FHIR Subgroup Meeting Notes 5/20/19 - 9/9/19

Quick link to this sign-in/notes document: http://tinyurl.com/fhirgenomics

Presiding co-chair: Gil Alterovitz gil_alterovitz@hms.harvard.edu

Schedule

May 20 - trackers from wgm
May 27 - X - Memorial Day
June 3 - trackers from wgm
June 10 - X - DevDays US
June 17 - non-ballot trackers
June 24 - non-ballot trackers
July 1 - connectathon/publication trackers
July 15 - connectathon/publication trackers
July 22 - connectathon/publication trackers (iron out DNA chg type proposal)
July 29 - implementation update
Aug 5 - implementation update
Aug 12 - implementation update
Aug 19 -
Aug 26 - Proposed IG deadline (for review prior to WGM)
Sept 2 - X - Labor Day
Sept 9 - WGM prep

FHIR Subgroup Meeting September 9th, 2019

https://join.freeconferencecall.com/clingenomics

Quick link to this sign-in/notes document: tinyurl.com/fhirgenomics

Sign In: (presiding co-chair - Gil Alterovitz - gil_alterovitz@hms.harvard.edu)

1. James Jones - BCH - james.jones.bch@gmail.com
2. Michael Stevens - Optum - jmichael.stevens@optum.com
3. Dora Finkeisen - MOLIT Institut - dora.finkeisen@molit.eu
4. Liz Amos - NLM - liz.amos@nih.gov
5. Alex Mankovich - Philips - alex.mankovich@philips.com
6. Bob Dolin - Elimu Informatics - bdolin@elimu.io
7. Lloyd McKenzie - Gevity - lmckenzie@gevityinc.com
8. Joel Schneider - NMDP/CIBMTR - jschneid@nmdp.org
9. Bret Heale - Intermountain Healthcare - bheale@gmail.com
10.

AGENDA:
1. Remaining trackers decision
   a. GForge Link
2. Remaining QA work
   a. IG QA Link
      i. “Name should be usable as an identifier for the module by machine
         processing applications such as code generation
         [name.matches('^[A-Z][A-Za-z0-9_]{0,254}$')]"
      ii. “Profile http://hl7.org/fhir/StructureDefinition/shareablevalueset, Element
         'ValueSet.publisher': minimum required = 1, but only found 0
   b. Need to populate
      http://build.fhir.org/ig/HL7/genomics-reporting/valueset-tbd-codes.html
   c. Need examples!
      i. Do the have to validate with the profile meta tags?
         1. Need to determine text for resolution of 19876
3. LOINC request issues
   a. Questions on clinical significance / level of evidence

DISCUSSION
1. 14 in GForge. List from last meeting below.
2. Recommend for 9/10 that we mark this list of 7 trackers as deferred and publish (other 7 will
   be finished by tomorrow)
   First/Second: Jamie/Bob D
   Discussion: specifically, defer (publish without applying)

16387
19947
16513
16876
19827
19876
15893
<table>
<thead>
<tr>
<th>ID</th>
<th>LOINC Request/Example</th>
<th>Text</th>
<th>Resolution/Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>16387</td>
<td>LOINC reference for HLA</td>
<td>Persuasive with mod - add guidance on sending multiple LOINC codes (will be included in resolution of 16408)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Current text: <a href="http://build.fhir.org/ig/HL7/genomics-reporting/index.html#understanding-fhir">http://build.fhir.org/ig/HL7/genomics-reporting/index.html#understanding-fhir</a>  &quot;Many Observation profiles and components in this guide require sending codes from <a href="http://loinc.org">http://loinc.org</a>. If necessary for implementation (e.g., to map to a local system), equivalent codes from other code systems may <em>also</em> be sent, following the guidance on observation.</td>
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<td>Bob M. and Joel will work on the text. (Should also have a generalized short discussion about dangers of using nomenclature. Could include a specialized discussion on PGx nomenclature)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>STRUCTURE (3)</strong></td>
<td></td>
</tr>
<tr>
<td>16513</td>
<td>need glossary</td>
<td>Persuasive - but need a formal proposal, and will have to update it when any definitions change and finalize before publishing.</td>
<td>Recommend Deferred</td>
</tr>
<tr>
<td></td>
<td></td>
<td>There was a consensus (FHIR subgroup Aug 13 2018) to provide a centralized statement of our definitions, updated once we decide how to proceed with &quot;variant/haplotype/genotype&quot; etc. and solidify definitions in the profiles themselves.</td>
<td></td>
</tr>
<tr>
<td>16876</td>
<td>Use of publically available external coding systems and autocomplete lookup tables - 2018-May Genomics #58</td>
<td>&quot;Deferred - Needs more work?&quot;</td>
<td>Recommend Deferred</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Asking for update from Patrick, Liz will send table with current text to Jamie so we can review it online in IG as voted on.</td>
<td></td>
</tr>
</tbody>
</table>
3.  
4. Need for the following table of concepts:  
   a. Narrative definition  
   b. (example) Answer lists/units of measure  
   c. Data type where applicable  
   d. Spell out valueset, improve text quality

Main Question:  
Can we publish IG requiring a LOINC code (that has an example/preferred list) and recommend a different list in the IG?

<table>
<thead>
<tr>
<th>Code</th>
<th>Display</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>grouper</td>
<td>grouper</td>
<td>No value, can simply describe use</td>
</tr>
<tr>
<td>mode-of-inheritance</td>
<td>mode-of-inheritance</td>
<td>Close code: <strong>Inheritance pattern based on family history</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>79742-3</td>
</tr>
<tr>
<td></td>
<td></td>
<td><a href="https://loinc.org/79742-3/">https://loinc.org/79742-3/</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Autosomal recessive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>X-linked dominant</td>
</tr>
<tr>
<td></td>
<td></td>
<td>X-linked recessive</td>
</tr>
</tbody>
</table>
Y-linked | Codominant | Mitochondrial
Close list, geared towards family history: **LL3731-8**

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect-transporter-function</td>
<td>Have example list</td>
</tr>
<tr>
<td>Somatic-diagnostic</td>
<td>Pathognomonic, Supportive, Argues Against, Rules Out</td>
</tr>
<tr>
<td>Somatic-diagnostic-medication</td>
<td>Consider matching this list with level of evidence</td>
</tr>
<tr>
<td>Somatic-prognostic</td>
<td>E.g. Better outcome, poorer outcome</td>
</tr>
<tr>
<td>Somatic-prognostic-medication</td>
<td>Rxnorm, others</td>
</tr>
<tr>
<td>Somatic-prognostic-treatment</td>
<td>??</td>
</tr>
<tr>
<td>Somatic-predictive</td>
<td>E.g. Resistant, Responsive, Not-Responsive, Sensitive, Reduced-Sensitivity, Adverse Response</td>
</tr>
<tr>
<td>Somatic-predictive-medication</td>
<td>Rxnorm, others</td>
</tr>
<tr>
<td>Associated-cancer</td>
<td>Text description,</td>
</tr>
<tr>
<td>Region-scope</td>
<td>Text description,</td>
</tr>
<tr>
<td>Region-coverage</td>
<td>Text description (further work ongoing)</td>
</tr>
</tbody>
</table>

5. LOINC issues Level of evidence
   a. ACMG/CAP/ASCO lists
   b. Recommendation, keep as unbound in IG
(copied from Tuesday, need to determine if action required)

Motion 2: Use 53037-8 for both germline and somatic variant clinical significance reporting, and
a. Add information to the Term description about the different guidelines for somatic and germline
variants;
b. Keep the Answer list the same, but update the Update the type from Preferred to Example

   c. 1st/2nd -
   d. Discussion - need a gforge tracker to track these if these are impacting IG. Need Jamie
      & Swapna to clarify what this impacts (LOINC vs IG)
   e. Abstain/Nay/Yea - / /
   f. Result -

Motion 3: Consider creating new codes for diagnostic, therapeutic, and prognostic significance (see
Quest screenshot, LabCorp report) and/or type of evidence (see Baylor report)

   ● 1st/2nd -
   ● Discussion -
   ● Abstain/Nay/Yea - / /
   ● Result -

Chat history:

Bret Heale
11:30 AM
48002-0 for mode of inheritance

Liz Amos
11:35 AM
https://loinc.org/79742-3/

Bret Heale
11:36 AM
thanks Liz! apologies for my mistake on the code

Joel Schneider
11:49 AM

FHIR terminology binding strengths: http://hl7.org/fhir/terminologies.html#strength

Bret Heale
11:49 AM

I'm much more of a molecular biologist. I'm thinking of condition where a gene is always 'on' (no longer regulated). The presence of the mutation would be dominant. But you would not need family history to determine it. Sorry. I'm a little off this morning. I'll try to be quieter

FHIR Subgroup Meeting August 26th, 2019
https://join.freeconferencecall.com/clingenomics

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14. Clem McDonald - NLM - clemmcdonald@mail.nih.gov
15. Joel Schneider - NMDP/CIBMTR - jschneid@nmdp.org
16. Michael Stevens - Optum - jmichael.stevens@optum.com
17. Deepak Sharma - Mayo Clinic - sharma.deepak2@mayo.edu
18. Kevin Power - Cerner - kpower@cerner.com
19. Bob Milius - NMDP/CIBMTR - bmilius@nmdp.org
20. Lloyd McKenzie - Gevity - lmckenzie@gevityinc.com
21.

