



Overview of ISO IDMP, Substances and HL7 Patient Care WG (allergy-intolerance)

Joint HL7 Biomedical Research & Regulation WG and Patient Care WG Meeting, May 10, Madrid, Spain

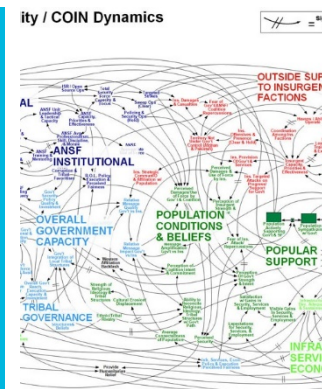
Panagiotis Telonis (EMA), Christian Hay (ISO/GS1), Herman Diederik (EMA/CBG), Larry Callahan (FDA), Frank Switzer (FDA), Tyler Peryea (NCATS/NIH), Noel Southall (NCATS/NIH)

1. High Level Overview of IDMP
2. Substances/ISO 11238/19844/G-SRS
3. HL7 PC - Allergy & Intolerance
4. Q&A and examples

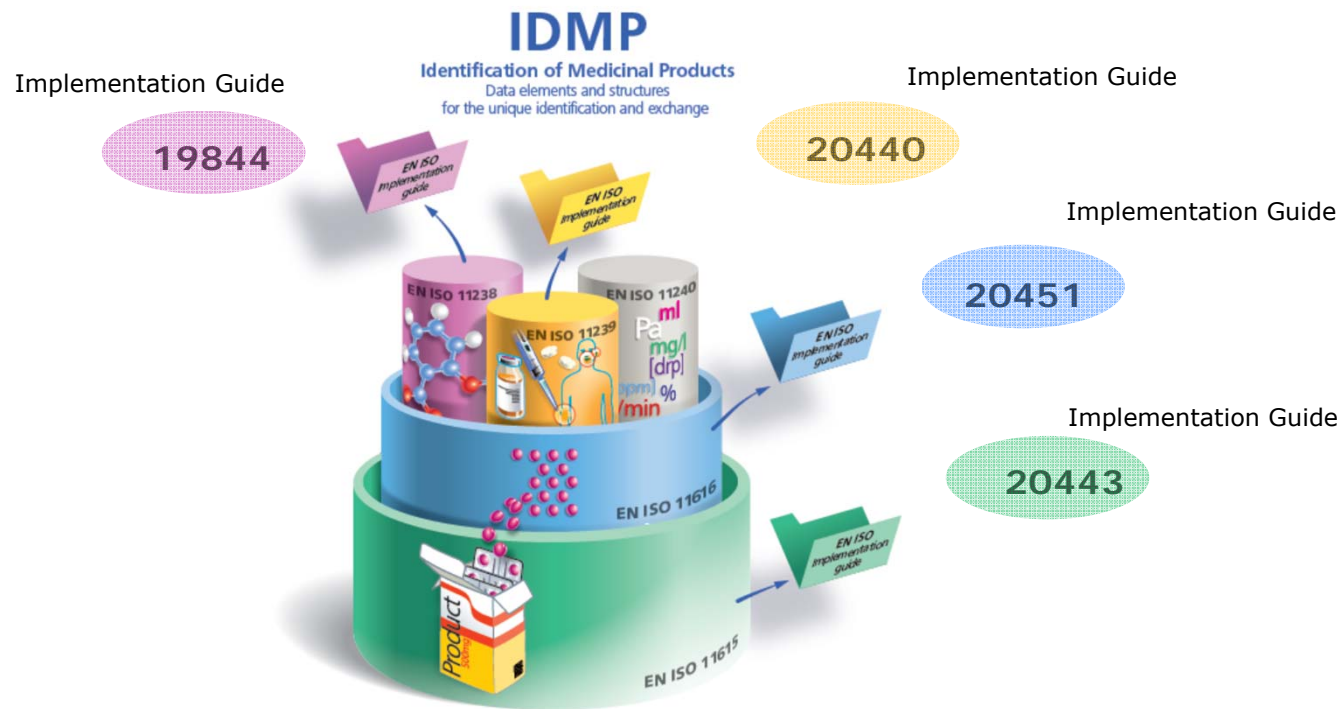


Overview of IDMP ...to introduce the discussion about allergies

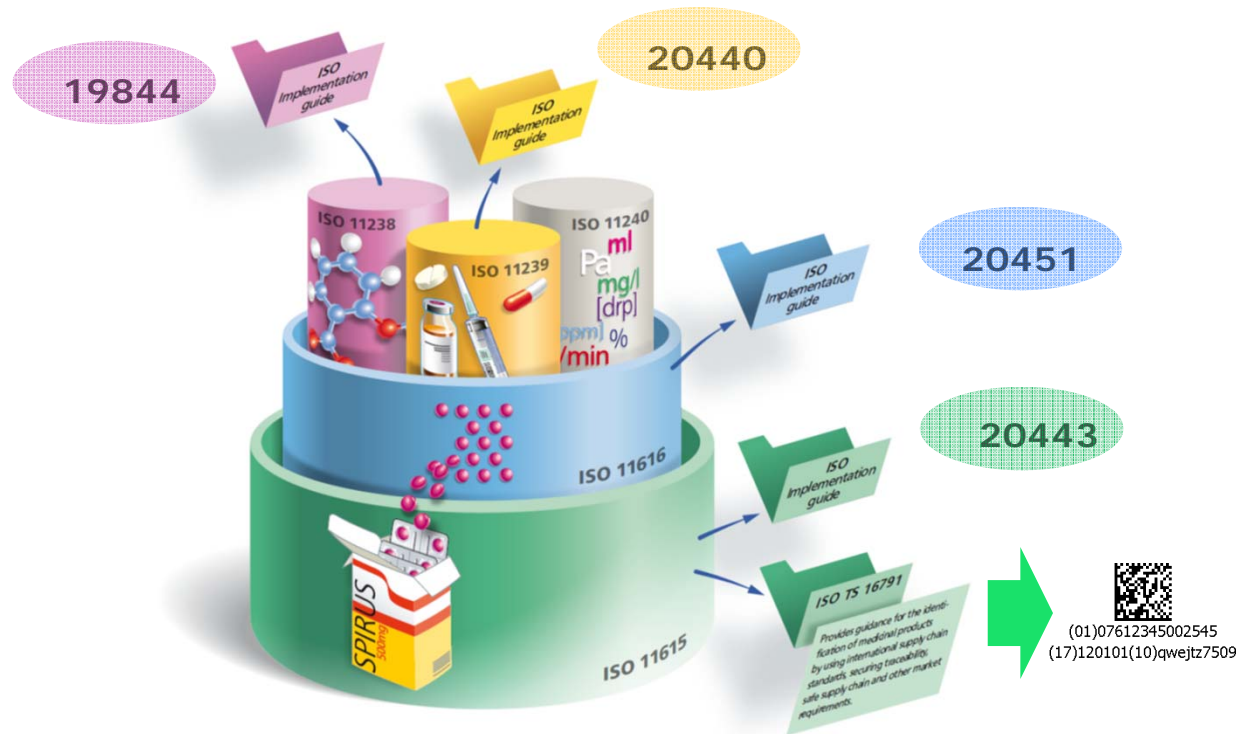
ity / COIN Dynamics



IDMP in a graphical representation



IDMP – the link to Supply Chain



DataMatrix, the preferred carrier



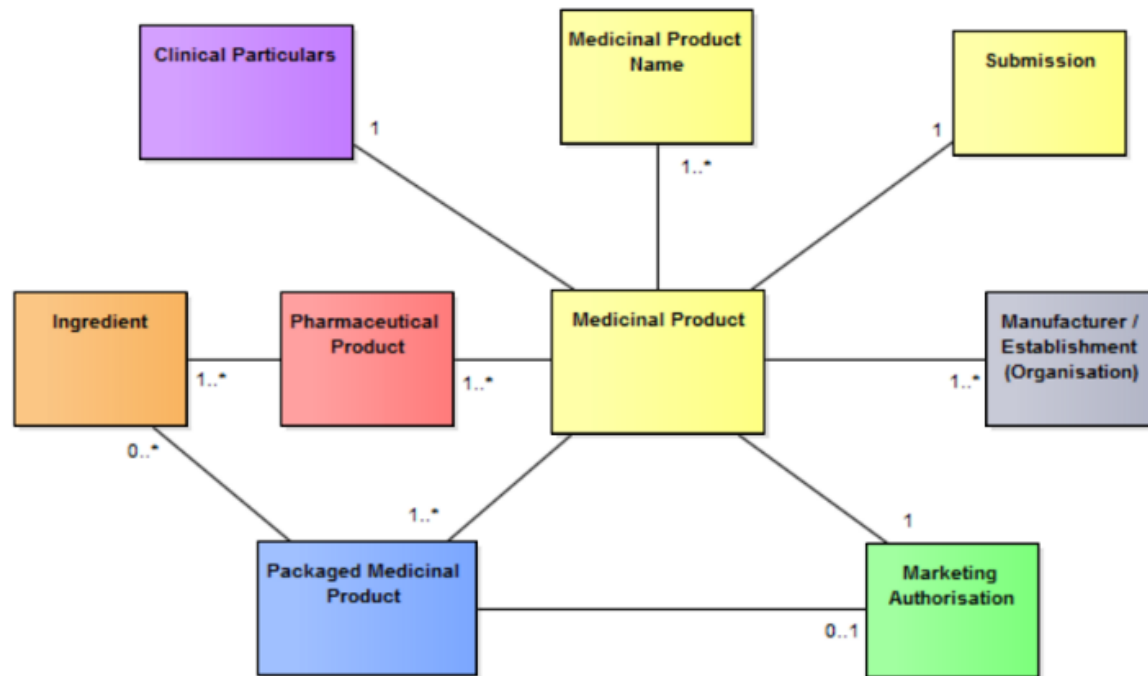
Product identifier (GTIN)

IDMP:
Packaged Item
Data Carrier Identifier
Code System* : 2.51.1.1
Value: 08699536160085

