

HL7 Clinical-Genomics SIG The Family History Model

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Introduction	2
The Family History Model.....	7
Model Walk -Through	8
Message Interactions of Person's Pedigree	15
Appendix A: The Family History (Pedigree) R-MIM	16
Appendix B: Hierarchical vs. Flat Representation	17
Appendix C: The GeneticLocus R-MIM	19
Appendix D: XML Schema and Samples	20
Appendix E: Relative Codes from the HL7 RoleCode Vocabulary - PersonalRelationshipRoleType.....	45
Appendix F : List of Changes through Ballot Cycles	67

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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:

Patient ID				
	Relative type (Self)			
	Cancer			
		Year diagnosed		
		Age diagnosed		
	Genetic syndrome suspected			
		Genetic test done		
			Genetic test result specific	
			Genetic test result interpretation	
	Mother ID number			
	Father ID number			
	Relative ID number			
		Relative type (Brother, sister...)		
		Cancer		
			Year diagnosed	
			Age diagnosed	
		Genetic syndrome suspected		
			Genetic test done	
				Genetic test result specific
				Genetic test result

				interpretation
		Mother ID number		
		Father ID number		
	Relative ID number			
		Relative type (Brother, sister...)		
		Cancer		
			Year diagnosed	
			Age diagnosed	
		Genetic syndrome suspected		
			Genetic test done	
				Genetic test result specific
				Genetic test result interpretation
		Mother ID number		
		Father ID number		

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/~gp/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 Proband⁴ 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

⁴ Proband: First affected family member coming to medical attention*.
 Consultand: Individual (s) seeking genetic counseling/testing*

*Bennett RL, Steinhaus KA, Uhrich SB, O'Sullivan CK, Resta RG, Lochner-Doyle D, Markel DS, Vincent V, Hamanishi J. Recommendations for standardized human pedigree nomenclature. Pedigree Standardization Task Force of the National Society of Genetic Counselors. Am J Hum Genet. 1995 Mar;56(3):745-52.

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 PCR'd.
- 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 PCR'd.
- 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).

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 DSTU 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

(Version POCG_RM000040.v12)

➤ **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 observation⁵, i.e., the ***ClinicalObservation*** class. It is used due to the absence of an age attribute in all HL7 classes. We have proposed to RIM harmonization⁶ the addition of an age attribute to the Act class as well as other classes, but were asked to try and model this piece of information using associated observations like this class.

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.

⁵ 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.

⁶ See appendix E for the RIM Harmonization proposals relevant to the Family History model.

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).

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 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 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**⁷ 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**⁸:
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

⁷ In general, the **code** attribute in HL7 is a specialization of the structural **classCode** attribute.

⁸ A shadow class means that all its attributes and traversable associations are identical to those of the class it shadows.

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). 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 by 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.

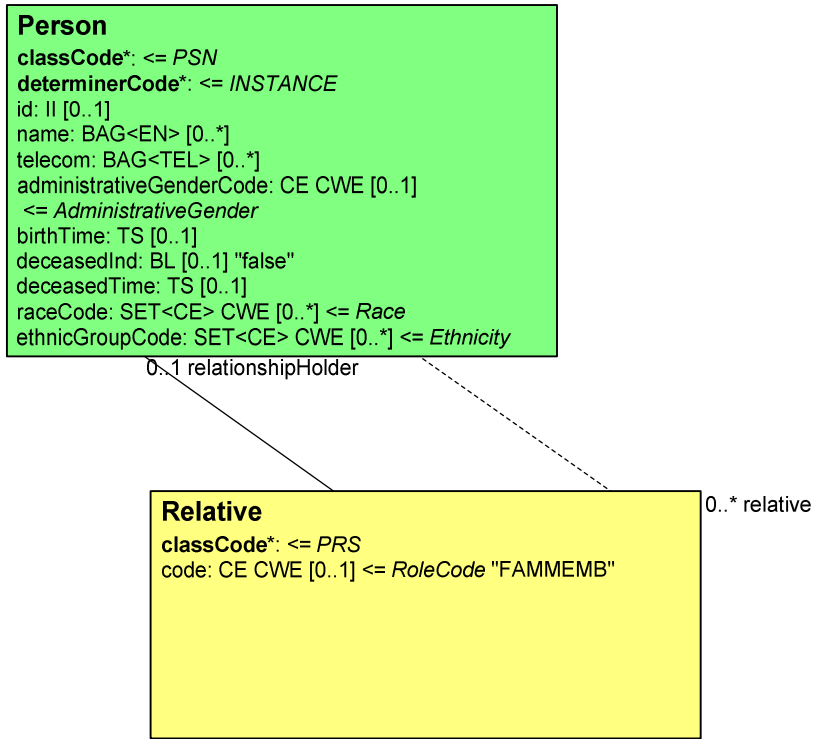


Figure 1: The recursive association of Person and relative which enables a hierarchical representation of a Pedigree to any depth needed.

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 B: Hierarchical vs. Flat Representation

- While a pedigree is hierarchical by nature, 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 (e.g., 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: Hierarchical and flat, where 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 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 and the above three ids are represented in the playing entity class (Person) id and in the associated Relative/Person classes of the mother and father of that relative
 - 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
- Personal relationships codes:
 - HL7 has a personal relationship vocabulary (RoleCode>PersonalRelationshipRoleType>FAMMEMB) bound to the Role.code attribute

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.

To assure consistency across different implementations of the Pedigree spec, the implementation guidance mandates the use of a flat representation, as follows:

- A Pedigree will have a flat representation with one nesting level
- The nesting level is used to represent mother and father ids of each relative
- Globally unique ids are assigned to the relative's mother & father using Entity (Person) id attribute
- Clinical and genomic data cannot be attached to the specification of the mother and father ID's

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 coreponding HMD⁹ and finally to the XML schema using the XML-ITS¹⁰ tools.

➤ The Pedigree Schema:

- ***POCG_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:

- ***FamilyHistorySample-POCG000040-v10.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.

- ***FamilyHistorySample-POCG000040-v10.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.

⁹ Hierarchical Message Definition.

¹⁰ Implementable Technology Specification.

POCG_MT000040.xsd

```
<?xml version="1.0" encoding="UTF-8" standalone="no"?>
<xs:schema xmlns:xs="http://www.w3.org/2001/XMLSchema" xmlns="urn:hl7-org:v3" xmlns:mif="urn:hl7-org:v3/mif"
targetNamespace="urn:hl7-org:v3" elementFormDefault="qualified">
  <!--
*****
* 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.
HMD to MIF Transform: $Id: RoseTreeHmdToMIFStaticModel.xml,v 1.12 2005/07/19 04:27:26 lmckenzi Exp $
Base transform: $Id: ConvertBase.xml,v 1.2 2005/04/17 03:20:15 lmckenzi Exp $
Package Id Conversion: $Id: TransformPackageIds.xml,v 1.3 2005/07/31 05:19:52 lmckenzi Exp $
HTML To MIF markup: $Id: HtmlToMIFMarkup.xml,v 1.2 2005/04/17 03:20:15 lmckenzi Exp $
Flat to Serialization Transform: $Id: MIFStaticModelFlatToSerialization.xml,v 1.3 2005/04/17 03:20:15 lmckenzi Exp $
Fix Names Transform: $Id: FixMifNames.xml,v 1.6 2005/04/17 03:20:15 lmckenzi Exp $
Base transform: $Id: ConvertBase.xml,v 1.2 2005/04/17 03:20:15 lmckenzi Exp $
Package Id Conversion: $Id: TransformPackageIds.xml,v 1.3 2005/07/31 05:19:52 lmckenzi Exp $
*
* Generated by XMLITS version 2.0
* MIF to XSD Transform $Id: StaticMifToXsd.xml,v 1.25 2005/07/09 20:20:15 lmckenzi Exp $
* Package Id Conversion: $Id: TransformPackageIds.xml,v 1.3 2005/07/31 05:19:52 lmckenzi Exp $
*
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* SUCH DAMAGE.
*
*****
-->
  <xs:annotation>
    <xs:documentation>Generated using schema builder version 2.0. Stylesheets:was rendered into XML using
software provided to HL7 by Beeler Consulting LLC.
HMD to MIF Transform: $Id: RoseTreeHmdToMIFStaticModel.xml,v 1.12 2005/07/19 04:27:26 lmckenzi Exp $
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HTML To MIF markup: $Id: HtmlToMIFMarkup.xml,v 1.2 2005/04/17 03:20:15 lmckenzi Exp $
Flat to Serialization Transform: $Id: MIFStaticModelFlatToSerialization.xml,v 1.3 2005/04/17 03:20:15 lmckenzi Exp $
Fix Names Transform: $Id: FixMifNames.xml,v 1.6 2005/04/17 03:20:15 lmckenzi Exp $
Base transform: $Id: ConvertBase.xml,v 1.2 2005/04/17 03:20:15 lmckenzi Exp $
Package Id Conversion: $Id: TransformPackageIds.xml,v 1.3 2005/07/31 05:19:52 lmckenzi Exp $.xml version
2.0</xs:documentation>
  </xs:annotation>
  <xs:include schemaLocation="..\coreschemas/infrastructureRoot.xsd"/>
  <xs:include schemaLocation="..\coreschemas/NarrativeBlock.xsd"/>
  <xs:include schemaLocation="COCT_MT930000.xsd"/>

