article name	name associated to the drug article, possibly specific for package sizes	string				0:1
<b>composedOf</b>	manufactured dose form	dose form presented in the manufactured item	manufactured dose form	dose form presented in the manufactured item, e.g. powder	Pharmaceutical Dose Form				0:1

General concept name	Cardinality for concept to Administrative Case	Cardinality for concept to Data Provider	Cardinality for concept to Subject Pseudo Identifier	Cardinality for concept to Source System
Drug Article	-	-	-	1:1

## 3.2 Drug Prescription

### 3.2.1 Currently released concept

Concept or concept compositions or inherited	General concept name	General description	Contextualized concept name	Contextualized description	Type	Standard	Value set or subset	Meaning binding	Cardinality for composedOf
<b>concept</b>	<b>Drug Prescription</b>	plan that defines at which frequency a drug should be administered to a patient with a given quantity; at every frequency time point a drug administration event should occur	<b>Drug Prescription</b>	plan that defines at which frequency a drug should be administered to a patient with a given quantity; at every frequency time point a drug administration event should occur				SNOMED CT: 33633005  Prescription of drug (procedure)	
<b>composedOf</b>	drug	any substance with the intent to prevent, diagnose, treat, or relieve symptoms of a disease or abnormal condition used in or causing the concept	drug	drug prescribed to a patient	Drug				1:1
<b>composedOf</b>	time pattern	type of time period during which a treatment was given or an	time pattern type	defines if the event is a single time point or a duration	Time Pattern				0:1

		assessment was performed		(continuous or intermittent)					
<b>composedOf</b>	drug quantity	quantity of a drug of the concept	drug quantity	quantity of a drug prescribed to an individual	Quantity				0:1
<b>composedOf</b>	frequency	number of events per unit of time	frequency	number of drug intakes prescribed per unit of time	Quantity				0:1
<b>composedOf</b>	first administration datetime	datetime of first administration	first administration datetime	datetime at which the prescribed drug has to be administered for the first time	temporal			SNOMED CT: 413946009  Date treatment started (observable entity)	1:1
<b>composedOf</b>	last administration datetime	datetime of last administration	last administration datetime	datetime at which the prescribed drug has to be administered for the last time	temporal			SNOMED CT: 413947000  Date treatment stopped (observable entity)	0:1
<b>composedOf</b>	administration route code	code, name, coding system and version describing the route of administration	administration route	route of administration of the prescription	Code	SNOMED CT	descendant of: 284009009  route of administration value (qualifier value)	SNOMED CT: 284009009  Route of administration value (qualifier value) ; LOINC: 74050-6 Actual route of administration - attempted or completed [AHRQ]	0:1

<b>composedOf</b>	intent	intention for the concept	intent	intention for drug prescription, e.g. palliative care	Intent				0:1
<b>composedOf</b>	indication to start	indication to start the concept	indication to start	indication to start the drug treatment; can be a specific diagnosis, or an intent	Diagnosis, Intent				0:1

General concept name	Cardinality for concept to Administrative Case	Cardinality for concept to Data Provider Institute	Cardinality for concept to Subject Pseudo Identifier
<b>Drug Prescription</b>	0:1	1:1	1:1

### 3.2.2 Proposed new concept

Concept or concept compositions or inherited	General concept name	General description	Contextualized concept name	Contextualized description	Type	Standard	Value set or subset	Meaning binding	Cardinality for composedOf
<b>concept</b>	<b>Drug Prescription</b>	plan that defines at which frequency a drug should be administered to a patient with a given quantity; at every frequency time point a drug administration	<b>Drug Prescription</b>	plan that defines at which frequency a drug should be administered to a patient with a given quantity; at every frequency time point a drug administration event should occur				SNOMED CT: 33633005  Prescription of drug (procedure)	



		event should occur							
<b>composedOf</b>	drug	medication associated to the concept	drug	drug prescribed to a patient	Drug				1:1
<b>composedOf</b>	time pattern	type of repetitive sequence of events over time of the concept	time pattern type	defines if the event is a single time point or a duration (continuous or intermittent)	Time Pattern				0:1
<b>composedOf</b>	frequency	number of events per unit of time	frequency	number of drug intakes prescribed per unit of time	Quantity				0:1
<b>composedOf</b>	first administration datetime	datetime of first administration	first administration datetime	datetime at which the prescribed drug has to be administered for the first time	temporal				1:1
<b>composedOf</b>	last administration datetime	datetime of last administration	last administration datetime	datetime at which the prescribed drug has to be administered for the last time	temporal				0:1
<b>composedOf</b>	administration route code	<b>coded information specifying</b> the route of administration	administration route	route of administration of the prescription	Code	SNOMED CT	descendant of: 284009009  route of administration value (qualifier value)		0:1

