Moving Family Health History & Genetic Test Result Data into the Electronic Health Record for Clinical Decision Support

HL7 - More Than You think

HIMSS

March 2, 2016

Grant M. Wood

Intermountain Healthcare Clinical Genetics Institute and HL7 Clinical Genomics workgroup
The White House Hosts a Precision Medicine Initiative Summit

Cohort Program RFA - Describe potential utilization of current and emerging standards to facilitate data exchange and analysis, such as:

- Standards for capture and representation of family health history such as SNOMED CT and HL7 Version 3 Implementation Guide: Family History/Pedigree for familial relationships.
- HL7 DIGITizE Actions Collaborative draft LOINC specification for pharmacogenomics.
- HL7 Clinical Genomics WG standards including CDA R2 Clinical Genetics Reporting, Clinical Genomics Pedigree Model, HL7 Genetic Testing Results Message (V2), and Clinical Sequencing Domain Analysis Model (DAM).
- SMART on FHIR Genomics standards to support development of clinico-genomic apps to communicate clinical genomics data between EHR systems.
Are Healthcare Systems Prepared

Health care systems risk being overwhelmed unless they start preparing for the complex demands of genetic screening programs.
Consortium and Collaborative Networks

- HL7 Clinical Genomics Workgroup
- Institute of Medicine – DIGITizE AC
- Global Alliance for Genomics and Health
- WEDI Genomics Workgroup
- National Human Genome Research Institute (NHGRI) - Global Genomic Medicine Collaborative (G2MC)
- eMERGE network
- ClinGen
HL7 Standards

- 2007, 2013 - Family Health History or Pedigree model
- 2009 to 2013 - Genetic Variation model and Cytogenetics model for laboratory reporting of genetic test results to the EHR
- 2011 to 2013 - Clinical Document Architecture (CDA) Genetic Test Results electronic document
- 2014 and beyond – Fast Health Information Resource (FHIR) for both family health history and genetic/genomic testing
Value of Family History in Clinical Care

Family history remains the best and least expensive genetic ‘test’ currently available for clinical use.

A major effort will entail developing tools to collect this information –

1. In a standardized format,
2. Store it in the patient’s electronic health record,
3. Apply risk assessment, and
4. Develop messages to clinicians that may alter patient care based on the information obtained.
A multi-stakeholder workgroup, including the private sector, federal health care providers, and federal Public Health Service agencies, should be formed to develop a core minimum data set and common data definition available for primary care collection of family health history information.

On July 31, 2007, the Personalized Health Care (PHC) Workgroup (http://www.hhs.gov/healthit/ahic/healthcare/) submitted a set of recommendations to the America Health Information Community (AHIC). These recommendations, subsequently adopted by AHIC, were aimed at enhancing the integration of interoperable family health history information into Electronic Health Records (EHRs).
Meaningful Use Stage 2
FHH Proposed Measure

- More than 20 percent of all unique patients seen by the EP, or admitted to the eligible hospital or CAH's inpatient or emergency department (POS 21 or 23) during the EHR reporting period have a structured data entry for one or more first-degree relatives.

- Information about second degree relatives may be useful for some diagnoses and conditions, we believe collecting medical history from first degree relatives is the floor, not the ceiling and encourage providers to collect additional information.
HL7 Version 3 Implementation Guide:
Family History/Pedigree Interoperability, Release 1
January 2013

HL7 Informative Ballot

Sponsored by:
Clinical Genomics Work Group

Pedigree R1 Co-Editors:
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What’s In the Family Health History Data Model

1) Record information
2) Person of focus (Proband)
3) Other persons in pedigree
4) Age of person / death date
5) Relationship
6) Disease
7) Age of disease onset / age of disease death
8) Genotypic data
9) Risk analysis
The Model Enables Risk Assessment

Risk Analysis

1. Risk scoring calculated by advanced programs can be shared.

2. Disease-specific risk algorithms can be provided by web services.
My Family Health Portrait
A tool from the Surgeon General

Using My Family Health Portrait you can:

- Enter your family health history.
- Create drawings of your family health history to share with family or health care worker.
- Use the health history of your family to create your own.

