



# GInAS/GSRS meeting November 16th, 2018

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COLLEGE TER  
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# IDMP and how we can support the health care domain



# Outline of the Presentation

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**Ing. Ciska Matai,**  
**presenter**  
CBG-MEB  
Quality Department,  
Substance & Medicinal  
Product Registration  
System



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**presenter**  
CBG-MEB  
Operational Management  
Department,  
Scientific lead EU-  
Substance Registration  
System

- The GInAS project, started in 2013
- IDMP Suite; Set of 5 standards and 4 Technical Specifications finalised with the ISO Award 2018 on the 30th Plenary Meeting, October 2018, Paestum Italy.  
Scope of IDMP Substance Standard and Implementation Guide, which is key for unique Substance identification and good Substance management
- Work in process on the future development of the ISO 11238 Substance Standard and ISO/TS 19844 Implementation Guide; Examples
- GSRS software and Europe

**IDentification of Medicinal Products (IDMP) is a set of five ISO Standards and Technical specifications that enable the transition to structured product information**

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- Introduction through legislation, regulators, but also for internal purposes
  - Provides structured medicinal, pharmaceutical product and substance data models
  - Provides mechanisms to uniquely identify products and its components
  - It is the only global standard for product information

ISO 11615 – Medicinal product information

ISO 11616 – Pharmaceutical product information

ISO 11238 – Information on Substances

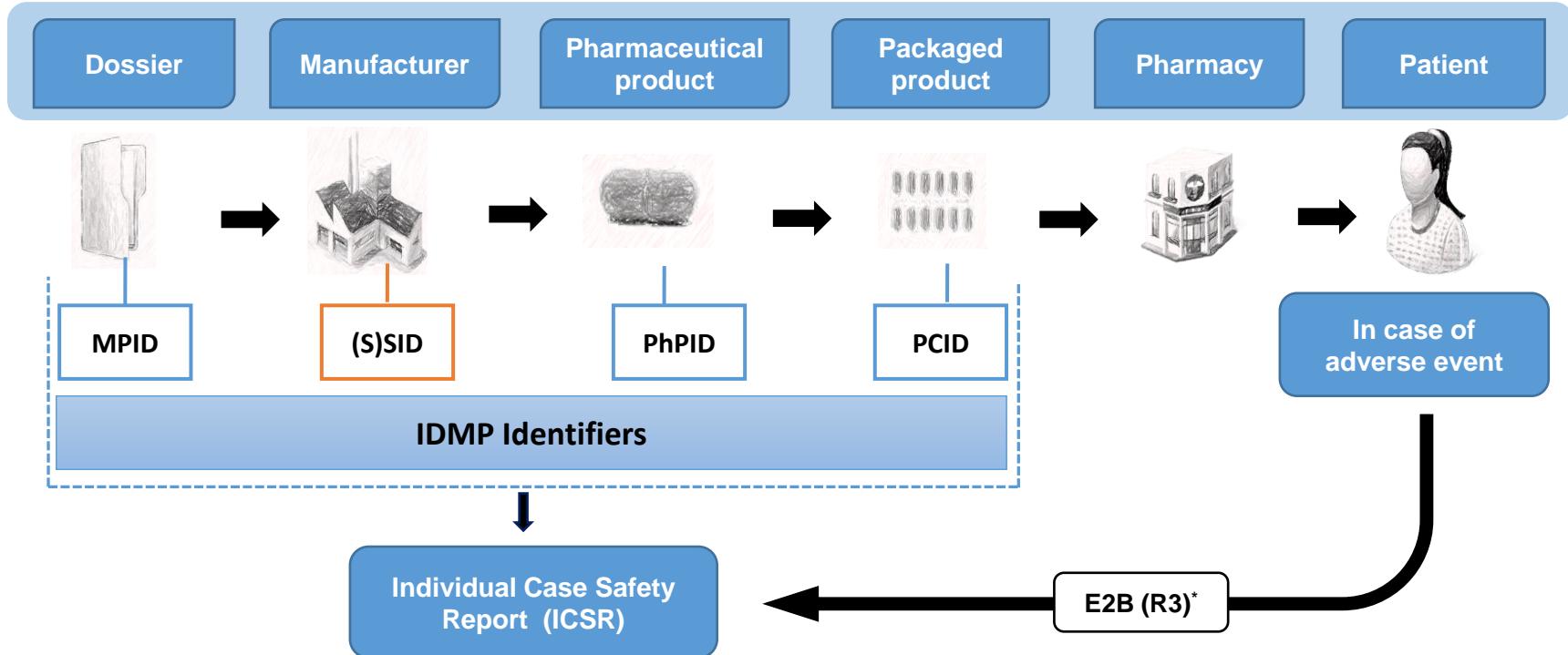
## **ISO 11239 – Information on pharmaceutical dose form, units of measure, routes of administration & packaging**

ISO 11240 – Units of measurement



# IDMP introduces identification numbers that enable communication

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Good substance management depends on adequate substance and specified substance identifiers (S)SID

*\*Example of a use case of IDMP\**

INTERNATIONAL  
STANDARDISO  
11238Second edition  
2018-07

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Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated information on substances

Informatique de santé — Identification des produits médicaux —  
Eléments de données et structures pour l'identification unique et  
l'échange d'informations réglementées sur les substances

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## Scope

This document provides an information model to define and **identify substances within medicinal products or substances used for medicinal purposes**, including dietary supplements, foods and cosmetics.

**The information model can be used in the human and veterinary domain since the principles are transferrable.**

Other standards and external terminological resources are referenced that are applicable to this document.



## Scope

This document provides detailed explanations of each type or grouping of substance information, an element-by-element description for implementation of ISO 11238, and many examples for a variety of Substances and Specified Substances.

The third edition of the document addresses Substances Groups 1 to 3 of the Specified Substances as defined in ISO 11238 and Annexes A, B, C, D, E, F, G, H, I, J and K.

It is anticipated that Specified Substances Group 4, as defined in ISO 11238, will be addressed in a subsequent edition of this document.

Some information that would typically fall under Specified

Substances Group 4 is covered in the Annexes of this document. This information, although not exclusively defining of either a Substance or a Specified Substance Group 1, might be essential to distinguishing substances. This document addresses the following:

- data elements necessary for defining Substances and Specified Substances Groups 1 to 3;
- the logical use of data elements as defined in ISO 11238;
- Substances and Specified Substances Groups 1 to 3 business rules for:
  - determining necessary data elements,
  - distinguishing and defining materials according to ISO 11238,
  - triggering the assignment of identifiers.

TECHNICAL  
SPECIFICATION

ISO/TS  
19844

Third edition  
2018-07

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Health informatics — Identification of medicinal products (IDMP) — Implementation guidelines for ISO 11238 for data elements and structures for the unique identification and exchange of regulated information on substances

*Informatic de santé — Identification des médicaments — Lignes directrices pour la mise en œuvre de l'ISO 11238 relative aux éléments de données et structures pour l'identification unique et l'échange d'informations réglementées sur les substances*



f.l.t.r: Christian Hay (ISO/TC 215, WG6 Convenor )-Michael Glickman(ISO/TC 215, Chair)-Panagiotis Telonis (EMA)-Herman Diederik (CBG-MEB)-Larry Callahan (FDA)-Christof Gessner (Gematik.de)-Tim Buxton (EMA)-Sabine Brosch (EMA)-Paolo Alcini (EMA)-Diana Warner (ISO/TC 215, Secretary)- Shirin Golyardi (NEN/Secretary ISO/TC 215, WG6)-Frits Elferink (KNMP, ISO/TC 215 WG6 Co-Convenor).

Awardees not shown:

Ilaria Del Seppia (EMA)- Vada Perkins (FDA)-Andrew Marr (BSI)- Chris Jarvis (EDQM).



