Public GSRS Meeting June 2018

CBG MEB

COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

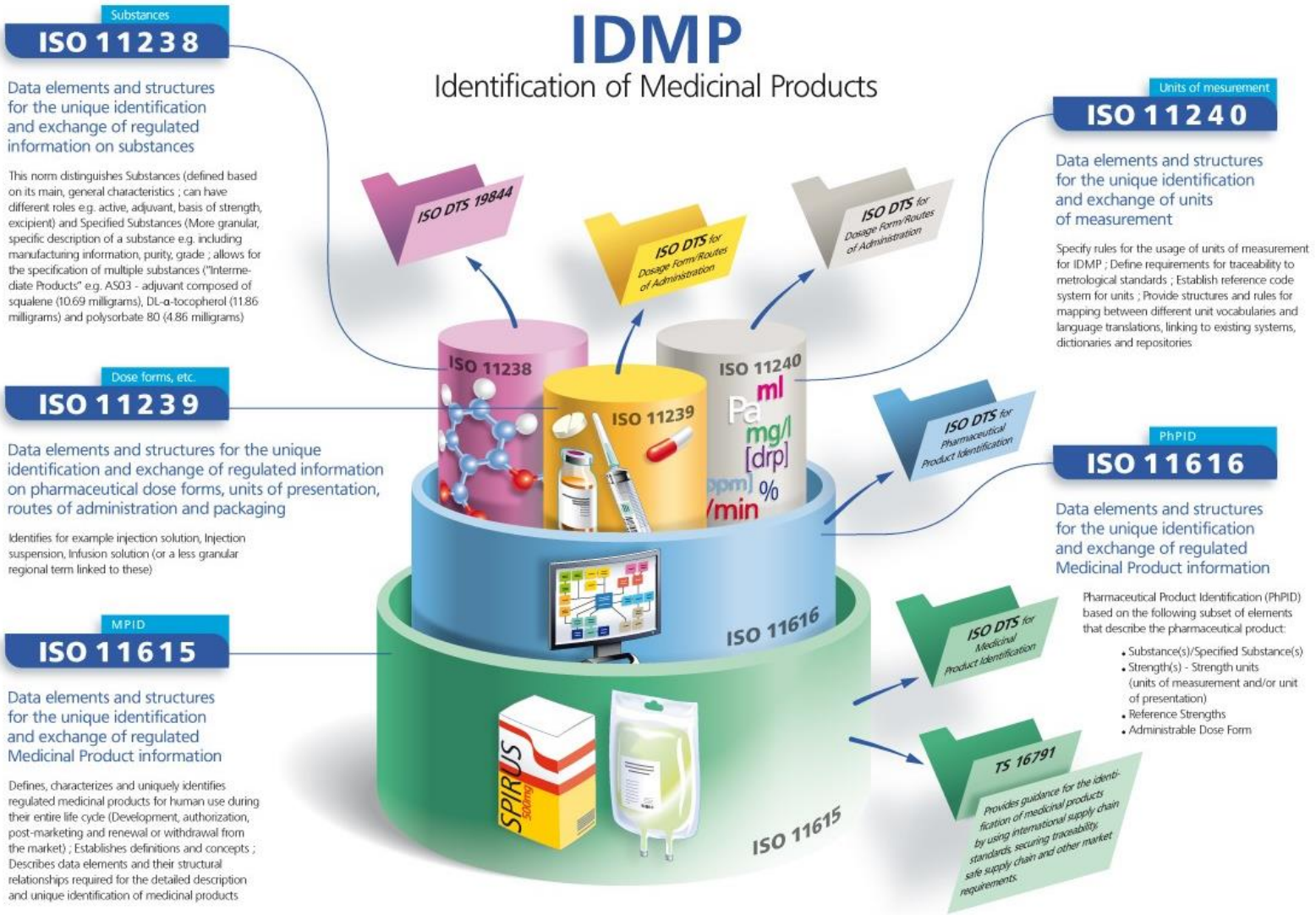
IDMP and how we can support the health care domain

GOEDE MEDICIJNEN GOED GEBRUIKT

GInAS 2013 consortium: software G-SRS

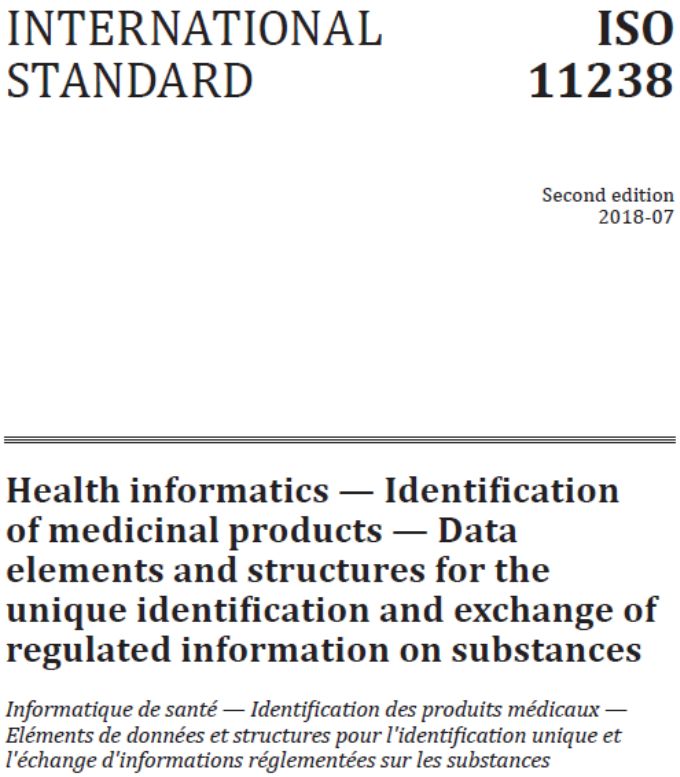
The main goal of GInAS is the production of software, called G-SRS, to assist agencies in registering and documenting information about substances found in medicines.
The **G**lobal **In**gredient **A**rchival **S**ystem provides a common identifier for all of the substances used in medicinal products, utilizing a consistent definition of substances globally, including active substances under clinical investigation, consistent with the ISO 11238 standard.

IDMP Standards



ISO 11238 International Substance Standard

Editors: Herman Diederik, CBG-MEB &
Larry Callahan, FDA



INTERNATIONAL STANDARD

ISO 11238

Second edition
2018-07

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

1 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

ISO TS 19844 implementatie guide

Editor: Herman Diederik, CBG-MEB in cooperation

with Panagiotis Telonis, EMA, Larry Callahan, FDA and Andrew Marr, BSI

1 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 examples for a variety of Substances and Specified Substances.
This 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 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.

ISO TS 19844:2018

ISO TC 215

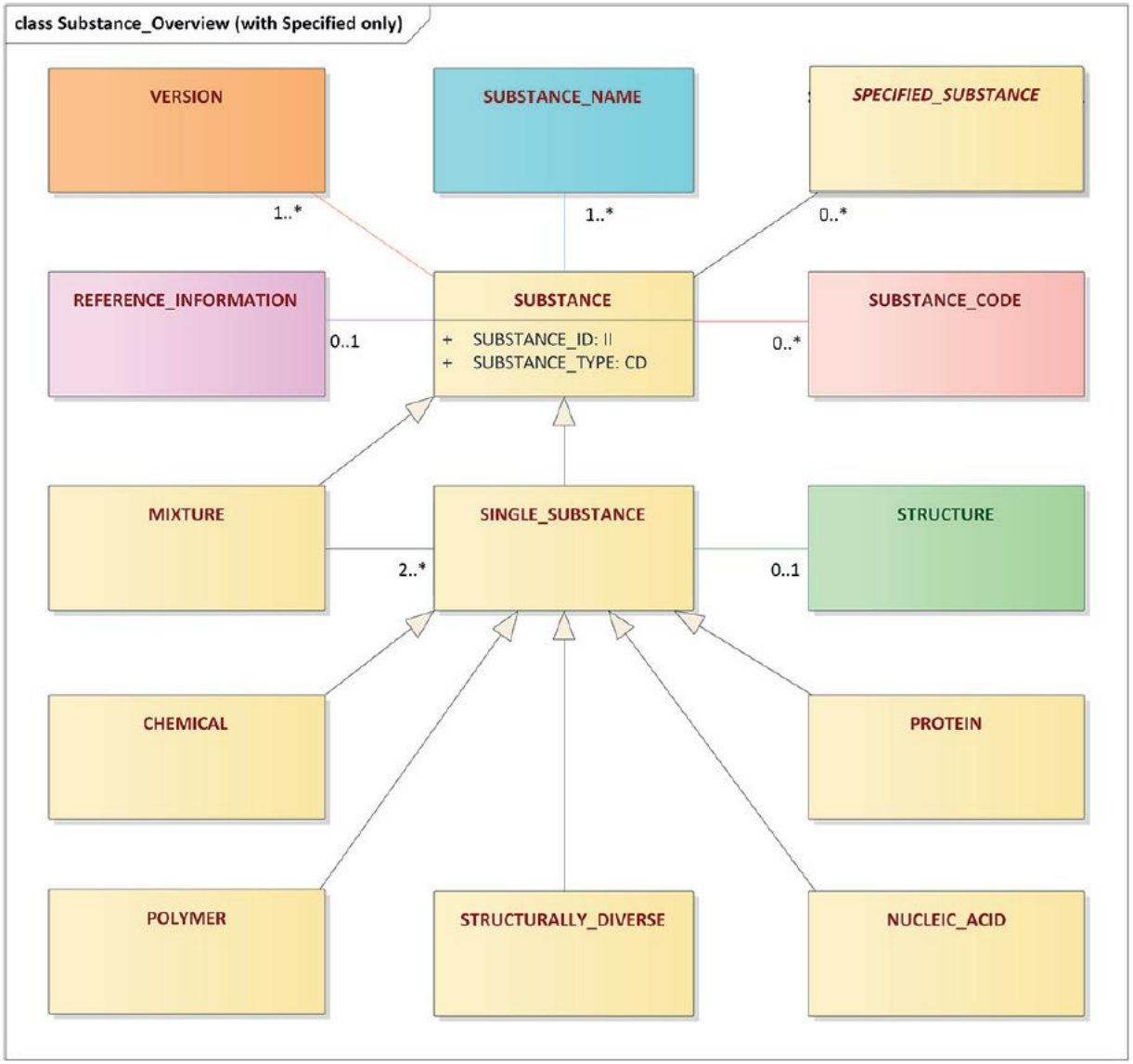
Date: 2018-xx

ISO TC 215/WG 6

Secretariat: ANSI

Health informatics – Identification of medicinal products – Implementation guidelines for data elements and structures for the unique identification and exchange of regulated information on substances

High-level information model of substances



TS 1984 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;

