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Standard Representation of Genomic Information

Yan Heras, PhD
Lantana Consulting Group

2013 Annual NAACCR Conference

Tuesday, June 11, Session 2, Section A

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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.

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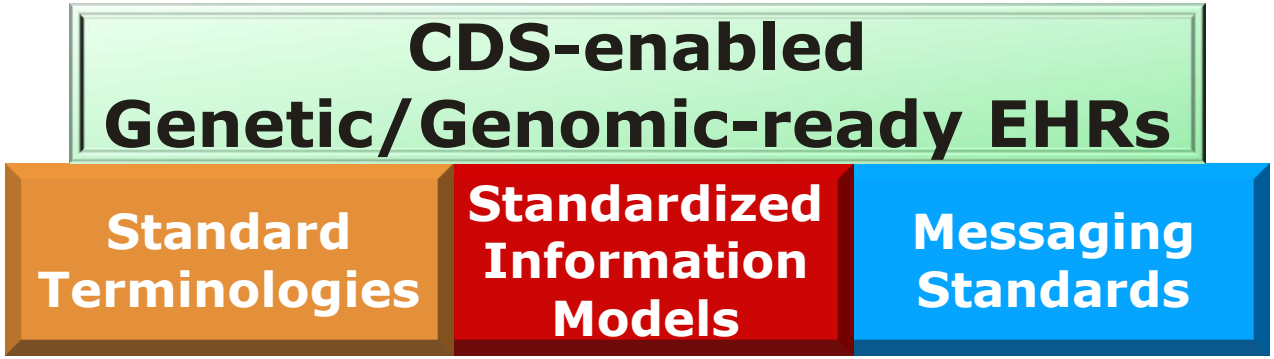
We need EHRs, but …

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.



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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)

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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

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HL7 V3 IG

Family History/ Pedigree Interoperability, Release 1

V3_IG_CANONPED_R1_INFORM_2013APR

HL7 Version 3 Implementation Guide: Family History/Pedigree Interoperability, Release 1 – US Realm