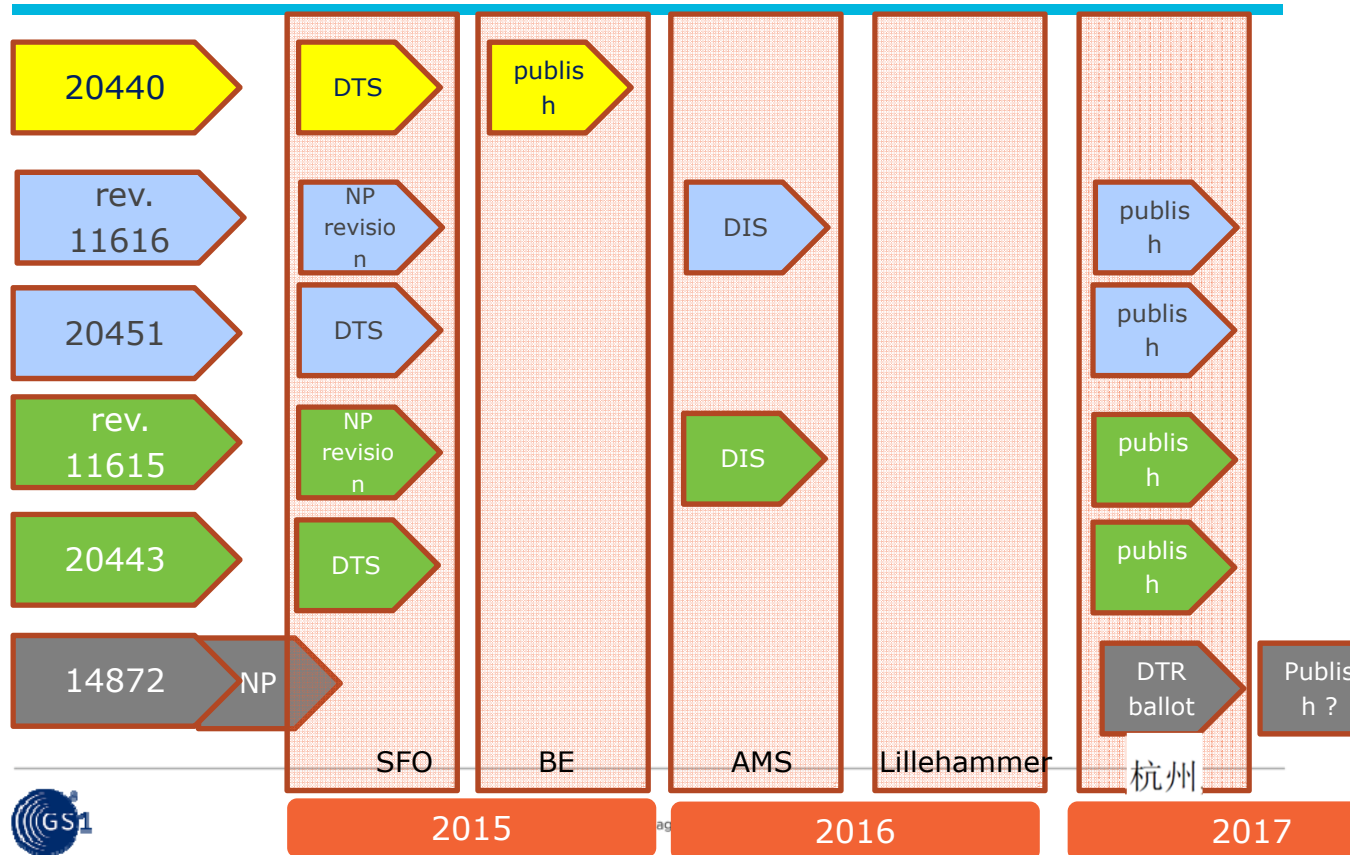
* OID for GS1 GTIN



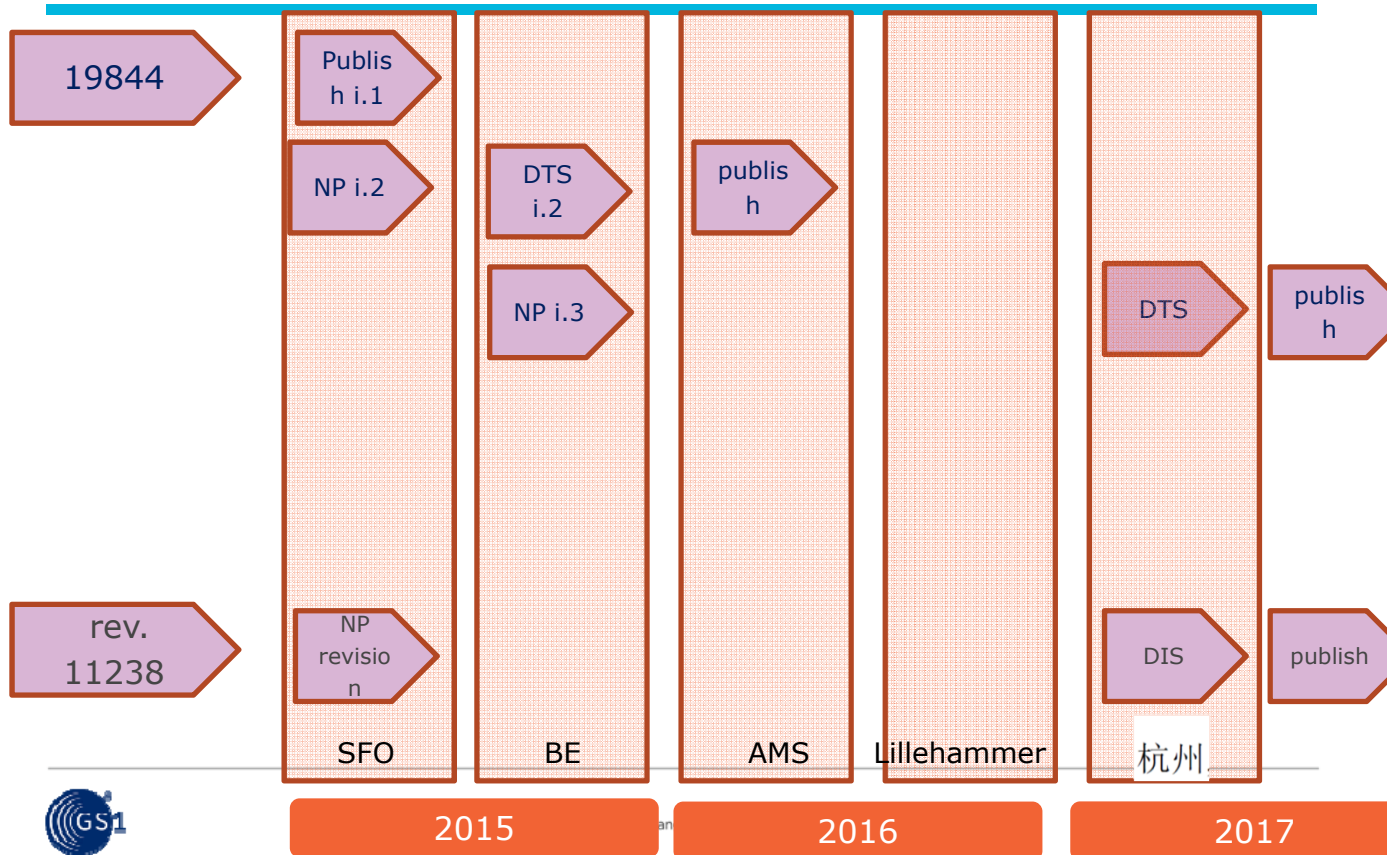
Medicinal Product overarching model



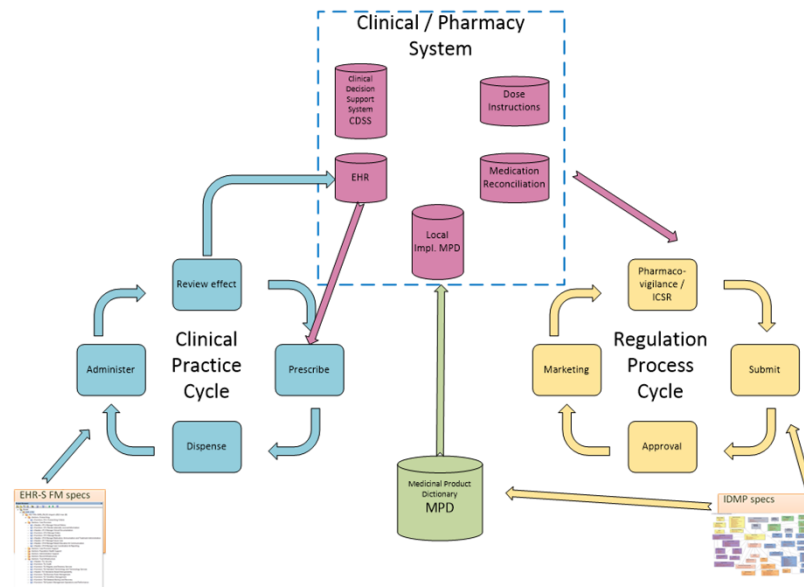
IDMP roadmap



IDMP roadmap

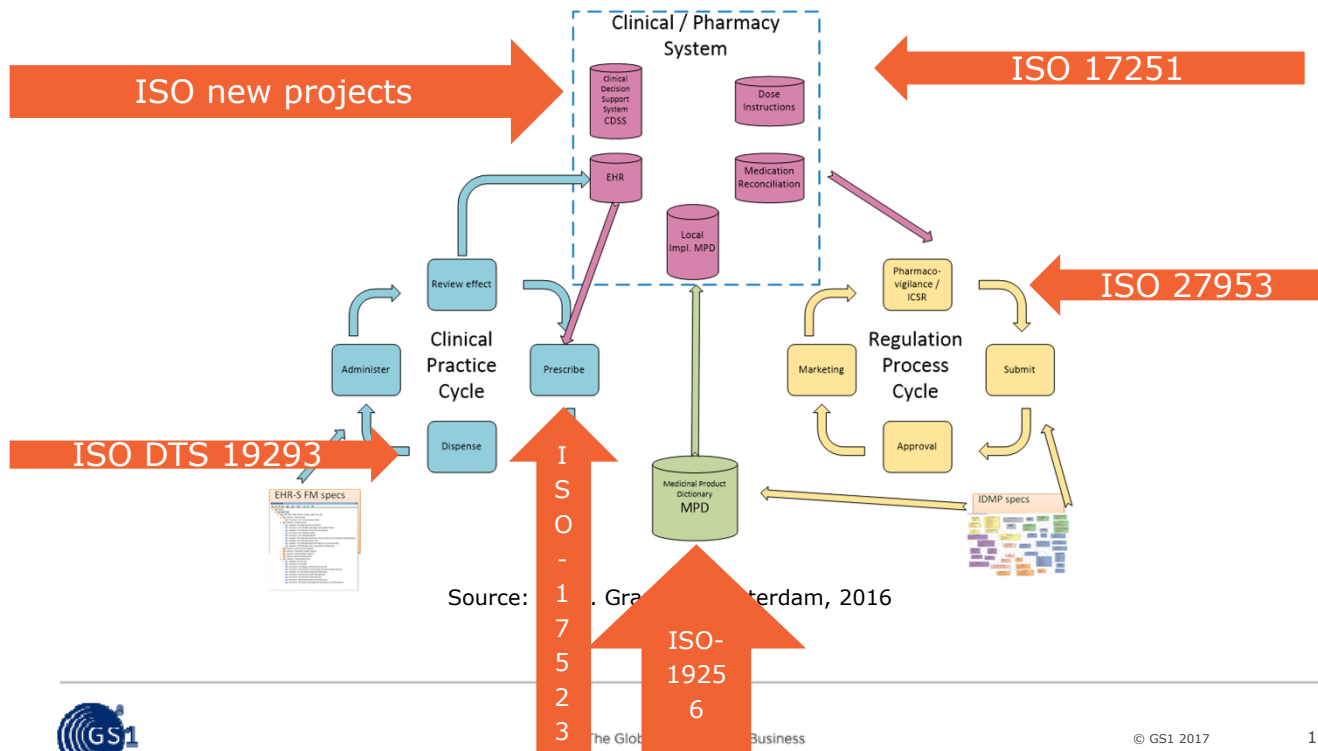


IDMP impact on Clinical Processes



Source: Dr. L. Grandia, Amsterdam, 2016

IDMP impact on Clinical Processes



Main IDMP identifiers



EUROPEAN MEDICINES AGENCY

ISO IDMP Global Harmonisation

Medicinal Product ID (MPID) 

- [Regional Identification](#)

Pharmaceutical Product ID (PhPID) [\(algorithm\)](#) 

- Based on core elements for identification of medicinal products

Substances 

- Global Substance Registration System [\(G-SRS\)](#)

Dosage forms and Routes of Administration 

- European Directorate for the Quality of Medicines [\(EDQM\)](#)

Units of measurement 

- Unified Code for Units of Measure [\(UCUM\)](#)



Why is substance (ID) important



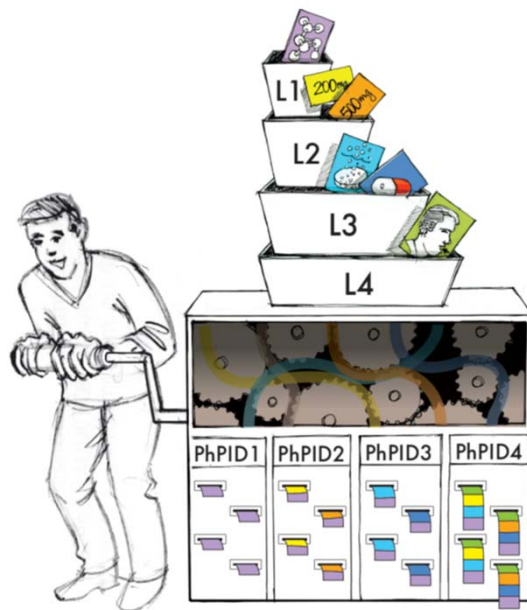
EUROPEAN MEDICINES AGENCY

Example: Paracetamol/Acetaminophen

• PhPID_SUB_L1 → paracetamol	• PhPID_SUB_L1 → paracetamol	• PhPID_SUB_L1 → paracetamol
• PhPID_SUB_L2 → paracetamol, 500 mg	• PhPID_SUB_L2 → paracetamol, 500 mg	• PhPID_SUB_L2 → paracetamol, 500 mg
• PhPID_SUB_L3 → paracetamol, tablet	• PhPID_SUB_L3 → paracetamol, caplet	• PhPID_SUB_L3 → paracetamol, capsule
• PhPID_SUB_L4 → paracetamol, 500 mg, tablet	• PhPID_SUB_L4 → paracetamol, 500 mg, caplet	• PhPID_SUB_L4 → paracetamol, 500 mg, capsule



