HL7 v3 Clinical Genomics – Overview

The HL7 Clinical Genomics Work Group

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HL7 Clinical Genomics WG
Co-chair and Modeling Facilitator

HL7 Structured Documents WG
CDA Co-editor
CCD Implementation Guide Co-editor
GTR Implementation Guide prime editor

HL7 RIMBAA WG
Past Co-chair
The Mission of HL7 Clinical Genomics Work Group

- The HL7 Clinical Genomics Work Group (CGWG) supports the HL7 mission to create and promote its standards by enabling the communication between interested parties of clinical and genomic data related to an individual. The focus of the CGWG efforts is the personalization of the genomic data, the so-called ’omics differences in an individual’s genomic – and its association with relevant phenotypic and clinical information. Associations to interpretive/expected phenotypes will be modeled as knowledge that can be utilized to transform an individual's data into meaningful information.

- CGWG will facilitate the development of common standards for clinical research information management across a variety of organizations -- including national and international government agencies and regulatory bodies, private research efforts, and sponsored research -- and thus the availability of safe and effective therapies by improving the processes and efficiencies associated with regulated clinical research.

- CGWG will strive to achieve common semantics across the clinical and research environments. Consequently, the group will start each standardization effort in Universal specifications that later on can be refined to specific realms.
Overview of Activities

Three Tracks:

**v3:**
- Family History (Pedigree) Topic
- Genetic Variations Topic
- Gene Expression Topic
- CMETs defined by the Domain

**v2:**
- Implementation Guides
  - *The IG “Genetic Test Result Reporting to EHR” is modeled after the HL7 Version 2.5.1 Implementation Guide: Orders And Observations; Interoperable Laboratory Result Reporting To EHR (US Realm), Release 1*

**CDA:**
- A CDA Implementation Guide for Genetic Testing Reports

**Common:**
- Domain Analysis Models for the various topics (e.g., gene.exp, c.seq)
- A Domain Information Model (v3) describing the common semantics
- Semantic alignment among the various specs
The Underlying Paradigm: Encapsulate & Bubble-up

- **Genomic Data Sources**
- **Clinical Practices**
- **EHR System**
- **Knowledge** (KBs, Ontologies, registries, reference DBs, Papers, etc.)
- **Decision Support Applications**
  - Bubble up the most clinically-significant raw genomic data into specialized HL7 objects and link them with clinical data from the patient EHR

Encapsulation by predefined & constrained bioinformatics schemas

Bubbling-up is done continuously by specialized DS applications
Current activities

- Family History US Implementation Guide
- GTR (Genetic Testing Report) – CDA Implementation Guide
- v2 genetic testing results message – Laboratory Message Implementation Guide
- Clinical Sequencing Domain Analysis Model
Enable Decision Support e.g., risk analysis algorithms

Population Research and Public Health

* Detailed description can be found in the Family History presentation
Example: Family History XML Encoding

Taken from a patient pedigree, the portion related to patient’s daughter
(in collaboration with Partners HealthCare & other HL7 CG SIG members)

<!-- DAUGHTER -->
- <relationshipHolder>
  <id extension="555.011"/>
  <code code="DAU"/>
+ <relationshipHolder>
  <!-- GENOMIC DATA -->
- <subjectOf>
  - <clinicalGenomicChoice>
    - <clinicalGenomicChoiceGenotype>
      - <Genotype>
        - <individualAllele>
          <code code="BRCA1" codeSystem="[insert GenBank OID]"
            codeSystemName="GenBank"/>
          <text>Homo sapiens breast and ovarian cancer susceptibility (BRCA1)
            complete cds.</text>
        </individualAllele>
      </Genotype>
    </clinicalGenomicChoiceGenotype>
  </clinicalGenomicChoice>
  </subjectOf>
<!-- CLINICAL DATA -->
+ <subjectOf>
  </relationshipHolder>
<!-- end of DAUGHTER data -->

Point back to the raw data of this relative providing “personal evidence”
XML Fusion: Encapsulation of Raw Genomic Data