Talking with your health care worker about your family health history can help you stay healthy!

Learn more about My Family Health Portrait

Create a Family History

Open a Saved History File
Continuity of Care Document (CCD)
Optional Sections

• Advanced Directives
• Functional Status
• Procedures
• Encounters
• Family History
• Social History

• Vital Signs
• Fetal Vital Signs
• Lab Results
• Plan of Care
Profile to support capturing pedigree within family history for genetics analysis

Adds additional information to a family history supporting both the capture of mother/father relationships as well as additional observations necessary to enable genetics-based risk analysis for patients

This profile was published on Wed, Oct 2, 2013 00:00+1000 as a draft by HL7 International - Clinical Genomics WG, and profiles the Resource

The id of this profile is

Content

<!-- Resources -->
<!-- GeneticPedigreeFamilyHistory -->
<FamilyHistory xmlns="http://hl7.org/fhir">
  <!-- from Element: extension -->
  <extension><!-- 0..* Extension Additional Content defined by implementations --></extension>
  <modifierExtension><!-- 0..* Extension Extensions that cannot be ignored --></modifierExtension>
  <text><!-- 0..1 Narrative Text summary of the resource, for human interpretation --></text>
  <contained><!-- 0..* Resource Contained, inline Resources --></contained>
  <identifier><!-- 0..* Identifier External Id(s) for this record --></identifier>
  <subject><!-- 1..1 Resource(Patient) Patient history is about --></subject>
  <note value="[string]"><!-- 0..1 Additional details not covered elsewhere -->
  <relation><!-- 1..* Relative described by history -->
  <!-- "Parent": -->
OPEN FOR COMMENTS | Posted: December 18, 2015

DRAFT 1

Family History Collection Tools - Statement of Best Practice

We would love to hear what you think of this draft.

Submit your feedback now!

About This Work Product

The purpose of this document is to highlight current approaches and challenges in enabling family history to guide clinical care to developers of clinically-oriented family history collection systems, including stand alone and EHR-integrated systems. Additionally, this document provides an overview of key design features (and supporting rationale) of family history systems for potential consumer/purchasers.
DRAFT 1

Family History Tool Inventory

We would love to hear what you think of this draft.

Submit your feedback now!

About This Work Product

The Family History Tool Inventory is a catalogue of family history tools currently available for documenting family health history information. It will be updated periodically and we encourage recommendations of other tools to include.

Downloads

- Family History Tool Inventory
  15KB
Possible Requirements for a FHH Consent Management Solution


System Issues

• Storage of consent directives
• Application and enforcement of consent directive
• Management: how they will be updated and monitored, and how to deal with conflicting instructions
• Overrides
• Integration (multiple inpoints; different EHRs with different CMS; thousands of end-points in the health system)
• Integrity
• Inter-jurisdictional movement of data
Next - Clinical Genetics
Precision Medicine includes

Thousands of genetic tests available in the clinic

AND

Commercially available direct-to-consumer genetic testing
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

Sponsored by:
Clinical Genomics Work Group

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Genetic Variation
Implementation Guide

Genetic analysis master panel (OBR)

Genetic Analysis Summary Panel (OBR)
(i.e. Case Definition in OBX’s)
including Medication or Disease Assessed,
Genomic Source Class, Analysis Report, and optional
Overall Interpretation

has a
1 to 1

Genetic Analysis Discrete Result Panel (OBR)

has a
0 to 1

has a
0 to many

DNA Analysis Discrete Sequence Variation Panel (OBR)
(i.e. Findings in OBX’s)
including Reference Sequence Identifiers, DNA Sequence
Variation, Genomic Source Class, and optional Allele Name
and Sequence Variation Interpretation
Genetic Variation
Implementation Guide