Substance ID as food for PhPID generation



- PhPID_SUB_L1 → paracetamol
- PhPID_SUB_L2 → paracetamol, **500 mg**
- PhPID_SUB_L3 → paracetamol, **tablet**
- PhPID_SUB_L4 → paracetamol, **500 mg, tablet**

Four levels of Information

- ❖ Substance (Global Unique identifier)
- ❖ Specified Substance (Global/can be implemented per Jurisdiction Regional)
- ❖ Pharmaceutical Product (Global Identifier) substance, strength, dosage form
- ❖ Medicinal Product (Regional per Jurisdiction)

NOTE: ISO 11238 standard and ISO/TS 19844 within ISO IDMP suite address both Substances and Specified Substances

ISO/DIS 11238 (revision of ISO 11238:2012)

ISO/TS 19844 (revision of ISO/TS 19844:2016)



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ISO/DIS 11238

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

Current status: Under development

Edition: 2 Number of pages: 57

Technical Committee: ISO/TC 215 Health Informatics

ICS: 35.240.80 IT applications in health care technology

Substances/Specified Substances -
the most challenging aspect of the
IDMP

General information

Current status: Under development

Edition: 2 Number of pages: 57

Technical Committee: ISO/TC 215 Health Informatics

ICS: 35.240.80 IT applications in health care technology

Life cycle

A standard is reviewed every 5 years

00 10 20 30 **40.00 Enquiry** 50 60 90 95

Revisions / Corrigenda

Previously
ISO 11238:2012

Now under development
ISO/DIS 11238

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ISO/AWI TS 19844

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

Current status: Under development

Edition: 3

Technical Committee: ISO/TC 215 Health Informatics

ICS: 35.240.80 IT applications in health care technology

General information

Current status: Under development

Edition: 3

Technical Committee: ISO/TC 215 Health Informatics

ICS: 35.240.80 IT applications in health care technology

Life cycle

A standard is reviewed every 5 years

00 10 **20.00 Preparatory** 30 40 50 60 90 95

Revisions / Corrigenda

Previously
ISO/TS 19844:2015

Now under development
ISO/AWI TS 19844

Substance

- ❖ Is defined on **what the substance is** (*e.g.* its main and general characteristics).
- ❖ Can have different roles *e.g.* active, adjuvant, basis of strength, excipient

Specified Substance

- ❖ More **granular, specific description of a substance** and **may have defining elements** *e.g.* including manufacturing information, purity, grade
- ❖ **Allows for the specification of multiple substances** (“Intermediate Products” *e.g.* AS03 - adjuvant composed of squalene (10.69 milligrams), DL- α -tocopherol (11.86 milligrams) and polysorbate 80 (4.86 milligrams))

G-SRS (open source)

- ❖ Provides a common tool and a repository of definitional substance information
- ❖ Will be linked to other information related to product/clinical trials/applications /quality /pharmacology
- ❖ It is freely distributable with bonus public domain information

Instead of relying on drug or chemical names which vary across countries, regions, jurisdictions, IDMP enables substances to be defined by standardised scientific descriptions. The substance is registered per type, as defined in the standard (e.g. chemicals, proteins, polymers, structurally diverse, nucleic acid, etc.) and then, certain criteria apply to distinguish substances in each category from one another (e.g., chemical structure, DNA sequence etc.). When enough information is available and validated, a substance is assigned a unique identification code, which can be used as a quick way to refer to that substance in the future.

- A Substance is defined based on **what something is** and **not on how it is made or, used**
 - Recombinant Salmon Calcitonin is the same substance as Synthetic Salmon Calcitonin
- A Substance is defined based on **immutable** properties independent of physical form, grade or level or purity
 - Most chemicals are defined by molecular structure
 - Proteins by their sequence and type of glycosylation
 - Complex materials from biological matrices that cannot be defined by a limited number of related chemical structures are defined based on taxonomic, anatomical and limited fractionation information

What is a Substance: Example

- ❖ Processes that irreversibly change the molecular structure results in a new substance
 - Hydrogenated castor oil is different from castor oil
 - An irreversibly-modification of a protein will be a different substance from a non-covalently modified protein
- ❖ Ambiguity will be limited
 - Vegetable oil would not be a substance need to specify the vegetable
 - Degree of polymerization or molecular weight needs to be specified for a polymer
 - Macrogol is not a substance but Macrogol 8000 is
 - Stereochemistry should be completely defined
- ❖ Materials that are defined as the same substance are not necessarily bioequivalent or pharmaceutical equivalents (Biosimilars are defined having the same amino acid sequence, but may differ for their Glycans).

❖ Five groups of elements are used to describe single substances.

- **Monodisperse***

- **Chemicals**

- Defined primarily by molecular structure (connectivity and stereochemistry)

- **Proteins**

- Amino Sequence, type of glycosylation, modifications

- **Nucleic Acids**

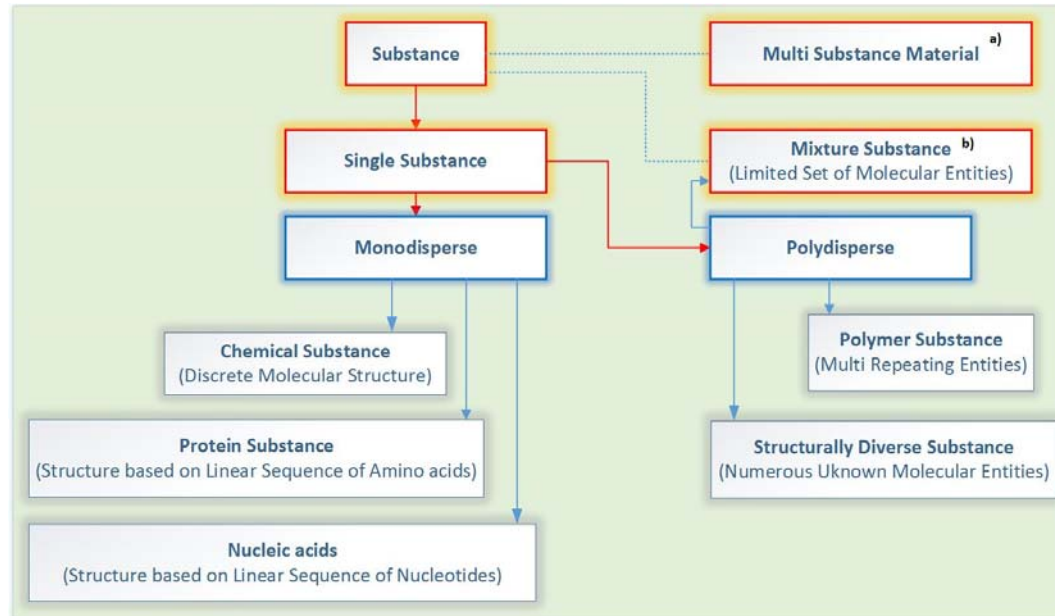
- Sequence, type of sugar and linkage, modifications

(*) Monodisperse substances are substances that can be described as a single molecular entity

- ❖ Five groups of elements are used to describe single substances (cont.)
 - **Polydisperse***
 - **Polymers** (Synthetic or biopolymers)
 - Structural repeating units, type, geometry, type of copolymer (block or random), ratio of monomers, modifications, molecular weight or properties related to molecular weight, biological source for many biopolymers.
 - **Structurally Diverse Substances**
 - Taxonomic, anatomical, fractionation, physical properties, modifications

(*) Polydisperse substances are substances that typically have multiple molecular entities that are too numerous or too diverse to be captured as a mixture (e.g. cells or tissues) or where the production of the substance inherently results in polydispersity (e.g. polymers).

Decision tree or process by which the type of substance is determined



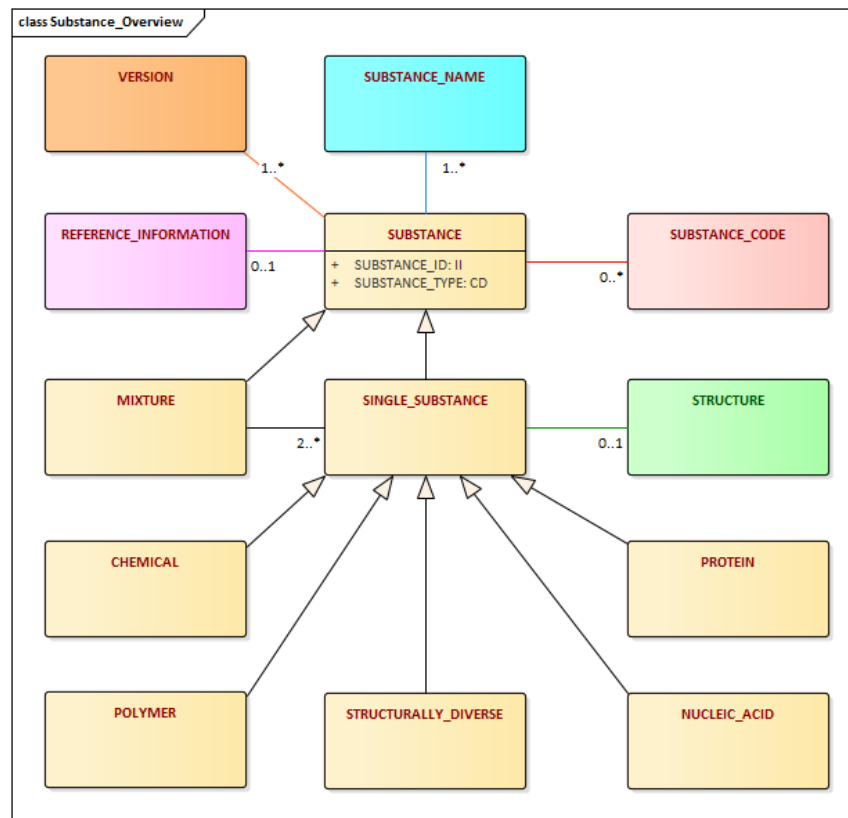
^a Multi-substance material: Multi Substances and/or Specified Substances of diverse origin.

^b Mixture: Type of polydisperse substance that is either a combination of single substances isolated together or synthesised/obtained or produced in the same process or an extract of a homologous group of substances (multi-substance starting material) resulting from the same synthetic process.

