

Interoperation and Analytics of EHR Data

James Campbell
Olivier Bodenreider
Robert Wynne
Stan Huff
W Scott Campbell



Agenda

- Introductions
- Acknowledgements
- Interoperation defined; relationship to SNOMED CT; Workshop Tooling: MRCM, ECL and OWL
- SNOMED Clinical Findings and Interoperation use cases for Problem Lists
- RxNorm Medicinal Products Interoperation for Research and Decision Support
- LOINC Laboratory results Observables Interoperation for Analytics and Decision support
- SNOMED Anatomic Pathology Observables Interoperation for Decision support and Cancer Research

2



Acknowledgements and Thank you is not enough

- Robert Wynne is a research programmer for the Lister Hill Center of the National Library of Medicine and data analyst for RxNorm OWL and Nebraska Lexicon preparation
- Jay Pedersen and Stefan Friesema are research software engineers working on Nebraska Public Health Lab and UNMC PCORnet datamart development
- B2I staff led us through the details of implementing the NLM OWL database into RF2 datasets and fixed our mistakes
- Rory Davidson and SNOMED International editorial have collaborated with the Regenstrief Institute to implement the LOINC extension and provide support for this workshop
- Toni Morrison, Julie James and the Drug Model Working Group have guided the development of the international drug and substance concept model
- Pathology and Laboratory Medicine CRG has spent long hours in developing content for Anatomic Pathology on behalf of the worldwide pathology informatics communities

3



Learning Objectives

- Be able to define interoperability and how this relates to data reuse in a Learning Healthcare system
- Understand the importance of an ontology as a computational tool for the management, manipulation and computation of clinical data and how the SNOMED CT-LOINC-RxNorm concept model supports interoperability and analytics in healthcare and research
- Identify key features of an integrated computable conceptualization for Clinical findings, Observable entities, Pharmaceutical and Biological products and appreciate use case for analytics and decision support



— Resources for this workshop

- Handout References: https://github.com/UNMC-CRANE/SNOMED_CT_Workshop_Nov_2023
- Expression Constraint Language-v50
- SNOMED CT Editorial Guide-v4-20230928
- International Medicinal Product model
- PCORnet common data model_v61
- RxNorm-in-OWL
- Computable Phenotypes ECL Exercises_20231025.docx
- <https://Browser.ihtsdotools.org/>
- <https://dev-nebraska-browser.ihtsdotools.org/>



— Interoperability

“Semantic interoperability is **the ability of computer systems to exchange data with unambiguous, shared (therefore computable) meaning.**

Semantic interoperability is a requirement to enable machine computable logic, inferencing, knowledge discovery, and data federation between information systems.”

-Wikipedia

- In healthcare, interoperability is key to achieving the vision of the Learning Health System proposed by the Institute of Medicine and taken up by several SNOMED member countries. That was one stimulus for the modern EHR



— Why is interoperability important?

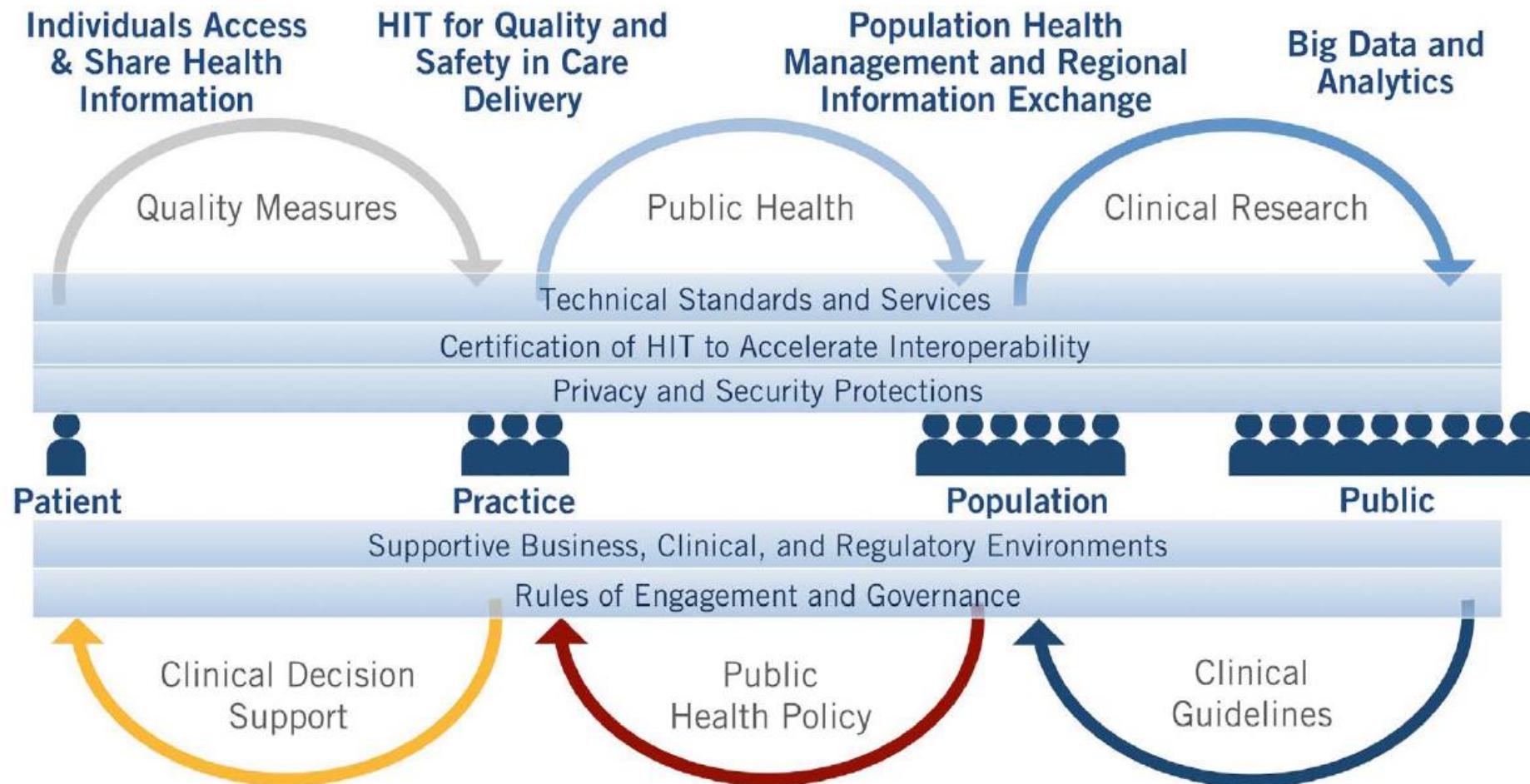
- In decision support for clinical healthcare, universal sharing of data definitions and structures supports transportability and reproducibility of knowledge tools
- In pragmatic research the ability to reliably and reproducibly retrieve EHR data across the breadth of the healthcare industry requires standardization of data definitions
- In public health, optimization and equity in healthcare for all society requires universal access and appreciation of healthcare process and outcomes

7



ONCHIT Vision for Learning Health System

Figure 1. Health IT Ecosystem



— Interoperation of EHR Information

- Information model (top level ontology)
- Vocabulary model (domain ontology): Terminology, Relationships, Descriptions
- Data representation model
- Interface (entrance) terminology and

The complete, unambiguous and consistent binding of these three standards-based elements among a community of users of (EHR) data employing shared query standards supports semantic interoperation



ONCHIT Vision for Interoperation: USCDI Top level ontology

- Is evolving from original HIE
- Identifies core clinical concepts
- Specification EHR implementation
- Use of application profiles “standard”
- Version 170.3
- Version 170.4

Allergies and Intolerances

- Substance (Medication)
- Substance (Drug Class)
- Substance (Non-Medication)
- Reaction

Care Team Member(s)

- Care Team Member Name
- Care Team Member Identifier
- Care Team Member Role
- Care Team Member Location
- Care Team Member Telecom

Clinical Notes

- Consultation Note
- Discharge Summary Note
- History & Physical
- Procedure Note
- Progress Note

Clinical Tests

- Clinical Test
- Clinical Test Result/Report

Diagnostic Imaging

- Diagnostic Imaging Test
- Diagnostic Imaging Report

Encounter Information

- Encounter Type
- Encounter Identifier
- Encounter Diagnosis
- Encounter Time
- Encounter Location
- Encounter Disposition

Facility Information

- Facility Identifier
- Facility Type
- Facility Name

Health Status Assessment

- Health Concerns
- Functional Status
- Disability Status
- Mental/Cognitive Status
- Pregnancy Status
- Alcohol Use
- Substance Use
- Physical Activity
- SDOH Assessment
- Smoking Status

Immunizations

- Immunizations

Laboratory

- Tests
- Values/Results
- Specimen Type
- Result Status
- Result Unit of Measure
- Result Reference Range
- Result Interpretation
- Specimen Source Site
- Specimen Identifier
- Specimen Condition Acceptability

Medical Devices

- Unique Device Identifier - Implantable

Medications

- Medications
- Dose
- Dose Unit of Measure
- Indication
- Fill Status
- Medication Instructions
- Medication Adherence

Patient Demographics/ Information (cont.)

- Sex
- Sexual Orientation
- Gender Identity
- Preferred Language
- Current Address
- Previous Address
- Phone Number
- Phone Number Type
- Email Address
- Related Person's Name
- Relationship Type
- Occupation
- Occupation Industry

Patient Summary and Plan

- Assessment and Plan of Treatment

Problems

- Problems
- SDOH Problems/Health Concerns
- Date of Diagnosis
- Date of Resolution

Procedures

- Procedures
- Performance Time
- SDOH Interventions
- Reason for Referral

Provenance

- Author Time Stamp
- Author Organization

Vital Signs

- Systolic Blood Pressure
- Diastolic Blood Pressure
- Average Blood Pressure

mandated

s for US

new
criterion,
(§



US Core Data for Interoperability v4 Vocabulary Standards 2024

- Integrated Domain ontologies
 - **SNOMED CT**
 - **LOINC**
 - **RxNorm**
- HIPAA Transaction Codesets
 - **ICD-10-CM, ICD-10-PCS, ICD-11**
 - **CPT-4, HCPCS, CDT**



Hypothesis: An integrated set of Domain Ontologies for Health System datasets employing shared elements and relationships promotes interoperability and advances the progress of the Learning Health System



Nebraska Lexicon SNOMED Extension

<https://dev-nebraska-browser.ihtsdotools.org>

<https://nelexicon.unmc.edu>

- Pending publication of LOINC laboratory extension by Regenstrief, we will use Nebraska namespace for the workshop

Components:

- SNOMED International edition 20230630
- 911754091000004101| Nebraska LOINC Laboratory module |
- 443651000004109|Nebraska NLM RxNorm Medication module |
- 911754081000004104|Nebraska Pathology Synoptic module |
- 32640001000004108|Nebraska Clinical extension module |



— SNOMED Concept Model Tooling for Semantic Interoperability

- Early experiments with post-coordination identified need for logical grammatical constraints in the use of defining attributes and valuesets
- 2009 - Machine Readable Concept Model
- Editorial guide: MRCM documentation: confluence.ihtsdotools.org/display/DOCEG/ ¹⁶
- MRCM documents and standardizes SNOMED concept model in promotion of interoperability: confluence.ihtsdotools.org/display/DOCMRCM/
- PDF in handouts: Clinical findings (pp 161ff), Substances (pp 503ff), Pharmaceutical and biological products (pp 283ff), Observable entities (pp 248ff)
- Provides a framework for designing and implementing tooling for interoperable URU analytics



— SNOMED Tooling: Expression Constraint Language

- PDF for version 5 ECL documentation included with handouts:

Expression Constraint Language - Specification and Guide-v50-20231001

- Expression Constraint Language: formalisms for computable query and manipulation of SNOMED CT metadata such as:

- * Terminology binding
- * Intensional reference sets (valuesets)
- * Computable Phenotype SNOMED content queries of EHR databases use valuesets
- * Specifications for SNOMED CT MRCM

			y	
255234002 After (attribute) ⁴³⁷	1	0..*	0..1	<< 272379006 Event (event) ⁴³⁸ OR << 404684003 Clinical finding (finding) ⁴³⁹ OR << 71388002 Procedure (procedure) ⁴⁴⁰
116676008 Associated morphology (attribute) ⁴⁴¹	1	0..*	0..1	<< 49755003 Morphologically abnormal structure (morphologic abnormality) ⁴⁴²
47429007 Associated with (attribute) ⁴⁴³	1	0..*	0..*	<< 105590001 Substance (substance) ⁴⁴⁴ OR << 260707004 Physical object (physical object)



EHR Interoperability Re-Use Cases

- Clinical and Healthcare Enterprise
 - Enterprise business management
 - Clinical decision support
 - Healthcare process improvement
- Research
 - Adverse event monitoring and safety: FDA Sentinel
 - Clinical data research networks: PCORnet, OHDSI, N3C
 - Patient-powered research networks
- Public and Population Health
 - Morbidity and Mortality monitoring

