Standard Representation of Genomic Information

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Challenges and Opportunities

• Genetic testing is rapidly becoming part of mainstream medicine. Will play a larger role in cancer risk assessment, prevention, detection, and personalized cancer treatment in the future

• Increased opportunities to automate cancer registry reporting from Electronic Health Records (EHRs):
  ▪ Meaningful Use Stage 2 (MU2)
  ▪ Health Information Exchange (HIE)

• Coded and structured genetic test results and family history data that are integrated into EHRs will be important for cancer registries.
We need EHRs, but …

Today’s EHRs are not ready for genetic/genomic information!

Lack of standards for data elements, terminology, structure, and interoperability is one of the key barriers for clinical decision support (CDS)-enabled EHRs.
Health Level Seven (HL7)

- American National Standards Institute (ANSI)-accredited standards organization
- Maintains messaging standards between systems
  - HL7 V2.x messaging standards are the most widely implemented healthcare standards in the world
  - HL7 V3, Clinical Document Architecture (CDA) Release 2 (R2)
HL7 Clinical Genomics Work Group

List of Standards:

• HL7 Family History/Pedigree Model
  A normative HL7 standard since 2007 and an ANSI standard

• HL7 V3 Implementation Guide (IG) - Family History/Pedigree Interoperability, Release 1

• HL7 V2.5.1 Genetic Variation Standard, Release 1 and Release 2

• HL7 V2.5.1 Cytogenetic Standard, Release 1

• HL7 V3 CDA R2 IG - Genetic Testing Report, Release 1
HL7 V3 IG
Family History/Pedigree Interoperability, Release 1

April, 2013

HL7 Informative Document
Sponsored by: Clinical Genomics Work Group

Pedigree R1 Co-Editors:
Dr. Amnon Shabo (Shvo), IBM Research Lab, Haifa; Co-chair & Modeling Facilitator
Dr. Kevin S. Hughes, Avon Comprehensive Breast Evaluation Center, Massachusetts General Hospital

US Realm IG Co-Editors:
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Dr. Yan Heras, Lantana Consulting Group
Nnadi Ihuegu, Life Technologies
Giant M. Wood, Intermountain Healthcare
Dr. Kevin S. Hughes
Dr. Brian Drohan, Comprehensive Breast Evaluation Center, Massachusetts General Hospital
Family History/Pedigree Model

Risk analysis

Genotypic data

Person of focus

Age, decease date, age of disease onset, etc.

Disease

Relatives

Family History

- Person of focus
  - Age, decease date, age of disease onset, etc.
  - Risk analysis
  - Relatives

Genotypic data

Disease
Pedigree Model Implementations

My Family Health Portrait

Using My Family Health Portrait you can:
- Enter your family health history.
- Print your family health history to share with family or your health care worker.
- Save your family health history so you can update it over time.

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

Create a Family Health History
En Español
Use a Saved History
Em Português

Hughes riskApps™

Cancer Risk Assessment Software

Risk Clinic Application Cancer Risk Assessment Software The Hughes riskApps™ software applications and modules are used by patients and clinics throughout the United States. For more information on our products visit our Products page.
Genetic Variation / Cytogenetics

Genetic Variation IG:
- Within one or a small number of genes
- Single nucleotide polymorphism (SNP) probes, genotyping, gene sequencing

Cytogenetics IG:
- Structure and copy number changes at the chromosome level
- G-banding, Fluorescence in situ hybridization (FISH), cytogenomics microarray
Design Principles

• Flexible and sustainable
  Use LOINC panel approach

• Reuse standard terminologies and bioinformatics standards wherever possible
  ▪ SNOMED, LOINC, RxNorm
  ▪ Human Gene Nomenclature Committee (HGNC) for gene names
  ▪ Human Genome Variation Society (HGVS) for sequence variation
  ▪ Single Nucleotide Polymorphism Database (dbSNP)
  ▪ National Center for Biotechnology Information (NCBI) Reference Sequence database (RefSeq) for baseline reference sequence
HL7 Genetic Variation Model

- Genetic Analysis Master Panel (OBR)
  - Has a 1 to 1
    - 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 0 to 1
    - DNA Region Analysis Test Coverage Panel (OBR)
      - Has a 0 to Many
    - DNA Region of Interest Panel (OBR)
      - (i.e. Region of Interest in OBX’s)
      - Including Reference Sequences, Region of Interest Start, Region of Interest Stop and potentially Reference Nucleotide and Variable Nucleotide (if a genotyping test) or Genechip information (if a genechip was used: Genechip Manufacturer, Genechip ID, Genechip Version)
    - Has a 0 to 1
      - Genetic Analysis Discrete Result Panel (OBR)
        - 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, Sequence Variation Interpretation, and Genetic Variant Assessment (for genotyping tests)
# LOINC Genetic Analysis Master Panel

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<thead>
<tr>
<th>LOINC#</th>
<th>LOINC Name</th>
<th>R/O/C</th>
<th>Cardinality</th>
<th>Data Type</th>
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HL7 Cytogenetics Model

62389-2: Chromosome Analysis Master Panel

1...1
62386-8: Chromosome analysis summary panel

1...1
62357-9: Chromosome analysis overall interpretation

1...1
62356-1: Chromosome analysis result in ISCN expression

1...1
48002-0: Genomic source class

0...M
51967-8: Genetic disease assessed

0...1
51969-4: Genetic analysis summary report

Details are shown in the Chromosome analysis G-banding panel

0...1
62355-3: Chromosome analysis – G-banding panel

Details are shown in the Chromosome analysis FISH panel

0...1
62367-8: Chromosome analysis – FISH panel

Details are shown in the Chromosome analysis arr panel

0...1
62343-9: Chromosome analysis – arr copy number change panel
## LOINC Chromosome Analysis Master Panel