Source: ISO/TS 19844

- ❖ Mixture substances are described as simple combinations of related single substances that are either isolated together or are the result of the same synthetic process.
 - Proportions are not captured
 - Variations in amounts can be significant.
 - Specifications would be captured the specified substance level.
 - All single entities typically present in amounts greater than 1% either by weight or mole percent could be part of the mixture
- ❖ Diverse material that is brought together to form a product or intermediate product is not defined as a substance. (Simethicone is not a substance)

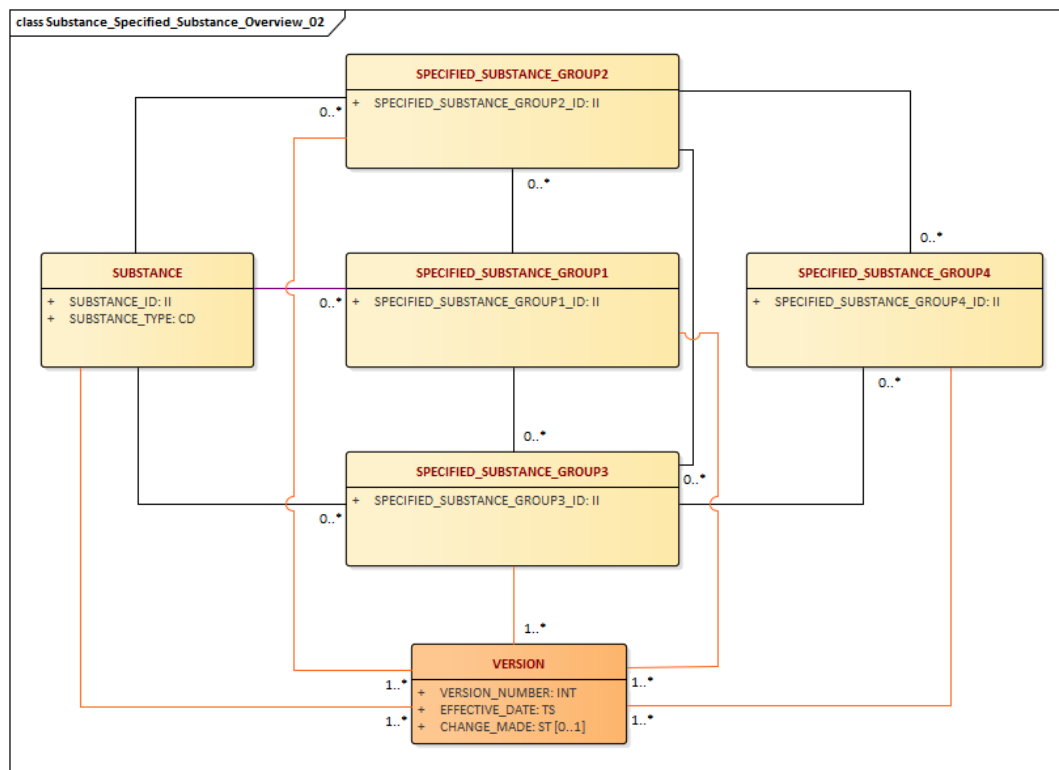
High level Substance model



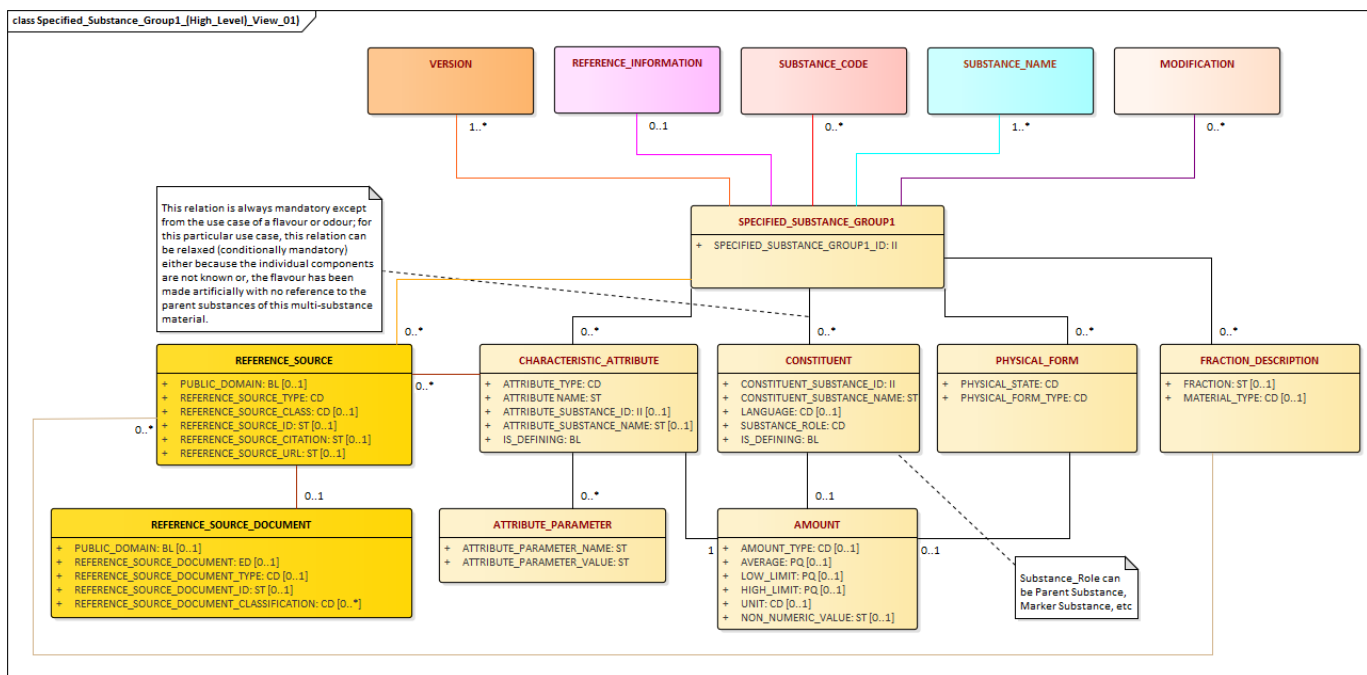
- ❖ Need to link material to a manufacturer and a process
- ❖ Need to tie material to a specific grade
- ❖ Need to obtain specification information
- ❖ Need to obtain information about processing materials
- ❖ Need to establish and monitor the supply chain

- ❖ **Specified Group 1:** Multiple substance materials (Coatings, Colorants, Flavorants); Physical Form; Extracts
- ❖ **Specified Group 2:** Manufacturer and minimal manufacturing information
- ❖ **Specified Group 3:** Grade of material (USP, EP, technical, standardized etc.)
- ❖ **Specified Group 4:**
 - Detailed manufacturing information
 - Specifications

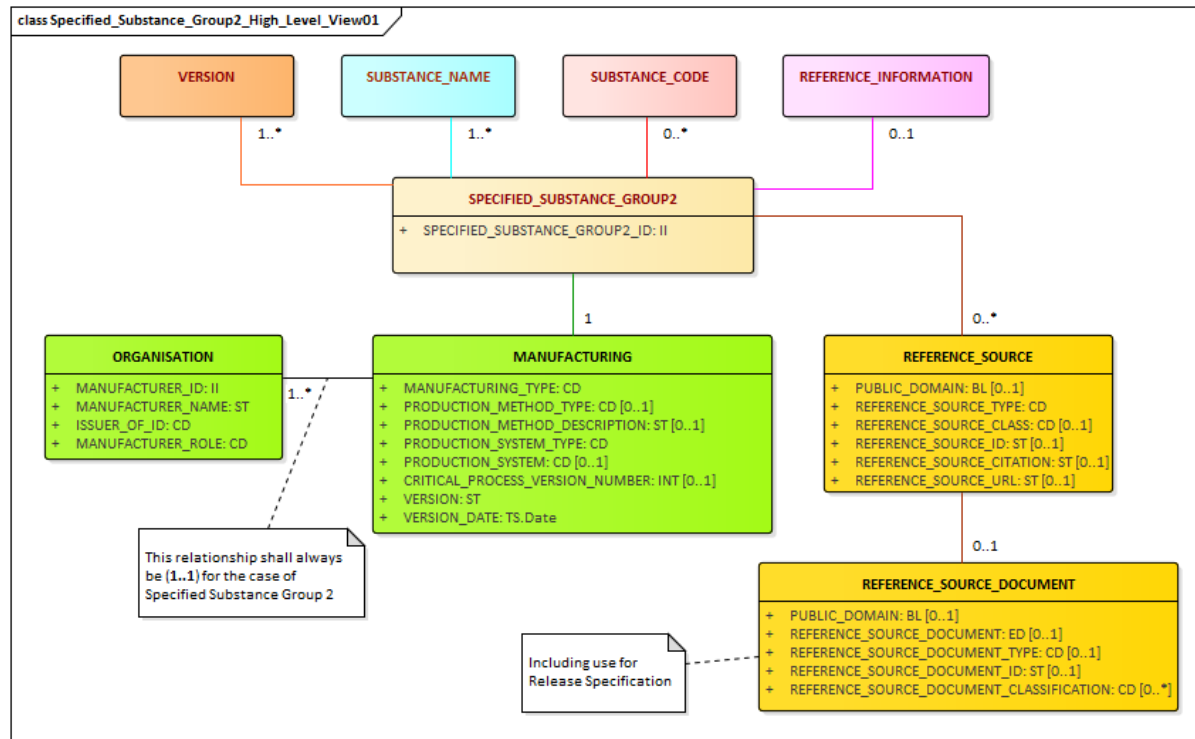
Specified Substance (high level)



