HL7 Clinical-Genomics Work Group
The Family History Standard
Pedigree Topic in the HL7 v3 Clinical Genomics Domain

Approved as an ANSI Normative Specification in 2007

Co-editors: Dr. Amnon Shabo (Shvo)\(^1\) and Dr. Kevin S. Hughes\(^2\)

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1 Research Staff Member at the IBM Research Lab in Haifa;
   HL7 SIG Clinical-Genomics Facilitator.
2 Surgical Director, Breast Screening;
   Co-Director, Avon Comprehensive Breast Evaluation Center, Massachusetts General Hospital.
Introduction

The Family History Model is part of the HL7 Clinical-Genomics SIG effort to accommodate various storyboards of using genomic data in healthcare practice. The need to represent a patient's pedigree information as associated with clinical and genomic data was introduced in the BRCA (Breast Cancer) storyboard developed by Dr. Kevin S. Hughes. This storyboard is described in detail in a separate document.

The BRCA storyboard includes a sample outline for the way the patient's pedigree should look:

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Relative type (Self)</th>
<th>Cancer</th>
<th>Year diagnosed</th>
<th>Age diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Genetic syndrome suspected</td>
<td></td>
<td>Genetic test done</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Genetic test result specific</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Genetic test result interpretation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother ID number</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father ID number</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relative ID number</td>
<td>Relative type (Brother, sister…)</td>
<td>Cancer</td>
<td>Year diagnosed</td>
<td>Age diagnosed</td>
</tr>
<tr>
<td></td>
<td>Genetic syndrome suspected</td>
<td>Genetic test done</td>
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<td>Genetic test result specific</td>
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<tr>
<th>Relative ID number</th>
<th>Relative type (Brother, sister…)</th>
<th>Cancer</th>
<th>Year diagnosed</th>
<th>Age diagnosed</th>
<th>Genetic syndrome suspected</th>
<th>Genetic test done</th>
<th>Genetic test result specific</th>
<th>Genetic test result interpretation</th>
</tr>
</thead>
</table>

**Table 1: Outline for family history of a cancer patient.**

Populating the above outline with actual data might result in a spreadsheet found in the package containing this document, by the name SamplePed.xls.

**Storyboard Presentation**

- Ms. Eve Everywoman has a family history of breast and ovarian cancer, and she is not of Ashkenazi Jewish descent.
- She believes she is at high risk of developing breast cancer.
- She goes to see her clinician (Medical oncologist, surgical oncologist, radiation oncologist, primary care provider) who takes a thorough family history. This history is recorded in the chart and the electronic medical record.
- The clinician reviews the family history, decides what genetic syndrome her family might have, and categorizes the patient as to degree of risk (Perhaps high, medium, or low risk). The clinician thinks the patient is at high risk of having a BRCA1/2 mutation.
- The clinician compares her Family History to tables of risk (Claus, Myriad) and runs computer models (algorithms such as BRCAPRO, see [http://www.isds.duke.edu/~qg/brcapro.html](http://www.isds.duke.edu/~qg/brcapro.html)). This gives a percentage risk of carrying a mutation and/or a risk of developing breast and/or ovarian cancer. Her risk of a mutation is 25%, because her father's 4 sisters had ovarian cancer.
The patient is considered to be at high risk of having a mutation, and this information is given to her.

She is referred to a Risk Clinic.

She agrees to go to the Risk Clinic.

Ms Eve Everywoman’s Genetic History details are sent to this clinic (the HL7 Interaction POCG_IN000001 is used), including her Family History, the syndrome suspected and her level of risk.

The counselor at the risk clinic (Nurse geneticist, genetic counselor, MD, etc.) reviews the family history information collected by the primary clinician, edits it and adds additional details.

The Counselor reviews the family history, decides what genetic syndrome her family might have, and categorizes the patient as to degree of risk (Perhaps high, medium, or low risk). The Counselor thinks the patient is at high risk of having a BRCA1/2 mutation.

The clinician compares the family history to tables of risk (Claus, Myriad) and runs computer models (algorithms such as BRCAPRO). This gives a percentage risk of carrying a mutation and/or a risk of developing breast and/or ovarian cancer. Her risk of a mutation is 25%, because her father's 4 sisters had ovarian cancer.

The patient is considered to be at high risk, and she is told she is a candidate for genetic testing. This includes a thorough discussion of the pros and cons of testing. This discussion is recorded in the electronic medical record.

Ms. Eve Everywoman wants to have testing, but as she is not affected, it is the standard of care to test a living affected relative first.

The Counselor suggests that her Aunt, Ms. Jeanne Aunt, is the most appropriate candidate for testing. Ms. Jeanne Aunt had ovarian cancer, and is still living.

Ms. Eve Everywoman agrees to contact Ms. Jeanne Aunt.

Ms Eve Everywoman signs consent to release her own Family History details to Ms Jeanne Aunt and her Provider.

Ms. Jeanne Aunt is a 39-year-old woman had been diagnosed with ovarian cancer at age 35.

Ms Jeanne Aunt agrees to discuss testing, and provides the name and address of the Risk Clinic she will attend.

Ms Eve Everywoman's FH details are sent to this clinic (the HL7 Interaction POCG_IN000001 is used).

The counselor at the risk clinic (Nurse geneticist, genetic counselor, MD, etc.) reviews the family history information collected by the primary clinician through a pedigree drawing program, and changes the Proband to Ms Jeanne Aunt, edits it and adds additional details (The family history message had had Ms Eve Everywoman as the Proband (Self), and Ms Jeanne Aunt as the aunt. The pedigree from the point of view of Ms Jeanne Aunt must have Jeanne Aunt as the Proband (Self) and must show Ms Eve Everywoman as the niece).

The Counselor reviews the family history, decides what genetic syndrome her family might have, and categorizes the patient as to degree of risk (Perhaps

3 Proband: First affected family member coming to medical attention*. Consultand: Individual (s) seeking genetic counseling/testing*

high, medium, or low risk). The Counselor thinks the patient is at high risk of having a BRCA1/2 mutation.

- The clinician compares the family history to tables of risk (Claus, Myriad) and runs computer models (algorithms such as BRCAPRO). This gives a percentage risk of carrying a mutation and/or a risk of developing breast and/or ovarian cancer. Ms. Jeanne Aunt is virtually at 100% risk of having a mutation.
- The patient is considered to be at high risk, and she is told she is a candidate for genetic testing. This includes a thorough discussion of the pros and cons of testing. This discussion is reviewed in the electronic medical record.
- Ms. Jeanne Aunt wants to have testing. She signs an informed consent document.
- The order for testing is issued, and the informed consent, and the family history are included with the lab requisition. All are MESSEGED to the blood drawing facility.
- The blood is drawn, and sent to the central testing facility along with the informed consent, the family history and the lab requisition.
- At the central testing facility, the specimen is checked in, and the DNA is separated and PCRed.
- Full gene sequencing of BRCA1 and BRCA 2 are undertaken.
- The sequence is assessed for mutations.
- Identified mutations are assessed for functional significance by determining if they are truncating (deleterious), or if they are irrelevant (No change in amino acid coded by that codon). All other mutations are compared to known mutations to determine if information is available on their functional significance.
- The actual mutation, and the assessment of functional significance are sent to the counselor.
- In this case, a mutation is identified in BRCA1 and the mutation is Deleterious.
- The counselor discusses the result with the patient.
- Management decisions (Screening, chemoprevention, prophylactic surgery) are probably beyond the scope of this storyboard.
- Ms Jeanne Aunt agrees to share this information with Ms Eve Everywoman's Clinician.
- This information is sent to Ms Eve Everywoman's Clinician.
- Ms. Eve Everywoman wants to have testing. She signs an informed consent document.
- The order for testing is issued, and the informed consent, and the family history are included with the requisition, as well as the results of Ms Jeanne Aunt’s test. All are MESSEGED to the blood drawing facility. In case the family history is messaged separately, then the HL7 Interaction POCG_IN000001 is used.
- The blood is drawn, and sent to the central testing facility along with the informed consent, the family history, the results of Ms Jeanne Aunt’s test, and the lab requisition.
- At the central testing facility, the specimen is checked in, and the DNA is separated and PCRed.
- Full gene sequencing is not needed. Testing only for the identified mutation is undertaken.
- The DNA is assessed for that specific mutation.
- The mutation is not found.
- The normal result is sent to the counselor.
- The counselor discusses the result with the patient.
- Management decisions (Screening, chemoprevention, prophylactic surgery) are probably beyond the scope of this storyboard.
The Family History Model

Following the above sample of a patient's pedigree as well as the contextual presentation, we have developed an HL7 model to allow the representation of such a pedigree with an unlimited depth of generations. The model addresses the Family History requirements and represents a patient's pedigree while making use of the Genotype model for genomic data.

Each family member object is represented in relation to another family member who ‘scopes’ its role and is designated by a code taken from the HL7 vocabulary "RoleCode", domain = "PersonalRelationshipRoleType". Appendix D includes a table that shows the codes of this domain (for more details about that vocabulary, see the HL7 V3 Ballot Package > Foundations > Vocabularies).

IMPORTANT NOTE: Unlike higher-level models presented in the other Clinical Genomics domain storyboards which are considered informative and aim at illustration purposes only, this model is part of the normative ballot and is used in a message interaction that can be implemented in actual family history information exchange. This model might be registered as a shared model, so it can be used by any other spec that needs to convey family history of the subject in the form of a pedigree.

General Notes:

- The Family History model is used in a message interaction designed to serve the need of information exchange between two disparate pedigree applications (see section on message interactions). This interaction does not serve other needs like sending genetic lab orders accompanied by family history. For the latter, there is a need to use Lab messages that might use this model as a payload.

- The model utilizes the GeneticLocus and GeneticLoci models (the Genotype Topic) in order to capture genomic data in any resolution needed. For that end, the GeneticLocus model was packaged as an internal CMET and was also moved to the HL7 Common Domains in the V3 Ballot Package. It is utilized in this model as one of the choices in the main Clinical Genomics choice box (see the model walk through below).

- The model suggests the use of the Clinical Statement shared model (under development in HL7) to represent the clinical data. Meanwhile, it has a generic ClinicalObservation class to hold common clinical data (e.g., problems, diagnoses, reactions to drugs, allergies, etc.).