AGENDA:
1. Review of local TBD-codes system
   a. Build errors/incorrect links should get resolved (thanks Lloyd)
   b. Pull together definition info on valueset page, including
      i. Narrative definition
      ii. (example) Answer lists/units of measure
      iii. Data type where applicable
      iv. Spell out valueset, improve text quality
   c. Had voted to update variant exact/inner/outer start-end as “new” local concepts, could be simpler to remain with current LOINC concepts. (22816 start-end of Variant confusing)

2. Final push to publication
   a. Remaining trackers to apply 14
      i. 2 textual
      ii. 3 structural (components, etc)
      iii. 2 pending LOINC requests (changes to IG finished)
      iv. 2 requests for web pages with info/links
      v. 5 re: more examples
         1. Need to resolve references not resolving issue
            a. Try fullurl approach and/or external
            b. Example.org is supposed to get ignored if root of endpoint
   2. Bob M will update some HLA page and examples for us

3. Other concerns?
   a. Ballot reconciliation spreadsheet
   b. Final timeline for publication (want to reach out to previous balloters before WGM)

DISCUSSION:

16387 LOINC reference for HLA

   Persuasive - with mod - add guidance on sending multiple LOINC codes (will be included in resolution of 16408) Current text: http://build.fhir.org/ig/HL7/genomics-reporting/index.html#understanding-fhir
"Many Observation profiles and components in this guide require sending codes from http://loinc.org. If necessary for implementation (e.g., to map to a local system), equivalent codes from other code systems may *also* be sent, following the guidance on observation.

**Is anything else needed? Bob taking care of**

**Update?**  
Bob Finishing up

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</tbody>
</table>
| 22814| Variant needs a component for variant type             | Updated proposal from FHIR subgroup discussion 7/22:  
|      |                                                       | 1. Update DNA-change type (48019-4) preferred binding to SO (anything under [SO:0002072](http://loinc.org))  
|      |                                                       | 2. Provide concept map to LOINC (code systems appendix??) (based on [this](http://loinc.org))  |
| 22815| Functional Annotation                                 | Add a component component (0..*) named "functional annotation" with a preferred binding to sequence ontology (everything under SO:0001060 - sequence_variant)  |
| 22816| start-end of Variant confusing                        | 3 new LOINC Concepts:  
|      |                                                       | **Variant exact start and end**  
|      |                                                       | The genomic coordinates of the exact genomic range in which the variant resides.  
|      |                                                       | **Variant inner start and end**  
|      |                                                       | The genomic coordinates of the inner genomic range in which the variant might reside.  
|      |                                                       | **Variant outer start and end**  |
The genomic coordinates of the outer genomic range in which the variant might reside.

Change LOINC codes of the existing start-end components in obs-variant.

Use temporary codes until LOINC adds these new concepts:

**WEB PAGES (2)**

**16513  need glossary**

Persuasive - but need a formal proposal, and will have to update it when any definitions change and finalize before publishing.

There was a consensus (FHIR subgroup Aug 13 2018) to provide a centralized statement of our definitions, updated once we decide how to proceed with "variant/haplotype/genotype" etc. and solidify definitions in the profiles themselves.

**16876  Use of publically available external coding systems and autocomplete lookup tables - 2018-May Genomics #58**

“Deferred - Needs more work?”

**LOINC REQUEST (2)**

**19841  LOINC: Sequence Phase Relationship code and value**

Use 82120-7, request LOINC Code naming to: Sequence Phase.

Request LOINC answer list as mentioned in: [https://gforge.hl7.org/gf/project/fhir/tracker/?action=TrackerItemEdit&tracker_item_id=19842&start=0](https://gforge.hl7.org/gf/project/fhir/tracker/?action=TrackerItemEdit&tracker_item_id=19842&start=0)

**19834  LOINC: Described Variant component (human reference**

Persuasive:
Missing item in the answer list, Liz has already submitted the change to LOINC.

Will have to confirm it is extensible short term. Jamie will send to Liz/Clem

https://loinc.org/62374-4/

needs 38

### EXAMPLES (5)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Actions</th>
</tr>
</thead>
</table>
| 19827 | Need guidance on housing extended test, methodology and reference information                  | Persuasive with mod-
|       |                                               | Increase cardinality of relatedArtifact extension on report to 0..* and add textual guidance/examples for observation.method |
| 20317 | Need better documentation and more examples that illustrate how reports with many results (bundles) should be structured. | Need examples of Observation.method, solidify our guidance here |
| 16510 | Need more examples                                                                           |         |
| 19876 | many examples do not validate against an IG profile using the FHIR Validator                  |         |
| 15893 | Decide what examples to bring across from existing profiles and convert them                  |         |

Chat History:

**Bret Heale** 11:12 AM just a friendly reminder, don’t need to have an exhaustive set of values for a LOINC code to be made - unless we want to restrict the profile to a specific value set.

**Bret Heale** 11:23 AM instead of VS spell out valueset

**Bret Heale** 11:23 AM just to make it clearer

**Bret Heale** 11:24 AM Cool!

**Kevin Power** 11:31 AM That was me, i commented those out :)

**Bret Heale** 11:50 AM Cis/Trans Phase

**Bret Heale** 11:50 AM Cis or Trans Phase

**Bret Heale** 11:50 AM Phased

**Bret Heale** 11:51 AM Phasing
FHIR Subgroup Meeting August 19th, 2019
https://join.freeconferencecall.com/clingenomics

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26. Dora Finkeisen - MOLIT Institut - dora.finkeisen@molit.eu
27. Bob Dolin - Elimu Informatics - bdolin@elimu.io
28. Deepak Sharma - Mayo Clinic - sharma.deepak2@mayo.edu
29. Kevin Power - Cerner - kpower@cerner.com (joined at :26 minutes)
30.

Agenda:

1. Other guides discussion, potential connectathon thoughts
   a. MCODE and/or phenopackets
   b.
2. Updated diagrams
3. Examples for Connectathon re: discussion last week
4. Textual description component
5. 12 TBD LOINCs need creating/resolving
6.

Discussion:

1. Other guides discussion, potential connectathon thoughts
   a. MCODE and/or phenopackets
      i. Reconciliation might be interesting here
b. Genomics England has their own codesets (derived from 1000 genomes) would be interesting to compare/connect
c. Will look for breakout rooms

2. Diagrams
   a. Want to confirm inheritance properties are needed (eg seqphasere1)
   b. Rather than “not defined in this guide”, “Resource defined in core spec”

3. Examples for connectathon (discussion from last week)
   a. Concern over if only groupers are referenced directly on the report, the lower level observations may not be found.
      i. Less advanced systems may have to be smarter about their queries.
      ii. Let’s build this into a Connectathon scenario, **see who can see what with what queries**

4. Text component:
   Clem proposed to align with emerge. Alignment in progress here:  

   **Comment Patrick:** I think we could use related Artifact here.
   (related Artifact needs to be extended to fit this purpose, needs a coding of what kind of artifact it represents)
   Proposed resolution from Patrick: persuasive with mod

   ===Update 6. Aug ===
   Alligned with emerge:

   Created example profile:
   https://simplifier.net/patrickssandbox/comment

   Alligns nicely with GF to O&O:
   http://gforge.hl7.org/gf/project/fhir/tracker/?action=TrackerItemEdit&tracker_item_id=22102

   ● Larry was not fully happy with the proposal, would rather have 3 options, one for methodology notes, one for interpretation (references, etc), and additional comments. Would like to have it on variants and also **on the overall report**
      ○ If it is information about the items contained in a grouper, it must be on the items themselves, they can’t inherit info
      ○ Curious this hasn’t come up in other issues with O&O
   ●
   ● Concern over adding an extension for something critical for interpretation
   ● Observation.narrative can’t hold info that isn’t contained in other fields
• Observation.note can provide additional info about the Observation itself is typically captured after the observation is already “final”
• Gil: confirm options are considered and reconcile with tracker
• Should also consider simply getting this into a component

Need to finish up changes and produce updated frozen version for other guides to reference. Should be here next week!

5. TBD LOINC
   a. Need to create local codes so we can validate profiles before LOINC gets the concepts fully integrated

Chat History
Clinical Genomics Work Group
11:02 AM
https://docs.google.com/document/d/1FGCQRtxJKyHhnC1uB_t4sJZ9yXbLMGOqPXHPr5tSLLQ/edit#heading=h.yntd678x4fjv

Bret Heale
11:03 AM
finally reviewed mcode closely. Definitely a difference in the target of our IG - which is more focused on lab reporting - and theirs - reporting data elements in oncology care. However, theirs are some good overlaps. Recommend checking it out.

Bret Heale
11:14 AM
anyone know if Phenopackets or mCODE have FHIR, or otherwise, servers with data using their IGs?

