CPIC Term Standardization: LOINC Codes

CPIC
December 3, 2015

Robert R. Freimuth

CPIC Term Standardization Project: Results

Allele Functional Status (allele descriptive)*:

1) Drug Metabolizing Enzymes (e.g., CYP enzymes, *UGT1A1*, *TPMT*, *DPYD*) and Transporters (e.g., *SLCO1B1*)
    a. Increased Function
    b. Normal Function
    c. Decreased Function
    d. No Function

https://www.pharmgkb.org/page/cpicTermProject
https://cpicpgx.org/resources/

Phenotype (diplotype descriptive)*:

1) Drug Metabolizing Enzymes (e.g., CYP enzymes, UGT1A1, TPMT, DPYD)
    a. Ultra-rapid Metabolizer
    b. Rapid Metabolizer
    c. Normal Metabolizer
    d. Intermediate Metabolizer
    e. Poor Metabolizer
2) Transporters (e.g., SLCO1B1)
    a. Increased Function
    b. Normal Function
    c. Decreased Function
    d. Poor Function
3) High-risk alleles (e.g., *HLA-B*15:02*)
    a. *HLA-B*15:02* positive
    b. HLA-B*15:*02* negative

Next step: LOINC codes

MAYO CLINIC

HL7 Version 2 Implementation Guide: Clinical Genomics; Fully LOINC-Qualified Genetic Variation Model, Release 2

March 2013

HL7 Informative Document: HL7 V2IG CG LOINCGENVAR R2-2013

A Technical Report prepared by Health Level Seven International and registered with ANSI:

5/5/2013

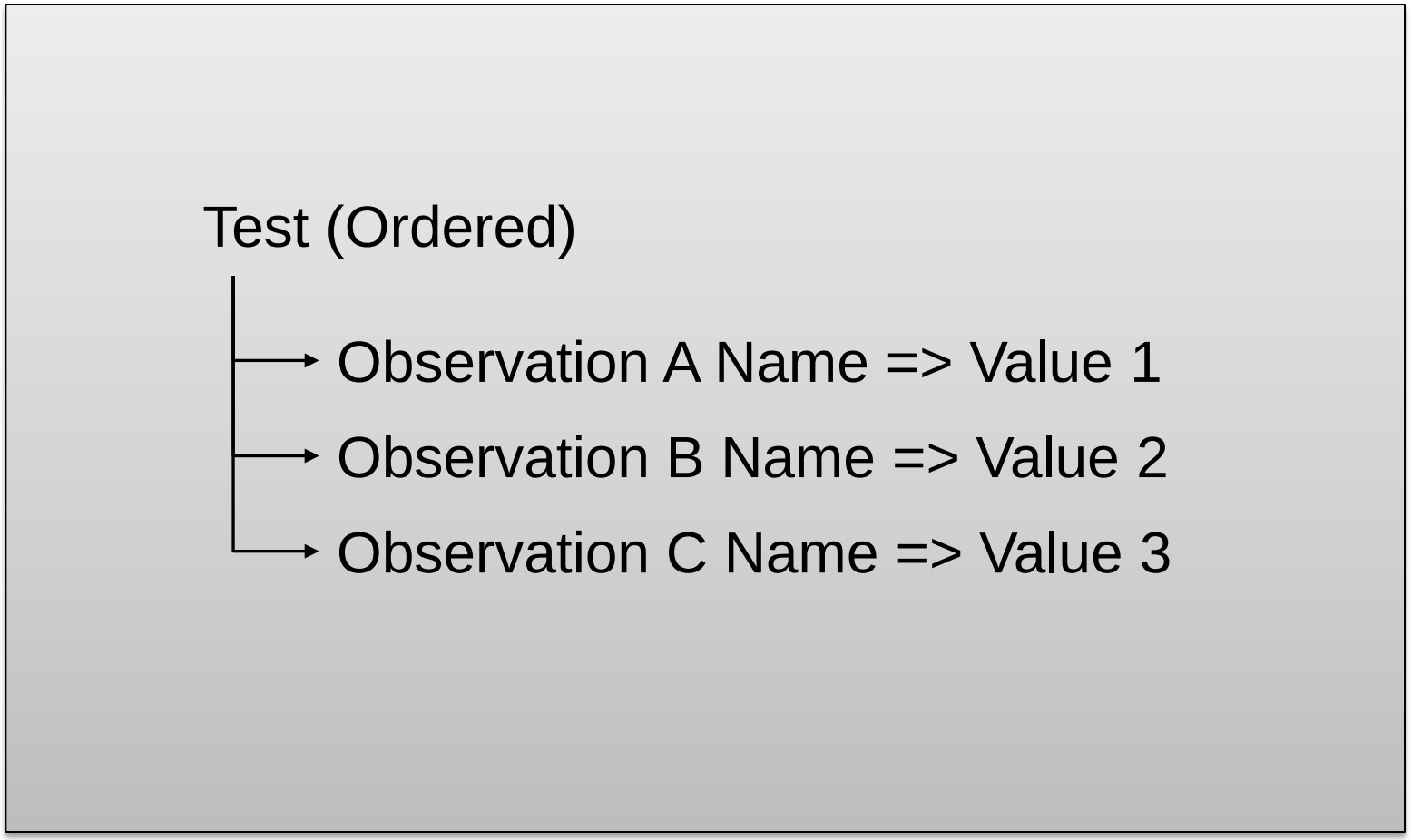
1.6 SCOPE

This guide covers the reporting of DNA based genetic test results performed using sequencing or genotyping technology for the identification of DNA sequence variations contained within a gene. This includes testing for DNA variants associated with disease or pharmacogenomic response to drugs (efficacy or metabolism).