- Appendix A shows the model and is also available in separate files in the distribution zip containing this document.
Model Walk-Through
(Specification ID = POCG_RM000040)

- **Entry Point - FamilyHistory:**
The starting point of the model is the FamilyHistory Observation class. This class has several associations, one of which is subject participation of the Patient role played by a Person entity. The latter scopes the Relative class which can hold information about the patient's relatives. This constitutes the backbone of the model. In addition, the entry point is associated with risk analysis results and with problems that can not be attributed to specific family members.

  Attributes:
  - **id:** holds a unique identifier of this family history instance
  - **code:** The code attribute shall hold a code representing Family History data in general, for example: the LOINC code 10157-6, HISTORY OF FAMILY MEMBER DISEASES or any other code that carries similar semantics.
  - **statusCode:** indicates whether the act of family history observation as a whole has completed, still active, etc. (based on the HL7 RIM Act State Machine)
  - **methodCode:** The methodCode holds the identification of the program creating the family history data

- **Patient & Person:**
The Patient role class is the root of the pedigree but in terms of data, it only captures an id assigned by the family history application on behalf of the provider hosting the family history application. Note that the id is optional and so is the class Provider (the scoping entity of the Patient role). Person is the player entity of Patient and holds general information about the person like gender, birth time, deceased indication, etc.

Note that the gender attribute of the Person class is an "administrative gender" and the way to represent genotypic / phenotypic gender is to populate an instance of the clinical observation class in the clinical genomic choice box.

- **Clinical & Genomic Data:**
At the right side of the Patient role there is a 'subjectOf2' participation that associates the patient (as a 'subject of') to a choice box of zero to many ClinicalObservation objects as well as genomic data represented by the GeneticLocus model (represented here as a CMET). Note that this association is shadowed at the bottom of the model, associated with the Relative class, which represents a role of a patient's relative.

  - **ClinicalObservation**
The ClinicalObservation class represents any clinical data that is part of the Person clinical history. Currently, the class has the **classCode** of
'OBS' which means that it is capable of representing only observations. However, the full expression of a clinical statement will be available when this single class will be replaced by the HL7 Clinical Statement model (under development). The Clinical Statement model will provide the 'grammar' of how various discrete acts (observations, procedures, substance administrations, etc.) are associated to a meaningful clinical statement.

Nevertheless, in the January 2007 ballot we added a recursive ActRelationship (sourceOf) to the clinical observation to address use cases where a richer clinical statement is need, as introduced to us by early adopters of the model. The addition of this association is in consistent with the Clinical Statement model, so that when eventually this single observation is replaced with the Clinical Statement model or a derivative of it, this current addition is in consistent with it and will not require substantive changes to the family history implementations.

- **DataEstimatedAge**
  The *DataEstimatedAge* class is used to hold the estimated age of the subject at the effective time of the observation (e.g., the diagnosis time). The diagnosis is represented by the source observation\(^4\), i.e., the *ClinicalObservation* class. It is used due to the absence of an age attribute in all HL7 classes. The data type is an interval to allow a range of ages such as in cases when the patient only remembers that the diagnosis was made when the family member was in her forties for example.

  Attributes:
  - code:
    The code attribute shall hold a code representing age of subject at the effective time when the source observation was made for that subject.

- **GeneticLocus** (The *A_GeneticLocus* CMET)
  This CMET is the main model we are developing at the HL7 Clinical Genomics SIG. In principle, the *GeneticLocus* model can hold relevant genomic data in any resolution required. In the BRCA storyboard, it could be information on mutations that the patient's relatives have or full DNA sequences of the patient's genes at stake.

  Note that in the sample attached to this document, the *GeneticLocus* model is being utilized to illustrate the representation of genomic data for one of the relatives (the sample can also be found in appendix C).

\(^4\) By 'source' observation we mean the source of the HL7 ActRelationship class (named 'subject' in this model) that associates a source act to a target act while its type code attribute carries the semantics of this association.
Note: samples might be outdated so contact the editors for the latest versions.

- **GeneticLoci** (The A_GeneticLoci CMET)
  This CMET allows the association of data on a set of loci such as genetic test panel results or gene expression assay.

- **informant**
  This class optionally represents the source of information from which this family history was collected.

- **PedigreeAnalysisResults**
  This class represents the results of analysis done to the data captured in the family history pedigree.
  Use the code attribute to identify the disease or variation for which the probabilities/risks/etc. are calculated.
  Use the methodCode to hold the type of the algorithm used to analyze the pedigree.
  Attributes:
  - **code**: identifies the disease or variation for which the probabilities/risks/etc. are calculated. Note that this class can be populated as many times as needed, for each clinical condition which is the is the focus of the risk calculations
  - **negationInd**: can be used to represent the fact that there is no risk found for this family history and the clinical condition in the code attribute
  - **methodCode**: holds the type of the algorithm used to analyze the pedigree (e.g., BRCAPRO)

- **risk**
  The risk association links the FamilyHistory class to the PedigreeAnalysisResults class and represents the risk associated with that family history. The risk Act Relationship is defined in the RIM as follows: "A noteworthy undesired outcome of a patient's condition that is either likely enough to become an issue or is less likely but dangerous enough to be addressed." The patient condition in this model is the patient's family history and the risk is represented through the classes associated with PedigreeAnalysisResults class.

  Consequently, the PedigreeAnalysisResults class and the observation classes associated with it are in 'risk' mood (moodCode= RSK) to express the fact that these are not observations that happened rather they represent a risk associated with the family history.

- **InputParameters**
  The controlVariable association links PedigreeAnalysisResults to input parameters used in the analysis like sensitivity and specificity in the BRCAPRO algorithm. For example, if the code attribute holds
"sensitivity" then the value attribute holds the sensitivity itself.

- **Choice**
  The component association links *PedigreeAnalysisResults* to a choice box that contains several options to represent the actual results:

  - **AnalysisResult**
    This class is a catcher for any analysis that cannot be represented through the other classes in this choice box.

  - **Probability**
    The value holds a probability of having what is represented in the *PedigreeAnalysisResults* code attribute (e.g., disease, variation). The code attribute holds a value that indicates that this is a probability observation.

  - **PercentageRisk**
    The value holds a percentage risk of having what is represented in the *PedigreeAnalysisResults* code attribute (e.g., disease, variation). The code attribute holds a value that indicates that this is a percentage risk observation.

  - **Relative Risk**
    The value holds a relative risk of having what is represented in the *PedigreeAnalysisResults* code attribute (e.g., disease, variation). The code attribute holds a value that indicates that this is a relative risk observation.

  - **Age & Probability**
    The pertinentInformation association links *Age* to *Probability* and multiple traversals of the *Age* class along with *Probability* can hold pairs of age-probability data for what is represented in the *PedigreeAnalysisResults* code attribute (e.g., disease, variation). The code attribute can hold the value 397659008 ("Age") in SNOMED CT.

> **Relative:**
This refinement of the HL7 Role Class represents a patient's relative and is scoped by the *Person* entity which plays the *Patient* role in the first traversal of the model (see further explanation in the "Person and Relative" bullet below). The cardinality of this association is 0..* which allows for the representation of any number of relatives who all relate to the *Person* who scopes the role.

The *Relative* class has a classCode = "PRS", defined as "links two people in a personal relationship… the character of the relationship must be defined by a *PersonalRelationshipRoleType* code…” The latter code is defined by the
Relative.code\(^5\) attribute whose value set is drawn from the domain "PersonalRelationshipRoleType".

Appendix E includes a table that shows the codes of this domain. Using values from this domain it is possible to designate the relation to the patient or to the patient's family member. Thus, in this model it is possible to use, for example, the code GRMTH (grandmother) for Relative associated directly to the patient, or use the code NMTH (mother) for Relative associated to the mother of the patient. This makes the model more flexible.

- The basis of this part of the model is in the RIM definition of family member relationships which are based on the relationship between a scoping entity and a role. For example, the code CHILD is defines as "The player of the role is a child of the scoping entity", and the same goes for any type of family relationship. Note that this is valid not only to the relationship between the patient and a relative directly associated with the patient, rather this is true for any relationship between family members on this pedigree, for example, between the patient's mother (the scoper) and her father (the role).

  - SubjectEstimatedAge
    This choice box is associated with the Relative class and holds two classes concerned with estimated ages of the subject as follows:
    - The DeceasedEstimatedAge class is used to hold the estimated age when the subject died. It is used due to a lack of age attribute in all HL7 classes. We have proposed to RIM harmonization the addition of age attribute to hold the deceased age as well as the subject age at the time a diagnosis was made (see above in the DataEstimatedAge class description), but were asked to try and model this piece of information using associated observations like this class.
    - The LivingEstimatedAge class is used to hold the estimated age of a living relative whose birth date is unknown.
    - The code shall represent semantics similar to the LOINC code "21611-9" that represents the concept of an estimated age (as opposed to precise age). For deceased subject, the code shall represent semantics similar to the LOINC code 39016-1 (AGE AT DEATH).

- subjectOf2 Shadow\(^6\):
  This class is a shadow of the subjectOf2 class associated with Patient and thus also includes all its associated classes. This means that the same clinical and genomic data structures attached to the patient could be optionally attached to any of his/her relatives represented by the Relative class. It could be that the clinical data of any of the persons involved in this pedigree model exist elsewhere (in the same message or document, or in the person medical records).

\(^5\) In general, the code attribute in HL7 is a specialization of the structural classCode attribute.
\(^6\) A shadow class means that all its attributes and traversable associations are identical to those of the class it shadows.
In this case it is possible to point to that data by including stub classes which only hold ids of the actual data, thus enabling applications to get the information if needed.

- **Person and Relative:**
  The Person class allows the representation of personal information like gender and birth time of each of the patient's relatives. It is also linked back to the Relative class, an association which enables a recursive traversal a pedigree at any level of depth in a pure XML hierarchical fashion (i.e., only by nesting elements). Note that in each new traversal of this recursive association, the scoping *Person* represents another family member, and consequently the *Relative* class relates to this family member and not directly to the patient. The recursive association is shown in figure 1.