FHIR Subgroup Meeting August 12th, 2019
https://join.freeconferencecall.com/clingenomics

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37. Bob Dolin - Elimu Informatics - bdolin@elimu.io
38. Deepak Sharma - Mayo Clinic - sharma.deepak2@mayo.edu
39. Clem McDonald - NLM - clemmcdonald@mail.nih.gov
40. Bob Milius - NMDP/CIBMTR - bmilius@nmdp.org
41. Bret Heale - Intermountain - bheale@gmail.com

Agenda:

1. Trackers applying towards draft publication:
   a. 31 last week >> 26 this week
2. New build errors fixed, thanks Kevin and Lloyd!
3. Added Groupers to OncologyReport example
   b. Concern over if only groupers are referenced directly on the report, the lower level
      observations may not be found.
      i. Less advanced systems may have to be smarter about their queries.
      ii. Let’s build this into a Connectathon scenario, see who can see what with
           what queries
4. Added compound heterozygote example using hasMember
   a. Clem: could also use the compound HGVS as one variant
      
      NM_022787.3(NMNAT1):c.[53A>G];[769G>A]
   b. Issue where multiple ways to display this info, some of which is unavoidable,
      whether “full” annotation is done, if lowest level observations are only reported, etc.
5. Reconsidering LOINC binding levels from
   https://docs.google.com/document/d/1E-nal_OPhJ8SSaI_N_f9XqiL5lyuGyhTlbUae8MWLMU/edit
   a. Patrick went over as well, will update in IG
6. Comments on region-studied:
   a. from Clem re: clarifying region-studied component “region-coverage”
   b. 19975 obs-region-studied Region Scope duplicates method?
      i. Current example answer list: Genome|Exome|GenePanel|SpecificVariants
      ii. Potentially duplicates region-description (string)
      iii. Mark tracker for vote, remove region scope to simplify model and push
           for publication
   c. Consideration on method and extension requested by eMerge

d. Text for methodology may still be most effective

7. High level diagram
   a. Observations Inheritance

   ![High level diagram](image)

   b. Should we make seq-phase-rel inherit from computable finding as well and remove “computable” from the name?
      i. (adds optional components Gene studied ID, Cytogenetic (chromosome) location, Human reference sequence assembly version)
      ii. Cleans up later diagrams referring to Findings

1. **Add as follow-up to high-level diagram tracker and flag ready for vote**
Bret Heale
11:33AM
a little glib ...but FHIR already got the easy 80 percent, we're stuck with the edges: ^ )
Bret Heale
11:58AM
if it is just the LOINC submission and creating definitions for tbd I can commit to pursuing the codes

FHIR Subgroup Meeting August 5th, 2019
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48. Patrick Werner - MOLIT Institut - patrick.werner@molit.eu
49. Dora Finkeisen - MOLIT Institut - dora.finkeisen@molit.eu
Agenda:

8. Trackers applying towards draft publication:
   a. 31 to apply, 10 currently unassigned, several requesting clarification below

9. New build errors:
   a. Issue with value[x] properties not resolving (eg, valueCodeableConcept, valueQuantity, etc)
   b. Agreed in R4 to change how differentials work on polymorphic types
   c. Old: for value[x], if you declare valueCoding, it would automatically constrain to coding. Realistically, want to be able to specify rules and performing constraints separately. First do a value[x] and then declare what the type is.
   d. https://chat.fhir.org/#narrow/stream/179304-genomics.2Fcommitters/topic/Publication.20Prep.202019

10. Possible comments on PGX profiles/LOINC TBD’s by Clem tomorrow if available

Discussion:

Update on Cytogenetic Nomenclature: name was changed on 19936 following Jan WGM, said we’d consider moving it into a component. (see ObsStructuralGeneticFinding should be a component of obs-variant).

   Update: voted to move into Variant last week.

<table>
<thead>
<tr>
<th>Tracker</th>
<th>Request</th>
<th>Proposal</th>
</tr>
</thead>
</table>
| obs-variant complex variant component should be merged | "add guidance for using 81263-6 and Observation.hasMember if and only if sending complex variant information." | "When sending a grouping of non-contiguous variants that are meant to be interpreted together but do not signify a named haplotype, one can send the type of complex variant here (determined by where the individual changes are in relation to each other), and use Observation.hasMember to reference the individual variants, which would then be described as normal."

   Patrick: still worried about the level of components in Variant,
   Kevin: seems like a good middle ground approach as we had discussed before, may re-address after feedback. Had found an example in Clingen at some point.
<table>
<thead>
<tr>
<th>Will update Compound Heterozygous example into FHIR and link to text about the component.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Panel is allowed but it is confusing</strong></td>
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<tr>
<td><strong>Add high level diagram to the IG</strong></td>
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<tr>
<td>Inherited Disease Pathogenicity - ValueCodeableConcept non LOINC value</td>
</tr>
<tr>
<td>---</td>
</tr>
</tbody>
</table>
| Usage of "genetics" and "genomics" | “Review IG (text, profile names/documentation) and ensure consistent usage of genetics/genomics.” | Options:  
1. Replace all genetic with **genomic**  
   a. (genomics) supercedes genetics so may be more appropriate  
2. Replace all genomic with genetic  
3. Add text to **background**,  
   a. “In this guide, the terms **genetic** and **genomic** will be used interchangeably.”  

Update all genetic to genomic, add disclaimer text for anyone looking for the term ‘genetic’ (options 1&3 above)  

**applied** |
| Region Studied is an arbitrary location | Textual guidance for how to use this profile (more about what was actually found). | Current definition: “The Region Studied profile is used to assert actual regions studied for the performed test(s). Intended coverage areas may differ from actual coverage areas (e.g. due to technical limitations during test performance).”  

Current description under diagram: “These are observations describing the region or regions that were studied as part of this Genomics Report.”  

Could say, “The Region Studied profile can assert and describe actual regions studied for the performed test(s).” |
Will revisit linking with intended/ordered regions after publication and feedback.
Will add text to Region-Studied variant group for sending arbitrary location using last 3 components

FHIR Subgroup Meeting July 29th, 2019
https://join.freeconferencecall.com/clingenomics

Quick link to this sign-in/notes document:
tinyurl.com/fhirgenomics

Sign In: (presiding co-chair - Gil Alterovitz - gil_alterovitz@hms.harvard.edu)

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56. Dora Finkeisen - MOLIT Institut - dora.finkeisen@molit.eu
57. Lloyd McKenzie - Gevity - lmckenzie@gevityinc.com
58. Liz Amos - NLM - liz.amos@nih.gov
59. Bob Dolin - Elimu Informatics - bdolin@elimu.io

Agenda:
1. Tracker implementation:
   a. 19998 Add more details about what the figure is attempting to describe. - CG #31
   
      16253 Enhance overall understandability of CG IG

      19870 Add high level diagram to the IG
Potentially remove last (lowest) level of profiles on the diagram,

mCode and Breast cancer have high level diagrams (see http://standardhealthrecord.org/guides/mcode-r4/modeling.html)

Patrick: maybe de-emphasize the implications that are less mature in our IG
- Add to Variant reporting diagram to show how they sit on the report itself

Remove extra diagram (6)

File a new tracker: group ISCN into Variant as component

Concerns with properties of variant being geared toward NGS, not fish results or other macroscopic data

1. Other topics of concern:
   a. Region studied - make sure full description is listed on profile itself, leave off variant diagram

2. Discussion:
   1. Ballot commenting deadlines (for content other than Genomics Reporting, which is not up for ballot) other content may be relevant to our space
      a. Day before ballot opens (EOD August 7th)

**FHIR Subgroup Meeting July 22nd, 2019**

[https://join.freeconferencecall.com/clingenomics](https://join.freeconferencecall.com/clingenomics)

Quick link to this sign-in/notes document: [tinyurl.com/fhirgenomics](https://tinyurl.com/fhirgenomics)

**Sign In:** (presiding co-chair - Gil Alterovitz - gil.Alterovitz@hms.harvard.edu)

60. James Jones - BCH - james.jones.bch@gmail.com
61. Patrick Werner - MOLIT Institut - patrick.werner@molit.eu
62. Dora Finkeisen - MOLIT Institut - dora.finkeisen@molit.eu
63. Deepak Sharma - Mayo Clinic - sharma.deepak2@mayo.edu
Agenda:

1. Call for Connectathon attendance/scenarios/input
   a. [https://confluence.hl7.org/display/FHIR/2019-09+Clinical+Genomics+Track](https://confluence.hl7.org/display/FHIR/2019-09+Clinical+Genomics+Track)
      i. September 14-15 Atlanta, GA
2. Non-ballot trackers towards publication
   a. Previous recommendation:
      i. [Inclusion of Sanger confirmation information](https://confluence.hl7.org/display/FHIR/2019-09+Clinical+Genomics+Track)
   b. Still to discuss:
      i. [Ability to include interpretation text/findings and recommendations to Observation](https://confluence.hl7.org/display/FHIR/2019-09+Clinical+Genomics+Track)
      ii. [Need guidance on housing extended test, methodology and reference information](https://confluence.hl7.org/display/FHIR/2019-09+Clinical+Genomics+Track)
      iii. functional annotation [GF#22815](https://confluence.hl7.org/display/FHIR/2019-09+Clinical+Genomics+Track) and variant type [GF#22814](https://confluence.hl7.org/display/FHIR/2019-09+Clinical+Genomics+Track)

Discussion:

   a. Attending (September 14-15 Atlanta, GA)
      i. Gil, Jamie, Lloyd, Joel, Patrick, Alex…
      ii. Anyone else confirm?
   b. Deadline is July 31 for finalizing page
   c. Zulip topic:
      [https://chat.fhir.org/#narrow/stream/179197-genomics/topic/Atlanta.20Connectathon.202019](https://chat.fhir.org/#narrow/stream/179197-genomics/topic/Atlanta.20Connectathon.202019)
      i. Possible cancer/genomics IG interoperability probe scenario?

