

Nebraska Lexicon© Release Notes: Cancer Protocols and Observables Ontology

A collaboration with the College of American Pathologists,
IHTSDO Observables Project and the Regenstrief Institute

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1 Purpose

This document summarizes the content and explains use of the terminology, maps and Annotated CAP® Cancer Protocols published as derivative work by the University of Nebraska Medical Center (Nebraska Medicine) in conjunction with the Nebraska Lexicon® extension (IHTSDO 1000004) namespace for SNOMED CT®.

2 Audience of interest for this document

Interested parties may include:

- National release centers, terminology middleware vendors and vendors of electronic health record software with interests or research projects in precision medicine or genomics in cancer medicine.
- Anatomic and molecular pathology laboratories, vendors of pathology departmental software who wish to deploy fully encoded synoptic data for cancer care within their healthcare institution
- Terminology developers who wish to evaluate or employ a LOINC-SNOMED CT compatible observables ontology for laboratory and pathology medicine

3 Content scope and history

3.1 Nebraska Lexicon® clinical terminology

Since February 2004, University of Nebraska Medical Center (Nebraska Medicine) has maintained an extension namespace (extension identifier 1000004 registered with IHTSDO) to support clinical terminology development required for electronic health record (EHR) deployment at its hospital and clinics. Content developed for this namespace has been driven pragmatically by recording requirements reported by Nebraska clinicians in the course of their daily work. This content has been deployed in records over three generations of EHRs including PHAMIS, IDX-GE and now is in use in Epic®. Beginning in 2015, new content has been developed which relates to Observables and precision medicine as described in 3.2-3.4.

3.2 IHTSDO Technology Preview: Observables ontology build for laboratory medicine and pathology

In 2014, the Observables project of the IHTSDO and Regenstrief Institute published a draft convergent concept model for harmonization of content between LOINC® and SNOMED CT®. In January 2017 the project published a set of SNOMED CT® formatted expressions which define the meaning of

~13000 laboratory LOINC® observables employing the harmonized concept model. An expanded technology preview of ~20000 concepts has been released by the IHTSDO but is not included in this publication. UNMC has converted the earlier expression set into SNOMED CT® formatted extension concepts employing LOINC® long names as the SNOMED CT® fully specified name and assigning class supertypes within the Observable entity hierarchy in SNOMED CT®. ‘Grouper’ concepts have been modeled and deployed within the Observable entity hierarchy in order to enhance clinical navigation and to support common query use cases in laboratory medicine and pathology.

Anatomic and molecular pathology observables defined by semantic analysis of the CAP Annotated Cancer Protocols explained in 3.3 are included. Some pre-existing SNOMED CT® Observable entity content has been fully defined using the harmonized concept model with permission of the IHTSDO. Grouper concepts have been included to organize the ontology and support common query use cases proposed by CAP.

All content was run through the description logic classifier and both ‘stated’ and ‘inferred’ relationships are included in this release. This “Observables ontology” for laboratory medicine and pathology is being published for evaluation and comment by the informatics community.

3.3 Annotated Cancer Protocols from the College of American Pathologists© CAP 2017

In 2015, at the request of Nebraska Medicine leadership, the departments of Pathology and Internal Medicine began a joint project to structure and encode pathology data for clinical care and research in cancer. The core semantic content for this project is that found in 82 Cancer protocols published by the College of American Pathologists(CAP). Content is inclusive of both anatomic (AP) and molecular pathology(MP includes protein and genetic) observations.

CAP Protocols are required content for synoptic reporting of cancer cases across the US. The majority of the associated terminology development is modeled within 363787002|Observable entity| hierarchy and have been developed in compliance with the harmonized observables model referenced in 3.2. The content is published with permission of CAP. Copies of the source protocols annotated with coded observables and valuesets of SNOMED CT® codes as answer sets for coded datatypes have been developed. Types of cancer that have been encoded and completed for publication are summarized as follows.

Publication date	Version	Content
3/13/2017	1.0	Encoded synoptic protocols: 1) colorectal and 2) breast cancer.

3.4 Maps to Genomic Ontologies and LOINC®

Development of observables content for molecular pathology required extensions of the SNOMED CT® concept model for modeling of genes, proteins and related subcellular features. These SNOMED CT® features were developed to reflect scientific research content documented in the ontologies of the National Center for Biomedical Ontology (<http://www.bioontology.org/>), specifically the Gene Ontology and related resources. This release includes maps from SNOMED CT® content to HUGO Human Gene Nomenclature Committee(<http://www.genenames.org/>) records and to LOINC® (<http://www.loinc.org/>) codes for observables concepts.