```

```

<xs:complexType name="POCG_MT000040.Age">
  <xs:sequence>
    <xs:group ref="InfrastructureRootElements"/>
    <xs:element name="code" type="CD" minOccurs="0"/>
    <xs:element name="value" type="IVL_PQ" minOccurs="0"/>
    <xs:element name="pertinentInformation" type="POCG_MT000040.PertinentInformation"
nillable="true"/>
  </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"/>
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<xs:complexType name="POCG_MT000040.AnalysisResult">
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    <xs:group ref="InfrastructureRootElements"/>
    <xs:element name="code" type="CD" minOccurs="0"/>
    <xs:element name="value" type="ANY" minOccurs="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.ClinicalObservation">
  <xs:sequence>
    <xs:group ref="InfrastructureRootElements"/>
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    <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"/>
    <xs:element name="value" type="ANY" minOccurs="0"/>
    <xs:element name="methodCode" type="CE" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="subject" type="POCG_MT000040.Subject4" nillable="true" minOccurs="0"/>
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maxOccurs="unbounded"/>
  </xs:sequence>
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</xs:complexType>
<xs:complexType name="POCG_MT000040.Component">
  <xs:sequence>
    <xs:group ref="InfrastructureRootElements"/>
    <xs:choice>
      <xs:element name="age" type="POCG_MT000040.Age" nillable="true"/>
      <xs:element name="analysisResult" type="POCG_MT000040.AnalysisResult"
nillable="true"/>
      <xs:element name="percentageRisk" type="POCG_MT000040.PercentageRisk"
nillable="true"/>
      <xs:element name="probability" type="POCG_MT000040.Probability" nillable="true"/>
      <xs:element name="relativeRisk" type="POCG_MT000040.RelativeRisk"
nillable="true"/>
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  </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:group ref="InfrastructureRootElements"/>
    <xs:choice>
      <xs:element name="geneticLocus" type="COCT_MT930000.GeneticLocus"
nillable="true"/>
      <xs:element name="clinicalObservation" type="POCG_MT000040.ClinicalObservation"
nillable="true"/>
    </xs:choice>
  </xs:sequence>
  <xs:attributeGroup ref="InfrastructureRootAttributes"/>
  <xs:attribute name="typeCode" type="ActRelationshipHasComponent" use="optional" default="COMP"/>

```

```

</xs:complexType>
<xs:complexType name="POCG_MT000040.Component3">
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    <xs:element name="pedigreeAnalysisResults" type="POCG_MT000040.PedigreeAnalysisResults"
nillable="true"/>
  </xs:sequence>
  <xs:attributeGroup ref="InfrastructureRootAttributes"/>
  <xs:attribute name="typeCode" type="ActRelationshipHasComponent" use="optional" default="COMP"/>
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<xs:complexType name="POCG_MT000040.ControlVariable">
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    <xs:group ref="InfrastructureRootElements"/>
    <xs:element name="inputParameters" type="POCG_MT000040.InputParameters" nillable="true"/>
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  <xs:attribute name="typeCode" type="ActRelationshipType" use="optional" fixed="CTRLV"/>
</xs:complexType>
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    <xs:element name="value" type="IVL_PQ" minOccurs="0"/>
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  <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.DeceasedEstimatedAge">
  <xs:sequence>
    <xs:group ref="InfrastructureRootElements"/>
    <xs:element name="code" type="CD" minOccurs="0"/>
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  <xs:attributeGroup ref="InfrastructureRootAttributes"/>
  <xs:attribute name="classCode" type="ActClassObservation" use="optional" default="OBS"/>
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    <xs:element name="code" type="CD" minOccurs="0"/>
    <xs:element name="text" type="ED" minOccurs="0"/>
    <xs:element name="effectiveTime" type="TS" minOccurs="0"/>
    <xs:element name="confidentialityCode" type="CE" minOccurs="0" maxOccurs="unbounded"/>
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    <xs:element name="languageCode" type="CE" minOccurs="0"/>
    <xs:element name="methodCode" type="CE" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="subject" type="POCG_MT000040.Subject5" nillable="true" minOccurs="0"/>
    <xs:element name="component1" type="POCG_MT000040.Component2" nillable="true"
minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="component2" type="POCG_MT000040.Component3" nillable="true"
minOccurs="0" maxOccurs="unbounded"/>
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  <xs:attributeGroup ref="InfrastructureRootAttributes"/>
  <xs:attribute name="classCode" type="ActClassObservation" use="optional" default="OBS"/>
  <xs:attribute name="moodCode" type="ActMood" use="optional" fixed="EVN"/>
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    <xs:element name="value" type="ANY" minOccurs="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.CRT"/>
</xs:complexType>

```

```

<xs:complexType name="POCG_MT000040.LivingEstimatedAge">
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  </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.Patient">
  <xs:sequence>
    <xs:group ref="InfrastructureRootElements"/>
    <xs:element name="id" type="II" minOccurs="0"/>
    <xs:element name="patientPerson" type="POCG_MT000040.Person" nillable="true"/>
    <xs:element name="provider" type="POCG_MT000040.Provider" nillable="true" minOccurs="0"/>
    <xs:element name="subjectOf1" type="POCG_MT000040.Subject3" nillable="true"
minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="subjectOf2" type="POCG_MT000040.Subject" nillable="true" minOccurs="0"
maxOccurs="unbounded"/>
  </xs:sequence>
  <xs:attributeGroup ref="InfrastructureRootAttributes"/>
  <xs:attribute name="classCode" type="RoleClass" use="optional" fixed="PAT"/>
</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="code" type="CD" minOccurs="0"/>
    <xs:element name="derivationExpr" type="ST" minOccurs="0"/>
    <xs:element name="text" type="ED" minOccurs="0"/>
    <xs:element name="effectiveTime" type="IVL_TS" minOccurs="0"/>
    <xs:element name="methodCode" type="CE" minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="component" type="POCG_MT000040.Component" nillable="true"
minOccurs="0" maxOccurs="unbounded"/>
    <xs:element name="controlVariable" type="POCG_MT000040.ControlVariable" nillable="true"
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  </xs:sequence>
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  <xs:attribute name="negationInd" type="bl" use="optional"/>
</xs:complexType>
<xs:complexType name="POCG_MT000040.PercentageRisk">
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    <xs:element name="value" type="INT" minOccurs="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.Person">
  <xs:sequence>
    <xs:group ref="InfrastructureRootElements"/>
    <xs:element name="id" type="II" minOccurs="0"/>
    <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"/>
    <xs:element name="birthTime" type="TS" minOccurs="0"/>
    <xs:element name="deceasedInd" type="BL" minOccurs="0"/>
    <xs:element name="deceasedTime" type="TS" minOccurs="0"/>
    <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" nillable="true" minOccurs="0"
maxOccurs="unbounded"/>
  </xs:sequence>
  <xs:attributeGroup ref="InfrastructureRootAttributes"/>
  <xs:attribute name="classCode" type="EntityClass" use="optional" fixed="PSN"/>

```



```

        <xs:attribute name="determinerCode" type="EntityDeterminer" use="optional" fixed="INSTANCE"/>
    </xs:complexType>
    <xs:complexType name="POCG_MT000040.PertinentInformation">
        <xs:sequence>
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        </xs:sequence>
        <xs:attributeGroup ref="InfrastructureRootAttributes"/>
        <xs:attribute name="typeCode" type="ActRelationshipPertains" use="optional" default="PERT"/>
    </xs:complexType>
    <xs:complexType name="POCG_MT000040.Probability">
        <xs:sequence>
            <xs:group ref="InfrastructureRootElements"/>
            <xs:element name="code" type="CD" minOccurs="0"/>
            <xs:element name="value" type="PQ" minOccurs="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.Provider">
        <xs:sequence>
            <xs:group ref="InfrastructureRootElements"/>
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            <xs:element name="name" type="EN" minOccurs="0" maxOccurs="unbounded"/>
        </xs:sequence>
        <xs:attributeGroup ref="InfrastructureRootAttributes"/>
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        <xs:attribute name="determinerCode" type="EntityDeterminer" use="optional" fixed="INSTANCE"/>
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    <xs:complexType name="POCG_MT000040.Relative">
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            <xs:element name="relationshipHolder" type="POCG_MT000040.Person" nillable="true"
minOccurs="0"/>
            <xs:element name="subjectOf1" type="POCG_MT000040.Subject3" nillable="true"
minOccurs="0" maxOccurs="unbounded"/>
            <xs:element name="subjectOf2" type="POCG_MT000040.Subject" nillable="true" minOccurs="0"
maxOccurs="unbounded"/>
        </xs:sequence>
        <xs:attributeGroup ref="InfrastructureRootAttributes"/>
        <xs:attribute name="classCode" type="RoleClass" use="optional" fixed="PRS"/>
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    <xs:complexType name="POCG_MT000040.RelativeRisk">
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            <xs:element name="value" type="PQ" minOccurs="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.SourceOf">
        <xs:sequence>
            <xs:group ref="InfrastructureRootElements"/>
            <xs:element name="clinicalObservation" type="POCG_MT000040.ClinicalObservation"
nillable="true"/>
        </xs:sequence>
        <xs:attributeGroup ref="InfrastructureRootAttributes"/>
        <xs:attribute name="typeCode" type="ActRelationshipType" use="required"/>
    </xs:complexType>
    <xs:complexType name="POCG_MT000040.Subject">
        <xs:sequence>
            <xs:group ref="InfrastructureRootElements"/>
            <xs:choice>
                <xs:element name="geneticLocus" type="COCT_MT930000.GeneticLocus"
nillable="true"/>

