HL7 Clinical Genomics and Next Generation Sequencing

An Introduction to HL7

and the Clinical Genomics workgroup

September 14, 2011

Grant M. Wood

Intermountain Healthcare Clinical Genetics Institute

The HL7 Organization

- Founded in 1987, Health Level Seven International (HL7), with members in over 55 countries, is a not-for-profit, ANSI-accredited standards developing organization

- HL7 is dedicated to providing a comprehensive framework and related standards for the exchange, integration, sharing, and retrieval of electronic health information that supports clinical practice and management, delivery and evaluation of health services

- HL7's 2,300+ members include approximately 500 corporate members who represent more than 90% of the information systems vendors serving healthcare

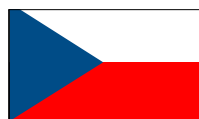- Over 43 healthcare standards from anatomic pathology to vocabulary
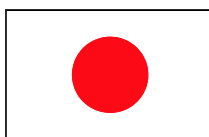
Take a Flash tour at
http://www.hl7.org/documentcenter/public/training/IntroToHL7/player.html

An International Organization with Over 30+ HL7 Affiliates

Argentina

Australia

Austria

Brazil

Canada

Chile

China

Columbia

Croatia

Czech Republic

Denmark

Finland

France

Germany

Greece

Hong Kong

India

Italy

Japan

South Korea

And growing

Luxembourg

Mexico

New Zealand

The Netherlands

Romania

Russia

Singapore

Spain

Sweden

Switzerland

Taiwan

Turkey

United Kingdom

United States

Uruguay
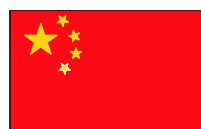
HL7 High Level Goals

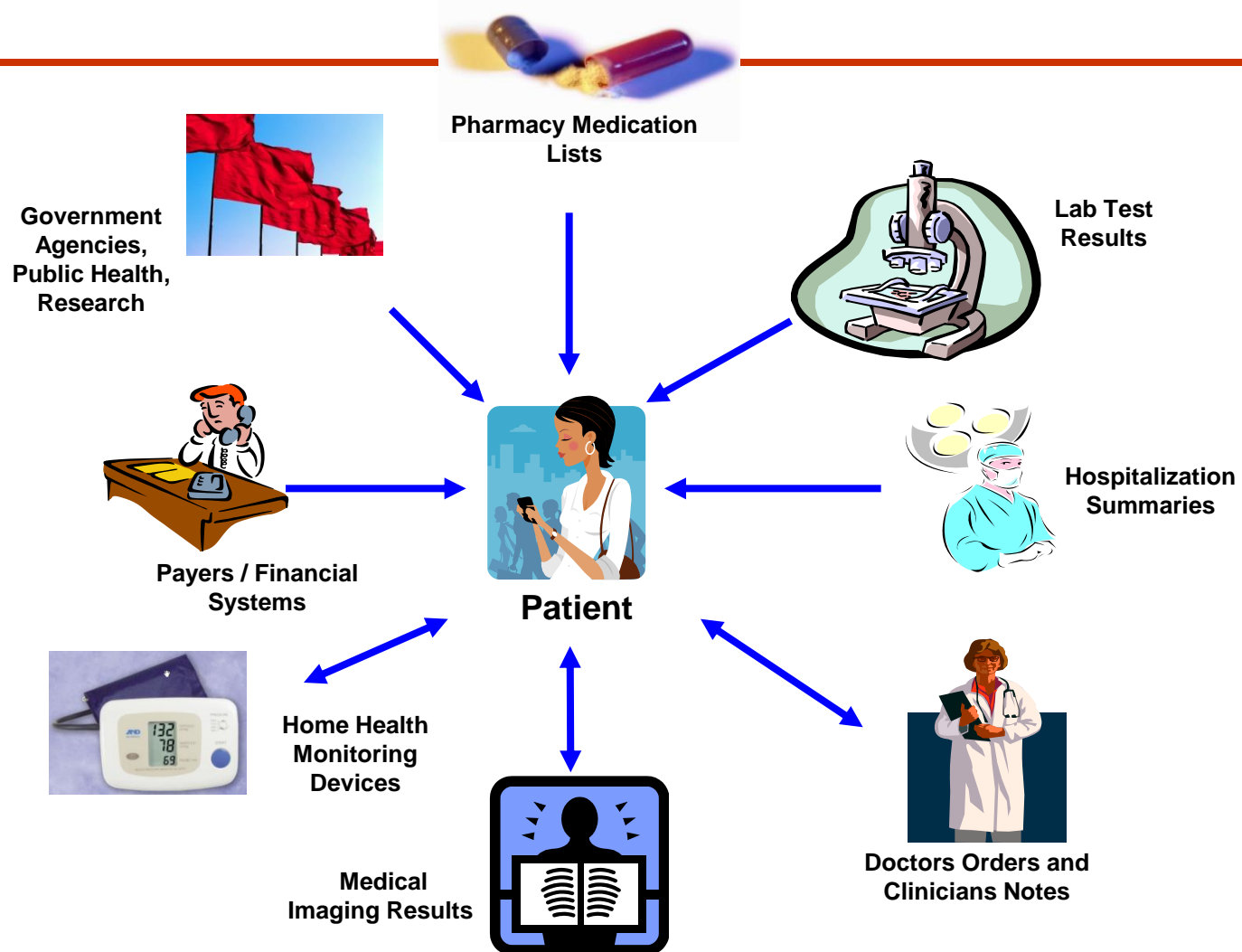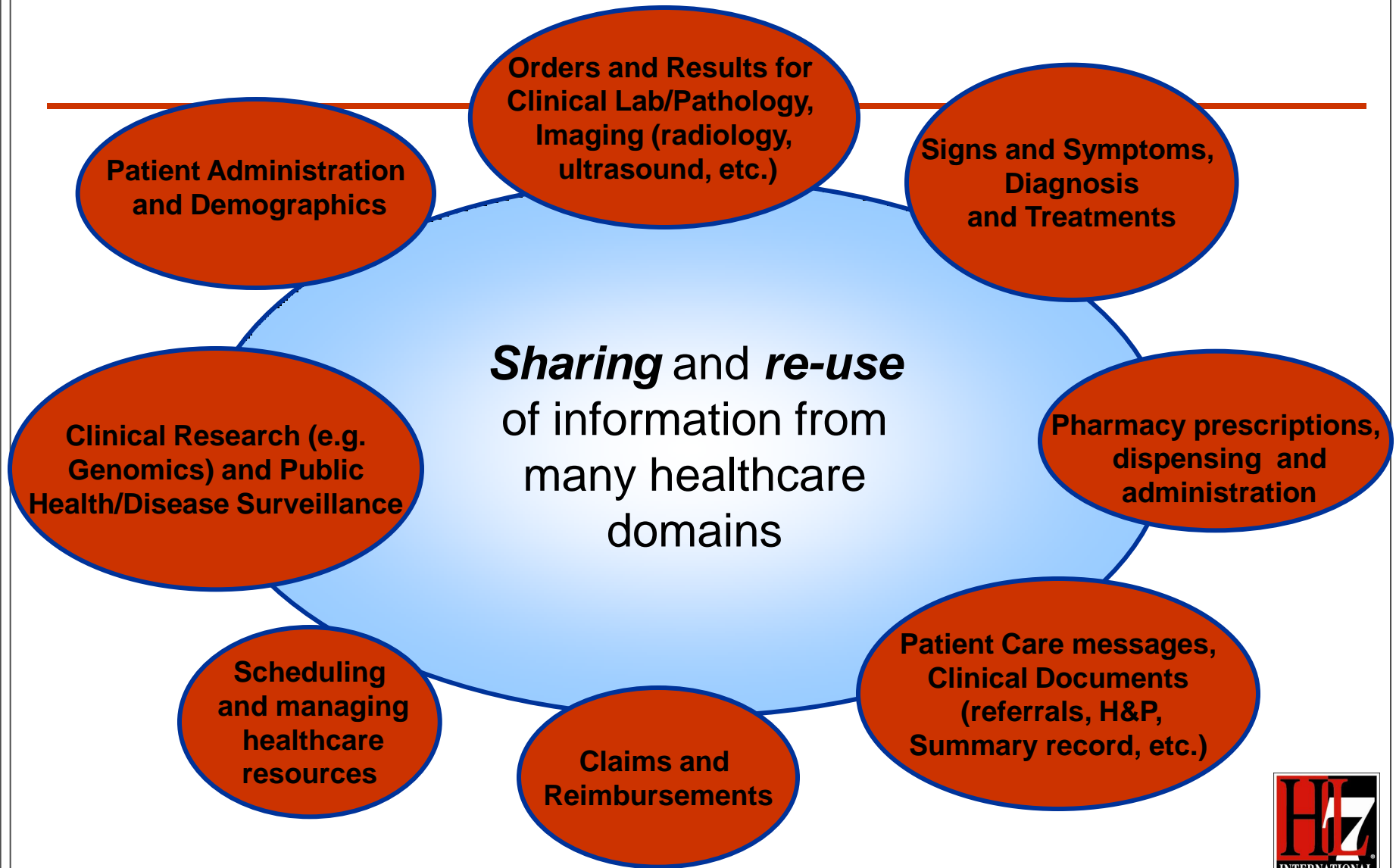➢ Stimulate, encourage and facilitate domain experts from healthcare industry stakeholder organizations to participate in HL7 to develop healthcare information standards in their area of expertise