<b>composedOf</b>	intent	intention for the concept	intent	intention for drug prescription, e.g. palliative care	Intent				0:n
<b>composedOf</b>	indication to start	indication to start the concept	indication to start	indication to start the drug treatment; can be a specific diagnosis, or an intent	Diagnosis				0:n
<b>composedOf</b>	record datetime	datetime the concept was recorded	record datetime	datetime the drug prescription was recorded	temporal				0:1

General concept name	Cardinality for concept to Administrative Case	Cardinality for concept to Data Provider	Cardinality for concept to Subject Pseudo Identifier	Cardinality for concept to Source System
Drug Prescription	0:1	1:1	1:1	1:1

### 3.3 Drug Administration Event

#### 3.3.1 Currently released concept

Concept or concept compositions or inherited	General concept name	General description	Contextualized concept name	Contextualized description	Type	Standard	Value set or subset	Meaning binding	Cardinality for composedOf
<b>concept</b>	<b>Drug Administration Event</b>	single event at which a drug was administered to the patient; this could be a single time point in case of a pill/cream or a duration in case of a single infusion pack or a single patch; one or many drug administration events are initiated by a drug prescription depending on the frequency stated in the prescription	<b>Drug Administration Event</b>	single event at which a drug was administered to the patient; this could be a single time point in case of a pill/cream or a duration in case of a single infusion pack or a single patch; one or many drug administration events are initiated by a drug prescription depending on the frequency stated in the prescription				<b>SNOMED CT: 182832007  Procedure related to management of drug administration (procedure) </b>	
<b>composedOf</b>	drug	any substance with the intent to prevent, diagnose, treat, or relieve symptoms of a disease or abnormal condition used in or causing the concept	drug	drug administered to a patient	Drug				1:1

<b>composedOf</b>	time pattern	type of time period during which a treatment was given or an assessment was performed	time pattern type	defines if the event is a single time point or a duration (continuous or intermittent)	Time Pattern				0:1
<b>composedOf</b>	drug quantity	quantity of a drug of the concept	drug quantity	quantity of a drug administered to an individual at a given time point or over a given time span continuously	Quantity				0:1
<b>composedOf</b>	duration	duration of an event	duration	time interval during which a substance was administered; it is only used for continuously administered substances	Quantity				0:1
<b>composedOf</b>	start datetime	datetime at which the concept started	event start datetime	actual datetime of the start of the administration	temporal				1:1
<b>composedOf</b>	end datetime	datetime at which the concept ended	event end datetime	actual datetime of the end of the administration; the actual end time could be earlier than the calculated end time from start time plus duration; this can occur if the administration is stopped early due to a problem	temporal				0:1

<b>composedOf</b>	administration route code	code, name, coding system and version describing the route of administration	administration route	route of administration of the drug administration event	Code	SNOMED CT	descendant of: 284009009  route of administration value (qualifier value)	SNOMED CT: 284009009  Route of administration value (qualifier value) ; LOINC: 74050-6 Actual route of administration - attempted or completed [AHRQ]	0:1
<b>composedOf</b>	reason to stop code	code, name, coding system and version indicating the reason to stop the concept	reason to stop	indication to stop the drug administration event	Code	SNOMED CT	441308009  New diagnosis (observable entity) ; 395009001  Medication stopped - side effect (situation) ; 182872003  Drug discontinued - too expensive (situation) ; 182846007  Doctor stopped drugs - medical aim achieved (situation) ; 395007004  Medication stopped - ineffective (situation) ; 31438003  Drug resistance (disorder) ; 182845006  Doctor stopped drugs - avoid interaction (situation) ; 182844005  Doctor stopped drugs - patient dislikes (situation) ; 419620001  Death		0:1

							(event)); 399307001  Lost to follow-up (finding)); 74964007  Other (qualifier value)		
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General concept name	Cardinality for concept to Administrative Case	Cardinality for concept to Data Provider Institute	Cardinality for concept to Subject Pseudo Identifier
Drug Administration Event	0:1	1:1	1:1