4 Instructions for use

4.1 RF2 refsets in this publication

There are multiple RF2 refsets in this release including:

- Terminology refsets for Nebraska Lexicon© 20170331 release
- Map refset from genes modeled in SNOMED CT® to the HUGO Human Gene Nomenclature Committee data
- Refset conformant with simple map refset specifying all LOINC® term identifiers that have been imported as expressions from the IHTSDO technology preview supplemented by observable entities developed within laboratory and pathology medicine modeled and authored by Nebraska.

The LOINC community of practice is welcome to employ these terminology sets to evaluate and deploy the terminology in support of an Observables ontology. Subsequent releases of Nebraska Lexicon will support OWL or other formats for maintaining an ontology of LOINC terms.

The refsets we are publishing meet all format requirements specified by the IHTSDO - EXCEPT THAT LOINC® CODES HAVE BEEN SUBSTITUTED FOR SNOMED CT® CONCEPT IDENTIFIERS for all content employing the Observables harmonized concept model. The SNOMED CT® community of practice may deploy this material into their SNOMED CT® enhanced system if they have programmer support to manage this code format difference. Those sites which do not have such support can obtain a licensed extension namespace from the IHTSDO and Nebraska will provide code which will translate the refsets into IHTSDO terminology RF2 format by substituting local extension concept identifiers for the LOINC® codes and creating map refsets linking local SCTIDs to the LOINC® counterpart. Those refsets will be loadable using usual SNOMED CT® distribution utilities. SNOMED CT sites wishing to proceed with this conversion should contact Jim Campbell (campbell@unmc.edu; office +1-402-559-7505).

4.2 PDF files: Annotated Cancer Protocols from the College of American Pathologists© CAP 2017

With permission of the College of American Pathologists (CAP), we enclose the CAP Cancer Protocol documents in PDF format supplemented with hyperlinks in context to the Observable entity coded 'question' and the valuesets of 'answers' for all protocol data items. In most cases the Observables codes are one-to-one matches with CAP protocol data items. In a minority of cases, the information model implied by the protocol structure was expanded or reorganized in order to properly define the nature of the observation. An example of this can be found in the colorectal cancer anatomic pathology protocol on page 6. Since the protocol valueset for Microscopic tumor extension required four types of observations, the last three items in the list (organ adherence, direct invasion and penetration of visceral peritoneum) have unique observable entities defined for a total of four observables for this component of the protocol. The comprehensive set of observable entities, valuesets and concept model definition are included immediately following the CAP PDF document.

To use the annotated CAP Cancer Protocol, simply open the document in an Adobe browser. Scrolling down the CAP protocol to individual data sections, a 'hand' widget will appear when hovering over a checklist item. Clicking on this portion of the document will take the reader to the SNOMED CT® observable entity – the fully specified name, concept identifier and diagrammatic model of the concept. The associated valueset of 'answers' will be listed in tabular form. Clicking a second time on the valueset table will return the reader to the CAP document at the point of departure.

Publication date	File name	Content
6/5/2016	CAP_colorectal_cancer_anatomic_pathology_20160610	Annotated colorectal AP protocol with observables and valuesets
6/13/2016	CAP_colorectal_cancer_biomarkers_20160613	Annotated colorectal biomarker (MP) protocol
6/13/2016	CAP_invasive_breast_cancer_anatomic_pathology_20160613	Annotated breast cancer AP protocol
6/14/2016	CAP_brest_cancer_biomarkers_20160614	Annotated breast cancer biomarker (MP) protocol

5 Quality assurance, validation and maintenance

Addition of Observable entity concepts applicable for anatomic and molecular pathology has been accomplished in close collaboration with the Observables project team of the IHTSDO. Nebraska and the project team have systematically applied the harmonized Observables concept model to the terminology use cases presented by the CAP cancer protocols and have collaborated with Regenstrief Institute on LOINC® code assignment for all newly

modeled content. Historical LOINC® terms which are within scope of the project have been modeled in SNOMED CT® and deployed as extension concepts. Extension and map content has been reviewed by all participating organizations.

6 Acknowledgements

6.1 Nebraska Lexicon©

Nebraska Lexicon© is copyright by the University of Nebraska Medical Center (Nebraska Medicine).