➢ Collaborate with healthcare information technology users to ensure that HL7 standards meet real-world requirements, and that appropriate standards development efforts are initiated by HL7 to meet emergent requirements

Many Types of Healthcare Information Need to be Exchanged

Pharmacy Medication Lists

Government Agencies, Public Health, Research

Lab Test Results

Payers / Financial Systems

Patient

Hospitalization Summaries

Home Health Monitoring Devices

Medical Imaging Results

Doctors Orders and Clinicians Notes

HL7 Has Produced a Family of Standards

Orders and Results for Clinical Lab/Pathology, Imaging (radiology, ultrasound, etc.)

Patient Administration and Demographics

Signs and Symptoms, Diagnosis and Treatments

Clinical Research (e.g. Genomics) and Public Health/Disease Surveillance

Sharing and *re-use* of information from many healthcare domains

Pharmacy prescriptions, dispensing and administration

Scheduling and managing healthcare resources

Claims and Reimbursements

Patient Care messages, Clinical Documents (referrals, H&P, Summary record, etc.)
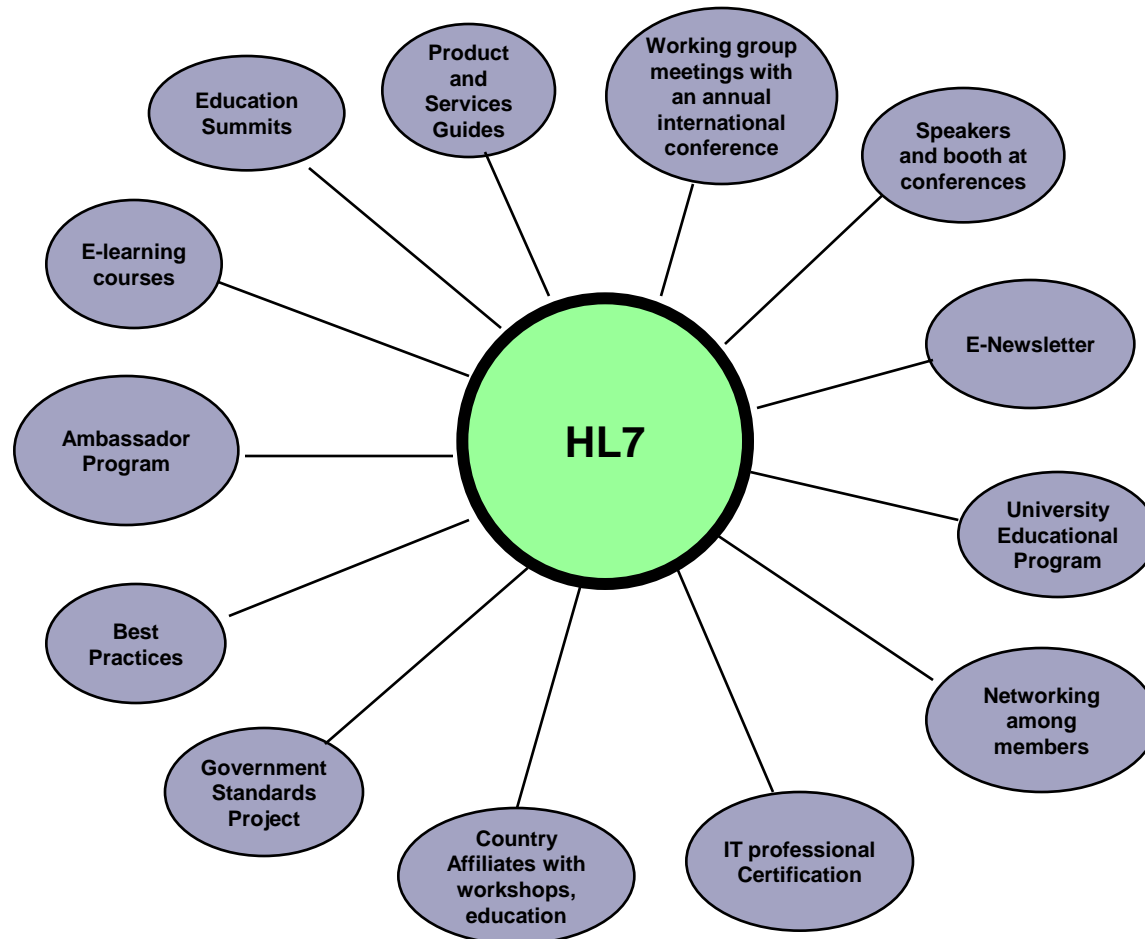
Domains in the Normative HL7 V3 standard

- Accounting & Billing
- Claims & Reimbursement
- Materials Management
- Patient Administration
- Personnel Management
- Scheduling
- Blood bank
- Care Provision
- Clinical Decision Support
- Clinical Document Architecture
- Clinical Genomics
- Diagnostic Imaging
- Immunization
- Laboratory
- Medical Records
- Medication
- Orders and Observation
- Pharmacy
- Public Health
- Regulated Products
- Regulated Studies
- Specimen
- Therapeutic Devices

Additional HL7 Programs and Activities

- Education Summits
- Product and Services Guides
- Working group meetings with an annual international conference
- Speakers and booth at conferences
- E-learning courses
- E-Newsletter
- Ambassador Program
- HL7
- University Educational Program
- Best Practices
- Networking among members
- Government Standards Project
- Country Affiliates with workshops, education
- IT professional Certification

The HL7 Clinical Genomics workgroup

Family Health History

Genetic Variation

Value of Family History in Clinical Care
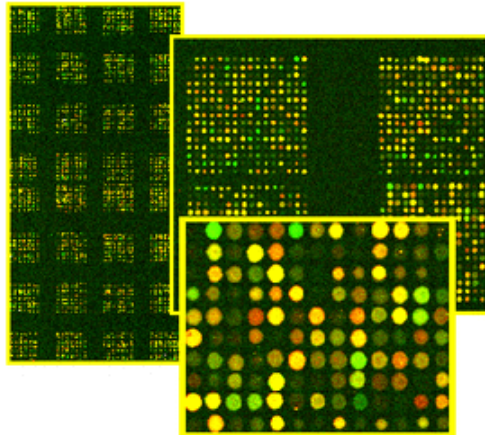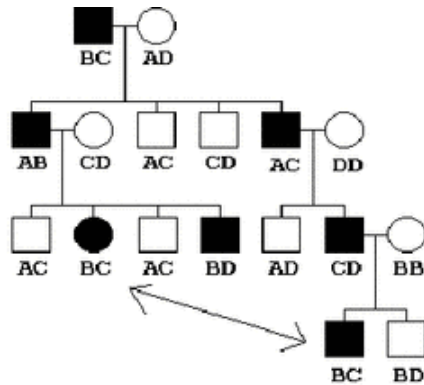
Family history remains the best and least expensive genetic 'test' currently available for clinical use.