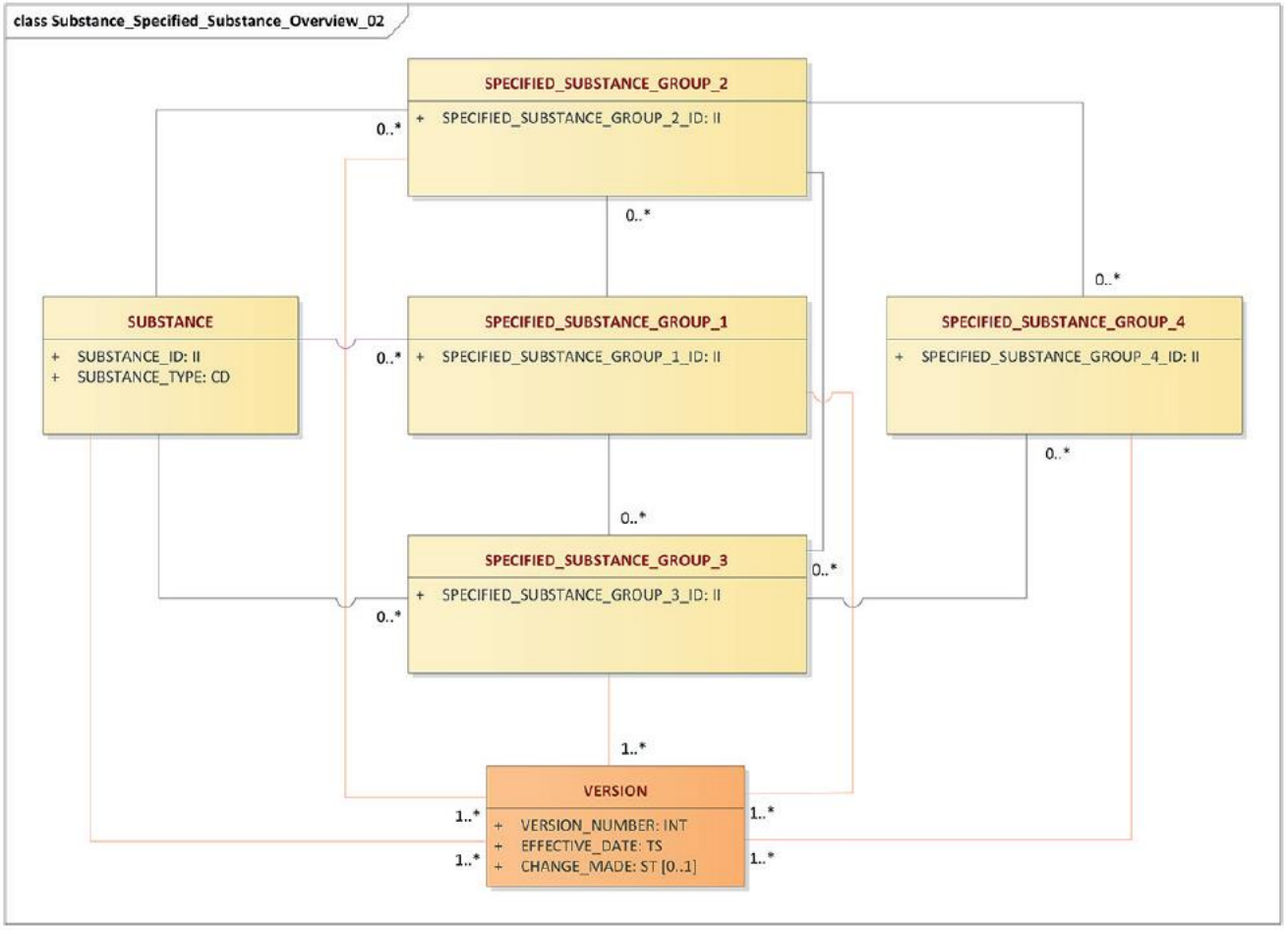
I) Structurally Diverse, Vaccines;

J) Structurally Diverse, Allergen

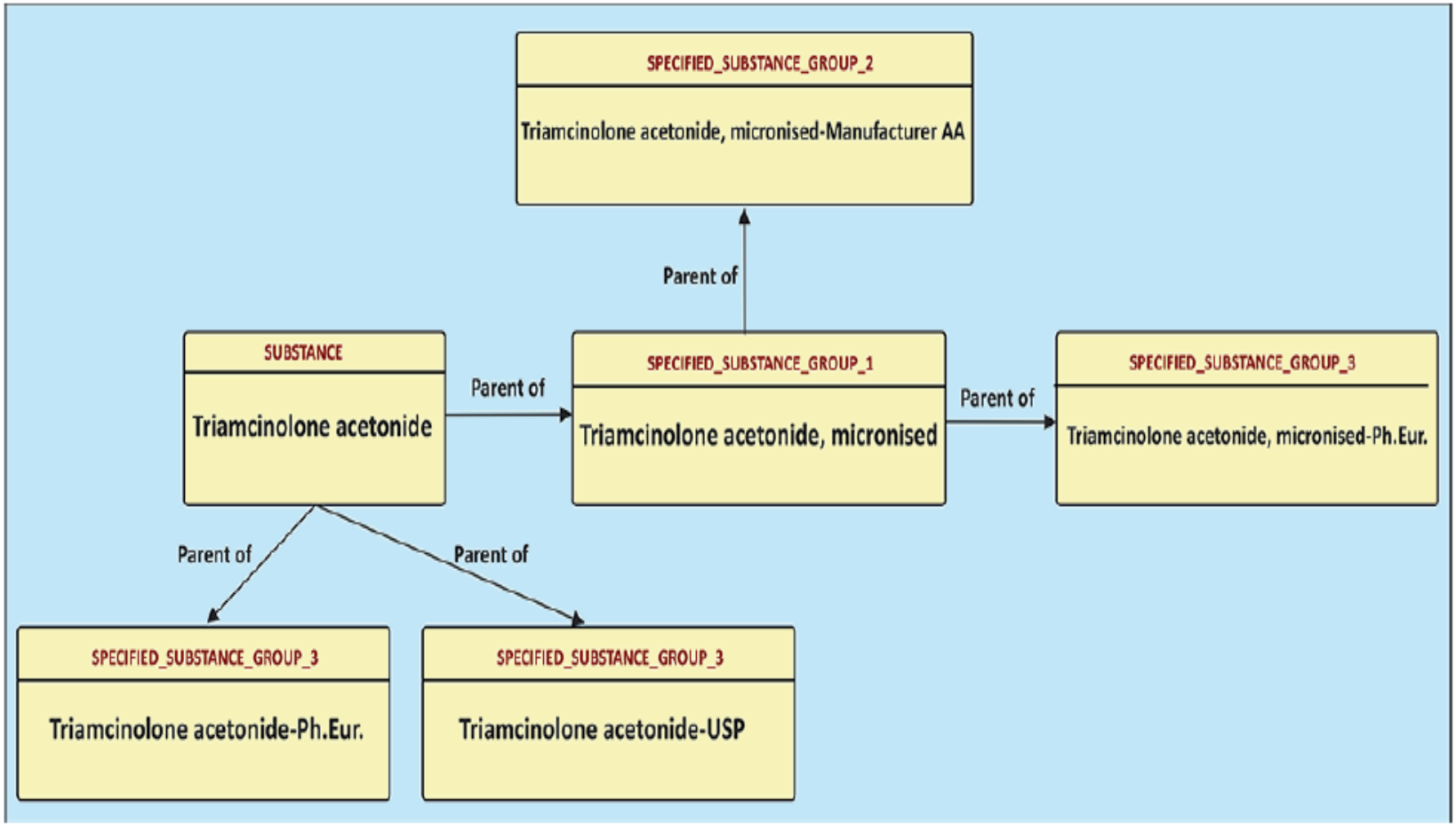
and

K) Structurally Diverse, Advanced Therapies and Advanced Vaccines (Genes, Modified Viruses, Cells and Tissues as Substances)

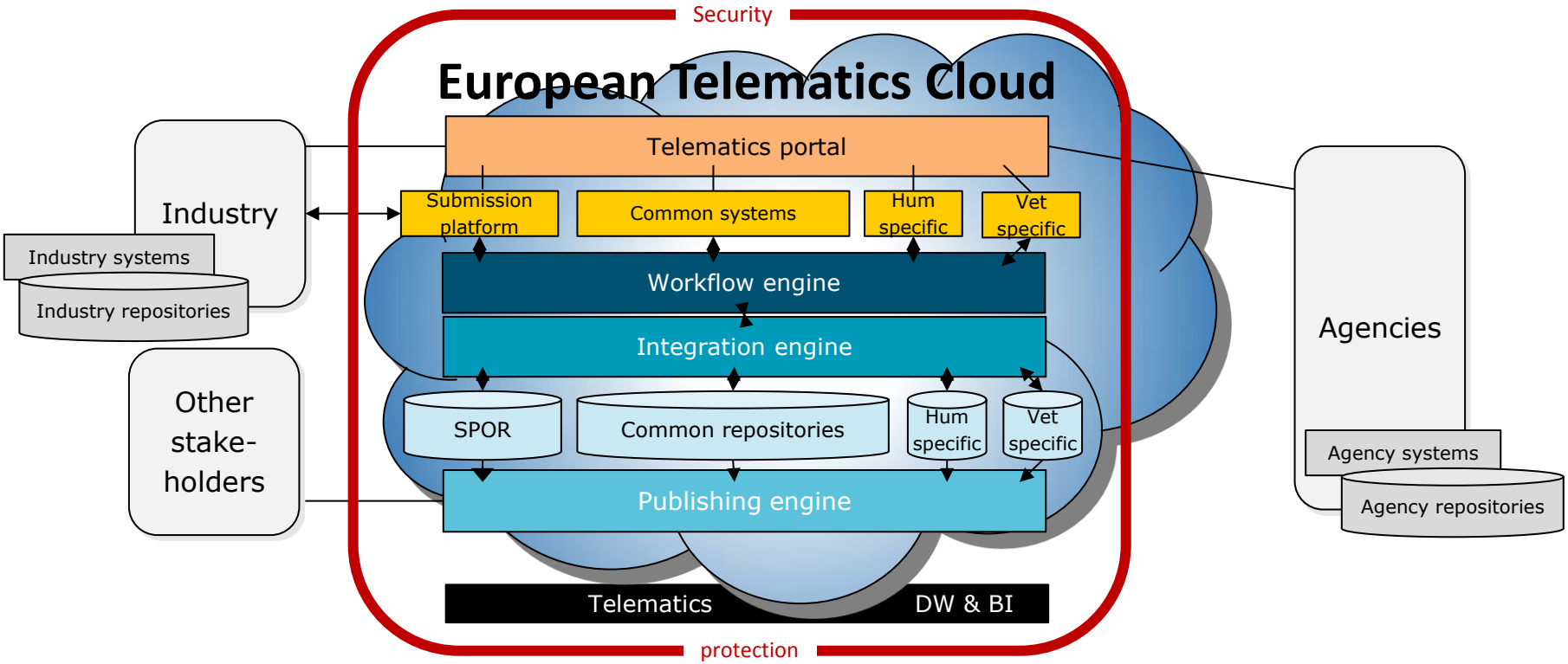
High-level Substance - Specified substance information model



Parent Substance and Specified Substances Groups relationships of Triamcinolone acetonide