```

```

nillable="true"/>
        <xs:element name="clinicalObservation" type="POCG_MT000040.ClinicalObservation"
            </xs:choice>
        </xs:sequence>
        <xs:attributeGroup ref="InfrastructureRootAttributes"/>
        <xs:attribute name="typeCode" type="ParticipationTargetSubject" use="optional" default="SBJ"/>
    </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:attributeGroup ref="InfrastructureRootAttributes"/>
        <xs:attribute name="typeCode" type="ParticipationTargetSubject" use="optional" default="SBJ"/>
    </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:attributeGroup ref="InfrastructureRootAttributes"/>
        <xs:attribute name="typeCode" type="ActRelationshipType" use="optional" fixed="SUBJ"/>
    </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:attributeGroup ref="InfrastructureRootAttributes"/>
        <xs:attribute name="typeCode" type="ParticipationTargetSubject" use="optional" default="SBJ"/>
    </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). 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"/>
  <subject>
    <patient>
      <!-- the following id could be the id assigned to the patient by the healthcare provider, not necessarily related to the pedigree ids -->
      <!-- The OID 2.16.840.1.113883.6.117 represents the entity "Computer-Stored Ambulatory Records (COSTAR). Boston (MA): Massachusetts General Hospital, 1989-1995.", per the HL7 OID Registry. This OID has been used below for illustration purposes only -->
      <id root="2.16.840.1.113883.6.117" extension="555"/>
      <!-- PATIENT -->
      <patientPerson>
        <!-- The following id belongs to the Patient class (Entity). In this sample, all persons (i.e., patient and relatives) were assigned a single id through the Person.id attribute which either nests within the 'patientPerson' element (for the patient) or within 'relationshipHolder' for all relatives. Only the extension component of the id value was populated in this sample. The root needs to be populated. 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. -->
        <id root="2.16.840.1.113883.6.117" extension="555.001"/>
        <administrativeGenderCode code="F"/>
        <birthTime value="1957"/>
        <!-- MOTHER -->
        <relative>
          <code code="NMTH"/>
          <relationshipHolder>
            <id root="2.16.840.1.113883.6.117" extension="555.002"/>
            <!-- The value 'true' means that this person is dead. Default value is 'false' -->
            <deceasedInd value="true"/>
            <relative>
              <!-- MATERNAL GRANDFATHER -->
              <code code="NFTH"/>
              <relationshipHolder>
                <id root="2.16.840.1.113883.6.117" extension="555.004"/>
              </relationshipHolder>
            </relative>
            <relative>
              <!-- MATERNAL GRANDMOTHER -->
              <code code="NMTH"/>
              <relationshipHolder>
                <id root="2.16.840.1.113883.6.117" extension="555.005"/>
              </relationshipHolder>
            </relative>
          </relationshipHolder>
        </relative>
        <!-- The following construct represents the estimated deceased age (72) -->
        <subjectOf1>
          <deceasedEstimatedAge>
            <value value="72" unit="year"/>
          </deceasedEstimatedAge>
        </subjectOf1>
        <subjectOf2>
          <clinicalObservation>
```

```

mother-->
<!-- Ovarian Cancer observation of the patient's
<code code="V1043" codeSystemName="ICD"
displayName="HX OF OVARIAN MALIGNANCY"/>
<!-- The following construct represents the estimated
age at which the above diagnosis was made (40)-->
<subject>
  <dataEstimatedAge>
    <value value="40" unit="year"/>
  </dataEstimatedAge>
</subject>
</clinicalObservation>
</subjectOf2>
</relative>
<!--maternal grandparents-->
<relative>
  <!-- MATERNAL GRANDFATHER -->
  <code code="GRFTH"/>
  <relationshipHolder>
    <id root="2.16.840.1.113883.6.117" extension="555.004"/>
  </relationshipHolder>
  <subjectOf1>
    <livingEstimatedAge>
      <value value="98" unit="year"/>
    </livingEstimatedAge>
  </subjectOf1>
</relative>
<!-- end of maternal grandfather data-->
<relative>
  <!-- MATERNAL GRANDMOTHER -->
  <code code="GRMTH"/>
  <relationshipHolder>
    <id root="2.16.840.1.113883.6.117" extension="555.005"/>
  </relationshipHolder>
  <subjectOf1>
    <livingEstimatedAge>
      <value value="67" unit="year"/>
    </livingEstimatedAge>
  </subjectOf1>
  <subjectOf2>
    <clinicalObservation>
      <code code="V1043" codeSystemName="ICD"
      displayName="HX OF OVARIAN MALIGNANCY"/>
      <subject>
        <dataEstimatedAge>
          <value value="50" unit="year"/>
        </dataEstimatedAge>
      </subject>
    </clinicalObservation>
  </subjectOf2>
</relative>
<!-- 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"/>
    <relative>
      <!-- PATERNAL GRANDFATHER -->
      <code code="GRFTH"/>
      <relationshipHolder>
        <id root="2.16.840.1.113883.6.117"
        extension="555.006"/>
      </relationshipHolder>
    </relative>
  </relationshipHolder>
</relative>
<relative>
  <!-- PATERNAL GRANDMOTHER -->
  <code code="GRMTH"/>
  <relationshipHolder>

```

```

                                <id root="2.16.840.1.113883.6.117"
extension="555.007"/>
                                </relationshipHolder>
                                </relative>
                                </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"/>
                                        <deceasedInd value="true"/>
                                        <relative>
                                            <code code="NMTH"/>
                                            <relationshipHolder>
                                                <id root="2.16.840.1.113883.6.117"
extension="555.002"/>
                                            </relationshipHolder>
                                        </relative>
                                    </relationshipHolder>
                                </relative>
                                <code code="NFTH"/>
                                <relationshipHolder>
                                    <id root="2.16.840.1.113883.6.117"
extension="555.003"/>
                                </relationshipHolder>
                                </relative>
                                </relationshipHolder>
                                <subjectOf1>
                                    <deceasedEstimatedAge>
                                        <value value="67" unit="year"/>
                                    </deceasedEstimatedAge>
                                </subjectOf1>

```

```

        <subjectOf2>
          <clinicalObservation>
            <!-- Ovarian Cancer observation of the patient's sister-->
            <code code="V1043" codeSystemName="ICD"
            </code>
            <subject>
              <dataEstimatedAge>
                <value value="60" unit="year"/>
              </dataEstimatedAge>
            </subject>
          </clinicalObservation>
        </subjectOf2>
      </relative>
      <!-- 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"
              </id>
            </relationshipHolder>
          </relative>
          <relative>
            <code code="NFTH"/>
            <relationshipHolder>
              <id root="2.16.840.1.113883.6.117"
              </id>
            </relationshipHolder>
          </relative>
        </relationshipHolder>
      </relative>
      <subjectOf1>
        <deceasedEstimatedAge>
          <value value="55" unit="year"/>
        </deceasedEstimatedAge>
      </subjectOf1>
      <subjectOf2>
        <clinicalObservation>
          <!-- Ovarian Cancer observation of the patient's sister-->
          <code code="V1043" codeSystemName="ICD"
          </code>
          <subject>
            <dataEstimatedAge>
              <value value="50" unit="year"/>
            </dataEstimatedAge>
          </subject>
        </clinicalObservation>
      </subjectOf2>
    </relative>
    <!-- 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>
    </relative>
    <!-- end of HUSBAND data-->
    <!-- DAUGHTER-->

```

```

<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="555.001"/>
      </relationshipHolder>
    </relative>
    <relative>
      <code code="NFTH"/>
      <relationshipHolder>
        <id root="2.16.840.1.113883.6.117"
extension="555.01"/>
      </relationshipHolder>
    </relative>
  </relationshipHolder>
</subjectOf1>
  <deceasedEstimatedAge>
    <value value="33" unit="year"/>
  </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" codeSystem="HGNC"/>
    </value>
    <component3>
      <sequenceVariation moodCode="EVN">
        <value xsi:type="CE"
code="185delAG"/>
        <!-- The 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
typeCode="PERT">
          <clinicalPhenotype
classCode="ORGANIZER">
            <component2>
              <!-- the following construct hold a known phenotype in the literature, in this example,
is a study taken from OMIM under -BRCA1 entry with OMIM id 113705, where .0003 standas for this specific
variation-->
              <knownClinicalPhenotype>
                <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>
                <value xsi:type="CE" code="113705.0003" codeSystemName="OMIM"/>
              </knownClinicalPhenotype>
            </component2>
          </clinicalPhenotype>
        </pertinentInformation>
      </sequenceVariation>
    </component3>
  </geneticLocus>
</subjectOf2>

```

```

                                </clinicalPhenotype>
                                </pertinentInformation>
                                </sequenceVariation>
                                </component3>
                                </geneticLocus>
                                </subjectOf2>
                                <!-- CLINICAL DATA-->
                                <subjectOf2>
                                <clinicalObservation>
                                <!-- Ovarian Cancer observation of the patient's
daughter-->
                                <code code="V1043" codeSystemName="ICD"
displayName="HX OF OVARIAN MALIGNANCY"/>
                                <subject>
                                <dataEstimatedAge>
                                <value value="30" unit="year"/>
                                </dataEstimatedAge>
                                </subject>
                                </clinicalObservation>
                                </subjectOf2>
                                </relative>
                                <!-- 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-->
                                <text>PROBABILITY OF DEVELOPING BREAST CANCER BEFORE THE AGE
INDICATED</text>
                                <effectiveTime value="200601132301"/>
                                <methodCode code="BRCAPRO"/>
                                <component>
                                <age>
                                <value>
                                <low nullFlavor="QS"/>
                                <high value="53" unit="year"/>
                                </value>
                                <pertinentInformation>
                                <probability>
                                <value value="0.000168"/>
                                </probability>
                                </pertinentInformation>
                                </age>
                                </component>
                                <component>
                                <age>
                                <value>
                                <low value="54" unit="year"/>
                                <high value="57" unit="year"/>
                                </value>
                                <pertinentInformation>
                                <probability>
                                <value value="0.000368"/>
                                </probability>