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
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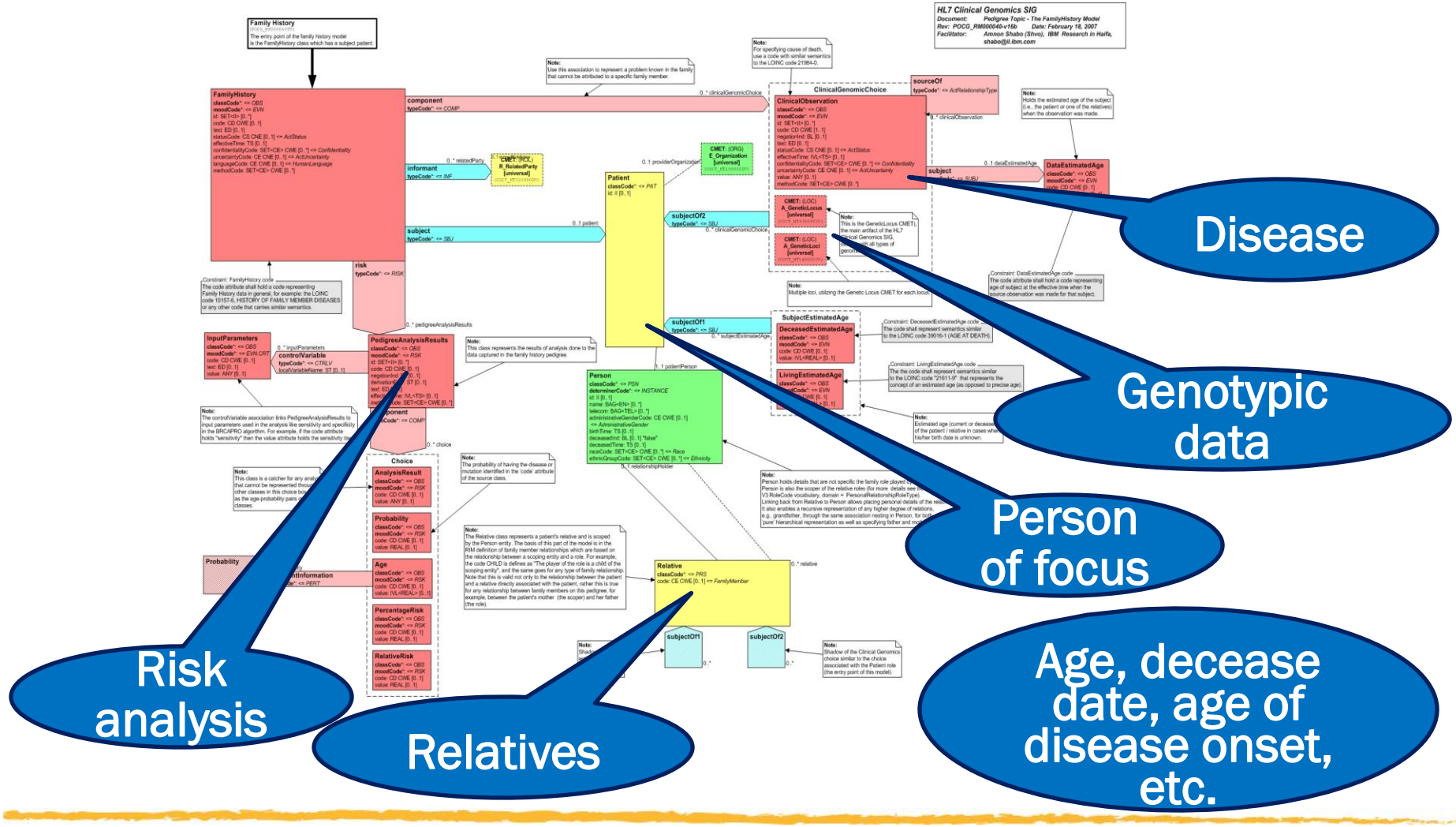
Family History/Pedigree Model



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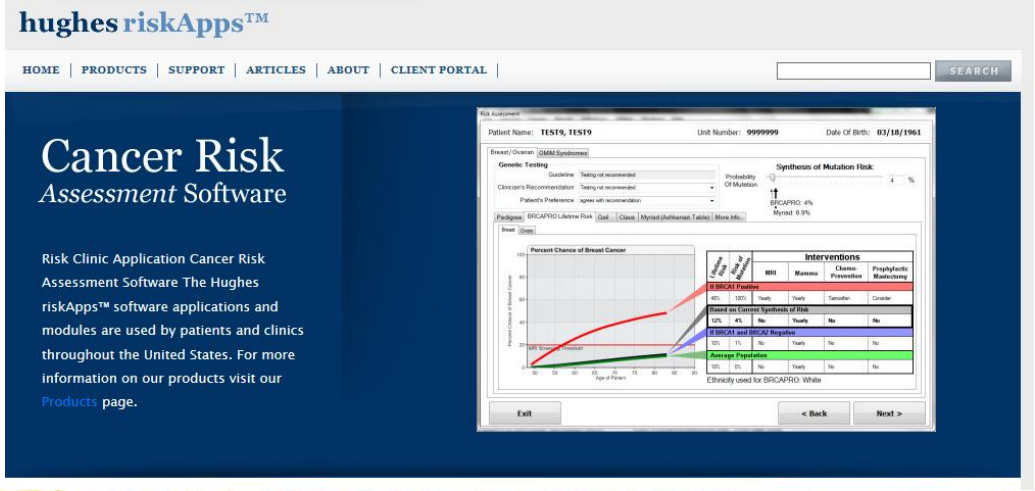
Pedigree Model Implementations

HealthVault



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Genetic Variation / Cytogenetics

Genetic Variation IG:

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

V2IG_CG_LOINCGENVAR_R2_INFORM_2013MAR

HL7 INTERNATIONAL

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

March 2013

HL7 Informative Document

Sponsored by:
Clinical Genomics Work Group

Principal Contributors:

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Grant Wood
Stan Huff
Clement McDonald
Amnon Shabo

Cytogenetics IG:

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

HL7 VERSION 2 IMPLEMENTATION GUIDE: CLINICAL GENOMICS; FULLY LOINC-QUALIFIED CYTOGENETICS MODEL, RELEASE 1

ORU^R01

HL7 Version 2.5.1

December, 2011

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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

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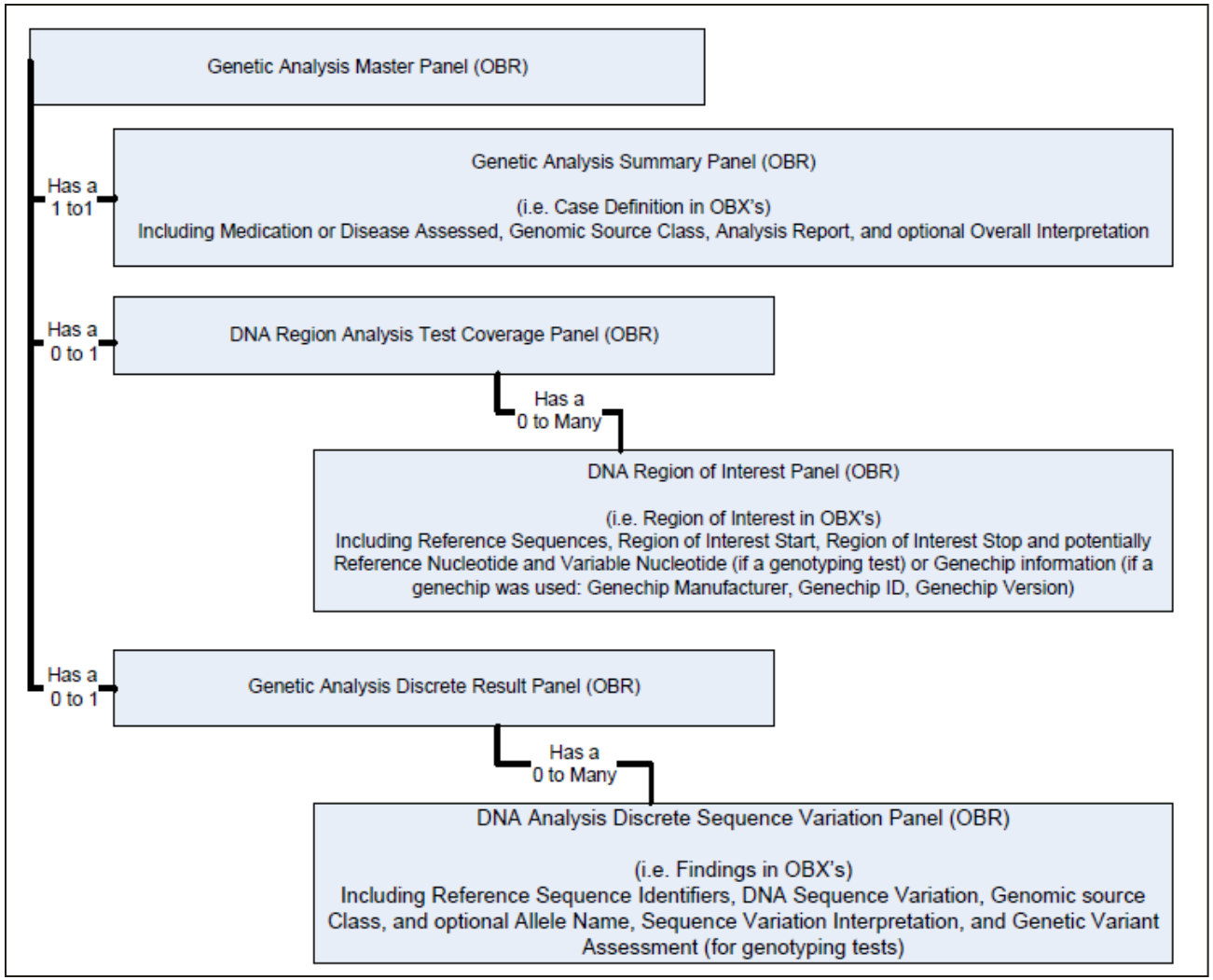
HL7 Genetic Variation Model