In general, the issue of recursion and XML hierarchy relate to the representation of pedigree data which is hierarchical by nature but could be represented in various ways using XML nesting elements on the one hand or mother and father ids for each relative thus constituting the hierarchy via links and pointers and not via nesting elements. The latter format also allows the flat outline of the pedigree. These issues are discussed in more detail in appendix B.

- **Relative's Mother and Father Identifiers:**
  In a flat XML representation of a pedigree it is often required to maintain mother and father ids for each relative, in order to allow the family history application to reconstruct the pedigree. These ids should be placed in the id attribute of the Person class. That class should be populated for each parent if available. The first XML sample in appendix D shows a flat representation of a pedigree with the ids populated in the Person class (XML element is relationshipHolder.id).

  It is required to use globally unique ids as mandated from the use of the II data type for the id attribute. Regarding the generation of these ids, there can be two situations: (1) The application generating the pedigree has a 'root' OID dedicated to this purpose and it extends it for each pedigree it creates. Then, it generates arbitrary unique ids for each relative who doesn't have a globally unique id and places it in the extension component. The concatenation of the pedigree root and relative extension creates a globally unique id for the person; (2) The application knows a globally unique id of a relative and uses it. Note that in a certain pedigree there can be a mixture of the two situations.
Figure 1: The recursive association of Person and relative which enables a hierarchical representation of a Pedigree to any depth needed.
**Message Interactions of Person's Pedigree**

A number of pedigree applications are in use by healthcare professionals (e.g., CAGENE) as well as by patients (e.g., the US Surgeon General’s Family History Program), which each have their own internal proprietary format of representing data for pedigree drawing and maintenance of family history information. We envision that any pedigree application will be able to send and receive an individual's family history information using this HL7 specification, either electronically or through import/export routines that will be developed for each Pedigree application.

For that vision to be realized, we developed a message interaction between two disparate pedigree applications where a person's pedigree is sent from one application to the other for a general purpose use case (i.e., not as part of a lab order/result or a specific patient care scenario).

For example, the interaction can serve the following short storyboard (derived from the full-blown Family History storyboard presented in the Clinical Genomics domain of the V3 Ballot Package):

Ms. Eve Everywoman is 48 years old. Her mother had ovarian cancer and was found to have a deleterious BRCA1 mutation. She has two sisters, a husband and a daughter. She is not of Ashkenazi Jewish descent

She makes an appointment at a Risk Clinic. The Clinic instructs the patient to use the Surgeon General’s Family History Tool to prepare for the visit. She downloads the Surgeon General’s Family History Tool onto her computer at home, and enters her family history.

She then exports the data as an HL7 MESSAGE, places it on Portable Media (CD, Flash drive) and brings it to her Risk Clinic appointment.

The counselor at the risk clinic (Nurse geneticist, Nurse Practitioner, Genetic Counselor, MD, etc.) imports the HL7 MESSAGE into CAGENE, a pedigree drawing program that runs risk models. The counselor edits the data after confirming and clarifying various issues with the patient, and adds additional information that had not been entered at home.

The patient is considered to be at high risk, and she is told she is a candidate for genetic testing. This includes a thorough discussion of the pros and cons of testing. The patient decides not to have testing, and leaves.

**Trigger event description:**
This is a notification of the availability of a person's family history information to be sent to another pedigree application.

**Application roles:**
A role of sending a person's pedigree to a Pedigree Receiver.

A role of receiving a person's pedigree from a Pedigree Sender.
Appendix A: The Family History (Pedigree) R-MIM
Appendix B: Hierarchical vs. Flat Representation

- A pedigree is hierarchical by nature… however, consider the following:
  - Sometimes the patient knows about a relative disease but cannot recall the precise position of that relative on the pedigree (or only knows parental affiliation, i.e., is he/she on the paternal or maternal side)
  - There are intermarriages
  - People are more comfortable with looking at flat representations when they look at the raw data (underlying representation like XML) and at the same time the preferred visualization/manipulation format of a pedigree is a graph (see all drawing features in the family history applications)

- Possible representations:
  - Pure hierarchical representation: the patient as well as all relatives are only associated with their first-degree relatives:
    Pros: No need for relationship codes such as uncle, cousin, etc. beyond the codes for the first degree relatives, i.e., mother, father and siblings
    Cons: In order to infer that this relative is a paternal aunt you need to traverse the pedigree; it's hard to read in XML though easy to read when it's being drawn as a pedigree diagram
  - Pure flat representation: all relatives are directly associated with the patient (proband):
    Pros: Easy to get to each relative; ease to read; allows the representation of fuzzy data (e.g., when you don't know the exact location of a relative on the pedigree or you only know that this relative is paternal or maternal)
    Cons: need too many relationship codes to represent multiple generations (e.g., grand grand mother's uncle); must have pointers to the father and mother of each relative in order for the parsing application to be able to reconstruct the hierarchy of the pedigree
  - Mixed representation: Some relatives are directly associated with the patient (mainly those whose position cannot be determined):
    Pros: a flexible structure that enables the representation of all use cases
    Cons: a complex model with optionality that might create confusion

- HL7 Modeling considerations:
  - Flat:
    - Using the flat representation (which is preferred by our early adopters) requires the use of three ids for each person:
      - Person id
      - Person's mother id
      - Person's father id
    - These ids allow the parsing application to construct the proper relationships necessary for the risk assessment procedures
Each relative is represented by a Role class where the id attribute can have the cardinality of 0..3 for holding the above three ids, nevertheless, its hard to capture the semantics of each id within the II (instance identifier) data type

- Alternatively, we are trying to use Entity ids instead of Role ids
- Hierarchical:
  - Using hierarchical representation requires recursive association of the Role class through its playing Person class and back to another Role which is scoped by the Person class (see the Clinical Genomics model)

- Personal relationships codes:
  - HL7 has a personal relationship vocabulary (RoleCode> PersonalRelationshipRoleType>FAMMEMB) used the Role.code attribute. This attribute has a CE datatype and thus doesn't allow you to qualify a code with parental qualification in a post-coordination manner (in the Clinical Genomics specs we also need this qualification at the genomic level, for example – a paternal or maternal allele)

Figure 1 (in the model walk-through) shows a portion of the Clinical Genomics Family History model which is the backbone of the pedigree 'mixed representation' as described above.

Note that our current implementation mandates the use of a flat representation.
Appendix C: The GeneticLocus R-MIM

This model has the HL7 name "POCG_RM000010" and it can be found in a MS-Visio file by the name GeneticLocus-v10.vsd.

Note that this model is in Draft Standard for Trial Use and is subject to change. Look for the latest version in the HL7 V3 Ballot Package, at the Clinical Genomics Domain.
Appendix D: XML Schema and Samples

In the package containing this document you can find the following files aimed at illustrating the way the model is implemented in specific instances that could be sent through the wire. The content of the files are also embedded in-line in this appendix, however, it's easier to view those files in an XML browser.

Note that the schema was generated using the HL7 tooling, going from the Visio model through the corresponding HMD\textsuperscript{7} and finally to the XML schema using the XML-ITS\textsuperscript{8} tools.

- The Pedigree Schema:
  - \textit{POCG\textunderscore MT000040.xsd}  
    The schema describes the pedigree model and in addition it includes the Genotype schema as a CMET, used to represent genomic data of the patient and any his/her relatives.

- Pedigree Samples:
  - \textit{FamilyHistorySample-POCG000040-v12.s2.xml}  
    Consists of a sample pedigree: patient, father, mother and grandparents of both sides. Also, two sisters, husband and daughter. It illustrates a certain way to implement a specific pedigree, and shows the use of pedigree ids, birth year, vital status and clinical data. It’s a 'flat' pedigree as all relatives are directly associated with the patient.
    
    In addition it shows an example of genomic data (BRCA1 mutation and optionally full DNA sequence in the extended sample).
    
    The data items currently demonstrated in that file are taken from the spreadsheet "SamplePed" contributed by Dr. Hughes. The file is part of the package where this document is found.

  - \textit{FamilyHistorySample-POCG000040-v12.s2-extended.xml}  
    Consists of a sample pedigree – the same is the above, with the addition of illustrative raw genomic data (BRCA gene sequence) to demonstrate the use of encapsulation of raw genomic data within the same pedigree structure.

\textsuperscript{7} Hierarchical Message Definition.  
\textsuperscript{8} Implementable Technology Specification.
POCG_MT000040.xsd

<?xml version="1.0" encoding="UTF-8" standalone="no"?>


*****
* XML schema for message type POCG_MT000040.
* Source information:
*  * Rendered by: RoseTree 4.0.2
*  * Rendered on:
* HMD was rendered into XML using software provided to HL7 by Beeler Consulting LLC.
* MIF to XSD Transform Std: StaticMifToXsd.xsl,v 1.25 2005/07/09 20:20:15 lmckenzi Exp $ * Package Id Conversion: Std: TransformPackageIds.xsl,v 1.3 2005/07/31 05:19:52 lmckenzi Exp $ * * Copyright (c) 2002, 2003, 2004, 2005 Health Level Seven. All rights reserved.
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* LIABILITY, OR TORT (INCLUDING NEGLIGENCE OR OTHERWISE) ARISING IN ANY WAY
* OUT OF THE USE OF THIS SOFTWARE, EVEN IF ADVISED OF THE POSSIBILITY OF
* SUCH DAMAGE.
* *

********************************************
********

<xs:annotation>

<xs:documentation>

<xs:include schemalocation="../coreschemas/infrastructureRoot.xsd"/>
<xs:include schemalocation="../coreschemas/NarrativeBlock.xsd"/>
<xs:include schemalocation="COCT_MT93000000 xd"/>