Nomenclatures, Code Systems and Value Sets

- LOINC
- SNOMED
- RxNORM
- HGNC
- HGVS
- DbSNP
- RefSeq
# Genetic Variation Implementation Guide

## Table 7-2: Genetic Analysis Summary Panel

<table>
<thead>
<tr>
<th>OBR/OBX</th>
<th>OBX-2 Value Type</th>
<th>Usage*</th>
<th>Cardinality</th>
<th>Value Set</th>
<th>LOINC Code</th>
<th>LOINC Element Name</th>
<th>Description/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>OBR</td>
<td></td>
<td>R</td>
<td>1..n</td>
<td></td>
<td>55232-3</td>
<td>Genetic Analysis Summary Panel</td>
<td>The summary panel for a genetic analysis for one or more laboratory tests (e.g. analysis for disease risk, diagnosis or pharmacogenetics) on a single accession.</td>
</tr>
<tr>
<td>OBX</td>
<td>CWE</td>
<td>C1</td>
<td></td>
<td>SNOMED</td>
<td>51967-8</td>
<td>Genetic disease assessed</td>
<td>A coded disease (recommend SNOMED) which is associated with the region of DNA covered by the genetic test.</td>
</tr>
<tr>
<td>OBX</td>
<td>CWE</td>
<td>C1</td>
<td></td>
<td>RxNORM</td>
<td>51963-7</td>
<td>Medication Assessed</td>
<td>A coded medication accessed in a pharmacogenetic test (recommend RxNorm).</td>
</tr>
<tr>
<td>OBX</td>
<td>CWE</td>
<td>R</td>
<td></td>
<td></td>
<td>48002-0</td>
<td>Genomic Source Class</td>
<td>The genomic class of the specimen being analyzed: Germline for inherited genome, somatic for cancer genome (e.g. DNA from tumor cells), and prenatal for fetal genome. LOINC Answer List values can be seen in Table 7.6.</td>
</tr>
</tbody>
</table>

*If the study is intended to assess disease risk or diagnosis based on genetic findings, then the Genetic Disease Analysis Overall Interpretation is used (see below).*
Genetic Variation
Implementation Guide

<table>
<thead>
<tr>
<th>LOINC #</th>
<th>Component Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>47998-0</td>
<td>DNA Sequence Variation display name</td>
</tr>
<tr>
<td>47999-8</td>
<td>DNA region name</td>
</tr>
<tr>
<td>48002-0</td>
<td>Genomic source class</td>
</tr>
<tr>
<td>48003-8</td>
<td>DNA Sequence Variation identifier</td>
</tr>
<tr>
<td>48004-6</td>
<td>DNA Sequence Variation</td>
</tr>
<tr>
<td>48005-3</td>
<td>Amino acid change</td>
</tr>
<tr>
<td>48006-1</td>
<td>Amino acid change type</td>
</tr>
<tr>
<td>48008-7</td>
<td>Allele name</td>
</tr>
<tr>
<td>48013-7</td>
<td>Genomic reference sequence identifier</td>
</tr>
<tr>
<td>48018-6</td>
<td>Gene identifier</td>
</tr>
<tr>
<td>48019-4</td>
<td>DNA Sequence Variation type</td>
</tr>
<tr>
<td>51958-7</td>
<td>Transcript reference sequence identifier</td>
</tr>
<tr>
<td>51959-5</td>
<td>DNA region of interest</td>
</tr>
<tr>
<td>51961-1</td>
<td>Drug efficacy sequence variation interpretation</td>
</tr>
<tr>
<td>51963-7</td>
<td>Medication assessed</td>
</tr>
<tr>
<td>51964-5</td>
<td>Drug efficacy analysis overall interpretation</td>
</tr>
<tr>
<td>51967-8</td>
<td>Genetic disease assessed</td>
</tr>
<tr>
<td>51968-6</td>
<td>Genetic Disease Analysis Overall Interpretation</td>
</tr>
<tr>
<td>51969-4</td>
<td>Genetic analysis summary report</td>
</tr>
<tr>
<td>51971-0</td>
<td>Drug metabolism analysis overall interpretation</td>
</tr>
<tr>
<td>53034-5</td>
<td>Allelic state</td>
</tr>
<tr>
<td>53037-8</td>
<td>Genetic disease sequence variation interpretation</td>
</tr>
<tr>
<td>53039-4</td>
<td>Genetic disease analysis overall carrier interpretation</td>
</tr>
<tr>
<td>53040-2</td>
<td>Drug metabolism sequence variation interpretation</td>
</tr>
</tbody>
</table>
# Genetic Variation Implementation Guide