18



Interoperation of Problem List for Clinical Research

James Campbell



— ADAPTABLE© Pragmatic Trial

- Hypothesis: The optimal dosage of aspirin (81 or 325 mg) for secondary prevention of heart disease outcomes has the best benefit/side effect ratio
- Design: Randomized dosing cohort observational trial
- Inclusion criteria: Documented atherosclerotic coronary disease with one or more coronary risk factors
- Exclusion criteria: Adults, aspirin allergy, pregnant, nursing mother, recent GI bleeding, hemorrhagic disorder, requires anticoagulant therapy
- Intervention: Randomized to 81mg or 325 mg aspirin
- Outcomes: Mortality, heart attack or stroke
- Safety endpoint: Major bleeding complication

Schuyler-Jones et all. Comparative Effectiveness of Aspirin Dosing in Cardiovascular Disease. NEJM; May 15, 2021. DOI:
[10.1056/NEJMoa2102137](https://doi.org/10.1056/NEJMoa2102137)



Analyzing Data Management for ADAPTABLE Trial Recruitment Criteria

22

Study design

Patients with known ASCVD

(ie MI, OR cath $\geq 75\%$ stenosis of ≥ 1 epicardial vessel OR PCI/CABG)

AND ≥ 1 Enrichment Factor*

Identified through EHR (computable phenotype) by CDRNs
(PPRN pts. already part of a CDRN are eligible)

Pts. contacted with trial information and link to eConsent;
Treatment assignment provided directly to patient

Exclusion Criteria

- Age < 18 yrs
- ASA allergy or contraindication (including pregnancy or nursing)
- Significant GI bleed within past 12 mos
- Significant bleeding disorder
- Requires warfarin or NOAC or Ticagrelor

ASA 81 mg QD

ASA 325 mg QD

Electronic F/U Q 3-6 months;
supplemented with EHR/CDM/claims data

Duration: Enrollment over 24 months;
maximum f/u of 30 months

*Enrichment factors

- Age > 65 years
- Creatinine > 1.5
- Diabetes (Type 1 or 2)
- 3-vessel coronary artery disease
- Cerebrovascular disease and/or peripheral artery disease,
- EF $< 50\%$ by echo,cath, nuclear study
- Current smoker

Primary Endpoint: Composite of all-cause mortality,
nonfatal MI, nonfatal stroke

Primary Safety Endpoint: Major bleeding complications



Oct 14 2015



— Computable Phenotypes and LHS

- A **Computable phenotype** refers to a set of clinical data that can be evaluated via a standardized computerized query to an EHR or clinical data research network”

Richesson RL, Smerek MM, Cameron CB. A Framework to Support the Sharing and Reuse of Computable Phenotype Definitions Across Health Care Delivery and Clinical Research Applications. eGEMS: 2016; Vol. 4: Issue 3, Article 2.

- A requirement for reproducible, accurate and valid scientific network research in healthcare

23



— Pragmatics of developing computable phenotype

- Semantic analysis 1: Translate language of the request into the (USCDI/PCORnet) top level data classes(tables) for query of the database
- Identify the components (attributes or columns) of the class that are essential to the request and determine the relevant domain ontologies that are required (for Nominal datatypes)
- Semantic analysis 2: For nominal data identify the relevant elements (codes) of the domain ontology that are required by the query; this is typically referred to as a “Valueset”
- Construct the query defining the computable phenotype

24



— Interoperable Valuesets for ADAPTABLE

“Patients with ASCVD (Arteriosclerotic Coronary Vascular Disease)”

DATA CLASS

PROBLEMS

Condition, diagnosis, or reason for seeking medical attention.

DATA ELEMENT	APPLICABLE VOCABULARY STANDARD(S)
	<p>Standards listed are required. If more than one is listed, at least one is required unless otherwise noted. If a cell is empty, an applicable vocabulary standard has not been identified.</p>
Problems Condition, diagnosis, or reason for seeking medical attention.	<ul style="list-style-type: none">Systematized Nomenclature of Medicine Clinical Terms (SNOMED CT) U.S. Edition, March 2023 ReleaseInternational Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) 2023
SDOH Problems/Health Concerns Social Determinants of Health-related health concerns, conditions, or diagnoses	<ul style="list-style-type: none">Systematized Nomenclature of Medicine Clinical Terms (SNOMED CT) U.S. Edition, March 2023 Release

:CONDITION_STATUS =
st”

“coronary vascular disease”?
lication from CDC leads to

:CONDITION_STATUS =
st”



— Interoperable Intensional Valuesets for ADAPTABLE

“Patients with ASCVD”

- ??? → CONDITION TABLE: CONDITION = “ASCVD”, CONDITION_STATUS = “Active”; CONDITION_STATUS = “Healthcare Problem List”
- What are the SNOMED CT codes for “Arteriosclerotic coronary vascular disease”?
- ??? → CONDITION TABLE: CONDITION IN
(<< 64572001 |Disease (disorder)| : << 363698007 |Finding site (attribute)| = << 41801008 |Coronary artery structure (body structure)|, << 116676008 |Associated morphology (attribute)| = << 28960008 |Arteriosclerosis (morphologic abnormality)|),
CONDITION_STATUS = “AC”; CONDITION_STATUS = “HC”
“37 concepts”

Why bother?

- US Datamarts have varying editions of SNOMED CT installed; historically complete code systems are a requirement; reproducible computable phenotypes are a challenge

27



— Interoperable Intensional Valuesets for ADAPTABLE

- . Myocardial Infarction???
- . Cerebrovascular disease???
- . Peripheral vascular disease???
- . Coronary artery bypass graft???
- . Coronary angioplasty???

28



Use Cases: Computable Phenotypes

- **Alcohol and Colorectal Cancer**

J. Burns, J. G. McDonnell, S. M. Gryziak, C. Hinschius, A. D. Bossler, T. McClay, et al.

Hypothesis: Patients with advanced colorectal carcinoma residing in rural areas are less likely to be treated with molecular cancer therapies than those in urban areas.

Inclusion criteria: Adult patients (age > 18 years) with metastatic colorectal cancer

- **Coronary Artery Disease**

Cardiovascular Disease

Independent variables: Gender, race and ethnicity, chemotherapy, molecular-guided therapies

- **Cancer Outcomes**

Campbell WS, Campbell JR, McDowell BD, Smith NC, Gryziak BM, Hinschius EA. Exploration of PCORnet data resources for assessing use of molecular-guided cancer treatment. JCO Clin Cancer Inform 2020 Aug;4:724-735.

Att T, McClay
e disorder of
mortality.

29

Dosing in

Bossler AD,



— Use Cases: Computable Phenotypes

CAUSATIVE AGENT

- Alcohol use disorder
- Streptococcal diseases???

30

AND/OR/MINUS; AFTER; DURING

- Colorectal Carcinoma
- Coronavirus disease or complications???
- Complications of eye surgery???



— Use Cases: Computable Phenotypes

- **Alcohol use disorder:** Bailey KL, Sayles H, Campbell JR, Khalid N, Anglim M, Ponce J, Wyatt T, McClay J, Burnham EL, Anzalone A, Hanson C. COVID-19 patients with documented alcohol use disorder or alcohol-related complications are more likely to be hospitalized and have higher all-cause mortality. *Alcoholism Clin Exp Research* 2022 Apr; 1:1-13.

- **Coronavirus Disease 2019 (COVID-19) and Alcohol Use Disorders**
 - Hypothesis:** Adult patients with Alcohol use disorders that are infected with COVID-19 are more likely die from their illness.
 - Inclusion criteria:** Adult patients (age > 18 years) with history of alcohol use disorder
 - Independent variables:** Gender, race and ethnicity, comorbidities
 - Outcomes:** Survival from onset of infection with COVID-19



— Use Cases: Computable Phenotypes

AND/OR/MINUS; AFTER; DURING

- Colorectal Carcinoma
- Coronavirus disease or complications???
- Complications of eye surgery???

32

PATHOLOGICAL PROCESS

- Types of pathology: < 64572001 |Disease (disorder)| . 370135005 |Pathological process (attribute)|
- Infections??? (7974 Clinical findings)
- Parasitic infection/Infestation??? (1337 Diseases)



RxNorm Medicinal Products Interoperation for Research and Decision Support

33

Olivier Bodenreider, Robert Wynne



— Outline

- SNOMED CT International Medicinal Product Model
- RxNorm drug model vs. SNOMED CT's
- Converting RxNorm clinical drugs to the SNOMED CT model
- Querying RxNorm and SNOMED CT drugs

34





ICBO 2018
Corvallis, Oregon
August 8, 2018

35

The New SNOMED CT International Medicinal Product Model

Olivier Bodenreider and Julie James

Lister Hill National Center
for Biomedical Communications
Bethesda, Maryland - USA

Bodenreider O, James J.

The new SNOMED CT international medicinal product model.

Proceedings of the 7th International Conference on Biomedical Ontology (ICBO 2018) 2018:
(electronic proceedings: http://ceur-ws.org/Vol-2285/ICBO_2018_paper_36.pdf).



* Each film-coated tablet contains amlodipine besylate, USP equivalent to 10 mg of amlodipine and atorvastatin calcium, USP equivalent to 10 mg of atorvastatin.

Usual Dosage: See accompanying prescribing information.

Keep this and all medication out of the reach of children.

Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

Manufactured for:

Mylan Pharmaceuticals Inc.
Morgantown, WV 26505 U.S.A.

Made in India



Mylan.com

RMX4517H1

NDC 0378-4517-93

Amlodipine Besylate and Atorvastatin Calcium Tablets

10 mg/10 mg*

AA8

PHARMACIST: Dispense the accompanying Patient Information Leaflet to each patient.

Rx only

30 Tablets

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure. Keep container tightly closed. Code No.: MH/DRUGS/25/NKD/89

(27 x 12 mm)
Vamish Free area
for Coding



N 3 0378-4517-93 2

75056717



Medicinal products in SNOMED CT

- Medicinal products vs. substances
 - MPs have substances as ingredients
- Types of medicinal products
 - Ingredient + dose form + strength
 - Ingredient + dose form
 - Ingredient
 - Drug classes
- Limited scope
 - No packaging or brand information

37

International Medicinal Product Model

<https://confluence.ihtsdotools.org/display/DOCMPM/SNOMED+CT+Medicinal+Product+Model+Specification>



Use cases

- To facilitate international interoperability of medication concepts
 - e.g., for use in patient summaries and for cross-border care
- To provide a strong foundation for member countries to develop their national medicinal product terminology
 - e.g., by adding package and branded product information
- To support medication analytics for research purposes
- To support the development of international medication decision support
 - e.g., allergy checking and duplicate therapy checking

38

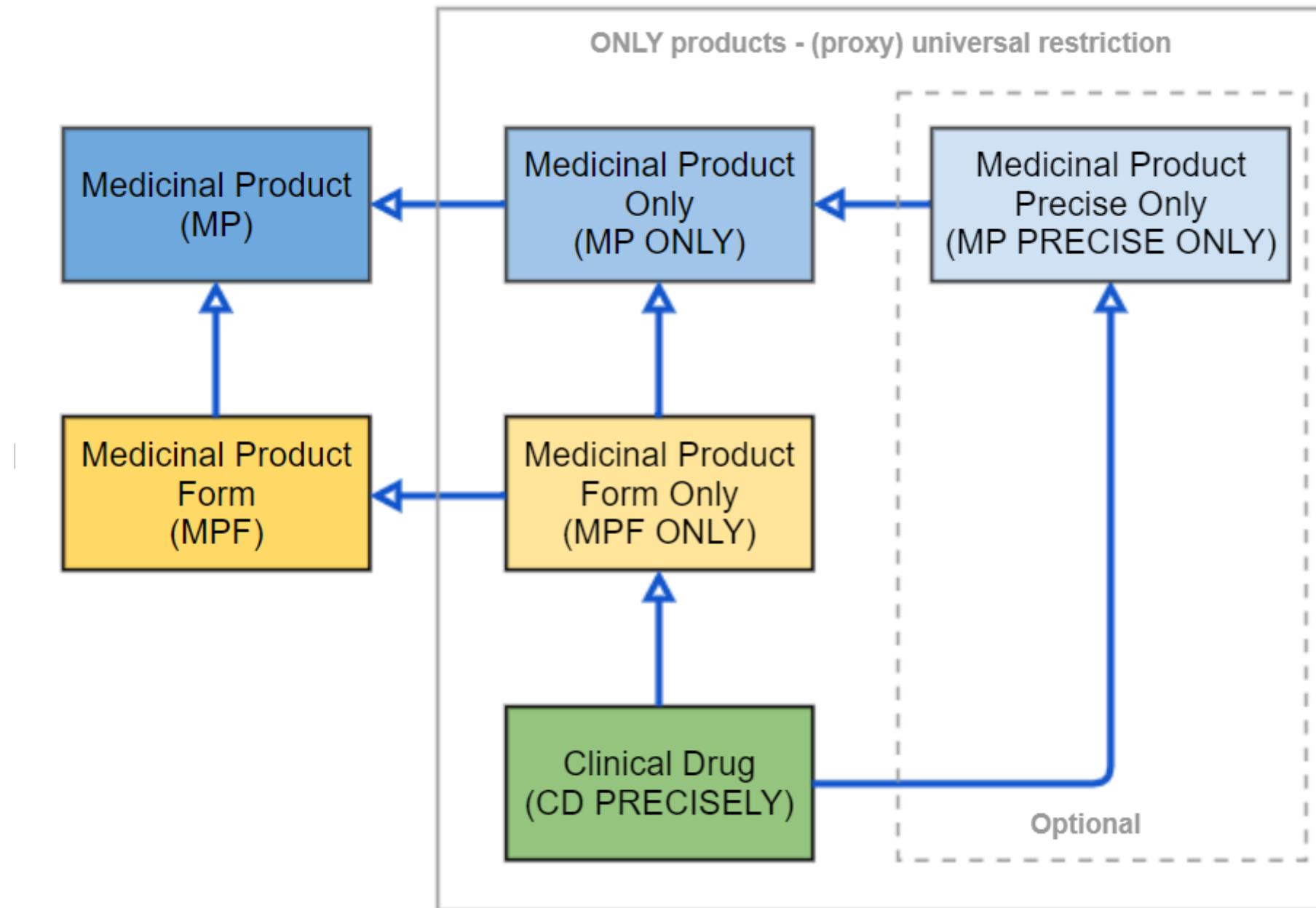


Patterns for types of medicinal products

- Clinical drug
 - *Precise* ingredient + dose form + strength
- Medicinal product form
 - Ingredient + dose form
- Medicinal product form “only”
 - Ingredient + dose form, *with universal restrictions*
- Medicinal product
 - Ingredient
- Medicinal product “only”
 - Ingredient, *with universal restrictions*
- Medicinal product “only” [optional]
 - Precise ingredient, *with universal restrictions*