# Why that level of detail of substances is necessary as provided in the Standard and Technical specification?

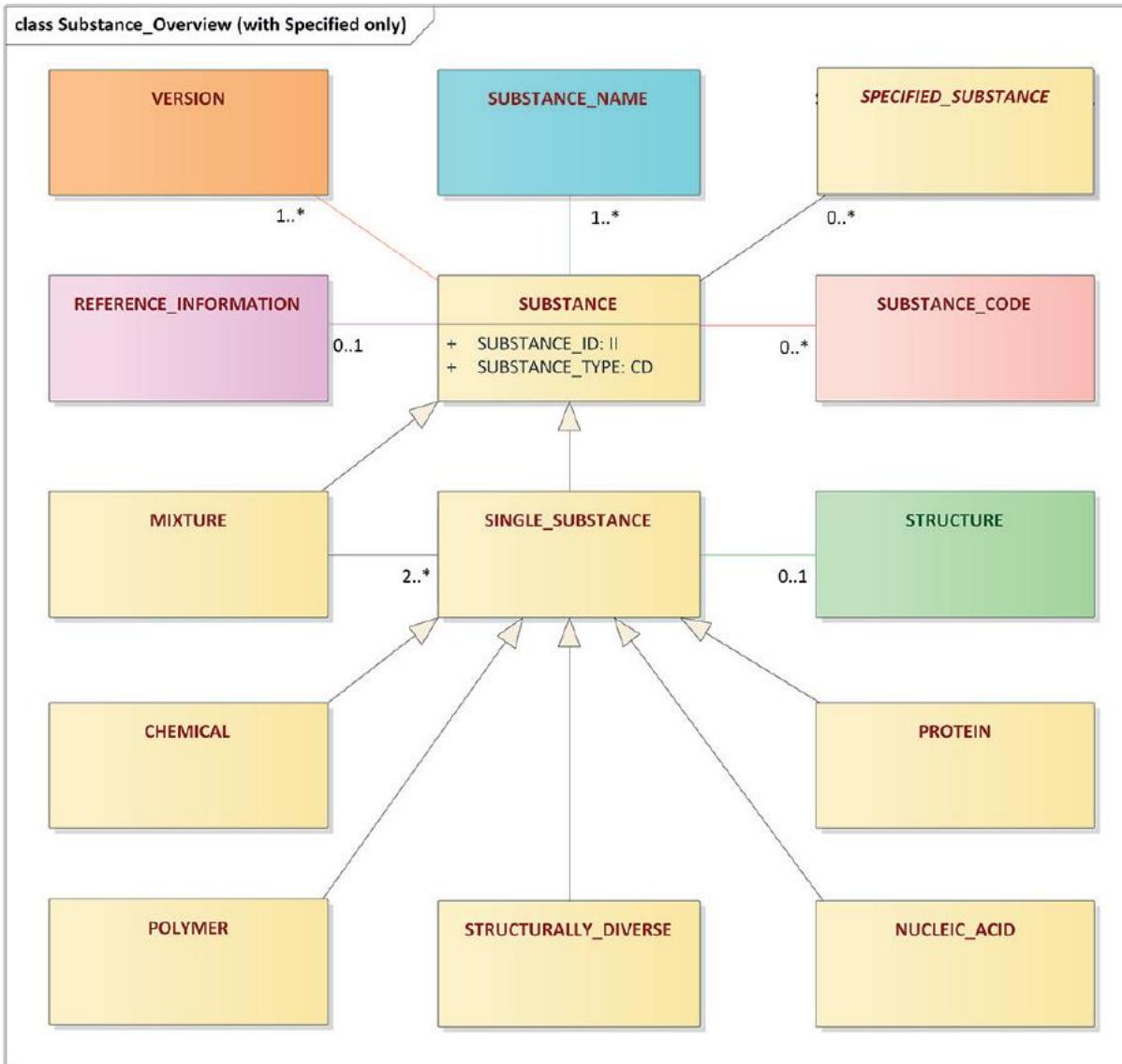
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- Unambiguously characterized substances according to **ISO11238 and ISO/TS 19844**
- Unique substance ID's and Specified Substance ID's to be used in several use cases and regulatory processes
- References, properties, methods and specifications in Regulatory documentation should be adequately covered in a structured way;
  - which implies sufficient detailed structured registration
  - by use of sufficient detailed data model attributes



# High-level information model of substances

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TS 19844 Single substance types

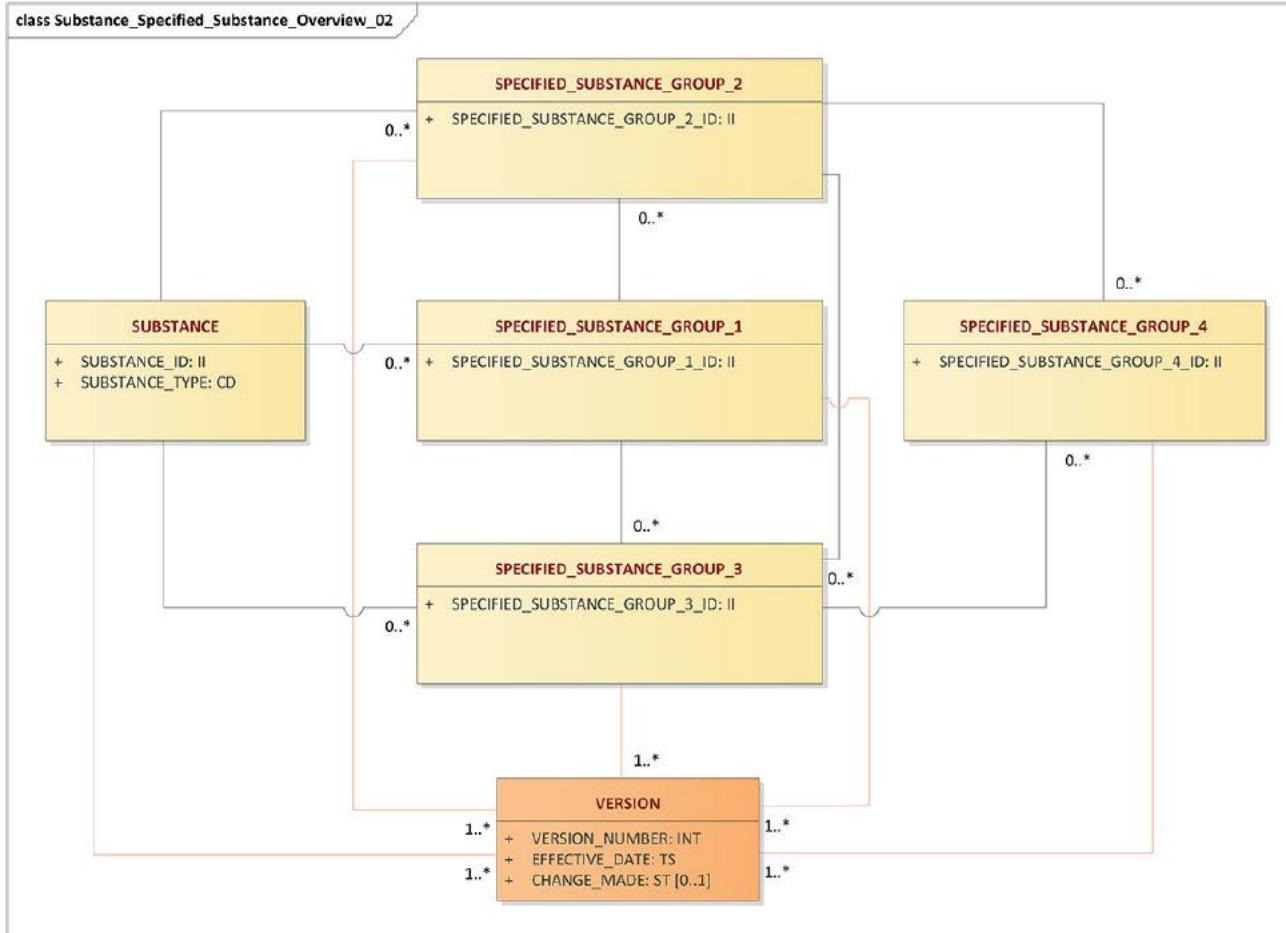
Annex:

- B) Chemical;
- C) Protein;
- D) Nucleic Acid;
- H) Polymer
- E) Structurally Diverse Substance, Herbal;
- F) Structurally Diverse Substance, Homeopathic;
- G) Structurally Diverse Substance, Plasma-derived;
- I) Structurally Diverse, Vaccines;
- J) Structurally Diverse, Allergen and
- K) Structurally Diverse, Advanced Therapies and Advanced Vaccines (Genes, Modified Viruses, Cells and Tissues as Substances)