Raw genomic data represented in Bioinformatics markup

<subjectOf2>
  <geneticLocus>
    <component1>
      <individualAllele moodCode="EVN">
        <text>breast cancer 1, early onset</text>
        <value code="83990" displayName="BRCA1" codeSystemName="NCBI Entrez">\n        \n        <translation code="20473" displayName="BRCA1" codeSystemName="HGNC"/>
        </value>
      </individualAllele>
    </component1>
    <component2>
      <sequence moodCode="EVN">
        <code code="BSMLcon3"/>
        <value mediaType="text/xml">
          <bsml:Bsmi xmlns:bsml="urn:bsml.org">
            <bsml:Definitions>
              <bsml:Sequences>
                <bsml:Seq-data>
                  <molecule>"dna" ic-acckey="U14680 REGION: 101..199" db-source="GenBank" title="BRCA1, exon 2" representation="raw" local-acckey="this could be used by the genetic lab">
                    GCTCCCA CTCCATGAGG TATTTCTTCA
                    CATCCGTGTC CCGGCACCGGC CGCGGGGAGG CCGGCTTCAT CGCGGCTTGGCC
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                    GAGGATGGAG CGCGGAGGC CGTGTAAGAG CAACGGAGGG CGCGAGTTT
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                  </bsml:Seq-data>
                </bsml:Seq-data>
                <bsml:Seq-data>
                  <molecule>"dna" ic-acckey="U14680 REGION: 200..253" db-source="GenBank" title="BRCA1, exon 3" representation="raw" local-acckey="this could be used by the genetic lab">
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                    TCCGCGGTTA CGCGAAGACGCCAGTACGAGCGAAGAGATTACATCGCCCTG
                    AACGAGGACC TGCGCTTTGGCAAGCAGGCGGCGGACATGGGCGCTACAGATCAC
                    CAAGCGGAAG TGGGAGGCGGCCATGGTGGC GGAGCAGCAG AGAGCCTACC
                    TGGATGGCAG GTGCCGTGAG TGCCCTGGCA GATACCTGGA GAACCGGAAG
                    GAGACGCTGC AGGCGACGG
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                </bsml:Seq-data>
              </bsml:Sequences>
            </bsml:Definitions>
          </bsml:Bsmi>
        </value>
      </sequence>
    </component2>
  </geneticLocus>
</subjectOf2>
The Pedigree Spec - Updates

- HL7 Normative Standard since 2007 and reaffirmed in May 2012 for 5 more years

- Pilots:
  - Hughes Risk Applications
  - Surgeon General’s My Family Health Portrait
  - Many more…

- HL7 US Realm IG
  - Under development with expected balloting in Sept 2012
  - Transmission supported in CCD
  - Accommodate MU Stage 2 requirements

- Release 2 in progress
  - Update representation of genetic data
  - Accommodating ISO ballot comments

- FHIR Pedigree?!
Pedigree Implementation Guide for US Realm

- Specify the exchange format to be compliant with MU
  - Reusing HITSP CCD exchange; CCD instance references a Pedigree

- Simplify the genetic representation by constraining out the full blown genomic CMETs and use GTR suggested conventions

- Specify clinical data using SNOMED (following HughesRiskApp IG)
  - Do we need dynamic binding?

- Representing interpretation as in GTR (constrain out the interpretation code attribute)
Pedigree R1 was adopted by MU 2 Final Ruling

"The HL7 Pedigree standard was originally released in 2007. Release 1 was recently reaffirmed by the American National Standards Institute (ANSI), which is a process that occurs every five years. We have adopted this reaffirmed version as it is the same version (Release 1) of the standard as the version we proposed. An implementation guide for this standard is scheduled to be published shortly after this final rule. Although EHR technology will not be required to conform to the implementation guide for certification, the implementation guide will provide important guidance for use of the HL7 Pedigree standard with EHR technology."

Balloted in January 2013:

- Passed as follows:
  HL7 Version 3 Implementation Guide: Family History/Pedigree Interoperability, Release 1 - US Realm Lvl. I1; Aff. 36; Neg. 3; Abst. 67; NV 13; TotP. 119; Q. 89.08%; A. 24
FHIR Pedigree

- **Scoping:**
  - Risk assessment results
  - Genetic models
  - Branching out to any no. of generation

- Backward compatible?

- Mapped back to the v3 model!

- Do we have the bandwidth to do it?