### 3.3.2 Proposed new concept

Concept or concept compositions or inherited	General concept name	General description	Contextualized concept name	Contextualized description	Type	Standard	Value set or subset	Meaning binding	Cardinality for composition
concept	Drug Administration Event	single event at which a drug was administered to the patient; this could be a single time point in case of a pill/cream or a duration in case of a single infusion pack or a single patch; one or many drug administration events are initiated by a drug prescription depending on the	Drug Administration Event	single event at which a drug was administered to the patient; this could be a single time point in case of a pill/cream or a duration in case of a single infusion pack or a single patch; one or many drug administration events are initiated by a drug prescription depending on the				SNOMED CT: 182832007  Procedure related to management of drug administration (procedure)	

		frequency stated in the prescription		frequency stated in the prescription					
<b>composedOf</b>	drug	medication associated to the concept	drug	drug administered to a patient	Drug				1:1
<b>composedOf</b>	time pattern	type of repetitive sequence of events over time of the concept	time pattern type	defines if the event is a single time point or a duration (continuous or intermittent)	Time Pattern				0:1
<b>composedOf</b>	duration	elapsed time from start to end of the concept	duration	time interval during which a substance was administered; it is only used for continuously administered substances	Quantity				0:1
<b>composedOf</b>	start datetime	datetime at which the concept started	event start datetime	actual datetime of the start of the administration	temporal				1:1
<b>composedOf</b>	end datetime	datetime at which the concept ended	event end datetime	actual datetime of the end of the administration; the actual end time could be earlier than the calculated end time from start time plus duration; this can occur if the administration is stopped early due to a problem	temporal				0:1

<b>composedOf</b>	administration route code	<b>coded information specifying</b> the route of administration	administration route	route of administration of the drug administration event	Code	SNOMED CT	descendant of: 284009009  route of administration value (qualifier value)		0:1
<b>composedOf</b>	reason to stop code	<b>coded information specifying</b> indicating the reason to stop the concept	reason to stop	indication to stop the drug administration event	Code	SNOMED CT	441308009  New diagnosis (observable entity); 395009001  Medication stopped - side effect (situation); 182872003  Drug discontinued - too expensive (situation); 182846007  Doctor stopped drugs - medical aim achieved (situation); 395007004  Medication stopped - ineffective (situation); 31438003  Drug resistance (disorder); 182845006  Doctor stopped drugs - avoid interaction (situation); 182844005  Doctor stopped drugs - patient dislikes (situation); 419620001  Death (event); 399307001  Lost to follow-up (finding); 74964007  Other (qualifier value)		0:1



General concept name	Cardinality for concept to Administrative Case	Cardinality for concept to Data Provider	Cardinality for concept to Subject Pseudo Identifier	Cardinality for concept to Source System
Drug Administration Event	0:1	1:1	1:1	1:1

## 4 Pros and cons

### 4.1 Advantages

For all proposals, the suggested addition of the composedOf 'quantity' makes the Drug concept consistent with the concept Substance which also features a 'quantity' attribute.

The adapted definition of "active ingredient" ("active component of the concept" instead of "pharmaceutically active component of the concept") allows the inclusion of components which do not show pharmaceutical activity yet are active components, for example contrast agents used for diagnosis purposes.

The addition of the composed 'record datetime' to 'Drug Prescription' improves traceability of prescriptions.

#### 4.1.1 Proposal A

	Type		Type		Type
concept	Drug	concept	Drug Administration Event	concept	Drug Prescription
composedOf	article code	composedOf	drug	composedOf	drug
composedOf	quantity	composedOf	time pattern	composedOf	time pattern
composedOf	active ingredient	composedOf	drug-quantity	composedOf	drug-quantity
composedOf	inactive ingredient	composedOf	duration	composedOf	frequency
composedOf	manufactured dose form	composedOf	start datetime	composedOf	first administration datetime
		composedOf	end datetime	composedOf	last administration datetime
		composedOf	administration route code	composedOf	administration route code
		composedOf	reason to stop code	composedOf	intent
				composedOf	indication to start
				composedOf	record datetime

Proposal A is "slim" and requires fewer changes of the current SPHN schema as compared to Proposal B or C. When used correctly, quantities of a drug in the context of Drug Prescription and Drug Administration Event can be described by Proposal A.