# High-level Substance - Specified Substance Relationship

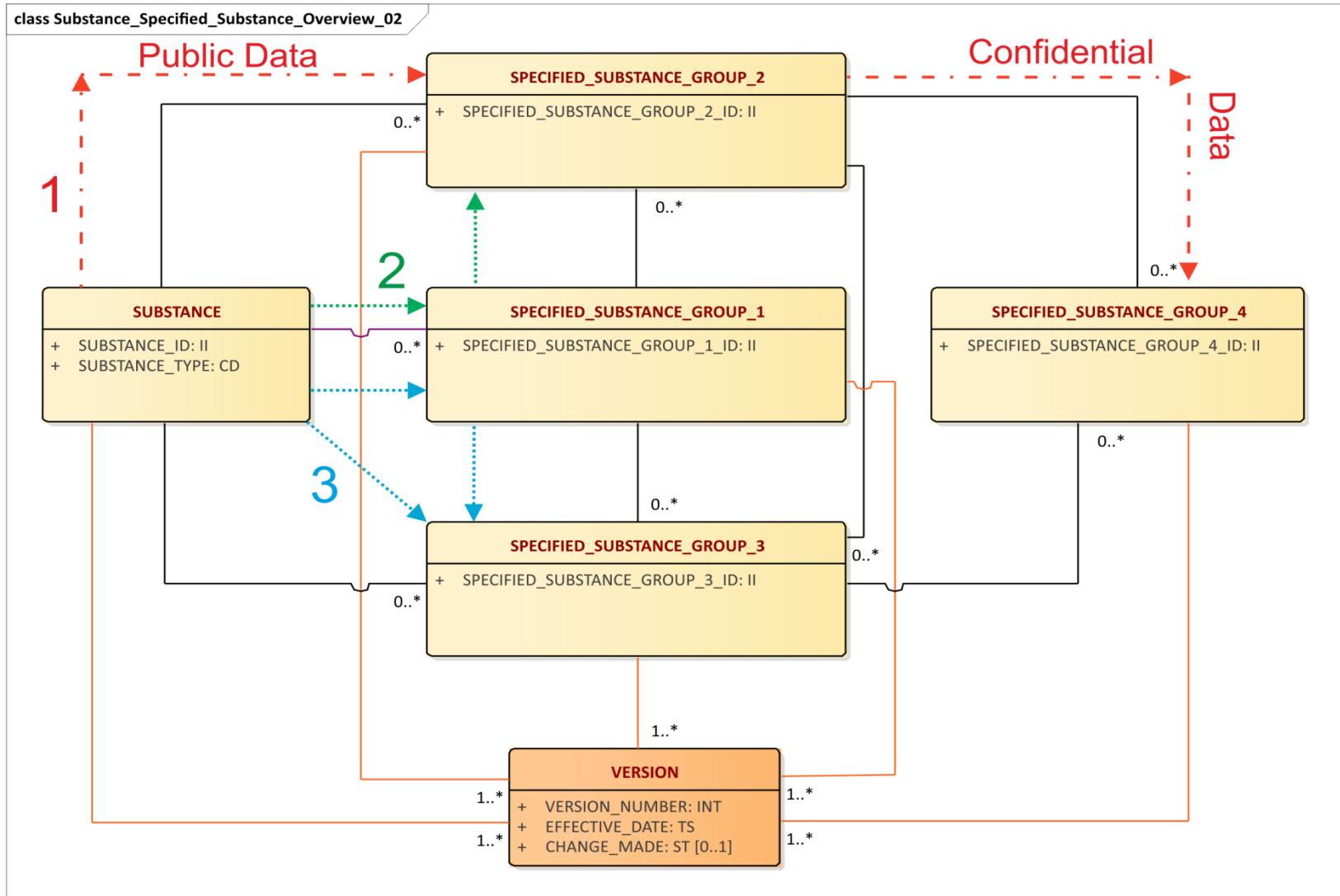
$$\frac{c \ B \ G}{M \ E^B}$$





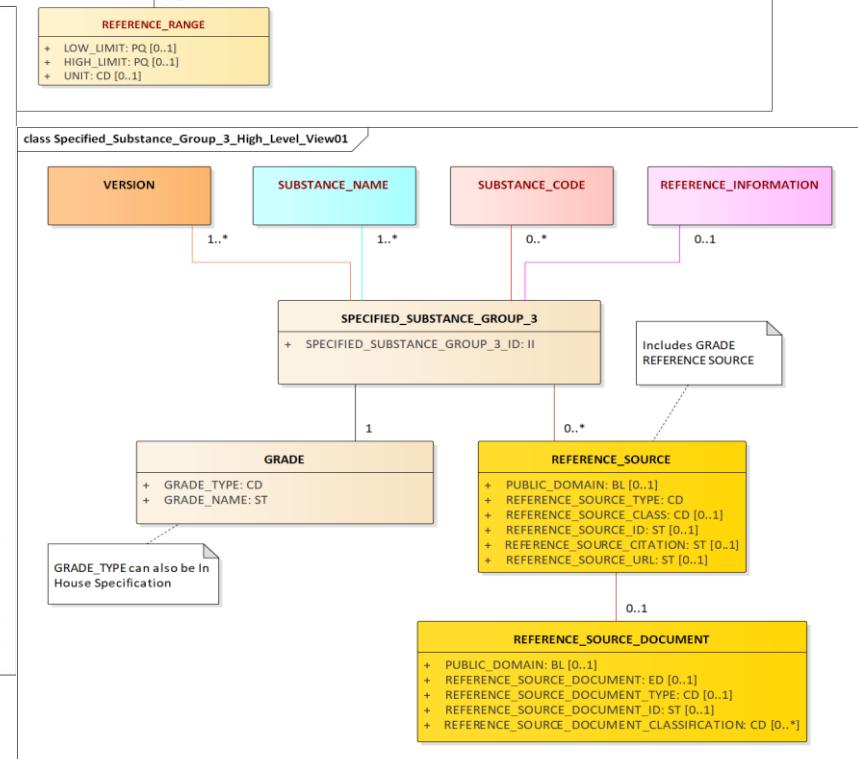
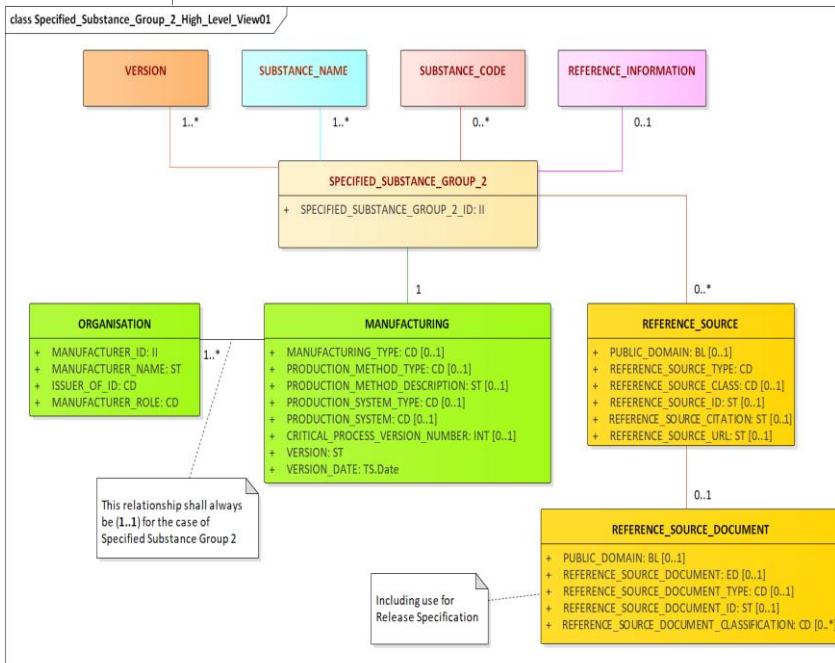
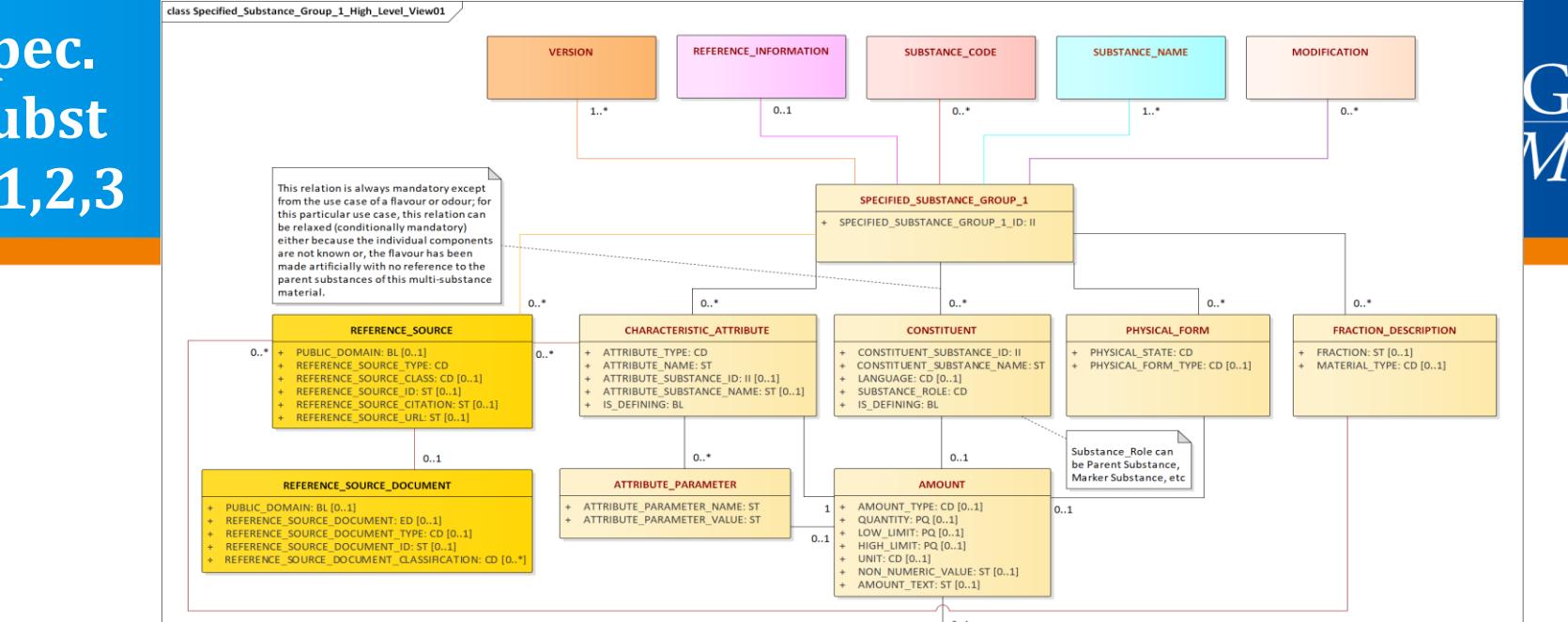
# High-level Substance – Specified Substance (2) MAIN ROUTES