- We’re asked on no. and scope of genomic resources
CDA IG: Genetic Testing Report (GTR)

- Define an implementation guide for a genetic testing report that is both human readable and machine-processable
  - Target at all types of GTR producers, e.g., genetic labs, clin. geneticists
  - Readable content is larger in scope
  - E.g., detailed description of the tests performed along with references
  - Machine-processable should be limited, e.g., exclude raw data

- Ballot a Universal IG; then derive → specific types of GTR:  
  - Healthcare & Research
  - Realm-specific guides
  - Omic-specific guides

- Developed using the MDHT open source tool (OHT)
GTR - Design Principles

- Follow **existing report formats** commonly used in healthcare & research

- Emphasize **interpretations & recommendations**

- Provide general **background information** on tests performed

- Reference **HL7 Clinical Genomics instances** (e.g., v3 or v2 GeneticVariation and Pedigree) as the place holders of full-blown raw genomic data and fully-structured family history data

- Utilize patterns of ‘**genotype-phenotype’** associations in the HL7 v3 Clinical Genomics Domain
  - Implement them as ‘**clinical genomic statement’** entry-level templates (see next slide), enabling **meaningful use** of the data
The Clinical Genomic Statement

- An abstract Clinical Genomic Statement (CGS) template that
  - Has at its core a genomic observation (e.g., a DNA sequence variation)
  - If it’s a reportable finding, then it should be associated with indications and interpretations, specimen and genomic source class
  - The major finding can be associated with associated observation (e.g., amino acid change)
  - Optionally, performers may be specified (overriding header performers)

- The CGS abstract template is instantiated by specialized CGS’s, e.g., for genetic variations or cytogenetics
Detailed description can be found in the GTR presentation
CDA GTR Ballot Status

- Balloted in several cycles for comments and DSTU
- Passed as DSTU in Oct. 10 & Sep. 12
- Decided to publish in December 2012
- Motion passed to approve the Publication Request Form
Collaboration with APWG around CDA IGs

- **Development:**
  - How do we share templates with AP (Anatomic Pathology)?
  - MDHT SVN could be an option

- **Harmonization:**
  - One consolidated document template or two interrelated and harmonized docs?
  - Workflows could dictate the way documents shape up…
  - Could we share specimen templates?
  - Could we harmonize summary / diagnosis templates?
  - Could we agree on a clinical statement approach where all pieces are tied together in one coherent structure?

- **Comments on the APSR sample:**
  - Is problem == reason for AP procedure?
  - Why “Left upper outer quadrant breast palpable mass” is considered illness?
  - APSR sample has CDA Validation issues
V2 Implementation Guides

- A v2 laboratory message implementation guide for genetic testing result
  - A message from the genetic lab to the EHR
  - An approved informative spec

- It is modeled after the HL7 Version 2.5.1 Implementation Guide: Orders And Observations; Interoperable Laboratory Result Reporting To EHR (US Realm), Release 1

- Is used in a pilot of information exchange between Partners Healthcare and Intermountain Health Care
The v2 Message Structure

- 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
  - Genetic Analysis Discrete Result Panel (OBR)
    - has a 0 to 1 relationship
    - has a 0 to many relationship
      - 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
V2 Sample Message

- **OBR|1||PM-08-J00094^HPCGG-LMM|^2.16.840.1.113883.3.167.1^ISO|Im_DCM-pnlB_L^Dilated Cardiomyopathy Panel B (5 genes)^99LMM-ORDER-TEST-ID||20080702000000||20080702100909||234567891^Pump^Patrick^^^^^^NP|^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
Clinical Sequencing Analysis Model

- Extends ONC Personalized Healthcare Use Case (2008) for support of clinical sequencing and current understanding of the field
- Serve as
  - Roadmap for further standards development/extension
  - Develop use cases and requirements for related projects (e.g. Specimen DAM and Specimen CMET Release 2)
C. Seq. Workflows

Different compatible standards may need to be used at different parts in the workflow (e.g. lab order vs. result reporting). Therefore, starting with workflow definition and key data needs is important (e.g. clinical indication for ordering the test).

<table>
<thead>
<tr>
<th>Patient</th>
<th>Healthcare Provider</th>
<th>Laboratory</th>
<th>Geneticist / Medical Geneticist / Molecular Pathologist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consent to Test</td>
<td>Indication for Genetic Testing</td>
<td>Specimen collection</td>
<td>Receiving Accession order and specimens</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Specimen Processing</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Testing</td>
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<td></td>
<td></td>
<td></td>
<td>Bioinformatic Analysis</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Transcoding</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Interpretation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reporting</td>
</tr>
</tbody>
</table>

Primary Clinical Sequencing Workflow

- Consent to Test
- Indication for Genetic Testing
- Specimen Collection
- Receiving Accession order and specimens
- Specimen Processing
- Testing
- Bioinformatic Analysis
- Transcoding
- Interpretation
- Reporting