2. Draft release planning:
   a. Content issues:
      i. Should fix breaking issues (dna-change type has no binding, the corresponding LOINC AL is not complete)
   b. Bob D: have to get this published in the timeline, should prioritize finalizing for that
      i. Goal: Final version ready Aug 26th (5 weeks left)
   c. Technical/logistic issues:
      i. Validation/QA
         1. Fix errors in examples
         2. Target is for there to be 0 errors and 0 warnings
         3. Can report exceptions due to tooling errors (requires approval)
4. Warnings require documentation and/or suppression (can add to the suppression file as needed but should be conscious choices)
   ii. Reconciliation package

3. Non-ballot trackers towards publication
   a. Window for logging new trackers is closing (will need August to finish applying and validation testing)
   b. Previous Discussion led to a recommendation (not yet voted on, any second thoughts?)
      i. 2 new Variant components: “ConfirmationMethod” (codeableConcept: sanger, MLPA, extensible, ...), “ConfirmationStatus” (codeableConcept: confirmed, needs confirmation, determined high confidence, unknown)
   c. Sending/structuring interpretation and methodology text
      i. Requests for more structure to send text in both Observation and DiagnosticReport

<table>
<thead>
<tr>
<th>Ability to include interpretation text/findings and recommendations to Observation</th>
<th>Request is to allow interpretive text on base genetic observation (resource has interpretation codeableConcept we have restricted to 0..0). Preferably in a coded/component sense.</th>
<th>Not Persuasive with mod</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Current options for Observation: Observation.text (Narrative) Observation.note (0..* Annotation)</td>
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<td>There was a similar request at the report level: <a href="https://chat.fhir.org/#narrow/stream/189875-genomics-/2F.20merge.20Pilot/topic/methodology">https://chat.fhir.org/#narrow/stream/189875-genomics-/2F.20merge.20Pilot/topic/methodology</a> to allow sending coded information of this sort on DR (which lacks components). Patrick filed 22101 with O&amp;O to see if they would like to include this functionality. Until then, do we want to include as extension or provide other textual guidance?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Little to no guidance given on use of Observation.method. Note is difficult to use for methodology, etc. Need to be sure we can give proper guidance using relatedartifact and confirm if it does what is required.</td>
<td>Persuasive with mod- increase cardinality of extension on report and add textual guidance/examples for observation.method</td>
</tr>
<tr>
<td></td>
<td>(base data type) <a href="http://build.fhir.org/metadatatypes.html#relatedartifact">http://build.fhir.org/metadatatypes.html#relatedartifact</a> -JJ: currently set at 0..1, is this a mistake?</td>
<td></td>
</tr>
</tbody>
</table>
c. functional annotation GF#22815 and variant type GF#22814

(Discussion from 7/16):
Bob D: seems to overlap with DNA change type; thinks of functional and variant type are different
(DNA change type uses https://s.details.loinc.org/LOINC/48019-4.html?sections=Comprehensive)
Patrick: definitely some overlap; simpler to merge, but can keep separate. What's the difference?
Bob D: maybe merging but name it to be clear to be different from DNA change type?
Patrick: sure, that would work
Bob M: Can we remove DNA change type and just use this?
Bob M: can we use this as our value set (prefer to point to one instead of creating our own)?
Bob F: has had difficulty with SO; for our uses we should document clearly what we want to use;
important to distinguish function from structural/physical changes.
Bob D: can we take DNA change type and these two and describe exactly what we use them for;
then after that bind the value set.
Bob M: make a zulip chat thread, define there.
Patrick: will start thread
https://chat.fhir.org/#narrow/stream/179197-genomics/topic/DNA.20change.20type

Patrick Werner: quick solution: create our own DNA change type valueSet with concepts from SO

Patrick Werner: could look like this:

Patrick Werner: This includes all concepts below sequence_comparison which is more than the LOINC
list but includes everything from the LOINC list

Patrick Werner: this is the mapping:
https://docs.google.com/spreadsheets/d/1IZYGLR18hYwKMhNjxG_NO-JhSS1ZxTJ5RviqDx8iBe0/edit?usp=sharing

Proposal:
1. Update DNA-change type (48019-4) preferred binding to SO (anything under SO:0002072)
   a. Provide concept map to LOINC (code systems appendix??) (based on this)
   b. Add slice for Coding with system = loinc.org
2. Add variant annotation (TBD) bound to SO (anything under SO:0001537)
3. Get feedback

Comment:
Still using LOINC for codes for sending profiles/components wherever possible, adding in SO values where domain-specific descriptions and lists are the most suitable. Will provide concept mappings where possible as well.
For a FHIR valueset, can have a mixture of terms if we need (though SO may be broad enough to cover everything in one list).
Lloyd: 2 cautions- don’t want concepts to overlap within a valueset, terminology services may
struggle to validate over multiple systems.
Bret: LOINC can only do intentional, SO can perform subsumption testing as it is hierarchical
Lloyd: can make valuesets from LOINC question and/or answer codes, eg
Gil: Need to reassess reasons against using SO, check with GA4GH, etc. Are there validator concerns?
Bret: would even like to consider moving more molecular concepts to SO
Jamie: double check no unnecessary concept overlap with amino acid change type
https://r.details.loinc.org/AnswerList/LL380-7.html

CHAT:

○ Bret Heale 11:31AM
  ● I believe the field is extensible in values used so you can certainly use your value set, or we can modify a version from the working group
  ● i.e a hybrid LOINC and SO value set - which is planned to be only LOINC once LOINC adds the additional terms this way users only point to one value set
  ● new item: totally. SO will likely always be more granular than LOINC answer lists (personally LOINC should point to SO terms as mappings for LA codes or just dispense with LA codes and indicate some example values and point to SO as a way to encode them)

FHIR Subgroup Meeting July 15th, 2019
https://join.freeconferencecall.com/clingenomics

Quick link to this sign-in/notes document: tinyurl.com/fhirgenomics

Sign In: (presiding co-chair - Gil Alterovitz - gil_alterovitz@hms.harvard.edu)
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6. Patrick Werner - MOLIT Institut - patrick.werner@molit.eu
7. Deepak Sharma - Mayo Clinic - sharma.deepak2@mayo.edu
8. Lloyd McKenzie - Gevity - lmckenzie@gevityinc.com
Agenda:

1. Call for Connectathon attendance/scenarios/input
   a. [https://confluence.hl7.org/display/FHIR/2019-09+Clinical+Genomics+Track](https://confluence.hl7.org/display/FHIR/2019-09+Clinical+Genomics+Track)
      i. September 14-15 Atlanta, GA
      ii. Likely attending:
          1. Gil, Jamie, Lloyd, Joel, Patrick,
      iii. Deadline is July 31 for finalizing

2. Non-ballot trackers towards publication
   a. Window for logging new trackers is closing (will need August to finish applying)
   b. Variant confirmation method and confirmation status
      i. Components for simplicity or separate Observation for completeness?
   c. Sending/structuring interpretation and methodology text
      i. Requests for more structure to send text in both Observation and DiagnosticReport

Discussion:

Confirmation and Confidence

1. 1 optional component:
   a. status of whether a variant is confirmed, needs to be, or doesn’t need to be could be computed based on how/whether this component is filled out.
      i. Ideally we’d want to iron out an extensible list for this but it doesn’t exist yet. Current example idea (please suggest others too): **Sanger, MLPA, High Confidence True Positive**: (eg, per [https://jmd.amjpathol.org/article/S1525-1578(18)30291-5/fulltext](https://jmd.amjpathol.org/article/S1525-1578(18)30291-5/fulltext)), **Not performed**: likely needs confirmation to be clinically used, **Unknown**: sender had no information on confidence of variant

   b. Most flat approach, if we want to suggest this information be included for every variant.

2. 2 optional components:
   a. **ConfirmationMethod** (codeableConcept: sanger, MLPA, extensible, ...), **ConfirmationStatus** (codeableConcept: confirmed, needs confirmation, determined high confidence, unknown)
   b. More clear concept delineation semantically, still quite flat
3. Separate Observation profile “confirmation”
   a. valueCodeableConcept for status, Observation.method for method
   b. More flexible for reporting performer/device and adding extensions or other info
   c. Refer to Variant with Observation.focus 1..*

4. Not suggest any particular structure for sending this info

Bob D: simple flag for confirmation is needed, but IG seems to already be a bit of a barrier. Why not keep it simple at first for the requirements currently known?
Bob M: what about the observation.method plus component that indicates confidence?
Bob D: if a lab is saying a variant is high confidence (either from computational analysis or testing methods that aren’t 100% standardized) I would trust them on it.
Bob M: Observation.method needs discussion overall, especially if we have multiple places talking about method.
Kevin: I was thinking option 2 but option 3 seems appropriate
Patrick: concern we are turning variant into a key value store with all these components. can do inline “contained” reference for confirmation observations.
Bob D: i worry that nobody is asking for that much structure yet, we’re looking forward for it but could try it with simplicity first.
Clem: I like simplicity here but we should check with clinical labs, they shouldn’t be reporting variants they haven’t confirmed.
Deepak: Clinically, method is important and what sort of parameters used. I like #3
Bob D: in #2, method backs up status
In #3, have to consider using focus to point to variant or derivedFrom from within variant itself.