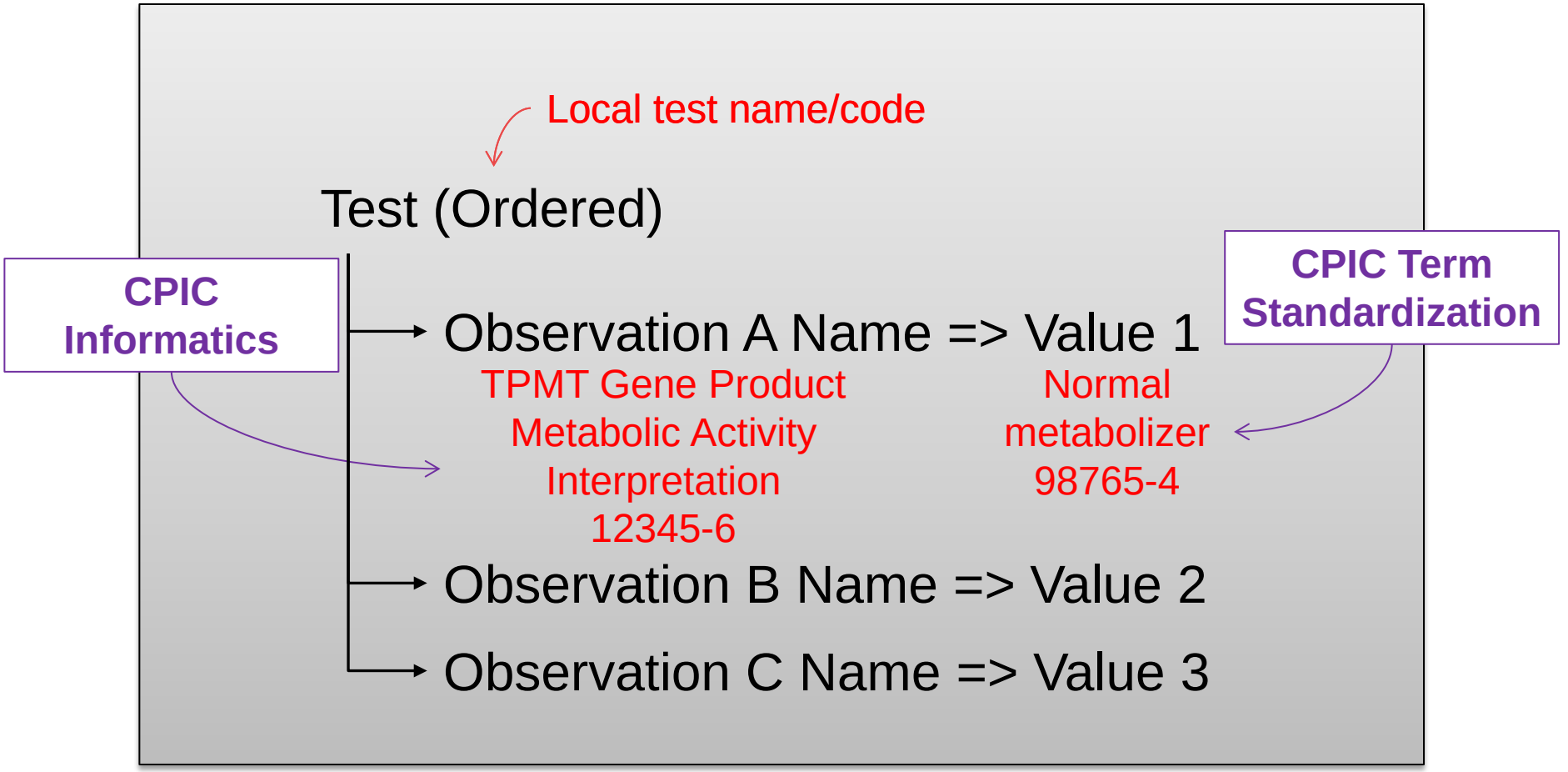
HL7 Genetic Variation Model

- Genetic tests: LOINC
- Interpretation code: LOINC
- Associated disease: SNOMED-CT
- Drug: RxNorm
- Gene: HGNC
- Variant(s): HGVS, dbSNP, COSMIC
- Reference sequence(s): NCBI RefSeq, LRG

Simplified HL7 Message Structure



Simplified HL7 Message Structure



Gene List for Current & Upcoming CPIC Guidelines

Drug Metab'g Enzymes

- CYP2C19
- CYP2D6
- CYP2C9
- CYP3A5
- UGT1A1
- TPMT
- DPYD
- CYP2B6†
- CYP4F2†

Transporters & non-DMEs

- SLCO1B1

Carrier Status

- HLA alleles
  - HLA-B*15:02
  - HLA-B*57:01
  - HLA-B*58:01
  - HLA-A*31:01†

† *Upcoming guideline*

LOINC Observation Names

Overall Gene Phenotypic Interpretation

e.g., "TPMT Gene Product Metabolic Activity Interpretation"

Phenotype-Drug Metabolizing Enzymes (*CYP2C19, CYP2D6, CYP3A5, CYP2C9, TPMT, DPYD, UGT1A1*)	Ultra-rapid Metabolizer
	Rapid Metabolizer
	Normal Metabolizer
	Intermediate Metabolizer
	Poor Metabolizer

e.g., "SLCO1B1 Gene Product Functional Interpretation"

Phenotype-Transporters and non-drug metabolizing enzymes[b] (*SLCO1B1*)	Increased Function
	Normal Function
	Decreased Function
	Poor Function

e.g., "HLA-B*57:01 [Presence]"

Phenotype-Carrier status (*HLA-B*)	Positive
	Negative

LOINC Observation Names

Overall Gene Phenotypic Interpretation

Drug Metab'g Enzymes

- CYP2C19 Gene Product Metabolic Activity Interpretation
- CYP2D6 Gene Product Metabolic Activity Interpretation
- CYP2C9 Gene Product Metabolic Activity Interpretation
- CYP3A5 Gene Product Metabolic Activity Interpretation
- UGT1A1 Gene Product Metabolic Activity Interpretation
- TPMT Gene Product Metabolic Activity Interpretation
- DPYD Gene Product Metabolic Activity Interpretation
- CYP2B6 Gene Product Metabolic Activity Interpretation
- CYP4F2 Gene Product Metabolic Activity Interpretation
- NAT2 Gene Product Metabolic Activity Interpretation

- Ultra-rapid Metabolizer
- Rapid Metabolizer
- Normal Metabolizer
- Intermediate Metabolizer
- Poor Metabolizer

Transporters & non-DMEs

- SLCO1B1 Gene Product Functional Interpretation

- Increased Function
- Normal Function
- Decreased Function
- Poor Function

Carrier Status

- HLA-B*15:02 [Presence]
- HLA-B*57:01 [Presence]
- HLA-B*58:01 [Presence]
- HLA-A*31:01 [Presence]