Clinical Sequencing Workflow – Germline Testing

- Consent to Test
- Indication for Genetic Testing
- Specimen Collection
- Receiving Accession order and specimens
- Specimen Processing
- Testing
- Bioinformatic Analysis
- Transcoding
- Interpretation
- Reporting

Patient Access to Data and Results (preparation for future)

Care Plan Development

Review Results/Report

Review Findings with Patient

Receiving Accession order and specimens

Specimen Processing

Testing

Bioinformatic Analysis

Transcoding

Interpretation

Reporting

Different compatible standards may need to be used at different parts in the workflow (e.g. lab order vs. result reporting). Therefore, starting with workflow definition and key data needs is important (e.g. clinical indication for ordering the test).
Alternative Workflows

Alternative Flow 1:
Chart Review

- Clinical request for updated interpretation
- Look-up Case
- Interpretation/Translation Tool(s)
- Reporting
- Continue with primary workflow

Alternative Flow 2:
New Genetic Knowledge

- Continue with primary workflow
- Automated Reinterpretation - Update Previous Results with New Clinical Knowledge

Alternative Flow 3:
New Clinical Indication

- Clinical request for interpretation for new clinical use
- Reinterpretation to Update Previous Results with New Clinical Knowledge
- Continue with Primary Workflow
These serve as potential integration points (e.g. dbSNP ID for links to dbSNP variant record).

<table>
<thead>
<tr>
<th>Internal and External Systems for Each Stakeholder Group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Systems</strong></td>
</tr>
<tr>
<td>PHR (Patient Controlled)</td>
</tr>
<tr>
<td>Patient Portal (Part of EHR)</td>
</tr>
</tbody>
</table>
Clinical Sequencing – Ballot Results

- Balloted in January 2013 for comments only

- Results:
  - Didn’t pass, tally follows:
    HL7 Version 3 Domain Analysis Model: Clinical Sequencing, Release 1
    Lvl. O1; Aff. 38; Neg.0; Abst. 75; NV 19; TotP. 132; Q. 85.61%; A 0
For v3 standards – see backup slides
Alignment Among the Various Specs

- v3 specs and CDA are all based the RIM
  - CDA GTR-IG will be based on CDA R3
  - Depending on the “right side” of R3, if it allows RIM-based domain models, then alignment is trivial

- v3-v2 alignment:
  - Proposal: represent semantics with UML and implement it in various ways, e.g., v3 using the existing v3 ITS and v2 being another format (develop an “v2 ITS” for the UML models)
  - See proposal made by Amnon in a separate presentation

- FHIR can be the single source of semantics
Selected Implementation

- **v2**
  - Exchange of genetic testing results between Intermountain and Harvard

- **v3**
  - The Family History spec is used in Mass General Hospital
  - Expanding to other family history applications including the US Surgeon General Family History tool
  - The Genetic Variation model is used in Hypergenes (a European project on essential hypertension, [http://www.hypergenes.eu/](http://www.hypergenes.eu/))
  - The Pedigree and Genetic Variation models are used in Italy, the Rizzoli institute in Bologna

- **CDA**
  - GTR has been used in uHealth – a PHR/EHR system in Korea
Other Domain Analysis Models

Work in progress...

- Clinical Genomics DAM
- Gene Expression DAM
- Harmonize with NCI LS-DAM and CDISC BRIDG
- Specimen (led by OO and AP Work Groups)
  - Specimen DAM
  - Specimen Unique ID
  - Specimen CMET Release 2
Omics in the LS DAM - Experiment (outdated)
Omics in the LS DAM - Specimen (outdated)
Gene Expression Topic (outdated)

- Domain Analysis Model (DAM)
  - Passed informative ballot
  - Based on several models for gene expression data along with extensions
Looking forward....
The rise of the 'narciss-ome'...

- Transformative paper in the Cell Journal


- iPOP – Integrative Personal Omics Profile
  - Our personal omics change over time!
  - Longitudinal examinations of genome, proteome, metabolome, autoantibodies, etc. of an individual (one of the authors)
  - Monitor healthy and disease states
  - Predict and act accordingly (the data predicted diabetes and diabetes was diagnosed; life style changes make it manageable!)
iPOP – Integrative Personal Omics Profile

Should be standardized and be part of the lifetime EHR!!
HL7 WG Health Check – Need to Improve!