6.2 SNOMED CT; IHTSDO Observables project

This material includes SNOMED Clinical Terms® (SNOMED CT®) which is used by permission of the International Health Terminology Standards Development Organisation (IHTSDO). All rights reserved. SNOMED CT®, was originally created by The College of American Pathologists. “SNOMED” and “SNOMED CT” are registered trademarks of the IHTSDO.

We wish to thank Farzaneh Ashrafi, Suzanne Santamaria, Daniel Karlsson and all members of the Observables project team for their assistance and advice in developing this material.

6.3 College of American Pathologists

We acknowledge the kind agreement of CAP in allowing us to publish the annotated protocols and wish to thank Raj Dash, Mary Kennedy, Alexis Carter and Ted Carithers as well as members of the International Pathology and Laboratory Medicine (IPaLM) Special Interest group of the IHTSDO for their work and advice in developing this material.

6.4 LOINC®

This material contains content from LOINC® (<http://loinc.org>). The LOINC table, LOINC codes, LOINC panels and form file, LOINC linguistic variants file, LOINC/RSNA Radiology Playbook, and LOINC/IEEE Medical Device Code Mapping Table are copyright © 1995-2016, Regenstrief Institute, Inc. and the Logical Observation Identifiers Names and Codes (LOINC) Committee and is available at no cost under the license at <http://loinc.org/terms-of-use>.

We wish to thank Daniel Vreeman, Katie Allen and Swapna Abhyankar of Regenstrief Institute for the hours they have spent creating LOINC® term sets and advising us on this development.

6.5 National Library of Medicine

We wish to thank Vivian Auld, Susan Roy and James Case of the NLM for their kind advice and support in this project. We are grateful for support of publication of the Nebraska Lexicon© by reference on the UMLS Terminology Server.

7 Appendix: File format specifications

7.1 Module Dependency refset

(Refset.Metadata.der2_ssRefSet_ModuleDependencySnapshot_INT_yyyymmdd)

Field	Data type	Purpose
id	UUID	A 128 bit unsigned integer, uniquely identifying the map category record
effectiveTime	Time	Specifies the inclusive date at which this change becomes effective.
active	Boolean	Specifies whether the member's state was active (=1) or inactive (=0) from the nominal release date specified by the effectiveTime field.
moduleId	SctId	Identifies the member version's module. Set to a child of 900000000000443000 Module within the metadata hierarchy.
refSetId	SctId	Set to one of the children of the 447250001 Complex map type concept in the metadata hierarchy.
referencedComponentId	SctId	A reference to the module on which this module depends, a descendant of 900000000000443000 Module in the metadata hierarchy.
sourceEffectiveTime	String	The effective time of the source module. This allows a specific module version to be selected as having a dependency. The effectiveTime must match exactly.
targetEffectiveTime	String	The effective time of the target module. This allows a specific module version to be selected as being the subject of a dependency. The effectiveTime must match exactly.

7.2 Nebraska Lexicon© Terminology

7.2.1 Concepts

(Terminology.sct2_Concept_Snapshot_INT_yyyymmdd)

Field	Data type	Purpose
id	SctId / LOINC®	The SNOMED CT® source concept ID OR by agreement with Regenstrief all Observables concept identifiers authored for this work will be represented by LOINC® code
effectiveTime	Time	Specifies the inclusive date at which this change becomes effective.
active	Boolean	Specifies whether the member's state was active (=1) or inactive (=0) from the nominal release date specified by the effectiveTime field.
moduleId	SctId	Identifies the member version's module. Set to a child of 9000000000000443000 Module within the metadata hierarchy.
DefinitionStatusId	SctId	Identifies the definition status of the concept, a child of metadata concept 9000000000000444006 Definition status (core metadata concept)

7.2.2 Descriptions

(Terminology.sct2_Description_Snapshot_en-us_INT_yyyymmdd)

Field	Data type	Purpose
id	SctId	A 128 bit unsigned integer, uniquely identifying the description record
effectiveTime	Time	Specifies the inclusive date at which this change becomes effective.
active	Boolean	Specifies whether the member's state was active (=1) or inactive (=0) from the nominal release date specified by the effectiveTime field.
moduleId	SctId	Identifies the member version's module. Set to a child of 9000000000000443000 Module within the metadata hierarchy.
conceptId	SctId / LOINC®	The SNOMED CT® source concept ID OR by agreement with Regenstrief all Observables concept identifiers authored for this work will be represented by LOINC® code
languageCode	String	Identifier for the language subset of which the description is a member. ISO 639-1 two character code.
typeId	SctId	Metadata concept identifying the type of the description.
term	String	Full text description
caseSignificanceId	SctId	Metadata concept identifying the significance of capitalization in the description term. A child of 9000000000000447004 Case significance(core metadata)