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# Spec. Subst G1,2,3

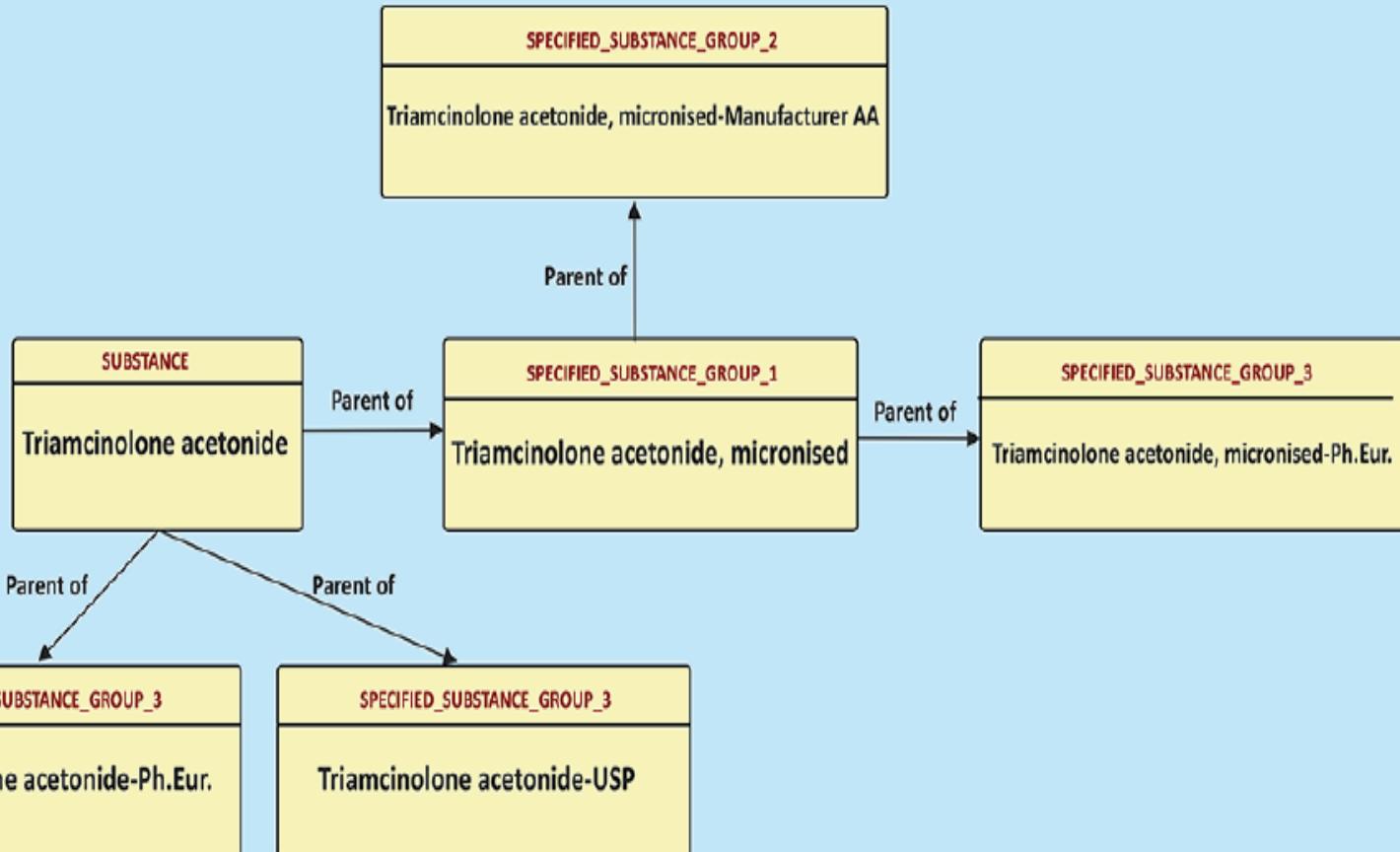
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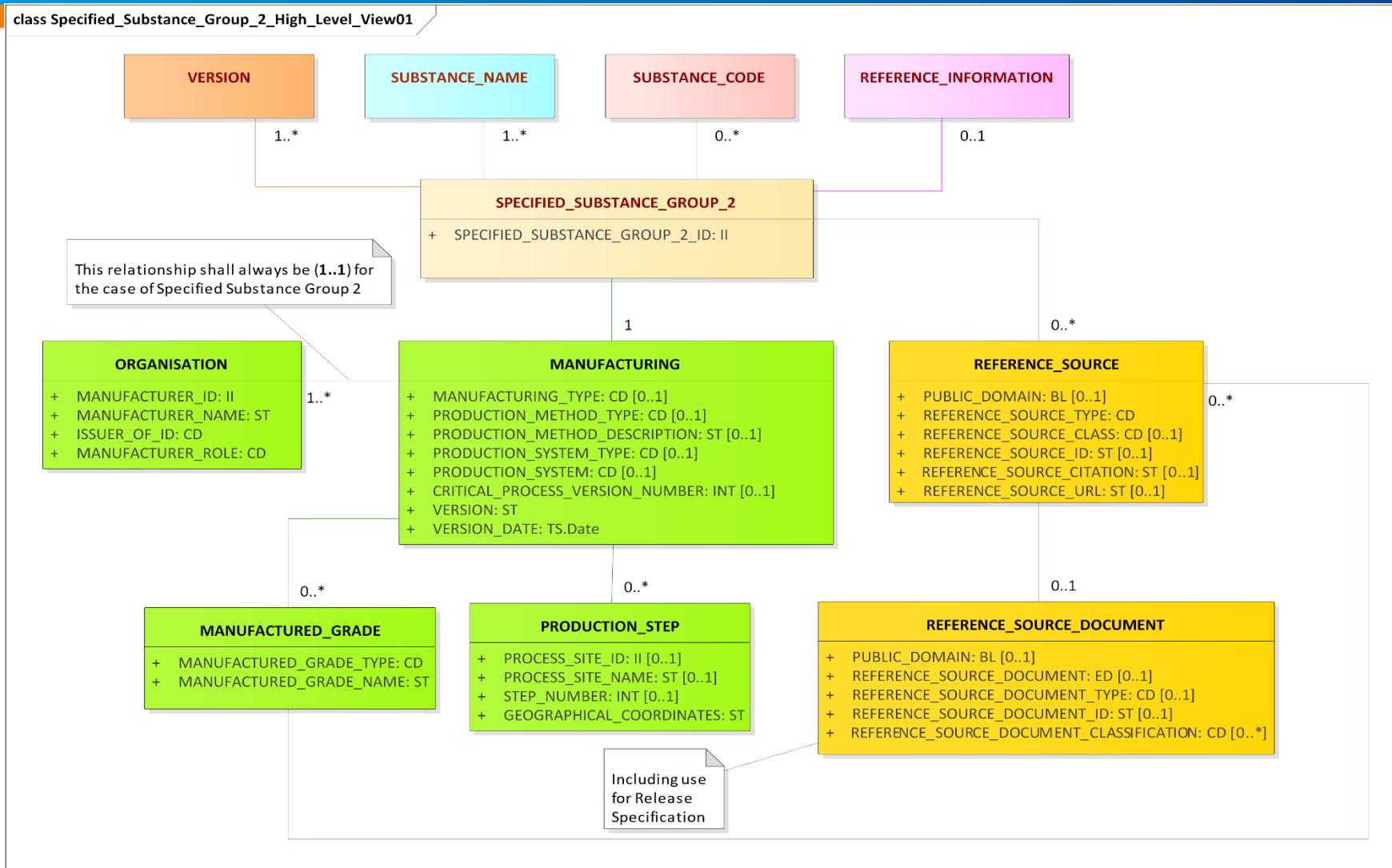
# Substance and Specified Substance Groups 'Parent' relationships of Triamcinolone acetonide

