FHIR Genomics Snapshot

HL7 International Working Group Meeting 2019

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5/6/2019
Welcome to Montreal!

**Helpful Links**

- Confluence Links:  
  - WGM Attendance
  - WGM Minutes
  - Weekly CG Minutes

- FHIR Subgroup Webcall notes:  
  - tinyurl.com/fhirgenomics

- FHIR R4 Spec:  

- Implementation Guide (current):  
  - http://build.fhir.org/ig/HL7/genomics-reporting/

- Domain Analysis Model:  
  - http://tinyurl.com/damcgdoc

- Gforge:  
  - gForge

- FHIR Chat (Zulip):  
  - https://chat.fhir.org/

- ListServ:  
  - clingenomics@lists.hl7.org (signup on HL7.org)

These slides:  
- tinyurl.com/cgwgmslides
Today

FHIR Genomics
Motivation

FHIR Genomics
Tools

Connectathon 21
Update

https://confluence.hl7.org/display/FHIR/2019-05+Clinical+Genomics+Track
FHIR Genomics Motivation
FHIR Genomics Motivation

• Modernizing Genomic Lab Reports

• Integrating Genomic Test Results in Patient Portals

• Point of Care apps for Precision Medicine

• Facilitation of Downstream Research/Reanalysis
Genomics Lab Reports

• How best to deliver genomics results to improve patient care?
Genomics Lab Reports

As PDFs …
Genomics Lab Reports

... or computable data?
Patient Portal Integration

Expand use cases
• Structured Genomic results
• Enable apps with an app store ecosystem

Open environments
• Enable standards-based environments and tools
• Foster Innovation

SMART on FHIR with Genomics

1. Order Panel or Sequencing

2. Return Data Results

3. Send Data to Clinicogenomic App

SMART on FHIR Clinical + Genomics Data

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Warner & Alterovitz, JAMIA 2016

https://smart-cancer-navigator.github.io
FHIR Genomics

Motivation

Point of Care Apps for Precision Medicine

Contextual, dynamic clinico-genomics information and decision support
For a specific gene mutation in a specific lung cancer patient, show information for most common KRAS in lung cancer populations.
Securely links **patient-specific** data from EHRs via FHIR and multiple laboratory/reference knowledge bases for **information and treatment options**.

https://smart-cancer-navigator.github.io

Facilitating Downstream Use

Clinical Care

- SMART Apps Clinician & Patient
- SMART on FHIR
- Clinical Data
- EHR (+ GACS) System
- FHIR Clinical Data
- FHIR Genomic Data
- Sequencing Lab
- Genomic Data
- SMART on FHIR
- Pharmacogenomics Cancer Genomics...

Research

- Research Data Warehouse
- All of Us Cohort Program, etc.
What is a GACS?

• **GACS = Genomics Archiving and Communication System**
  
  – System akin to PACS, for housing Genomics data
  
  – Enables extra-EHR storage of genomic data, to be served on demand to SMART apps and/or CDS Hooks cards using FHIR
  
  – Highlighted in [May 2019 HL7 Newsletter](https://www.hl7.org) following Connectathon 20:
EHR+GACS Integration for PGx using CDS Hooks
Automated results directly appear in clinician’s workflow!

**Genomic Data stored and queried remotely**

EHR+GACS Integration for PGx using CDS Hooks
EHR+GACS Integration for PGx using CDS Hooks

CDS Hook Information Card in Cerner Prescribing workflow
FHIR Genomics Toolkit
FHIR Genomics Toolkit

• **HL7 Domain Analysis Model: Clinical Genomics (2018)**
  – Identifies stakeholders, use cases, and workflows
    • Iterative feedback needed

• **Implementation Guide - Genomics Reporting (draft)**
  – Large Focus on structuring/encoding genomic test results
    • Feedback and examples needed
  – Describes sample SMART on FHIR Genomics apps
    • Ongoing storage and querying considerations for raw data
New Standard Publication on Use Cases

**HL7 Clinical Genomics Domain Analysis Model: Clinical Genomics**

- Contains use cases and workflows for clinical genomics, including WES, RNA-sequencing, proteomics
- Published July 2018
- Approximately 100 pages

Recent Calls for additional use cases regarding Law Enforcement scenarios and synthetic sequences

Timeline of FHIR Genomics

- **Dec 2018 - Now**
  - Work towards R5

- **Dec 2018**
  - Ballot Complete
  - R4

- **Dec 2016**
  - Ballot Complete
  - STU3

- **Dec 2016**
  - Ballot Complete
  - DSTU2

- **Sep 2015**
  - Ballot Complete

FHIR Genomics

Level 1 Maturity Achieved

“...Substantially complete and ready for implementations...”
Timeline of FHIR Genomics