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.
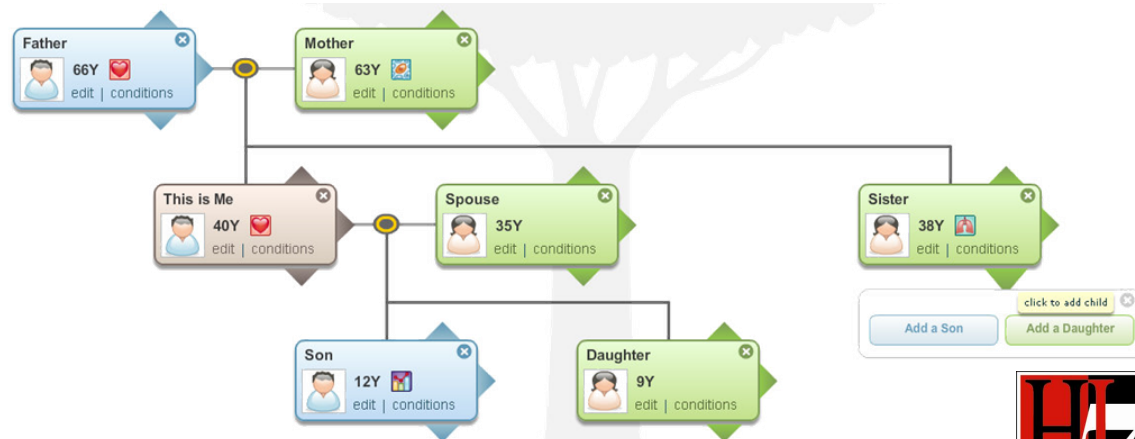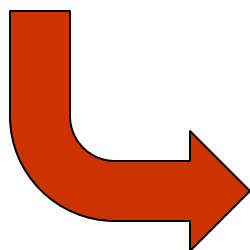
What's In the Pedigree Data Model

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

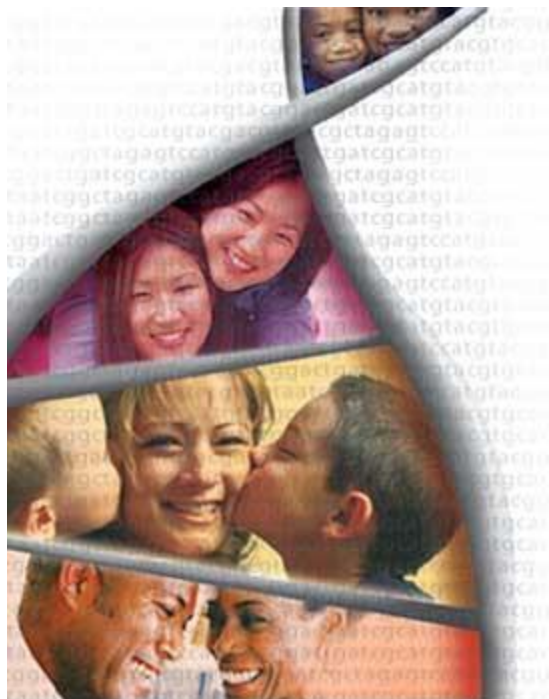# Data That Can Be Transmitted
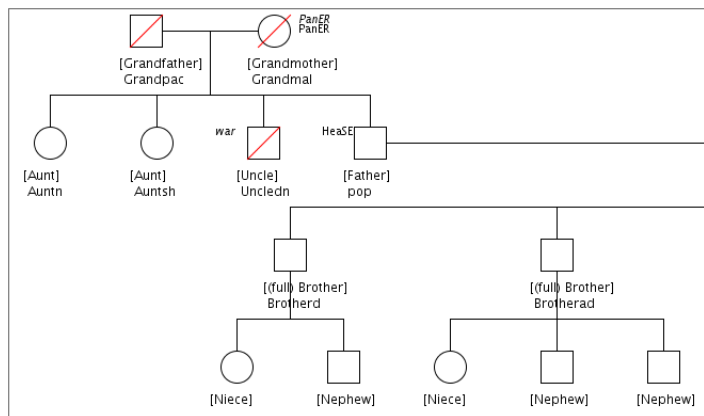
Full pedigree data
from one application
and completely
re-drawn in another

Data That Can Be Transmitted

Genetic Test Results in XML

```
<!-- GENOMIC DATA  -->
 <subjectOf2>
 <geneticLocus moodCode="EVN">
 <component1>
 <individualAllele moodCode="EVN">
 <text>breast cancer 2, early onset</text>
 <value code="U43746" displayName="BRCA2"
codeSystemName="HUGO" />
 <component3>
 <sequenceVariation moodCode="EVN">
 <value xsi:type="CE" code="185delAG" />
 <interpretationCode code="DELETERIOUS" />
```
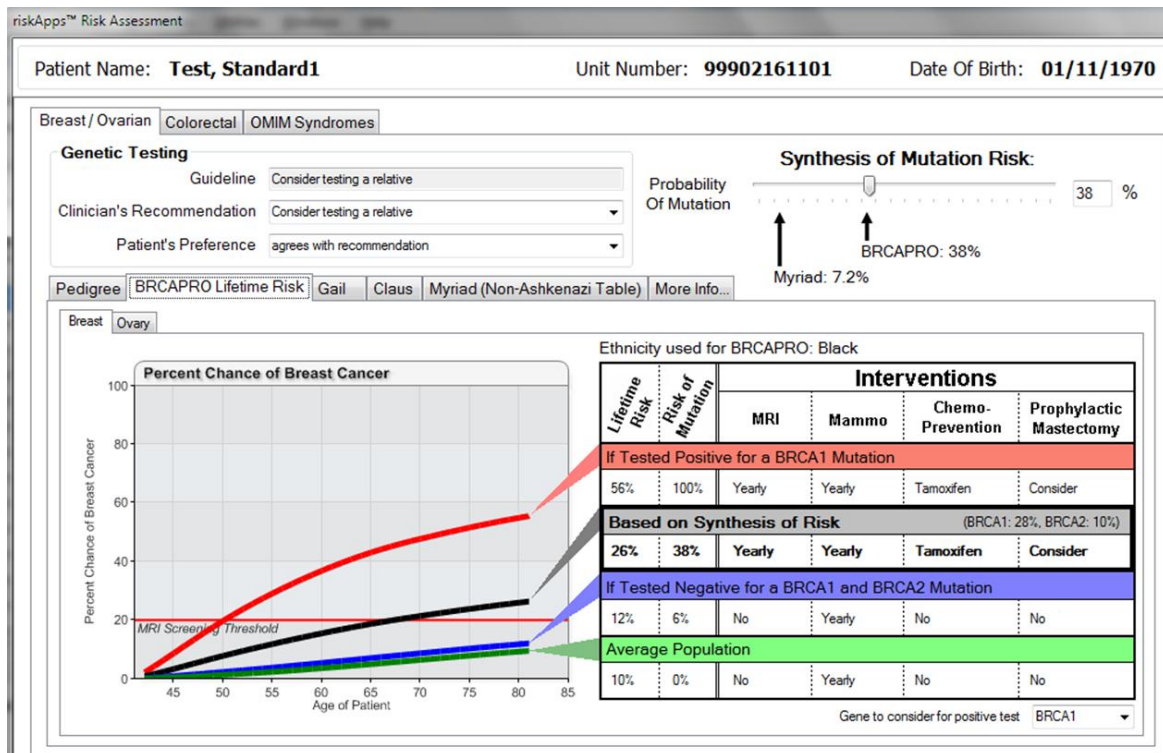
Data That Can Be Transmitted