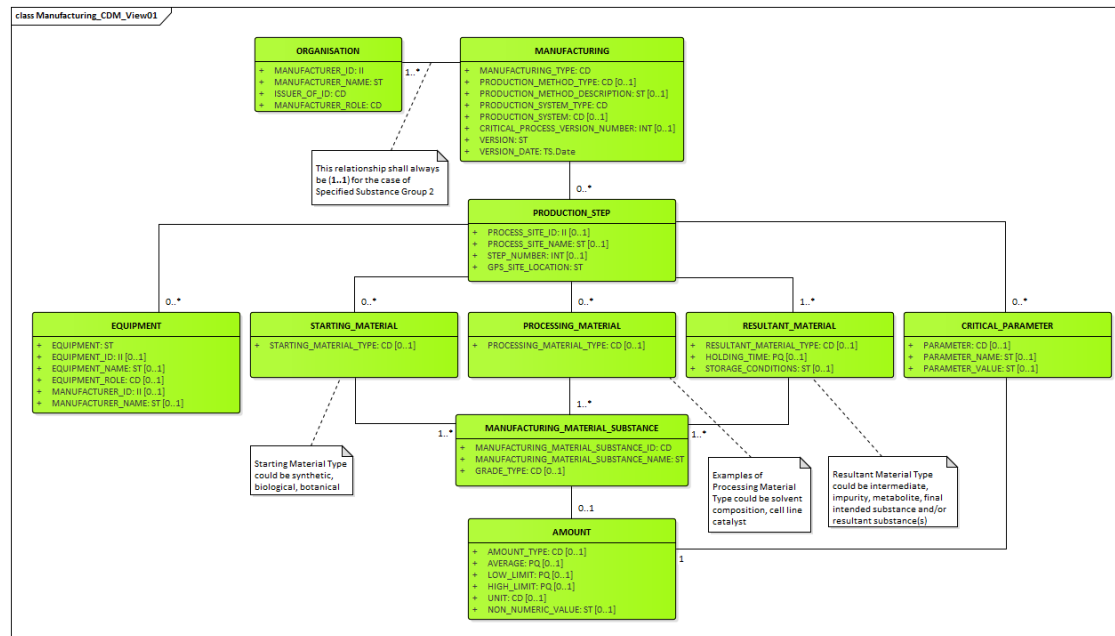
Specified Substance Group 1



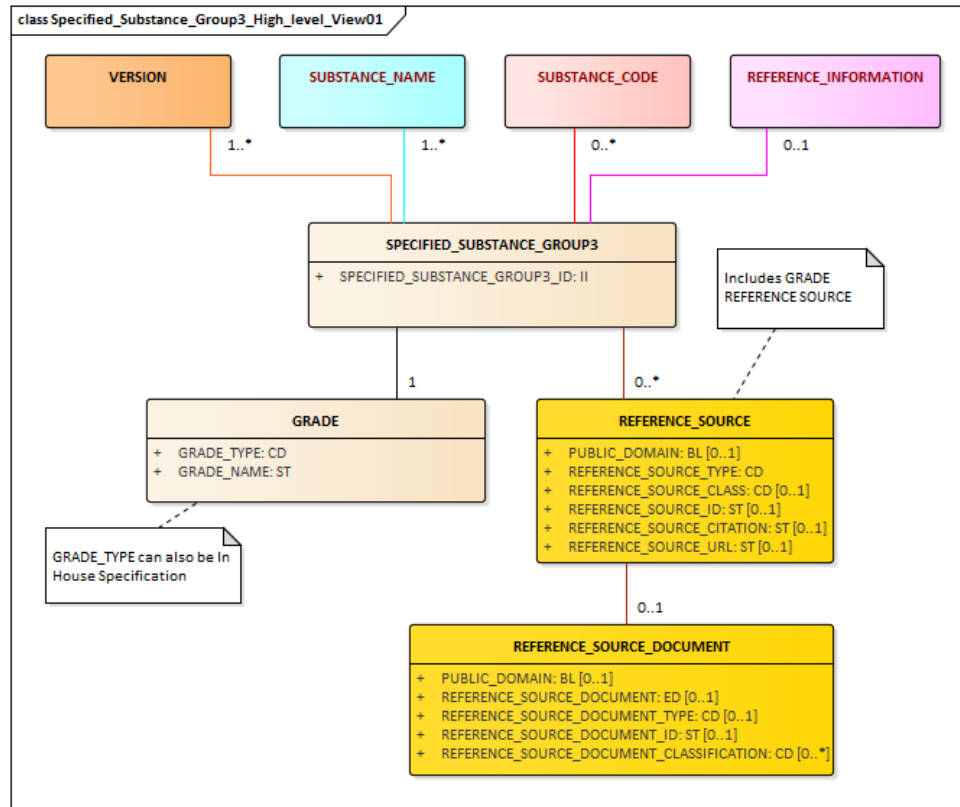
Specified Substance Group 2



Manufacturing Model



Specified Substance Group 3



HL7 Patient Care - Allergy & Intolerance Drug Sub-project



Allergy & Intolerance Drug Sub-project

Purpose

Produce a list of unique substances and multiple substance medications used in allergy & intolerance lists, ordered by frequency of incidence. This list will support the use of common elements for data capture and validation of data exchange. This list is not intended to prevent the recording of unusual substances where necessary, whether by code or text. We would like to provide a set of standard coded identifiers for these substances. The codes for such a list would need to be free, readily available, and accepted for use by international establishments. Note that the criterion is clinical use, not chemical specificity, i.e. if all we know is that the patient reports an allergy to "fish," that's what we can record. Similarly, if a patient has a reaction to penicillin, and the clinician doesn't have evidence that suggests identification of a specific ingredient, then "penicillin" is what we know.

Goal

- A list of substances ordered by frequency of incidence, with frequency codes
- Identifiers for these substances, using freely available standard identifiers

Plan

- Confirm goals
- Assess assets
- Estimate gaps
- Fill gaps

Open questions

1. Safe: We assume that salt forms are included, and that incidences recorded on salt forms should be recorded as general forms (e.g., ceftriaxone vs ceftriaxone sodium), is this always true?
 - a. Is it true for any other chemical modifications, e.g., salts? (Which would make require an instance of a salt/acid)
2. Classes
 1. For classes that are commonly assessed but do not actually designate cross-reactive substances, how do we proceed?
3. Negative
 1. Included contrast media
4. Scope
 1. Ingredients
 2. Active components
 3. Excipients/requirements
5. What systems should be used for encoding?
 1. International: do we need to choose, or can we provide a list of substances with all pertinent code assignments?
 2. Criteria
 1. Maximal coverage of identified requirements
 2. Ability to add missing items
 3. Freely available
 4. International
 3. Candidates
 1. SHIMED CT: substances, classes, includes only as products, Licensing issue
 2. RxNorm: medications & includes, no terms about salt/acid
 3. NDF-RT: classes only, Class definitions problematic
 4. UMLS: substances only, US terms, no relationships (e.g., of salts)
 5. ATC: classes only, Class definitions problematic
 6. WHO: no access to list, but
 7. Prepared to use substance Q-IDs (classes to use IIR available when available)

Specific Questions

1. Morphine derivatives, Morphine and related. List on Morphine and list drug checks every about a readability?
2. Beta Lactamase Inhibitors
3. Sulphonylureas: a class? other typical sulphonylureas? include SGLT?
 1. ADA (sulphonylureas)
4. Influenza virus vaccine, Inactivated (IN): CIV (seems too specific, but no general terms available for components)
5. Immunologic adjuvants, Classed?
 1. Adjuvants/SUPPLEMENTS
6. Tetanus Botulinum toxin vaccine, inactivated?
7. Insulin, Digitalin
8. Heparin, coded sulfate
9. Povidone Iodine
10. Inactivated glycerol
11. are very topical
12. Vaccines
13. vaccine and analogues
14. Topical/Inhalation, or like product?
15. Salt/Isotonic

Closed Questions

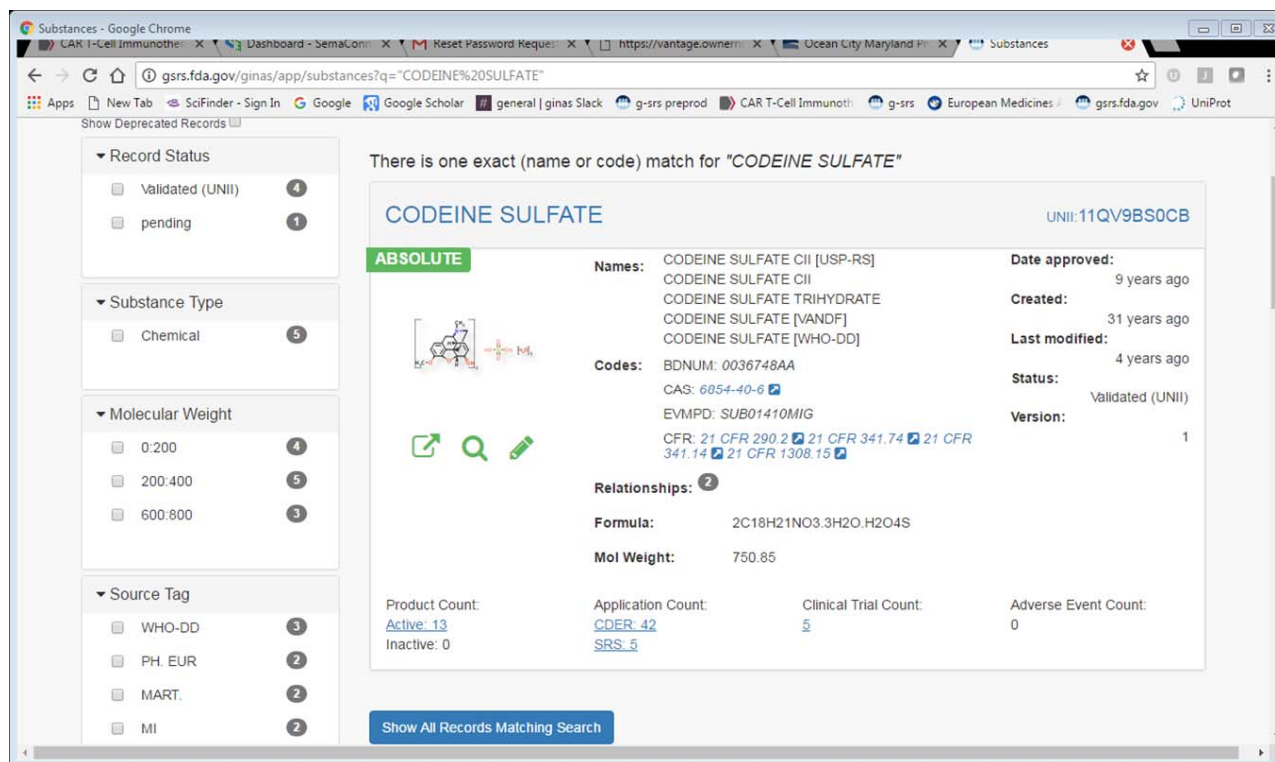
[http://wiki.hl7.org/index.php?title=Allergy %26 Intolerance Drug Sub-project](http://wiki.hl7.org/index.php?title=Allergy_%26_Intolerance_Drug_Sub-project)

Question: Salts: We assume that salt forms are irrelevant, and that incidences recorded as salt forms should be recorded as general forms (e.g., codeine vs codeine sulfate). Is this always true?

Answer: **This is not always true:**

- *Different salt forms can dramatically change the performance of a medicine*
- *Some salts will dramatically delay the absorption of a drug or change where a drug may be absorbed, the stability of a drug.*
- *Some drug allergies are not necessarily due to the drug but the impurities in the drugs and the salt form can have an effect on the impurities that will form over the lifetime of the drug.*
- *In the IDMP/G-SRS we always have an explicit relationship between the salt form and the parent (non-salt) as well as the active moiety*

Dashboard for Codeine Sulfate in G-SRS



There is one exact (name or code) match for "CODEINE SULFATE"

CODEINE SULFATE

UNII:11QV9BS0CB

ABSOLUTE

Names: CODEINE SULFATE CII [USP-RS]
CODEINE SULFATE CII
CODEINE SULFATE TRIHYDRATE
CODEINE SULFATE [VANDF]
CODEINE SULFATE [WHO-DD]

Codes: BDNUM: 0036748AA
CAS: 6054-40-6
EVMPD: SUB01410MIG
CFR: 21 CFR 290.2, 21 CFR 341.74, 21 CFR 341.14, 21 CFR 1308.15

Relationships: 2

Formula: 2C18H21NO3.3H2O.H2O4S

Mol Weight: 750.85

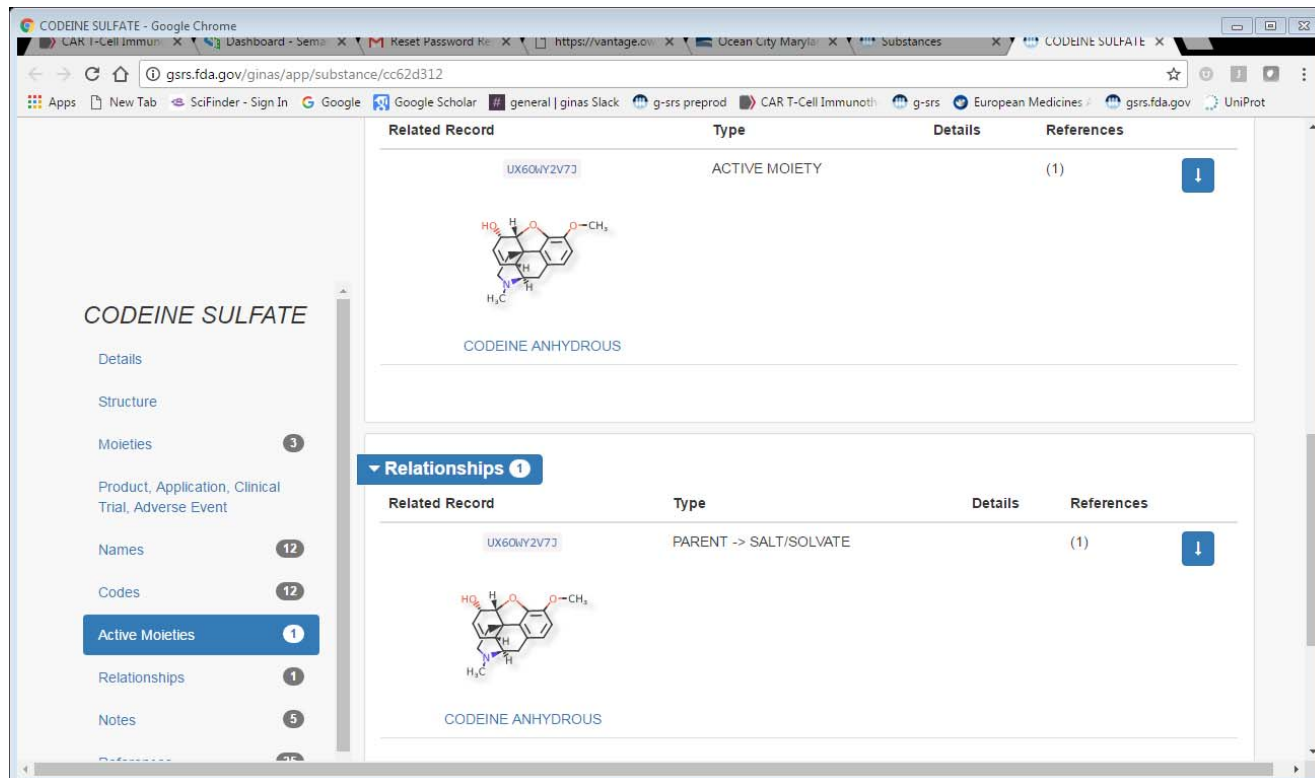
Date approved: 9 years ago
Created: 31 years ago
Last modified: 4 years ago
Status: Validated (UNII)
Version: 1

Product Count: Active: 13, Inactive: 0
Application Count: CDER: 42, SRS: 5
Clinical Trial Count: 5
Adverse Event Count: 0

Show All Records Matching Search

A Codeine Sulfate Trihydrate = Preferred term US. Actually the Preferred term should be Codeine hemisulfate sesquihydrate (1:0.5: 1.5). Per ISO definition we only use stoichiometric complete values, the mol. formula 2: 1: 3. and therefore the mol. weight = 750.85 refers to two molecules codeine as base.