#### 4.1.2 Proposal B

	Type		Type		Type
concept	Drug	concept	Drug Administration Event	concept	Drug Prescription
composedOf	article	composedOf	drug	composedOf	drug
composedOf	quantity	composedOf	time pattern	composedOf	time pattern
composedOf	active ingredient	composedOf	drug-quantity	composedOf	drug-quantity
composedOf	inactive ingredient	composedOf	duration	composedOf	frequency
		composedOf	start datetime	composedOf	first administration datetime
		composedOf	end datetime	composedOf	last administration datetime
		composedOf	administration route code	composedOf	administration route code
		composedOf	reason to stop code	composedOf	intent
				composedOf	indication to start
				composedOf	record datetime
concept	Drug Article				
inherited	code				
inherited	name				
inherited	manufacturer				
composedOf	active ingredient				
composedOf	inactive ingredient				
composedOf	manufactured dose form				

Proposal B introduces the new concept 'Drug Article' which combines several composedOfs of the 'Drug'-concept which apply to a specific article rather than the drug in general in a separate concept. In addition to the advantages of Proposal A, Proposal B offers a clear solution where to provide amounts of active and inactive ingredients for a single unit of the drug ("drug strength"), e.g., one tablet or one milliliter of a liquid drug. The lack of possibility to reflect this information in the RDF schema has been the cause for ongoing discussions revolving around 'Drug' and 'Drug'-related concepts.

### 4.1.3 Proposal C

		Type			Type			Type
concept	Drug		concept	Drug Administration Event		concept	Drug Prescription	
composedOf	article	Drug Article	composedOf	drug	Drug	composedOf	drug	Drug
composedOf	quantity	Quantity	composedOf	time pattern	Time Pattern	composedOf	time pattern	Time Pattern
composedOf	active ingredient	Substance	composedOf	drug-quantity	Quantity	composedOf	drug-quantity	Quantity
composedOf	inactive ingredient	Substance	composedOf	duration	Quantity	composedOf	frequency	Quantity
			composedOf	start datetime	temporal	composedOf	first administration datetime	temporal
		Type	composedOf	end datetime	temporal	composedOf	last administration datetime	temporal
concept	Drug Article		composedOf	administration route code	Code	composedOf	administration route code	temporal
inherited	code	Code [restricted to: GTIN]	composedOf	reason to stop code	Code	composedOf	intent	Intent
inherited	name	string				composedOf	indication to start	Diagnosis
composedOf	manufactured dose form	Pharmaceutical Dose Form				composedOf	record datetime	temporal

Proposal C offers the same advantages as Proposal A. Like Proposal B, Proposal C introduces the concept 'Drug Article', however, with a more limited scope. The variant of 'Drug Article' of Proposal C is therefore less prone to being overloaded.

Once a solution is available for representing drug properties in a terminology, it can readily be connected to Proposal C. This would apply for example if an agreement with HCI solutions could be reached on providing the HCI Compendium to university hospitals in a suitable format.

## 4.2 Disadvantages

The changes and their implications need to be communicated very clearly for all proposals to avoid delivery of wrong or low-quality data (see Discussion).

### 4.2.1 Proposal A

Proposal A does not resolve the confusion around the question of how to provide amounts of active and inactive ingredients for a single unit of the drug, e.g., one tablet or one milliliter of a liquid drug.

### 4.2.2 Proposal B

The concept 'Drug Article' offers useful information but may easily be overloaded: In principle, the codes for article or product already specify name, manufacturer, active ingredients, inactive ingredients, and manufactured dose form, yet this information can be entered separately as well. This is beneficial for drugs without article code, but could possibly lead to inconsistencies for drugs with article codes if data is not curated well.

The composedOf 'manufacturer' is of type string because a suitable standard is missing. This impedes interoperability and would require additional coordination efforts between data providers. Unique identifiers (UIDs) from the [UID register](#) are only used in Switzerland, and international standards like the "Data Universal Numbering System" ([DUNS](#)) are not available as a terminology.

### 4.2.3 Proposal C

Like Proposal A, Proposal C does not offer a solution on how to provide amounts of active and inactive ingredients for a single unit of the drug. The 'Drug Article' concept of Proposal C is less exhaustive compared to the variant of Proposal B which comes as a price for the reduced risk of overloading the concept.