Risk Analysis

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

2. Disease-specific risk algorithms can be provided by web services.

Going Beyond Family History

After 10 years,
what does it all mean?

There was just one problem at all the parties, press conferences, and publications celebrating the completion of the Human Genome Project (again and again and again) — 10 years later healthcare providers do not have the knowledge, education, and **informatics tools** to implement clinical genetics, genomics, proteomics, metabolics, and epigenetics into personalized medicine

Are Healthcare Systems Prepared

The bad news is that most health care systems risk being overwhelmed unless they start preparing for the complex and costly demands of genetic screening programs

Bio·IT World "Quote"

"We have to start thinking about genetics as just another component of data information and knowledge that has to be integrated into the electronic health record. Stop labeling genetics as something different and new and completely outside the mainstream medical establishment and move it back into the fundamental foundational effort of medical activity."

- Peter Tonellato, September 2010

HL7 Genetic Variation Data Model

The model facilitates the electronic transmission of genetic testing results and interpretations from –

- Genetic testing laboratories to medical practitioners, electronic health records, personal health records and associated clinical decision support systems able to receive and process such information

- Genetic testing laboratories to drug and medical device companies that have ordered such information as part of a clinical trial

- Drug and medical device companies to regulatory agencies that need to review such information as part of a new drug or device marketing application
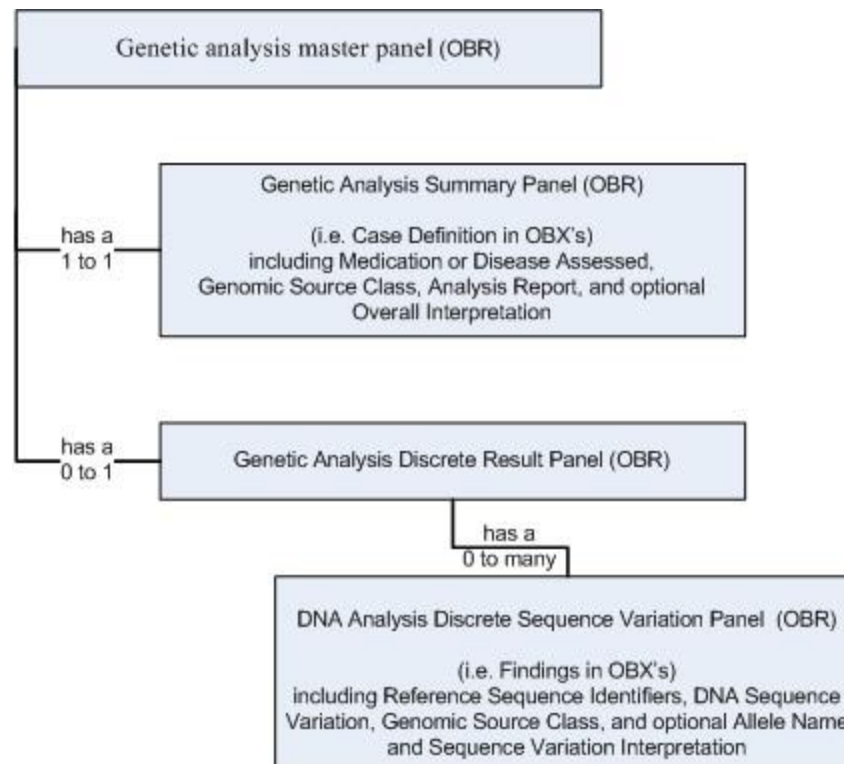
HL7 Version 2 Implementation Guide: Clinical Genomics; Fully LOINC-Qualified Genetic Variation Model, Release 1

September, 2009

HL7 Informative Document

Principal Contributors:

Amon Schabo
Mollie Ullman-Cullere
Phil Pochon
Grant Wood
Clement McDonald
Clinical Genomics Working Group

Genetic Variation Implementation Guide

Genetic Variation Implementation Guide

TABLE 7–2 –GENETIC ANALYSIS SUMMARY PANEL

OBR/ OBX	OBX-2 Value Type	Usage*	Card-inality	Value Set	LOINC Code	LOINC Element Name	Description/Comments
OBR		R	1..n		55232-3	Genetic Analysis Summary Panel	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.
OBX	CWE	C1		SNOMED	51967-8	Genetic disease assessed	A coded disease (recommend SNOMED) which is associated with the region of DNA covered by the genetic test.
OBX	CWE	C1		RxNORM	51963-7	Medication Assessed	A coded medication accessed in a pharmacogenic test (recommend RxNorm).
OBX	CWE	R			48002-0	Genomic Source Class	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.

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).