Parent-Salt Relationship



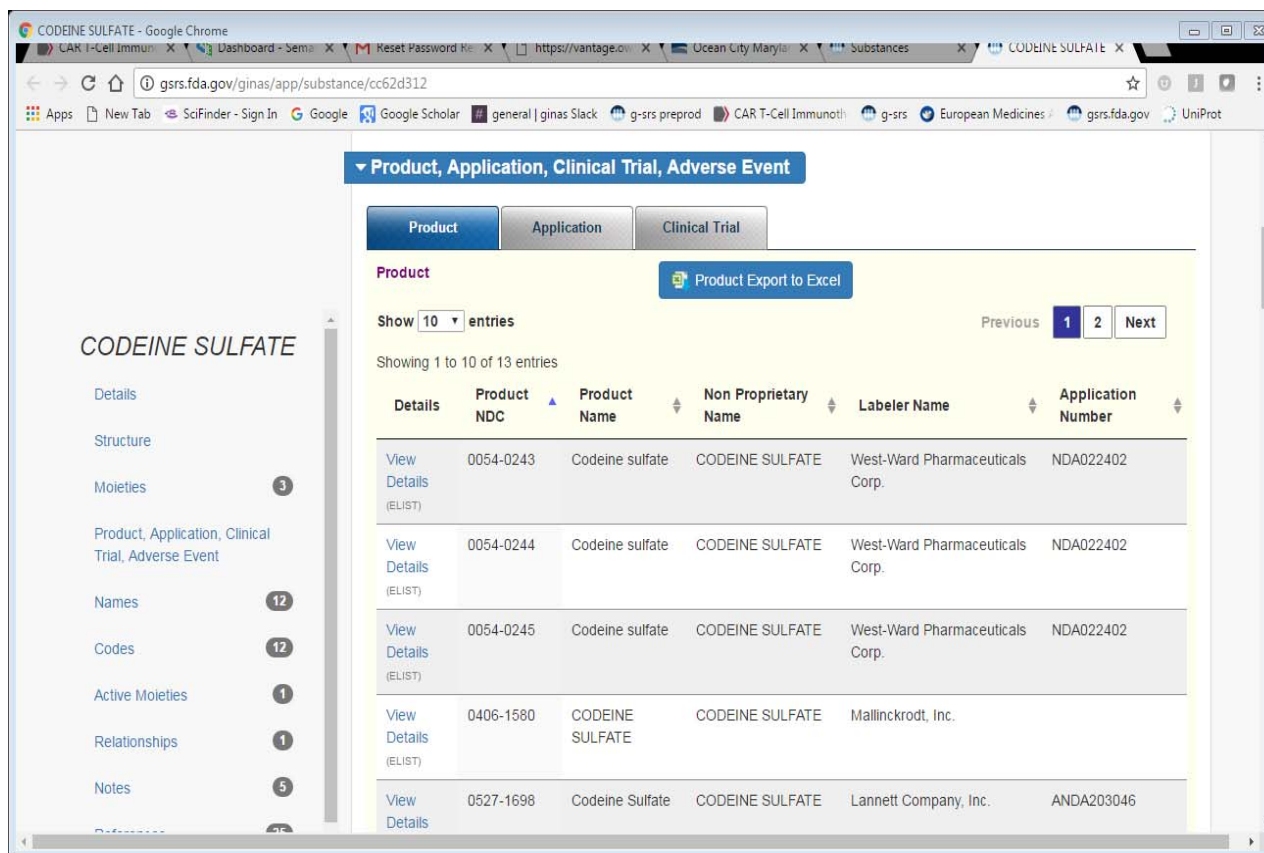
The screenshot displays the gsr.s.fda.gov/ginas application interface for the substance CODEINE SULFATE. The left sidebar contains a navigation menu with the following items: Details, Structure, Moieties (3), Product, Application, Clinical Trial, Adverse Event, Names (12), Codes (12), Active Moieties (1), Relationships (1), Notes (5), and References (7). The main content area is divided into two sections. The top section, titled 'Related Record', shows a table with one entry: 'UX60iY2V7J' of type 'ACTIVE MOIETY' with one reference. Below this is the chemical structure of CODEINE ANHYDROUS. The bottom section, titled 'Relationships', shows a table with one entry: 'UX60iY2V7J' of type 'PARENT -> SALT/SOLVATE' with one reference. Below this is the same chemical structure of CODEINE ANHYDROUS.

Related Record	Type	Details	References
UX60iY2V7J	ACTIVE MOIETY		(1)

Relationships

Related Record	Type	Details	References
UX60iY2V7J	PARENT -> SALT/SOLVATE		(1)

Products that Contain Codeine Sulfate



The screenshot shows a web browser window displaying the FDA's ginas app. The main heading is "Product, Application, Clinical Trial, Adverse Event". Under the "Product" tab, there is a "Product Export to Excel" button and a "Show 10 entries" dropdown menu. The table below lists five products containing Codeine Sulfate.

Details	Product NDC	Product Name	Non Proprietary Name	Labeler Name	Application Number
View Details (ELIST)	0054-0243	Codeine sulfate	CODEINE SULFATE	West-Ward Pharmaceuticals Corp.	NDA022402
View Details (ELIST)	0054-0244	Codeine sulfate	CODEINE SULFATE	West-Ward Pharmaceuticals Corp.	NDA022402
View Details (ELIST)	0054-0245	Codeine sulfate	CODEINE SULFATE	West-Ward Pharmaceuticals Corp.	NDA022402
View Details (ELIST)	0406-1580	CODEINE SULFATE	CODEINE SULFATE	Mallinckrodt, Inc.	
View Details	0527-1698	Codeine Sulfate	CODEINE SULFATE	Lannett Company, Inc.	ANDA203046

Product Details

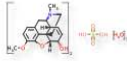


gins - Google Chrome
gsrs.fda.gov/ginas/app/productDetailsElist?productId=2dddb421-6023-4db6-8729-fc42a91831f1

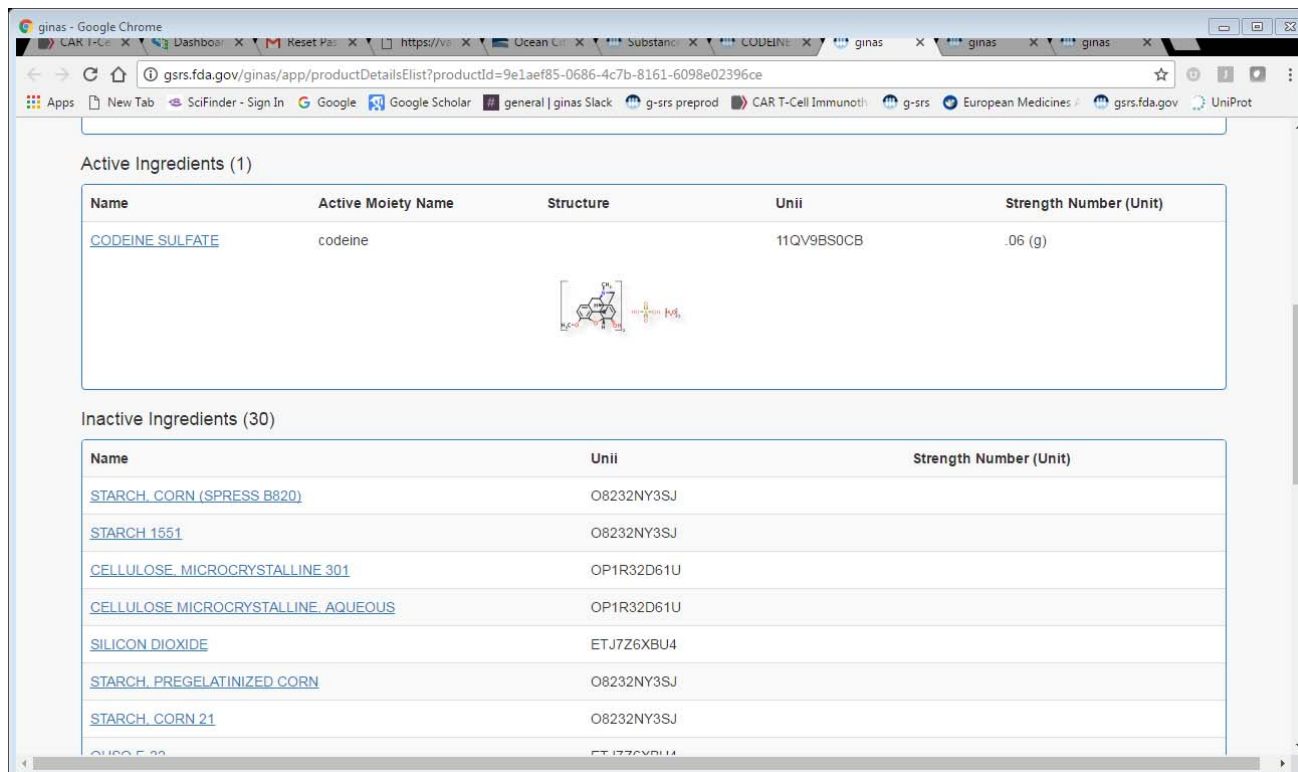
Product Details

Product NDC:	0054-0243	Application Number:	NDA022402
Product Name:	Codeine sulfate	Product Name Type:	HUMAN PRESCRIPTION DRUG
Non Proprietary Name:	CODEINE SULFATE	Proprietary Name Suffix:	
Labeler Name:	West-Ward Pharmaceuticals Corp.	Dosage Form Name:	TABLET
Marketing Category Name:	NDA	Start Marketing Date:	20090716
Route Name:	ORAL	End Marketing Date:	
Color:	WHITE	Flavor:	
Shape:	ROUND	Imprint Text:	15;54;613
Size (mm):	6	Number of Fragments:	2

Active Ingredients (1)

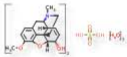
Name	Active Moiety Name	Structure	Unii	Strength Number (Unit)
CODEINE SULFATE	CODEINE ANHYDROUS		11QV9BS0CB	.015 (g)

Product Details cont.