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# Update Specified Substance Group 2 proposed High-level Information

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# Proposed

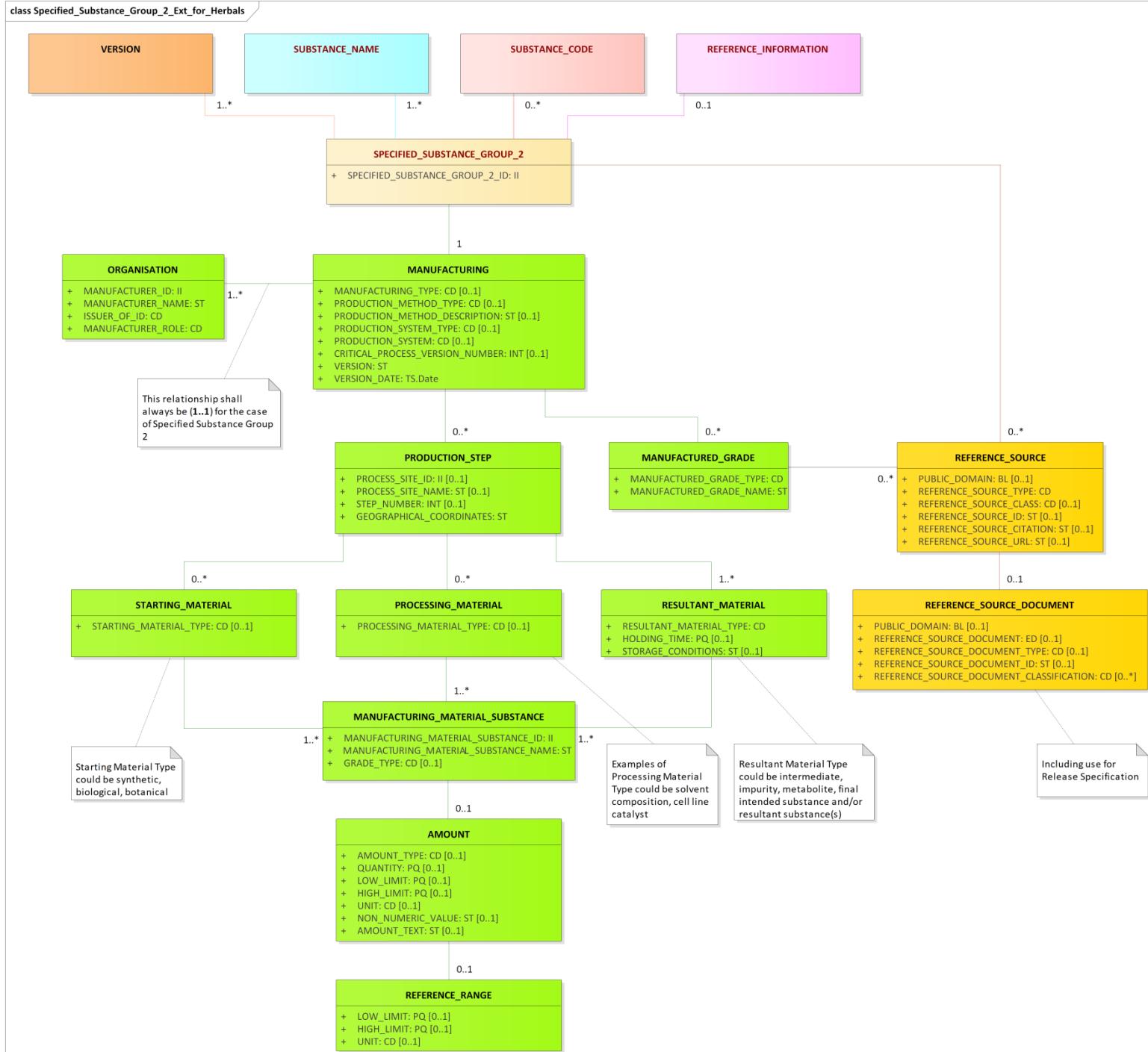
## Update

### Specified Substance

### Group 2

### Extended

### Information



# Herbal Substance information of *Salvia miltiorrhiza*, Rhizome and Root

**Herbal Substance:** [Nomenclature based on the CFDA (China Food and Drug Administration)]

**Scientific Name:** *Salvia miltiorrhiza* Bunge; Family: Labiatae (Lamiaceae)

**Parts of the plant:** Dried, fragmented root and rhizome, cut pieces NMT 5 cm.

**Supplier of Herbal Substance:** e.g. Tasly Plant Pharmaceutical, Shaanxi province, China

**Harvest time, Cultivated plants:** In the autumn of the next year after seeding when the aerial parts of the plants are wilting (Shaanxi province of China). The harvested material is dried at 50°C – 60°C as soon as possible after harvesting (loss on drying ≤13%) and stored in closed PP bags under low relative humidity conditions.

**Marker Substance for specification:**

- Salvianolic acid B (Mol. Form.: C<sub>36</sub>H<sub>30</sub>O<sub>16</sub>; Mol. Weight: 718,6 Da); NLT 3,0 %
- Tanshinone IIA (Mol. Form.: C<sub>19</sub>H<sub>18</sub>O<sub>3</sub>; Mol. Weight: 294,3 Da) ; NLT 0,12 %

**Analytical marker:** Rosmarinic acid (Mol. Form.: C<sub>18</sub>H<sub>16</sub>O<sub>8</sub>; Mol. Weight: 360,3 Da);

BP-spec.:NLT 0,17 %



Rosmarinic acid

**CAS Registry Name:**

Benzene propanoic acid, .alpha.-[[[(2E)-3-(3,4-dihydroxyphenyl)-1-oxo-2-propen-1-yl]oxy]-3,4-dihydroxy-, (.alpha.R)-  
CAS No.: 20283-92-5



*Salvia miltiorrhiza*, also known as red sage, tan shen, or danshen, is a perennial plant of the genus *Salvia*, highly valued for its roots in traditional Chinese medicine.

Native to China and Japan, it grows at 90 to 1,200 m (300 to 3,900 ft) elevation, preferring grassy places in forests, hillsides, and along stream banks.

Sample of the Root and Rhizoma. Cylindrical, slightly curved segments, 5 cm long. The external surface is reddish brown, rough with longitudinal striations.



## SALVIA MILTIORRHIZA ROOT AND RHIZOME

Salviae miltiorrhizae radix et rhizoma

### DEFINITION

Dried, whole or fragmented rhizome and root of *Salvia miltiorrhiza* Bunge, collected in spring or autumn.

### Content:

- salvianolic acid B (C<sub>36</sub>H<sub>30</sub>O<sub>16</sub>; M<sub>r</sub> 719): minimum 3.0 per cent (dried drug);
- tanshinone II<sub>A</sub> (C<sub>19</sub>H<sub>18</sub>O<sub>3</sub>; M<sub>r</sub> 294.3): minimum 0.12 per cent (dried drug). EP monograph no.: 2663

# Formulation of a Traditional Herbal Medicinal Product, e.g. Danshen Capsule (Cont. *Salvia miltiorrhiza* Radix Extract)