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LOINC Genetic Analysis Master Panel

55233-1 Genetic analysis master panel - Blood or Tissue by Molecular genetics method

PANEL HIERARCHY

LOINC#	LOINC Name	R/O/C	Cardinality	Data Type
55233-1	Genetic analysis master panel - Blood or Tissue by Molecular genetics method		1..n	
55232-3	Genetic analysis summary panel - Blood or Tissue by Molecular genetics method		1..n	
51967-8	Genetic disease assessed [Identifier] in Blood or Tissue by Molecular genetics method	C	0..n	CWE
51963-7	Medication assessed [Identifier] in Blood or Tissue by Molecular genetics method	C	0..n	CWE
48002-0	Genomic source class [Type] in Blood or Tissue by Molecular genetics method	R	1..1	CWE
51968-6	Genetic disease analysis overall interpretation [interpretation] in Blood or Tissue by Molecular genetics method	C	0..1	CWE
53039-4	Genetic disease analysis overall carrier interpretation [interpretation] in Blood or Tissue by Molecular genetics method	C	0..1	CWE
51964-5	Drug efficacy analysis overall interpretation [interpretation] in Blood or Tissue by Molecular genetics method	C	0..1	CWE
51971-0	Drug metabolism analysis overall interpretation [interpretation] in Blood or Tissue by Molecular genetics method	C	0..1	CWE
51969-4	Genetic analysis summary report in Blood or Tissue Document by Molecular genetics method	O	0..1	FT
53577-3	Reason for study additional note [Text] in Blood or Tissue by Molecular genetics method Narrative	O	0..1	ST
55207-5	Genetic analysis discrete result panel - Blood or Tissue by Molecular genetics method		1..n	
55208-3	DNA analysis discrete sequence variation panel - Blood or Tissue by Molecular genetics method		1..n	
48018-6	Gene [Identifier] in Blood or Tissue by Molecular genetics method	O	0..1	CWE
48013-7	Genomic reference sequence [Identifier] in Blood or Tissue by Molecular genetics method	C	0..1	CWE
51958-7	Transcript reference sequence [Identifier] in Blood or Tissue by Molecular genetics method	C	0..1	CWE
48008-7	Allele name [Identifier] in Blood or Tissue by Molecular genetics method	O	0..1	CWE
48003-8	DNA sequence variation identifier [Identifier] in Blood or Tissue by Molecular genetics method	O	0..1	CWE
48004-6	DNA sequence variation in Blood or Tissue by Molecular genetics method	C	0..1	CWE
48019-4	DNA sequence variation type in Blood or Tissue by Molecular genetics method	O	0..1	CWE
48005-3	Amino acid change in Blood or Tissue by Molecular genetics method	C	0..1	CWE
48006-1	Amino acid change type in Blood or Tissue by Molecular genetics method	O	0..1	CWE
47999-8	DNA region name [Identifier] in Blood or Tissue by Molecular genetics method	O	0..1	CWE
53034-5	Allelic state in Blood or Tissue by Molecular genetics method	O	0..1	CWE
48002-0	Genomic source class [Type] in Blood or Tissue by Molecular genetics method	R	1..1	CWE
47998-0	DNA sequence variation display name [Text] in Blood or Tissue by Molecular genetics method Narrative	O	0..1	ST
53037-8	Genetic disease sequence variation interpretation [interpretation] in Blood or Tissue by Molecular genetics method	C	0..1	CWE
53040-2	Drug metabolism sequence variation interpretation [interpretation] in Blood or Tissue by Molecular genetics method	C	0..1	CWE
51961-1	Drug efficacy sequence variation interpretation [interpretation] in Blood or Tissue Qualitative by	C	0..1	CWE