Straw Poll:
Kevin: While I still like #3, given how this is going, I say +1 to propose option #2
Peter: I like #2
Patrick: a confirmation is an observation so I would prefer #3

- Kevin Power
- Host
- 11:53AM

- Maybe option #4 (defer) is the right answer given all this uncertainty
  - 0Patrick
  - Host
  - 11:54AM
+1 maybe people with a need for this will create something for their use case and then can bring them upstream?
  ○ Deepak Sharma
  ○
  ○
  ○
  ○
  ○
  ○ 11:57AM

#2 or #3
  ○ Kevin Power
  ○
  ○
  ○
  ○
  ○
  ○ 11:59AM

Yup vote on #2
  ○ Joel Schneider
  ○
  ○
  ○
  ○
  ○
  ○ 11:59AM

+1 for #2

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**FHIR Subgroup Meeting July 1st, 2019**

[https://join.freeconferencecall.com/clingenomics](https://join.freeconferencecall.com/clingenomics)

Quick link to this sign-in/notes document: [tinyurl.com/fhirgenomics](http://tinyurl.com/fhirgenomics)

**Sign In: (presiding co-chair - Gil Alterovitz - gil_alterovitz@hms.harvard.edu)**

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4. Liz Amos - NLM - liz.amos@nih.gov
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6. Patrick Werner - MOLIT Institut - patrick.werner@molit.eu
7. Joel Schneider - NMDP/CIBMTR - jschneid@nmdp.org
8. Bob Dolin - Elimu Informatics - bdolin@elimu.io
9. Bret Heale - Intermountain - Heale@imail.org
10. Lloyd McKenzie - Gevity - lmckenzie@gevityinc.com

11. Agenda:

3. Call for Connectathon attendance/scenarios/input
   a. [https://confluence.hl7.org/display/FHIR/2019-09+Clinical+Genomics+Track](https://confluence.hl7.org/display/FHIR/2019-09+Clinical+Genomics+Track)
      i. September 14-15 Atlanta, GA
      ii. Deadline is July 31 for finalizing

   1. Joel: HLA nomenclature uploading with HAPI, may work with Rob from Terminology
      a. Recent pull request on HAPI containing terminology upload api (LOINC, SNOMED, etc) to create CodeSystem resource. [https://github.com/jamesagnew/hapi-fhir/pull/1330](https://github.com/jamesagnew/hapi-fhir/pull/1330)
      b. Once finished, HAPI would be able to validate GL String codes for HLA use cases. (eventual goal is to support GLSC: [https://glstring.org/](https://glstring.org/))
      c. Bret: how complex is GLString to HGVS conversion?
         i. GL string covers multiple alleles and ambiguity, with gene-level named haplotypes. HGVS conversion wouldn’t necessarily be useful to HLA stakeholders as well.
      d. NMDP hosting another DaSSH fhir hackathon in August (Bob M has more info)

   2. Could look at opening up to non-HLA use cases: clinvar terminology service, sequence ontology, etc. LOINC has one but building out others will be very helpful in the future.
      a. Once a terminology server is hosted, validation can be done by accessing the server rather than every server needing to perform the upload (implementation concerns here).

   3. May from MITRE also mentioned mCODE may attend

4. Non-ballot trackers towards publication
   a. Window for logging new trackers is closing (will need August to finish applying)
   b. 20549-related items:
i. “Required” LOINC answer lists that may cause issues
   ii. “Required” (missing) LOINC codes that can’t validate
   c. Other trackers pulled from last week
d. Sending/structuring interpretation and methodology text
e. Sanger confirmation and general confidence

| LOINC-related |
|---------------|-----------------|-----------------|
| **Inherited Disease Pathogenicity - ValueCodeableConcept non LOINC value** | Would like to confirm all “required” LOINC lists | Persuasive with mod - update list binding to extensible |
| 20549 | [https://docs.google.com/document/d/1E-nal_OPhJ8SSaIN_f9XgiL5lyuGyhTlbUae8MWLMU/edit](https://docs.google.com/document/d/1E-nal_OPhJ8SSaIN_f9XgiL5lyuGyhTlbUae8MWLMU/edit) | Will follow-up on ZULIP need to hash out a lot of text and request/make placeholder codes |

| Text-related |
|---------------|-----------------|-----------------|
| **Ability to include interpretation text/findings and recommendation s to Observation** | Request is to allow interpretive text on base genetic observation (resource has interpretation codeableConcept we have restricted to 0..0). Preferably in a coded/component sense. | Not Persuasive with mod |
| 20978 | Current options for Observation: Observation.text (Narrative) Observation.note (0..* Annotation) | |
| | There was a similar request at the report level: [https://chat.fhir.org/#narrow/stream/189875-genomics.-2F.20eM erge.20Pilot/topic/methodology](https://chat.fhir.org/#narrow/stream/189875-genomics.-2F.20eM erge.20Pilot/topic/methodology) to allow sending coded information of this sort on DR (which lacks components). Patrick filed [22101](https://chat.fhir.org/#narrow/stream/189875-genomics.-2F.20eM erge.20Pilot/topic/methodology) with O&O to see if they would like to include this functionality. | |
| | Until then, do we want to include as extension or provide other textual guidance? | |
| | Current options: DR.text | |
| **Need guidance on housing extended test.** | Little to no guidance given on use of Observation.method. | Persuasive with mod - increase cardinality of extension on report |
| 19827 | | |
| methodology and reference information | Note is difficult to use for methodology, etc. Need to be sure we can give proper guidance using relatedArtifact [http://build.fhir.org/ig/HL7/genomics-reporting/extension-dr-relatedArtifact.html](http://build.fhir.org/ig/HL7/genomics-reporting/extension-dr-relatedArtifact.html) -JJ: currently set at 0..1, is this a mistake? and add textual guidance/examples for observation.method |

| Confirmation/Confidence | Would this be another Variant profile duplicating many components? Or a generic Observation stating the method of confirmation?

Is confidence a separate component?

Zulip chat for this topic: [https://chat.fhir.org/#narrow/stream/179197-genomics/topic/Sanger.confirmation.2Ftesting](https://chat.fhir.org/#narrow/stream/179197-genomics/topic/Sanger.confirmation.2Ftesting)

Should it be confirmationMethod rather than status?

Need to hash out example list:

Sanger, etc

“Not performed” for research tests, etc.

“Not needed, high confidence region” etc for

Will follow up on Zulip and listserv as proposal solidifies. |

| Inclusion of Sanger confirmation information | 19829 |

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**FHIR Subgroup Meeting June 24th, 2019**

[https://join.freeconferencecall.com/clingenomics](https://join.freeconferencecall.com/clingenomics)

Quick link to this sign-in/notes document: [tinyurl.com/fhirgenomics](https://tinyurl.com/fhirgenomics)

**Sign In:** (presiding co-chair - Gil Alterovitz)

12. James Jones - BCH - james.jones.bch@gmail.com
13. Joel Schneider - NMDP/CIBMTR - jschneid@nmdp.org
14. Liz Amos - NLM - liz.amos@nih.gov
15. Deepak Sharma - Mayo Clinic - sharma.deepak2@mayo.edu
16. Bob Dolin - Elimu Informatics - bdolin@elimu.io
17. Clem McDonald - NLM - clemmcdonald@mail.nih.gov

Agenda:

5. Call for Connectathon attendance/scenarios/input
   a. [http://www.hl7.org/events/working_group_meeting/2019/09/](http://www.hl7.org/events/working_group_meeting/2019/09/)
      i. September 14-15 Atlanta, GA
   b. Will draft Confluence page this week

6. Non-ballot trackers towards publication
   a. Recommendations:
      i. 22728 - Profile names should meet FHIR naming standards
         recommendation: Persuasive - Update ALL profiles names to follow the guidelines and use CamelCase naming. (voted but Kevin has follow-up)
      ii. 18988 - CG IG should support: MSI, TMB, PD-L1 recommendation: Persuasive with mod - add “Other observations” to figure 1 as report results. Add textual guidance under the figure for sending other tests.
      iii. 19829 - Inclusion of Sanger confirmation information Proposal: Persuasive with mod - add a component for confidence, (example values: High/Medium/Low/unknown)
   b. Still considering (needs more discussion/solidification of proposals):
      i. Need guidance on housing extended test, methodology and reference information
      ii. Usage of LOINC code 81247-9 for Genetic tests
      iii. Inherited Disease Pathogenicity - ValueCodeableConcept non LOINC value
      iv. Ability to include interpretation text/findings and recommendations to Observation

Discussion:

<table>
<thead>
<tr>
<th>Profile names should meet FHIR naming standards</th>
<th>Name should be usable as an identifier for the module by machine processing applications such as code generation [name.matches('A-Z{0,254}')]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zulip</td>
<td>It seems our choice of '-' conflicts with this warning. From a review of other IG's, it seems that the most common way</td>
</tr>
<tr>
<td>22728</td>
<td>Persuasive - Update ALL profiles names to follow the guidelines and use CamelCase naming.</td>
</tr>
</tbody>
</table>
1. **Resource/profile selection**: Should a test like this be a single Observation matching one of our "Finding" profiles, a "Grouper" of Observations, or a whole sub-report? Should we just use Variant and tack on an additional component?

2. **Code to send**: Should users look through LOINC to find whatever code is closest and use that? Is there a generic LOINC code we can point them to and tell them to enter additional context into coding.text or Observation.note? Is just sending it as text okay?

3. **Value**: If an Observation, is HIGH/LOW/etc okay?
   1. Recommend we give guidance on sending computational values with unit descriptions and context as much as possible.

4. **Interpretation**: since Obs-base is not meant to be "implementable", do we want to enforce interpretations are still zeroed out and other Implication/etc profiles are used?

5. **Method/Device/RegionStudied**: How descriptive is Observation.method meant to be? Is text okay or how can we code our own tests?

6. **RegionStudied**: How does this get linked? HasMember? DerivedFrom? Being in the same grouper? We still lack guidance on how to include this resource apart from as another result on a report.

PD-L1 would be a numeric RNA-expression test, may generalize easily. Could flag if RNA vs IHC.

Patrick: suggest we don’t attempt to cover all biomarkers
Bret: do we want to try and link these with region-studied or at least the gene-studied component?
Would be great if LOINC had an internal database for which tests applied to which genes by name…

**Persuasive with mod**
- add "Other observations" to figure 1 as report results for TMB/MSI and biomarkers as. Add textual guidance under the figure.

and expand guidance in application of 16408:

"1: add text for how to send multiple codes 2: add textual examples of where this is important and adds value

Additionally, we will request interested parties to create ontology-specific tables and guidance for matching up our LOINC items. Work group is open to publish this content as appendices and link to them from the main text."

**Need guidance on housing**

**Persuasive** - add guidance/examples for
| **Inclusion of Sanger confirmation information** | 19829 | Would this be another Variant profile duplicating many components? Or a generic Observation stating the method of confirmation?

Is confidence a separate component?