## Herbal Preparation:

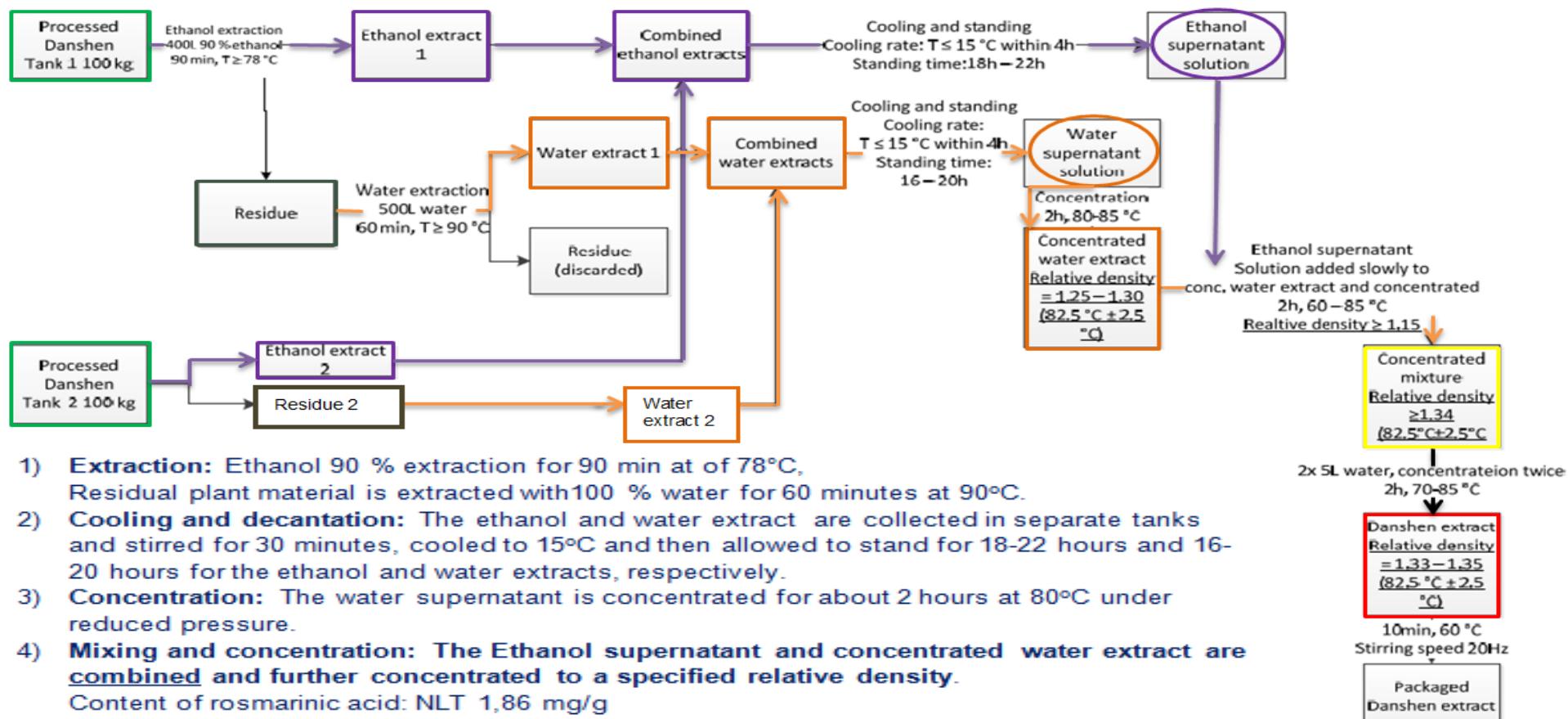
**Extract:** Danshen extract is a brown to dark brown soft (semi-solid) extract, made through the process of extraction and concentration (4,5 – 6 = 1).

**Name:** *Salvia miltiorrhiza* root and rhizome Ethanolic (90 pCt.)-water liquid extract (4,5 – 6 = 1).

**DER:** 4,5 – 6 Parts Herbal Substance = 1,0 Part Extract;

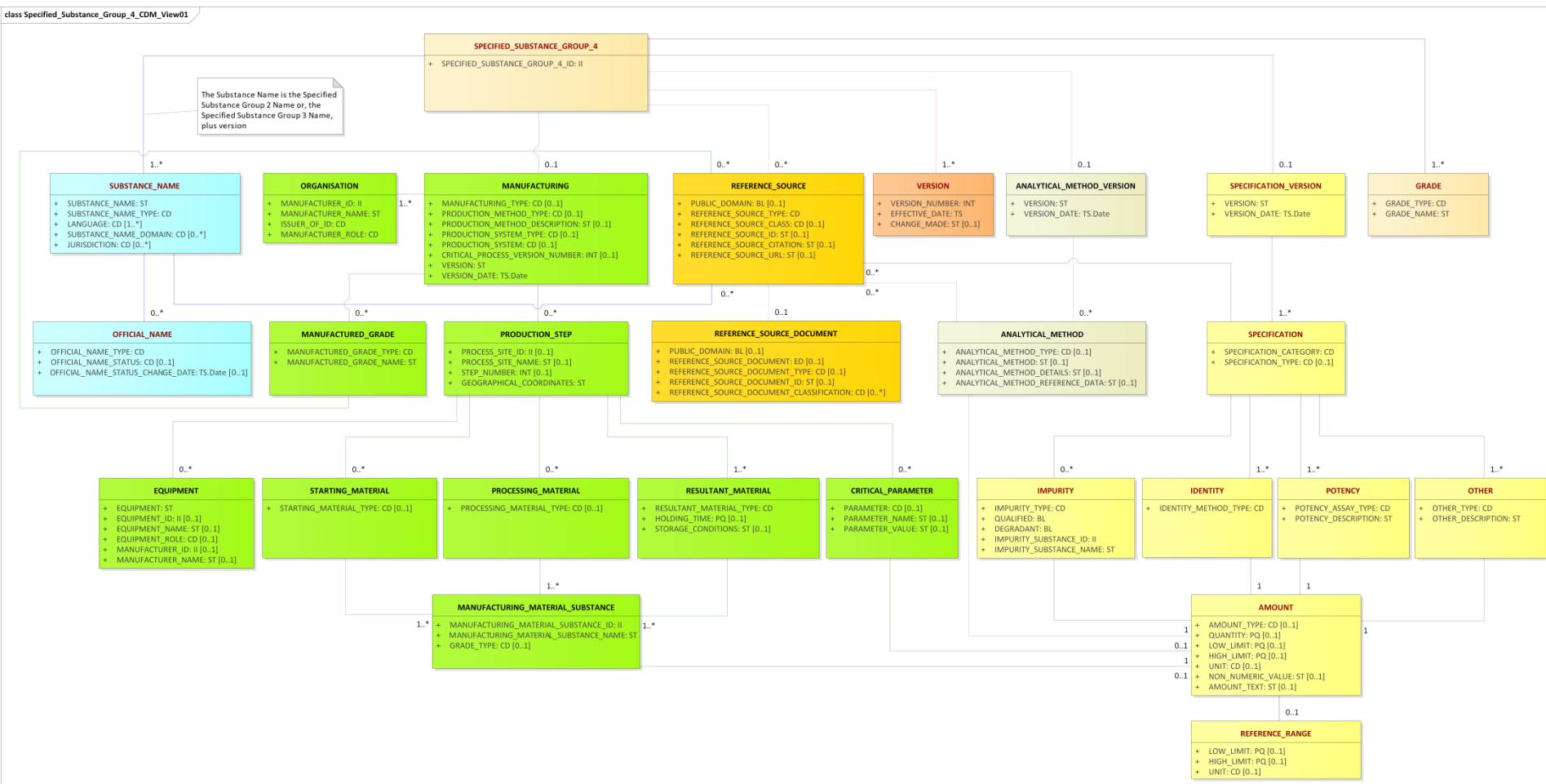
**Extraction solvent:** Ethanol (90) – Water (10) = Ethanol 90 pCt.

Manufacturer of Herbal Preparation: e.g. TXXXX, Pharmaceutical Group Co., Ltd, China



# Proposed Update Specified Substance Group 4

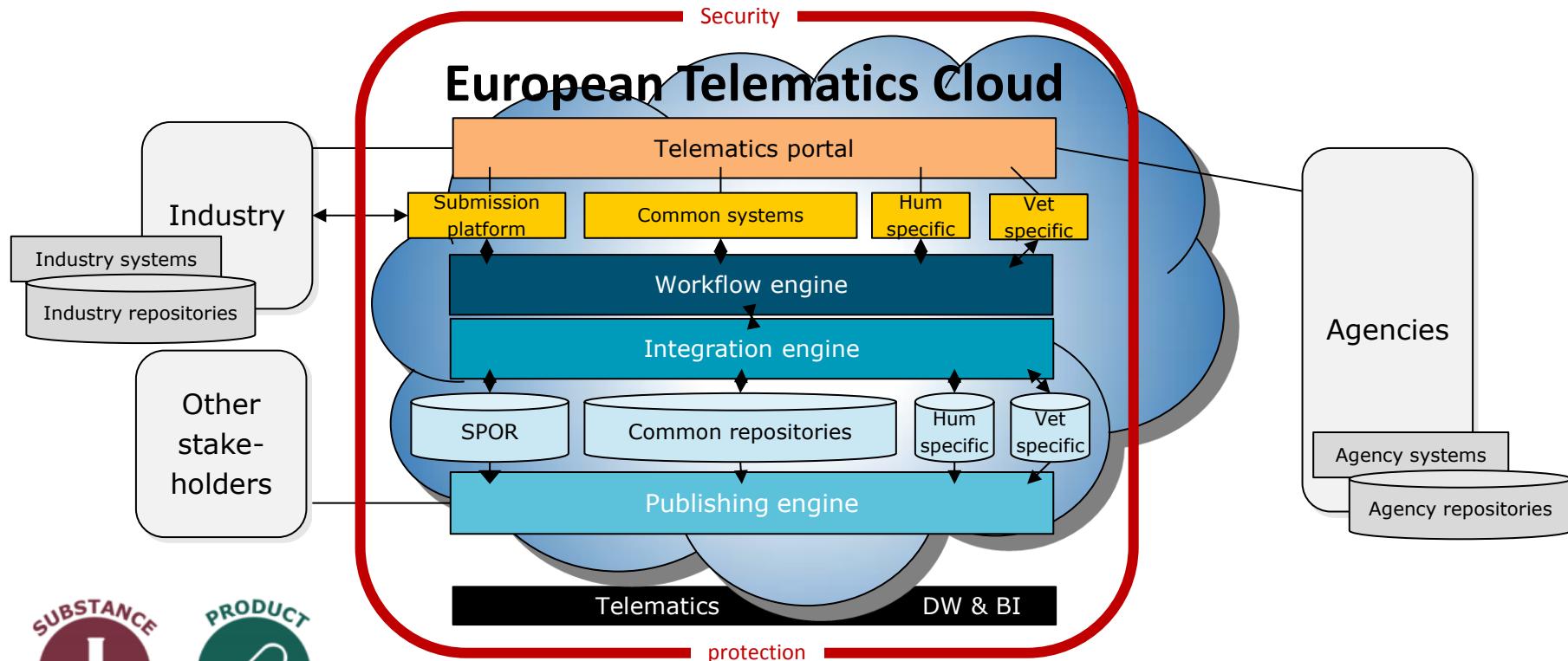
## Extended Information





# In Europe IDMP is an important part of the Telematics Roadmap

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**S**= Identification of Ingredients; **P**= Identification medicinal products in accordance with EU Directives and Guidelines;  
**O**= Names, address, Geographic location; **R**= List of terms ('controlled vocabularies') to describe product attributes



# Why and What?

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## Why?