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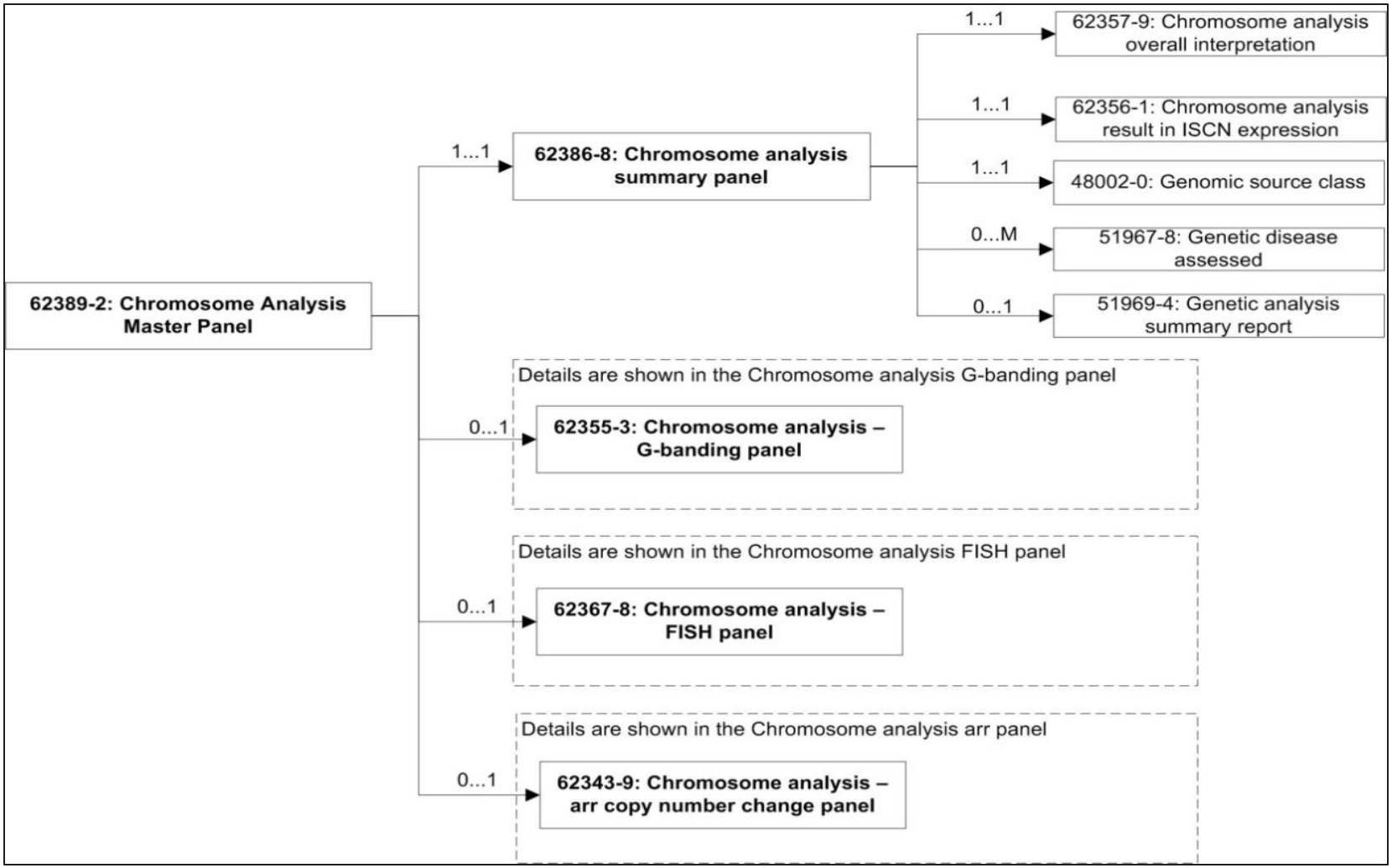
HL7 Cytogenetics Model