HL7 Version 2 Message
Genetic Disease Analysis

8.2.1 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

Advanced Genetic Testing Workflow
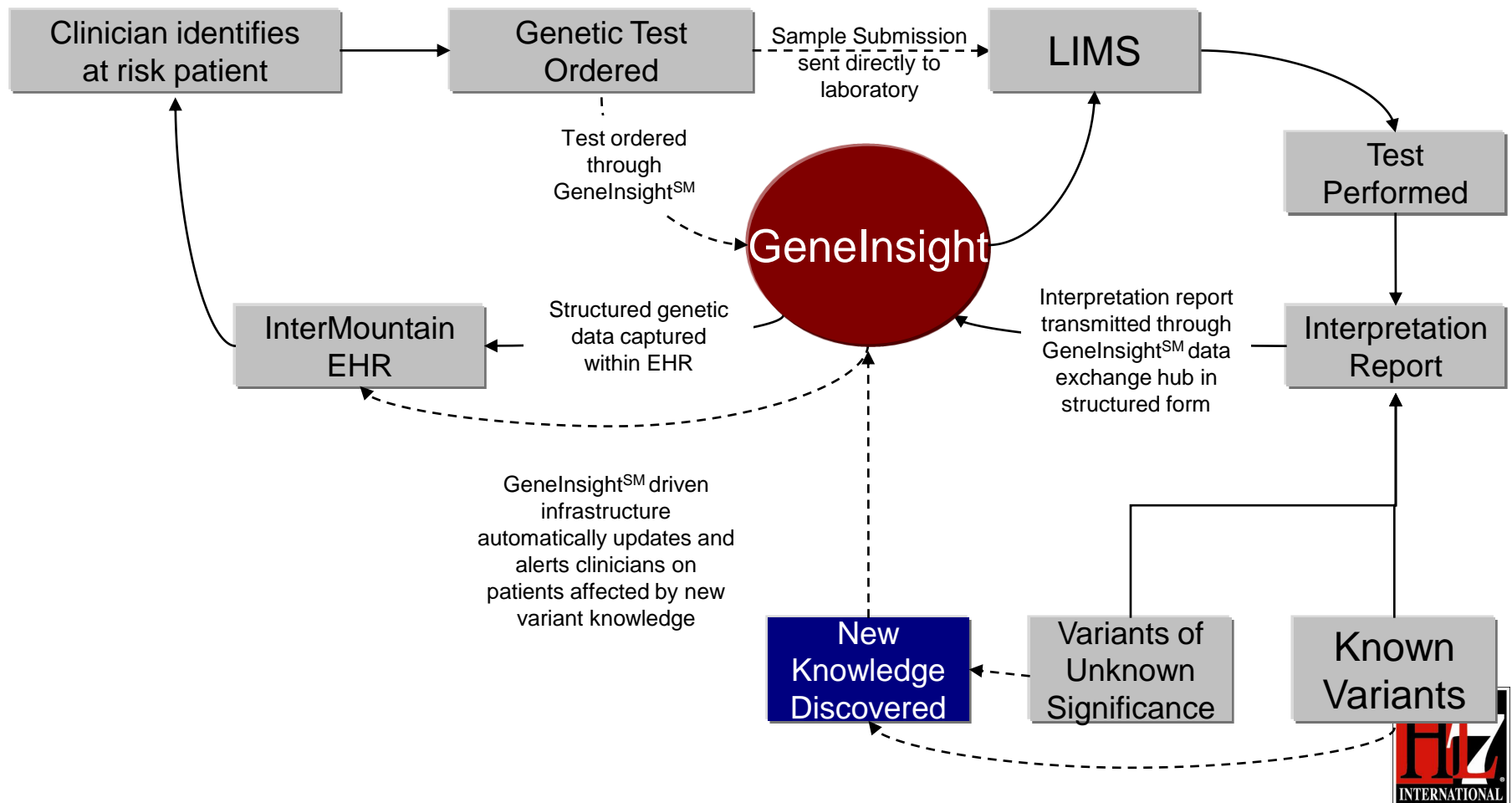
Other Areas of Activity

- CDA template – for CDA-based transfer of genetic test results

- Cytogenetics – for chromosomal-based tests in the clinic

- Gene Expression – for laboratory research and drug discovery

Implementation Guide for CDA Release 2
Genetic Testing Report (GTR)
(Universal Realm)

Draft For Comment

September 2011

CDAR2_IG_GENTESTRPT_R1_O2_2011SEP

What is a Continuity of Care Document?

- A medical summary representing the continuity of care record core data set covering one or more healthcare encounters.

- A snapshot in time for a patient, in CDA form, containing the pertinent:

  - clinical,
  - demographic, and
  - administrative data

CCD Required Sections

- Conditions (Problems)

- Allergies and Intolerances

- Medications

Optional Sections

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

- Immunizations
- Vital Signs
- Fetal Vital Signs
- Lab Results
- Plan of Care

CDA is the Basis For ...

- Continuity of Care Document
- Consult Note
- Diagnostic Imaging Report
- Discharge Summary
- Healthcare-associated Infections, Public Health Case Reports
- History and Physical
- Operative Note
- Personal Health Monitoring
- Plan-2-Plan Personal Health Record
- Quality Reporting Document
- Unstructured Documents

- Emergency Care Summary
- Summary Documents Using HL7 CCD
- Patient Level Quality Data Document Using IHE Medical Summary (XDS-MS)
- Encounter Document constructs
- Consult and History & Physical Note Document
- Immunization Document
- Scanned document
- … and many more …

Hearing Loss: Connexin 26 and 30 Full Gene Sequencing Panel Test Report

Patient	John Doe		
Date of birth	May 5, 1947	Sex	Male
Contact info	address not available Telecom information not available	Patient IDs	123456789 2.16.840.1.113883.18.12.7.30.9.2