In Europe IDMP is an important part of the Telematics Roadmap



EMA implements ISO IDMP by four domains: SPOR

Substances : Identification of Ingredients

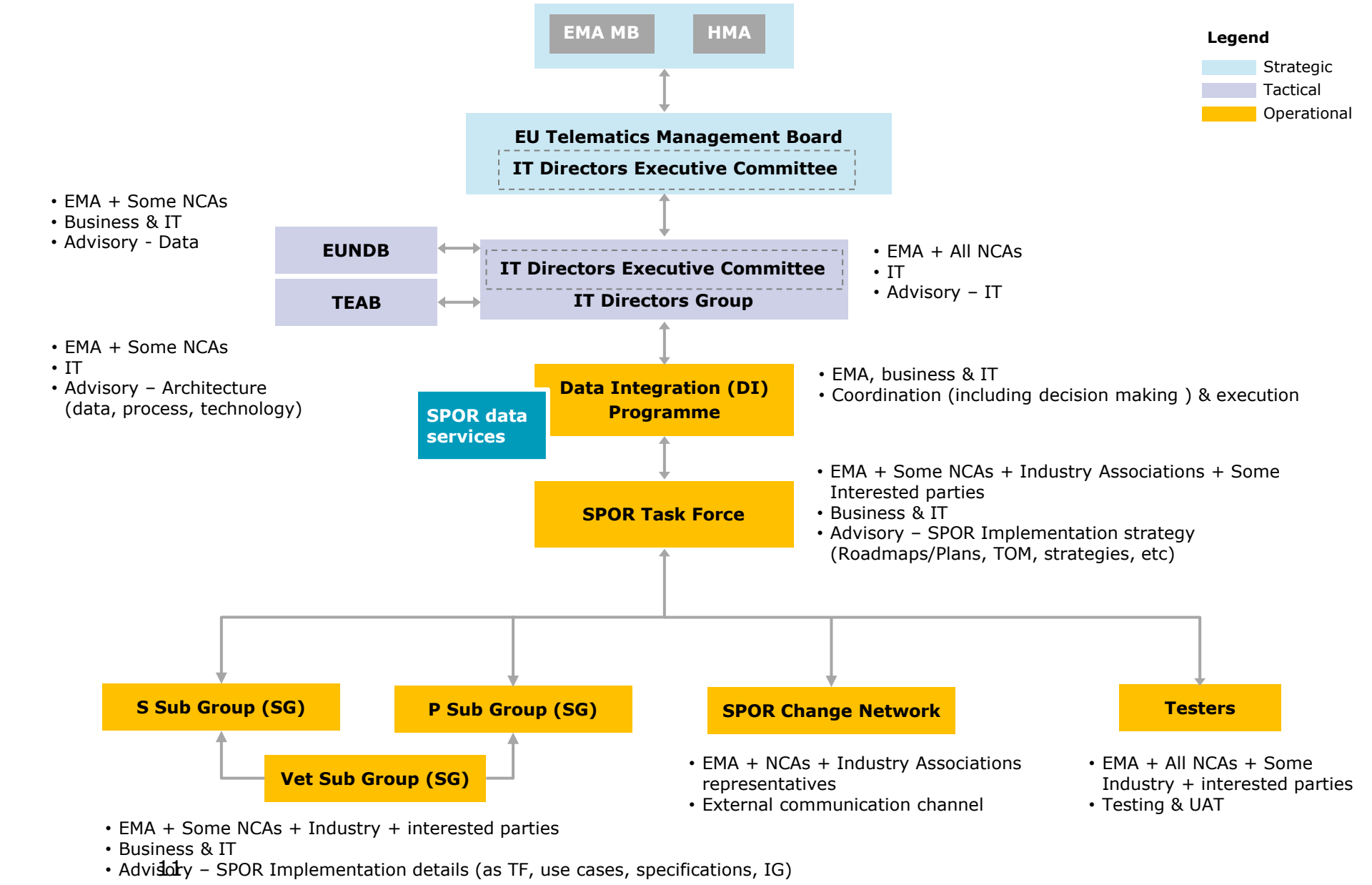
Products: Identification medicinal products in accordance with EU Directives and Guidelines

Organisations: Names, address, Geographic location

Referentials: List of terms (‘controlled vocabularies’) to describe product attribues

SPOR within the Telematics Governance

EUROPEAN MEDICINES AGENCY



Why and What?

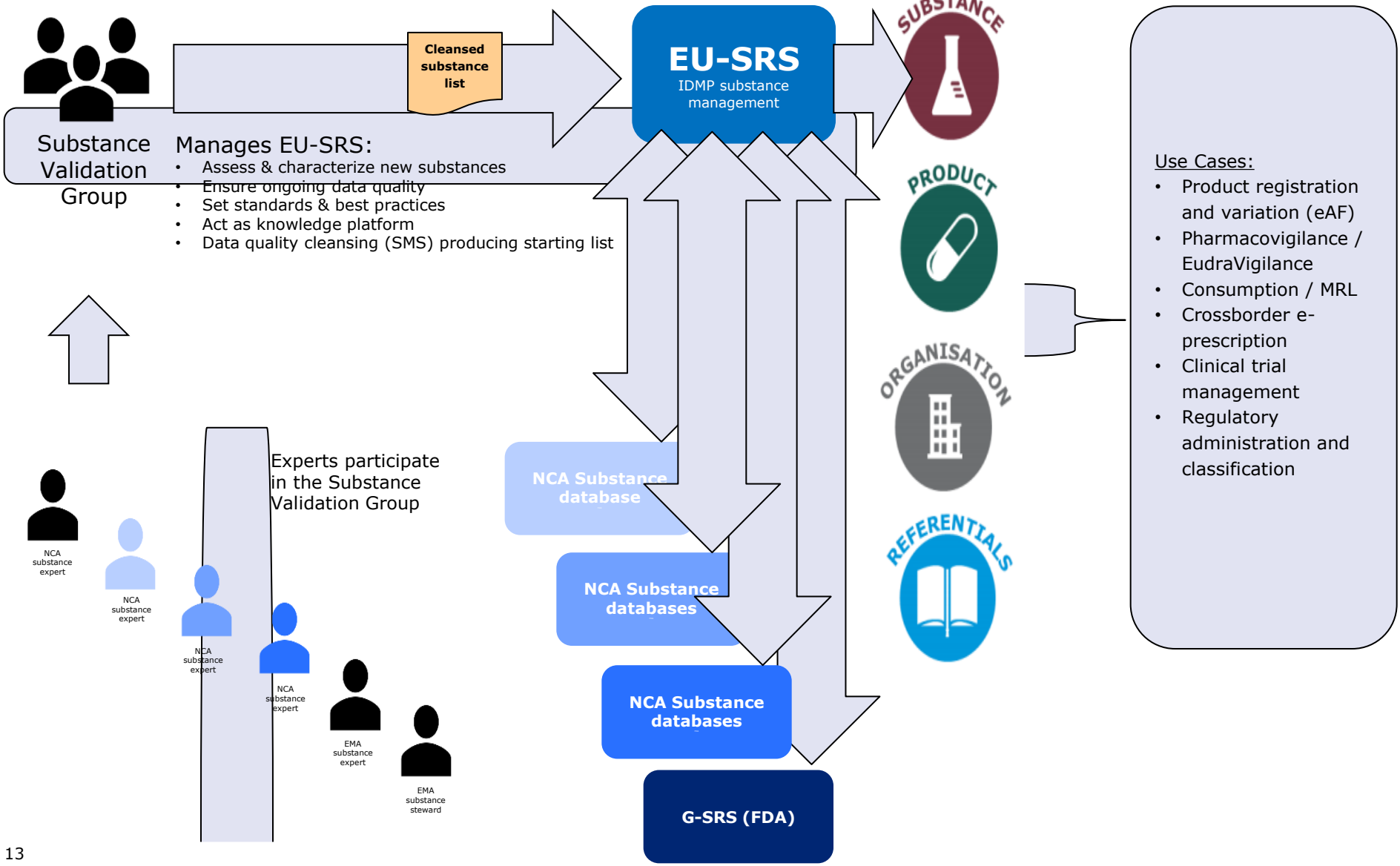
Why?

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.

Outcomes


Substance Validation Group
Cleansed substance list
EU-SRS
IDMP substance management
Manages EU-SRS:
• Assess & characterize new substances
• Ensure ongoing data quality
• Set standards & best practices
• Act as knowledge platform
• Data quality cleansing (SMS) producing starting list
SUBSTANCE
PRODUCT
ORGANISATION
REFERENTIALS
Use Cases:
• Product registration and variation (eAF)
• Pharmacovigilance / EudraVigilance
• Consumption / MRL
• Crossborder e-prescription
• Clinical trial management
• Regulatory administration and classification
Experts participate in the Substance Validation Group
NCA substance expert
NCA substance expert
NCA substance expert
NCA substance expert
EMA substance expert
EMA substance steward
NCA Substance database
NCA Substance databases
NCA Substance databases
G-SRS (FDA)

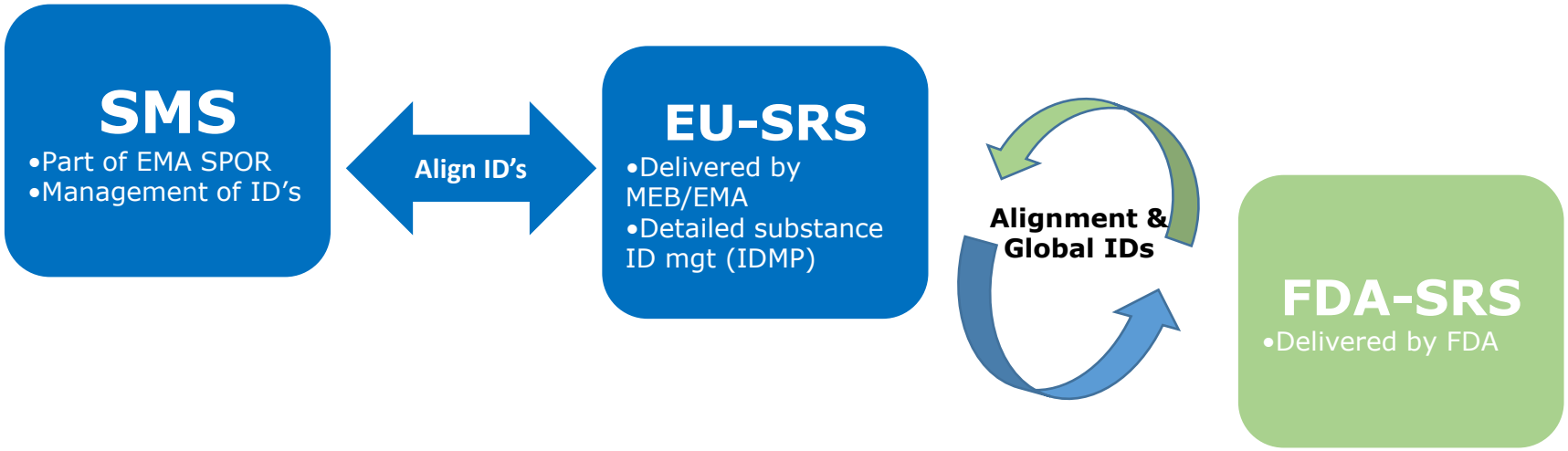
Objectives of EU-SRS implementation

- Implement IDMP compliant solution for management of substances in medicinal products (actives and excipients) - Human and veterinary*
- Support the IDMP Legal Remit (EMA) – by complementing required functionality of SMS (substance management service in SPOR)
- Ensure contents of EU-SRS is managed by suitable level of experts (Substance Validation Group) ensuring data quality and scientific correctness
- Execute cleansing of substances content for use in SMS (2018)
- **Maximize re-use of existing FDA system to allow for efficient implementation in Europe**