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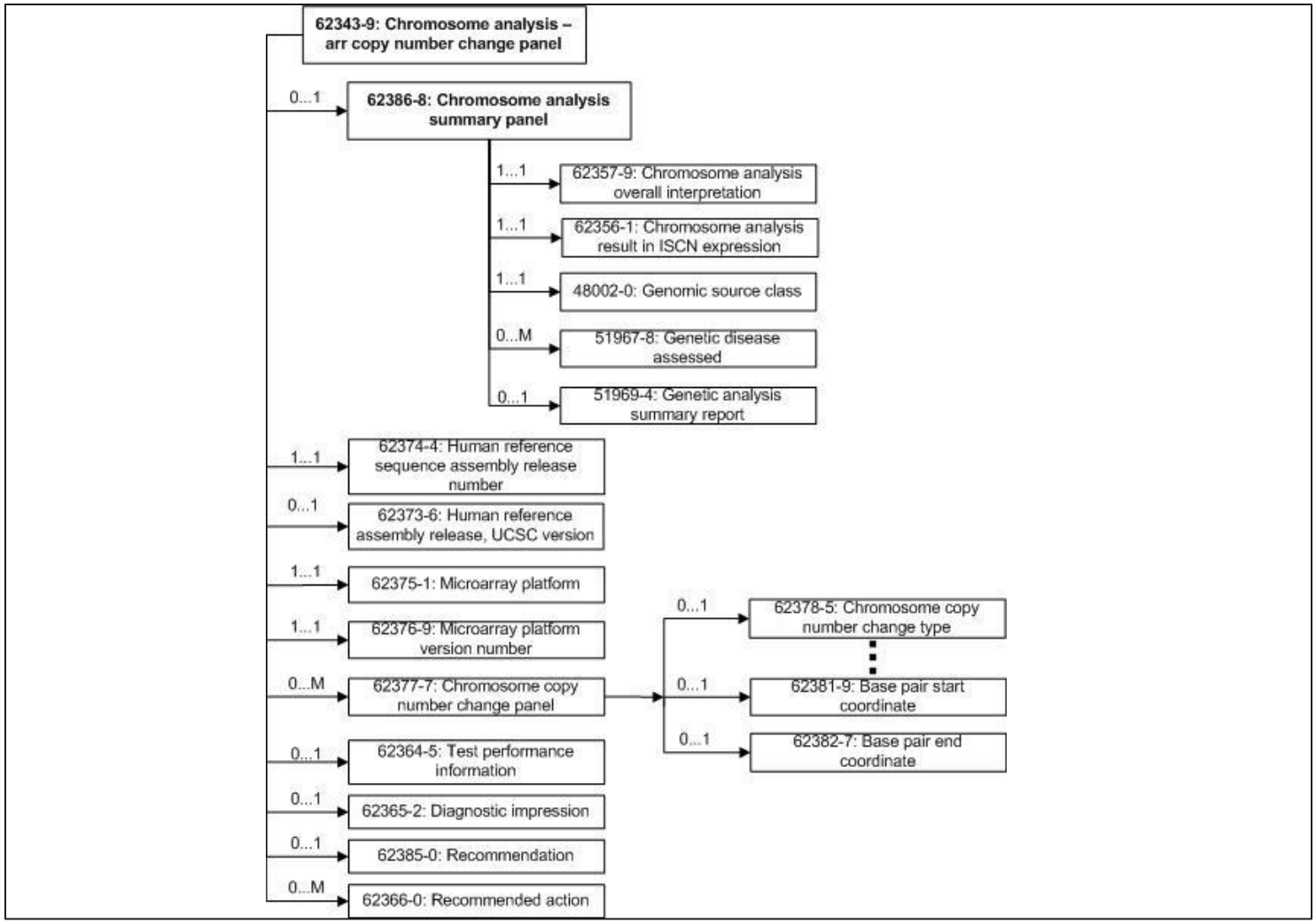
HL7 Cytogenetics Model