39

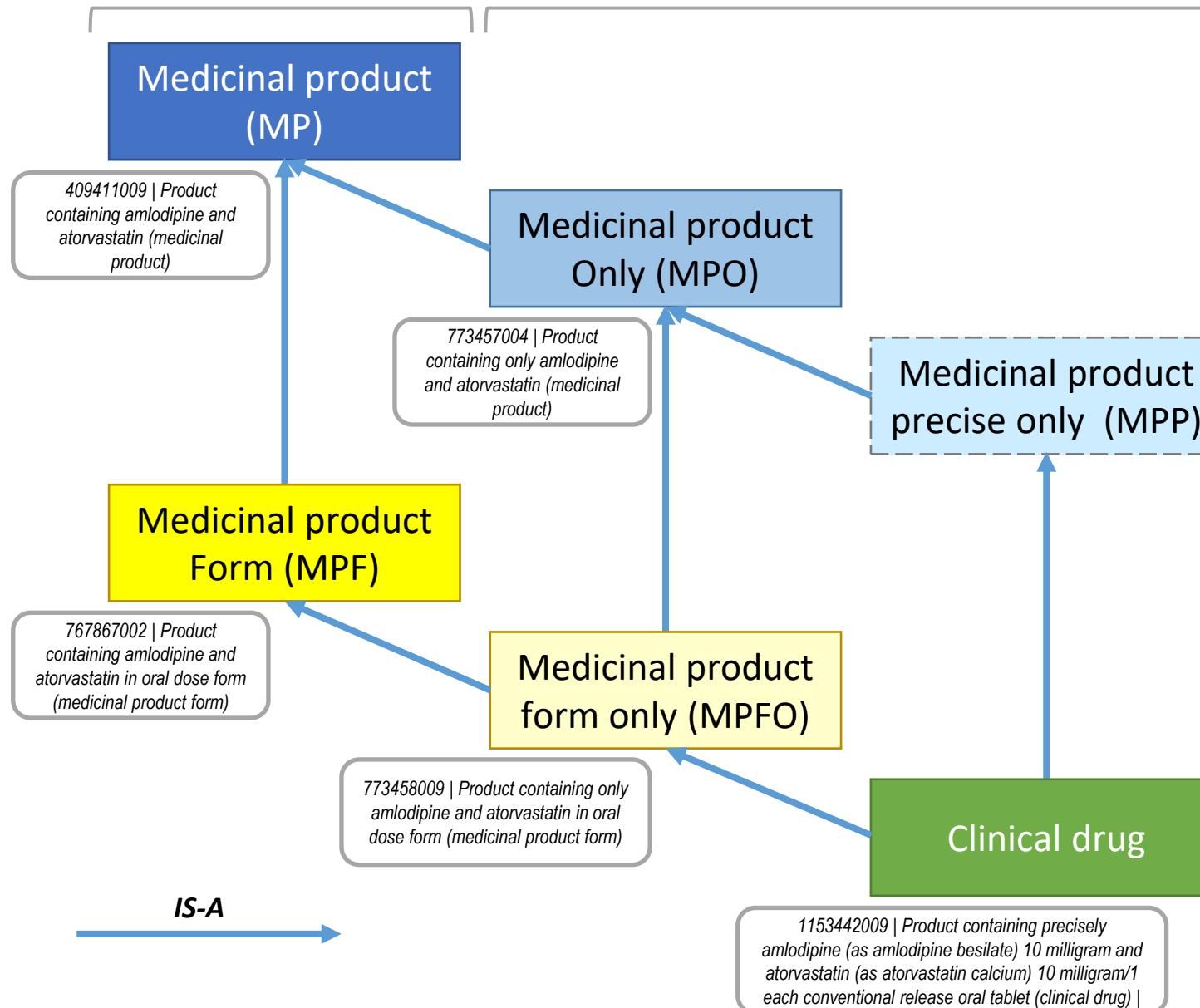




SNOMED CT
EXPO 2023

OCTOBER 26 - 27 2023 - ATLANTA USA & ONLINE

Open-world entities



Pattern for Clinical Drug

- Presentation strength
 - As opposed to normalized strength
 - To support the distinction among iso-concentration products
 - 4 discrete elements
 - Numerator (value and unit), denominator (value and unit)
- Basis of strength substance
 - Substance in reference to which strength is defined
- Dose form and unit of presentation
 - Harmonized with international standards

42



Pattern for Clinical Drug

- Closure axiom
 - Required to restrict a clinical drug to exactly its ingredients (only vs. some)
 - Should be implemented through universal restrictions
 - Has_ingredient SOME atorvastatin
 - Has_ingredient SOME amlodipine
 - **Has_ingredient ONLY (atorvastatin OR amlodipine)**
 - Universal restrictions not supported in EL++
 - Workaround: count of active ingredients
 - 2 active ingredients

43



New SNOMED CT model

1153442009 | Product containing precisely amlodipine (as amlodipine besilate) 10 milligram and atorvastatin (as atorvastatin calcium) 10 milligram/1 each conventional release oral tablet (clinical drug) |

Equivalent To +

- 'Medicinal product (product)'
 - and ('Has manufactured dose form (attribute)' some 'Conventional release oral tablet (dose form)')
 - and ('Role group (attribute)' some
 - (('Has basis of strength substance (attribute)' some 'Atorvastatin (substance)')
 - and ('Has presentation strength numerator unit (attribute)' some 'milligram (qualifier value)')
 - and ('Has presentation strength denominator unit (attribute)' some 'Tablet (unit of presentation)')
 - and ('Has precise active ingredient (attribute)' some 'Atorvastatin calcium (substance)')
 - and ('Has presentation strength numerator value (attribute)' value 10)
 - and ('Has presentation strength denominator value (attribute)' value 1)))
 - and ('Role group (attribute)' some
 - (('Has basis of strength substance (attribute)' some 'Amlodipine (substance)')
 - and ('Has presentation strength numerator unit (attribute)' some 'milligram (qualifier value)')
 - and ('Has presentation strength denominator unit (attribute)' some 'Tablet (unit of presentation)')
 - and ('Has precise active ingredient (attribute)' some 'Amlodipine besilate (substance)')
 - and ('Has presentation strength numerator value (attribute)' value 10)
 - and ('Has presentation strength denominator value (attribute)' value 1)))
 - and ('Has unit of presentation (attribute)' some 'Tablet (unit of presentation)')
 - and ('Count of base of active ingredient (attribute)' value 2)



Drug classes (Groupers)

- Based on disposition
 - Product containing 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitor
- Based on chemical structure
 - Product containing aminoglycoside
- Based on intended site of administration
 - Product manufactured as parenteral dosage form
- Based on therapeutic role
 - Conserved when intimately related to mechanism of action
 - Product containing antimalarial
 - Removed from the medicinal product hierarchy when purely regulatory information (non-definitional)
 - Antilipemic agent, Cardiovascular drug

45



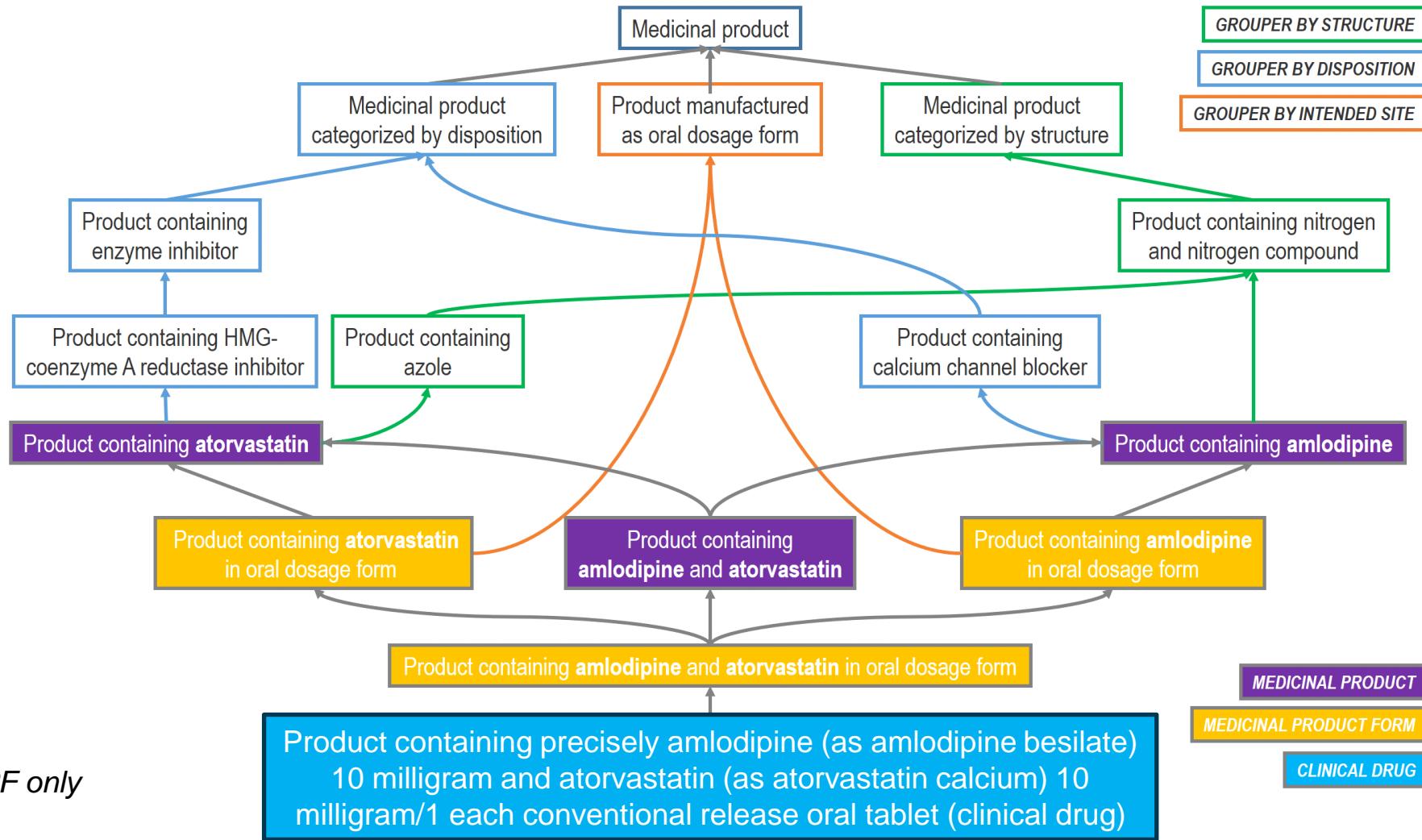
Inference of product groupers from substance groupers

- Groupers asserted in the substance hierarchy
 - Amlodipine (substance)
 - SubClassOf Substance with calcium channel blocker mechanism of action [substance grouper]
- Groupers *inferred* in the product hierarchy
 - Product containing amlodipine (medicinal product)
 - SubClassOf Product containing calcium channel blocker [product grouper]
 - Has_active_ingredient Substance with calcium channel blocker mechanism of action [substance grouper]