## 5 Impact on SPHN Dataset

Addition of a composedOf of Type 'Quantity' to the 'Drug' concept renders the composedOf 'drug quantity' of the concepts 'Drug Administration Event' and 'Drug Prescription' obsolete (release 2023.2). Hence, they should be removed.

## 6 Discussion

The change requests for 'Drug Administration Event' and 'Drug Prescription' as well as the proposals A and B for 'Drug' and 'Drug Article' have been discussed during the Semantic Working Group meeting on 30.08.2023. The proposals for 'Drug Administration Event' and 'Drug Prescription' will be included in release 2024.1 of the SPHN schema.

For 'Drug' and 'Drug Article', a preference for Proposal B materialized because of its clarity and ability to provide useful meta-information, in spite of the additional complexity when compared to Proposal A. Due to the risk of overloading the concept 'Drug Article' of Proposal B and potential issues with reusing drug master data from the HCI Compendium, however, a third proposal (Proposal C) has been launched with a variant of 'Drug Article' with reduced scope.

Proposal C of 'Drug' and 'Drug Article' will be included in release 2024.1 of the SPHN schema. They can be extended as needed in future releases (for example, addressing points raised in section [Limitations](#)) and can readily be linked to a potential drug terminology once it becomes available (negotiations with HCI Solutions ongoing).

### 6.1 Definitions

To explain the correct use of 'quantity' in the context of Drug and Drug-related concepts, it is helpful to recall the definition laid out in the SPHN dataset:

- **Drug Prescription:** *"plan that defines at which frequency a drug should be administered to a patient with a given quantity; **at every frequency time point a drug administration event should occur**"*
- **Drug Administration Event:** *"single event at which a drug was administered to the patient; this could be a single time point in case of a pill/cream or a duration in case of a single infusion pack or a single patch; **one or many drug administration events are initiated by a drug prescription** depending on the frequency stated in the prescription"*

### 6.2 Quantity

Following the definitions above, the composedOf 'quantity' of the Drug concept represents different aspects in the context of Drug Prescription and Drug Administration Event:

- **Drug Prescription:** 'quantity' of the Drug represents the quantity intended to be administered during a single Drug Administration Event launched by the Drug Prescription, e.g. "2 tablets" if "2 tablets 3 times per day" are prescribed: "2 tablets" is covered by quantity of the Drug, "3 times a day" by the frequency of the Drug Prescription.
- **Drug Administration Event:**

The 'quantity'-attribute of the Drug represents the total quantity of a drug administered during a single Drug Administration Event, e.g., 2 tablets between start and end datetime, or 500 ml during the duration.

**Note:** The 'quantity'-attributes of the active and inactive ingredients of Drug represent the total amount of the specific ingredient administered during the Drug Administration Event.

## 6.3 Total quantities

### 6.3.1 Drug amount

Total quantities of Drug over a specific period can (and need to) be calculated, either including all Drug Administration Events during the time period of interest, or spanning the time between first and last administration datetime for Drug Prescription.

The total amount of drug **administered over a period of time** involving multiple identical Drug Administration Event is calculated as follows:

$$total\ amount_{drug\ administered} = quantity_{Drug} \times number\ of\ Drug\ Administration\ Events\ during\ period\ of\ interest$$

For a **single Drug Administration Event** this therefore simplifies to:

$$total\ amount_{drug\ administered} = quantity_{Drug} \times 1 = quantity_{Drug}$$

The total amount of drug **prescribed over a period of time** is calculated as follows (assuming full days for the administration datetimes):

$$total\ amount_{drug\ prescribed} = quantity_{Drug} \times frequency_{Drug\ Prescription} \times (last\ administration\ datetime - first\ administration\ datetime + 1)_{Drug\ Prescription}$$

### 6.3.2 (Active) Ingredients

In the context of Drug Administration Events, not only the amount of drug but also the total amount of active ingredients(s) is of particular interest. For a single Drug Administration Event it is calculated as follows:

$$total\ amount_{active\ ingredient\ administered} = \frac{amount\ active\ ingredient}{dosage\ form} \times quantity_{Drug}$$

**This total amount is to be stored under the 'quantity' of the active ingredient of the Drug** as attributes are context-dependent and describe the instance of the concept they refer to.