</xs:annotation>
</xs:documentation>
</xs:schema>
<xs:complexType name="POCG_MT000040.Age">
  <xs:sequence>
    <xs:element ref="InfrastructureRootElements" />
    <xs:element name="code" type="CD" minOccurs="0" maxOccurs="unbounded" nillable="true" />
    <xs:element name="text" type="ED" minOccurs="0" maxOccurs="unbounded" />
    <xs:element name="effectiveTime" type="IVL_TS" minOccurs="0" maxOccurs="unbounded" />
    <xs:element name="confidentialityCode" type="CE" minOccurs="0" maxOccurs="unbounded" nillable="true" />
    <xs:element name="uncertaintyCode" type="CE" minOccurs="0" maxOccurs="unbounded" nillable="true" />
    <xs:element name="value" type="ANY" minOccurs="0" maxOccurs="unbounded" />
    <xs:element name="methodCode" type="CE" minOccurs="0" maxOccurs="unbounded" />
    <xs:element name="sourceOf" type="POCG_MT000040.SourceOf" nillable="true" minOccurs="0" maxOccurs="unbounded" />
  </xs:sequence>
  <xs:attributeGroup ref="InfrastructureRootAttributes" />
  <xs:attribute name="classCode" type="ActClassObservation" use="optional" default="OBS" />
  <xs:attribute name="moodCode" type="ActMood" use="optional" fixed="EVN" />
</xs:complexType>

<xs:complexType name="POCG_MT000040.AnalysisResult">
  <xs:sequence>
    <xs:element ref="InfrastructureRootElements" />
    <xs:element name="code" type="CD" minOccurs="0" maxOccurs="unbounded" />
    <xs:element name="text" type="ED" minOccurs="0" maxOccurs="unbounded" />
    <xs:element name="effectiveTime" type="IVL_TS" minOccurs="0" maxOccurs="unbounded" />
    <xs:element name="confidentialityCode" type="CE" minOccurs="0" maxOccurs="unbounded" nillable="true" />
    <xs:element name="uncertaintyCode" type="CE" minOccurs="0" maxOccurs="unbounded" nillable="true" />
    <xs:element name="value" type="ANY" minOccurs="0" maxOccurs="unbounded" />
    <xs:element name="methodCode" type="CE" minOccurs="0" maxOccurs="unbounded" />
    <xs:element name="sourceOf" type="POCG_MT000040.SourceOf" nillable="true" minOccurs="0" maxOccurs="unbounded" />
  </xs:sequence>
  <xs:attributeGroup ref="InfrastructureRootAttributes" />
  <xs:attribute name="classCode" type="ActClassObservation" use="optional" default="OBS" />
  <xs:attribute name="moodCode" type="ActMood" use="optional" fixed="EVN" />
</xs:complexType>

<xs:complexType name="POCG_MT000040.ClinicalObservation">
  <xs:sequence>
    <xs:element ref="InfrastructureRootElements" />
    <xs:element name="code" type="CD" />
    <xs:element name="text" type="ED" minOccurs="0" />
    <xs:element name="effectiveTime" type="IVL_TS" minOccurs="0" />
    <xs:element name="confidentialityCode" type="CE" minOccurs="0" maxOccurs="unbounded" />
    <xs:element name="uncertaintyCode" type="CE" minOccurs="0" maxOccurs="unbounded" />
    <xs:element name="value" type="ANY" minOccurs="0" maxOccurs="unbounded" />
    <xs:element name="methodCode" type="CE" minOccurs="0" maxOccurs="unbounded" />
    <xs:element name="sourceOf" type="POCG_MT000040.SourceOf" nillable="true" minOccurs="0" maxOccurs="0" />
  </xs:sequence>
  <xs:attributeGroup ref="InfrastructureRootAttributes" />
  <xs:attribute name="classCode" type="ActClassObservation" use="optional" default="OBS" />
  <xs:attribute name="moodCode" type="ActMood" use="optional" fixed="EVN" />
</xs:complexType>

<xs:complexType name="POCG_MT000040.Component">
  <xs:sequence>
    <xs:element ref="InfrastructureRootElements" />
    <xs:element name="age" type="POCG_MT000040.Age" nillable="true" />
    <xs:element name="analysisResult" type="POCG_MT000040.AnalysisResult" />
    <xs:attribute name="percentageRisk" type="POCG_MT000040.PercentageRisk" />
    <xs:attribute name="probability" type="POCG_MT000040.Probability" nillable="true" />
    <xs:attribute name="relativeRisk" type="POCG_MT000040.RelativeRisk" />
  </xs:sequence>
  <xs:attributeGroup ref="InfrastructureRootAttributes" />
  <xs:attribute name="typeCode" type="ActRelationshipHasComponent" use="optional" default="COMP" />
</xs:complexType>

<xs:complexType name="POCG_MT000040.Component2">
  <xs:sequence>
    <xs:element ref="InfrastructureRootElements" />
    <xs:element name="geneticLocus" type="COCT_MT930000.GeneticLocus" />
    <xs:element name="clinicalObservation" type="POCG_MT000040.ClinicalObservation" />
  </xs:sequence>
  <xs:attributeGroup ref="InfrastructureRootAttributes" />
  <xs:attribute name="typeCode" type="ActRelationshipHasComponent" use="optional" default="COMP" />
</xs:complexType>
<xs:complexType name="POCG_MT000040.LivingEstimatedAge">
  <xs:sequence>
    <xs:group ref="InfrastructureRootElements"/>
    <xs:element name="code" type="CD" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="value" type="IVL_PQ" minOccurs="0" maxOccurs="unbounded"/>
  </xs:sequence>
</xs:complexType>

<xs:complexType name="POCG_MT000040.Component">
  <xs:sequence>
    <xs:group ref="InfrastructureRootElements"/>
    <xs:element name="id" type="II" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="derivationExpr" type="ST" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="type" type="ED" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="subjectOf1" type="POCG_MT000040.Subject" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="component" type="POCG_MT000040.Component" minOccurs="0" maxOccurs="unbounded"/>
  </xs:sequence>
</xs:complexType>

<xs:complexType name="POCG_MT000040.AgeEstimate">
  <xs:sequence>
    <xs:group ref="InfrastructureRootElements"/>
    <xs:element name="value" type="IVL_PQ" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="valueSecondary" type="IVL_PQ" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="valueQuoted" type="IVL_PQ" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="system" type="CD" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="code" type="CD" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="codeSystem" type="CD" minOccurs="0" maxOccurs="unbounded"/>
  </xs:sequence>
</xs:complexType>

<xs:complexType name="POCG_MT000040.Patient">
  <xs:sequence>
    <xs:group ref="InfrastructureRootElements"/>
    <xs:element name="id" type="II" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="providerPerson" type="POCG_MT000040.Provider" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="subjectOf1" type="POCG_MT000040.Subject" minOccurs="0" maxOccurs="unbounded"/>
  </xs:sequence>
</xs:complexType>

<xs:complexType name="POCG_MT000040.PedigreeAnalysisResults">
  <xs:sequence>
    <xs:group ref="InfrastructureRootElements"/>
    <xs:element name="id" type="II" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="text" type="ED" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="subjectOf1" type="POCG_MT000040.Subject" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="component" type="POCG_MT000040.Component" minOccurs="0" maxOccurs="unbounded"/>
  </xs:sequence>
</xs:complexType>

<xs:complexType name="POCG_MT000040.Relative">
  <xs:sequence>
    <xs:group ref="InfrastructureRootElements"/>
    <xs:element name="id" type="II" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="type" type="ED" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="relative" type="POCG_MT000040.Relative" minOccurs="0" maxOccurs="unbounded"/>
  </xs:sequence>
</xs:complexType>

<xs:complexType name="POCG_MT000040.Person">
  <xs:sequence>
    <xs:group ref="InfrastructureRootElements"/>
    <xs:element name="id" type="II" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="name" type="EN" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="telecom" type="TEL" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="administrativeGenderCode" type="CE" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="birthTime" type="TS" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="deceasedInd" type="BL" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="deceasedTime" type="TS" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="raceCode" type="CE" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="ethnicGroupCode" type="CE" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="relative" type="POCG_MT000040.Relative" minOccurs="0" maxOccurs="unbounded"/>
  </xs:sequence>
</xs:complexType>
<xs:element name="clinicalObservation" type="POCG_MT000040.ClinicalObservation"
nillable="true"/>
</xs:choice>
</xs:sequence>
<xs:complexType>
<xs:complexType name="POCG_MT000040.Subject3">
<xs:sequence>
<xs:group ref="InfrastructureRootElements"/>
<xs:choice>
<xs:element name="deceasedEstimatedAge" type="POCG_MT000040.DeceasedEstimatedAge" nillable="true"/>
<xs:element name="livingEstimatedAge" type="POCG_MT000040.LivingEstimatedAge" nillable="true"/>
</xs:choice>
</xs:sequence>
</xs:complexType>
<xs:complexType name="POCG_MT000040.Subject4">
<xs:sequence>
<xs:group ref="InfrastructureRootElements"/>
<xs:element name="dataEstimatedAge" type="POCG_MT000040.DataEstimatedAge" nillable="true"/>
</xs:sequence>
</xs:complexType>
<xs:complexType name="POCG_MT000040.Subject5">
<xs:sequence>
<xs:group ref="InfrastructureRootElements"/>
<xs:element name="patient" type="POCG_MT000040.Patient" nillable="true"/>
</xs:sequence>
</xs:complexType>
</xs:schema>
FamilyHistorySample-POCG000040-v12.s2.xml

<?xml version="1.0" encoding="UTF-8"?>
<!-- Sample of Family History model showing a flat version of a patient's pedigree as well as the ability to represent clinical and genomic data the patient and any of his/her relatives. The pedigree represented in this sample file is as follows: has two sisters, a husband, a daughter, and a mother and a father (each has two parents). For comments, please email to Amnon Shabo (Shvo) at shabo@il.ibm.com (IBM Research Lab in Haifa). -->