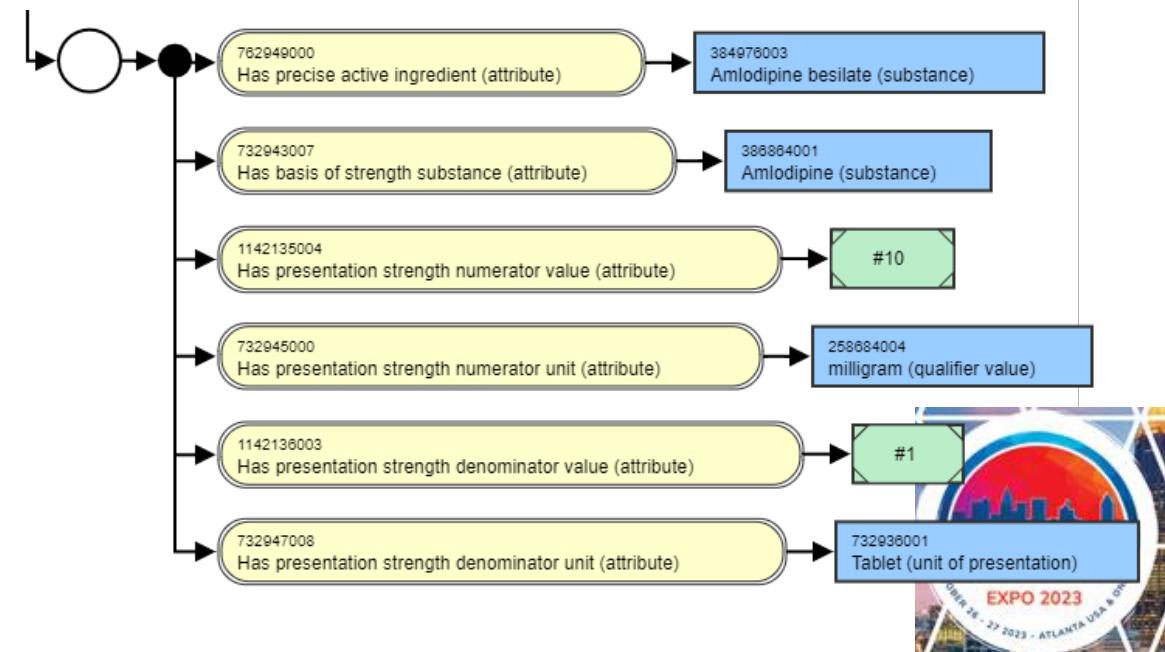
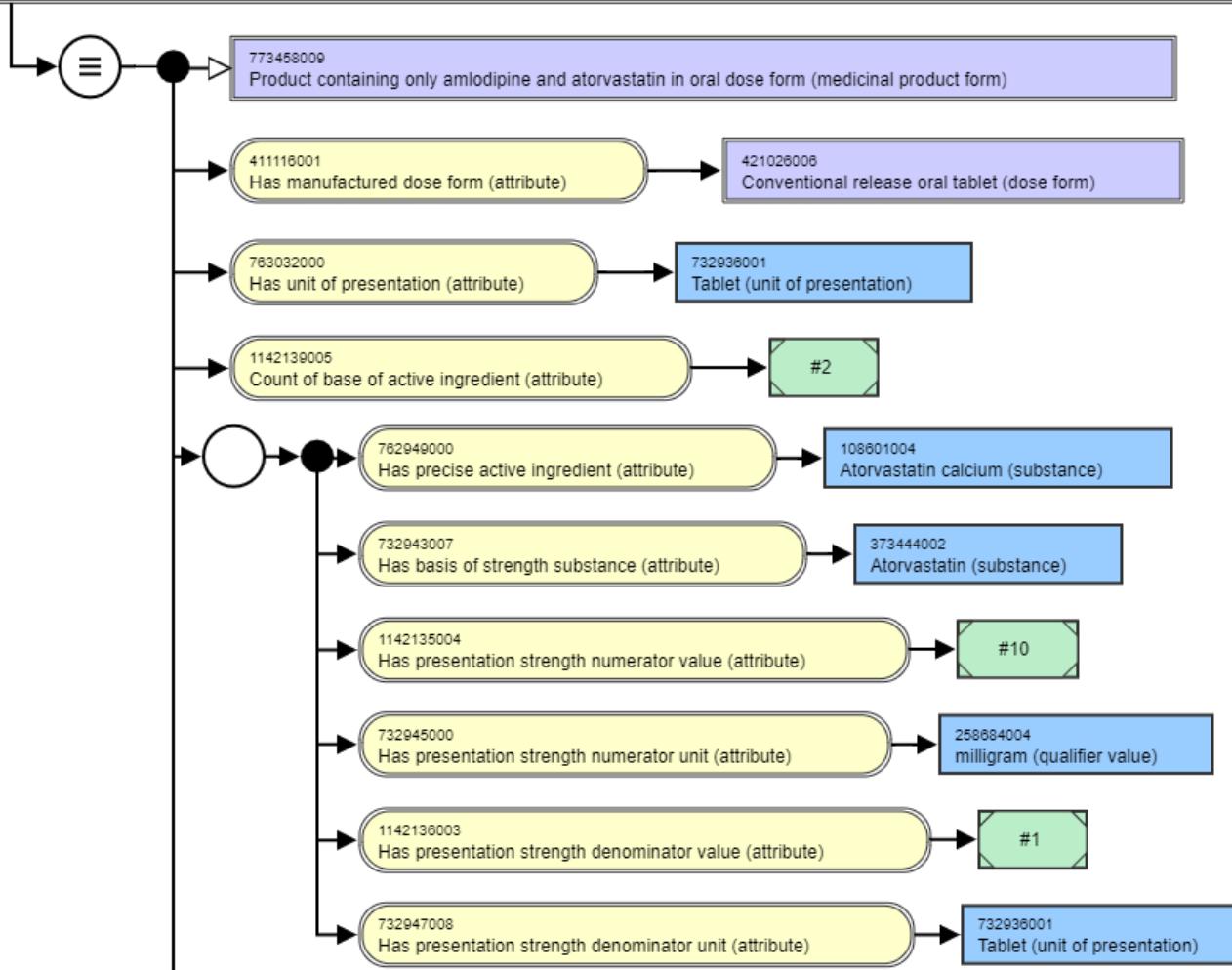
46



Medicinal product hierarchy (simplified*)



* MP only and MPF only entities omitted



Discussion

- Benefits
 - More comprehensive representation of medicinal products (MPs)
 - Necessary and sufficient classes for all MPs
 - MP hierarchy completely inferred
 - Support identification of equivalent classes
 - Interoperability with national extensions
 - Strong foundation for developing national extensions
 - Distinction among types of groupers
 - Compliance with international standards

49



Discussion

- Limitations
 - Unorthodox closure axiom
 - Based on count of active ingredients
 - In the absence of universal restrictions in EL++
 - Partially implemented in the July 2018 release
 - Mostly oral solid dose form drugs
 - Ongoing work for oral solutions, parenteral drugs and topical drugs
 - Interoperability with national drug extensions not fully demonstrated yet
 - Ongoing work with RxNorm

50





ICBO 2019
August 1, 2019
University at Buffalo

10th International Conference on Biomedical Ontology

Comparing the representation of medicinal products in RxNorm and SNOMED CT *Consequences on interoperability*

51

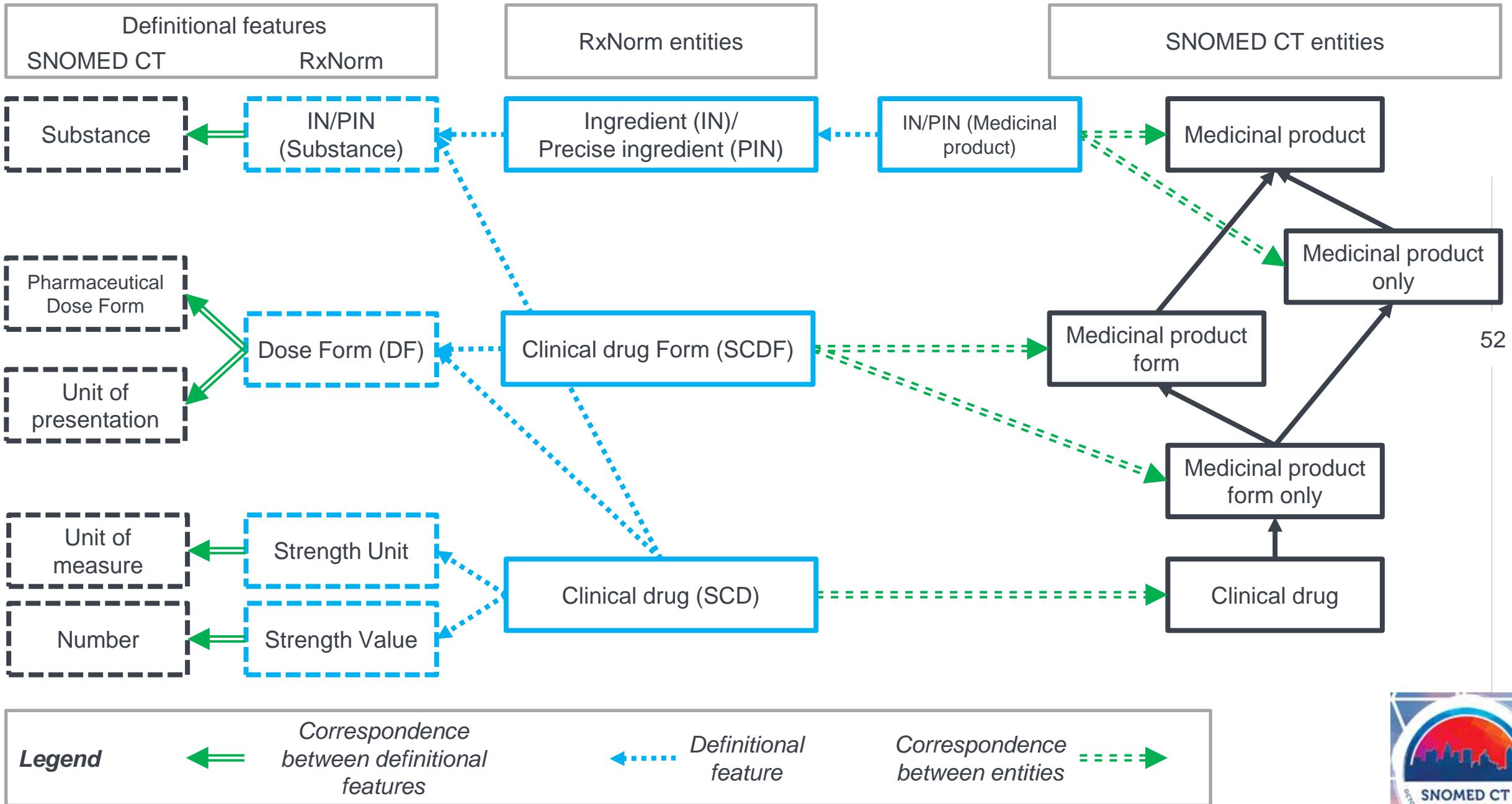
Jean-Noël Nikiema & Olivier Bodenreider

National Institutes of Health, Bethesda, Maryland, USA

Nikiema J-N, Bodenreider O.

Comparing the representation of medicinal products in RxNorm and SNOMED CT – Consequences on interoperability.
Proceedings of the 10th International Conference on Biomedical Ontology (ICBO 2019):
(electronic proceedings: http://ceur-ws.org/Vol-2931/ICBO_2019_paper_21.pdf)





Findings: Consequences on interoperability

- Can RxNorm be translated into SNOMED CT?
 - Yes, for the most part
- Specifically
 - Ingredients
 - Trivial disambiguation
 - Strength
 - Different editorial conventions for units (minor)
 - Presentation strength / Concentration strength / Both (depending on unit of presentation)
 - Dose form – requires detailed analysis to identify dose form and unit of presentation



Conclusions

- Similarities and differences between the representation of medicinal products in RxNorm and SNOMED CT
- Both models share major definitional features including ingredient (or substance), strength and dose form
- Subtle differences between the two models
- Translation of RxNorm into SNOMED CT is possible, but not straightforward

54



Lessons learned from instantiating the SNOMED CT international medicinal product model with RxNorm drugs products

Olivier Bodenreider
Robert Wynne

Thursday October 26

14:00 Room: Hub 4



— Creating DL definitions for RxNorm products

- Create logical definitions in OWL for each RxNorm generic drug product based on the SNOMED CT model
 - [Adding branded products as children of the (generic) clinical drugs for convenience]
- Classify these definitions using the OWL 2 EL Reasoner, ELK, together with the OWL version of SNOMED CT
- ELK inferred logical equivalences between the RxNorm products and the corresponding products in SNOMED CT

56



Exploring medications (Browser)

Follow-along Activity

- Tooling: SNOMED CT Browser
(<https://browser.ihtsdotools.org/>)
 - International edition
 - RxNorm extension (experimental)
- ECL (Expression Constraint Language) queries
 - Constraints on definitional and other features
- Retrieval across SNOMED CT and RxNorm medications
 - Equivalent SNOMED CT and RxNorm medications shown as distinct classes

57



— Q01 - ANTIBACTERIAL CLINICAL DRUGS AVAILABLE FOR ORAL USE

- Constraints
 - Medicinal product [type]
 - Therapeutic role [**Plays role**]
 - Dose form [**Has manufactured dose form**]
- ECL query