```



```

    </pertinentInformation>
  </age>
</component>
<component>
  <age>
    <value>
      <low value="58" unit="year"/>
      <high value="62" unit="year"/>
    </value>
    <pertinentInformation>
      <probability>
        <value value="0.000594"/>
      </probability>
    </pertinentInformation>
  </age>
</component>
<component>
  <age>
    <value>
      <low value="63" unit="year"/>
      <high value="67" unit="year"/>
    </value>
    <pertinentInformation>
      <probability>
        <value value="0.000838"/>
      </probability>
    </pertinentInformation>
  </age>
</component>
<component>
  <age>
    <value>
      <low value="68" unit="year"/>
      <high value="72" unit="year"/>
    </value>
    <pertinentInformation>
      <probability>
        <value value="0.001089"/>
      </probability>
    </pertinentInformation>
  </age>
</component>
<component>
  <age>
    <value>
      <low value="73" unit="year"/>
      <high value="77" unit="year"/>
    </value>
    <pertinentInformation>
      <probability>
        <value value="0.001327"/>
      </probability>
    </pertinentInformation>
  </age>
</component>
<component>
  <age>
    <value>
      <low value="78" unit="year"/>
      <high value="82" unit="year"/>
    </value>
    <pertinentInformation>
      <probability>
        <value value="0.001530"/>
      </probability>
    </pertinentInformation>
  </age>
</component>
<component>
  <age>

```

```
<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>
```

FamilyHistorySample-POCG000040-v12.s2-extended.xml

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).
-->
<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"/>
  <subject>
    <patient>
      <!--the following id could be the id assigned to the patient by the healthcare provider, not necessarily
related to the pedigree ids-->
      <!-- The OID 2.16.840.1.113883.6.117 represents the entity "Computer-Stored Ambulatory Records
(COSTAR). Boston (MA): Massachusetts General Hospital, 1989-1995.", per the HL7 OID Registry. This OID has been used below
for illustration purposes only-->
      <id root="2.16.840.1.113883.6.117" extension="555"/>
      <!-- PATIENT-->
      <patientPerson>
        <!-- The following id belongs to the Patient class (Entity). In this sample, all persons (i.e.,
patient and relatives) were assigned a single id through the Person.id attribute which either nests within the 'patientPerson' element
(for the patient) or within 'relationshipHolder' for all relatives. Only the extension component of the id value was populated in this
sample. The root needs to be populated. 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.-->
        <id root="2.16.840.1.113883.6.117" extension="555.001"/>
        <administrativeGenderCode code="F"/>
        <birthTime value="1957"/>
        <!-- MOTHER-->
        <relative>
          <code code="NMTH"/>
          <relationshipHolder>
            <id root="2.16.840.1.113883.6.117" extension="555.002"/>
            <!-- The value 'true' means that this person is dead. Default value is
'false'-->
            <deceasedInd value="true"/>
            <relative>
              <!-- MATERNAL GRANDFATHER -->
              <code code="NFTH"/>
              <relationshipHolder>
                <id root="2.16.840.1.113883.6.117"
extension="555.004"/>
              </relationshipHolder>
            </relative>
            <relative>
              <!-- MATERNAL GRANDMOTHER -->
              <code code="NMTH"/>
              <relationshipHolder>
                <id root="2.16.840.1.113883.6.117"
extension="555.005"/>
              </relationshipHolder>
            </relative>
          </relationshipHolder>
        </relative>
        <!-- The following construct represents the estimated deceased age (72)-->
        <subjectOf1>
          <deceasedEstimatedAge>
            <value value="72" unit="year"/>
          </deceasedEstimatedAge>
        </subjectOf1>
      </patientPerson>
    </patient>
  </subject>
</FamilyHistory>
```

```

        </deceasedEstimatedAge>
    </subjectOf1>
    <subjectOf2>
        <clinicalObservation>
            <!-- Ovarian Cancer observation of the patient's
mother-->
            <code code="V1043" codeSystemName="ICD"
displayName="HX OF OVARIAN MALIGNANCY"/>
            <!-- The following construct represents the estimated
age at which the above diagnosis was made (40)-->
            <subject>
                <dataEstimatedAge>
                    <value value="40" unit="year"/>
                </dataEstimatedAge>
            </subject>
        </clinicalObservation>
    </subjectOf2>
</relative>
<!--maternal grandparents-->
<relative>
    <!-- MATERNAL GRANDFATHER -->
    <code code="GRFTH"/>
    <relationshipHolder>
        <id root="2.16.840.1.113883.6.117" extension="555.004"/>
    </relationshipHolder>
    <subjectOf1>
        <livingEstimatedAge>
            <value value="98" unit="year"/>
        </livingEstimatedAge>
    </subjectOf1>
</relative>
<!-- end of maternal grandfather data-->
<relative>
    <!-- MATERNAL GRANDMOTHER -->
    <code code="GRMTH"/>
    <relationshipHolder>
        <id root="2.16.840.1.113883.6.117" extension="555.005"/>
    </relationshipHolder>
    <subjectOf1>
        <livingEstimatedAge>
            <value value="67" unit="year"/>
        </livingEstimatedAge>
    </subjectOf1>
    <subjectOf2>
        <clinicalObservation>
            <code code="V1043" codeSystemName="ICD"
displayName="HX OF OVARIAN MALIGNANCY"/>
            <subject>
                <dataEstimatedAge>
                    <value value="50" unit="year"/>
                </dataEstimatedAge>
            </subject>
        </clinicalObservation>
    </subjectOf2>
</relative>
<!-- 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"/>
        <relative>
            <!-- PATERNAL GRANDFATHER -->
            <code code="GRFTH"/>
            <relationshipHolder>
                <id root="2.16.840.1.113883.6.117"
extension="555.006"/>
            </relationshipHolder>
        </relative>
    </relationshipHolder>
</relative>

```

```

        <relative>
            <!-- PATERNAL GRANDMOTHER -->
            <code code="GRMTH"/>
            <relationshipHolder>
                <id root="2.16.840.1.113883.6.117"
extension="555.007"/>
            </relationshipHolder>
        </relative>
    </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"/>
        <deceasedInd value="true"/>
        <relative>
            <code code="NMTH"/>
            <relationshipHolder>
                <id root="2.16.840.1.113883.6.117"
extension="555.002"/>
            </relationshipHolder>
        </relative>
    </relationshipHolder>
    <relative>
        <code code="NFTH"/>
        <relationshipHolder>
            <id root="2.16.840.1.113883.6.117"
extension="555.003"/>
        </relationshipHolder>
    </relative>
</relationshipHolder>
</subjectOf1>

```

```

        <deceasedEstimatedAge>
          <value value="67" unit="year"/>
        </deceasedEstimatedAge>
      </subjectOf1>
    <subjectOf2>
      <clinicalObservation>
        <!-- Ovarian Cancer observation of the patient's sister-->
        <code code="V1043" codeSystemName="ICD"
        displayName="HX OF OVARIAN MALIGNANCY"/>
        <subject>
          <dataEstimatedAge>
            <value value="60" unit="year"/>
          </dataEstimatedAge>
        </subject>
      </clinicalObservation>
    </subjectOf2>
  </relative>
  <!-- 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>
      <relative>
        <code code="NFTH"/>
        <relationshipHolder>
          <id root="2.16.840.1.113883.6.117"
          extension="555.003"/>
        </relationshipHolder>
      </relative>
    </relationshipHolder>
  </relative>
  <subjectOf1>
    <deceasedEstimatedAge>
      <value value="55" unit="year"/>
    </deceasedEstimatedAge>
  </subjectOf1>
  <subjectOf2>
    <clinicalObservation>
      <!-- Ovarian Cancer observation of the patient's sister-->
      <code code="V1043" codeSystemName="ICD"
      displayName="HX OF OVARIAN MALIGNANCY"/>
      <subject>
        <dataEstimatedAge>
          <value value="50" unit="year"/>
        </dataEstimatedAge>
      </subject>
    </clinicalObservation>
  </subjectOf2>
</relative>
<!-- 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>
</relative>

```

```

        </subjectOf1>
    </relative>
    <!-- end of HUSBAND data-->
    <!-- DAUGHTER-->
    <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="555.001"/>
                </relationshipHolder>
            </relative>
            <relative>
                <code code="NFTH"/>
                <relationshipHolder>
                    <id root="2.16.840.1.113883.6.117"
extension="555.01"/>
                </relationshipHolder>
            </relative>
        </relationshipHolder>
    </subjectOf1>
    <deceasedEstimatedAge>
        <value value="33" unit="year"/>
    </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" codeSystem="HGNC"/>
        </value>
        <component3>
            <sequenceVariation moodCode="EVN">
                <value xsi:type="CE"
code="185delAG"/>
                <!-- The 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.-->
            </sequenceVariation>
        </component3>
        <interpretationCode
code="DELETERIOUS"/>
        <pertinentInformation
typeCode="PERT">
            <clinicalPhenotype
classCode="ORGANIZER">
                <component2>
                    <!-- the following construct hold a known phenotype in the literature, in this example,
is a study taken from OMIM under -BRCA1 entry with OMIM id 113705, where .0003 standas for this specific
variation-->
                    <knownClinicalPhenotype>
                        <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>
                        <value xsi:type="CE" code="113705.0003" codeSystemName="OMIM"/>
                    </knownClinicalPhenotype>
                </component2>
            </clinicalPhenotype>
        </pertinentInformation>
    </geneticLocus>
</subjectOf2>

```