The EU-SRS implementation is aligned to Telematics strategy to ensure high quality master data via SPOR for use in efficiency improvements in the EU Network

* Different requirements exist for Veterinary – see note

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

General Introduction to FDA-EU-SRS

From Name/ Text substance data base, i.e. ICI

Structure substance Database, i.e. FDA-SRS

Our examples (1-2)

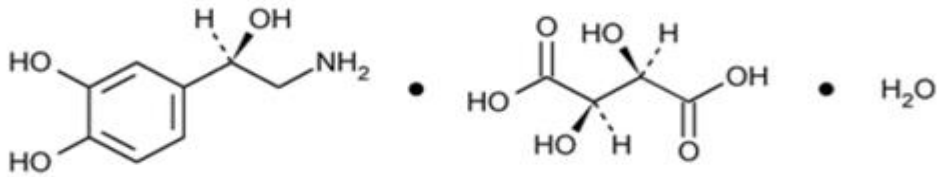
UC	Description	Clarification
1	Choice of **Preferred term** Why Substance terms are ambiguous Example: Norepinephrine tartrate	We need to couple one preferred term to be coupled 1:1 to an ID. Humans work with names, machines work with identifiers, primary and secondary keys. However, what is in a name and what reflects the name? This is different per substance type. Example: for Chemicals the name (=Preferred term)should reflect the Structure, since the structure is an unambiguous representation of the substance.
2	How EU-SRS Substance data will support a correct Medicinal Product composition. Example: **Two common excipients** used in a simple product composition. Copovidone and Croscarmellose Sodium	Unambiguous defined substances, reflected by the precise and detailed enough Preferred term can be used and selected into a Product composition. When the product composition is established a human should be able to get a characteristic fingerprint information of that substance used in that product. The information should be available not more than two clicks away. In this example is explained that the term Copovidone is insufficiently defined to get an Identifier (UNII). The term should be replaced by Copovidone K25-31.

Choice of Preferred term

Why Substance terms are ambiguous
Example: Norepinephrine tartrate;

- INN: Norepinephrine
- Ph. Eur: Noradrenaline tartrate
- USP: Norepinephrine bitartrate
- **Preferred term:**
  Norepinephrine hydrogen tartrate monohydrate

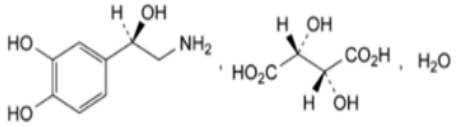
- The USP Name = Official Name of the monograph fo **Norepinephrine Bitartrate**
  (nor'' ep i nef' rin bye tar' trate).



- 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:
- Systhematic name / structure of the Substance.

NORADRENALINE TARTRATE

Noradrenalini tartras



$C_{12}H_{17}NO_9,H_2O$

[108341-18-0]

DEFINITION

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

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

$C_8H_{11}NO_3 \cdot C_4H_6O_6 \cdot H_2O$ 337.28
$C_8H_{11}NO_2 \cdot C_4H_6O_6$ 319.27

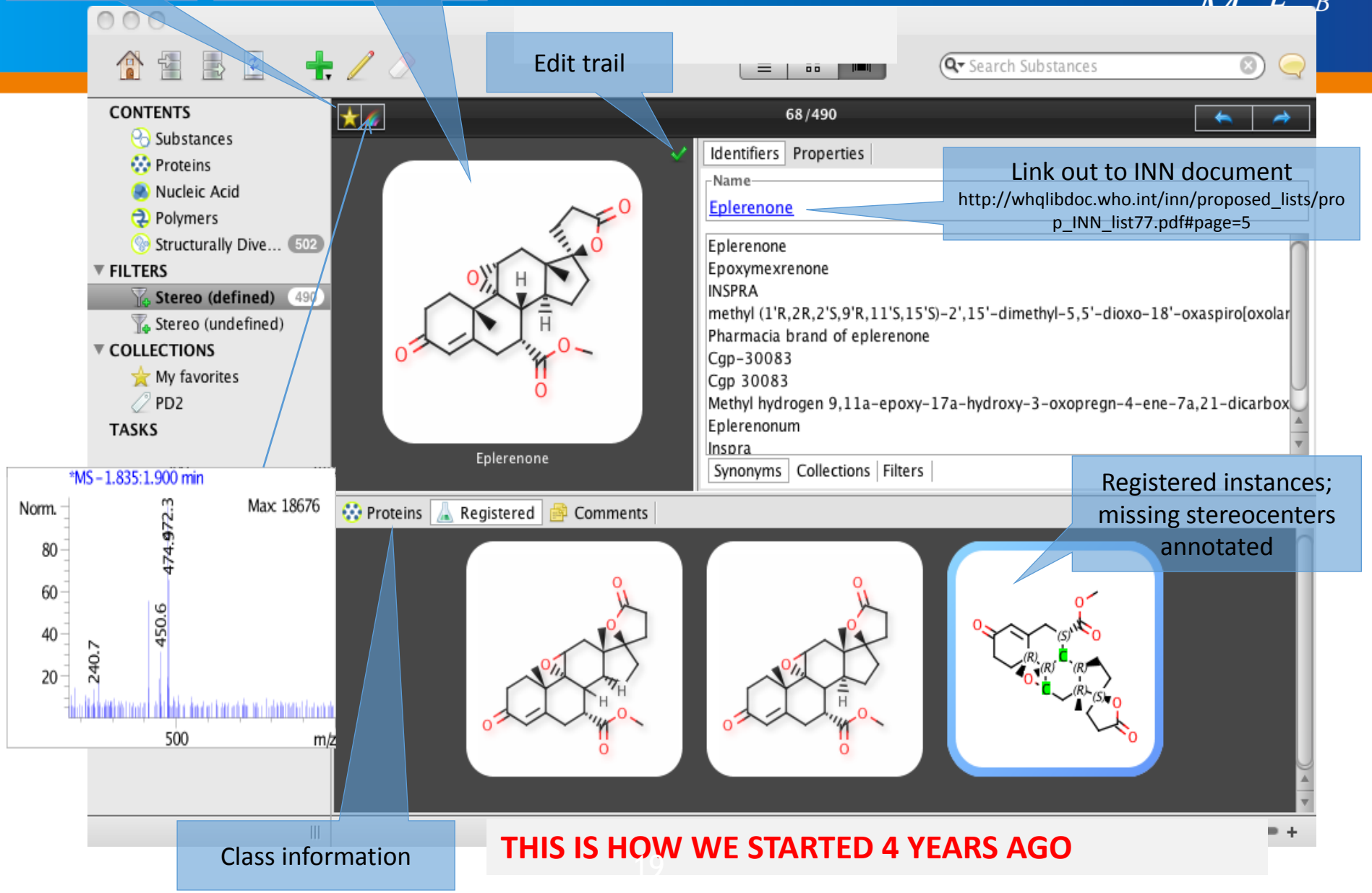
1,2-Benzenediol, 4-(2-amino-1-hydroxyethyl)-, (*R*)-,[*R*-(*R**,*R**)]-2,3-dihydroxybutanedioate (1:1) (salt), monohydrate;
(−)-α-(Aminomethyl)-3,4-dihydroxybenzyl alcohol tartrate (1:1) (salt), monohydrate
[108341-18-0]; UNII: IFY5PE3ZRW.

Display of INN, IUPAC name, Structure and properties all in one place

Curation status

Preferred structure

Edit trail



Link out to INN document
http://whqlibdoc.who.int/inn/proposed_lists/prop_INN_list77.pdf#page=5

Registered instances; missing stereocenters annotated

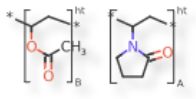
Class information

THIS IS HOW WE STARTED 4 YEARS AGO

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

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

Complete defined properties for mass ratio between Monomers and molecular weight indicated by the display of the facet region in the screen after entering the substance record

COPOVIDONE K25-31 [D9C330MD8B]

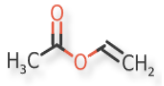
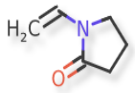
COPOVIDONE K25-31

- Details
- Display Structure
- Monomers 2
- Structural Repeat Units 0
- Names 7
- Codes 4
- Relationships 2
- Properties 1
- Notes 5
- References 10

COPOVIDONE

POVIDONE/VINYL ACETATE COPOLYME

Monomers 2

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

Relationships 2

Properties 1

Name	Property Type	Amount
MOL_WEIGHT:NUMBER AVERAGE	CHEMICAL	NUMBER AVERAGE [15000 to 20000] Da (limits)

Monomer and Mw are defining elements for Polymer

What can go wrong when you don't select the correct substance?

Applicant:

- In control of your submission?

Assessor:

- Assessing the correct molecule, strength, activity profile, interaction profile?

Pharmacovigilance:

- Connecting the correct ADRs to the relevant substance, missing relations?

Clinical:

- Not overseeing the total exposure due to unrelated substances?

Pharmacist:

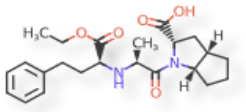
- Using the information (electronic) from the NCA needs to lead to the correct dose, ..

Example: Ramipril

RAMIPRIL

L35JN3I7SJ

ABSOLUTE



Names: CARDACE
RAMIPRIL [USP-RS]
HOPACE
CYCLOPENTA(B)PYRROLE-2-CARBOXYLIC A...
RAMIPRIL [JAN]

Codes: CAS: *87333-19-5*

WHO-ATC: *C09BB07* *C09BB05* *C10BX04* *C09BA05* *C09AA05* *C10BX06*

EVMPD: *SUB10248MIG*

ChEMBL: *CHEMBL1168*

Active Moiety

Relationships: 22

Created: 3 months ago

Last modified: 3 months ago

Status: Validated (UNII)