- Active projects
- SWOT current
- 3 year plan current
- Mission and charter current
- Co-chair post-WGM survey participation
- Ballot presence
- Minutes posted since last WGM
- Last listserv activity
- Wiki presence
- WG conference calls schedules
- Steering division conference call participation
- Steering division co-chair (TSC representation) election participation
- WG rep at steering division WGM
- WG meetings at WGM scheduled
- WG has an approved DMP based on review of the updated template
Planning ahead

- **May 2013 WGM (Atlanta)**
  - Schedule (from Tuesday Q4 to Thursday Q1)
  - Joint meetings with:
    - Wed. Q1: OO+AP+II
    - Wed. Q3: AP

- **Weekly conf. calls**
  - Continue Tuesday’s 11EST

- **Three year plan update**
Summary

- Small group coping with
  - Various HL7 formats: v3, v2 and CDA
  - Clinical & Research environments

- Developing a DAM and component models (CMETs) to be used in other HL7 domains
  - Genetic Variation
  - Gene Expression

- CDA Genetic Testing Report (GTR)
  - Bridge from raw data to human readable reports and bubbled-up data
  - Model-driven development of standards (use of MDHT CDA Editor)
A new member? Here is how to participate:

- Through our mailing list (open to nonmembers as well)

- Provide comments to specs
  - Formally through the balloting process
  - Informally through the list or by corresponding with spec editors

- Weekly conference calls

- Project specific conf. calls:
  - Clinical sequencing
  - CG & GE DAMs
  - Specimen
• Thank you for your attention… 😊

• Questions? Contact Amnon at shabo@il.ibm.com

• Comments of general interest should be posted to the CG mailing list at clingenomics@lists.hl7.org

• See backup slides for more info on v3 standards
HL7 Clinical Genomics v3 Static Models

Family History

CDA IG

Reference

RCRIM

LAB

Utilize

Genetic Locus (DSTU Expired)

Constrained

Genetic Variation

Gene Expression

Implementation Topic

Implementation Topic

Domain Information Model: Genome

Phenotype

(utilizing the HL7 Clinical Statement)
To achieve semantic interoperability...

...we need standard specs derived from a Central Health RIM:

Central Health RIM (e.g., an extended HL7 V3 Reference Information Model): Bio & medical-informatics standard specs are derived from the same RIM.
The DSTU Genetic Locus Model (deprecated) Focal Areas:

- Expression Data
- The Locus and its Alleles
- Sequence Variations
- (Clinical) Phenotypes
- Sequence and Proteomics
The Underlying Paradigm: Encapsulate & Bubble-up

Genomic Data Sources

Bridging is the challenge...

Clinical Practices

Knowledge
(KBs, Ontologies, registries, reference DBs, Papers, etc.)

EHR System

Decision Support Applications
Bubble up the most clinically-significant raw genomic data into specialized HL7 objects and link them with clinical data from the patient EHR

Encapsulation by predefined & constrained bioinformatics schemas

HL7 CG Messages with encapsulated data associated with HL7 clinical objects (phenotypes)

Bubbling-up is done continuously by specialized DS applications

HL7 CG Messages with mainly Encapsulating HL7 Objects

Encapsulated HL7 Objects

Haifa Research Lab
**Encapsulate & Bubble-up Example**

- **DNA Lab**
- **Genetic Counseling**

**Sequencing Example…**

- HL7 CG Messages with a Sequence
  - HL7 Object encapsulating the raw sequencing results

- EHR System

- Knowledge Sources on genetic variants
  - (e.g., OMIM)

- Encapsulation by a constrained BSML schema

- Bubbling-up is done dynamically by specialized applications, e.g., sequence analyzing programs

**Decision Support Applications**

- Bubble up the most clinically-significant SNP data into HL7 SNP and Mutation objects and link them with clinical data from the patient EHR

- Sequencing Example…

- EHR System

- HL7 CG Messages with encapsulated sequencing data associated with clinical phenotypes
Example: Family History XML Encoding

<!-- DAUGHTER -->
- <relationshipHolder>
  <id extension="555.011" />
  <code code="DAU" />
- <subjectOf>
  - <clinicalGenomicChoice>
    - <clinicalGenomicChoiceGenotype>
      - <Genotype>
        - <individualAllele>
          <code code="BRCA1" codeSystem="[insert GenBank OID]" codeSystemName="GenBank" />
          <text>Homo sapiens breast and ovarian cancer susceptibility (BRCA1) complete cds.</text>
        </individualAllele>
      </Genotype>
    </clinicalGenomicChoiceGenotype>
  </clinicalGenomicChoice>
</subjectOf>

To phenotype and beyond...

Bubble up...

Point back...