```

</knownClinicalPhenotype>
</component2>
</clinicalPhenotype>
</pertinentInformation>
</sequenceVariation>
</component3>
<component4>
<sequence moodCode="EVN">
<!-- full sequence of the
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 -->
(note that the actual sequences
<code code="BSMLcon3"/>
<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 CGCGGGGAGC CCCGCTTCAT CGCCGTGGGC
ACACGCAGTT CGTGCGGTTT GACAGCGACG CCGCGAGCCA
CCGCGGGGCGC CGTGGATAGA GCAGGAGGGG CCGGAGTATT
GACACGGAAT GTGAAGGCC AGTCACAGAC TGACCGAGTG
CCCTGCGCGG CTAACAAC 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
TGCGCTTTG GACCGCGGCG GACATGGCGG CTCAGATCAC
TGGGAGGCGG CCCATGTGGC GGAGCAGCAG AGAGCCTACC
GTGCGTGGAG TGGCTCCGCA GATACCTGGA GAACGGGAAG
AGCGCACGG
</bsml:Seq-data>
</bsml:Sequence>
</bsml:Sequences>

```


<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>

belongs to the HL7 Sequence class and represents the sequencing method.

down yet and several options are suggested in the Genotype documentation.-->

moodCode="EVN">

code="DNA"/>

<!-- The HL7 'text' attribute is of ED data type and this data type has a reference tag that allows the to the BSML Isoform element.

referencing enables the linking between the bubbled-up object like this sequence variation one,

the encapsulated data in the Sequence class.-->

<reference value="#SNP456"/>

xsi:type="CE" code="633delC"/>

interpretationCode value should be drawn from the ObservationInterpretation vocabulary that doesn't have the DELETERIOUS value (abnormal is the closest)

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 theinstance of the referred diagnosis resides (e.g., in the patient medical records)-->

<component3>

<externalObservedClinicalPhenotype>

<id root="2.16.840.1.113883" extension="diagnosis1"/>

</bsml:BsmI>

</value>

<!-- The following attribute

vocabulary has not been nailed

<methodCode code="SBT"/>

<derivedFrom3>

<sequenceVariation

<code

<text>

</text>

<value

<!-- The

has been proposed to

```

        </externalObservedClinicalPhenotype>
    </component3>
</clinicalPhenotype>
</pertinentInformation>
<derivedFrom>
<associatedProperty>
<code code="TYPE"/>
<value xsi:type="CV" code="MUTATION"/>
</associatedProperty>
</derivedFrom>
</sequenceVariation>
</derivedFrom3>
</sequence>
</component4>
</geneticLocus>
</subjectOf2>
<!-- CLINICAL DATA-->
<subjectOf2>
<clinicalObservation>
    <!-- Ovarian Cancer observation of the patient's
daughter-->
    <code code="V1043" codeSystemName="ICD"
displayName="HX OF OVARIAN MALIGNANCY"/>
    <subject>
        <dataEstimatedAge>
            <value value="30" unit="year"/>
        </dataEstimatedAge>
    </subject>
</clinicalObservation>
</subjectOf2>
</relative>
    <!-- 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-->
        <text>PROBABILITY OF DEVELOPING BREAST CANCER BEFORE THE AGE
INDICATED</text>
        <effectiveTime value="200601132301"/>
        <methodCode code="BRCAPRO"/>
        <component>
            <age>
                <value>

```

```

        <low nullFlavor="QS"/>
        <high value="53" unit="year"/>
    </value>
    <pertinentInformation>
        <probability>
            <value value="0.000168"/>
        </probability>
    </pertinentInformation>
</age>
</component>
<component>
    <age>
        <value>
            <low value="54" unit="year"/>
            <high value="57" unit="year"/>
        </value>
        <pertinentInformation>
            <probability>
                <value value="0.000368"/>
            </probability>
        </pertinentInformation>
    </age>
</component>
<component>
    <age>
        <value>
            <low value="58" unit="year"/>
            <high value="62" unit="year"/>
        </value>
        <pertinentInformation>
            <probability>
                <value value="0.000594"/>
            </probability>
        </pertinentInformation>
    </age>
</component>
<component>
    <age>
        <value>
            <low value="63" unit="year"/>
            <high value="67" unit="year"/>
        </value>
        <pertinentInformation>
            <probability>
                <value value="0.000838"/>
            </probability>
        </pertinentInformation>
    </age>
</component>
<component>
    <age>
        <value>
            <low value="68" unit="year"/>
            <high value="72" unit="year"/>
        </value>
        <pertinentInformation>
            <probability>
                <value value="0.001089"/>
            </probability>
        </pertinentInformation>
    </age>
</component>
<component>
    <age>
        <value>
            <low value="73" unit="year"/>
            <high value="77" unit="year"/>
        </value>
        <pertinentInformation>
            <probability>

```