There is no EU wide list of substances of adequate quality for use in regulatory use cases, leading to errors in submissions, rework by assessors and duplication of substance expert work across the network.

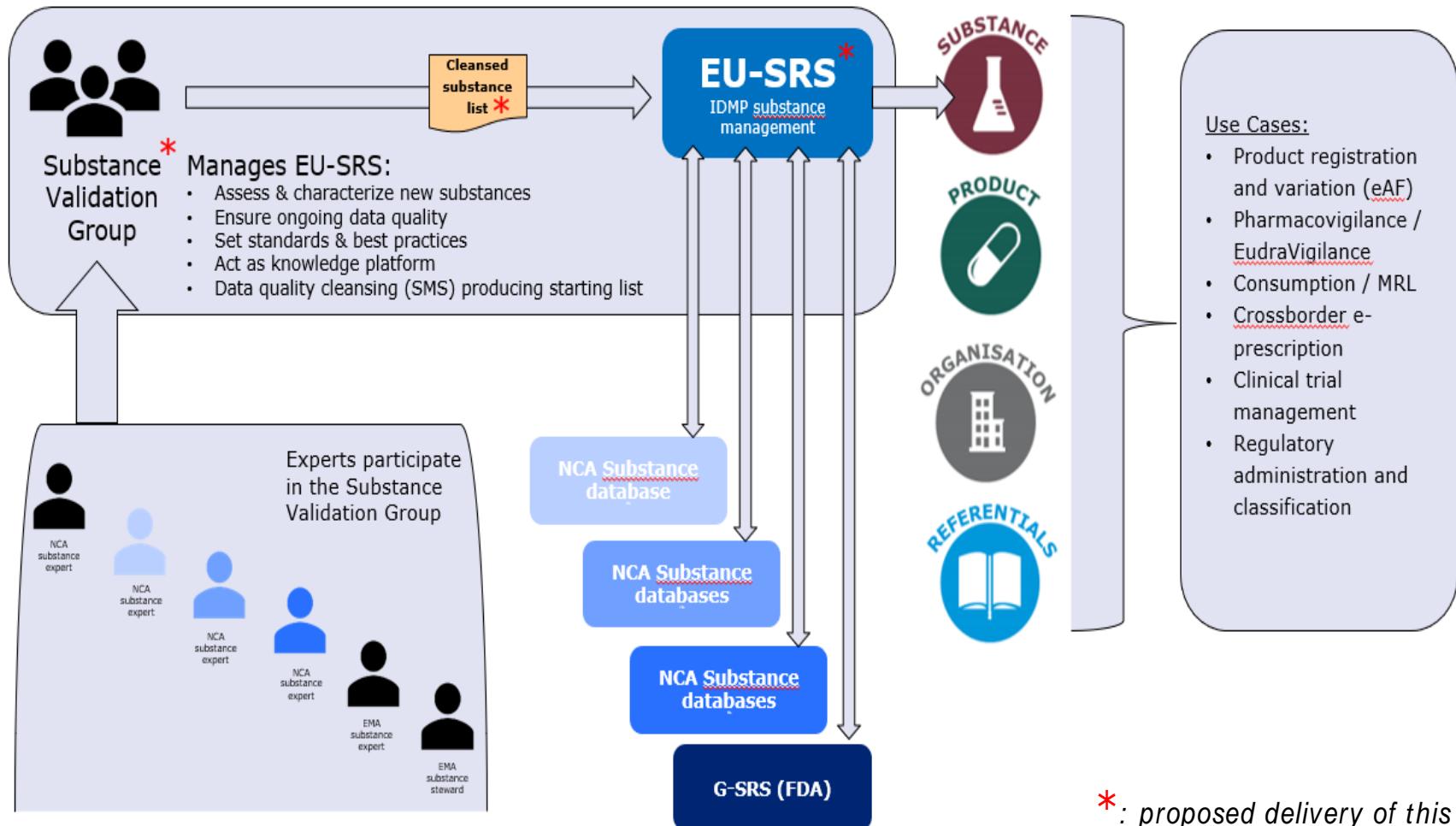
## What?

This project proposes to install an EU Network wide substances database (based on IDMP standards), governed by a group of NCA substance experts (=Substance Validation Group), who ensure data quality is fit for use.



# Outcome of the EU-SRS Project

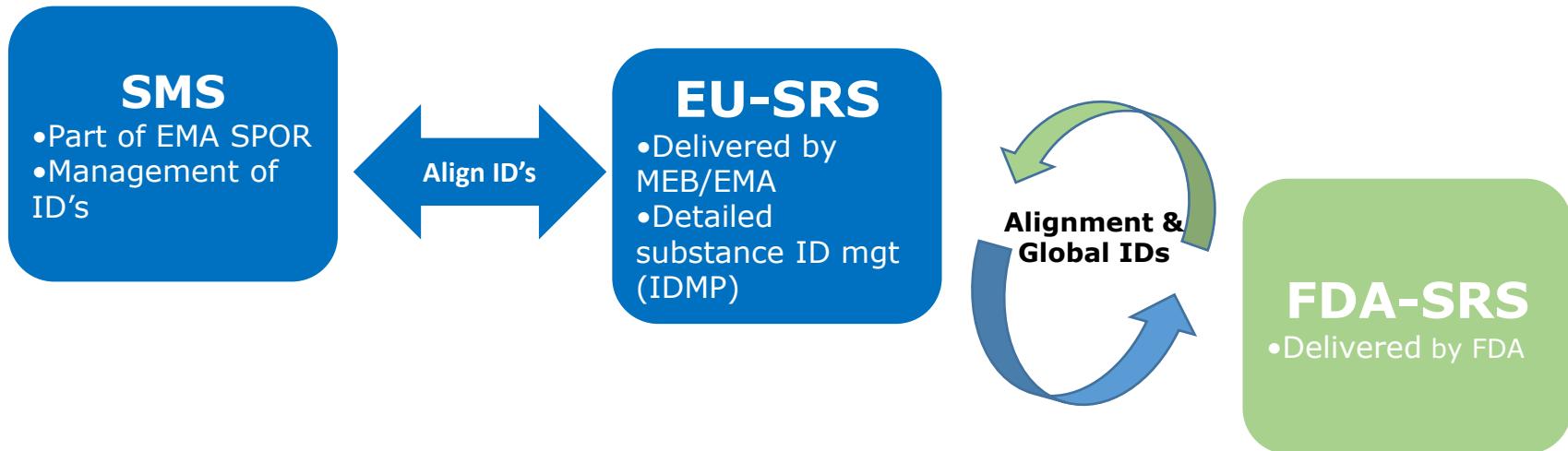
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# Role of EU-SRS



In the first Iteration EU-SRS database will focus on structurally diverse substances:

- Vaccines
- Biologicals (e.g. monoclonal antibodies, plasma-derived substances)
- Herbals
- Homeopathics
- Allergens

EU-SRS will complement SMS on these substances



# Preferred Name

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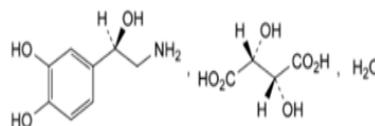
Substance name are ambiguous: Example Norepinephrine tartrate

- Norepinephrine (INN)
- Noradrenaline tartrate (Ph.Eur.)
- Norepinephrine bitartrate (USP)

- Leading is the Structure of the Active moiety
- Then: name as described for the active moiety by INN
- The Ph.Eur. Name = Official Name of the monograph 0285 and is the Grade name used in SSG3:
- Systematic name / structure of the Substance.