7.2.3 Relationships (inferred from classification of the extension with all related modules)

(Terminology.sct2_Relationship_Snapshot_INT_yyyymmdd)

Field	Data type	Purpose
id	UUID	A 128 bit unsigned integer, uniquely identifying the map record
effectiveTime	Time	Specifies the inclusive date at which this change becomes effective.
active	Boolean	Specifies whether the member's state was active (=1) or inactive (=0) from the nominal release date specified by the effectiveTime field.
moduleId	SctId	Identifies the member version's module. Set to a child of 9000000000000443000 Module within the metadata hierarchy.
sourceId	SctId	The conceptId of the origin of the relationship
destinationId	SctId	The conceptId of the target of the relationship.
relationshipGroup	Integer	The integer identifying the role group of the relationship instance
typeId	SctId	The concept identifier (attribute) of the name of the relationship
characteristicTypeId	String	Metadata concept identifying the manner in which this relationship instance participates in the definition of the SNOMED CT® concept. A child of metadata concept 9000000000449001 Characteristic type (core metadata) .
modifierId	String	Metadata concept identifying whether this relationship enforces existential or universal restriction.

7.2.4 Stated relationships (only those relationships invoked by the authors in modeling the extension concepts)

(Terminology.sct2_StatedRelationship_Snapshot_INT_yyyymmdd)

Table structure and content is identical to 7.2.3.

7.3 HGNC Equivalence map

(Refset.Map.der2_sRefset_SNOMEDNebraskaLexicon-HGNCEquivalenceMapSnapshot_INT_yyyymmdd)

Field	Data type	Purpose
id	UUID	A 128 bit unsigned integer, uniquely identifying the map record
effectiveTime	Time	Specifies the inclusive date at which this change becomes effective.
active	Boolean	Specifies whether the member's state was active (=1) or inactive (=0) from the nominal release date specified by the effectiveTime field.
moduleId	SctId	Identifies the member version's module. Set to a child of 900000000000443000 Module within the metadata hierarchy.
refSetId	SctId	A unique identifier for this type of map refset
referencedComponentId	SctId	The SNOMED CT® source concept ID that is the subject of the map record. This map asserts equivalencies for human genes which are subtypes of 1350001000004100 Nucleotide sequence(cell structure)
mapTarget	String	Format "HGNC:NNNN^http://URL" where NNNN is the unique identifier of the Human Gene Nomenclature record and URL is the RESTful service call for descriptive information about the referenced component.

7.4 LOINC® term subset modeled as 363787002|Observable entity| (Refset.Map.der2_sRefset_LOINCHarmonizationTechnicalPreviewMapSnapshot_INT_yyyymmdd)

Field	Data type	Purpose
id	UUID	A 128 bit unsigned integer, uniquely identifying the map record
effectiveTime	Time	Specifies the inclusive date at which this change becomes effective.
active	Boolean	Specifies whether the member's state was active (=1) or inactive (=0) from the nominal release date specified by the effectiveTime field.
moduleId	SctId	Identifies the member version's module. Set to a child of 900000000000443000 Module within the metadata hierarchy.
refSetId	SctId	A unique identifier for this type of map refset
cancerreferencedComponentId	LOINC®	By agreement with Regenstrief all Observables concept identifiers authored for this work will be represented by LOINC® code
mapTarget	LOINC®	By agreement with Regenstrief all Observables concept identifiers authored for this work will be represented by LOINC® code

7.5 College of American Pathologist Annotated Cancer Protocols

7.5.1 Breast cancer and biomarkers

7.5.1.1 Invasive breast cancer

(Cancer worksheets.CAP_Invasive_breast_cancer_encoded_20170331)

7.5.1.2 Breast cancer biomarkers

(Cancer worksheets.CAP_Breast_biomarker_encoded_20170331)

7.5.2 Colorectal cancer and biomarkers

7.5.2.1 Colorectal cancer

(Cancer worksheets.CAP_Colorectal_encoded_20170331)

7.5.2.2 Colorectal biomarkers

(Cancer worksheets.CAP_Colorectal_biomarkers_encoded_20170331)