<FamilyHistory xmlns="urn:hl7-org:v3" xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance" xsi:schemaLocation="urn:hl7-org:v3 OutputFiles\Schemas\ClinicalGenomicsElements.xsd">
  <!-- General attributes of the pedigree as a whole, e.g., date of creation, version of software used, etc. -->
  <effectiveTime value="200512241729"/>
  <methodCode displayName="CAGENE Version 3.4"/>
  <patient>
    <id root="2.16.840.1.113883.6.117" extension="555"/>
    <administrativeGenderCode code="F"/>
    <birthTime value="1957"/>
    <!-- The following id could be the id assigned to the patient by the healthcare provider, not necessarily related to the pedigree ids -->
    <relative>
      <id root="2.16.840.1.113883.6.117" extension="555.001"/>
      <relationshipHolder>
        <id root="2.16.840.1.113883.6.117" extension="555.002"/>
        <deceasedInd value="true"/>
        <relative>
          <id root="2.16.840.1.113883.6.117" extension="555.002"/>
          <relationshipHolder>
            <id root="2.16.840.1.113883.6.117" extension="555.004"/>
          </relationshipHolder>
          <!-- MATERNAL GRANDFATHER -->
          <relative>
            <code code="NFTH"/>
            <relationshipHolder>
              <id root="2.16.840.1.113883.6.117" extension="555.005"/>
            </relationshipHolder>
            <!-- MATERNAL GRANDMOTHER -->
            <relative>
              <code code="NMTH"/>
              <relationshipHolder>
                <id root="2.16.840.1.113883.6.117" extension="555.006"/>
              </relationshipHolder>
              <!-- The following construct represents the estimated deceased age (72) -->
              <!-- Note that in a certain pedigree there can be a mixture of the two situations -->
              <subjectOf1>
                <deceasedEstimatedAge>
                  <value value="72" unit="year"/>
                </deceasedEstimatedAge>
              </subjectOf1>
            </relative>
          </relative>
        </relative>
      </relationshipHolder>
    </relative>
    <relative>
      <!-- PATIENT -->
      <subjectOf1>
        <subject>...</subject>
      </subjectOf1>
    </relative>
  </patient>
</FamilyHistory>
Ovarian Cancer observation of the patient's mother

displayName="HX OF OVARIAN MALIGNANCY"/>

age at which the above diagnosis was made (40)->

code code="V1043" codeSystemName="ICD"

displayName="HX OF OVARIAN MALIGNANCY"/>

subject>

dataEstimatedAge>
-value="40" unit="year"/>

</dataEstimatedAge>

</subject>

</clinicalObservation>

<subjectOf2>

(relative>

!--maternal grandparents-->>

(relative>

<code code="GRFTH"/>

<relationshipHolder>

{id root="2.16.840.1.113883.6.117" extension="555.004"}/

<subjectOf1>

<livingEstimatedAge>

-value="98" unit="year"/>

</livingEstimatedAge>

</subjectOf1>

</relative>

<subjectOf2>

<clinicalObservation>

displayName="HX OF OVARIAN MALIGNANCY"/>

<subject>

dataEstimatedAge>

-value="50" unit="year"/>

</dataEstimatedAge>

</subject>

</clinicalObservation>

</subjectOf2>

<!-- end of maternal grandfather data-->>

(relative>

<code code="GRMTH"/>

<relationshipHolder>

{id root="2.16.840.1.113883.6.117" extension="555.005"}/

<subjectOf1>

<livingEstimatedAge>

-value="67" unit="year"/>

</livingEstimatedAge>

</subjectOf1>

</relative>

<subjectOf2>

</clinicalObservation>

<code code="V1043" codeSystemName="ICD"

displayName="HX OF OVARIAN MALIGNANCY"/>

<subject>

dataEstimatedAge>

-value="50" unit="year"/>

</dataEstimatedAge>

</subject>

</clinicalObservation>

</subjectOf2>

<!-- end of maternal grandmother data-->>

<!-- end of MOTHER data-->>

<!-- FATHER -->

(relative>

<code code="NFTH"/>

<relationshipHolder>

{id root="2.16.840.1.113883.6.117" extension="555.003"}/

<subjectOf2>

(relative>

<!-- PATERNAL GRANDFATHER -->

<code code="GRFTH"/>

<relationshipHolder>

{id root="2.16.840.1.113883.6.117" extension="555.006"}/

<subjectOf2>

(relative>

<!-- PATERNAL GRANDMOTHER -->

<code code="GRMTH"/>

<relationshipHolder>
<id root="2.16.840.1.113883.6.117" extension="555.007"/>

The following construct represents the estimated age (75) that the code element will be fixed in the schema to the LOINC code below, there is no need to send it in each instance and it appears here for illustration purposes.

<subjectOf1>
  <livingEstimatedAge>
    <code code="21611-9" displayName="ESTIMATED AGE" codeSystemName="LOINC"/>
    <value value="75" unit="year"/>
  </livingEstimatedAge>
</subjectOf1>

</relative>

<!-- paternal grandparents -->

<relative>
  <!-- PATERNAL GRANDFATHER -->
  <code code="GRFTH"/>
  <relationshipHolder>
    <id root="2.16.840.1.113883.6.117" extension="555.006"/>
  </relationshipHolder>
  <subjectOf1>
    <livingEstimatedAge>
      <value value="78" unit="year"/>
    </livingEstimatedAge>
  </subjectOf1>
</relative>

<!-- end of paternal grandfather data -->

<!-- end of FATHER data -->

<!-- SISTER -->

<relative>
  <code code="SIS"/>
  <relationshipHolder>
    <id root="2.16.840.1.113883.6.117" extension="555.008"/>
    <deceasedInd value="true"/>
    <relative>
      <code code="NMTH"/>
      <relationshipHolder>
        <id root="2.16.840.1.113883.6.117" extension="555.008"/>
      </relationshipHolder>
    </relative>
    <subjectOf1>
      <deceasedEstimatedAge>
        <value value="67" unit="year"/>
      </deceasedEstimatedAge>
    </subjectOf1>
  </relationshipHolder>
</relative>

extension="555.002"/>

</relative>

<relative>
  <code code="NFTH"/>
  <relationshipHolder>
    <id root="2.16.840.1.113883.6.117" extension="555.003"/>
  </relationshipHolder>
</relative>

extension="555.003"/>

</relative>

</relationshipHolder>

<subjectOf1>
Ovarian Cancer observation of the patient's sister:

displayName="HX OF OVARIAN MALIGNANCY"/

<subject>
  <dataEstimatedAge>
    <value value="60" unit="year"/>
  </dataEstimatedAge>
</subject>

Ovarian Cancer observation of the patient's sister's sister:

displayName="HX OF OVARIAN MALIGNANCY"/

<subject>
  <dataEstimatedAge>
    <value value="50" unit="year"/>
  </dataEstimatedAge>
</subject>

Ovarian Cancer observation of the patient's husband:

displayName="HX OF OVARIAN MALIGNANCY"/

<subject>
  <livingEstimatedAge>
    <value value="57" unit="year"/>
  </livingEstimatedAge>
</subject>
<relative>
  <code code="DAU"/>
  <relationshipHolder>
    <id root="2.16.840.1.113883.6.117" extension="555.011"/>
    <deceasedInd value="true"/>
    <relative>
      <code code="NMTH"/>
      <relationshipHolder>
        <id root="2.16.840.1.113883.6.117" extension="555.011"/>
      </relationshipHolder>
    </relative>
  </relationshipHolder>
  <extension="555.001"/>
</relative>

<relative>
  <code code="NMTH"/>
  <relationshipHolder>
    <id root="2.16.840.1.113883.6.117" extension="555.001"/>
  </relationshipHolder>
</relative>

<relative>
  <code code="NFTH"/>
  <relationshipHolder>
    <id root="2.16.840.1.113883.6.117" extension="555.01"/>
  </relationshipHolder>
</relative>

<subjectOf1>
  <deceasedEstimatedAge>
    <value value="33" unit="year"/>
  </deceasedEstimatedAge>
</subjectOf1>

<subjectOf2>
  <geneticLocus moodCode="EVN">
    <text>breast cancer 1, early onset</text>
    <value code="83990" displayName="BRCA1" codeSystemName="NCBI Entrez"/>
    <translation code="20473">
      <sequenceVariation moodCode="EVN">
        <value xsi:type="CE" code="185delAG"/>
      </sequenceVariation>
    </translation>
  </geneticLocus>
  <interpretationCode code="DELETERIOUS"/>
  <pertinentInformation typeCode="PERT">
    <clinicalPhenotype classCode="ORGANIZER">
      <component2>
        <text>Roa et al. (1996) found the 185delAG mutation in 1.09% of approximately 3,000 Ashkenazi Jewish individuals and found the 5382insC mutation (113705.0018) in 0.13%. BRCA2 analysis on 3,085 individuals from the same population showed a carrier frequency of 1.52% for the 6174delT mutation (600185.0009). The expanded population-based study confirmed that the BRCA1 185delAG mutation and the BRCA2 6174delT mutation constituted the 2 most frequent mutant alleles predisposing to hereditary breast cancer among Ashkenazim and suggested a relatively lower penetrance for the 6174delT mutation in BRCA2.</text>
      </component2>
      <knownClinicalPhenotype>
        <value xsi:type="CE" code="113705.0003" codeSystemName="OMIM"/>
      </knownClinicalPhenotype>
    </clinicalPhenotype>
  </pertinentInformation>
</subjectOf2>
Clinical phenotype

pertinent information

sequence variation

component 3

genetic locus

subject of 2

Clinical data

Ovarian Cancer observation of the patient's daughter
display name="HX OF OVARIAN MALIGNANCY"

subject

data estimated age

value=value="30" unit="year"

subject

related

end of DAUGHTER data

patient person

PATIENT personal and clinical data

subject of 1

deceased estimated age

value=value="47" unit="year"

dead

subject of 2

"end of PATIENT data"

patient

pedigree analysis results

PROBABILITY OF DEVELOPING BREAST CANCER BEFORE THE AGE INDICATED

effective time value="200601132301"

method code="BRCAPRO"

component

age

value

null flavor="QS"

high value="53" unit="year"

pertinent information

probability

value=value="0.000168"

pertinent information

age

value

low value="54" unit="year"

pertinent information

probability

value=value="0.000368"
<pertinentInformation>
  <value>
    <low value="58" unit="year"/>
    <high value="62" unit="year"/>
  </value>
  <pertinentInformation>
    <probability>
      <value value="0.000594"/>
    </probability>
  </pertinentInformation>
</pertinentInformation>

<pertinentInformation>
  <value>
    <low value="63" unit="year"/>
    <high value="67" unit="year"/>
  </value>
  <pertinentInformation>
    <probability>
      <value value="0.000838"/>
    </probability>
  </pertinentInformation>
</pertinentInformation>

<pertinentInformation>
  <value>
    <low value="68" unit="year"/>
    <high value="72" unit="year"/>
  </value>
  <pertinentInformation>
    <probability>
      <value value="0.001089"/>
    </probability>
  </pertinentInformation>
</pertinentInformation>

<pertinentInformation>
  <value>
    <low value="73" unit="year"/>
    <high value="77" unit="year"/>
  </value>
  <pertinentInformation>
    <probability>
      <value value="0.001327"/>
    </probability>
  </pertinentInformation>
</pertinentInformation>

<pertinentInformation>
  <value>
    <low value="78" unit="year"/>
    <high value="82" unit="year"/>
  </value>
  <pertinentInformation>
    <probability>
      <value value="0.001530"/>
    </probability>
  </pertinentInformation>
</pertinentInformation>
<value>
  <low value="83" unit="year"/>
  <high value="88" unit="year"/>
</value>
<pertinentInformation>
  <probability>
    <value value="0.001663"/>
  </probability>
</pertinentInformation>
</age>
</component>
</pedigreeAnalysisResults>
</component2>
</FamilyHistory>
This sample shows high resolution genomic data (i.e., gene sequence) embedded in the same sample as the above.