Notably, for Proposal A and C **this amount needs to be delivered pre-calculated by the data provider** as the RDF schema (release 2023.2) holds no place to store the amount of active ingredient per dosage form (e.g., amount of active ingredient per 1 tablet or 1 ml).

Proposal B would offer an opportunity and allow a better transparency on how amounts of active ingredients are derived, albeit with its own limitations (see [6.5 Limitations](#)).

The total amount of active ingredient for multiple identical Drug Administration Events over a specific period is often of particular clinical interest, e.g., in cancer therapy, and calculated as follows:

$$\text{total amount}_{\text{active ingredient administered}} = \frac{\text{amount active ingredient}}{\text{dosage form}} \times \text{quantity}_{\text{Drug}} \times \text{number of Drug Administration Events during period of interest}$$

## 6.4 Drug metainformation (“Drug Article”)

Initially, the name ‘Drug Properties’ was considered for ‘Drug Article’. As the concept references a specific article due to the lack of a system for unambiguous product codes, however, the name “Drug Article” was chosen instead.

Notably, the introduction of the drug metainformation in the concept ‘Drug Article’ of Proposal B makes the composedOfs ‘active ingredient’ and ‘inactive ingredient’ of ‘Drug’ in principle redundant. While they offer a slot for the total amount per substance in the context the drug is used, these quantities could be computed using the quantity-attribute of ‘Drug’ (=the drug amount) and the quantity attributes of the ingredient-attributes of ‘Drug Article’ representing the drug strength.

Different extents of metainformation provided each have their own advantages and disadvantages (see [4. Pros and cons](#)).

## 6.5 Limitations

The current proposals, in particular proposal B, resolves several issues of the current Drug and Drug-related SPHN concepts (release 2023.2).

Some remaining issues, however, have been identified and should be addressed in one of the next releases of the SPHN schema. These limitations were in part touched on during meeting of the Semantic Working Group (30.08.2023) and discussed in more detail during a meeting of a subgroup (14.09.2023; Ramirez Ramos Amanda, Harald Witte, external data expert Josip Matic (USZ)).

- Non-standard units of drugs cannot be represented properly, e.g., drops, sachets, ampoules etc. One option would be to extend the allowed codes in the current Unit-concept by children of SNOMED CT-code 408102007 (Unit dose (qualifier value)) which holds such non-standard units. Alternatively, a concept ‘Drug Dosage Unit’ allowing unit doses in addition to UCUM units could be created and then be used by a hypothetical concept ‘Drug Amount’ (akin to ‘Quantity, with an extended unit-range).
- Non-standard units like “drop” need to be represented in SI-units for full transparency, e.g., 1 drop = 0.036 ml.  
Example: GANFORT Gtt Opht (eye-drops for glaucoma treatment; GTIN #7680576300013 or 7680576300037).

This information is available in the HCI compendium (which needs to be licensed) or directly from the drug manufacturer but it cannot be represented in the current SPHN schema. This undermines efforts to provide all elements for the calculation of amounts of active ingredients for a specific dose. The representation of such a drug dosage equivalence involves a calculation which is out of scope of the current SPHN concepts.

- For some drugs the reference amount is not a single unit.  
Example: SPRAVATO Nasenspray 28 mg (antidepressant nasal spray; GTIN # 7680671030013, 7680671030020, or 7680671030037) where a dose of 28 mg Esketamin is contained in 2 puffs (presumably one puff per nostril intended). Such a reference amount could be represented in an extended 'Drug Article'-concept in the future.

Some drugs are not applied as is but need to be pre-processed, for example, dissolved.

Example: Fibrogammin 1'250 I.E. (GTIN # 7680006710061) containing 1'250 I.U. dried coagulation factor XIII (human) is to be dissolved in 20 ml water for injection or infusion. Without this reference amount information, the information that a specific volume was administered is not informative.

In this particular case, dissolving the drug represents a processing step which cannot be represented using the current SPHN concepts.

- Some drugs need to be diluted before use to reach a recommended concentration. This involves both a processing step and a calculation which again is out of scope of the current SPHN concepts.  
Example: of LAVASEPT Konz (GTIN # 7680504450704; containing 200 mg/ml Polihexanidum) which is recommended to be diluted to a final concentration of 0.2 to 0.4 mg/ml Polihexanidum.