## TABLE 7-6 - LOINC ANSWER LISTS

<table>
<thead>
<tr>
<th>LOINC code</th>
<th>LOINC component</th>
<th>Sequence</th>
<th>Answer text</th>
<th>LOINC answer code</th>
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<tbody>
<tr>
<td>53034-5</td>
<td>Allelic state</td>
<td></td>
<td>1 Heteroplasmic</td>
<td>LA6703-8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 Homoplasmic</td>
<td>LA6704-6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 Homozygous</td>
<td>LA6705-3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 Heterozygous</td>
<td>LA6706-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5 Hemizygous</td>
<td>LA6707-9</td>
</tr>
<tr>
<td>48006-1</td>
<td>Amino acid change type</td>
<td></td>
<td>1 Wild type</td>
<td>LA9658-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 Deletion</td>
<td>LA6692-3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 Duplication</td>
<td>LA6686-5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 Frameshift</td>
<td>LA6694-9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5 Initiating Methionine</td>
<td>LA6695-6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6 Insertion</td>
<td>LA6687-3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7 Insertion and Deletion</td>
<td>LA9659-9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>8 Missense</td>
<td>LA6698-0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>9 Nonsense</td>
<td>LA6699-8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10 Silent</td>
<td>LA6700-4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>11 Stop Codon Mutation</td>
<td>LA6701-2</td>
</tr>
<tr>
<td>48019-4</td>
<td>DNA sequence variation type</td>
<td></td>
<td>1 Wild type</td>
<td>LA9658-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 Deletion</td>
<td>LA6692-3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 Duplication</td>
<td>LA6686-5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 Insertion</td>
<td>LA6687-3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5 Insertion/Deletion</td>
<td>LA6688-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6 Inversion</td>
<td>LA6689-9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7 Substitution</td>
<td>LA6690-7</td>
</tr>
<tr>
<td>51964-5</td>
<td>Drug efficacy analysis overall interpretation</td>
<td></td>
<td>1 Responsive</td>
<td>LA6677-4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 Resistant</td>
<td>LA6676-6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 Negative</td>
<td>LA6577-6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 Inconclusive</td>
<td>LA9663-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5 Failure</td>
<td>LA9664-9</td>
</tr>
<tr>
<td>51961-1</td>
<td>Drug efficacy sequence variation interpretation</td>
<td></td>
<td>1 Resistant</td>
<td>LA6676-6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 Responsive</td>
<td>LA6677-4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 Presumed resistant</td>
<td>LA9660-7</td>
</tr>
</tbody>
</table>
HL7 Implementation Guide
for CDA ® Release 2:
Genetic Testing Report (GTR), DSTU Release 1

(Universal Realm)
Draft Standard For Trial Use
February 2013
**Example Report**

DOB/Sex: 58 Female
Printed: 07-Oct-10 09:35:48

### Hemochromatosis Interpretation

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Result</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFE PCR Specimen</td>
<td>Whole Blood</td>
<td></td>
</tr>
<tr>
<td>C282Y Hemochromatosis Mutation</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>H63D Hemochromatosis Mutation</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>S65C Hemochromatosis Mutation</td>
<td>Negative</td>
<td></td>
</tr>
</tbody>
</table>

