HL7 FHIR Proposal for Variant Inheritance Basis

Willie Chang

Version 2

> **What's new in this version?** Added short name, definition (p. 1), and other options considered (p. 2).

In JIRA ticket FHIR-32101, we propose to add a new component to the R4 Variant profile for expressing the method of determination for variant inheritance below.

- Component: variant-inheritance-basis
- Short name: Evidential basis for variant inheritance
- Definition: The method by which the variant inheritance is determined.
- Code: LOINC 82309-6 (Basis for allelic phase)
- Value binding: LOINC Answer List LL4050-2
  - Directly measured
  - Family DNA
  - Family history
  - Inferred from population data

Consistent with other places where this answer list is used (e.g., the **method** of **Haplotype** and **Sequence Phase Relationship** profiles), we propose making the value set extensible, not required.

Epic currently uses an extension to send this information.

For reference, the variant-inheritance component has the following specification:

component:variant-inheritance	0..1	BackboneElement	Variant Inheritance
code	1..1	CodeableConcept	variant-inheritance **Required Pattern:** At least the following
coding	1..*	Coding	Code defined by a terminology system **Fixed Value:** (complex)
system	1..1	uri	Identity of the terminology system **Fixed Value:** http://hl7.org/fhir/uv/genomics-reporting/CodeSystem/tbd-codes-cs
code	1..1	code	Symbol in syntax defined by the system **Fixed Value:** variant-inheritance
value[x]	1..1	CodeableConcept	Maternal | Paternal | Unknown **Binding:** Variant Inheritances (extensible)

And for genomic-source-class:

component:genomic-source-class	0..1	BackboneElement	Genomic Source Class
code	1..1	CodeableConcept	48002-0 **Required Pattern:** At least the following
coding	1..*	Coding	Code defined by a terminology system **Fixed Value:** (complex)
system	1..1	uri	Identity of the terminology system **Fixed Value:** http://loinc.org
code	1..1	code	Symbol in syntax defined by the system **Fixed Value:** 48002-0
value[x]	1..1	CodeableConcept	Germline | Somatic | Fetal | Likely germline | Likely somatic | Likely fetal | Unknown genomic origin | De novo **Binding:** LOINC Answer List LL378-1 (extensible)

The value sets for variant-inheritance and genomic-source-class do not overlap, which should address Robert Freimuth's concerns in the JIRA ticket.

Other options considered

1. Adding a **method** extension on the **variant-inheritance** component: the pattern of adding a **method** extension on components would be useful if there were multiple components for which a component-specific method would commonly be specified in reports. However, we did not identify such other components as of writing. If, in the future, there are proposals with such other components, we can revisit this option. A potential downside to this approach is **method** on the component can be confused with **method** on the observation.

2. Specifying **method** on the **Sequence Phase Relationship** profile: While **method** on the **Sequence Phase Relationship** profile has the same answer list that we propose in this new component, implementers would need to send an observation of this profile even if the sequence phase relationship is not known or has not been determined. This new component allows implementers to express the method of determining variant inheritance without documenting sequence phase relationship.