## 6.6 Removal of meaning bindings of composedOfs

As of release 2024.1, the use of meaning bindings for composedOfs is discouraged. Meaning bindings have been removed from composedOfs of Drug Prescription and/or Drug Administration Event according to Table 1.

**Table 1: Removal of meaning bindings in release 2024.1**

composedOf	previous meaning binding (removed for release 2024.1)	concept affected
first administration datetime	SNOMED CT: 413946009  Date treatment started (observable entity)	Drug Prescription
last administration datetime	SNOMED CT: 413947000  Date treatment stopped (observable entity)	Drug Prescription
administration route code	SNOMED CT: 284009009  Route of administration value (qualifier value) ; LOINC: 74050-6 Actual route of administration - attempted or completed [AHRQ]	Drug Administration Event Drug Prescription

## 7 Example

### 7.1 Proposal A

**Example:** Two tablets of ALGIFOR Dolo Duo Filmtabl 150 mg/500 mg (GTIN #7680677370014), each tablet containing 500 mg Paracetamol and 150 mg Ibuprofen

#### Drug

article code:

identifier: 7680677370014

name: ALGIFOR Dolo Duo Filmtabl 150 mg/500 mg

coding system and version: GTIN

active ingredient:

substance:

code: 387517004 |Paracetamol (substance)|

generic name: -

quantity:

value: 1000

unit: mg

comparator: -

active ingredient:

substance:

code: 387207008 |Ibuprofen (substance)|

generic name: -

quantity:

value: 300

unit: mg

comparator: -

inactive ingredient:

substance:

code: 229936000 |Cornflour (substance)|

generic name: -

quantity:

value: -

unit: -

comparator: -

inactive ingredient:

substance:

code:

identifier: -

name: -

coding system and version: -

generic name: Lactose-1-Wasser

quantity:

value: 3.81

unit: mg

comparator: -

manufactured dose form:

code: 421026006 |Conventional release oral tablet (dose form)|



quantity:

value: 2

unit: {#} [ {#} represents "number"]

comparator: -

## 7.2 Proposal B

**Example:** Two tablets of ALGIFOR Dolo Duo Filmtabl 150 mg/500 mg (GTIN #7680677370014), each tablet containing 500 mg Paracetamol and 150 mg Ibuprofen

### Drug

active ingredient:

code: 387517004 |Paracetamol (substance)|

generic name: -

quantity:

value: 1'000

unit: mg

active ingredient:

code: 387207008 |Ibuprofen (substance)|

generic name: -

quantity:

value: 300

unit: mg

inactive ingredient:

code: 229936000 |Cornflour (substance)|

quantity:

value: 2

unit: {#}

### drug article

article code:

identifier: 7680677370014

name: ALGIFOR Dolo Duo Filmtabl 150 mg/500 mg

coding system and version: GTIN

name: ALGIFOR Dolo Duo Filmtabl 150 mg/500 mg (or use name without dosage?)

manufacturer: VERFORA SA

active ingredient:

code: 387517004 |Paracetamol (substance)|

generic name: -

quantity:

value: 500

unit: mg

active ingredient:

code: 387207008 |Ibuprofen (substance)|

generic name: -

quantity:

value: 150  
unit: mg  
inactive ingredient:  
code: 229936000 |Cornflour (substance)|  
manufactured dose form:  
code: 1163573008 |Conventional release film-coated oral tablet (dose form)|

### 7.3 Proposal C

**Example:** Two tablets of ALGIFOR Dolo Duo Filmtabl 150 mg/500 mg (GTIN #7680677370014), each tablet containing 500 mg Paracetamol and 150 mg Ibuprofen

#### Drug

active ingredient:  
code: 387517004 |Paracetamol (substance)|  
generic name: -  
quantity:  
value: 1'000  
unit: mg

active ingredient:  
code: 387207008 |Ibuprofen (substance)|  
generic name: -  
quantity:  
value: 300  
unit: mg

inactive ingredient:  
code: 229936000 |Cornflour (substance)|  
quantity:  
value: 2  
unit: {#}

#### drug article

article code:  
identifier: 7680677370014  
name: ALGIFOR Dolo Duo Filmtabl 150 mg/500 mg  
coding system and version: GTIN  
name: ALGIFOR Dolo Duo Filmtabl 150 mg/500 mg  
manufactured dose form:  
code: 1163573008 |Conventional release film-coated oral tablet (dose form)|