Hemochromatosis Mutation Interpretation: See Note f

25-Sep-10 10:15:00  Hemochromatosis Mutation Interpretation

Hemochromatosis Interpretive Results:

**C282Y:** Negative -- The patient is negative for the HFE C282Y mutation.

**H63D:** Negative -- The patient is negative for the HFE H63D mutation.

**S65C:** Negative -- The patient is negative for the HFE S65C mutation.

Mutations in unidentified genes or other mutations in the HFE gene are not ruled out.

25-Sep-10 10:15:00  HFE PCR:
Client Accession number: [Accession Number]
Is the Patient Fasting? Yes

This result has been reviewed and approved by Hunter Bost, Ph.D.

25-Sep-10 10:15:00  Hemochromatosis Mutation Interpretation:

BACKGROUND INFORMATION: Hemochromatosis (HFE) 3 Mutations

**CHARACTERISTICS:** Disorder of iron metabolism resulting in excessive iron storage leading to increased skin pigmentation, arthritis, hypogonadism, diabetes mellitus, heart arrhythmias/failure, cirrhosis and liver carcinoma.

**INCIDENCE:** One in 300 individuals of Northern European descent; unknown in other ethnicities.

**INHERITANCE:** Autosomal recessive.

**PENETRANCE:** 5 percent of C282Y homozygotes, 1 percent of C282Y/H63D compound heterozygotes and rare H63D homozygotes develop clinical symptoms.

**CAUSE:** Two pathogenic HFE gene mutations on opposite chromosomes.


**CLINICAL SENSITIVITY:** 85 percent of hereditary hemochromatosis in Northern Europeans is caused by C282Y homozygosity and 5 percent by C282Y/H63D compound heterozygosity.

**METHODOLOGY:** PCR and fluorescence monitoring.

**ANALYTICAL SENSITIVITY AND SPECIFICITY:** 99 percent.

**LIMITATIONS:** HFE mutations, other than those targeted, will not be detected. Rare diagnostic errors may occur due to primed site mutations.

This test is performed pursuant to an agreement with BioRad Laboratories, Inc.

The performance characteristics of this test were validated by ARUP Laboratories. The U.S. Food and Drug Administration (FDA) has not approved or cleared this test. However, FDA approval or clearance is currently not required for clinical use of this test. The results are not intended to be used as the sole means for clinical diagnosis or patient
Genetic Testing Report

The GeneticTestingReport is a document template and thus serves as the root template for the GTR Implementation Guide. Its organization is described in the Approach section of this document. The sub-sections residing here constitute the backbone of the GTR. A specific genetic test is described in the TestDetailsSection which serves as a blueprint specialized sections describing testing like genetic variation or gene expression.

1. SHALL contain exactly one [1..1] code/code="51969-4" Genetic analysis summary report (CodeSystem: 2.16.840.1.113883.6.1 LOINC) (CONF-GTR-1)

2. SHALL contain exactly one [1..1] title (CONF-GTR-7)
   • Default title is "Genetic Testing Report".

3. SHALL contain exactly one [1..1] component
   a. Contains exactly one [1..1] Summary Section (templateId: 2.16.840.1.113883.10.20.20.1.1)

4. Contains at least one [1..*] component
   a. Contains exactly one [1..1] Test Details Section (templateId: 2.16.840.1.113883.10.20.20.1.8)

5. Contains zero or one [0..1] component
   a. Contains exactly one [1..1] Test Information Section (templateId: 2.16.840.1.113883.10.20.20.1.9)

6. Sections and subsections SHALL have a title and the title SHALL NOT be empty. Text of a section title can specialize the section code by being more specific, for example, a hearing loss genetic testing report.