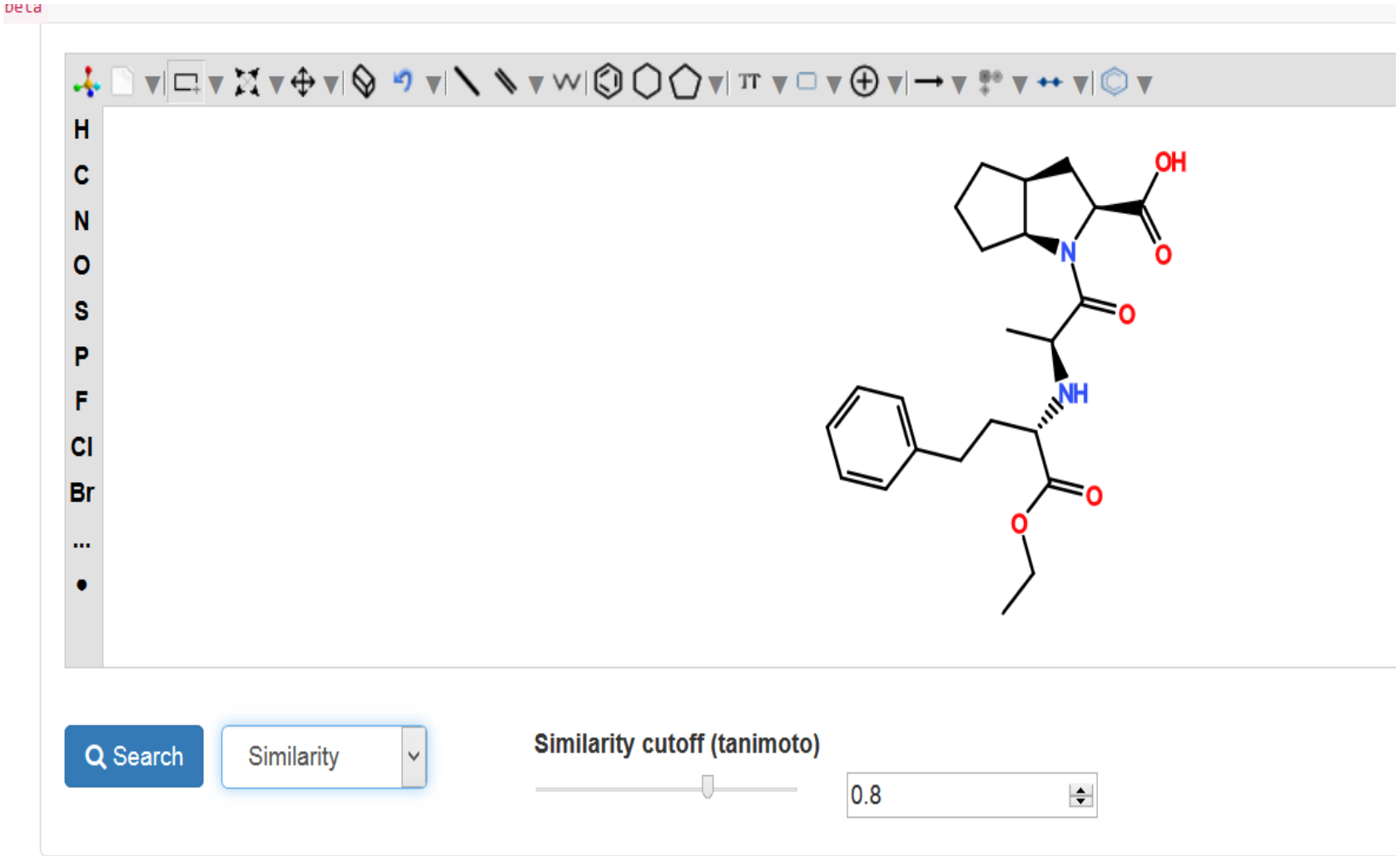
Version: 4

Formula: C23H32N2O5

Mol Weight: 416.51

- RAMIPRILAT [6N5U4QFC3G]
  - RAMIPRILAT [6N5U4QFC3G]
  - **RAMIPRIL [L35JN3I7SJ]**

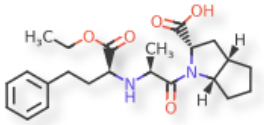
Example: Ramipril: Similarity Search



Ramipril: Similarity Search Results

L35JN3I7SJ

ABSOLUTE

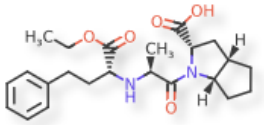


Similarity 1.000

RAMIPRIL

9947X9J31M

ABSOLUTE

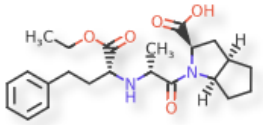


Similarity 1.000

RAMIPRIL EPIMER, (R,...

5COV0OAU1T

ABSOLUTE

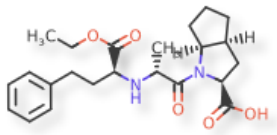


Similarity 1.000

RAMIPRIL, (-)-

E7CEJ08B2F

ABSOLUTE



Similarity 1.000

(2S,3AS,6AS)-1-((2R)-2-...

MFY4AI76OW

ABSOLUTE

2S4N8A063C

ABSOLUTE

1T0N3G9CRC

ABSOLUTE

7U47129S2I

ABSOLUTE

Quality aspects in relation to safety and efficacy of Biologicals

- Process control Strategy
- Comparability with development batches
- Characterisation of the drug substance
- Identity and content/potency of the active substance
- Purity
- Formulation
- Stability
- Microbial and viral safety

- Immunogenicity

- Legal texts:
  - European Pharmacopoeia (monographs)
  - European Directive

Recombinant proteins

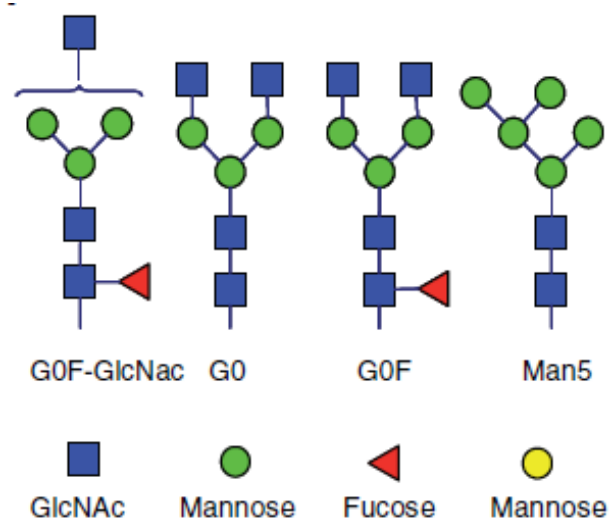
CDLPQTHSLG SRRTLMLLAQ MRX$_1$ISLFSCL KDRHDFGFPQ
KEFGNQFQKA ETIPVLHEMI QQIFNLFSTK DSSAAWDETL
LDKFYTELYQ QLNDLEACVI QGVGVTETPL MKEDSILAVR
KYFQRITLYL KEKKYSPCAW EVVRAEIMRS FSLTSNLQES
LRSKE

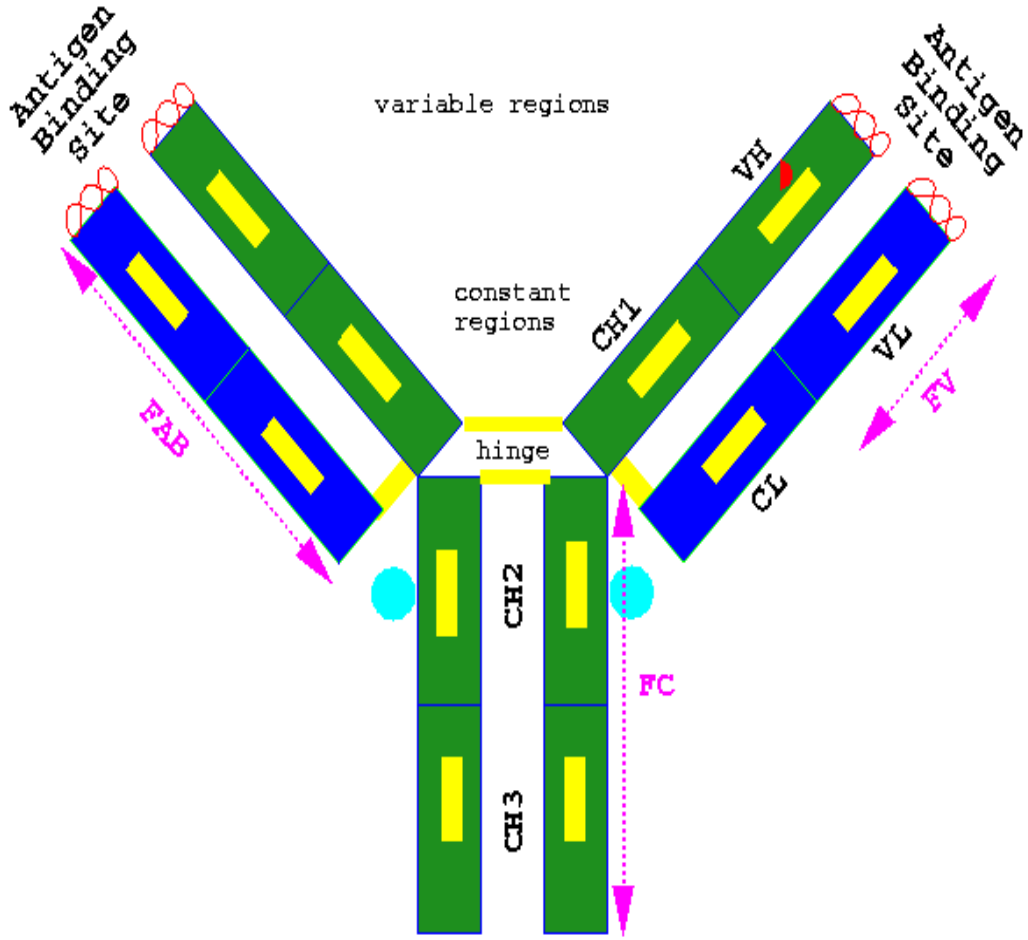
Which parameters?

AA sequence

Di-sulfide bridges

Glycosylation





Biosimilars or Production change:

- Well-documented
- Consistency in assessment

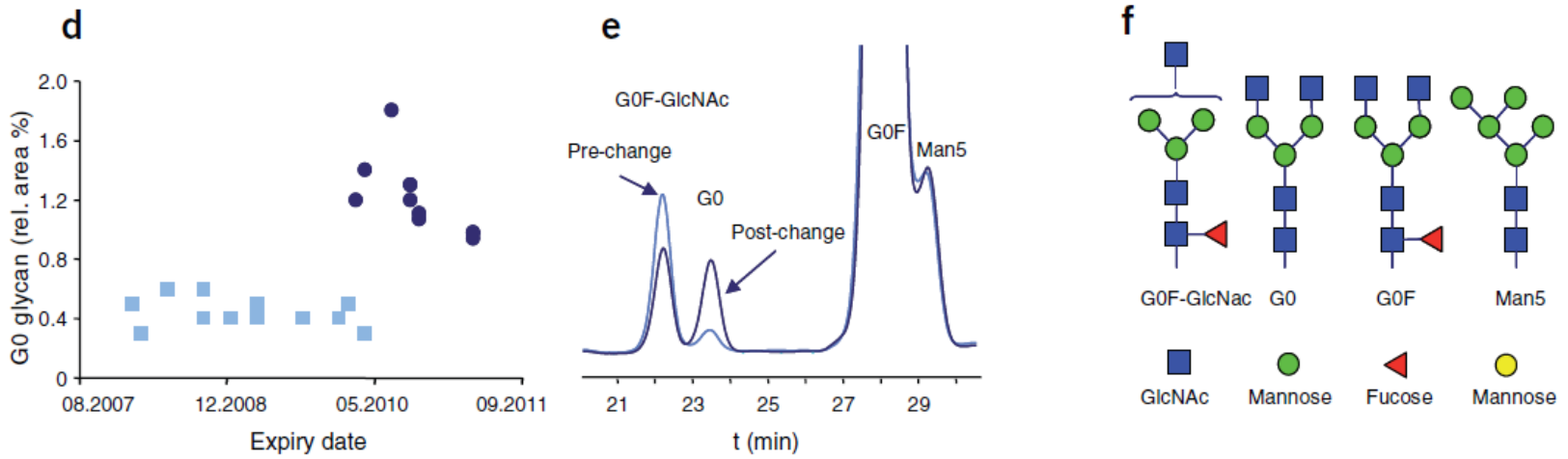


Figure 2 Comparison of the different pre- and post-change batches of Rituxan/Mabthera. (**a**) Exemplary CEX chromatograms. (**b**) Amount of basic variants of the pre-change ($n = 12$) and post-change ($n = 6$) batches as measured by CEX. (**c**) ADCC potency of the pre-change ($n = 11$) and post-change ($n = 8$) batches. (**d**) Relative amount of the G0 glycan of the pre-change ($n = 13$) and post-change ($n = 11$) batches. (**e**) Exemplary glycan mapping chromatograms. (**f**) Glycan legend.