<< 763158003 |Medicinal product (product)| : << 766939001 |Plays role (attribute)| = << 787994008 |Antibacterial therapeutic role (role)|, << 411116001 |Has manufactured dose form (attribute)| = << 385268001 |Oral dose form (dose form)|

- Results (2045 concepts)
- Examples

Follow-along Activity

58

Ciprofloxacin 250 MG Oral Tablet [Ciproflaxacin] (RxNorm:540707 SBD)	Ciprofloxacin 250 MG Oral Tablet [Ciproflaxacin]	1552061000004101
Product containing precisely ciprofloxacin (as ciprofloxacin hydrochloride) 250 milligram/1 each conventional release oral tablet (clinical drug)	Ciprofloxacin (as ciprofloxacin hydrochloride) 250 mg oral tablet	783329001

— Q02 - ANTIBACTERIAL CLINICAL DRUGS AVAILABLE FOR SYSTEMIC ADMINISTRATION

- Constraints
 - Medicinal product [type]
 - Therapeutic role [**Plays role**]
 - Dose form [**Has manufactured dose form**] ** multiple values
- ECL query

<< 763158003 |Medicinal product (product)| : << 766939001 |Plays role (attribute)| = << 787994008 |Antibacterial therapeutic role (role)|, << 411116001 |Has manufactured dose form (attribute)| = (<< 385268001 |Oral dose form (dose form)| OR <<385287007|Parenteral dose form|)

- Results (2970 concepts)
- Examples

Follow-along Activity

59

Rifampin 600 MG Injection [Rifadin] (RxNorm:207436 SBD)	Rifampin 600 MG Injection [Rifadin]	2613521000004109
Product containing precisely rifampicin 600 milligram/1 vial powder for conventional release solution for infusion (clinical drug)	Rifampin 600 mg powder for solution for infusion vial	1237155005

— Q03 - ANTIBACTERIAL EYE DROPS

- Constraints
 - Medicinal product [type]
 - Therapeutic role [**Plays role**]
 - Dose form [**Has manufactured dose form**]
- ECL query

<< 763158003 |Medicinal product (product)| : << 766939001 |Plays role (attribute)| = << 787994008 |Antibacterial therapeutic role (role)|, << 411116001 |Has manufactured dose form (attribute)| = <<385276004 |Ocular dose form (dose form)|

- Results (355 concepts)
- Examples ** not limited to clinical drugs

Follow-along Activity

60

Product containing prednisolone and sulfacetamide in ocular dose form (medicinal product form)	Prednisolone- and sulfacetamide-containing product in ocular dose form	783843003
Gentamicin 3 MG/ML / prednisolone acetate 10 MG/ML Ophthalmic Suspension (RxNorm:310469 SCD)	Gentamicin 3 MG/ML / prednisolone acetate 10 MG/ML Ophthalmic Suspension	250062100004107

— Q04 - EYE DROPS FOR GLAUCOMA

- Constraints
 - Medicinal product [type]
 - Therapeutic role [**Plays role**]
 - Dose form [**Has manufactured dose form**]
- ECL query

```
<< 763158003 |Medicinal product (product)| : << 766939001 |Plays role  
(attribute)| = << 773832000 |Antiglaucoma therapeutic role (role)|, <<  
411116001 |Has manufactured dose form (attribute)| = << 385276004 |Ocular  
dose form (dose form)|
```

- Results (402 concepts)
- Examples ** not limited to clinical drugs

Follow-along Activity

61



Latanoprost 0.05 MG/ML Ophthalmic Suspension (RxNorm:2056743 SCD)	Latanoprost 0.05 MG/ML Ophthalmic Suspension	1648081000004103
Product containing only latanoprost in ocular dose form (medicinal product form)	Latanoprost only product in ocular dose form	779661009

— Q05 - WHAT MEDICATIONS DO I HAVE TO TREAT GLAUCOMA?

- Constraints
 - Medicinal product [type]
 - Therapeutic role [**Plays role**]
 - ** no constraints on Dose form

- ECL query

<< 763158003 |Medicinal product (product)| : << 766939001 |Plays role (attribute)| = << 773832000 | Antiglaucoma therapeutic role (role) |

- Results (464 concepts)
- Examples ** include preparations other than eye drops

Follow-along Activity

62

Acetazolamide 250 MG Oral Tablet (RxNorm:197304 SCD)	Acetazolamide 250 MG Oral Tablet	1596811000004101
Product containing precisely acetazolamide 250 milligram/1 each conventional release oral tablet (clinical drug)	Acetazolamide 250 mg oral tablet	330601002

— Q06 - LISINOPRIL (BLOOD PRESSURE PILL) ORAL FORMULATIONS 5 MG AND STRONGER

- Constraints
 - Medicinal product [type]
 - Ingredient [**Has precise active ingredient**]
 - Strength [**Has numerator value, Has presentation strength numerator unit**]
 - Single-ingredient formulation [**Count of base of active ingredients**]
- ECL query

<< 763158003 |Medicinal product (product)| : << 762949000 |Has precise active ingredient (attribute)| = << 386873009 |Lisinopril (substance)|, 1142135004|Has numerator value| >= #5, << 732945000 |Has presentation strength numerator unit (attribute)| = 258684004 |milligram (qualifier value)|,
1142139005|Count of base of active ingredients| = #1
- Results (22 concepts)
- Examples

Follow-along Activity

63

Lisinopril 10 MG Oral Tablet [Carace] (RxNorm:201381 SBD)	Lisinopril 10 MG Oral Tablet [Carace]	1482851000004108
Product containing precisely lisinopril 40 milligram/1 each conventional release oral tablet (clinical drug)	Lisinopril 40 mg oral tablet	376772000

— Q07 - ALL ACTIVE INGREDIENTS IN AVAILABLE ANTICONVULSANT MEDICATIONS

- Constraints
 - Medicinal product categorized by therapeutic role
 - Active ingredient [**Has active ingredient**]
 - . operator
- ECL query

Follow-along Activity

< 63094006 |Medicinal product acting as anticonvulsant agent (product)| .
127489000 |Has active ingredient (attribute)|

- Results (48 concepts)
- Examples ** returns substances, not clinical drugs

64



Cenobamate (substance)	Cenobamate	830240007
Perampanel (substance)	Perampanel	703127006

Q08 - ANTIBACTERIAL CLINICAL DRUGS AVAILABLE FOR ORAL USE BUT *ALLERGY TO SULFA DRUGS*

- Constraints
 - Medicinal product [type]
 - Therapeutic role [**Plays role**]
 - Dose form [**Has manufactured dose form**]
 - **MINUS operator**
 - Active ingredient [**Has active ingredient**]

Follow-along Activity

- ECL query

```
(<< 763158003 |Medicinal product (product)| : << 766939001 |Plays role  
(attribute)| = << 787994008 |Antibacterial therapeutic role (role)|, << 411116001  
|Has manufactured dose form (attribute)| = << 385268001 |Oral dose form (dose  
form)|) MINUS (<< 763158003 |Medicinal product (product)| : 762949000 | Has  
precise active ingredient (attribute)| = << 372788003 |Substance with  
sulfonamide structure and antibacterial mechanism of action (substance)|)
```

- Results (1905 concepts)
- Examples *of excluded medications*

65



Sulfisoxazole 500 MG Oral Tablet [Gantrisin] (RxNorm:202248 SBD)	Sulfisoxazole 500 MG Oral Tablet [Gantrisin]	2612161000004104
Sulfadimethoxine 500 MG Oral Tablet (RxNorm:102797 SCD)	Sulfadimethoxine 500 MG Oral Tablet	2606531000004100

Interoperation and Analytics of EHR Data

Stan Huff



Interoperation of Laboratory Data for Standardization, Research and Decision Support

Stanley Huff

67



Why do we need clinical decision support?

68



Medical Error – Third Leading Cause of Death in the US

BMJ 2016; 353:i2139 (Published 3 May 2016)

Table

Table 1 | Studies on US death rates from medical error since the 1999 IOM report

Study	Dates covered	Source of information	Patient admissions	Adverse event rate (%)	Pooled results			
					Deaths due to preventable adverse event	% of admissions with a preventable lethal adverse event	Extrapolation to 2013 US admissions†	
Health Grades ¹¹	2000-02	Medicare patients	37 000 000	NR	389 576	0.71	251 454	
Office of Inspector General ¹²	2008	Medicare patients	37 000 000	1.4	44	12	0.62	219 579
Classen et al ¹³	2004		33.2	1.1	100	9	1.13	400 201
Landrigan et al ¹⁴			2341	18.1	0.6	63	14	0.38
Point estimate from all data			—	—	—	—	0.71	251 454‡

Physicians Do the Right Thing ~50% of the Time
 McGlynn EA, Asch SM, Adams J, Keesey J, Hicks J, DeCristofaro A,
 Kerr EA. N Engl J Med. 2003 Jun 26;348(26):2635-45.

— Core Assumptions

‘The complexity of modern medicine exceeds the inherent limitations of the unaided human mind.’

~ David M. Eddy, MD, Ph.D.

‘... man is not perfectible. There are limits to man’s capabilities as an information processor that assure the occurrence of random errors in his activities.’

~ Clement J. McDonald, MD

70



Decision Support Modules (Intermountain)

Antibiotic Assistant

Ventilator weaning

ARDS protocols

Nosocomial infection monitoring

MRSA monitoring and control

Prevention of Deep Venous Thrombosis

Infectious disease reporting to public health

Diabetic care

Pre-op antibiotics

ICU glucose protocols

Ventilator disconnect

Infusion pump errors

Lab alerts

Blood ordering

Order sets

Patient worksheets

Post MI discharge meds

71

All of these applications decrease cost and improve health!



— So what is one answer to better care?

Clinical Decision Support!

But ...

MedInfo 17th World Conference of Medical and Health Informatics, August 25-30, 2019 Lyon France

P1-07 History of Clinical Decision Support: A Six-Decade Retrospective* Casimir Kulikowsk, Robert Greenes, Ted Shortliffe, Don Detmer

Conclusion: The greatest challenge is being able to share CDS outside of the organization where it was created!



Moving Forward Together- Background

- **Shared goal:** Improve health and better care through standardized terminology



- Support enhanced clinical system functionality and interoperability by establishing principled relationships between SNOMED CT and LOINC
- Provide effective support for providers and users who implement different combinations of SNOMED CT and LOINC in health information systems

73



The LOINC Ontology: A LOINC and SNOMED CT Interoperability Solution

- Extension of SNOMED CT
 - SNOMED CT: ontological framework
 - LOINC: content
- Distribute LOINC content to LOINC and SNOMED CT users
 - Create SNOMED CT and LOINC codes for all concepts that are shared between the terminologies
- Easy for implementers to have a unified approach to implementing both standards, giving them a choice of which codes to use for ease of implementation
- Provide a single solution that meets clinical and regulatory requirements, globally

74



The LOINC Ontology: A LOINC and SNOMED CT Interoperability Solution

- Benefits
 - Provides LOINC pathology and lab content in an understood format to countries who do not currently use LOINC
 - Provides the ontological framework for LOINC to meet the needs of the community for a computable representation of LOINC
 - **Computable relationships to enable decision support**
 - Leverage LOINC and SCT subject matter expertise
 - Sets a precedent for other domains and standard collaborations

75



— Progress to date and other information

- Preview released mid October
 - ≈23K-24K Laboratory LOINC
- Created a user site: loincsnomed.org
- Browser: browser.loincsnomed.org
- Meetings:
 - Salt Lake City, Montreal, London
 - bi-monthly project team meetings
- Owned & maintained by Regenstrief, including responsibility for the model (concept model as well as the ontology)

76



More information

- All LOINC content will eventually be in the extension
- We will map existing SNOMED observables to LOINC codes and make new LOINC codes as needed
- We will map/match LOINC parts to SNOMED concepts, and create new SNOMED concepts as needed
- We will incrementally add domains of information (lab, clinical, documents, radiology, survey instruments)
- We are not creating grouper codes (we will use ECL instead)
- To support exchange of data between systems that use LOINC and systems that use SNOMED CT we have provided a simple translation/equivalence table
- FSNs in the LOINC Extension will be created by the rules for FSNs in the International Edition

77



The MRCN – Observable entity

SNOMED CT - Home SNOMED CT MRCM Maintenance Tool

browser.ihtsdotools.org/mrcm/?branch=MAIN%2F2023-10-01&domain=363787002

Intermountain links World Clock Meeti... Bookmarks HL7 stuff Graphite SHIELD Gmail U of Utah LOINC SNOMED

SNOMED International

SNOMED CT MRCM Maintenance Tool MAIN/2023-10-01

Observable entity (observable entity)

Domain

- Filter Domains...
- Basic dose form (basic dose form)
- Body structure (body structure)
 - Anatomical structure (body structure)
 - Lateralizable body structure reference set (foundation metadata concept)
- Clinical finding (finding)
- Event (event)
- Observable entity (observable entity)**
- Pharmaceutical / biologic product (product)
 - Medicinal product package (product)
- Pharmaceutical dose form (dose form)
- Physical object (physical object)
- Procedure (procedure)
 - Surgical procedure (procedure)

Domain Constraint

<< 363787002 |Observable entity (observable entity)|

Proximal Primitive Constraint

<< 363787002 |Observable entity (observable entity)|

Guide URL

<http://snomed.org/dom363787002>

Precoordination Domain Template

[[+id(<< 363787002 |Observable entity (observable entity)|))]: [[0..*]] { [[0...]] }

Postcoordination Domain Template

[[+scq(<< 363787002 |Observable entity (observable entity)|))]: [[0..*]] { [...]