7. Sections SHALL appear in the order they are presented in this guide. Thus, SummarySection which SHALL appear first and TestInformationSection which SHOULD appear last. In between, TestDetailsSection can be repeated per the no. of genetic tests performed. Note that a TestInformationSection can appear in each of the specific test sections.

<?xml version="1.0" encoding="UTF-8"?>
<ClinicalDocument xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
   xmlns="urn:hll-org:v3" xsi:schemaLocation="urn:hll-org:v3 CDA.xsd">
  <typeId root="2.16.840.1.113883.1.3" extension="POCD_HD000040"/>
  <templateId root="2.16.840.1.113883.10.20.20"/>
  <id root="2.16.840.1.113883.11.12.7.30.9.1" extension="c266"/>
  <code code="51969-4" codeSystem="2.16.840.1.113883.6.1" codeSystemName="LOINC" display="Genetic analysis summary report"/>
  <title>Genetic Testing Report</title>
  <effectiveTime value="20100809"/>
  <!-- Other elements go here -->
</ClinicalDocument>
Summary Section

Indications
- Clinical Diagnosis and Family History of DCM

Specimen and Genomic Source
- Peripheral Blood
- Genomic source class: Germline

Tests Performed
- Dilated Cardiomyopathy Panel B (5 genes)

Overall Interpretation
- **Positive**: DNA sequencing of the coding regions and splice sites of the ACTC, LDB3, LMNA, PLN and TAZ genes revealed a heterozygous R377C variant in exon 5 of the LMNA gene (NM_170707.1). The R377C variant has been reported in the literature (Mucir 2000, Ki 2002, Kubben 2006, van Tintelen 2007). As such, this variant is highly likely to be pathogenic and therefore causative for DCM. Genetic testing of this patient’s biological parents and other family members, particularly those who are affected, may help to confirm the significance of this variant. Please note that the laboratory can attempt testing on tissue specimens from deceased family members. It should be noted that the expression of DCM is the product not only of a DCM gene variant, but also of other modifier genes and environmental factors. The significance of a variant should always be interpreted in the context of the patient’s clinical manifestations. COMMENTS: Common sequence variants of unlikely clinical significance are not included in this report but are available upon request.

Recommendations
- If you would like more information about the clinical manifestations of DCM variants we recommend you visit a cardiology center with expertise in the management of dilated cardiomyopathy such as the Brigham Cardiovascular Genetics Center at 617-732-4837 (www.bwh.harvard.edu/centers/services/genetics). DCM caused by LMNA variants is inherited in an autosomal dominant manner where each first-degree relative of an individual with a DCM causing mutation has a 50% (or 1 in 2) chance of inheriting the mutation. Genetic testing is available for at-risk family members if desired. Genetic counseling is recommended for this patient and his family. For assistance in locating nearby genetic counseling services please call the laboratory at 617-732-8500 or email at LMM@partners.org.

Test Information

Background
- Dilated cardiomyopathy (DCM) is characterized by ventricular chamber enlargement and systolic dysfunction with normal left ventricular wall thickness. The estimated prevalence of DCM is 1/2,500 and about 20-35% of cases have a family history showing a predominantly autosomal mode of inheritance. Mutations in more than 20 genes have been shown to cause DCM, several of which (including MYH7, MYBPC3, TNNT2, TNNT1, TPM1, and ACTC), are also known to cause hypertrophic cardiomyopathy. Mutations in some genes cause additional abnormalities: Lamin A/C (LMNA) mutations are frequently found in DCM that occurs with progressive conduction system disease. Mutations in the Tafazzin (TAZ) gene cause Barth syndrome, an X-linked cardiomyopathy in infants. In addition, mutations in several genes (including LMNA, DES, SGCD and EMD) can cause DCM in conjunction with skeletal myopathy. Genetic testing can confirm the diagnosis of DCM in patients with disease as well as identify at-risk family members prior to the onset of symptoms.
# HL7 Version 2.5.1 Implementation Guide: Clinical Genomics; Fully LOINC-Qualified Cytogenetics Model, Release 1