```

        <value value="0.001327"/>
      </probability>
    </pertinentInformation>
  </age>
</component>
<component>
  <age>
    <value>
      <low value="78" unit="year"/>
      <high value="82" unit="year"/>
    </value>
    <pertinentInformation>
      <probability>
        <value value="0.001530"/>
      </probability>
    </pertinentInformation>
  </age>
</component>
<component>
  <age>
    <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>

```

Appendix E: Relative Codes from the HL7 RoleCode Vocabulary - PersonalRelationshipRoleType

| | | | |
|---------|--|------------------------------|--|
| 0-
A | _PersonalRelationshipRoleType
v:PersonalRelationshipRoleType | PersonalRelationshipRoleType | <p>Concept Relationships:
Generalizes (derived):
FAMMEMB FRND NBOR ROOM</p> <p>Concept Properties:
<i>internalId:</i> 21131</p> |
| 1-
S | . FAMMEMB
v:FamilyMember | Family Member | <p>Definition:
A relationship between two people characterizing their "familial" relationship</p> <p>Concept Relationships:
Specializes:
_PersonalRelationshipRoleType
Generalizes (derived):
CHILD EXT PRN SIB SIGOTHR</p> <p>Concept Properties:
<i>internalId:</i> 17926</p> |
| 2-
S | . . CHILD
v:Child | Child | <p>Definition:
The player of the role is a child of the scoping entity.</p> <p>Concept Relationships:
Specializes: FAMMEMB
Generalizes (derived):
CHLDADOPT CHLDFOST
CHLDINLAW DAUC NCHILD
SONC STPCHLD</p> <p>Concept Properties:
<i>internalId:</i> 16360</p> |
| 3-
S | . . . CHLDADOPT
v:AdoptedChild | adopted child | <p>Definition:
The player of the role is a child taken into a family through legal means and raised by the scoping person (parent) as his or her own child.</p> <p>Concept Relationships:
Specializes: CHILD
Generalizes (derived):
DAUADOPT SONADOPT</p> <p>Concept Properties:
<i>internalId:</i> 11564</p> |
| 4-
L | DAUADOPT | adopted daughter | <p>Definition:
The player of the role is a</p> |

| | | | |
|---------|---|-----------------|---|
| | | | <p>female child taken into a family through legal means and raised by the scoping person (parent) as his or her own child.</p> <p>Concept Relationships:
 Specializes: CHLDADOPT DAUC</p> <p>Concept Properties:
 <i>internalId:</i> 19756</p> |
| 4-
L | SONADOPT | adopted son | <p>Definition:</p> <p>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.</p> <p>Concept Relationships:
 Specializes: CHLDADOPT SONC</p> <p>Concept Properties:
 <i>internalId:</i> 19757</p> |
| 3-
S | CHLDFOST
v:FosterChild | foster child | <p>Definition:</p> <p>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.</p> <p>Concept Relationships:
 Specializes: CHILD
 Generalizes (derived): DAUFOST SONFOST</p> <p>Concept Properties:
 <i>internalId:</i> 11565</p> |
| 4-
L | DAUFOST | foster daughter | <p>Definition:</p> <p>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.</p> <p>Concept Relationships:
 Specializes: CHLDFOST DAUC</p> <p>Concept Properties:
 <i>internalId:</i> 19758</p> |
| 4-
L | SONFOST | foster son | <p>Definition:</p> <p>The player of the role is a male</p> |

| | | | |
|---------|--|-----------------|--|
| | | | <p>child receiving parental care and nurture from the scoping person (parent) but not related to him or her through legal or blood ties.</p> <p>Concept Relationships:
 Specializes: CHLDFOST
 SONC</p> <p>Concept Properties:
 <i>internalId:</i> 19759</p> |
| 3-
S | . . . CHLDINLAW
v:ChildInLaw | child in-law | <p>Definition:</p> <p>The player of the role is the spouse of scoping person's child.</p> <p>Concept Relationships:
 Specializes: CHILD
 Generalizes (derived):
 DAUINLAW SONINLAW</p> <p>Concept Properties:
 <i>internalId:</i> 11563</p> |
| 4-
L | DAUINLAW | daughter in-law | <p>Definition:</p> <p>The player of the role is the wife of scoping person's son.</p> <p>Concept Relationships:
 Specializes: CHLDINLAW</p> <p>Concept Properties:
 <i>internalId:</i> 19760</p> |
| 4-
L | SONINLAW | son in-law | <p>Definition:</p> <p>The player of the role is the husband of scoping person's daughter.</p> <p>Concept Relationships:
 Specializes: CHLDINLAW</p> <p>Concept Properties:
 <i>internalId:</i> 19761</p> |
| 3-
S | . . . DAUC | Daughter | <p>Definition:</p> <p>Description: The player of the role is a female child (of any type) of scoping entity (parent)</p> <p>Concept Relationships:
 Specializes: CHILD
 Generalizes (derived): DAU
 DAUADOPT DAUFOST STPDAU</p> <p>Concept Properties:</p> |

| | | | |
|---------|---|------------------------------|---|
| | | | <i>internalId:</i> 22915 |
| 4-
L | DAU | natural daughter
Daughter | <p>Definition:</p> <p>The player of the role is a female offspring of the scoping entity (parent).</p> <p>Concept Relationships:
Specializes: DAUC NCHILD</p> <p>Concept Properties:
<i>internalId:</i> 16361</p> |
| 4-
L | DAUADOPT | adopted daughter | <p>Definition:</p> <p>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.</p> <p>Concept Relationships:
Specializes: CHLDADOPT DAUC</p> <p>Concept Properties:
<i>internalId:</i> 19756</p> |
| 4-
L | DAUFOST | foster daughter | <p>Definition:</p> <p>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.</p> <p>Concept Relationships:
Specializes: CHLDFOST DAUC</p> <p>Concept Properties:
<i>internalId:</i> 19758</p> |
| 4-
L | STPDAU | stepdaughter | <p>Definition:</p> <p>The player of the role is a daughter of the scoping person's spouse by a previous union.</p> <p>Concept Relationships:
Specializes: DAUC STPCHLD</p> <p>Concept Properties:
<i>internalId:</i> 19762</p> |
| 3-
S | NCHILD
v:NaturalChild | natural child | <p>Definition:</p> <p>The player of the role is an offspring of the scoping entity</p> |

| | | | |
|---------|------------------|------------------------------|--|
| | | | <p>as determined by birth.</p> <p>Concept Relationships:
 Specializes: CHILD
 Generalizes (derived): DAU
 SON</p> <p>Concept Properties:
 <i>internalId:</i> 17930</p> |
| 4-
L | DAU | natural daughter
Daughter | <p>Definition:</p> <p>The player of the role is a female offspring of the scoping entity (parent).</p> <p>Concept Relationships:
 Specializes: DAUC NCHILD</p> <p>Concept Properties:
 <i>internalId:</i> 16361</p> |
| 4-
L | SON | natural son
Son | <p>Definition:</p> <p>The player of the role is a male offspring of the scoping entity (parent).</p> <p>Concept Relationships:
 Specializes: NCHILD SONC</p> <p>Concept Properties:
 <i>internalId:</i> 16362</p> |
| 3-
S | SONC | son | <p>Definition:</p> <p>Description: The player of the role is a male child (of any type) of scoping entity (parent)</p> <p>Concept Relationships:
 Specializes: CHILD
 Generalizes (derived): SON
 SONADOPT SONFOST STPSON</p> <p>Concept Properties:
 <i>internalId:</i> 22914</p> |
| 4-
L | SON | natural son
Son | <p>Definition:</p> <p>The player of the role is a male offspring of the scoping entity (parent).</p> <p>Concept Relationships:
 Specializes: NCHILD SONC</p> <p>Concept Properties:
 <i>internalId:</i> 16362</p> |
| 4-
L | SONADOPT | adopted son | <p>Definition:</p> |

| | | | |
|---------|--|--------------|--|
| | | | <p>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.</p> <p>Concept Relationships:
 Specializes: CHLDADOPT
 SONC</p> <p>Concept Properties:
 <i>internalId:</i> 19757</p> |
| 4-
L | SONFOST | foster son | <p>Definition:</p> <p>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.</p> <p>Concept Relationships:
 Specializes: CHLDFOST
 SONC</p> <p>Concept Properties:
 <i>internalId:</i> 19759</p> |
| 4-
L | STPSON | stepson | <p>Definition:</p> <p>The player of the role is a son of the scoping person's spouse by a previous union.</p> <p>Concept Relationships:
 Specializes: SONC STPCHLD</p> <p>Concept Properties:
 <i>internalId:</i> 19763</p> |
| 3-
S | STPCHLD
v:StepChild | step child | <p>Definition:</p> <p>The player of the role is a child of the scoping person's spouse by a previous union.</p> <p>Concept Relationships:
 Specializes: CHILD
 Generalizes (derived):
 STPDAU STPSON</p> <p>Concept Properties:
 <i>internalId:</i> 11562</p> |
| 4-
L | STPDAU | stepdaughter | <p>Definition:</p> <p>The player of the role is a daughter of the scoping person's spouse by a previous union.</p> |

| | | | |
|---------|----------------|------------------------|---|
| | | | <p>Concept Relationships:
Specializes: DAUC STPCHLD</p> <p>Concept Properties:
<i>internalId:</i> 19762</p> |
| 4-
L | STPSON | stepson | <p>Definition:</p> <p>The player of the role is a son of the scoping person's spouse by a previous union.</p> <p>Concept Relationships:
Specializes: SONC STPCHLD</p> <p>Concept Properties:
<i>internalId:</i> 19763</p> |
| 2-
S | . . EXT | extended family member | <p>Definition:</p> <p>Description: A family member not having an immediate genetic or legal relationship e.g. Aunt, cousin, great grandparent, grandchild, grandparent, niece, nephew or uncle.</p> <p>Concept Relationships:
Specializes: FAMMEMB
Generalizes (derived):
AUNT COUSN GGRPRN
GRNDCHILD GRPRN NIENEPH
UNCLE</p> <p>Concept Properties:
<i>internalId:</i> 22916</p> |
| 3-
S | . . . AUNT | aunt | <p>Definition:</p> <p>The player of the role is a sister of the scoping person's mother or father.</p> <p>Concept Relationships:
Specializes: EXT
Generalizes (derived):
MAUNT PAUNT</p> <p>Concept Properties:
<i>internalId:</i> 19748</p> |
| 4-
L | MAUNT | MaternalAunt | <p>Definition:</p> <p>Description:The player of the role is a biological sister of the scoping person's biological mother.</p> <p>Concept Relationships:
Specializes: AUNT</p> |

| | | | |
|---------|----------------|----------------|--|
| | | | Concept Properties:
<i>internalId:</i> 22017 |
| 4-
L | PAUNT | PaternalAunt | Definition:

Description: The player of the role is a biological sister of the scoping person's biological father.

Concept Relationships:
Specializes: AUNT

Concept Properties:
<i>internalId:</i> 22018 |
| 3-
S | . . . COUSN | cousin | Definition:

The player of the role is a relative of the scoping person descended from a common ancestor, such as a grandparent, by two or more steps in a diverging line.

Concept Relationships:
Specializes: EXT
Generalizes (derived):
MCOUSN PCOUSN

Concept Properties:
<i>internalId:</i> 19749 |
| 4-
L | MCOUSN | MaternalCousin | Definition:

Description: The player of the role is a biological relative of the scoping person descended from a common ancestor on the player's mother's side, such as a grandparent, by two or more steps in a diverging line.

Concept Relationships:
Specializes: COUSN

Concept Properties:
<i>internalId:</i> 22021 |
| 4-
L | PCOUSN | PaternalCousin | Definition:

Description: The player of the role is a biological relative of the scoping person descended from a common ancestor on the player's father's side, such as a grandparent, by two or more steps in a diverging line.

Concept Relationships:
Specializes: COUSN |

| | | | |
|---------|---|--------------------------|---|
| | | | Concept Properties:
<i>internalId:</i> 22022 |