Applicable Attributes

- Filter Attributes...
- Characterizes (attribute)
- Component (attribute)
- Direct site (attribute)
- Has realization (attribute)
- Inherent location (attribute)
- Inheres in (attribute)
- Precondition (attribute)
- Procedure device (attribute)
 - Using device (attribute)
- Process acts on (attribute)
- Process agent (attribute)
- Process duration (attribute)
- Process extends to (attribute)
- Process output (attribute)
- Property (attribute)
- Relative to (attribute)
- Relative to part of (attribute)
- Scale type (attribute)
- Technique (attribute)
- Time aspect (attribute)
- Towards (attribute)
- Units (attribute)

78

78



General Form of Clinical LOINC Names

LOINC codes are created using a six axis model

<component> : <property> :
<timing> : <system> :
<scale> : <**method**>

8331-1 Body Temperature :TEMP :PT :MOUTH :QN

The first 5 parts are mandatory, but method is optional. Subparts of the six axes are created as needed in specific subject areas.

MRCN and LOINC Axes

```

[[+id(<< 363787002 |Observable entity (observable entity)|)]]:  

...  

[[0..1]] 246093002 |Component| = [[+id(<< 105590001 |Substance (substance)|  

    OR << 123037004 |Body structure (body structure)|  

    OR << 123038009 |Specimen (specimen)|  

    OR << 260787004 |Physical object (physical object)|  

    OR << 373873005 |Pharmaceutical / biologic product (product)|  

    OR << 410607006 |Organism (organism)|  

    OR << 419891008 |Record artifact (record artifact)|)]],  

[[0..1]] 370130000 |Property| = [[+id(<< 118598001 |Property (qualifier value)|)]],  

[[0..1]] 370134009 |Time aspect| = [[+id(<< 7389001 |Time frame (qualifier value)|)]],  

[[0..1]] 704327008 |Direct site| = [[+id(<< 105590001 |Substance (substance)|  

    OR << 123037004 |Body structure (body structure)|  

    OR << 123038009 |Specimen (specimen)|  

    OR << 260787004 |Physical object (physical object)|  

    OR << 373873005 |Pharmaceutical / biologic product (product)|  

    OR << 410607006 |Organism (organism)|  

    OR << 419891008 |Record artifact (record artifact)|)]],  

[[0..1]] 370132008 |Scale type| = [[+id(<< 117362005 |Nominal value (qualifier value)|  

[[0..1]] 246501002 |Technique| = [[+id(<< 254291000 |Staging and scales (staging scale)|  

    OR << 117363000 |Ordinal value (qualifier value)|  

    OR << 117364006 |Narrative value (qualifier value)|  

    OR << 117365007 |Ordinal  

    OR quantitative value (qualifier value)|  

    OR << 117444000 |Text value (qualifier value)|  

    OR << 26716007 |Qualitative (qualifier value)|  

    OR << 30766002 |Quantitative (qualifier value)|)]],

```

LOINC Axis

Component

Property Timing System

80

Scale

Method

80



— Q09 - TESTS FOR COVID-19 ACTIVE DISEASE

- Constraints
 - Observable entity
 - Substance(s) [**RNA or Antigen**]
- ECL query

Follow-along Activity

(<< 363787002 |Observable entity (observable entity)| : 246093002 |Component (attribute)| = << 1240411000000107 |Ribonucleic acid of severe acute respiratory syndrome coronavirus 2 (substance)|)

OR

(<< 363787002 |Observable entity (observable entity)| : 246093002 |Component (attribute)| = << 840536004 |Antigen of severe acute respiratory syndrome coronavirus 2 (substance)|)

- Results (11 concepts)
- Examples

Measurement of severe acute respiratory syndrome coronavirus 2 antigen (observable entity)	Measurement of SARS-CoV-2 antigen
SARS-CoV-2 (COVID-19) RNA [Presence] in Nasopharynx by NAA with nonprobe detection (LOINC:94565-9)	SARS-CoV-2 (COVID-19) RNA [Presence] in Nasopharynx by NAA with nonprobe detection



— Q10 – FHIR Query: 2345-7 Glucose:MCnc:Pt:Ser/Plas:Qn

- Constraints
 - Glucose MCNC Pt Blood Qn
 - MINUS (Glucose MCNC Pt Blood Qn with Precondition)
- ECL query

```
(<< 6060001000004106 |Clinical laboratory observable (observable entity)| : << 246093002 |Component (attribute)| =  
<< 67079006 |Glucose (substance)|, << 370130000 |Property (attribute)| = << 118539007 |Mass concentration  
(property) (qualifier value)|, << 370134009 |Time aspect (attribute)| = << 123029007 |Single point in time (qualifier  
value)|, << 704327008 |Direct site (attribute)| = << 119297000 |Blood specimen (specimen)|)  
MINUS
```

```
(<< 6060001000004106 |Clinical laboratory observable (observable entity)| : << 246093002 |Component (attribute)| =  
<< 67079006 |Glucose (substance)|, << 370130000 |Property (attribute)| = << 118539007 |Mass concentration  
(property) (qualifier value)|, << 370134009 |Time aspect (attribute)| = << 123029007 |Single point in time (qualifier  
value)|, << 704327008 |Direct site (attribute)| = << 119297000 |Blood specimen (specimen)|, << 704326004  
|Precondition (attribute)| = << 703763000 |Precondition value (qualifier value)|)
```

- Results (7 concepts)
- Examples

Glucose [Mass/volume] in Blood by automated test strip (LOINC:2340-8)	Glucose [Mass/volume] in Blood by automated test strip	911753291000004107
Glucose [Mass/volume] in Venous blood (LOINC:41652-9)	Glucose [Mass/volume] in Venous blood	81121001000004108
Glucose [Mass/volume] in Arterial blood (LOINC:41651-1)	Glucose [Mass/volume] in Arterial blood	81111001000004100

Follow-along Activity

82



— Q11 – ALL TECHNIQUES THAT ARE PRE-COORDINATED WITH LAB OBSERVABLE

- Constraints
 - Clinical laboratory observable
 - Technique [EXISTS]
- ECL query

<< 6060001000004106 |Clinical laboratory observable (observable entity)| -

<< 246501002 |Technique (attribute)|

Results (160 concepts)

- Examples

Nucleic acid amplification with probe detection technique (qualifier value)

Unfractionated measurement technique (qualifier value)

Direct antiglobulin test technique (qualifier value)

Dilute Russell viper venom reduced phospholipid technique (qualifier value)

Follow-along Activity

83



How to query SNOMED CT encoded cancer pathology data sets (or synoptic reports)

Scott Campbell, PhD, MBA

An implementation overview of
the Cancer Synoptic Reporting
Working Group



*Global terminology enabling
quality information
exchange*

Summary of cancer pathology reporting project

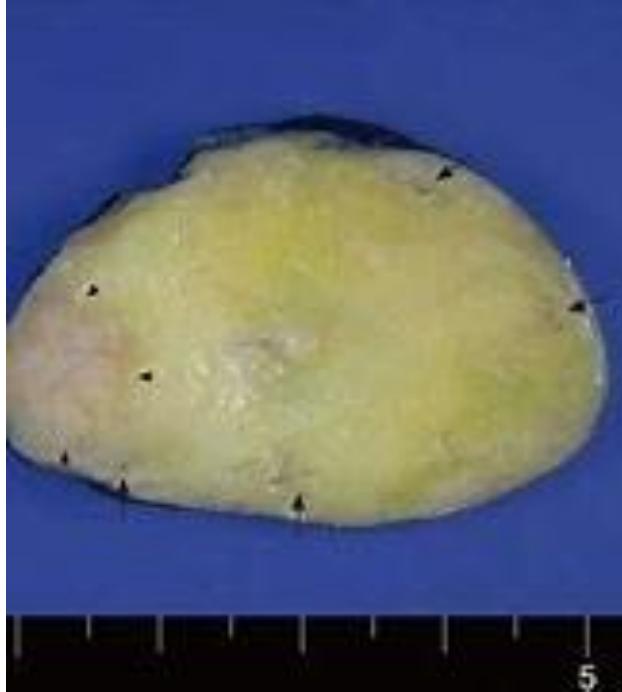
- Content covered today *briefly* discusses structured pathology reporting.
- Tomorrow's session is an in depth discussion of the Cancer Synoptic Reporting Working Group final product, electronic cancer pathology reporting, implementation and use
- General discussion on how to interrogate SNOMED CT encoded cancer pathology data sets
- Take aways:
 - Synoptic structure of pathology reporting
 - Data architectures suitable for synoptic data storage
 - Query use cases using ECL

The Histopathology Process



Surgery

Surgery performed to excise suspected lesions and/or remove tumor



Gross Exam

Tissue macroscopically examined, described, measured



Tissue Blocks

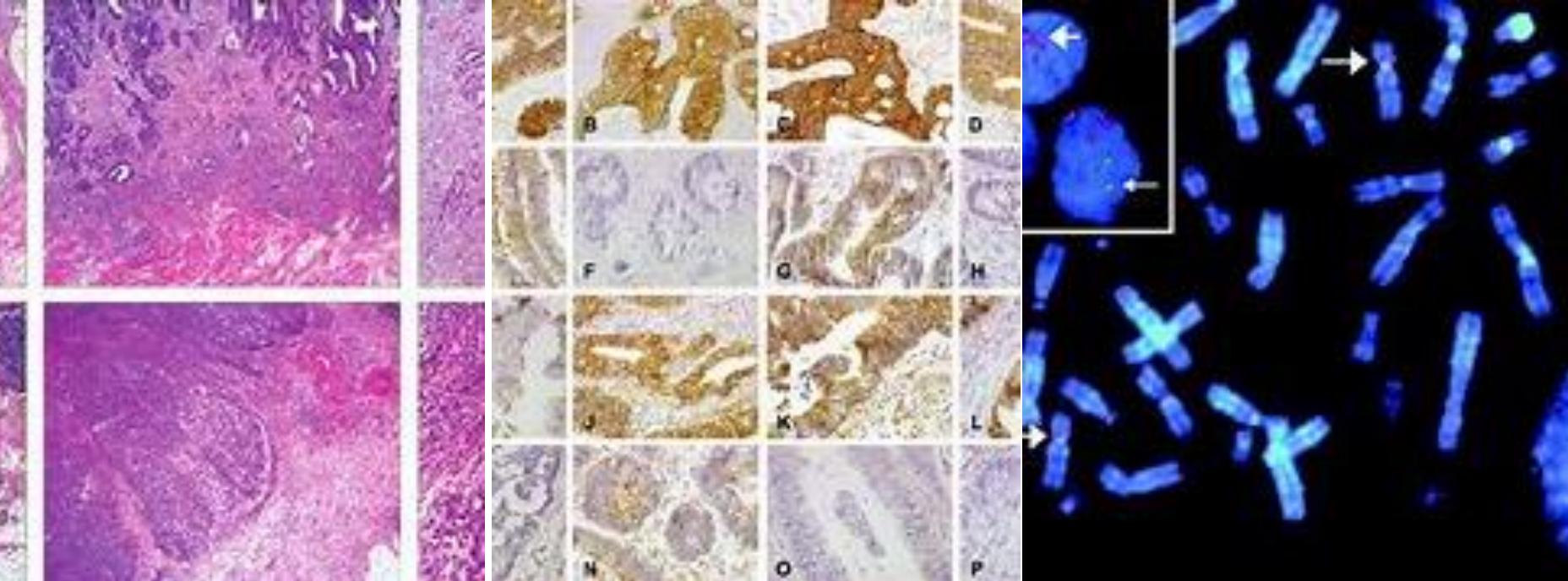
Tissue regions fixed in formalin and embedded in paraffin



Histopathology Slide

Tissue blocks cut, tissue placed on glass slide, and stained

Microscopic Exam



Hematoxylin and Eosin

H&E tissue examination to identify irregular tissue architecture

Immuno-histochemistry

IHC stains help differentiate between underlying pathologies

Cytogenetic and molecular genomics

Various genomic techniques used if needed

Report

Final report issued



Hospital Name
Address

Surgical Pathology Report

Patient: Last Name, First Name
MRN: Medical Record Number
DOB: Date of Birth (Age: #)
Gender: M/F

Accession Number: Specimen Identification
Procedure: Date
Attending: Doctor's Name

Clinical History: Large Gastric Mass

Specimen: Gastric Mucosa

Diagnosis:
Stomach, Partial Gastrectomy:

- Malignant Epithelioid Gastrointestinal Stromal Tumor
- Tumor Size 10 x 9 x 8 cm
- Cell Type: Epithelioid and Spindled
- High cellularity; present
- Mucosal Invasion: Focally present adjacent to ulceration
- Mucosal ulceration present
- Mitotic Count: 10/50 HPF
- Myxoid background: Focally present
- Foci of necrosis present
- CD117, vimentin, and CD34: uniformly positive

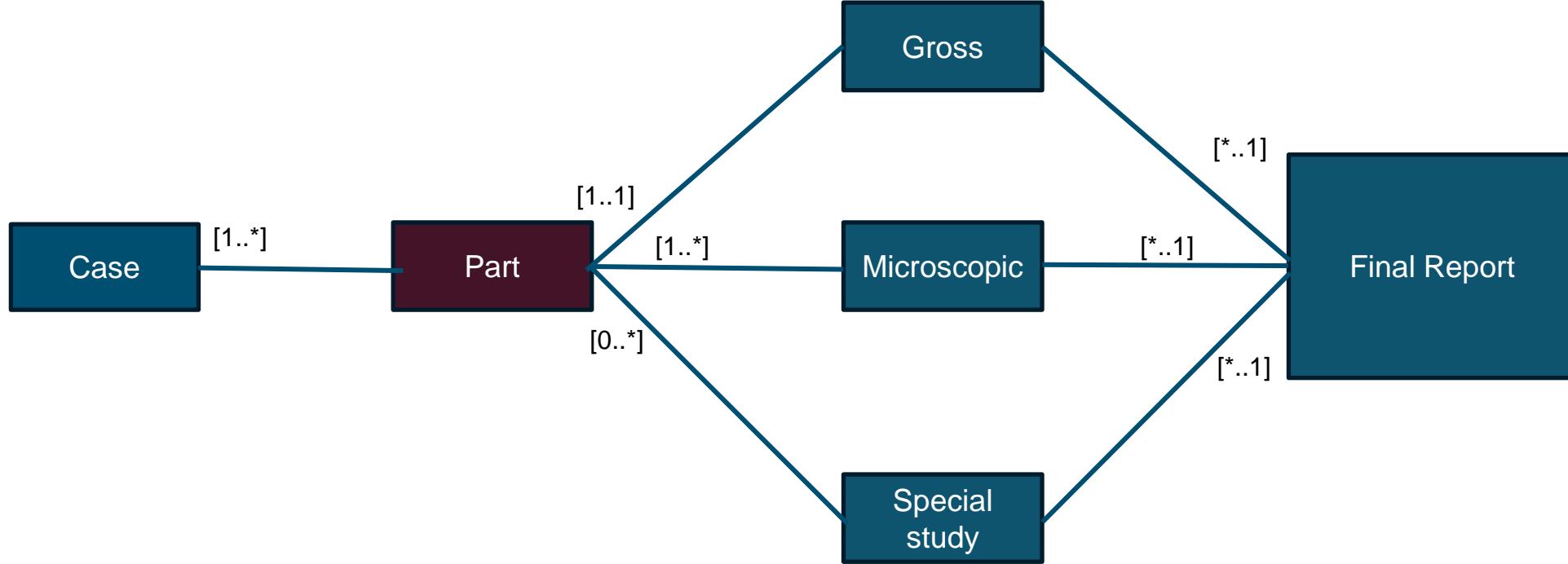
Gross Description:
The specimen consists of an approximately 5 x 7 cm portion of gastric mucosa that is surrounded and underlying by a lobulated mass which is 10 x 9 x 8 cm. The central portion of the mass appears to have an approximately 1.5-cm ulcer. The mucosa away from the area of ulceration is partially removed from the underlying tumor. The underlying mass appears encapsulated and lobular. Gross sections show the lesion to consist of several different patterns. A single area has a gray-tan pattern with an area of central necrosis showing a fairly uniform appearance whereas other regions of the tumor are gray white- and somewhat lobular in appearance. Areas of yellow necrosis are scattered through the tumor. Representative portions submitted.

Microscopic Description:
Sections through the neoplasm show it to be primarily a high cellular neoplasm. The cells are in part arranged in fascicles and clusters with enlarged elongate nuclei having relatively finely nucleoli. In some areas, the fascicles have an interwoven appearance. Mitotic figure up to 10/50 HPF. A few areas show foci of necrosis with the cells appearing to be surrounded by somewhat myxoid stroma. Foci of displayed necrosis are present. The lesions appear circumscribed, although not specifically encapsulated. It focally involved the mucosa and shows full thickness ulceration. The tumor immediately beneath the mucosal area of ulceration has a nearly lobular somewhat spindled growth pattern. Some areas of the tumor have a slightly more rounded nuclei and somewhat epithelioid appearance. The cells appear to be arranged in groups and clusters. Some of the cells have cytoplasmic vacuoles. These areas also show a prominent mitotic activity. Some mitotic figures are abnormal and atypical. The tumor contains numerous relatively open vascular channels which appear to be part of the neoplasm. The tumor has a pseudo capsule and in some areas appear to be nearly covered.

Immunostains are strongly positive for CD117 (C-kit), CD34, and Vimentin, Smooth muscle actin, Desmin, Synaptophysin, S-100, and CK8/18 are negative.

Comment:
Immunostains were performed on the core biopsy and demonstrate that the tumor cells are positive for CD117. The

Information Model



88



88

Final Report Using Synoptic Style

MICROSCOPIC TUMOR CHARACTERISTICS

Histologic type of neoplasm:

Mucinous adenocarcinoma (greater than 50% mucinous)

Histologic grade of neoplasm:

Low-grade (well to moderately differentiated) (%) : 95

Mucinous histologic fraction of neoplasm:

(%) : 0

Percent signet ring cells in adenocarcinoma:

None

Intratumoral Lymphocytic Response:

None

Peritumoral Lymphocytic Response:

None

Status of tumor budding in carcinoma:

None

Number of tumor buds per HPF (Average per 10 HPF): Average # per HPF: 0

Perineural Invasion:

Perineural invasion absent

Lymphatic (Small Vessel) Invasion (L):

Absent

Intramural vascular (Large vessel) invasion:

Absent

Extramural vascular (Large vessel) invasion:

Absent

Polyp Type in which invasive carcinoma arose:

None identified

89

ANCILLARY TESTING

Mismatch repair abnormality by IHC:

MLH1- Mismatch Repair (MMR) Proteins by IHC:

No: Mismatch repair proficient

Intact nuclear expression

MSH2-Mismatch Repair (MMR) Proteins by IHC:

Intact nuclear expression

MSH6-Mismatch Repair (MMR) Proteins by IHC:

Intact nuclear expression

PMS2-Mismatch Repair (MMR) Proteins by IHC:

Negative for cytoplasmic expression

89



Objective of CSRWG

- Develop SNOMED CT concepts necessary to fully, unambiguously represent all required cancer pathology synoptic reporting data elements
- SNOMED CT concepts authored must be able to be unambiguously and fully represent each data element AFTER the data is separated from the initial data capture device (e.g., paper, web portal, eCP)
 - Can the data elements be stored in database or registry such that the *meaning* of the data remains intact without reference to the data capture form?
 - Not acceptable to be a "number" associated with a word-string. The "number" *must* carry meaning...semantically computable.
- SNOMED CT content developed must be suitable for major protocol publishing bodies – CAP, ICCR, RCPATH, RPCA, Palga, others.
 - Project used CAP infrastructure and inventory capability of data elements as a base framework for concept enumeration and initial authoring
 - ICCR, RCPATH content used to clarify meaning of common data elements across data set publications.

90

90



Project Status

- > 1000 new concepts created and/or fully modeled
- 100% of CAP required data elements for all solid tumors
 - 61 data sets
 - Includes both adult and pediatric data sets
 - CAP PERT committee reviewing and approving SNOMED CT terminology binding and association with C-keys.
 - CAP to include SNOMED CT terminology bindings in eCP and other release formats
- 24 ICCR data sets initially mapped to SNOMED CT
 - Terminology binding on-going for remaining data sets
 - Terminology binding to be reviewed and validated for use by ICCR

Synoptic structure

- Structured pathology cancer reporting is built as a series of questions and answers that summarize the key, actionable features of the cancer for patient care
- The "Questions" are features of the tumor that the pathologist is to observe, measure or describe
- The "Answers" represent what the pathologist observed.
- In the pathology cancer report protocols, each question or tumor feature to be assessed is paired with a constrained set of acceptable answers or "measurements"
- Pathology societies and other domain authorities define what features of tumors should be assessed and how those assessments should be made

92



92



Content developed

- Procedure used to collect the specimen(s)
- Tumor site
- Tumor dimensions
- Histologic type
- Histologic grade
- Anatomic location(s) involved by direct, contiguous extension of the neoplasm
 - Tissue layers
 - Adjacent tissue structures
 - Lymph/vascular invasion
 - Perineural invasion
- Presence of neoplasm at surgical margins
- Lymph node metastasis
 - Number lymph nodes involved by metastasis
 - Number lymph nodes examined
 - Location of lymph nodes
- Anatomic locations involved by metastatic, discontinuous spread of the neoplasm
- TNM staging (Tumor, Node, Metastasis)

93



93

Design Assumptions and Approach

- Observable entity hierarchy used
- Question carries the context to unambiguously interpret the observation
- Explicit pathology knowledge NOT carried by SNOMED CT
- Pathologist carries and expresses their knowledge when recording their observation

94

Part	Type	Description	
Question	CODED_TEXT	<< Observable entity (observable entity)	The question
Observation	CODED_TEXT	<< 123037004 Body structure (body structure) OR ???	The coded result of the observation
Interpretation	Implied - Context dependent	N/A	The interpretation of the observation based on agreed guidelines/rules

94

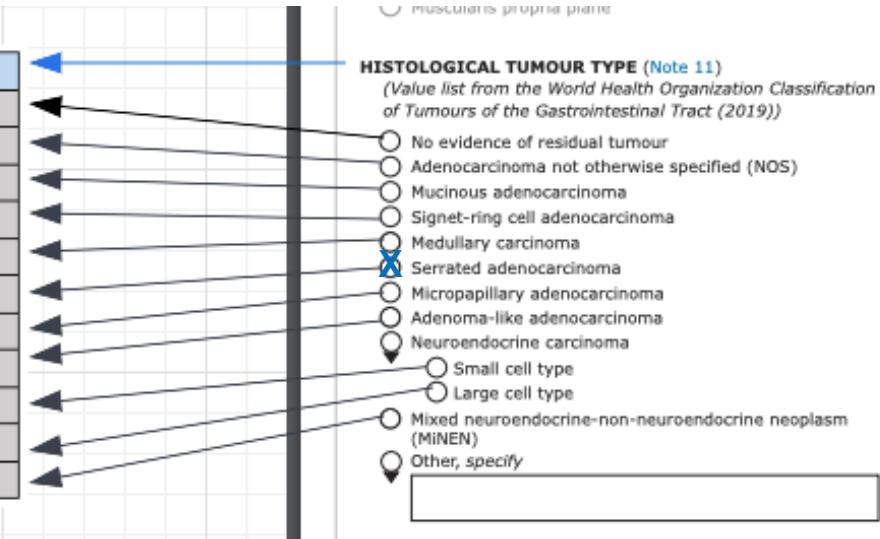


Example – Colon Histology

SNOMED CT Bindings

1284862009 Histologic type of primary malignant neoplasm of cecum and/or colon and/or rectum (observable entity)
41647 Change Page Orientation [textual qualifier] (qualifier value)
1187332001 Adenocarcinoma (morphologic abnormality)
72495009 Mucinous adenocarcinoma (morphologic abnormality)
87737001 Signet ring cell carcinoma (morphologic abnormality)
32913002 Medullary carcinoma (morphologic abnormality)
450948005 Serrated adenocarcinoma (morphologic abnormality)
450895005 Micropapillary carcinoma (morphologic abnormality)
1187332001 Adenocarcinoma (morphologic abnormality)
719105002 Small cell neuroendocrine carcinoma (morphologic abnormality)
128628002 Large cell neuroendocrine carcinoma (morphologic abnormality)
785766008 Mixed neuroendocrine-non neuroendocrine neoplasm (morphologic abnormality)

ICCR Data Elements



95

1284862009 |Histologic type of primary malignant neoplasm of cecum and/or colon and/or rectum (observable entity)|
 = 450948005 |Serrated adenocarcinoma (morphologic abnormality)|

Similar terminology bindings are complete and ready for ICCR review for 24 data sets

95



Observable entity defining attributes

96

Attribute	Description
[Property]	This attribute is used to assert the property, or feature, being assessed by the pathologist. Target values for this attribute include: <<410668003 Length property (qualifier value) ; <<30001000004102 Histologic feature (property) (qualifier value) ; <<1300001000004107 Location property (qualifier value) ; 705057003 Presence (property) (qualifier value) ; 118582008 Percent (property) (qualifier value) ; 758637006 Anatomic location (property) (qualifier value)
[Inheres in]	This attribute is used to assert the entity that carries the property being measured. In most cases, the target values are <<108369006 Neoplasm (morphologic abnormality)
[Inherent location]	The inherent location attribute is used to describe the anatomical location of the entity that carries the property being assessed. In most cases, the inherent location indicates the anatomical location of the primary malignant neoplasm, that is the primary organ affected by the malignancy.
[Component]	This attribute is used to indicate an entity that is being assessed for presence such as necrosis within a neoplasm. It is also used to represent the numerator in an percent observation.
[Relative to]	This attributed is used for the denominator in a percent or number fraction observable.
[Direct site]	Direct site is specifically used to define the specimen in which the observation is being made.
[Technique]	Technique is used to define the method by which the observation is being made. This attribute is used to specific methods of tumor staging, histologic grading methods, direct vision (gross) evaluation, microscopy and immunohistochemistry methods.
[Time aspect]	The time aspect for all cancer pathology observable entities is 123029007 Single point in time (qualifier value) .
[Scale type]	This attribute is used to describe the evaluation scale used for the observation. 117362005 Nominal value (qualifier value) is used to describe observable entities assessing morphologies, body structures, and procedures. 117363000 Ordinal value (qualifier value) is used in histologic grade observations and observations indicating the presence, absence or degree of presence. 30766002 Quantitative (qualifier value) is used for numerical observations.
[Characterizes]	Characterizes is used to represent the underlying processes of the neoplasm. These include <<1204295007 Malignant proliferation of neoplasm (qualifier value) and 1255587009 Regression of neoplasm (qualifier value)
[Process extends to]	This attribute is used to define the "end point" of the process indicated by the characterized attribute/value pair. In most concepts, this associated value of this attribute is <<123037004 Body structure (body structure) to indicate where the neoplasm has grown or metastasized.