Document Id	c266 2.16.840.1.113883.18.12.7.30.9.1
Document Created:	August 9, 2010

Author	Jean Geome,

Legal authenticator	Jean Genome of The New Genetic Testing Laboratory signed at February 12, 2006

Document maintained by	2.16.840.1.113883.19.3.2409

Table of Contents

Summary

Indications

- Indication: Profound sensorineural hearing loss

Specimen and Genomic Source Class

- Peripheral Blood
- Genomic source class: Germline

Summary of Tests Performed

- GJB2 Full Gene Test
- GJB6-D13S1830 deletion terminology
- Mitochondrial Hearing Loss Mutation Test

Overall Interpretation

- **Inconclusive.**
- DNA sequencing detected two changes in the GJB2 gene, 79G>A (V27I) and 109G>A (V37I). The V27I change has been reported as a benign variant (references) and is not believed to cause hearing loss. The V37I mutation has been previously reported in patients with hearing loss. This mutation, in homozygosity or combined with another GJB2 disease causing mutation, typically results in a mild to moderate hearing loss (Cryns et al. 2005). Mutations in both copies of the GJB2 gene are necessary to assume that GJB2 is responsible for the hearing loss. Although two mutations were identified in this patient, we would assume that the combination of a benign variant and a mild pathogenic mutation would result in a mild to moderate hearing loss rather than a moderately-severe one, as in this patient. It is most likely that the hearing loss in this patient is the result of the V37I mutation and an unknown second pathogenic mutation. It should be noted that a second mutation is not identified in a large percentage (10-50%) of patients with nonsyndromic hearing loss and GJB2 mutations (del Castillo et al. 2003).
- GJB6-D13S1830 Deletion: A PCR-based analysis of the GJB6-D13S1830 region of chromosome 13 was performed and did not detect the deletion. This test does not assess the DNA sequence of the GJB6 gene or detect other mutations that could affect the expression of the gene.
- Mitochondrial Hearing Loss mutations: Targeted bidirectional sequencing of mitochondrial DNA 1555 and 7445 regions did not detect the presence of these mutations. Although this test examines all regions known to contain pathogenic mutations in these genes, it does not include sequencing of the 5' end of the MTRNR1 gene.

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

ORU^R01

HL7 Version 2.5.1

September, 2011

Chapter Chair:	Amnon Shabo IBM
Chapter Chair and Contributing Author:	Mollie Ullman-Cullere Dana-Farber Cancer Institute
Project Chair and Contributing Author:	Stan Huff Intermountain Healthcare
Principal Author:	Yan Heras Lantana Consulting Group Dept. of Biomedical Informatics, University of Utah
Contributing Author	Clement McDonald Lister Hill Center for Biomedical Communication, National Library of Medicine
Contributing Author	Grant Wood Intermountain Healthcare
Subject Matter Advisor	Arthur Brothman ARUP Laboratories

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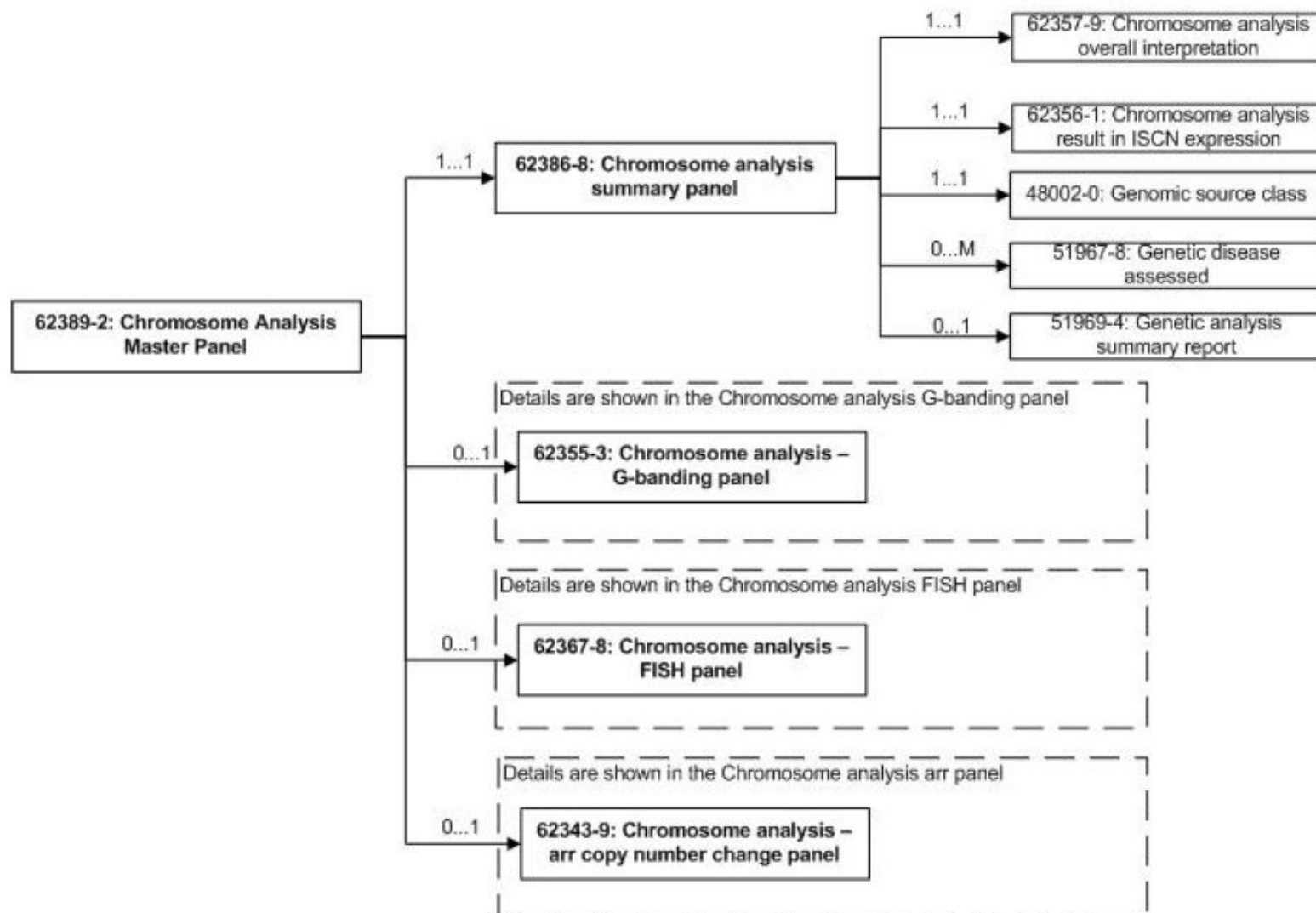