- Positive
- Negative

PGx LOINC Codes

LOINC	LOINC Component
50956-2	HLA-B*57:01
57979-7	HLA-B*15:02
79711-8	HLA-B*58:01
79712-6	HLA-A*31:01
79713-4	TPMT gene product metabolic activity interpretation
79714-2	CYP2C19 gene product metabolic activity interpretation
79715-9	CYP2D6 gene product metabolic activity interpretation
79716-7	CYP2C9 gene product metabolic activity interpretation
79717-5	CYP3A5 gene product metabolic activity interpretation
79718-3	UGT1A1 gene product metabolic activity interpretation
79719-1	DPYD gene product metabolic activity interpretation
79720-9	CYP2B6 gene product metabolic activity interpretation
79721-7	CYP4F2 gene product metabolic activity interpretation
79722-5	SLCO1B1 gene product functional interpretation

Answer ID	Answer (CPIC Phenotype Term)
LA6576-8	Positive
LA6577-6	Negative
LA10315-2	Ultrarapid metabolizer
LA25390-8	Rapid metabolizer
LA25391-6	Normal metabolizer
LA10317-8	Intermediate metabolizer
LA9657-3	Poor metabolizer
LA25392-4	Increased function
LA25393-2	Normal function
LA25395-7	Decreased function
LA25394-0	Poor function