<?xml version="1.0" encoding="UTF-8"?>
<!--Sample of Family History model showing a flat version of a patient's pedigree as well as the ability to represent clinical and genomic data the patient and any of his/her relatives. The pedigree represented in this sample file is as follows: has two sisters, a husband a daughter, and a mother and a father (each has two parents).

comments, please email to Amnon Shabo (Shvo) at shabo@il.ibm.com (IBM Research Lab in Haifa).

-->
<clinicalObservation>
  <subjectOf1>
    <subjectOf2>
      <clinicalObservation display="HX OF OVARIAN MALIGNANCY">
        <code code="V1043" codeSystemName="ICD">
          <displayName>HX OF OVARIAN MALIGNANCY</displayName>
        </code>
        <subject>
          <dataEstimatedAge value="40" unit="year"/>
        </subject>
      </clinicalObservation>
    </subjectOf2>
  </subjectOf1>
</clinicalObservation>

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    <subjectOf2>
      <clinicalObservation display="HX OF OVARIAN MALIGNANCY">
        <code code="V1043" codeSystemName="ICD">
          <displayName>HX OF OVARIAN MALIGNANCY</displayName>
        </code>
        <subject>
          <dataEstimatedAge value="50" unit="year"/>
        </subject>
      </clinicalObservation>
    </subjectOf2>
  </subjectOf1>
</clinicalObservation>

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    <subjectOf2>
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        </code>
        <subject>
          <dataEstimatedAge value="98" unit="year"/>
        </subject>
      </clinicalObservation>
    </subjectOf2>
  </subjectOf1>
</clinicalObservation>

<clinicalObservation display="HX OF OVARIAN MALIGNANCY">
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    <subjectOf2>
      <clinicalObservation display="HX OF OVARIAN MALIGNANCY">
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        </code>
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        </subject>
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  </subjectOf1>
</clinicalObservation>

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    <subjectOf2>
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        </code>
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</clinicalObservation>

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    <subjectOf2>
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        </code>
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</clinicalObservation>

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</clinicalObservation>

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  </subjectOf1>
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</clinicalObservation>

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        </code>
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</clinicalObservation>

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</clinicalObservation>

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        </code>
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</clinicalObservation>

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          <displayName>HX OF OVARIAN MALIGNANCY</displayName>
        </code>
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        </subject>
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  </subjectOf1>
</clinicalObservation>

<clinicalObservation display="HX OF OVARIAN MALIGNANCY">
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    <subjectOf2>
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          <displayName>HX OF OVARIAN MALIGNANCY</displayName>
        </code>
        <subject>
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        </subject>
      </clinicalObservation>
    </subjectOf2>
  </subjectOf1>
</clinicalObservation>

<clinicalObservation display="HX OF OVARIAN MALIGNANCY">
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    <subjectOf2>
      <clinicalObservation display="HX OF OVARIAN MALIGNANCY">
        <code code="V1043" codeSystemName="ICD">
          <displayName>HX OF OVARIAN MALIGNANCY</displayName>
        </code>
        <subject>
          <dataEstimatedAge value="67" unit="year"/>
<relative>
  <!-- PATERNAL GRANDMOTHER -->
  <code code="GRMTH"/>
  <relationshipHolder>
    <id root="2.16.840.1.113883.6.117" extension="555.007"/>
  </relationshipHolder>
  <!-- The following construct represents the estimated age (75) that the code element will be fixed in the schema to the LOINC code below, there is no need to send it in each instance and it appears here for illustration purposes. -->
  <subjectOf1>
    <livingEstimatedAge>
      <code code="21611-9" displayName="ESTIMATED AGE" codeSystemName="LOINC"/>
      <value value="75" unit="year"/>
    </livingEstimatedAge>
  </subjectOf1>
</relative>
<!-- paternal grandparents -->
<relative>
  <!-- PATERNAL GRANDFATHER -->
  <code code="GRFTH"/>
  <relationshipHolder>
    <id root="2.16.840.1.113883.6.117" extension="555.006"/>
  </relationshipHolder>
  <subjectOf1>
    <livingEstimatedAge>
      <value value="78" unit="year"/>
    </livingEstimatedAge>
  </subjectOf1>
</relative>
<!-- end of paternal grandfather data -->
<relative>
  <!-- PATERNAL GRANDMOTHER -->
  <code code="GRMTH"/>
  <relationshipHolder>
    <id root="2.16.840.1.113883.6.117" extension="555.007"/>
  </relationshipHolder>
  <subjectOf1>
    <livingEstimatedAge>
      <value value="87" unit="year"/>
    </livingEstimatedAge>
  </subjectOf1>
</relative>
<!-- end of paternal grandmother data -->
<!-- end of FATHER data -->
<!-- SISTER -->
<relative>
  <code code="SIS"/>
  <relationshipHolder>
    <id root="2.16.840.1.113883.6.117" extension="555.008"/></id>
    <deceasedInd value="true"/>
    <relative>
      <code code="NMTH"/>
      <relationshipHolder>
        <id root="2.16.840.1.113883.6.117" extension="555.002"/>
      </relationshipHolder>
      <subjectOf1>
    </relative>
  </relationshipHolder>
</relative>
<relative>
  <code code="NFTH"/>
  <relationshipHolder>
    <id root="2.16.840.1.113883.6.117" extension="555.003"/>
  </relationshipHolder>
  <subjectOf1>
</relative>
<deceasedEstimatedAge><value value="67" unit="year"/></deceasedEstimatedAge>
</subjectOf1>
<subjectOf2>
<branch>

<!-- Ovarian Cancer observation of the patient's sister-->
<clinicalObservation>
<displayName>"HX OF OVARIAN MALIGNANCY"/></clinicalObservation>

<!-- end of first SISTER data-->
<!-- SISTER--> 
<relative>
<code code="SIS"/>
<relationshipHolder>
<id root="2.16.840.1.113883.6.117" extension="555.009"/>
<deceasedInd value="true"/>
<relative>
<code code="NMTH"/>
<relationshipHolder>
<id root="2.16.840.1.113883.6.117" extension="555.002"/>
</relationshipHolder>
<relative>
<code code="NFTH"/>
<relationshipHolder>
<id root="2.16.840.1.113883.6.117" extension="555.003"/>
</relationshipHolder>
</relative>
</relative>
</subjectOf2>
<branch>

<!-- end of second SISTER data-->
<!-- HUSBAND--> 
<relative>
<code code="HUSB"/>
<relationshipHolder>
<id root="2.16.840.1.113883.6.117" extension="555.01"/>
</relationshipHolder>
<subjectOf1>
<deceasedEstimatedAge>
<value value="55" unit="year"/>
</deceasedEstimatedAge>
</subjectOf1>
<subjectOf2>
<branch>

<!-- Ovarian Cancer observation of the patient's sister-->
<clinicalObservation>
<displayName>"HX OF OVARIAN MALIGNANCY"/></clinicalObservation>

<!-- end of first SISTER data-->
<!-- SISTER--> 
<relative>
<code code="SIS"/>
<relationshipHolder>
<id root="2.16.840.1.113883.6.117" extension="555.009"/>
<deceasedInd value="true"/>
<relative>
<code code="NMTH"/>
<relationshipHolder>
<id root="2.16.840.1.113883.6.117" extension="555.002"/>
</relationshipHolder>
<relative>
<code code="NFTH"/>
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</relationshipHolder>
</relative>
</relative>
</subjectOf2>
<branch>

<!-- end of second SISTER data-->
<!-- HUSBAND--> 
<relative>
<code code="HUSB"/>
<relationshipHolder>
<id root="2.16.840.1.113883.6.117" extension="555.01"/>
</relationshipHolder>
<subjectOf1>
<livingEstimatedAge>
<value value="57" unit="year"/>
</livingEstimatedAge>
</subjectOf1>
<subjectOf2>
<branch>
subjectOf1

relative
<!-- end of HUSBAND data-->
relative
code code="DAU"/>
relationshipHolder
<id root="2.16.840.1.113883.6.117" extension="555.011"/>
deceasedInd value=true/>
relationshipHolder
<id root="2.16.840.1.113883.6.117" extension="555.001"/>
relative
code code="NMTH"/>
relationshipHolder
<id root="2.16.840.1.113883.6.117" extension="555.001"/>
relative
code code="NFTH"/>
relationshipHolder
<id root="2.16.840.1.113883.6.117" extension="555.01"/>
relative
deceasedEstimatedAge value="33" unit="year"/>
deceasedEstimatedAge
subjectOf1
deceasedEstimatedAge
</subjectOf1>

GENETIC DATA
subjectOf2
geneticLocus moodCode="EVN">
text breast cancer 1, early onset</text>
value code="83990" displayName="BRCA1" codeSystemName="NCBI Entrez">
<translation code="20473" displayName="BRCA1"/>
component3>
sequenceVariation moodCode="EVN">
value xsi:type="CE" code="185delAG"/>
</sequenceVariation>
</component3>

codeSystemName="NCBI Entrez">
displayName="BRCA1" codeSystem="HGNC"/>

interpretationCode code="DELETERIOUS"/>
pertinentInformation typeCode="PERT">
classCode="ORGANIZER">

<component2>

<knownClinicalPhenotype>
Roa et al. (1996) found the 185delAG mutation in 1.09% of approximately 3,000 Ashkenazi Jewish individuals and found the 5382insC mutation (113705.0003) in 0.13%. BRCA2 analysis on 3,085 individuals from the same population showed a carrier frequency of 1.52% for the 6174delT mutation (600185.0009). The expanded population-based study confirmed that the BRCA1 185delAG mutation and the BRCA2 6174delT mutation constituted the 2 most frequent mutant alleles predisposing to hereditary breast cancer among Ashkenazim and suggested a relatively lower penetrance for the 6174delT mutation in BRCA2.