Zulip chat for this topic: [https://chat.fhir.org/#narrow/stream/179197-genomics/topic/Sanger.20confirmation.2Ftesting](https://chat.fhir.org/#narrow/stream/179197-genomics/topic/Sanger.20confirmation.2Ftesting)

**Proposal:** add a component for confirmationStatus and another for confidence, (values example: High/Medium/Low/Unknown)

**High:** generally true positive (eg, per [https://jmd.amjpathol.org/article/S1525-1578(18)30291-5/fulltext](https://jmd.amjpathol.org/article/S1525-1578(18)30291-5/fulltext)),

**Medium:** needs confirmation,

**Low:** likely false positive,

**Unknown:** sender has no information on confidence of variant.

| **Usage of LOINC code 81247-9 for Genetic tests** | 19831 | Request or provide guidance on different test codes?

Will confirm if actual request for additional codings here and/or if fully restricting the coding to 1..1 was a conscious choice.

| **Inherited Disease Pathogenicity - ValueCodeableConcept non LOINC value** | 20549 | Would like to confirm all "required" LOINC lists

(Genomic source class, Amino acid change type, Allelic state, Chromosome copy number change type, Genetic variation clinical significance, Genetic variation's effect on drug metabolism) are not just preferred lists that we entered incorrectly.

**Persuasive with mod - update list binding to preferred (in coordination with LOINC)**

| **Ability to include interpretation text/findings and recommendation** | 20978 | Note is difficult to use for methodology, etc. Need to be sure we can give proper guidance using relatedartifact

**Persuasive with mod - increase cardinality of extension on report and add textual** |
There was a request [https://chat.fhir.org/#narrow/stream/189875-genomics.-2F.20merge.20Pilot/topic/methodology](https://chat.fhir.org/#narrow/stream/189875-genomics.-2F.20merge.20Pilot/topic/methodology) to allow sending coded information of this sort on DR (which lacks components)

Current options:
- DR.text
- DR.renderedreport
- Observation.method/text/note on the relevant observations

---

**FHIR Subgroup Meeting June 17th, 2019**

[https://join.freeconferencecall.com/clingenomics](https://join.freeconferencecall.com/clingenomics)

---

*Quick link to this sign-in/notes document: tinyurl.com/fhirgenomics*

**Sign In: (presiding co-chair - Gil Alterovitz)**

1. James Jones - BCH - james.jones.bch@gmail.com
2. Patrick Werner - MOLIT Institut - patrick.werner@molit.eu
3. Dora Finkeisen - MOLIT Institut - dora.finkeisen@molit.eu
4. Joel Schneider - NMDP/CIBMTR - jschneid@nmdp.org
5. Lloyd McKenzie - Gevity - lmckenzie@gevityinc.com
6. Ning Xie - BCH - ningxie2018@gmail.com
7. Bret Heale - Intermountain Healthcare - bheale@gmail.com
8. Bob Dolin - Elimu Informatics - bdolin@elimu.io
9. Alex Mankovich - Philips - alex.mankovich@philips.com
10. Deepak Sharma - Mayo Clinic - sharma.deepak2@mayo.edu

**Agenda:**

1. September Connectathon: (Atlanta, GA)
   a. New pages to go up on confluence, aim for ~6 weeks before event
   b. Will confirm and draft page
      i. Additional track ideas?
      ii. Call for Participants
2. Non-ballot trackers (All ballot trackers have resolutions!)
   a. [https://docs.google.com/spreadsheets/d/1S1f-DtqBZ67zZxyhjNxy5zBDt55tRkMSCMgLYUc6SE/edit?ts=5d017514#gid=0](https://docs.google.com/spreadsheets/d/1S1f-DtqBZ67zZxyhjNxy5zBDt55tRkMSCMgLYUc6SE/edit?ts=5d017514#gid=0)
b. We selected 9 to review at higher priority based on recent work on examples/connectathons (see below)

c. any others looking to propose or recall (for addressing before IG publication - ASAP)

3. Applying “Resolved” trackers
   a. List of 45 still to apply
   b. Zulip: Genomics/Committers for tricky ones
   c. Any volunteers to help?
      i. Aim for 1 tracker per github commit

Discussion
1.

<table>
<thead>
<tr>
<th>Summary</th>
<th>Tracker</th>
<th>Notes</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IG to provide specifications around search</td>
<td>15884</td>
<td>Needs to use R4 search options for Observation, (<a href="http://build.fhir.org/observation.html#search">http://build.fhir.org/observation.html#search</a>) integrate with updated examples. Should also mention the potential need for genomics Operations for advanced queries.</td>
<td>Persuasive with mod - update the examples for latest version and guidance</td>
</tr>
<tr>
<td>Need a section that describes conversion from</td>
<td>15887</td>
<td>Add section describing use for systems locked into STU2? Current use case for integration with production EMRs using STU2. Should at least point people in the right direction for using guidance given here in other versions. Ambiguity as to which version of FHIG the guide is specifically aimed at in terms of validations (publishing as R4) Can provide short guidance/links to back-porting newer structures.</td>
<td>Persuasive with mod - make sure this page is current and include as “Appendix E”, remove incomplete mapping and provide brief guidance instead on compatibility.</td>
</tr>
<tr>
<td>STU 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CG IG should support: MSI, TMB, PD-L1</td>
<td>18988</td>
<td>7. <strong>Resource/profile selection</strong>: Should test like this be a single Observation matching one of our &quot;Finding&quot; profiles, a &quot;Grouper&quot; of Observations, or a whole sub-report? Should we just use Variant and tack on an additional component? 8. <strong>Code to send</strong>: Should users look through LOINC to find whatever code is closest and use that? Is there a generic LOINC code we can point them to and tell them to enter additional context into</td>
<td>Persuasive with mod - add “Other observations” to figure 1 as report results for TMB/MSI and biomarkers as. Add textual guidance under the figure asking</td>
</tr>
</tbody>
</table>
coding.text or Observation.note? Is just sending it as text okay?

9. **Value:** If an Observation, is HIGH/LOW/etc okay?
   1. Recommend we give guidance on sending computational values with unit descriptions and context as much as possible.

10. **Interpretation:** since Obs-base is not meant to be "implementable", do we want to enforce interpretations are still zeroed out and other Implication/etc profiles are used?

11. **Method/Device/RegionStudied:** How descriptive is Observation.method meant to be?
    Is text okay or how can we code our own tests?

12. **RegionStudied:** How does this get linked?
    HasMember? DerivedFrom? Being in the same grouper? We still lack guidance on how to include this resource apart from as another result on a report.

PD-L1 would be a numeric RNA-expression test, may generalize easily. Could flag if RNA vs IHC.

Patrick: suggest we don’t attempt to cover all biomarkers
Bret: do we want to try and link these with region-studied or at least the gene-studied component?
Would be great if LOINC had an internal database for which tests applied to which genes by name…

<table>
<thead>
<tr>
<th>update the TODO sections in the IG</th>
<th>19454</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need guidance on housing extended test, methodology and reference information</td>
<td>19827</td>
</tr>
<tr>
<td>Inclusion of Sanger confirmation information</td>
<td>19829</td>
</tr>
</tbody>
</table>

**Persuasive** - convert standing TODO sections with requests for feedback

**Persuasive** - add guidance/examples for observation.method

Would this be another Variant profile duplicating many components? Or a generic Observation stating the method of confirmation?
| **Usage of LOINC code 81247-9 for Genetic tests** | 19831 | Request or provide guidance on different test codes? |
| **Inherited Disease Pathogenicity - ValueCodeableConcept non LOINC value** | 20549 | Would like to move all "required" LOINC codes to recommended/extensible ... |
| **Ability to include interpretation text/findings and recommendations to Observation** | 20978 | Note is difficult to use for methodology, etc. Need to be sure we can give proper guidance using relatedartifact |

Zulip chat for this topic: https://chat.fhir.org/#narrow/stream/179197-genomics/topic/Sangerconfirmation/2Ftesting
I recall that Patrick and I volunteered. We've not done anything yet. Unless you have

I think it should be done as group effort.

parsed out to multiple people

Patrick

yes, still on my todo list (which is a mess atm)

Bret Heale

great. +1 Jaimie reviewing the searches in Zulip. please add the Zulip chat link to the
tracker/today's meeting notes : ^ )

11:33 AMthe gene studied is the importnat genetic portion. also a flag if this is

expression level by RNA or IHC

Bret Heale

just a note, not wanting to slow the flow. But, even though I made

a case on querying. There is nothing stopping a site from Creating a FHIR server

which does the LOINC computation to provide complete results to a query based on

a geneID.