**ORU^R01**

HL7 Version 2.5.1

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The hierarchical structures of panels are shown in the following diagrams:

Figure 1: Chromosome analysis master panel
Sample Clinical Workflow

1. Patient has encounter, fills out initial screening app
2. Patient fills out detailed FHH and medical Hx app
3. If patient is high risk, schedule genetic counselor
4. Screen patient for further testing
5. Case review, order genetic tests for patient and optionally family
6. Order placed with relevant clinical info
7. Return narrative, codified genomic result
8. Review results and recommend treatment

Risk Screening Applications
Dynamic Family Health History app
Risk assessment app
Diagnosis and Treatment Recommendation
Genomic Predictive Models w/ machine learning
Genomic inference Engine

CDS
Knowledge base
Risk Screening Data
Family Health History
Genomic Repository
CDR
EHR

More Than You Think
4.20.11 Standard Profile for Genetics

4.20.11.1 Overview

Observation genetics profile (i.e. Standard Profile for Genetics) extends Observation resource to enable reporting of structured genetic test results. In addition, the genetics profile contextualizes well established standards from the field of clinical genetics into the standards of healthcare (e.g. HGNC - HUGO Gene Nomenclature Committee’s international standard for gene names, symbols, and identifiers).

4.20.11.1 Genetic Standards and Resources include:

- Variant Databases: dbSNP, ClinVar, and COSMIC
- Reference Sequences: RefSeq and ENSEMBL
- Gene Symbols and Identifiers: HGNC - Human Gene Nomenclature Committee
- Variant Nomenclature: HGVS nomenclature from the Human Genome Variation Society
- Variant Feature Annotation: Sequence Ontology (SO) and LOINC
- Locus: Gene

4.20.11.2 Scope and Usage

The Standard Profile for Genetics supports reporting of a DNA variant at the genomic, cDNA, and protein change level. In addition, a condition context may be provided, as AssessedCondition. For large genomic tests, a condition may be used as an input into the analytic pipeline to aid in the identification of clinically relevant variants related to the test order. It is strongly encouraged to provide all available information in this profile for any reported variants, because receiving systems (e.g. discovery research, outcomes analysis, and public health reporting) may use this information to normalize variants over time or across sources. However, these data should not be used to dynamically correct/change variant representations for clinical use outside of the laboratory, due to insufficient information.

Implementers should be aware that semantic equivalency of results of genetic variants cannot be guaranteed unless there is an agreed upon standard between sending and receiving systems.

This FHIR genomics work is based on work of the HL7 Clinical Genomics Workgroup and modeled based on the Domain Analysis Model and SMART on FHIR Genomics as published in JAMIA 2015 (http://jamia.oxfordjournals.org/content/early/2015/07/21/jamia.ocv045.long).

The HL7 Clinical Genomics Work Group emphasizes the importance of transmitting structured genetic findings within the clinical, translational, and research environments fully integrated with other clinical data, in order to drive outcomes analysis, operational decision making, discovery research, and public health reporting. The standard doesn’t currently cover the reporting of clinically relevant negative or wild type results within genetic data portion of the message.

Here is the document of HL7 Version 3 Domain Analysis Model where the examples used in genetics profile are from (Page 5).
SMART on FHIR Genomics: Facilitating standardized clinico-genomic apps

Gil Alterovitz\textsuperscript{1,2,3,*}, Jeremy Warner\textsuperscript{4,5,*}, Peijin Zhang\textsuperscript{6,*}, Yishen Chen\textsuperscript{7}, Mollie Ullman-Cullere\textsuperscript{8}, David Kreda\textsuperscript{2}, Isaac S. Kohane\textsuperscript{1,2,3}

ABSTRACT

Background Supporting clinical decision support for personalized medicine will require linking genome and phenome variants to a patient’s electronic health record (EHR), at times on a vast scale. Clinico-genomic data standards will be needed to unify how genomic variant data are accessed from different sequencing systems.