The screenshot shows a web browser window with the URL <https://www.accessdata.fda.gov/drugsatfda/drugs/infopage.cfm?drugid=11QV9BS0CB>. The page displays the following information:

Active Ingredients (1)

Name	Active Moiety Name	Structure	Unii	Strength Number (Unit)
CODEINE SULFATE	codeine		11QV9BS0CB	.06 (g)

Inactive Ingredients (30)

Name	Unii	Strength Number (Unit)
STARCH_CORN (SPRESS B820)	O8232NY3SJ	
STARCH 1551	O8232NY3SJ	
CELLULOSE_MICROCRYSTALLINE 301	OP1R32D61U	
CELLULOSE MICROCRYSTALLINE_AQUEOUS	OP1R32D61U	
SILICON DIOXIDE	ETJ7Z6XBU4	
STARCH_PREGELATINIZED CORN	O8232NY3SJ	
STARCH_CORN 21	O8232NY3SJ	
SILICON DIOXIDE	ETJ7Z6XBU4	

Codeine Dashboard



Substances - Google Chrome

gdrs.fda.gov/ginas/app/substances?q="CODEINE%20ANHYDROUS"

Show Deprecated Records

Record Status

- Validated (UNII) 18
- pending 9
- Non-Validated 1

Substance Type

- Chemical 27
- Concept 1

Molecular Weight

- 0:200 20
- 200:400 25
- 400:600 6
- 600:800 4
- 800:1000 4

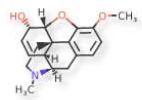
Source Tag

There is one exact (name or code) match for "CODEINE ANHYDROUS"

CODEINE ANHYDROUS

UNII: UX6OWY2V7J

ABSOLUTE



Names: CODEINE [WHO-DD]
CODEINE ANHYD
7,8-DIDEHYDRO-4,5 ALPHA-EPOXY-3-METHO...
CODEINE [MI]
CODEINE [HSDB]

Codes: BDNUM: 0535853AA
CAS: 76-57-3
EVMPD: SUB13424MIG SUB127261
CFR: 21 CFR 862.3270

Relationships: 25

Formula: C₁₈H₂₁NO₃

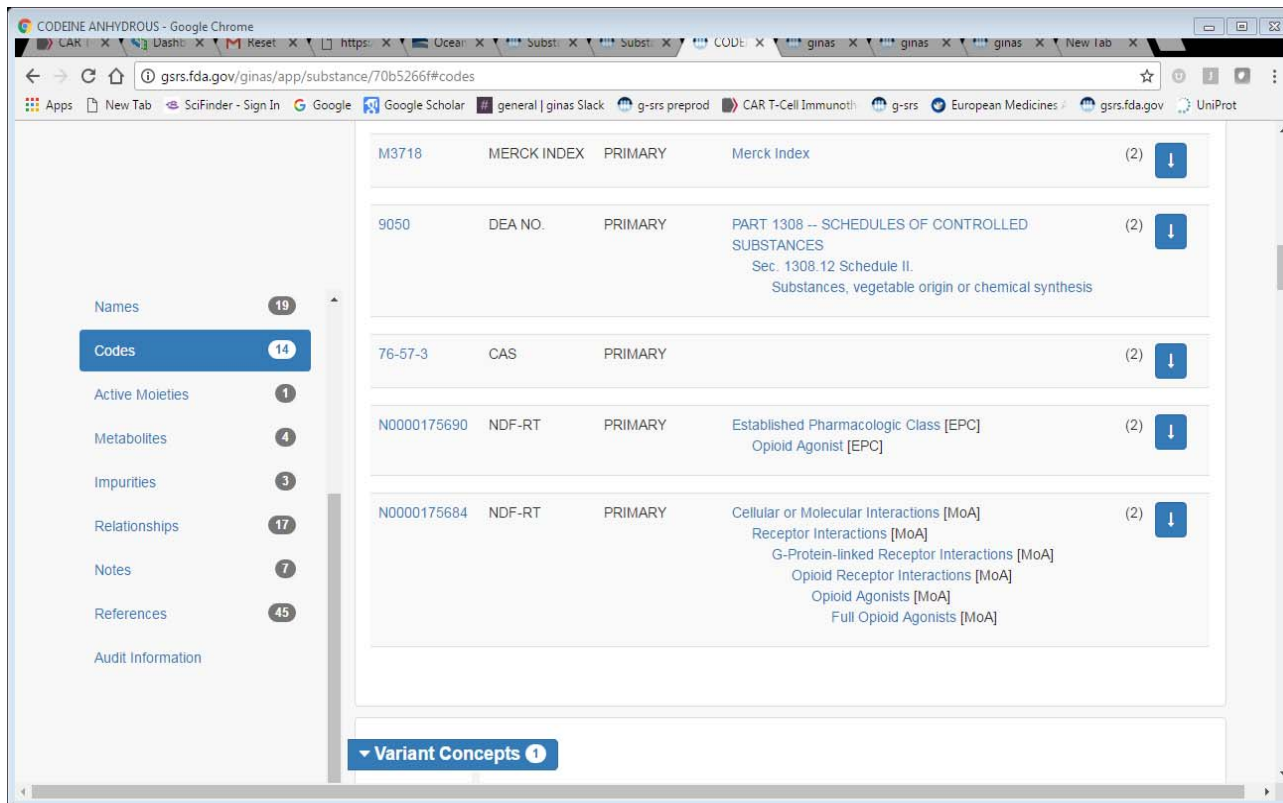
Mol Weight: 299.36

Date approved: 12 years ago
Created: 12 years ago
Last modified: 4 years ago
Status: Validated (UNII)
Version: 1

Product Count: Active: 7 Inactive: 0
Application Count: CDER: 0 SRS: 0
Clinical Trial Count: 0
Adverse Event Count: 16484

Show All Records Matching Search

Codeine Codes and Classification

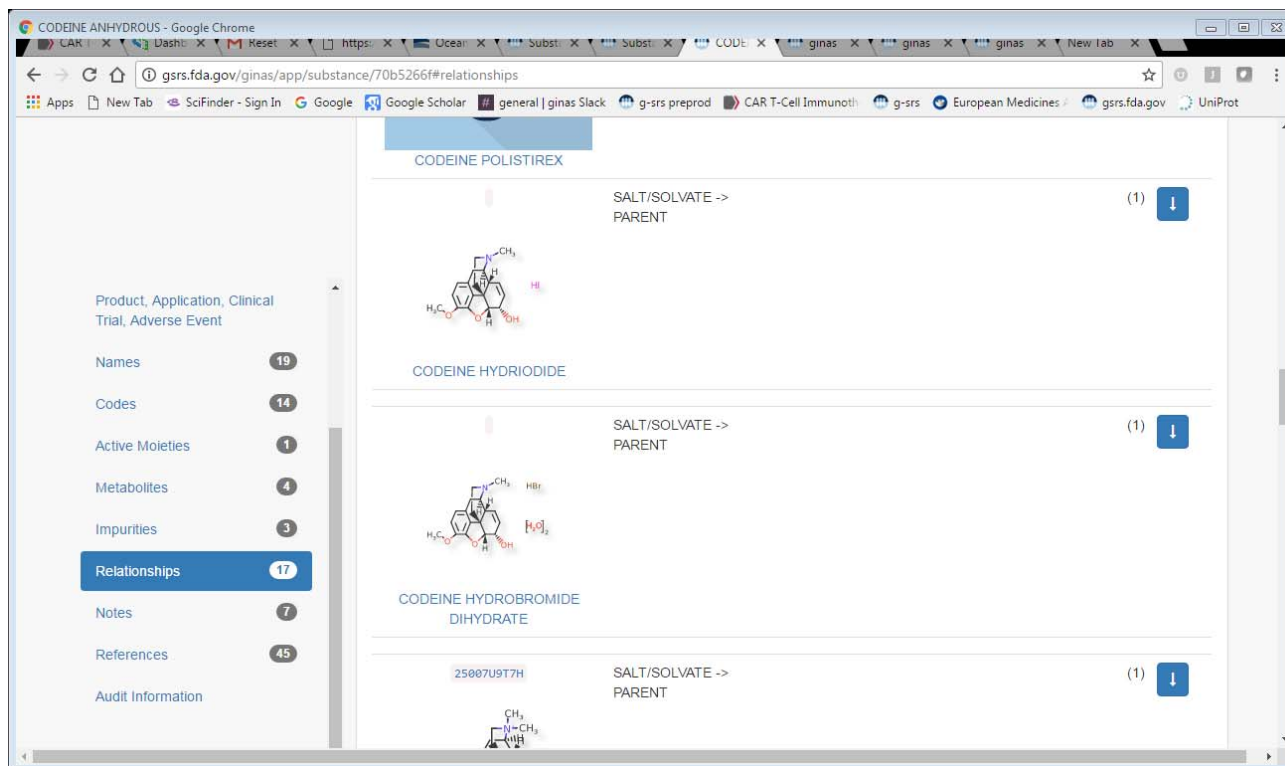


The screenshot displays the 'CODEINE ANHYDROUS' page in the gsr.fda.gov/ginas application. The left sidebar shows navigation options: Names (19), Codes (14), Active Moieties (1), Metabolites (4), Impurities (3), Relationships (17), Notes (7), References (45), and Audit Information. The main content area lists several codes and their classifications:

Code	System	Classification	Description	Count
M3718	MERCK INDEX	PRIMARY	Merck Index	(2)
9050	DEA NO.	PRIMARY	PART 1308 -- SCHEDULES OF CONTROLLED SUBSTANCES Sec. 1308.12 Schedule II. Substances, vegetable origin or chemical synthesis	(2)
76-57-3	CAS	PRIMARY		(2)
N0000175690	NDF-RT	PRIMARY	Established Pharmacologic Class [EPC] Opioid Agonist [EPC]	(2)
N0000175684	NDF-RT	PRIMARY	Cellular or Molecular Interactions [MoA] Receptor Interactions [MoA] G-Protein-linked Receptor Interactions [MoA] Opioid Receptor Interactions [MoA] Opioid Agonists [MoA] Full Opioid Agonists [MoA]	(2)

At the bottom, there is a 'Variant Concepts' button with a count of 1.

Codeine Relationships



CODEINE ANHYDROUS - Google Chrome

gdrs.fda.gov/ginas/app/substance/70b5266f#relationships

Product, Application, Clinical Trial, Adverse Event

Names 19

Codes 14

Active Moieties 1

Metabolites 4

Impurities 3

Relationships 17

Notes 7

References 45

Audit Information

CODEINE POLISTIREX

SALT/SOLVATE -> PARENT (1) ↓

CN1CC[C@]23[C@@H]4OC5=C(C=C(C=C5C2=O)OC)C(=O)C13

CODEINE HYDRIODIDE

SALT/SOLVATE -> PARENT (1) ↓

CN1CC[C@]23[C@@H]4OC5=C(C=C(C=C5C2=O)OC)C(=O)C13.I

CODEINE HYDROBROMIDE DIHYDRATE

25007U9T7H SALT/SOLVATE -> PARENT (1) ↓

CN1CC[C@]23[C@@H]4OC5=C(C=C(C=C5C2=O)OC)C(=O)C13.Br

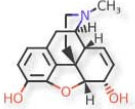
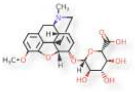
Codeine Relationships

CODEINE ANHYDROUS - Google Chrome

gdrs.fda.gov/ginas/app/substance/70b5266f#metabolites

8 WEIGHT PERCENT (average)

2,2,2-TRICHLOROETHANOL

Identifier	Classification	Comments	Count
76I766029C	METABOLITE ACTIVE -> PRODRUG	Comments: MINOR METABOLITE Interaction Type: MINOR	(2) ↓
 <p>MORPHINE</p>			
E2M937KY47	METABOLITE ACTIVE -> PRODRUG	Comments: MAJOR METABOLITE MAY BE RESPONSIBLE FOR ANALGESIC EFFECT Interaction Type: MAJOR	(2) ↓
 <p>CODEINE-6- GLUCURONIDE</p>			
32W9P3T4ML	METABOLITE INACTIVE -> PARENT	Comments: Metabolic Enzyme - cytochrome P-450 3A4	(2) ↓

Product, Application, Clinical Trial, Adverse Event

Names 19

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Adverse Events to Active Moiety



CODEINE ANHYDROUS - Google Chrome

gdrs.fda.gov/ginas/app/substance/70b5266f#advPt

Product, Application, Clinical Trial, Adverse Event

Product Adverse PT Adverse DME

Adverse Event PT Adverse Event PT Export to Excel

Show 10 entries Previous 1 2 3 4 5 ... 309 Next

Showing 1 to 10 of 3,086 entries

PT Term	Prim SOC	Case Count	PT Count	PRR
DRUG HYPERSENSITIVITY	IMMUNE SYSTEM DISORDERS	16484	2941	30.064
TOXICITY TO VARIOUS AGENTS	INJURY, POISONING AND PROCEDURAL COMPLICATIONS	16484	1588	14.184
DRUG ABUSE	PSYCHIATRIC DISORDERS	16484	1004	23.72
OVERDOSE	INJURY, POISONING AND PROCEDURAL COMPLICATIONS	16484	975	6.792
COMPLETED SUICIDE	PSYCHIATRIC DISORDERS	16484	948	12.238
VOMITING	GASTROINTESTINAL DISORDERS	16484	916	2.06
NAUSEA	GASTROINTESTINAL DISORDERS	16484	809	1.203
INTENTIONAL OVERDOSE	INJURY, POISONING AND PROCEDURAL COMPLICATIONS	16484	612	9.99