FHIR Subgroup Meeting June 3rd, 2019

https://join.freeconferencecall.com/clingenomics
Quick link to this sign-in/notes document: tinyurl.com/fhirgenomics

Sign In: (presiding co-chair - Gil Alterovitz)

1. James Jones - BCH - james.jones.bch@gmail.com
2. Bret Heale - Intermountain Healthcare - bheale@gmail.com
3. Joel Schneider - NMDP/CIBMTR - jschneid@nmdp.org
4. Jamie Parker - Carradora Health - jamie.parker@carradora.com
5. Deepak Sharma - Mayo Clinic - sharma.deepak2@mayo.edu
6. Kevin Power - Cerner - kpower@cerner.com
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8. Sameer Malhotra - Weill Cornell Medicine sam2032@med.cornell.edu
9. Alex Mankovich - Philips - alex.mankovich@philips.com
10. Lloyd McKenzie - Gevity - lmckenzie@gevityinc.com
11. Liz Amos - NLM - liz.amos@nih.gov
12. Clem McDonald - clemmcdonald@mail.nih.gov

Agenda:
1. Tracker from last week re: effectiveness of medication (Bret to go over proposal)
2. Remaining connectathon trackers

Updated recommendations:

21636: Remove components 81260-2 and 81262-8, add guidance for using 81263-6 and Observation.hasMember if and only if sending complex variant information.
21238: Persuasive, Continue to use unitsofmeasure but do not enforce % (sender could choose to use fraction)
21283: Persuasive, update binding to extensible (LOINC will move list from normative)
21275: Persuasive, Stop restricting performer type from base resource

Proposals in the works:

21638: Patrick to look at reports and clarify use case for potential component to add

<table>
<thead>
<tr>
<th>Tracker</th>
<th>Summary</th>
<th>Affirmative</th>
<th>Kanwarpreet Sethi</th>
</tr>
</thead>
<tbody>
<tr>
<td>19995</td>
<td>How do the genetic findings affect the effectiveness of medication? - CG #28,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resolution</td>
<td>Persuasive: From Bret this morning: Recommend changing the wording on IG page</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Notes</td>
<td><a href="http://hl7.org/fhir/uv/genomics-reporting/2019JAN/pharmacogenomics.html">http://hl7.org/fhir/uv/genomics-reporting/2019JAN/pharmacogenomics.html</a> which reads 'Medication Efficacy Impact describes how the associated genetic findings affect the</td>
<td></td>
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</tr>
</tbody>
</table>
Medication Efficacy Impact describes how the associated genetic findings affect the ability of the patient’s body to respond to the medication (predicted phenotype) - distinct from metabolic impact, this is in regards to molecular function...

---

Comment:
Can you please clarify? How do the genetic findings affect the effectiveness of medication? Wouldn't the findings either decrease or increase medication effectiveness? Consider rewording for clarity.
Also, is the valueCodeableConcept within this profile (StructureDefinition: Medication Efficacy Impact) correct? Here are the values listed: Resistant | Responsive | Presumed resistant | Presumed responsive | Unknown significance | Non-Responsive | Presumed non-responsive. Are these the measure of medication effectiveness or of the impact?

---

Summary:
How do the genetic findings affect the effectiveness of medication?

Disposition
resistant/responsive typically used for cancer, increases/decreases typically used for germline
Efficacy not due to metabolism? Yes, others exist.
Need to compare lists currently available. Bob D will forward one.
Note from Bret in above resolution

Bret will apply change per recent listserv email (after fixing a typo) and will update the top-level definition to match as well as was voted last Tuesday.

From recent work/Connectathons

<table>
<thead>
<tr>
<th>Tracker</th>
<th>Summary</th>
<th>Resolution Notes</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>21635</td>
<td>Variant.code shouldn't be fixed,</td>
<td>Up for discussion, likely defer</td>
<td>Currently obs-variant.code is fixed to TBD-Described. To enable search for specific variant types this should be bound to a ValueSet.Add suggestion:- SNV- Structural Variant (do we need complex variant?)</td>
</tr>
</tbody>
</table>
Clinvar codes can do many things, will discuss further along with 21636.

With so many components in Variant (covering use of discrete, structural, and complex variants), can be difficult to determine how the profile is being used just by its code.

Variant currently has a valid code \(69548-6\)

Could leave structure as is and add a new component to differentiate SNVs etc which is difficult currently.

Rough Proposal: add component (code=???) extensible list (Single Nucleotide | Structural | ???) maybe no preferred list but would like a code

Clem: how does this change things? It doesn’t alter phenotype, eg.

Bret: main concern here is querying. For a system that doesn’t have the ability to go through HGVS/Clinvar/etc to pull information,

Foundation1 seems to not differentiate between scale of variants anymore

**Group leading towards not persuasive (with potential mod of adding component after patrick looks into the use case further)**

<table>
<thead>
<tr>
<th>Tracker</th>
<th>Summary</th>
<th>N/A</th>
<th>Patrick Werner</th>
</tr>
</thead>
<tbody>
<tr>
<td>21636</td>
<td>obs-variant complex variant component should be merged,</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Links | N/A |

| Resolution Notes | Persuasive (approved) |

| Details | as we merged discrete and complex variant we now have some redundant components: Complex genetic variant code Complex variant HGVS name Complex variant type &lt; cave: different ValueSet i assume there are more redundancies, needs review. |

| Follow-ups | |

| Discussion | Remove components 81260-2 and 81262-8, add guidance for using 81263-6 and Observation.hasMember if and only if sending complex variant information. |

<table>
<thead>
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<tbody>
<tr>
<td>21238</td>
<td>allele frequency component shouldn't use %,</td>
<td></td>
</tr>
</tbody>
</table>

| Links | N/A |

| Resolution Notes | persuasive (approved) |
the allele frequency component could be further simplified/ needs correction:- NFr are usually reported as 0.41 or 0.73, so our fixed unit "%" is wrong as then we would have to write the NFr as 41 and 71 which would be unusual- instead of valueQuantity valueDecimal would be sufficient

<table>
<thead>
<tr>
<th>Details</th>
<th>Follow-ups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disposition</strong></td>
<td>Continue to use unitsofmeasure but do not enforce % (sender could choose to use fraction)</td>
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</table>

<table>
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<tr>
<th>Tracker</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>21283</strong></td>
<td>Change Observation.method value set binding from required to at least extensible or preferred,</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Links</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><a href="http://build.fhir.org/ig/HL7/genomics-reporting/obs-variant.html">http://build.fhir.org/ig/HL7/genomics-reporting/obs-variant.html</a></td>
<td>Persuasive (approved)</td>
</tr>
</tbody>
</table>

Suggest that "Method" should not have a required binding, because new methods come along all the time. At best, extensible. For cancer-related genetic tests, we use the following codes from NCI Thesaurus based on 1) input from ASCO/CancerLinQ, and 2) the set of matching coded elements. 

**ValueSet:** GeneticTestMethodVS 

**Description:** "The method used to perform a genetic test, drawn from NCI Thesaurus. Examples include Fluorescent in situ hybridization (FISH), polymerase chain reaction-based assays (PCR), and next-generation sequencing (NGS)."

- NCIT#C130179 'Allele Specific Primer Polymerase Chain Reaction'
- NCIT#C18084 'Comparative Genomic Hybridization'
- NCIT#C19641 'Dideoxy Chain Termination DNA Sequencing'
- NCIT#C63328 'DNA Methylation Analysis'
- NCIT#C17563 'Fluorescence In Situ Hybridization'
- NCIT#C16768 'Karyotyping'
- NCIT#C18477 'Microarray Analysis'
- NCIT#C139286 'Microsatellite Stability Assessment'
- NCIT#C116161 'Multiplex Ligation-dependent Probe Amplification'
- NCIT#C101293 'Next Generation Sequencing'
- NCIT#C17003 'Polymerase Chain Reaction'
- NCIT#C519522 'Real Time PCR'
- NCIT#C17093 'Restriction Fragment Length Polymorphism'
- NCIT#C18136 'Reverse Transcriptase-Polymerase Chain Reaction'
- NCIT#C18473 'RNA Analysis'
- NCIT#C17565 'Sequence Analysis'
- NCIT#C116151 'Single Nucleotide Polymorphism Array'
- NCIT#C16356 'Southern Blotting'

We considered the possibility of using one of the LOINC answer lists as a high level method with the more detailed term as an alternate code, but there are some tests (e.g.: Southern Blot) which might not be a good fit for any of these terms.

**Follow-ups**

**Disposition** | Update binding to extensible (LOINC will move list from normative) |

<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td>N/A</td>
</tr>
</tbody>
</table>
### 21275  Genomics DiagnosticReport Performer should allow more resources,

**Links**

**Resolution Notes** Persuasive, seems like error (approved)

**Details** performer should support all referenced resource types Zulip discussion:https://chat.fhir.org/#narrow/stream/189875-genomics-.2F.20eMerge.20Pilot/topic/performer

**Follow-ups**

**Disposition** Stop restricting performer type from base resource

### 20978  Ability to include interpretation text/findings and recommendations to Observation,

**Links** N/A

**Resolution Notes** Write up recent guidance regarding relatedArtifact extension.

**Details** As highlighted in the attached test reports, we include textual findings/interpretations and recommendations in a genetic report. For the eMERGE reports, while mapping to draft CG IG spec, these textual interpretations span multiple FHIR Observation profiles in our implementation e.g. Referencing file "highlighted..." test report, text highlighted in grey and yellow would be a fit for general profiles like obs-overall and obs-inh-dis-path; text highlighted in green would be a fit for PGx profiles and the recommendations text highlighted in blue is a recommendation for the provider but not exactly a recommended action; it would be up to the provider to decide on the recommended action. Considering the need for including this kind of interpretative/summary text (this is not the same as the "text" narrative element) spans multiple Observation resources, it would be very helpful if Interpretation Text and Recommendations were added as Narrative or String elements to the obs-base resource itself.

### 20315  Genomic Diagnostic reports should have better ability to reference another diagnostic report.,

**Links** N/A

**Resolution Notes** Persuasive, write up guidance on extensions and link to examples

**Details** Diagnostic reports should have better ability to reference another diagnostic report. This was a finding from the Sync for Genes Phase 2 Pilot sites that participated in the January 2019 Connectathon. A molecular pathologist may have to stitch together various tests/specimens. A single diagnostic report may have multiple specimens. 2 specimens may generate 2 separate results + a 3rd result referencing those 2. More help on the FHIR website for describing examples would be helpful. HLA typing via buccal swab or blood is a relevant example. Having a GDR that can refer to other GDRs...
to have a separate swab for buccal swab vs blood + another that summarizes the 2 of them. Needs an advocate at O&O to push this through. Would be helpful if diagnostic reports can point to other diagnostic reports.