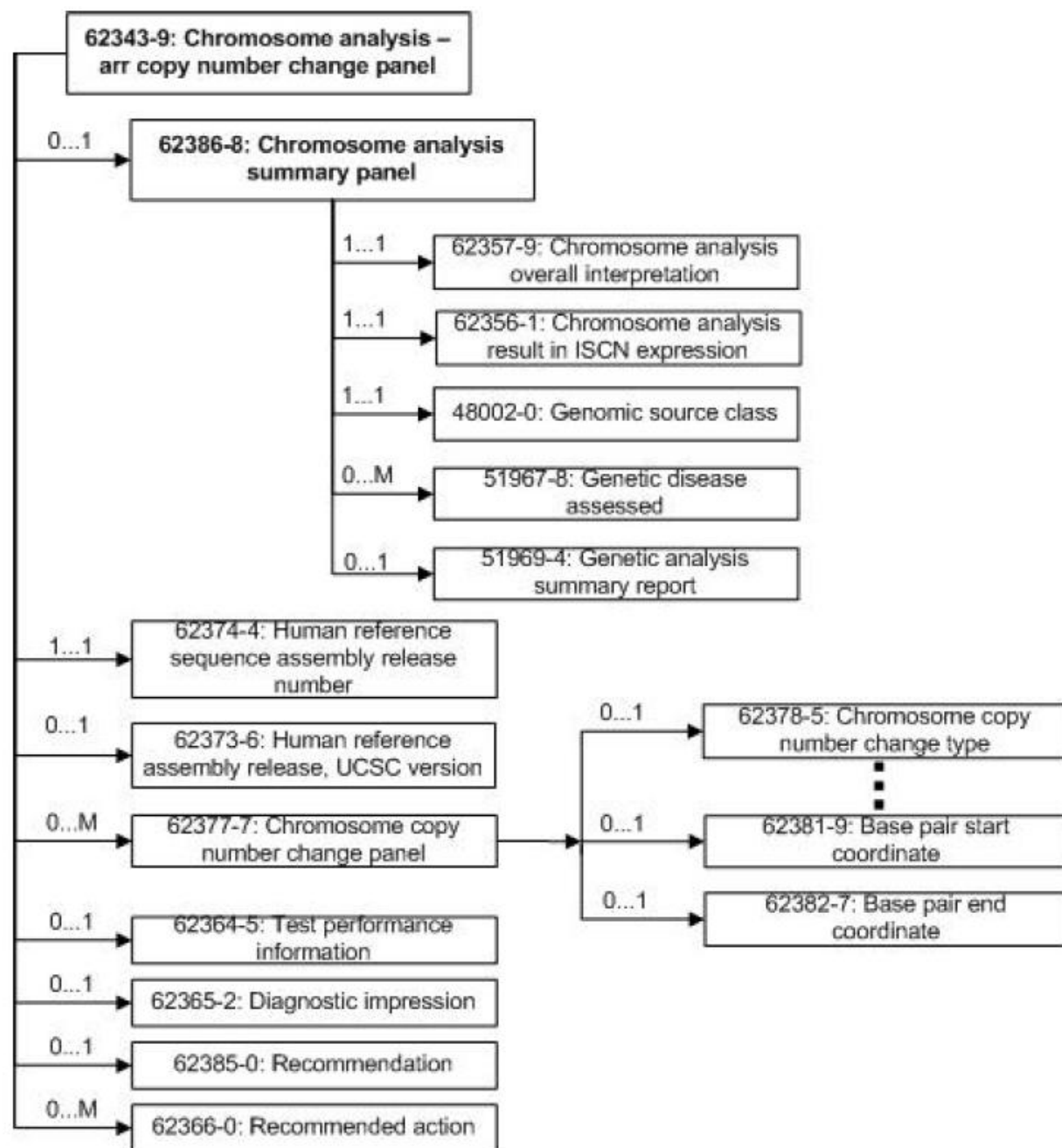
Figure 1: Chromosome analysis master panel

Figure 4: Chromosome analysis arr copy number change panel

Contact Information

- Find the HL7 Clinical Genomics workgroup at –

  - http://www.hl7.org/Special/committees/clingenomics/index.cfm
  - http://wiki.hl7.org/index.php?title=CG

- Contact the co-chairs:

  ★ Amnon Shabo
    IBM Haifa Research Lab
    shabo@il.ibm.com
  ★ Kevin Hughes MD
    Partners HealthCare
    kshughes@partners.org
  ★ Mollie Ullman-Cullere
    Dana-Farber Cancer Institute
    mollie_ullman-cullere@dfci.harvard.edu
  ★ Joyce Hernandez
    Merck
    joyce_hernandez@merck.com

- Contact Grant Wood
  Intermountain Healthcare Clinical Genetics Institute
  grant.wood@imail.org

Questions