<value xsi:type="CE" code="113705.0003" codeSystemName="OMIM"/>
daughter's BRCA1 gene goes here so that applications could look for more information such as SNPs that are not recognized as mutations below are not accurate and are presented for illustration purposes only) -->

<code code="BSMLev3"/>
<value mediaType="text/xml">
<bsml:Bsm1
 xmlns:bsml="urn:bsml.org">
<bsml:Definitions>
<bsml:Sequences>
<bsml:Sequence 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">
<bsml:Seq-data>
CTCCATGAGG TATTTCTTCA
CCGGCCCGGC CGCCGGGAGC CCCGCTTCAT CGCCGTGGGC
ACACGCAAGT CGTGCGGTTC GACAGCGACG CCGCGAGCCA
CCGCGGGGCGC CGTGGATAGA GCAGGAGGGG CCGGAGTATT
GACACGGAAT GTGAAGGCCC AGTCACAGAC TGACCGAGTG
CCCTGCGCGG CTACTACAAC CAGAGCGAGG CCG
</bsml:Seq-data>
</bsml:Sequence>
<bsml:Sequence id="seq2" 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">
<bsml:Seq-data>
ATAATGTATG GCTGCGACGT GGGGTCGGAC GGGCGCTTCC
CCGGCAGGAC GCCTACGACG GCAAGGATTA CATCGCCCTG
TGCGCTCTTG GACCGCGGCG GACATGCGCG CTCAGATCAC
TGGGAGGCGG CCCATGTGGC GGAGCAGCAG AGAGCCTACC
GTGCGTGAGG TGACGCCGCA GATACCTGGA GAACGGGAAG
AGCGCACGG
</bsml:Seq-data>
</bsml:Sequence>
</bsml:Sequences>
</bsml:Bsm1>
<bsml:Definitions>
  <bsml:Isoforms>
    <bsml:Isoform-set>
      <!-- The isoform tag in BSML can be used to represent a SNP. 'seqref' attribute is used to refer to the sequence where the SNP occurs. (Note that the SNPs are not based on real data, rather were made up for illustration purposes only) -->
      <bsml:Isoform id="SNP123" seqref="seq1" location="9" change="T"/>
      <bsml:Isoform id="SNP456" seqref="seq1" location="32" change="C"/>
      <bsml:Isoform id="SNP789" seqref="seq2" location="124" change="G"/>
    </bsml:Isoform-set>
  </bsml:Isoforms>
</bsml:Definitions>

The following attribute belongs to the HL7 Sequence class and represents the sequencing method. vocabulary has not been nailed down yet and several options are suggested in the Genotype documentation. -->

methodCode="SBT"/>
<derivedFrom3>
  <sequenceVariation moodCode="EVN">
    <code code="DNA"/>
    <text value xsi:type="CE" code="633delC"/>
    <!-- The HL7 'text' attribute is of ED data type and this data type has a reference tag that allows the referencing enables the linking between the bubbled-up object like this sequence variation one, the encapsulated data in the Sequence class -->
    <reference value="#SNP456"/>
  </text>
  <value xsi:type="CE" code="633delC"/>
</sequenceVariation>
</derivedFrom3>

interpretationCode value should be drawn from the ObservationInterpretation vocabulary that doesn't have the DELETERIOUS value (abnormal is the closest) has been proposed to RIM Harmonization in November 2004 and was accepted in principle. -->

<interpretationCode code="DELETERIOUS"/>
<pertinentInformation>
  <clinicalPhenotype classCode="ORGANIZER">
    <!-- The use of the id attribute populated with an OID value could facilitate the access to the location the instance of the referred diagnosis resides (e.g., in the patient medical records) -->
    <component3>
      <externalObservedClinicalPhenotype>
        <id root="2.16.840.1.113883" extension="diagnosis1"/>
      </externalObservedClinicalPhenotype>
    </component3>
  </clinicalPhenotype>
</pertinentInformation>
</value>
externalObservedClinicalPhenotype
</component3>
</clinicalPhenotype>
</pertinentInformation>
<derivedFrom>
<associatedProperty>
<code code="TYPE"/>
</associatedProperty>
</derivedFrom>
</sequenceVariation>
</component4>
</sequence>
</geneticLocus>
</subjectOf2>
<!- CLINICAL DATA-->
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<clinicalObservation>
<!- Ovarian Cancer observation of the patient's daughter-->
<displayName="HX OF OVARIAN MALIGNANCY"/>
<code code="V1043" codeSystemName="ICD">
<subject>
<dataEstimatedAge>
<value value="30" unit="year"/>
</dataEstimatedAge>
</subject>
</clinicalObservation>
</subjectOf2>
<!- end of DAUGHTER data-->
</patientPerson>
<!- PATIENT personal and clinical data-->
<subjectOf1>
<deceasedEstimatedAge>
<value value="47" unit="year"/>
</deceasedEstimatedAge>
</subjectOf1>
<subjectOf2>
<!- The patient did NOT have ovarian Cancer -->
<clinicalObservation negationInd="true">
<code code="V1043" codeSystemName="ICD" displayName="HX OF OVARIAN MALIGNANCY"/>
</clinicalObservation>
</subjectOf2>
<!- end of PATIENT data-->
</patient>
</subject>
<component2>
<pedigreeAnalysisResults>
<!- could add a code attribute to identify the disease or variation for which the probabilities are calculated--> 
</pedigreeAnalysisResults>
</component2>
</effectiveTime value="200601132301"/>
</methodCode code="BRCAPRO"/>
</component>
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<high value="53" unit="year" />
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<probability>
  <value value="0.000168" />
</probability>
</pertinentInformation>
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</component>
<value>
<low value="54" unit="year" />
<high value="57" unit="year" />
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  <value value="0.000368" />
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<high value="62" unit="year" />
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<high value="67" unit="year" />
</value>
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<probability>
<value value="0.001663"/>
</probability>
</pertinentInformation>
</age>
</component>
</pedigreeAnalysisResults>
</component2>
</FamilyHistory>
Appendix E: Relative Codes from the HL7 RoleCode Vocabulary

THIS VOCABULARY IS OUTDATED AS OUR HARMONIZATION PROPOSAL TO ADD MATERNAL/PATERNAL CODES WAS ACCEPTED.