CODEINE ANHYDROUS

- Details
- Structure
- Moieties 1
- Product, Application, Clinical Trial, Adverse Event
- Names 19
- Codes 14
- Active Moieties 1
- Metabolites 4
- Impurities 3

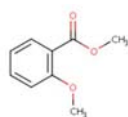
JSON message for Codeine



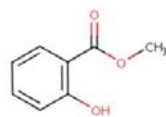
```
Object
  uuid: "70b5266f-4706-49ae-85cd-0ef23b9e50f8"
  created: 111647880000
  createdBy: "EAH"
  lastEdited: 1373642375000
  lastEditedBy: "SWITZERF"
  deprecated: false
  definitionType: "PRIMARY"
  definitionLevel: "COMPLETE"
  substanceClass: "chemical"
  status: "approved"
  version: "1"
  approvedBy: "J4"
  approved: 1121662800000
  names: Array [19]
    0: Object
      uuid: "78e88acd-0f64-4914-bdf8-2f81d7b0fcbc"
      created: 1405635086001
      createdBy: "SWITZERF"
      lastEdited: 1405635086001
      lastEditedBy: "SWITZERF"
      deprecated: false
      name: "CODEINE [WHO-DD]"
      type: "cn"
      domains: Array [0]
      languages: Array [1]
        0: "en"
      nameJurisdiction: Array [0]
      nameOrgs: Array [0]
      preferred: false
      displayName: false
```

Question (cont.): Is it true for any other chemical modifications, e.g., esters?
(Which would make aspirin an instance of a salicylate)?

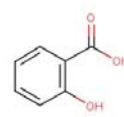
Answer: No, esters are different substances from their parent substances e.g. Methylsalicylate



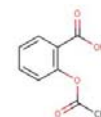
2-methoxy-methyl salicylate



Methyl salicylate



Salicylic acid (parent)



'Aspirin' Acetylsalicylic acid

Side effects:

Salicylic acid: contact dermatitis, penetration of the skin can be increased

Methyl salicylate: Methyl salicylate/menthol cream is a topical analgesic, interaction with coumarins. It is aggressive on the skin.

Dimethyl salicylate (2-methoxy-methyl salicylate, Benzoic acid, 2-methoxy, methylester, Methyl o-anisate): Causes serious eye irritation

Acetylsalicylic acid: Salicylic acid intolerance, since the substance can be metabolized into salicylic acid.

So differences per ester, some adverse effects in common.

Question: What system(s) should be used for encoding?

... UNII: substances only. US realm. no relationships (e.g., of salts)

Answer: This is not true:

- *extensive relationships, relationship to active moieties, metabolites, metabolic enzymes, extensively curated, capture, defines substances not just hierarchy.*
- *Realm is increasing, Europe will use and, perhaps Canada, codes directly into drug product.*
- *Maps to ATC, INN, RxNorm, WHO-DD, DEA list, yellow list etc.*
- *No license issue.*
- *UNII assigned early in the development process, ability to connect preclinical data to post marketing data. G-SRS links products, clinical trials, and adverse events from US systems; can be readily extended to products in other realms.*

Specific Questions

1. Morphine derivatives. Morphine and related. List as Morphine and let drug check worry about x-reactivity?
2. Beta Lactamase Inhibitors.
3. Salicylates. A class? Infer topical salicylates? Include ASA? ASA (salicylates)
4. influenza virus vaccine, inactivated. Etc. CVX seems too specific, but no general terms available for components.
5. narcotic analgesics. Opioids?
6. Estrogens. Class or IN.
7. ASPIRIN BUFFERED.
8. Tetanus. tetanus toxoid vaccine, inactivated?
9. Nitrates, Organic
10. Nickel, nickel sulfate
11. POVIDONE IODINE.
12. iodinated glycerol
13. aloe vera topical
14. VACCINES
15. quinine and analogues
16. Tegaderm. Adhesive, or this product?
17. sulfa topicals

Answer/Hint (1/2)

- ❖ *It is better to separate a classification (groups into categories based on similar properties), terminology (set of terms representing the system of concepts in a particular field) etc. since many of the specific questions may easily create confusion to a certain extent. G-SRS is based on the definition of a substance. Classification for example, is a separate exercise.*
- ❖ *IDMP captures strength, dosage form, and approved routes of administration and both active and inactive ingredient.*
- ❖ *In IDMP/G-SRS, products are defined in much more detail, mappings between substances and products required information, is freely available. Both active and inactive substances are captured. The G-SRS has distributable data and a distributable registration system that allows easy submission and use; it will also have a product registration system.*
- ❖ *Built in JSON message for detailed substance information exchange (also allows a relatively easier path to be adapted to HL7). API driven system. All FAERS data mapped to active moiety and actual ingredient.*

Answer/Hint (2/2)

- ❖ One of the many advantages of using “definitional” approach compared to a classification system approach is that additional information on inactive ingredients is conveyed to cover allergic reactions. Otherwise, neither patients or physicians would have any way to identify that an inactive ingredient like, for example, lactose, is present in a product.
- ❖ Many “allergenic-like” reactions can be due to lactose or other inactive ingredients. A classification or various terminology systems would not have any way of knowing this.

- ❖ IDMP/G-SRS System has been deployed in FDA environment
- ❖ Has implemented the Substance information level of ISO 11238 / ISO/TS 19844 and Specified Substance Group 1.
- ❖ Migration and supplementation of data
- ❖ IT tools developed for API access and Batch Updating
- ❖ Integrated product (SPL), application, clinical trial with current FDA systems
- ❖ Integrated modules for product and application information
- ❖ System will/is into production at FDA.
- ❖ EMA/EU in phased implementation (SPOR), O-R first, S-P follow http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000645.jsp&mid=WC0b01ac058078fbe2

Working Collaboratively



- ❖ Develop modules for Specified Substance Groups 2-4
- ❖ Start entering Specified Substance Group 1 information
- ❖ Develop better forms and presentation of data
- ❖ Expand quality (impurities) and pharmacology (targets, metabolite, cyp and transporter information)
- ❖ Deploy full instances with all public data at Open FDA and NLM
- ❖ Establish mechanism for system-system communication
- ❖ Integrate G-SRS into a clinical trial registry system (C-DISC)

Snapshots from EU/NCA Technical work



Substance mapping exercises (led by Herman Diederik)

Extract for the design of EU-G-SRS-14-04-2017-Mandatory fields for (S)PMs.xlsx (Read-Only) - Excel

Substance Code	Substance Class	Substance Preferred Name	AMOUNT/ Amount Type: Exact/ Non-Numeric Value	Official Name	Reference	EXTRA Translations of EN Preferred Name / Other values	Substance Name						
Substance XEVMPD code (Substance ID)	UNII Code	Pending IDMP Global Identifier (Placeholder)	Substance Type	Substance name (All Moieties included)	Equivalent factor (calculated by molecular weight of reference substance/ molecular weight substance [salt]) (v 1.00 No Reference substance)	Substance name type	Official Name Type	Reference Source (NAME)	Translation	Language	EU-Local Code	Substance Name Domain	Jurisdiction
3	SUB21605	XB13HY1RU	GFTDORJ65T (Artificial ID)	Protein		0.903	English Preferred		Desmopressin Monoacetas trihydratum	IA		Drug	EU

SOURCE-TEXT-EN	COPY OF SUBSTANCE-NAME-EN	SMILES/ Structure	Mol. Formula	Mol. Weight	UNII	InChIKey	CAS Number	FDA-SRS-Synonyms	FDA-Preferred term	REFERENC
Trivial name (trade name)	acetyl tributyl citrate	<chem>CCCCC(=O)CC(C)(C)C</chem>	C20H34O8	402.4792	QZBXM59RZ	InChIKey=QZCLKY	77-90-7	1,2,3-PROPANETRICAR ACETYLRIBUTYL CITRATE	FDA-SRS	
122 Official name	Acetylacetone	<chem>CC(=O)CC(=O)C</chem>	CSH8O2	100.1158	46R950BPAJ	InChIKey=YRKCRC	123-54-6	2,4-PENTANDIONE 3-FACETYLACETONE	FDA-SRS	
124 Chemical name	Acetylacetone	<chem>CC(=O)CC(=O)C</chem>				Key=YRKCRC	123-54-6	2,4-PENTANDIONE 3-FACETYLACETONE	FDA-SRS	
125 Official name	Acetylacetone	<chem>CC(=O)CC(=O)C</chem>				Key=YRKCRC	123-54-6	2,4-PENTANDIONE 3-FACETYLACETONE	FDA-SRS	
126 Trivial name (trade name)	ACETYLACETONE ALUMINUM SALT									
127 Trivial name (trade name)	ACETYLACETONE ALUMINUM SALT									
128 Chemical name	ACETYLACETONE ALUMINUM SALT									
129 Trivial name (trade name)	Acetylcysteine	<chem>CC(=O)N[C@@H](CS)C</chem>				Key=PWKSKI	616-91-1	5052 ACETADOTE ACI ACETYL CYSTEINE	FDA-SRS	
130 Official name	Acetylcysteine	<chem>CC(=O)N[C@@H](CS)C</chem>				Key=PWKSKI	616-91-1	5052 ACETADOTE ACI ACETYL CYSTEINE	FDA-SRS	
130 Official name	Acetylsalicylic acid									
131		<chem>CC(=O)OC1=CC=CC=C1</chem>				Key=BSYRNY	50-78-2	2-(ACETYLOXY)BENZOII ASPIRIN	FDA-SRS	
132 Official name	Acetyltryptophan	<chem>CC(=O)N(CC1=CNC2=CC=CC=C12)C</chem>				Key=DZTHIG	87-32-1	ACETYLRYPPTOPHAN, [ACETYLRYPPTOPHAN, DL-	FDA-SRS	
133 Chemical name	Acetyltryptophan	<chem>CC(=O)N(CC1=CNC2=CC=CC=C12)C</chem>				Key=DZTHIG	87-32-1	ACETYLRYPPTOPHAN, [ACETYLRYPPTOPHAN, DL-	FDA-SRS	
134 Chemical name	Acetyltryptophan, N-	<chem>CC(=O)N[C@@H](CC1=CC=CC=C1)C</chem>				Key=DZTHIG	1218-34-4	ACETYL-L-TRYPTOPHAN ACETYLRYPPTOPHAN, L-	opsin	
135 Chemical name	Acetyltryptophan, N-	<chem>CC(=O)N[C@@H](CC1=CC=CC=C1)C</chem>				Key=DZTHIG	1218-34-4	ACETYL-L-TRYPTOPHAN ACETYLRYPPTOPHAN, L-	opsin	
136 Trivial name (trade name)	ACETYLRYPPTOPHANE SODIUM	<chem>[Na].CC(=O)N[C@@H](C1=CC=CC=C1)C</chem>	C13H14N2NaO3	269.2516		InChIKey=ALSIRUSZLQONHW-LTCKWSDVSA-N			opsin	
137 Trivial name (trade name)	ACETYLRYPPTOPHANE SODIUM	<chem>[Na].CC(=O)N[C@@H](C1=CC=CC=C1)C</chem>	C13H14N2NaO3	269.2516		InChIKey=ALSIRUSZLQONHW-LTCKWSDVSA-N			opsin	
138	ACICLOVIRUM	<chem>NC1=NC(=O)C2=C(N1)N=CN=C2</chem>	C8H11N5O3	225.2046	X4HE5101F	InChIKey=MKUJA	59277-89-3	6H-PURIN-6-ONE, 2-AA ACYCLOVIR	PUBCHEM	

Thank you for your attention

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Convenor ISO/TC 215 WG6, GS1