Example: Monoclonal Anitibody

There is one exact (name or code) match for *"BRENTUXIMAB VEDOTIN"*

BRENTUXIMAB VEDOTIN

7XL5ISS668

PROTEIN

Names: CAC10-1006(4)
BRENTUXIMAB VEDOTIN [VANDF]
SGN-35
BRENTUXIMAB VEDOTIN [WHO-DD]
BRENTUXIMAB VEDOTIN [USAN]

Codes: CAS: *914088-09-8*
WHO-ATC: *L01XC12*
EVMPD: *SUB32397*
ChEMBL: *CHEMBL1742994*

Relationships: 7

Created: 3 months ago
Last modified: 3 months ago
Status: Validated (UNII)
Version: 18

Subunits: 4

- BRENTUXIMAB VEDOTIN [7XL5ISS668]
  - BRENTUXIMAB VEDOTIN [7XL5ISS668]

Monoclonal Anitibody: Sequence Subunit 1

CBG MEB

Subunits 4

Subunit 1

```
                10                  20                  30                  40                  50
QIQLQQSGPE  VVKPGASVKI  SCKASGYTFT  DYYITWVKQK  PGQGLEWIGW
                60                  70                  80                  90                 100
IYPGSGNTKY  NEKFKGKATL  TVDTSSSTAF  MQLSSLTSED  TAVYFCANYG
               110                 120                 130                 140                 150
NYWFAYWGQG  TQVTVSAAST  KGPSVFPLAP  SSKSTSGGTA  ALGCLVKDYF
               160                 170                 180                 190                 200
PEPVTVSWNS  GALTSGVHTF  PAVLQSSGLY  SLSSVVTVPS  SSLGTQTYIC
               210                 220                 230                 240                 250
NVNHKPSNTK  VDKKVEPKSC  DKTHTCPPCP  APELLGGPSV  FLFPPKPKDT
               260                 270                 280                 290                 300
LMISRTPEVT  CVVVDVSHED  PEVKFNWYVD  GVEVHNAKTK  PREEQYNSTY
               310                 320                 330                 340                 350
RVVSVLTVLH  QDWLNGKEYK  CKVSNKALPA  PIEKTISKAK  GQPREPQVYT
               360                 370                 380                 390                 400
LPPSRDELTK  NQVSLTCLVK  GFYPSDIAVE  WESNGQPENN  YKTTPPVLDS
               410                 420                 430                 440                 446
DGSFFLYSKL  TVDKSRWQQG  NVFSCSVMHE  ALHNHYTQKS  LSLSPG
```

Subunit 2

```
                10                  20                  30                  40                  50
```

Monoclonal Anitibody: Sequence Search, subunit 1

CBG MEB

Sequence Search

Search Identity: 0.65

Cutoff Type: Contains Alignment Match

Sequence Type: Protein

Query Sequence:

QIQLQQSGPEVVKPGASVKISCKASGYTFTDYYITWVKQKPGQGLEWIGWIYPGSGNTKYNEKFKGKATLTVDTSSSTAFMQLSSLTSE
DTAVYFCANYGNYWFAYWGQGTQVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG
LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRD
ELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP
G

Clean Sequence

Search

Monoclonal Anitibody: Sequence Search, subunit 1, Results

Sort By: Sort By

A10SJL62JY
Protein
OCRELIZUMAB

NYM5HO7I39
Protein
LONCASTUXIMAB

SK1LVT23A1
Protein
ELEZANUMAB

3A189DH42V
Protein
ALEMTUZUMAB

B800Z06O8K
Protein

H5324S1M7H
Protein

3S25202Z4X
Protein

6T8C155666
Protein

INFORMATION FLOW (HIGH LEVEL) & REQUIREMENTS TO REGISTER

- Organism Name
- Herbal substance (fresh)
  - Herbal substance (fresh), SSG 1, 2, 3 if needed
- Herbal drug (as described in a Pharmacopoeia)
  - Herbal drug, SSG 1, 2, 3
- Herbal preparation Substance level
  - Herbal preparation, SSG 1, 2, 3, 4
- Pre-registration of Constituents

OVERVIEW OF THE NAMING OF BOTANICAL MATERIAL AT THE SUBSTANCE AND SPECIFIED SUBSTANCE LEVELS

SUBSTANCE LEVEL

Substance (Fresh)
Definition: <Scientific genus/binomial/trinomial with Author>, <Part/s>
Example: *Ginkgo biloba* L., Leaf

SPECIFIED SUBSTANCE GROUP 1 LEVEL

Specified Substance Group 1 (Fresh)
Definition: <Scientific genus/binomial/trinomial **without** Author>, <Part/s>, <Fresh>
Example: *Ginkgo biloba*, Leaf, Fresh

Comment: This applies on the condition the substance (Fresh) does not have a corresponding monograph in a pharmacopoeia and has a Herbal Preparation (e.g. exudates, juices, etc.)

SPECIFIED SUBSTANCE GROUP 2 LEVEL

Specified Substance Group 2 (Fresh)
Definition: <Scientific genus/binomial/trinomial **without** Author>, <Part/s>, <Fresh>, <Manufacturer who harvests the Substance>
Example: *Ginkgo biloba*, Leaf, Fresh, CompanyXYZ S.A.

SUBSTANCE LEVEL

Substance (usually Dry, may be Fresh), (= **Herbal Drug**)
Definition: <Scientific genus/binomial/trinomial **without** Author>, <Part/s>
Example: *Ginkgo biloba*, Leaf

SPECIFIED SUBSTANCE GROUP 1 LEVEL

Specified Substance Group 1 (=**Herbal Drug**)
Definition: <Scientific genus/binomial/trinomial **without** Author>, <Part/s>, <Fresh/Dry>
Example: *Ginkgo biloba*, Leaf, Dry

SPECIFIED SUBSTANCE GROUP 2 LEVEL

Specified Substance Group 2 (=**Herbal Drug**)
Definition: <Scientific genus/binomial/trinomial **without** Author>, <Part/s>, <Fresh/Dry>, <Manufacturer who harvests/collects/stores the Herbal Drug>
Example: *Ginkgo biloba*, Leaf, Dry, CompanyXYZ S.A.

SPECIFIED SUBSTANCE GROUP 3 LEVEL (Pharmacopoeial GRADE)

Specified Substance Group 3 (=Herbal Drug)
Definition: <Scientific genus/binomial/trinomial **without** Author>, <Part/s>, <Fresh/Dry>, <EP/USP>
Example: *Ginkgo biloba*, Leaf, Dry- (EP/USP):
GRADE Name = Ginkgo Leaf

SUBSTANCE LEVEL

Substance (Herbal preparation)
Definition: <Scientific genus/binomial/trinomial **without** Author>, <Part/s>, <Fraction>
Example 1: *Ginkgo biloba*, Leaf, Extract (or Oil/Juice)
Example 2: *Mentha piperita*, Whole Plant, Oil

SPECIFIED SUBSTANCE GROUP 1 LEVEL

Specified Substance (Herbal preparation) [**Extended** information]
Definition: <Scientific genus/binomial/trinomial **without** Author>, <Part/s>, <Fraction>
[**Fraction** = <Dry/Liquid/Viscous Extract>, <extraction solvent composition/ unit>,<Herbal Substance (Herbal Drug)-Extract (mass) Ratio (DER)]
Example: *Ginkgo biloba*, Leaf, Dry Extract, Acetone-Water (60-40 w/w),(37-65: 1)

Limited or Extended Information

SPECIFIED SUBSTANCE GROUP 1 LEVEL

Specified Substance (Herbal preparation) [**Limited** information]
Definition: <Scientific genus/binomial/trinomial **without** Author>, <Part/s>, <Fraction>
[**Fraction** = <Dry/Liquid/Viscous Extract> or <Oil, Essential Oil, Juice>]
Example 1: *Ginkgo biloba*, Leaf, Liquid Extract/Viscous Extract/Dry Extract
Example 2: *Mentha piperita*, Whole aerial Plant, Essential Oil

SPECIFIED SUBSTANCE GROUP 2 LEVEL

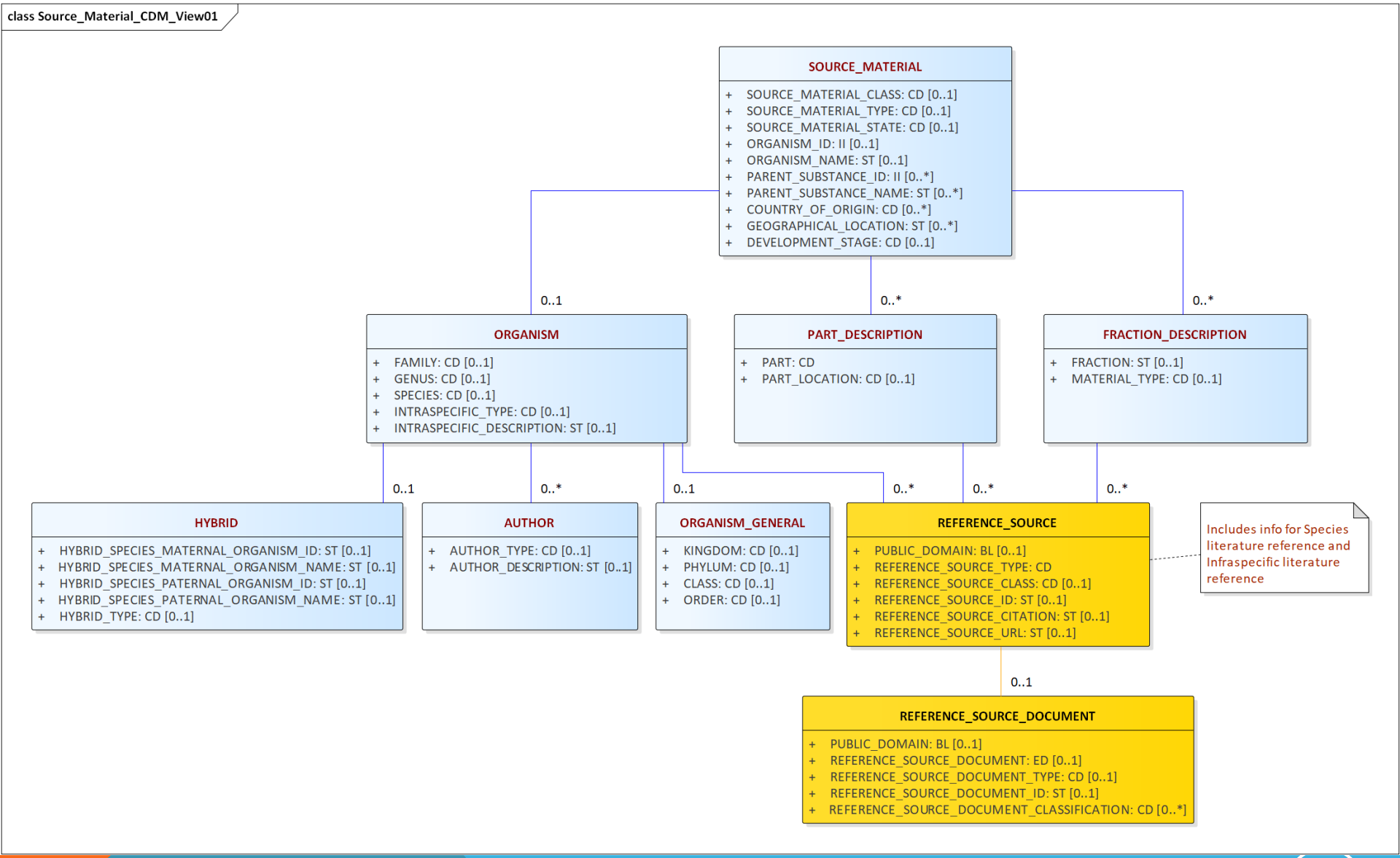
Specified Substance Group 2 (Herbal preparation) [**Limited** information]
Definition: <Scientific genus/binomial/trinomial **without** Author>, <Part/s>, <Fraction>-<Manufacturer of the Herbal Preparation>
Fraction = <Dry/Liquid/Viscous Extract> or <Oil, Essential Oil, Juice>
Example 1: *Ginkgo biloba*, Leaf, Liquid Extract/ Viscous Extract/ Dry Extract, CompanyOPQ S.A.
Example 2: *Mentha piperita*, Whole aerial Plant, Essential Oil, CompanyLMA S.A.