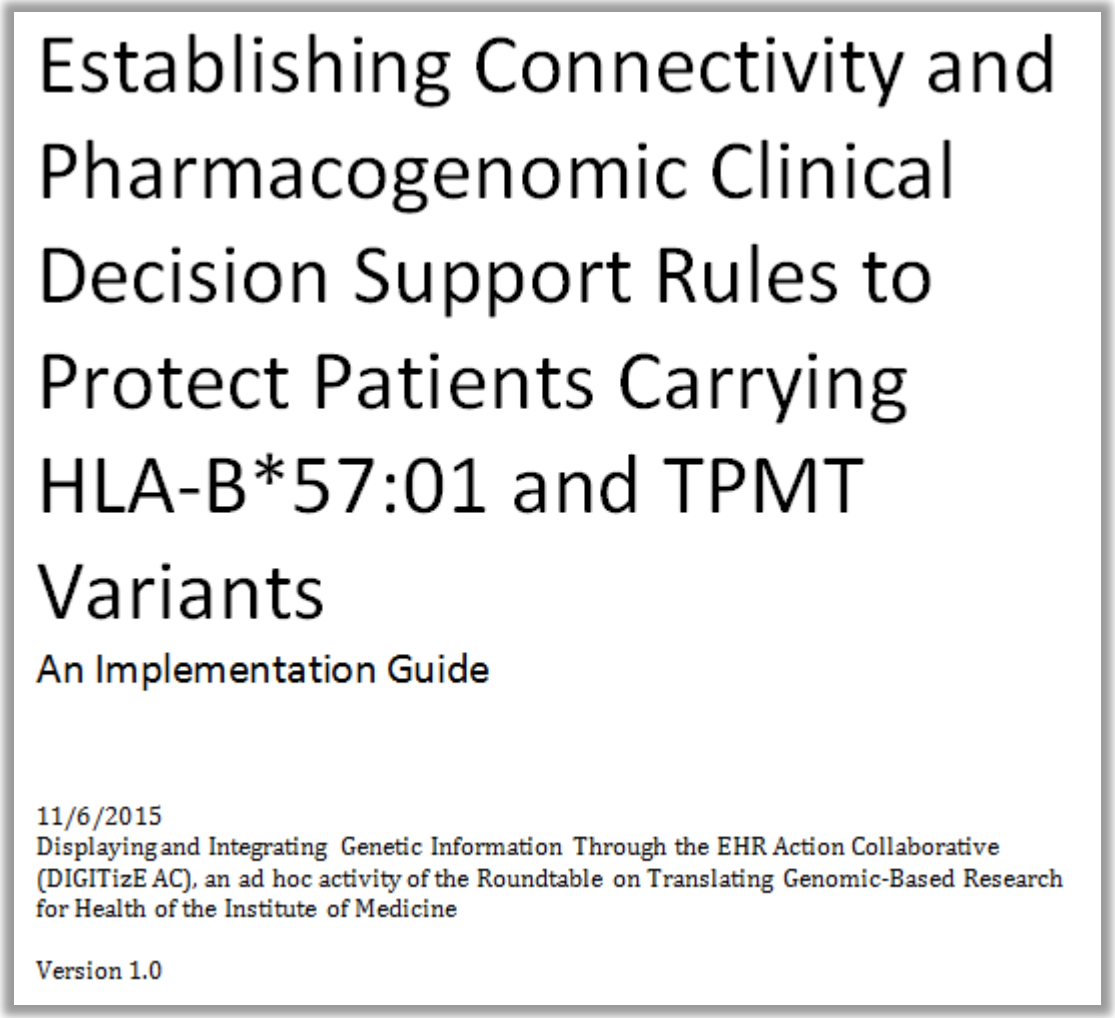
LOINC Release

- CPIC PGx terms will be in the next release of LOINC!

- Public laboratory LOINC meeting
  - Dec 2-3, 2015
  - Beta release available

- Public release of LOINC
  - ~Mid-Dec 2015

IOM DIGITizE AC Implementation Guide



Establishing Connectivity and Pharmacogenomic Clinical Decision Support Rules to Protect Patients Carrying HLA-B*57:01 and TPMT Variants

An Implementation Guide

11/6/2015

Displaying and Integrating Genetic Information Through the EHR Action Collaborative (DIGITizE AC), an ad hoc activity of the Roundtable on Translating Genomic-Based Research for Health of the Institute of Medicine

Version 1.0

IOM DIGITizE AC Implementation Guide

*HLA-B*57:01 [Presence]*

The existing LOINC code, 50956-2: *HLA-B*57:01*[Presence], is designed to communicate either the presence or absence of the specific *HLA-B*57:01* allele. Here are the details:

LOINC CD	Component	Long Common Name
50956-2	HLA-B*57:01	HLA-B*57:01 [Presence]
Part Definition/Description(s)		
Part of HLA-B57 allele family that is associated with Abacavir hypersensitivity reaction (AHSR)		

Answer List*			
	Seq #	Answer	Answer ID
	1	Positive	LA6576-8
	2	Negative	LA6577-6

For a positive finding of the *HLA-B*57:01* allele...

OBX|1|„|50956-2^HLA-B*57:01^LN ||10828004^Positive^SCT~LA6576-8^Positive^LN-ANS |...

And, for a negative finding of the *HLA-B*57:01* allele...

OBX|1|„|50956-2^HLA-B*57:01^LN ||260385009^Negative^SCT~LA6577-6^Negative^LN-ANS |...

IOM DIGITizE AC Implementation Guide

TPMT Gene Product Metabolic Activity Interpretation

A new LOINC observation code, 79713-4: TPMT gene product metabolic activity interpretation, has been created precisely to support the requirement for the azathioprine use case. The details of the LOINC code follow:

LOINC CD	Component	Long Common Name
79713-4	TPMT gene product metabolic activity interpretation	TPMT gene product metabolic activity interpretation in Blood or Tissue Qualitative by CPIC

Part Definition/Description(s)

The TPMT gene product metabolic activity interpretation is determined by the reporting lab and returned with the structured test results. It indicates the lab's interpretation of the phenotype that meets the Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for reporting TPMT gene product metabolic activity (phenotype), regardless of whether the lab assay's method was genetic or enzymatic. This specific interpretation would be considered a separate observation made by the lab in addition to the primary reported results (e.g., genotype or measured activity level) and it could be included with other assay-specific observations, which would ideally support the interpretation value. [https://cpicpgx.org/resources.html]

Answer List*

	Seq #	Answer	AnswerID
	1	Ultrarapid metabolizer	LA10315-2
	2	Rapid metabolizer	LA25390-8
	3	Normal metabolizer	LA25391-6
	4	Intermediate metabolizer	LA10317-8
	5	Poor metabolizer	LA9657-3

*based on the CPIC Delphi Survey

Here is an example of a partial OBX segment to show how this LOINC code would be applied:

For an Intermediate metabolizer TPMT gene product metabolic activity interpretation observation...

OBX|1|CWE|79713-4^ TPMT gene product metabolic activity interpretation ^LN || LA10317-8^Intermediate metabolizer^LN-ANS|...