| 3-
S | . . . GGRPRN
v:GreatGrandparent | great grandparent | Definition:

The player of the role is a parent of the scoping person's grandparent.

Concept Relationships:
Specializes: EXT
Generalizes (derived):
GGRFTH GGRMTH MGGRFTH
MGGRMTH MGGRPRN PGGRFTH
PGGRMTH PGGRPRN

Concept Properties:
<i>internalId:</i> 19739 |
| 4-
L | GGRFTH | great grandfather | Definition:

The player of the role is the father of the scoping person's grandparent.

Concept Relationships:
Specializes: GGRPRN

Concept Properties:
<i>internalId:</i> 19740 |
| 4-
L | GGRMTH | great grandmother | Definition:

The player of the role is the mother of the scoping person's grandparent.

Concept Relationships:
Specializes: GGRPRN

Concept Properties:
<i>internalId:</i> 19741 |
| 4-
L | MGGRFTH | MaternalGreatgrandfather | Definition:

Description: The player of the role is the biological father of the scoping person's biological mother's parent.

Concept Relationships:
Specializes: GGRPRN

Concept Properties:
<i>internalId:</i> 22013 |
| 4-
L | MGGRMTH | MaternalGreatgrandmother | Definition:

Description: The player of the role is the biological mother of the scoping person's biological |

| | | | |
|---------|---|--------------------------|--|
| | | | <p>mother's parent.</p> <p>Concept Relationships:
Specializes: GGRPRN</p> <p>Concept Properties:
<i>internalId:</i> 22015</p> |
| 4-
L | MGGRPRN | MaternalGreatgrandparent | <p>Definition:</p> <p>Description:The player of the role is a biological parent of the scoping person's biological mother's parent.</p> <p>Concept Relationships:
Specializes: GGRPRN</p> <p>Concept Properties:
<i>internalId:</i> 22011</p> |
| 4-
L | PGGRFTH | PaternalGreatgrandfather | <p>Definition:</p> <p>Description:The player of the role is the biological father of the scoping person's biological father's parent.</p> <p>Concept Relationships:
Specializes: GGRPRN</p> <p>Concept Properties:
<i>internalId:</i> 22014</p> |
| 4-
L | PGGRMTH | PaternalGreatgrandmother | <p>Definition:</p> <p>Description:The player of the role is the biological mother of the scoping person's biological father's parent.</p> <p>Concept Relationships:
Specializes: GGRPRN</p> <p>Concept Properties:
<i>internalId:</i> 22016</p> |
| 4-
L | PGGRPRN | PaternalGreatgrandparent | <p>Definition:</p> <p>Description:The player of the role is a biological parent of the scoping person's biological father's parent.</p> <p>Concept Relationships:
Specializes: GGRPRN</p> <p>Concept Properties:
<i>internalId:</i> 22012</p> |
| 3-
S | . . . GRNDCHILD
v:GrandChild | grandchild | <p>Definition:</p> |

| | | | |
|---------|--|---------------|---|
| | | | <p>The player of the role is a child of the scoping person's son or daughter.</p> <p>Concept Relationships:
 Specializes: EXT
 Generalizes (derived):
 GRNDDAU GRNDSON</p> <p>Concept Properties:
 <i>internalId:</i> 19745</p> |
| 4-
L | GRNDDAU | granddaughter | <p>Definition:</p> <p>The player of the role is a daughter of the scoping person's son or daughter.</p> <p>Concept Relationships:
 Specializes: GRNDCHILD</p> <p>Concept Properties:
 <i>internalId:</i> 19746</p> |
| 4-
L | GRNDSON | grandson | <p>Definition:</p> <p>The player of the role is a son of the scoping person's son or daughter.</p> <p>Concept Relationships:
 Specializes: GRNDCHILD</p> <p>Concept Properties:
 <i>internalId:</i> 19747</p> |
| 3-
S | . . . GRPRN
v:Grandparent | Grandparent | <p>Definition:</p> <p>The player of the role is a parent of the scoping person's mother or father.</p> <p>Concept Relationships:
 Specializes: EXT
 Generalizes (derived):
 GRFTH GRMTH MGRFTH
 MGRMTH MGRPRN PGRFTH
 PGRMTH PGRPRN</p> <p>Concept Properties:
 <i>internalId:</i> 16349</p> |
| 4-
L | GRFTH | Grandfather | <p>Definition:</p> <p>The player of the role is the father of the scoping person's mother or father.</p> <p>Concept Relationships:
 Specializes: GRPRN</p> <p>Concept Properties:</p> |

| | | | |
|---------|----------------|---------------------|--|
| | | | <i>internalId:</i> 16351 |
| 4-
L | GRMTH | Grandmother | <p>Definition:</p> <p>The player of the role is the mother of the scoping person's mother or father.</p> <p>Concept Relationships:
Specializes: GRPRN</p> <p>Concept Properties:
<i>internalId:</i> 16350</p> |
| 4-
L | MGRFTH | MaternalGrandfather | <p>Definition:</p> <p>Description:The player of the role is the biological father of the scoping person's biological mother.</p> <p>Concept Relationships:
Specializes: GRPRN</p> <p>Concept Properties:
<i>internalId:</i> 22009</p> |
| 4-
L | MGRMTH | MaternalGrandmother | <p>Definition:</p> <p>Description:The player of the role is the biological mother of the scoping person's biological mother.</p> <p>Concept Relationships:
Specializes: GRPRN</p> <p>Concept Properties:
<i>internalId:</i> 22007</p> |
| 4-
L | MGRPRN | MaternalGrandparent | <p>Definition:</p> <p>Description:The player of the role is the biological parent of the scoping person's biological mother.</p> <p>Concept Relationships:
Specializes: GRPRN</p> <p>Concept Properties:
<i>internalId:</i> 22005</p> |
| 4-
L | PGRFTH | PaternalGrandfather | <p>Definition:</p> <p>Description:The player of the role is the biological father of the scoping person's biological father.</p> <p>Concept Relationships:</p> |

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|---------|--|---------------------|---|
| | | | <p>Specializes: GRPRN</p> <p>Concept Properties:
<i>internalId:</i> 22010</p> |
| 4-
L | PGRMTH | PaternalGrandmother | <p>Definition:</p> <p>Description:The player of the role is the biological mother of the scoping person's biological father.</p> <p>Concept Relationships:
Specializes: GRPRN</p> <p>Concept Properties:
<i>internalId:</i> 22008</p> |
| 4-
L | PGRPRN | PaternalGrandparent | <p>Definition:</p> <p>Description:The player of the role is the biological parent of the scoping person's biological father.</p> <p>Concept Relationships:
Specializes: GRPRN</p> <p>Concept Properties:
<i>internalId:</i> 22006</p> |
| 3-
S | NIENEPH
v:NieceNephew | niece/nephew | <p>Definition:</p> <p>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.</p> <p>Concept Relationships:
Specializes: EXT
Generalizes (derived):
NEPHEW NIECE</p> <p>Concept Properties:
<i>internalId:</i> 19750</p> |
| 4-
L | NEPHEW | nephew | <p>Definition:</p> <p>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.</p> <p>Concept Relationships:
Specializes: NIENEPH</p> <p>Concept Properties:
<i>internalId:</i> 19751</p> |
| 4-
L | NIECE | niece | <p>Definition:</p> |

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|---------|-------------------------------------|---------------|--|
| | | | <p>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.</p> <p>Concept Relationships:
Specializes: NIENEPH</p> <p>Concept Properties:
<i>internalId:</i> 19752</p> |
| 3-
S | . . . UNCLE | uncle | <p>Definition:</p> <p>The player of the role is a brother of the scoping person's mother or father.</p> <p>Concept Relationships:
Specializes: EXT
Generalizes (derived): MUNCLE PUNCLE</p> <p>Concept Properties:
<i>internalId:</i> 19753</p> |
| 4-
L | MUNCLE | MaternalUncle | <p>Definition:</p> <p>Description:The player of the role is a biological brother of the scoping person's biological mother.</p> <p>Concept Relationships:
Specializes: UNCLE</p> <p>Concept Properties:
<i>internalId:</i> 22019</p> |
| 4-
L | PUNCLE | PaternalUncle | <p>Definition:</p> <p>Description:The player of the role is a biological brother of the scoping person's biological father.</p> <p>Concept Relationships:
Specializes: UNCLE</p> <p>Concept Properties:
<i>internalId:</i> 22020</p> |
| 2-
S | . . PRN
v:Parent | Parent | <p>Definition:</p> <p>The player of the role is one who begets, gives birth to, or nurtures and raises the scoping entity (child).</p> <p>Concept Relationships:
Specializes: FAMMEMB
Generalizes (derived): FTH</p> |

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|---------|---|-------------------------|--|
| | | | MTH NPRN PRNINLAW STPPRN
Concept Properties:
<i>internalId:</i> 16346 |
| 3-
L | . . . FTH | Father | Definition:

The player of the role is a male who begets or raises or nurtures the scoping entity (child).

Concept Relationships:
Specializes: PRN

Concept Properties:
<i>internalId:</i> 16348 |
| 3-
L | . . . MTH | Mother | Definition:

The player of the role is a female who conceives, gives birth to, or raises and nurtures the scoping entity (child).

Concept Relationships:
Specializes: PRN

Concept Properties:
<i>internalId:</i> 16347 |
| 3-
S | . . . NPRN
v:NaturalParent | natural parent | Concept Relationships:
Specializes: PRN
Generalizes (derived):
NFTH NMTH

Concept Properties:
<i>internalId:</i> 19764 |
| 4-
S | NFTH | natural father | Definition:

The player of the role is a male who begets the scoping entity (child).

Concept Relationships:
Specializes: NPRN
Generalizes (derived):
NFTHF

Concept Properties:
<i>internalId:</i> 19765 |
| 5-
L | NFTHF | natural father of fetus | Definition:

Indicates the biologic male parent of a fetus.

Concept Relationships:
Specializes: NFTH

Concept Properties: |

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|---------|--|----------------|--|
| | | | internalId: 21455 |
| 4-
L | NMTH | natural mother | <p>Definition:</p> <p>The player of the role is a female who conceives or gives birth to the scoping entity (child).</p> <p>Concept Relationships:
Specializes: NPRN</p> <p>Concept Properties:
internalId: 19766</p> |
| 3-
S | . . . PRNINLAW
v:ParentInLaw | parent in-law | <p>Definition:</p> <p>The player of the role is the parent of scoping person's husband or wife.</p> <p>Concept Relationships:
Specializes: PRN
Generalizes (derived): FTHINLAW MTHINLAW</p> <p>Concept Properties:
internalId: 19770</p> |
| 4-
L | FTHINLAW | father-in-law | <p>Definition:</p> <p>The player of the role is the father of the scoping person's husband or wife.</p> <p>Concept Relationships:
Specializes: PRNINLAW</p> <p>Concept Properties:
internalId: 19771</p> |
| 4-
L | MTHINLAW | mother-in-law | <p>Definition:</p> <p>The player of the role is the mother of the scoping person's husband or wife.</p> <p>Concept Relationships:
Specializes: PRNINLAW</p> <p>Concept Properties:
internalId: 19772</p> |
| 3-
S | . . . STPPRN
v:StepParent | step parent | <p>Definition:</p> <p>The player of the role is the spouse of the scoping person's parent and not the scoping person's natural parent.</p> <p>Concept Relationships:
Specializes: PRN</p> |

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|---------|---|--------------|---|
| | | | <p>Generalizes (derived):
STPFTH STPMTH</p> <p>Concept Properties:
<i>internalId:</i> 19767</p> |
| 4-
L | STPFTH | stepfather | <p>Definition:</p> <p>The player of the role is the husband of scoping person's mother and not the scoping person's natural father.</p> <p>Concept Relationships:
Specializes: STPPRN</p> <p>Concept Properties:
<i>internalId:</i> 19768</p> |
| 4-
L | STPMTH | stepmother | <p>Definition:</p> <p>The player of the role is the wife of scoping person's father and not the scoping person's natural mother.</p> <p>Concept Relationships:
Specializes: STPPRN</p> <p>Concept Properties:
<i>internalId:</i> 19769</p> |
| 2-
S | . . SIB
v:Sibling | Sibling | <p>Definition:</p> <p>The player of the role shares one or both parents in common with the scoping entity.</p> <p>Concept Relationships:
Specializes: FAMMEMB
Generalizes (derived): BRO HSIB NSIB SIBINLAW SIS STPSIB</p> <p>Concept Properties:
<i>internalId:</i> 11567</p> |
| 3-
L | . . . BRO | Brother | <p>Definition:</p> <p>The player of the role is a male sharing one or both parents in common with the scoping entity.</p> <p>Concept Relationships:
Specializes: SIB</p> <p>Concept Properties:
<i>internalId:</i> 16359</p> |
| 3-
S | . . . HSIB
v:HalfSibling | half-sibling | <p>Definition:</p> |

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|---------|--|-----------------|--|
| | | | <p>The player of the role is related to the scoping entity by sharing only one biological parent.</p> <p>Concept Relationships:
 Specializes: SIB
 Generalizes (derived):
 HBRO HSIS</p> <p>Concept Properties:
 <i>internalId:</i> 19776</p> |
| 4-
L | HBRO | half-brother | <p>Definition:</p> <p>The player of the role is a male related to the scoping entity by sharing only one biological parent.</p> <p>Concept Relationships:
 Specializes: HSIB</p> <p>Concept Properties:
 <i>internalId:</i> 19777</p> |
| 4-
L | HSIS | half-sister | <p>Definition:</p> <p>The player of the role is a female related to the scoping entity by sharing only one biological parent.</p> <p>Concept Relationships:
 Specializes: HSIB</p> <p>Concept Properties:
 <i>internalId:</i> 19778</p> |
| 3-
S | NSIB
v:NaturalSibling | natural sibling | <p>Definition:</p> <p>The player of the role has both biological parents in common with the scoping entity.</p> <p>Concept Relationships:
 Specializes: SIB
 Generalizes (derived):
 NBRO NSIS</p> <p>Concept Properties:
 <i>internalId:</i> 19773</p> |
| 4-
L | NBRO | natural brother | <p>Definition:</p> <p>The player of the role is a male having the same biological parents as the scoping entity.</p> <p>Concept Relationships:
 Specializes: NSIB</p> <p>Concept Properties:</p> |

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|---------|---|----------------|---|
| | | | internalId: 19774 |
| 4-
L | NSIS | natural sister | <p>Definition:</p> <p>The player of the role is a female having the same biological parents as the scoping entity.</p> <p>Concept Relationships:
Specializes: NSIB</p> <p>Concept Properties:
internalId: 19775</p> |
| 3-
S | . . . SIBINLAW
v:SiblingInLaw | sibling in-law | <p>Definition:</p> <p>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.</p> <p>Concept Relationships:
Specializes: SIB
Generalizes (derived):
BROINLAW SISINLAW</p> <p>Concept Properties:
internalId: 19782</p> |
| 4-
L | BROINLAW | brother-in-law | <p>Definition:</p> <p>The player of the role is: (1) a brother of the scoping person's spouse, or (2) the husband of the scoping person's sister, or (3) the husband of a sister of the scoping person's spouse.</p> <p>Concept Relationships:
Specializes: SIBINLAW</p> <p>Concept Properties:
internalId: 19783</p> |
| 4-
L | SISINLAW | sister-in-law | <p>Definition:</p> <p>The player of the role is: (1) a sister of the scoping person's spouse, or (2) the wife of the scoping person's brother, or (3) the wife of a brother of the scoping person's spouse.</p> <p>Concept Relationships:
Specializes: SIBINLAW</p> <p>Concept Properties:
internalId: 19784</p> |

| | | | |
|---------|--|-------------------|--|
| 3-
L | . . . SIS | Sister | <p>Definition:</p> <p>The player of the role is a female sharing one or both parents in common with the scoping entity.</p> <p>Concept Relationships:
Specializes: SIB</p> <p>Concept Properties:
<i>internalId:</i> 16358</p> |
| 3-
S | . . . STPSIB
v:StepSibling | step sibling | <p>Definition:</p> <p>The player of the role is a child of the scoping person's stepparent.</p> <p>Concept Relationships:
Specializes: SIB
Generalizes (derived): STPBRO STPSIS</p> <p>Concept Properties:
<i>internalId:</i> 19779</p> |
| 4-
L | STPBRO | stepbrother | <p>Definition:</p> <p>The player of the role is a son of the scoping person's stepparent.</p> <p>Concept Relationships:
Specializes: STPSIB</p> <p>Concept Properties:
<i>internalId:</i> 19780</p> |
| 4-
L | STPSIS | stepsister | <p>Definition:</p> <p>The player of the role is a daughter of the scoping person's stepparent.</p> <p>Concept Relationships:
Specializes: STPSIB</p> <p>Concept Properties:
<i>internalId:</i> 19781</p> |
| 2-
S | . . SIGOTHR
v:SignificantOtherRoleType | significant other | <p>Definition:</p> <p>A person who is important to one's well being; especially a spouse or one in a similar relationship. (The player is the one who is important)</p> <p>Concept Relationships:
Specializes: FAMMEMB
Generalizes (derived):</p> |

| | | | |
|---------|--|------------------|--|
| | | | <p>DOMPART SPS</p> <p>Concept Properties:
<i>internalId:</i> 19755</p> |
| 3-
L | . . . DOMPART | domestic partner | <p>Definition:</p> <p>The player of the role cohabits with the scoping person but is not the scoping person's spouse.</p> <p>Concept Relationships:
Specializes: SIGOTHR</p> <p>Concept Properties:
<i>internalId:</i> 19754</p> |
| 3-
S | . . . SPS
v:Spouse | spouse | <p>Definition:</p> <p>The player of the role is a marriage partner of the scoping person.</p> <p>Concept Relationships:
Specializes: SIGOTHR
Generalizes (derived):
HUSB WIFE</p> <p>Concept Properties:
<i>internalId:</i> 19742</p> |
| 4-
L | HUSB | husband | <p>Definition:</p> <p>The player of the role is a man joined to a woman (scoping person) in marriage.</p> <p>Concept Relationships:
Specializes: SPS</p> <p>Concept Properties:
<i>internalId:</i> 19743</p> |
| 4-
L | WIFE | wife | <p>Definition:</p> <p>The player of the role is a woman joined to a man (scoping person) in marriage.</p> <p>Concept Relationships:
Specializes: SPS</p> <p>Concept Properties:
<i>internalId:</i> 19744</p> |
| 1-
L | . FRND | unrelated friend | <p>Definition:</p> <p>The player of the role is a person who is known, liked, and trusted by the scoping person.</p> |

| | | | |
|---------|--------|----------|--|
| | | | <p>Concept Relationships:
 Specializes:
 _PersonalRelationshipRoleType</p> <p>Concept Properties:
 <i>internalId:</i> 19737</p> |
| 1-
L | . NBOR | neighbor | <p>Definition:</p> <p>The player of the role lives near or next to the scoping person.</p> <p>Concept Relationships:
 Specializes:
 _PersonalRelationshipRoleType</p> <p>Concept Properties:
 <i>internalId:</i> 19738</p> |
| 1-
L | . ROOM | Roommate | <p>Definition:</p> <p>One who shares living quarters with the subject.</p> <p>Concept Relationships:
 Specializes:
 _PersonalRelationshipRoleType</p> <p>Concept Properties:
 <i>internalId:</i> 16364</p> |

Appendix F: List of Changes through Ballot Cycles

Membership Level#1:

- In general, non-substantive changes were made in the Family History static model in order to accommodate the ballot comments of the previous cycle, as follows:
 - Relaxation of several fixed code requirements so that implementations will not be obligated to use certain code schemes like LOINC. Note that no change in the required semantics was made.
 - Replacement of several uses of PQ data type with REAL. The latter was the original intention but due to limitation in the R-MIM Designer tool it was not possible to assign the REAL data type to an attribute. The selection of the REAL data type was made possible with the version that came out after San Diego meeting in January 2007.

Committee Level #2:

- Submitted harmonization proposal to add a new code (FHX) to the ActClass vocabulary so that it can be fixed to the classCode attribute of the entry point class FamilyHistory and allow parsers of Family History instances to understand the semantics of this class without needing to look at the clone name. The proposal was not accepted so instead the code attribute is fixed to LOINC code: 10157-6 (HISTORY OF FAMILY MEMBER DISEASES).
- Changed the moodCode of the PedigreeAnalysisResults class and all its outbound associated observations to RSK (risk).
- Added a recursive ActRelationship to the class Clinical Observation which is supposed to be replaced eventually with a Clinical Statement CMET. The ActRelationship added is in consistent with the current Clinical Statement Shared model and serves the needs of implementers.
- Added an informant participant.
- Add the GeneticLoci CMET to ClinicalGenomicChoice so that it would be possible to associate data on a set of loci such as genetic test panel results or gene expression assay.
- Changed the scoping Provider class to the E_Organization CMET to allow for the representation of more details about the provider scoping the patient while the family history had been collected.
- Added constraint on the code attribute of the DataEstimatedAge class: The code attribute is fixed to 397659008 (“Age”) in SNOMED CT (2.16.840.1.113883.6.96).
- Refined the storyboard narrative to indicate more clearly at which point a messaging interaction would occur.
- Added attribute level definitions.

Committee Level #1:

- Moved the place holder for mother and father ids from the Relative class to the Person class so that there is no use of Role id in general, and in particular there is no use of multiple values in the same id attribute.

- For diagram clarity purposes only, the association between Person and Relative is done directly and not through a shadow of the Person class as was done in the previous version. Note that the semantics of this structure is identical to the former structure that consisted of the Person shadow.

DSTU Update #1:

- Added a new class of FamilyHistory to represent the pedigree as a whole.
- Made the FamilyHistory class an entry point (in case we wish to register this model as a CMET and thus need it to be distinguished from CMETs starting with Patient).
- Added classes to hold results of risk assessment procedures analyzing the whole pedigree (e.g., probabilities).
- Added an association from FamilyHistory to the ClinicalGenomicChoice which allows the representation of problems known in the family that cannot be attributed to specific family members.
- Made the age value an interval to accommodate age estimation such as 'she was diagnosed in her forties'.
- Added input parameters hanging off the PedigreeAnalysisResults class to specify input from a specific analysis, such as specificity and sensitivity in BRACPRO.
- Changed the class name PersonalRelationship to Relative for more clarity.
- Added a constraint box to explicitly mandate the use of the Relative.id attribute.