SPECIFIED SUBSTANCE GROUP 3 LEVEL (Pharmacopeial GRADE)

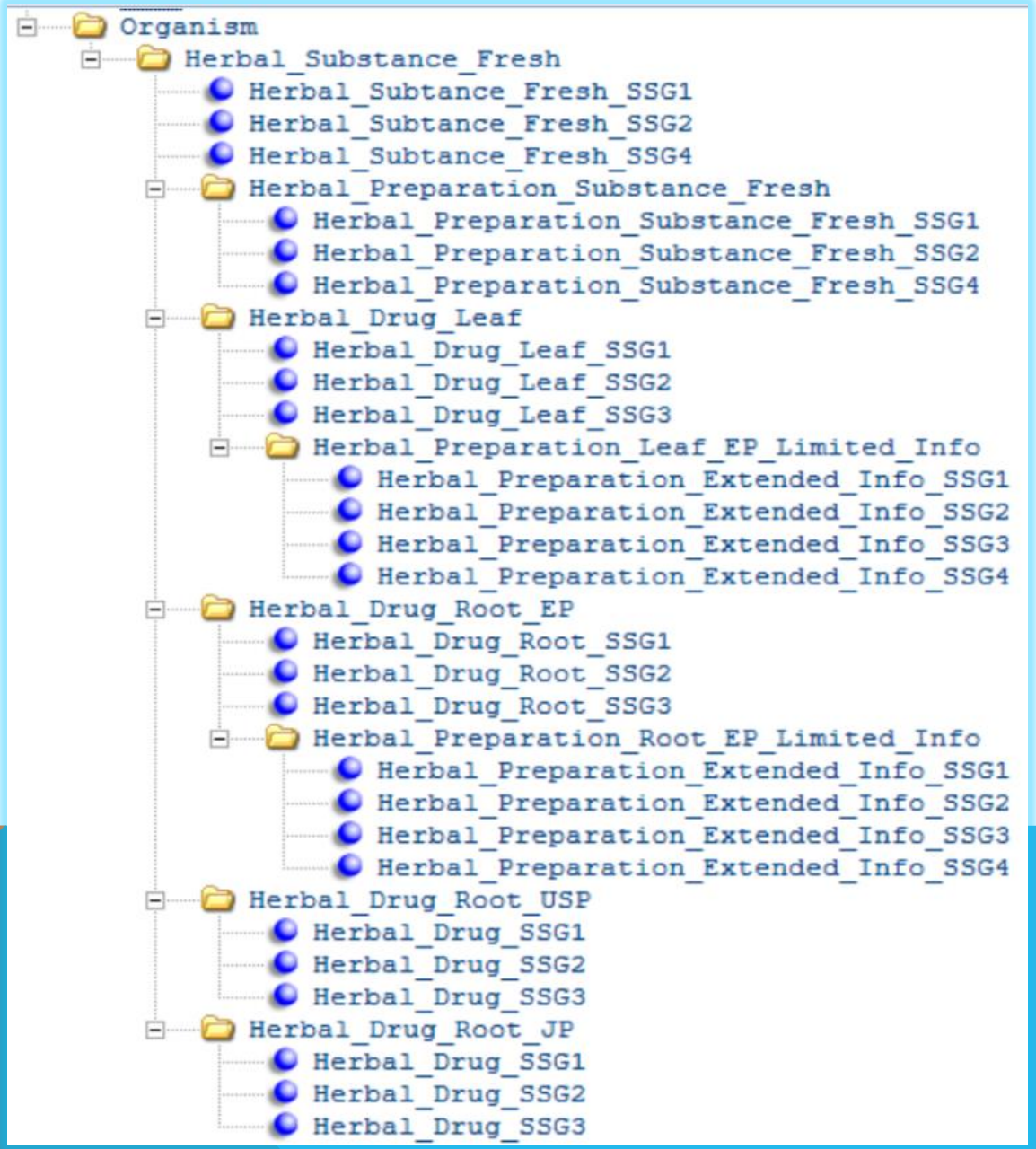
Specified Substance Group 3 (Herbal preparation) [**Limited/Extended** information]
Definition: <Scientific genus/binomial/trinomial **without** Author>, <Part/s>, <Fraction>, <EP/USP>
Limited Information: [**Fraction** = <Dry/Liquid/Viscous Extract> or <Oil, Essential Oil, Juice>]
Extended Information: [Fraction = <extraction solvent composition/ unit>,<Herbal Substance (Herbal Drug)-Extract (mass) Ratio (DER)]
Example: *Ginkgo biloba*, Leaf, Dry Extract, Acetone-Water (60-40 w/w),(37-65:1)- (EP/USP):
EP GRADE Name = Ginkgo Leaf refined Dry Extract, quantified

by Herman Diederik & Panagiotis Telonis, Sep 2016

SOURCE MATERIAL, DETAILED INFORMATION



INFORMATION FLOW: TERMS AND ID'S FOR STRUCTURALLY DIVERSE SUBSTANCES/SPECIFIED SUBSTANCES IN EU-SRS



REPORT TO SMS (2)

Assignment of Active substance Preferred term to be used in SMS:

[ID= SSG1E-UTWER8419E]; Active substance Preferred term:

***Puerariae lobatae,* root , dry extract, Ethanol-Water (85-15v/v), (DER 7.8-8.5=1)**

- *Pueraria montana var. lobata* (Willd.), Maesen & S.M. Almeida ex Sanjapp a & Predeep, (Whole) = **EUSUB-PUERT23456 (Organism)**
- *Pueraria montana var. lobata* (Willd.), Maesen & S.M. Almeida ex Sanjappa & Predeep, Root = **EUSUB-OYURT89765 (Subst Fresh)**
- *Puerariae lobatae*, root = **EUSUB-12345678HS (Herbal drug)**
- ***Puerariae lobatae*, root, dried, fragmented = SSG1E-JKHGR45327 (SSG1, Herbal drug)**
- ***Puerariae lobatae*, root, dried, fragmented-Company B, China = SSG2E-HJGYS78453 (SSG2, Herbal drug)**
- ***Puerariae lobatae*, root--Ph.Eur. = SSG3E-LDGQP45281 (SSG3, Herbal drug)**
- *Puerariae lobatae*, root, dry ethanolic extract = **EUSUB-PUEHP74521 (Herbal preparation)**
- ***Puerariae lobatae*, root , dry extract, Ethanol-Water (85-15v/v), (7.8-8.5=1) = SSG1E-UTWER8419E (SSG1, Herbal preparation)**
- ***Puerariae lobatae*, root , dry extract, Ethanol-Water (85-15v/v),(7.8-8.5=1)-Company B, China = SSG2E-MANUF74532 (SSG2, Herbal preparation)**
- ***Puerariae lobatae*, root ,dry extract, Ethanol-Water (85-15v/v),(7,8-8.5=1)-V001 (SSG4, Herbal preparation)**

Herbals: Organism/ Herbal Substance/ Herbal Drug/ Extracts, Hierarchy

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SAFFRON CROCUS EXTR...

E849G4X5YJ

CONCEPT

Names: CROCUS SATIVUS STIGMA EXTRACT
FEMA NO. 2999
SAFFRON CROCUS EXTRACT
CROCUS SATIVUS EXTRACT [WHO-DD]
CROCUS SATIVUS STIGMA EXTRACT [INCI]

Relationships: 1

Created: 3 months ago
Last modified: 3 months ago
Status: non-approved
Version: 1

- SAFFRON [E849G4X5YJ]
  - SAFFRON [E849G4X5YJ]
  - **SAFFRON CROCUS EXTRACT [E849G4X5YJ]**
- CROCUS SATIVUS WHOLE [Z5C927G4XF]
  - CROCUS SATIVUS FLOWER [00IF91KFKQ]
    - CROCUS SATIVUS FLOWER EXTRACT [00IF91KFKQ]
  - SAFFRON OIL [56H35HBB69]
  - SAFFRON [E849G4X5YJ]
    - SAFFRON [E849G4X5YJ]
    - **SAFFRON CROCUS EXTRACT [E849G4X5YJ]**

EU-SRS Signature fields

- Definition:
  - Signature fields describe field values containing Essential Characteristics of a substance or specified substance used for unambiguous description of a substance or specified substance;
  - Signature fields are not used for exhausting definition of the substance giving a 100% unique identified substance, but provide a ‘fingerprint’ of the characteristics covering the overall, but not complete defining identity of a substance;
  - Selection of the Signature fields does NOT replace the ISO 11238 standard or ISO 19844 TS