Methods A specification for the basis of a clinic-genomic standard, building upon the current Health Level Seven International Fast Healthcare Interoperability Resources (FHIR\textsuperscript{®}) standard, was developed. An FHIR application protocol interface (API) layer was attached to proprietary sequencing platforms and EHRs in order to expose gene variant data for presentation to the end-user. Three representative apps based on the SMART platform were built to test end-to-end feasibility, including integration of genomic and clinical data.

Results Successful design, deployment, and use of the API was demonstrated and adopted by HL7 Clinical Genomics Workgroup. Feasibility was shown through development of three apps by various types of users with background levels and locations.

Conclusion This prototyping work suggests that an entirely data (and web) standards-based approach could prove both effective and efficient for advancing personalized medicine.
Roundtable on Translating Genomic-Based Research for Health
Action Collaborative to Develop Principles for Integrating Genomic Information Into the Electronic Health Record Ecosystem
# Key Pharmacogenomic Use Case Types

<table>
<thead>
<tr>
<th>#</th>
<th>Use Case Types</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Incorporating Genetic Results into EHR User Interfaces</td>
</tr>
<tr>
<td>2</td>
<td>Adding genetic tests in order sets</td>
</tr>
<tr>
<td>3</td>
<td>Clinical Decision Support (CDS) identifies when a test should be ordered (pre-test alert*)</td>
</tr>
<tr>
<td>4</td>
<td>CDS identifies when a drug order is inconsistent with a test result (post-order alert*)</td>
</tr>
</tbody>
</table>

* Note pre and post order status refers to the status of the test order as opposed to the drug order.
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:

<table>
<thead>
<tr>
<th>LOINC CD</th>
<th>Component</th>
<th>Long Common Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>79713-4</td>
<td>TPMT gene product metabolic activity interpretation</td>
<td>TPMT gene product metabolic activity interpretation in Blood or Tissue Qualitative by CPIC</td>
</tr>
</tbody>
</table>

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*

<table>
<thead>
<tr>
<th>Seq #</th>
<th>Answer</th>
<th>AnswerID</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Ultrarapid metabolizer</td>
<td>LA10315-2</td>
</tr>
<tr>
<td>2</td>
<td>Rapid metabolizer</td>
<td>LA25390-8</td>
</tr>
<tr>
<td>3</td>
<td>Normal metabolizer</td>
<td>LA25391-6</td>
</tr>
<tr>
<td>4</td>
<td>Intermediate metabolizer</td>
<td>LA10317-8</td>
</tr>
<tr>
<td>5</td>
<td>Poor metabolizer</td>
<td>LA9657-3</td>
</tr>
</tbody>
</table>
Proposal for V2 HL7 Genomics Reporting-Lite

- Develop an approach that would be compatible with both V2 and in FHIR for the smaller variations
Whitepaper on Genetics/Genomics in Care Coordination

- Genetic/Genomic data repositories in support of care coordination
- Genetic/Genomic data linked to electronic health record
- Genetic/Genomic data linked to other predictive data for broader association studies (i.e. medical claims data)
- Clinical Decision Support including clinical, genetic, family, occupational, and environmental health history
- Patient genomic profile (includes data beyond DNA, includes proteomic, gene expression, epigenomic, and microbiome, to complete a metabolic pathway)
Value Proposition

- The combination of detailed family health history, medical history, clinical evaluation, and genomic sequencing, could shed more light on accurate disease risk prediction, diagnosis, with more informed treatment recommendations and better patient outcomes.
QUESTIONS

Moving Family Health History & Genetic Test Result Data into the Electronic Health Record for Clinical Decision Support

HL7 - More Than You think

HIMSS
March 2, 2016

Grant M. Wood
Intermountain Healthcare Clinical Genetics Institute and HL7 Clinical Genomics workgroup