Point back to the raw data of this relative providing "personal evidence"
XML Fusion: Encapsulation of Raw Genomic Data

Raw genomic data represented in Bioinformatics markup

XML: <subjectOf>
  <geneticLocus>
    <component1>
      <individualAllele moodCode="EVN">
        <text>breast cancer 1, early onset</text>
        <value code="83990" displayName="BRCA1" codeSystemName="NCBI Entrez">
          <translation code="20473" displayName="BRCA1" codeSystemName="HGNC"/>
        </value>
      </individualAllele>
    </component1>
    <sequence moodCode="EVN">
      <code code="BSMLcon3"/>
      <value mediaType="text/xml">
        <bsml:Bsm xmlns:bsm="urn:bsml.org">
          <bsml:Definitions>
            <bsml:Sequences>
              <bsml:Seq-data id="seq1" molecule="dna" ic-acckey="U14680 REGION: 101..199" db-source="GenBank" title="BRCA1, exon 2" representation="raw" local-acckey="this could be used by the genetic lab">
                GCTCCA CTCCATGAGG TATTTCTTCA
                CATCCCGTGC CCGGCGCGGC CCGGGGAGAC CGGCGTTACG CGCGTGAGGC
                TACGTCGGAC ACACGCAGTT CTTGCGGTTC GACAGCGACG CCGCGAGCCA
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                AAGCGGAGAC TGGCGTCGTC GACGCGGCGG GACATGGCGG CTCAGATCAC
                CAAGCGCAAG TGGAGGCGCG CCGATGAGG CAGAAGCAAG AGACGTATCC
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                GAGCGCTGC AGCGACGGG
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          </bsml:Definitions>
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      </value>
    </sequence>
  </geneticLocus>
</subjectOf>
Other v3 Models / Efforts

- **The Genome**
  - An HL7 Domain Information Model (DIM)
  - Evolved as generalization of the Genotype DSTU models
  - Was not balloted
  - Will be updated based on the DAM efforts
  - In the future, DAM balloting will require the mapping to DIM

- **The RCRIM use of our DSTU CMETs**

- **Query model**
The Domain Information Model - Genome

- Individual Allele
- Encapsulating Obj.
- Bubbled-up Obj.
- Entry Point: Genome
- Genetic Locus
- Genetic Loci
- Bio Sequence
- Polypeptide
- Expression Data
- Expression Attributes
- Sequence Variation (SNP, Mutation, Polymorphism, etc.)
- Variation Attributes
- Non-locus specific data
- Phenotype
- genotype<->phenotype

Haifa Research Lab
The HL7 RCRIM CT Laboratory Model - The Pharmacogenomics Extension

- Enrolled Subject
- Specimen
- Clinical Trial
- Consent to Genotype
- Pharmacogenomics Test
- Genetic Lab
- Utilizes the Clinical Genomics CMET
The CG V3 Query Model: Query by Parameter

Starting point with query identifiers and attributes

GeneticLocus parameters

Phenotype parameters

participants parameters

GeneticLoci parameters

Miscellaneous parameters
HL7 Clinical Genomics CMETs

- CMET – a shared v3 model used by domain models

- Current CMET efforts:
  - Phenotype
  - Genetic Variation
  - Gene Expression
  - Pedigree
The Phenotype CMET Model

Observed Phenotype

Interpretive Phenotype

Note: Use this CMET to describe complex phenotypes that occur in the context of a specific mutation, which is embedded in instances compliant with this model and not just referenced. The complex phenotype is either known in the scientific literature or a possible phenotype, or has been actually observed in the patient.

Note: Use this CMET to describe medication components related to this phenotype (e.g., pharmacogenomics uses), when the administration of the drug is described elsewhere.
The Genetic Variation CMET (passed normative in Jan. 2010)

- Genetic Loci
- Genetic Testing Order
- Participants (including specimen)
- Associated data (vocab. Controlled)
- Observed or Interpretive phenotypes
- Timing issues: collecting specimen, extracting genetic material, identifying genomic observations, interpretation

- Sequence Variation
- Sequence (observed or reference)
- Individual Allele
- Genetic Report (CDA)
The Gene Expression CMET Draft
Utilizations in HL7

- **Clinical Trials:**
  HL7 RCRIM Work Group (clinical trials specs) utilized the CG DSTU model (Genetic Locus) in their **Pharmacogenomics message**, which was an extension of the CTLab message (an approved but expired DSTU).

- **Laboratory:**
  The Lab Work Group might utilize a constrained version of the Genetic Variation model in their next release if the Lab Result message