## NORADRENALINE TARTRATE

Noradrenalin tartras



C<sub>12</sub>H<sub>17</sub>NO<sub>5</sub>.H<sub>2</sub>O

[108341-18-0]

## DEFINITION

(1R)-2-Amino-1-(3,4-dihydroxyphenyl)ethanol hydrogen (2R,3R)-2,3-dihydroxybutanedioate monohydrate.

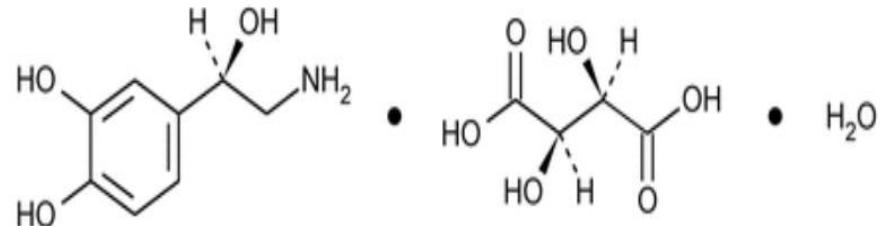
Content: 98.5 per cent to 101.0 per cent (anhydrous substance).

**Preferred name: Norepinephrine hydrogen tartrate monohydrate**

The USP Name = Official Name of the monograph and is the Grade name for SSG3

## Norepinephrine Bitartrate

(nor' ep i nef' rin bye tar' rate).



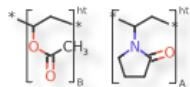
C<sub>8</sub>H<sub>11</sub>NO<sub>3</sub>·C<sub>4</sub>H<sub>6</sub>O<sub>6</sub>·H<sub>2</sub>O      337.28

C<sub>8</sub>H<sub>11</sub>NO<sub>2</sub>·C<sub>4</sub>H<sub>6</sub>O<sub>6</sub>      319.27

1,2-Benzenediol, 4-(2-amino-1-hydroxyethyl)-, (R)-,[R-(R\*,R\*)]-2,3-dihydroxybutanedioate (1:1) (salt), monohydrate;  
(-)-α-(Aminomethyl)-3,4-dihydroxybenzyl alcohol tartrate (1:1) (salt), monohydrate  
[108341-18-0]; UNII: IFY5PE3ZRW.

# COPovidone K25-31

## POLYMER



**Names:** COPovidone (PLASDONE-S630)

COPovidone K26-29

KOLLIDON VA 64

COPOLYMER OF 1-VINYL-2-PYRROLIDONE A...

PLASDONE-S630

**Codes:** CAS: 25086-89-9

EVMPD: SUB126855 SUB180567

NCI THESAURUS: C80921



**Relationships:** 2

## COPOVIDONE K25-31 [D9C330MD8B]

COPOVIDONE [D9C330MD8B]

POVIDONE/VINYL ACETATE COPOLYMER [D9C330MD8B]

## COPovidone K2...

D9C330MD8B

Overview

Variant Concepts 2

Names 7

Identifiers 4

Display Structure

Relationships 2

Characteristic Attributes 1

Notes 5

Audit Info

References 10



POVIDONE/VINYL ACETATE COPOLYMER

# COPOLYMER OF 1-VINYL-2-PYRROLIDONE AND VINYL ACETATE IN THE MASS PROPORTION OF 3:2 (MW=40000)

Complete defined properties for mass ratio between monomers and molecular weight (Mw) indicated by the display of the navigation column in the substance record

## Monomers 2

| Material | Material Name        | Amount     | Type    |
|----------|----------------------|------------|---------|
|          | VINYL ACETATE        | MOLE RATIO | MONOMER |
|          | N-VINYLPYRROLIDINONE | MOLE RATIO | MONOMER |

## Characteristic Attributes

### Properties

| Name                      | Property Type | Amount   |
|---------------------------|---------------|--|
| MOL_WEIGHT:NUMBER AVERAGE | CHEMICAL      | NUMBER AVERAGE<br>[15000 to 20000] Da (limits) |



Monomer and Mw are defining elements for Polymer



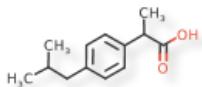
# EU-SRS Preview

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## IBUPROFEN

### Links to sources and other codes

## RACEMIC



- Names:** IBUPROFEN COMPONENT OF ADVIL ALLERG...  
IB-100  
IBUPROFEN COMPONENT OF SINE-AID IB  
IBUPROFEN COMPONENT OF CHILDREN'S M...  
IBUPROFEN [INN]
- Codes:** CAS: 15687-27-1 □ 58560-75-1 □ 139466-08-3 □  
WHO-ATC: G02CC01 □ M01AE51 □ R02AX02 □  
M01AE01 □ C01EB16 □ M02AA13 □  
EVMPD: SUB08098MIG  
ChEMBL: CHEMBL521 □



## List of substances

- Formula:** C13H18O2  
**Mol Weight:** 206.28
- [IBUPROFEN \[WK2XYI10QM\]](#)
  - [IBUPROFEN \[WK2XYI10QM\]](#)
  - [IBUPROFEN MEGLUMINE \[56SFW97YYQ\]](#)
  - [IBUPROFEN POTASSIUM \[48304089JJ\]](#)
  - [IBUPROFEN LYSINE \[N01ORX9D6S\]](#)
  - [IBUPROFEN SODIUM \[RM1CE97Z4N\]](#)
  - [IBUPROFEN PICONOL \[B0F91K5U4N\]](#)
  - [IBUPROFEN ALUMINUM \[D0YGZ1VO1B\]](#)
  - [IBUPROFEN SODIUM ANHYDROUS \[O0PJ4UZ01U\]](#)

### Links to Structure/search details

#### VEDOTIN FRAGMENT

Q3606FDE0B

##### ABSOLUTE

Names: CONJUGATED FORM OF MC-VC-PAB-MMAE

Created: 3 months ago

VEDOTIN (USAN)

Last modified: 3 months ago

VEDOTIN FRAGMENT

Status: 3 months ago

VEDOTIN RADICAL

Version: Validated (UNII)

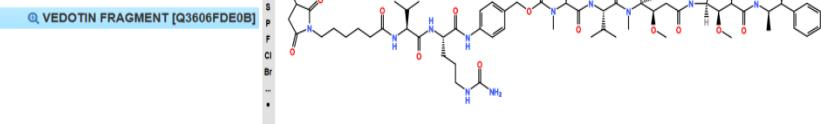
Codes: ChEMBL: CHEMBL2364667 □

Relationships: 7



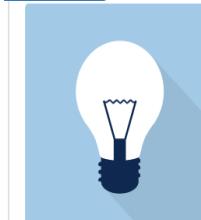
Formula:

Mol Weight:



### Hierarchy to related substances

#### CONCEPT



Names: EUPHORBIA PILULIFERA EXTRACT

Created: 3 months ago

Relationships: 1

Last modified: 3 months ago

Status: non-approved

Version: 1



▫ [EUPHORBIA HIRTA \[L13YF113GN\]](#)

▫ [EUPHORBIA HIRTA \[L13YF113GN\]](#)

▫ [EUPHORBIA HIRTA EXTRACT \[L13YF113GN\]](#)

▫ [EUPHORBIA HIRTA LEAF \[243K8QF0MS\]](#)

▫ [EUPHORBIA PILULIFERA EXTRACT \[243K8QF0MS\]](#)

▫ [EUPHORBIA HIRTA FLOWERING TOP \[6H89ZY31MR\]](#)

▫ [EUPHORBIA HIRTA FLOWERING TOP \[6H89ZY31MR\]](#)



# EU-SRS preview: Use of hierarchy for selection/ Parent-Child relationship

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Select the correct Preferred term by direct name/ID and Structure display

IBUPROFEN LYSINE

Search Structure

IBUPROFEN LYSINE [N01ORX9D6S]

IBUPROFEN SODIUM [RM1CE97Z4N]

IBUPROFEN PICONOL [B0F91K5U4N]

IBUPROFEN ALUMINUM [D0YGZ1VO1B]

IBUPROFEN SODIUM ANHYDROUS [O0PJ4UZ01U]

EVMPD: SUB08098MIG

ChEMBL: CHEMBL521

Relationships: 32

Formula: C13H18O2

Mol Weight: 206.28

K2XYI10QM]

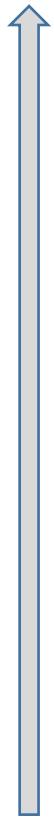
[WK2XYI10QM]

MEGLUMINE [56SF97YYQ]

POTASSIUM [48304089JJ]



**Support the health care domain**



**Structure/relational substance  
data base**



**GInAS Project/  
G-SRS Software**



**Name/ Text  
substance data base**

Thank you for your attention



**Ciska Matai ([cg.matai@cbg-meb.nl](mailto:cg.matai@cbg-meb.nl))**

**Herman Diederik ([h.diederik@cbg-meb.nl](mailto:h.diederik@cbg-meb.nl))**

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