**Follow-ups**

- Tue, 19 Mar 2019 - by Eric Haas-look at v2 examples-will mock up extensions in DR.

**Discussion**

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>18988</td>
<td>CG IG should support: MSI, TMB, PD-L1,</td>
<td></td>
</tr>
</tbody>
</table>

**Links**

N/A

**Resolution Notes**

Persuasive, request Loinc codes for TMB, MSI status, PD-L1 test?

**Details**

Currently MSI, TMB, PD-L1 can't be captured with the CG IG. As these a relevant observations in oncology CG reports these values should be supported.

- Mon, 01 Oct 2018 - by Alexander Mankovich-Will follow up with a more detailed overview of MSI, TMB, PD-L1 attributes required for oncology CG reporting.-Mon, 07 Jan 2019 - by Alexander Mankovich-Please find sample descriptions for MSI, TMB, and PD-L1 (generally found in reports) below.-MSI:-Microsatellite Instability (MSI) by PCR Method-DNA extracted from tumor and normal (if available) tissue is amplified by PCR using fluorescently labeled primers for five mononucleotide repeat markers (BAT-25, BAT-26, NR-21, NR-24 and MONO-27). The PCR products are separated by capillary electrophoresis and the genotype of each marker is scored as stable or unstable by comparison of the tumor to the matched normal. If normal tissue is not available, the genotype of each marker is scored as stable or unstable by comparing the size of the tumor alleles to the size distribution of alleles present in a pool of normal tissues. -MSI Classification (Tumor and Matched Normal)-High - ≥40% of microsatellite markers are altered (≥2 altered markers out of 5)-Low - 1 altered marker-Stable - 0 altered markers-MSI Classification (Tumor Only)-MSI Positive - ≥2 altered markers-MSI Indeterminate - 1 altered marker-MSINegative - No altered markers--TMB:-Tumor mutation burden (TMB) testing measures the number of somatic variants per megabase of sequenced DNA. Results are reported as low, indeterminate, or high. The cutoffs were determined across a number of tumor types in an internal validation study. Tumor mutation burden is a biomarker associated with the production of neoantigens within the tumor. A high TMB score has been shown to predict sensitivity to treatment and duration of response to treatment with a checkpoint inhibitor immunotherapy. In contrast, a patient with a low TMB score may be less likely to respond, based on TMB alone; however, it is uncertain how a patient with an indeterminate TMB score might respond. An example of the cutoff values used to report the patient’s TMB is: &lt;7 is “low,” 7-19 is “indeterminate,” and &gt;19 is “high”. Different cutoffs are adapted based on the data source and variant selection (whole genome, exome or a gene panel).-PD-L1 IHC-Drugs inhibiting the PD-1/PD-L1 checkpoint have been approved by the Food and Drug Administration for several cancers – including lung, bladder, and kidney cancers, squamous cell cancer of the head and neck, and Hodgkin lymphoma – and are in clinical testing for a variety of other cancer types. A PD-L1 test measures how much PD-L1 a tumor “expresses,” or produces. Tumors that express high amounts of PD-L1 may be more susceptible to checkpoint inhibitors than those that express less. Patients should ask their cancer physicians whether a PD-L1 test is appropriate for them.-For a range of cut-off values, please consult the table 2 in the publication below:-https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5807740/
Patrick: Discussion last week about multiple specimen:
https://chat.fhir.org/#narrow/stream/179256-Orders-and.20Observation.20WG/topic/Specimen.20Cardinality/near/166095545 (there was some interest in O&O to have this as an core extension)

FHIR Subgroup Meeting May 20th, 2019
https://join.freeconferencecall.com/clingenomics

Quick link to this sign-in/notes document:
tinyurl.com/fhirgenomics

Sign In: (presiding co-chair - Gil Alterovitz)

11. James Jones - BCH - james.jones.bch@gmail.com
12. Liz Amos - NLM - liz.amos@nih.gov
13. Joel Schneider - NMDP/CIBMTR - jschneid@nmdp.org
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15. Dora Finkeisen - MOLIT Institut - dora.finkeisen@molit.eu
16. Alex Mankovich - Philips - alex.mankovich@philips.com
17. Kevin Power - Cerner - kpowers@cerner.com
18. Bob Dolin - Elimu Informatics - bdolin@elimu.io
19. Deepak Sharma - Mayo Clinic - sharma.deepak2@mayo.edu
20. May Terry - MITRE - mayT@mitre.org
21. Clem McDonald - NLM - clemmcdonald@mail.nih.gov
22. Lloyd McKenzie - Gevity - lmckenzie@gevityinc.com

Agenda:

1. Connectathon recap
   a. Slides on confluence
   b. HSPC sandbox validator tool
      i. https://chat.fhir.org/#narrow/stream/179197-genomics/topic/Montreal.20Connectathon.202019
ii. Patrick created a HSPC Sandbox with all CG profiles contained to validate (won’t be updated as trying to switch to a CI build which uploads profiles)
https://api-v8-r4.hspconsortium.org/CGTest/open

iii. Questions on “Must Support”
   1. May to file tracker, current meaning of “support” is not defined in the IG and FHIR structure may be updating on this as well.

iv. Make sure we find the TMB/MSI status tracker from before
https://gforge.hl7.org/gf/project/fhir/tracker/?action=TrackerItemEdit&tracker_item_id=18988&start=0

c. Upcoming work prototyping custom Operations
   i. Slot for call in future

d. Brainstorm/call for topics for next connectathon
   i. Atlanta, GA in Sept
   ii. tinyurl.com/damcgdoc

2. Remaining trackers to address before publication
   a. ballot trackers overview (2 Jan, 2 May)
   b. Trackers from connectathon and recent work that ought to be addressed (7)
   c. Any others?

3. Examples recap
   a. https://docs.google.com/spreadsheets/d/1kYzfQMbTXwb4yt-tOKh9FfNcYjiK0W-PXwOJyoPH8PU/edit#gid=0

<table>
<thead>
<tr>
<th>Tracker</th>
<th>Summary</th>
<th>Affirmative</th>
<th>Bob Dolin</th>
</tr>
</thead>
<tbody>
<tr>
<td>19842</td>
<td>LOINC: Sequence Phase Relationship valueCodeableConcept binding,</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Resolution | create internal list (CodeSystem) containing: cis/trans/indeterminate/unknown ? |

Notes | Existing wording: Sequence Phase Relationship observation.valueCodeableConcept Binding: (unbound) (example) Ballot comment: Create a LOINC answer list containing (at least) ’Cis’, Trans’. |

Follow-ups | -Tue, 26 Mar 2019 - by FHIR Bot-Vote: #64 - A-S-Submitted by: Bob Dolin (Elimu Informatics)-On behalf of: (bdolin@elimu.io) |

Disposition | Loinc list used to just say Cis/Trans, |

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<thead>
<tr>
<th>Tracker</th>
<th>Summary</th>
<th>Affirmative</th>
<th>Kanwarpreet Sethi</th>
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<tr>
<td>19995</td>
<td>How do the genetic findings affect the effectiveness of medication? - CG #28,</td>
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Resolution | Persuasive: |
Existing Wording: Medication Efficacy Impact describes how the associated genetic findings affect the effectiveness of the medication.

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Comment:
Can you please clarify? How do the genetic findings affect the effectiveness of medication? Wouldn't the findings either decrease or increase medication effectiveness? Consider rewording for clarity. Also, is the valueCodeableConcept within this profile (StructureDefinition: Medication Efficacy Impact) correct? Here are the values listed: Resistant | Responsive | Presumed resistant | Presumed responsive | Unknown significance | Non-Responsive | Presumed non-responsive. Are these the measure of medication effectiveness or of the impact?

---

Summary:
How do the genetic findings affect the effectiveness of medication?

Follow-ups
resistant/responsive typically used for cancer, increases/decreases typically used for germline Efficacy not due to metabolism? Yes, others exist. Need to compare lists currently available. Bob D will forward one.

Note from Bret in above resolution

From last May

1 Request made with 2 example answer lists, "others may be appropriate"

ACMG
- Very strong evidence pathogenic
- Strong evidence pathogenic
- Moderate evidence pathogenic
- Supporting evidence pathogenic
- Supporting evidence benign
- Strong evidence benign
- Uncertain significance

CPIC
- Level 1A - Annotation for a variant-drug combination in a CPIC or medical society-endorsed PGx guideline, or implemented at a PGRN site or in another major health system.
- Level 1B - Annotation for a variant-drug combination where the preponderance of evidence shows an association. The association must be replicated in more than one cohort with significant p-values, and preferably will have a strong effect size.
- Level 2A - Annotation for a variant-drug combination that qualifies for level 2B where the variant is within a VIP (Very Important Pharmacogene) as defined by PharmGKB. The variants in level 2A are in known pharmacogenes, so functional significance is more likely.
- Level 2B - Annotation for a variant-drug combination with moderate evidence of an association. The association must be replicated but there may be some studies that do not show statistical
significance, and/or the effect size may be small.

- Level 3 - Annotation for a variant-drug combination based on a single significant (not yet replicated) study or annotation for a variant-drug combination evaluated in multiple studies but lacking clear evidence of an association.
- Level 4 - Annotation based on a case report, non-significant study or in vitro, molecular or functional assay evidence only.

Notes:
Somatic tends to use AMP guidelines, question on alignment between AMP and ACMG. There's also CIVIC and potentially COSMIC. Effort in GA4GH to unify these...

https://civicdb.org/help/evidence/evidence-levels

Deadline is last week for changes but Clem has chips he can spend. Code is showing up as "on-hold" Liz and Jamie to attempt to add AMP as another example list in the code request over the listserv ASAP.

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<thead>
<tr>
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<th>Sequence quality</th>
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