96



Where to find content in browser

- Majority of “question” content <<1145211006 |Proliferative mass observable (observable entity)| and <<1149283006 |Tissue specimen observable (observable entity)|
- “Answer” content is found in hierarchies consistent with Property target Concept in Observable entity definition.
 - Example: Presence (property):
< 272519000 |Absence findings (qualifier value)| or
< 260411009 |Presence findings (qualifier value)|
 - Example: Anatomic location (property):
<<91723000 |Anatomical structure (body structure)|
- Important: Many historical observable entity concepts developed by the College of American Pathologists (effective dates 2001/2002) are primitive
- *MOST* but not all new concepts are fully defined.



Examples of terminology bindings

- Association of synoptic data elements with properly constructed SNOMED CT concepts critical to effective, reliable and consistent implementation
- SNOMED International and CSRWG can provide initial bindings, BUT users should confirm with national/regional authorities for prescribed bindings (e.g., CAP, ICCR, RCPA, RCPPath)

Question SCTID	Description	Answer SCTID
911750741000004104 Histologic type of primary malignant neoplasm of lung (observable entity)	Squamous cell carcinoma	1162767002 Squamous cell carcinoma (morphologic abnormality)
911750741000004104 Histologic type of primary malignant neoplasm of lung (observable entity)	Keratinizing	18048008 Squamous cell carcinoma, keratinizing (morphologic abnormality)
911750741000004104 Histologic type of primary malignant neoplasm of lung (observable entity)	Non-keratinizing	45490001 Squamous cell carcinoma, large cell, nonkeratinizing (morphologic abnormality)
911750741000004104 Histologic type of primary malignant neoplasm of lung (observable entity)	Basaloid	128634009 Basaloid squamous cell carcinoma (morphologic abnormality)

8

98

Data storage and analytics

- Question/answer pairs
- Questions carry context of answers
- Grouping by information model to retain linkage to case and other data
- Bindings to SNOMED CT

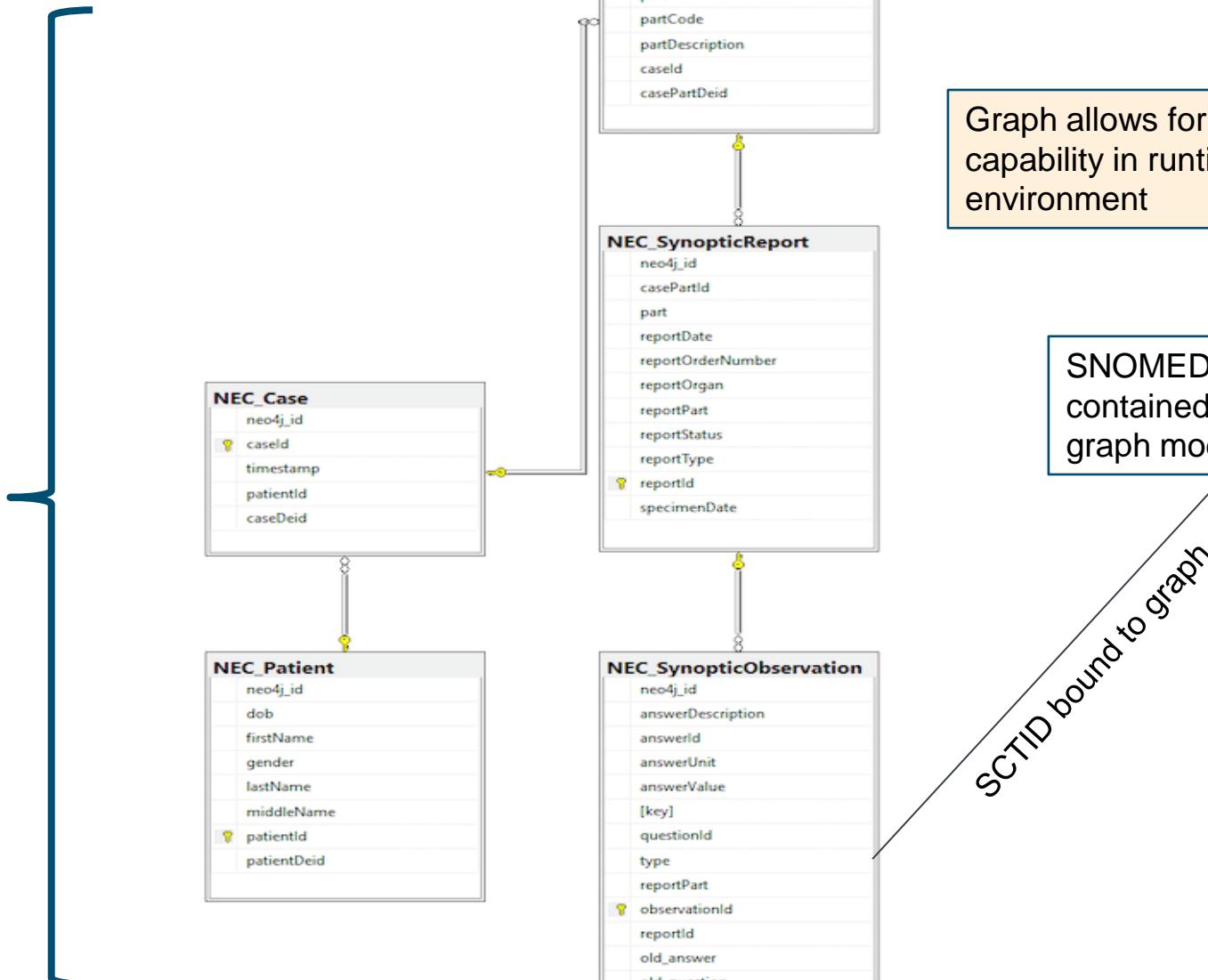
99



UNMC Tumor Biorepository Model

Synoptic Observations stored in RDBMS MS SQL structure

RDBMS allows easy to understand patient, report-level data



Graph allows for ECL-like query capability in runtime environment

SNOMED CT contained in MS SQL graph model

SCTID bound to graph



Why we care – Utility of Description Logic

Enter an ECL query (ECL Version: 2.0)

<< 512001000004108 |Histologic type of primary malignant neoplasm (observable entity) :<< 718497002 |Inherent location (attribute) = << 86762007 |Structure of digestive system (body structure)|

ECL Builder **Execute**

Enter additional search filter (optional)

Description type: Language Refsets Modules

Results: Found 19 concepts

Concept	Preferred Term	
Histologic type of primary malignant neoplasm of oral mucosa (observable entity)	Histologic type of primary malignant neoplasm of oral mucosa	911753741000004106
Histologic type of primary malignant neoplasm of appendix (observable entity)	Histologic type of primary malignant neoplasm of appendix	911753681000004106
Histologic type of primary malignant neoplasm of ampulla of Vater (observable entity)	Histologic type of primary malignant neoplasm of ampulla of Vater	911753671000004108
Histologic type of primary malignant neoplasm of liver (observable entity)	Histologic type of primary malignant neoplasm of liver	911753551000004103
Histologic type of primary malignant neoplasm of gallbladder (observable entity)	Histologic type of primary malignant neoplasm of gallbladder	911753531000004106
Histologic type of primary malignant neoplasm of pancreas (observable entity)	Histologic type of primary malignant neoplasm of pancreas	911753511000004104
Histologic type of primary malignant neoplasm of small intestine (observable entity)	Histologic type of primary malignant neoplasm of small intestine	911753501000004102
Histologic type of primary malignant neoplasm of stomach (observable entity)	Histologic type of primary malignant neoplasm of stomach	911753491000004106
Histologic type of primary malignant neoplasm of esophagus (observable entity)	Histologic type of primary malignant neoplasm of oesophagus	911753481000004108
Histologic type of primary malignant neoplasm of colon (observable entity)	Histologic type of primary malignant neoplasm of colon	798721000004104
Histologic type of primary malignant neoplasm of pharynx (observable entity)	Histologic type of primary malignant neoplasm of pharynx	1149008006
Histologic type of primary malignant neoplasm of minor salivary gland (observable entity)	Histologic type of primary malignant neoplasm of minor salivary gland	1149004008
Histologic type of primary malignant neoplasm of major salivary gland (observable entity)	Histologic type of primary malignant neoplasm of major salivary gland	1149003002
Histologic type of primary malignant neoplasm of oral soft tissue (observable entity)	Histologic type of primary malignant neoplasm of oral soft tissue	1149002007

All histologic types of malignant neoplasms of digestive system

Returns 19 concepts from oral cavity to anus

Logical queries/Clinical Decision Support

<< 51200100004108 |Histologic type of primary malignant neoplasm (observable entity)| : << 718497002 |Inherent location (attribute)| = << 122865005 |Gastrointestinal tract structure (body structure)|

ECL Builder Execute

Enter additional search filter (optional)

Description type: ▾ Language Refsets ▾ Modules ▾

Results: Found 7 concepts

Refinement by attribute-value pairs based on logical inference

GI tract => 7 concepts

Concept	Preferred Term	ID
Histologic type of primary malignant neoplasm of appendix (observable entity)	Histologic type of primary malignant neoplasm of appendix	911753681000004106
Histologic type of primary malignant neoplasm of ampulla of Vater (observable entity)	Histologic type of primary malignant neoplasm of ampulla of Vater	911753671000004108
Histologic type of primary malignant neoplasm of small intestine (observable entity)	Histologic type of primary malignant neoplasm of small intestine	911753501000004102
Histologic type of primary malignant neoplasm of stomach (observable entity)	Histologic type of primary malignant neoplasm of stomach	911753491000004106
Histologic type of primary malignant neoplasm of esophagus (observable entity)	Histologic type of primary malignant neoplasm of oesophagus	911753481000004108
Histologic type of primary malignant neoplasm of colon (observable entity)	Histologic type of primary malignant neoplasm of colon	798721000004104
Histologic type of primary malignant neoplasm of anus (observable entity)	Histologic type of primary malignant neoplasm of anus	1148991003

Showing all 7 inferred matches

10
2



Logical inference along multiple axes

Enter an ECL query (ECL Version: 2.0)

<< 371441004 |Histologic type of proliferative mass (observable entity)| : << 718497002 |Inherent location (attribute)| = << 122865005 |Gastrointestinal tract structure (body structure)|

ECL Builder

Execute

Enter additional search filter (optional) ×

Description type:

Language Refsets

Modules

Results: Found 8 concepts

Concept	Preferred Term	Id
Histologic type of primary malignant neoplasm of appendix (observable entity)	Histologic type of primary malignant neoplasm of appendix	91175368100004106
Histologic type of primary malignant neoplasm of ampulla of Vater (observable entity)	Histologic type of primary malignant neoplasm of ampulla of Vater	91175367100004108
Histologic type of primary malignant neoplasm of small intestine (observable entity)	Histologic type of primary malignant neoplasm of small intestine	91175350100004102
Histologic type of primary malignant neoplasm of stomach (observable entity)	Histologic type of primary malignant neoplasm of stomach	91175349100004106
Histologic type of primary malignant neoplasm of esophagus (observable entity)	Histologic type of primary malignant neoplasm of oesophagus	91175348100004108
Histologic type of primary malignant neoplasm of colon (observable entity)	Histologic type of primary malignant neoplasm of colon	798721000004104
Histologic type of polyp of colon (observable entity)	Histologic type of polyp of colon	1237195007
Histologic type of primary malignant neoplasm of anus (observable entity)	Histologic type of primary malignant neoplasm of anus	1148991003

Showing all 8 inferred matches

Logical queries done on multiple axes

Neoplasm vs. Malignant Neoplasm & GI tract vs. Digestive System