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LOINC Chromosome Analysis Master Panel

62389-2 Chromosome analysis master panel - Blood or Tissue

PANEL HIERARCHY

LOINC#	LOINC Name	R/O/C	Cardinality	Data Type
62389-2	Chromosome analysis master panel - Blood or Tissue			
62386-8	Chromosome analysis summary panel - Blood or Tissue by Molecular genetics method		1..1	
62356-1	Chromosome analysis result in ISCN expression in Blood or Tissue by Molecular genetics method		1..1	
62357-9	Chromosome analysis overall interpretation [interpretation] in Blood or Tissue Qualitative by Molecular genetics method		1..1	
48002-0	Genomic source class [Type] in Blood or Tissue by Molecular genetics method		1..1	CWE
51967-8	Genetic disease assessed [Identifier] in Blood or Tissue by Molecular genetics method		0..n	CWE
51969-4	Genetic analysis summary report in Blood or Tissue Document by Molecular genetics method		0..1	FT
62355-3	Chromosome analysis panel - Blood or Tissue by Banding			
62386-8	Chromosome analysis summary panel - Blood or Tissue by Molecular genetics method		1..1	
62356-1	Chromosome analysis result in ISCN expression in Blood or Tissue by Molecular genetics method		1..1	
...	...			
62343-9	Chromosome analysis microarray copy number change panel - Blood or Tissue by arrCGH			
62386-8	Chromosome analysis summary panel - Blood or Tissue by Molecular genetics method		1..1	
62356-1	Chromosome analysis result in ISCN expression in Blood or Tissue by Molecular genetics method		1..1	
62357-9	Chromosome analysis overall interpretation [interpretation] in Blood or Tissue Qualitative by Molecular genetics method		1..1	
48002-0	Genomic source class [Type] in Blood or Tissue by Molecular genetics method		1..1	CWE
51967-8	Genetic disease assessed [Identifier] in Blood or Tissue by Molecular genetics method		0..n	CWE
51969-4	Genetic analysis summary report in Blood or Tissue Document by Molecular genetics method		0..1	FT
62373-6	Human reference assembly release, UCSC version [Identifier] in Blood or Tissue		0..1	
62374-4	Human reference sequence assembly release number in Blood or Tissue by Molecular genetics method		1..1	
62375-1	Microarray platform [Identifier] in Blood or Tissue by Molecular genetics method Narrative		1..1	
62376-9	Microarray platform version number in Blood or Tissue by Molecular genetics method Narrative		1..1	
62377-7	Chromosome copy number change panel - Blood or Tissue by Molecular genetics method		0..n	
62378-5	Chromosome copy number change [Type] in Blood or Tissue by Molecular genetics method		0..1	
62379-3	Chromosome band involved start in Blood or Tissue by Molecular genetics method		0..1	
62380-1	Chromosome band involved end in Blood or Tissue by Molecular genetics method		0..1	
62381-9	Base pair start coordinate [#] in Blood or Tissue by Molecular genetics method		0..1	
62382-7	Base pair end coordinate [#] in Blood or Tissue by Molecular genetics method		0..1	
62383-5	Flanking normal region before start in Blood or Tissue by Molecular genetics method		0..1	
62384-3	Flanking normal region after end in Blood or Tissue by Molecular genetics method		0..1	
62364-5	Test performance information in Unspecified specimen Narrative		0..1	
62365-2	Diagnostic impression [interpretation] in Unspecified specimen by Molecular genetics method Narrative		0..1	
62385-0	Recommendation [interpretation] Document		0..1	