### 62389-2  
**Chromosome analysis master panel - Blood or Tissue**

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<th>LOINC#</th>
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### 62342-9

### 62386-8

### 62335-9

### 48002-0

### 51967-8

### 51968-4

### 62373-8

### 62374-4

### 62375-1

### 62376-9

### 62377-7

### 62378-5

### 62379-3

### 62380-1

### 62381-9

### 62382-7

### 62383-3

### 62384-3

### 62384-5

### 62385-2

### 62385-0

LOINC Panel Hierarchies and HL7 V2

Observation/Result Segment

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<th>OBX-3</th>
<th>OBX-3</th>
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LOINC Panel Code

| 3 | PO-1000-2^ARUP | 62386-8^Chromosome analysis summary panel^LN | 20100702000000|2010072100909|201007021410|12345^Dr.Jones|201070201410||F||PO-1000^ARUP |

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LOINC Panel Code

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<th>LA6626-1^Normal^LN</th>
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<th>ARUP Laboratories</th>
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Sample Cytogenetics HL7 V2 Message

1st OBR

OBR-3: (Filler Order Number) PO-1000^ARUP
OBR-4: (Universal Service Identifier) use LOINC
panel code where apply, or use local code
OBR-50: (Parent Universal Service Identifier)
Chromosome analysis master panel

OBR

OBR-3: PO-1001^ARUP
OBR-4: Chromosome analysis G-banding panel
OBR-29: (Parent) PO-1000^ARUP

OBX

OBX-3: (Observation Identifier) ISCN band level

OBX

OBX-3: Chromosome analysis result overall interpretation

OBX

OBX-3: Chromosome analysis result in ISCN

OBR|1|PO-1000^ARUP|200291^Chromosome analysis chorionic villus sampling^99ARU-ORDER-TEST-ID||20100702000000|20100702100909|12345^Dr.Jones||120080703000000|||F|||Fet al demise|62389-2^Chromosome analysis master panel^LN

SPM|1|^Placental tissue-Villi|20100702100909

OBR|2|PO-1000-1^ARUP|62355-3^Chromosome analysis G-banding^LN||20100702000000|20100702100909|12345^Dr.Jones|||201070201410|F|PO-1000^ARUP

OBX|1|CWE|62358-7^ISCN band level^LN||LA14112-9^425^LN|201070201410|ARUP Laboratories

OBX|2|CWE|62357-9^Chromosome analysis result overall interpretation^LN||LA6626-1^Normal^LN|||F|201070201410|ARUP Laboratories

OBX|2|CWE|62356-1^Chromosome analysis result in ISCN expression^LN||47,XY^2.16.840.1.113883.6.299^2005|||M|201070201410|ARUP Laboratories

Sample HL7 V2 Message

Example: Genetic Disease Analysis (e.g., Dilated Cardiomyopathy)

- **MSH**→As according to HL7 VERSION 2.5.1 IMPLEMENTATION GUIDE: ORDERS AND OBSERVATIONS; INTEROPERABLE LABORATORY RESULT REPORTING TO EHR (US REALM), RELEASE 1, ORU^R01, HL7 Version 2.5.1, November, 2007.

- **OBR|1|**|PM-08-J00094^HPCGG-LMM^2.16.840.1.113883.3.167.1^ISO|Im_DCML-
pnB_L^Dilated Cardiomyopathy Panel B (5 genes)^99LMM-ORDER-TEST-ID||20080702000000|20080702100909|||234567891^Pump^Patrick^^^^^NPI^L||20080703000000||F||I||00000009^Cardiovascular^99HPCGG-GVIE-INDICATION^^^^^Clinical Diagnosis and Family History of DCM|&Geneticist&Gene&&&NPI^^^^^HPCGG-LMM&2.16.840.1.113883.3.167.1^ISO|55233-1^Genetic analysis master panel ^LN

- **SPM|1|**|119273009&Peripheral blood&SNM3&&&0707Intl&Blood, Peripheral|||20080702000000

- **OBR|2|**|PM-08-J00094-1^HPCGG-LMM^2.16.840.1.113883.3.167.1^ISO|55232-3^Genetic analysis summary panel^LN|20080702000000|||20080703000000||F|||PM-08-
J00094&HPCGG-LMM&2.16.840.1.113883.3.167.1^ISO

- **OBX|1|**|CWE|51967-8^Genetic disease assessed^LN|39902009^DCM-Dilated Cardiomyopathy^SNM3^0707Intl|||F|20080702100909||Laboratory for Molecular Medicine^L^22D1005307^CLIA&2.16.840.1.113883.4.7^ISO|1000 Laboratory Lane^Ste. 123^Cambridge^MA^99999^USA^B
Implementation Guide for CDA Release 2
Genetic Testing Report (GTR)
(Universal Realm)

Draft Standard for Trial Use
Second Ballot
May 2011
CDAR2_IG_GENTESTRPT_R1_O2_2011MAY
Conclusions

• An essential infrastructure needs to be developed to fit the rapidly changing and evolving nature of the field of genetic testing so that EHRs and cancer registries will be able to handle the high volume of genomic information.

• Coded and structured standard representation of genomic information and family history data are critical to interoperability between EHRs and cancer registries.

• Active involvement of the NAACCR community is critical.
Acknowledgments

- HL7 Clinical Genomics Work Group
- Amnon Shambo (Shvo), PhD, IBM Research Lab
- Grant Wood, Intermountain Healthcare
- Mollie Ullman-Cullere, Dana-Farber Cancer Institute and Partners Healthcare
- Kevin Hughes, MD, Avon Comprehensive Breast Evaluation Center, Massachusetts General Hospital