<table>
<thead>
<tr>
<th>Code</th>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>FAMMEmb</td>
<td>Family Member</td>
</tr>
<tr>
<td></td>
<td>Family Member</td>
<td>A relationship between two people characterizing their &quot;familial&quot; relationship</td>
</tr>
<tr>
<td>3</td>
<td>CHILD</td>
<td>Child</td>
</tr>
<tr>
<td></td>
<td>Child</td>
<td>The player of the role is a child of the scoping entity.</td>
</tr>
<tr>
<td>4</td>
<td>CHLDADOPT</td>
<td>adopted child</td>
</tr>
<tr>
<td></td>
<td>adopted child</td>
<td>The player of the role is a child taken into a family through legal means</td>
</tr>
<tr>
<td></td>
<td></td>
<td>and raised by the scoping person (parent) as his or her own child.</td>
</tr>
<tr>
<td>5</td>
<td>DAUADOPT</td>
<td>adopted daughter</td>
</tr>
<tr>
<td></td>
<td>adopted daughter</td>
<td>The player of the role is a female child taken into a family through legal means and raised by the scoping person (parent) as his or her own child.</td>
</tr>
<tr>
<td>5</td>
<td>SONADOPT</td>
<td>adopted son</td>
</tr>
<tr>
<td></td>
<td>adopted son</td>
<td>The player of the role is a male child taken into a family through legal means and raised by the scoping person (parent) as his or her own child.</td>
</tr>
<tr>
<td>4</td>
<td>CHLDINLAW</td>
<td>child in-law</td>
</tr>
<tr>
<td></td>
<td>child in-law</td>
<td>The player of the role is the spouse of scoping person’s child.</td>
</tr>
<tr>
<td>5</td>
<td>DAUINLAW</td>
<td>daughter in-law</td>
</tr>
<tr>
<td></td>
<td>daughter in-law</td>
<td>The player of the role is the wife of scoping person’s son.</td>
</tr>
<tr>
<td>5</td>
<td>SONINLAW</td>
<td>son in-law</td>
</tr>
<tr>
<td></td>
<td>son in-law</td>
<td>The player of the role is the husband of scoping person’s daughter.</td>
</tr>
<tr>
<td>4</td>
<td>CHLDFOST</td>
<td>foster child</td>
</tr>
<tr>
<td></td>
<td>foster child</td>
<td>The player of the role is a child receiving parental care and nurture from the scoping person (parent) but not related to him or her through legal or blood ties.</td>
</tr>
<tr>
<td>5</td>
<td>DAUFOST</td>
<td>foster daughter</td>
</tr>
<tr>
<td></td>
<td>foster daughter</td>
<td>The player of the role is a female child receiving parental care and nurture from the scoping person (parent) but not related to him or her through legal or blood ties.</td>
</tr>
<tr>
<td>5</td>
<td>SONFOST</td>
<td>foster son</td>
</tr>
<tr>
<td></td>
<td>foster son</td>
<td>The player of the role is a male child receiving parental care and nurture from the scoping person (parent) but not related to him or her through legal or blood ties.</td>
</tr>
<tr>
<td>4</td>
<td>NCHILD</td>
<td>natural child</td>
</tr>
<tr>
<td></td>
<td>natural child</td>
<td>The player of the role is an offspring of the scoping entity as determined by birth.</td>
</tr>
<tr>
<td>5</td>
<td>DAU</td>
<td>natural daughter</td>
</tr>
<tr>
<td></td>
<td>natural daughter</td>
<td>The player of the role is a female offspring of the scoping entity (parent).</td>
</tr>
<tr>
<td>5</td>
<td>SON</td>
<td>natural son</td>
</tr>
<tr>
<td></td>
<td>natural son</td>
<td>The player of the role is a male offspring of the scoping entity (parent).</td>
</tr>
<tr>
<td>4</td>
<td>STPC1HD</td>
<td>step child</td>
</tr>
<tr>
<td></td>
<td>step child</td>
<td>The player of the role is a child of the scoping person's spouse by a previous union.</td>
</tr>
<tr>
<td>5</td>
<td>STPDAU</td>
<td>stepdaughter</td>
</tr>
<tr>
<td></td>
<td>stepdaughter</td>
<td>The player of the role is a daughter of the scoping person's spouse by a previous union.</td>
</tr>
<tr>
<td>5</td>
<td>STPSON</td>
<td>stepson</td>
</tr>
<tr>
<td></td>
<td>stepson</td>
<td>The player of the role is a son of the scoping person's spouse by a previous union.</td>
</tr>
<tr>
<td>3</td>
<td>GRNDC1HD</td>
<td>grandchild</td>
</tr>
<tr>
<td></td>
<td>grandchild</td>
<td>The player of the role is a child of the scoping person's son or daughter.</td>
</tr>
<tr>
<td>4</td>
<td>GRNDDAU</td>
<td>granddaughter</td>
</tr>
<tr>
<td></td>
<td>granddaughter</td>
<td>The player of the role is a daughter of the scoping person's son or daughter.</td>
</tr>
<tr>
<td>4</td>
<td>GRNDSON</td>
<td>grandson</td>
</tr>
<tr>
<td></td>
<td>grandson</td>
<td>The player of the role is a son of the scoping person's son or daughter.</td>
</tr>
<tr>
<td>3</td>
<td>GRPRN</td>
<td>Grandparent</td>
</tr>
<tr>
<td></td>
<td>Grandparent</td>
<td>The player of the role is a parent of the scoping person's mother or father.</td>
</tr>
<tr>
<td>4</td>
<td>GRFTH</td>
<td>Grandfather</td>
</tr>
<tr>
<td></td>
<td>Grandfather</td>
<td>The player of the role is the father of the scoping person's mother or father.</td>
</tr>
<tr>
<td>Code</td>
<td>Title</td>
<td>Definition</td>
</tr>
<tr>
<td>-------</td>
<td>-------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>4</td>
<td>GRMTH great mother</td>
<td>The player of the role is the mother of the scoping person's mother or father.</td>
</tr>
<tr>
<td>3</td>
<td>GGRPRN great grandparent</td>
<td>The player of the role is a parent of the scoping person's grandparent.</td>
</tr>
<tr>
<td>4</td>
<td>GGRFTH great grandfather</td>
<td>The player of the role is the father of the scoping person's grandparent.</td>
</tr>
<tr>
<td>4</td>
<td>GGRMTH great grandmother</td>
<td>The player of the role is the mother of the scoping person's grandparent.</td>
</tr>
<tr>
<td>3</td>
<td>NIE/NPH niece/nephew</td>
<td>The player of the role is a child of scoping person's brother or sister or of the brother or sister of the scoping person's spouse.</td>
</tr>
<tr>
<td>4</td>
<td>NEPHEW nephew</td>
<td>The player of the role is a son of the scoping person's brother or sister or of the brother or sister of the scoping person's spouse.</td>
</tr>
<tr>
<td>4</td>
<td>NIECE niece</td>
<td>The player of the role is a daughter of the scoping person's brother or sister or of the brother or sister of the scoping person's spouse.</td>
</tr>
<tr>
<td>3</td>
<td>PRN Parent</td>
<td>The player of the role is one who begets, gives birth to, or nurtures and raises the scoping entity (child).</td>
</tr>
<tr>
<td>4</td>
<td>NPRN natural parent</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>NFTH natural father</td>
<td>The player of the role is a male who begets the scoping entity (child).</td>
</tr>
<tr>
<td>5</td>
<td>NMTH natural mother</td>
<td>The player of the role is a female who conceives or gives birth to the scoping entity (child).</td>
</tr>
<tr>
<td>4</td>
<td>PRNILAW parent in-law</td>
<td>The player of the role is the parent of scoping person's husband or wife.</td>
</tr>
<tr>
<td>5</td>
<td>FTHINLAW father-in-law</td>
<td>The player of the role is the father of the scoping person's husband or wife.</td>
</tr>
<tr>
<td>5</td>
<td>MTHINLAW mother-in-law</td>
<td>The player of the role is the mother of the scoping person's husband or wife.</td>
</tr>
<tr>
<td>4</td>
<td>STPPRN step parent</td>
<td>The player of the role is the spouse of the scoping person's parent and not the scoping person's natural parent.</td>
</tr>
<tr>
<td>5</td>
<td>STPXTH stepfather</td>
<td>The player of the role is the husband of scoping person's mother and not the scoping person's natural father.</td>
</tr>
<tr>
<td>5</td>
<td>STPMTH stepmother</td>
<td>The player of the role is the wife of scoping person's father and not the scoping person's natural mother.</td>
</tr>
<tr>
<td>4</td>
<td>FTH Father</td>
<td>The player of the role is a male who begets or raises or nurtures the scoping entity (child).</td>
</tr>
<tr>
<td>4</td>
<td>MTH Mother</td>
<td>The player of the role is a female who conceives, gives birth to, or raises and nurtures the scoping entity (child).</td>
</tr>
<tr>
<td>3</td>
<td>SIB Sibling</td>
<td>The player of the role shares one or both parents in common with the scoping entity.</td>
</tr>
<tr>
<td>4</td>
<td>HSIB half-sibling</td>
<td>The player of the role is related to the scoping entity by sharing only one biological parent.</td>
</tr>
<tr>
<td>5</td>
<td>HBRO half-brother</td>
<td>The player of the role is a male related to the scoping entity by sharing only one biological parent.</td>
</tr>
<tr>
<td>5</td>
<td>HSIS half-sister</td>
<td>The player of the role is a female related to the scoping entity by sharing only one biological parent.</td>
</tr>
<tr>
<td>4</td>
<td>NSIB natural sibling</td>
<td>The player of the role has both biological parents in common with the scoping entity.</td>
</tr>
<tr>
<td>5</td>
<td>NBRO natural brother</td>
<td>The player of the role is a male having the same biological parents as the scoping entity.</td>
</tr>
<tr>
<td>5</td>
<td>NSIS natural sister</td>
<td>The player of the role is a female having the same biological parents as the scoping entity.</td>
</tr>
<tr>
<td>4</td>
<td>SIBINLAWS sibling in-law</td>
<td>The player of the role is: (1) a sibling of the scoping person's spouse, or (2) the spouse of the scoping person's sibling, or (3) the spouse of a sibling of the scoping person's spouse.</td>
</tr>
<tr>
<td>Code</td>
<td>Role</td>
<td>Definition</td>
</tr>
<tr>
<td>------</td>
<td>------</td>
<td>------------</td>
</tr>
<tr>
<td>5</td>
<td>BROINLAW</td>
<td>brother-in-law</td>
</tr>
<tr>
<td>5</td>
<td>SISLINLAW</td>
<td>sister-in-law</td>
</tr>
<tr>
<td>4</td>
<td>STPSIB</td>
<td>step sibling</td>
</tr>
<tr>
<td>5</td>
<td>STPBR</td>
<td>stepbrother</td>
</tr>
<tr>
<td>5</td>
<td>STPSIS</td>
<td>stepsister</td>
</tr>
<tr>
<td>4</td>
<td>BRO</td>
<td>Brother</td>
</tr>
<tr>
<td>4</td>
<td>SIS</td>
<td>Sister</td>
</tr>
<tr>
<td>3</td>
<td>SPS</td>
<td>spouse</td>
</tr>
<tr>
<td>4</td>
<td>HUSB</td>
<td>husband</td>
</tr>
<tr>
<td>4</td>
<td>WIFE</td>
<td>wife</td>
</tr>
<tr>
<td>3</td>
<td>AUNT</td>
<td>aunt</td>
</tr>
<tr>
<td>3</td>
<td>COUSN</td>
<td>cousin</td>
</tr>
<tr>
<td>3</td>
<td>DOMPART</td>
<td>domestic partner</td>
</tr>
<tr>
<td>3</td>
<td>ROOM</td>
<td>Roommate</td>
</tr>
<tr>
<td>3</td>
<td>SIGOTH</td>
<td>significant other</td>
</tr>
<tr>
<td>3</td>
<td>UNCLE</td>
<td>uncle</td>
</tr>
</tbody>
</table>
Appendix F: Accepted RIM Harmonization Proposals

The following codes with all combinations like "Maternal Cousin", "Paternal Cousin", etc. were added to the appropriate HL7 personal relationship vocabulary:

Maternal AUNT
Paternal AUNT

Maternal BROINLAW
Paternal BROINLAW

Maternal COUSN
Paternal COUSN

Maternal GGRFTH
Paternal GGRFTH

Maternal GGRMTH
Paternal GGRMTH

Maternal GGRPRN
Paternal GGRPRN

Maternal GRFTH
Paternal GRFTH

Maternal GRMTH
Paternal GRMTH

Maternal GRPRN
Paternal GRPRN

Maternal HBRO
Paternal HBRO

Maternal HSIB
Paternal HSIB

Maternal HSIS
Paternal HSIS

Maternal NBRO
Paternal NBRO

Maternal NEPHEW
Paternal NEPHEW

Maternal NIECE
Paternal NIECE

Maternal NIENEPH
Paternal NIENEPH

Maternal NSIB
Paternal NSIB

Maternal NSIS
Paternal NSIS

Paternal SIBINLAW
Maternal SIBINLAW
Paternal SISLINLAW
Maternal SISLINLAW
Paternal STPBRO
Maternal STPBRO
Paternal STPSIB
Maternal STPSIB
Paternal STPSIS
Maternal STPSIS
Paternal UNCLE
Maternal UNCLE

Note that this gives us maternal and paternal. ‘Both’ is implied by the family member relationship of those types (Brother is always both). Unknown is denoted by the lack of a modifier and the lack of mother and father ID [an Aunt with a mother and father ID can be determined to be paternal or maternal. One without is unknown)