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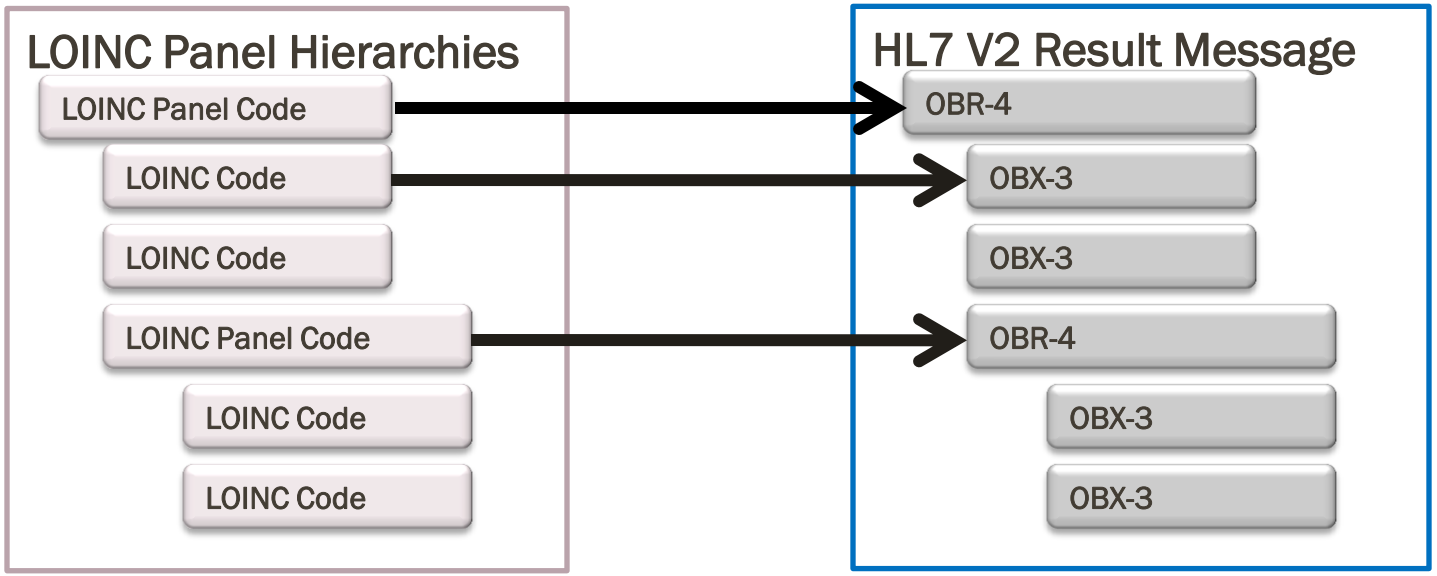
LOINC Panel Hierarchies and HL7 V2



Observation Request Segment

LOINC Panel Code

|3||PO-1000-2^ARUP|**62386-8**^Chromosome analysis summary panel^LN|
|20100702000000|20100702100909||||||201070201410||12345^Dr.Jones|||||
|201070201410|||F||||PO-1000^ARUP

Observation/Result Segment

LOINC Panel Code

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

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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

…

OBR

OBR-3: PO-1002^ARUP
OBR-4: Chromosome analysis summary panel
OBR-29: (parent) PO-1000^ARUP

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|||||| 201070201410||12345^Dr.Jones|||||20080703000000 |||F||||||^Fetal 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||||||201070201410||12345^Dr.Jones||||| |201070201410|||F||||PO-1000^ARUP

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

…

OBR|3||PO-1000-2^ARUP|62386-8^Chromosome analysis summary panel^LN||20100702000000 |20100702100909| ||||||201070201410||12345^Dr.Jones||||||201070201410|||F||| |PO-1000^ARUP

OBX|1|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

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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|lm_DCM-pnlB_L^**Dilated Cardiomyopathy Panel B (5 genes)**^99LMM-ORDER-TEST-ID||20080702000000|20080702100909||||||||234567891^Pump^Patrick^^^^^^NPI^L||||||20080703000000|||F||||||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||399020009^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

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HL7 V3 CDA R2 IG

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

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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.

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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

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