Fields taken from (specified) Substance information levels

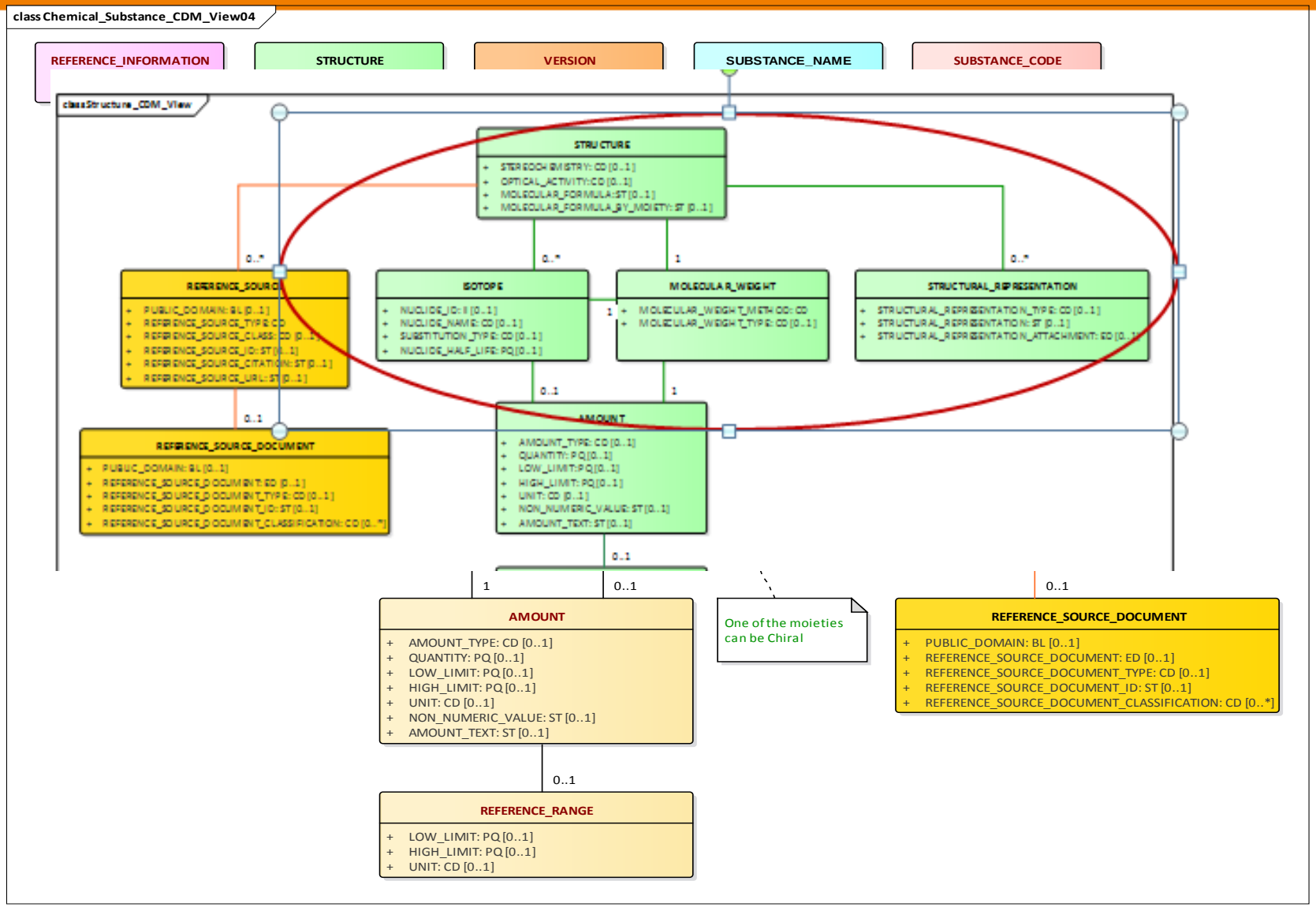
A) General Fields:

- EU-SRS ID; Preferred Name; Official Name;
  Systematic Name; CAS-RN; Codes and Reference Source information

B) Chemical fingerprint fields:

1. Structural Representation/ Isomeric SMILES
2. Molecular formula
3. Molecular formula by Moiety
4. Molecular weight
5. Physical form state/ type (e.g. solid, polymorphic form)
6. Characteristic attribute name (e.g. particle size,)
7. Production method type (e.g. extraction, semi-synthetic, fermentation, fractionation, biosynthetic)
8. Pharmaceutical Grade (e.g. Ph. Eur., USP, In-House

EU-SRS Signature fields, Ex. Chemical Substance

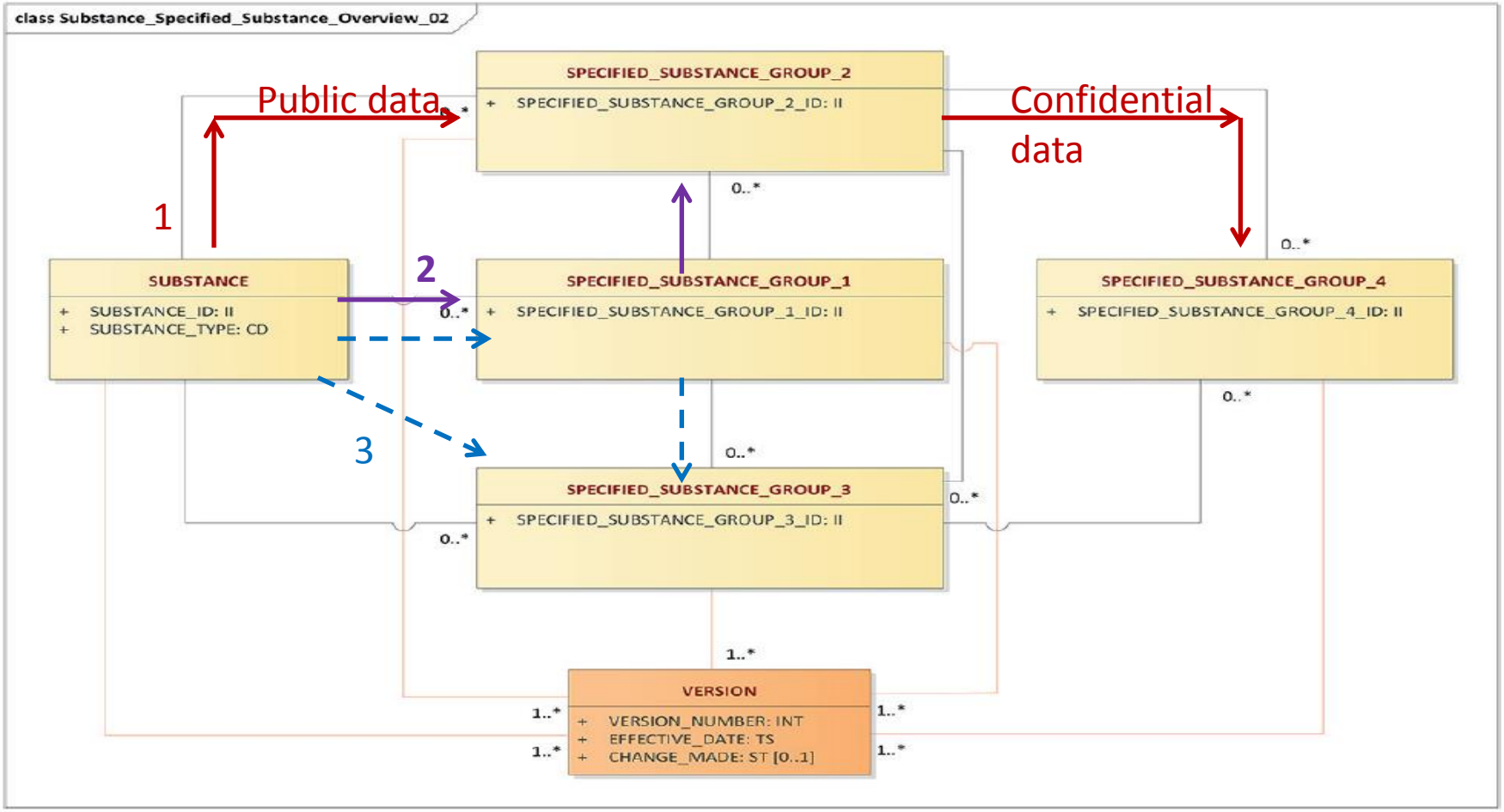


Stepwise approach in registering substances: Signature Fields

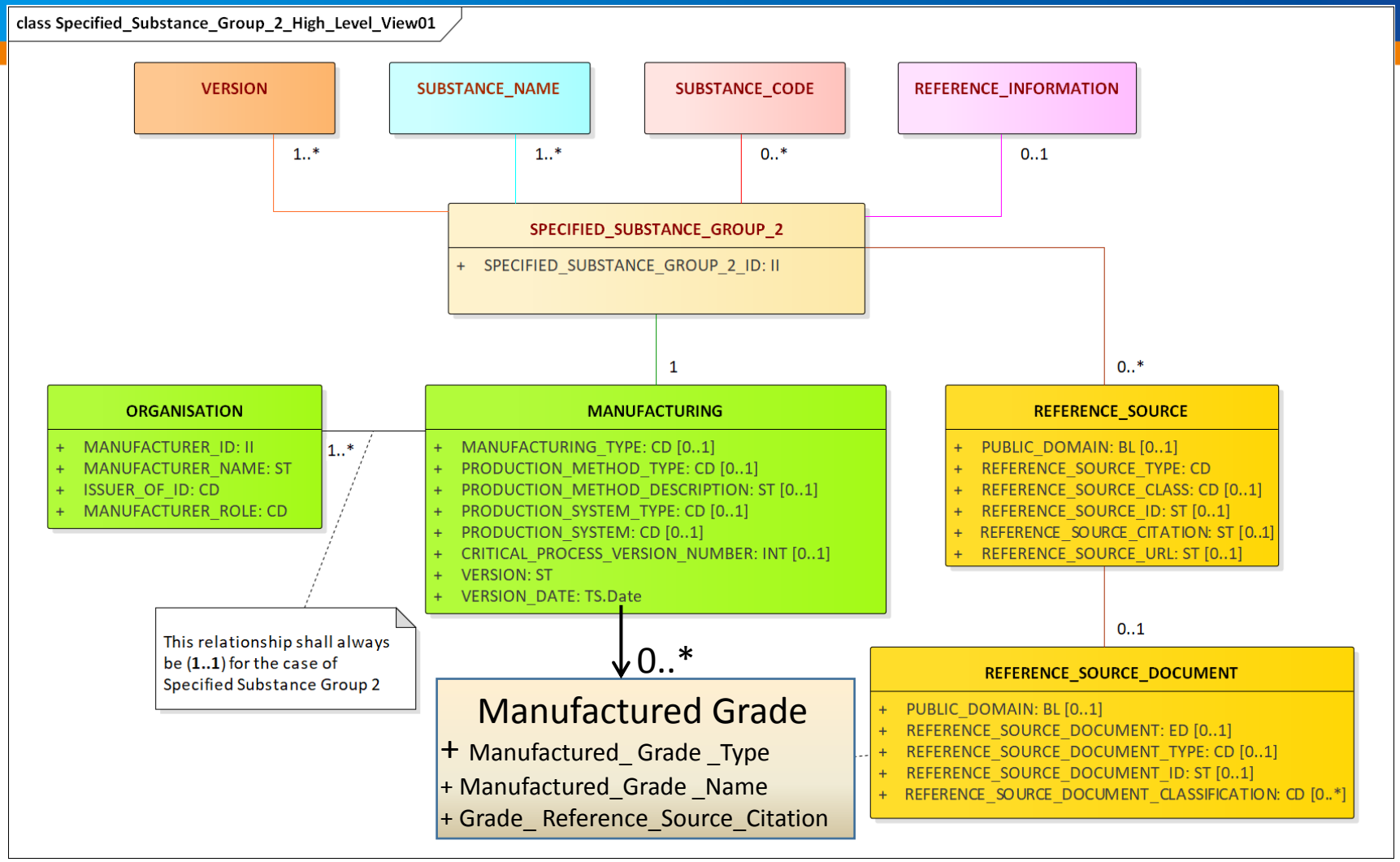
Class	Minimum signature fields to initially identify substance without general fields	Absolute minimum fields to identify substance
Chemicals	8	30
Proteins	14	73
Polymers	10	34
Nucleic acids	10	24
Vaccines	14	43
Advanced Therapies	10	43
Allergens	12	43
Homeopathics	6	43
Plasma Derived	10	43
Herbals	12	43
Mixture	10	15

If the substance needs to be created newly (to be identified) – you will need these fields to describe it (once)

Main Route from Substance to SSG4 Using the Highway 1 or 2, Incidental need for 3



Updated/ Revised Specified Substance Group 2



CBG MEB
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GOOD MEDICINES USED BETTER