• R3 to R4 Resource Changes

- ProcedureRequest
- ServiceRequest
- Sequence
- MolecularSequence
Timeline of FHIR Genomics

Other Guidance Applied in the Implementation Guide:

➢ Constrain R4 for genomics reporting
  ○ Maximize use of Observation Resource (normative!)
  ○ Hierarchy of Observation profiles

➢ Minimize use of Extensions

http://build.fhir.org/ig/HL7/genomics-reporting/index.html
Timeline of FHIR Genomics (R5 Considerations)

The Clinical Genomics Work Group will continue to work on:

1. Refining MolecularSequence
2. Moving content of current profiles of core resources (e.g., Observation-Genetics, etc) to the Genomics Reporting IG to remove redundancy
3. Updating genetics examples in core resources to improve accuracy and completeness
4. Working with Patient Care on the family history pedigree representation/profiles.
Genetics Test: Core Resources

Genetic Profiles

ServiceRequest

DiagnosticReport

FamilyMemberHistory

Observation
Multiple Observations: Genetic Findings, Implications, Interpretations.
gForge Items January Ballot

61 comments logged in January ballot

11 Remain for resolution
FHIR Connectathon Update
Landscape of Adoption Programs and Iterative Genomics Standard Feedback

Pre-production to production

Connectathons: Develop/test
Pilots: Apply/Test
Pre/Production: Use/deploy

Genomics
Standard, Use Cases, Tools, and Processes

Utilize standard
Feedback to standard

FHIR Genomics Pilots
FHIR Connectathons
Connectathon 21 Scenarios

Scenario 1
Registering New IG-compliant FHIR Resources

Scenario 2
Querying FHIR Resources/GACS Operations

Scenario 3
EHR+GACS Integration for PGx using CDS Hooks

https://confluence.hl7.org/display/FHIR/2019-05+Clinical+Genomics+Track
Registering New IG-compliant Resources

• Gap analysis between MITRE’s mCODE (minimal Common Oncology Data Elements) model and the Genomics Reporting IG was completed.

• Philips’ panel-based molecular genomics report was converted to an R4 CG-IG compliant bundle, with additional Observations for Tumor Mutational Burden (TMB) and Microsatellite Instability (MSI).

• Project to refactor hapi-fhir code begun to integrate terminology upload support covering HLA nomenclature CodeSystems.
Registering New IG-compliant Resources

• Work generated multiple gForge change requests, follow-ups to discussion streams on Zulip, IG build error/warning fixes, and uploading of new examples to the IG.

• Resulting examples were validated against an open FHIR endpoint on HSPC populated with IG structure definitions using the newly integrated “Profiles” module.

  – https://api-v8-r4.hspconsortium.org/CGTest/open/
Registering New IG-compliant Resources

gForge Trackers from Connectathon 21

<table>
<thead>
<tr>
<th>Issue</th>
<th>Description</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>21238</td>
<td>allele frequency component shouldn't use %</td>
<td>Patrick Werner</td>
</tr>
<tr>
<td>21283</td>
<td>Change Observation.method value set binding from required to at least extensible or preferred.</td>
<td>May Terry</td>
</tr>
<tr>
<td>21275</td>
<td>Genomics DiagnosticReportPerformer should allow more resources</td>
<td>Patrick Werner</td>
</tr>
<tr>
<td>21296</td>
<td>NullPointerException error generated when validating genomics diagnosticReport</td>
<td>May Terry</td>
</tr>
</tbody>
</table>
Once complex FHIR genomics resources are created and registered in a server, what guidance can we give on storing, searching, and retrieving them?

Additionally, how can we support reuse/reanalysis of NGS results— for instance in reclassifying variants of unknown significance or when new drug-gene interactions are found?
Querying FHIR Resources/GACS Operations

Answer being explored:

Store large raw data (FASTQ/VCF/BAM/etc) remotely, enable querying by gene/region through custom search Operations and tooling.
Example Operation being explored:

• Input parameters:
  – [Patient, Reference Sequence, integer Range]

• Output Bundle:
  – [All variants in range, summary of region]

• Test case:
  – De-identified data from 1000 Genomes VCFs
  – Caution: Many uncallable regions, difficult to describe
Connectathon 21

Clinical Genomics Track Recap

IG-Compliant Genomics Resources are being created and consumed
• Still a handful of codes, values, and mappings that need to be solidified for proper validation before publication

Examples outlining DAM use cases in FHIR are being collected and aligned with the IG
• Over half of main use cases represented in some form

GACS prototypes for archiving and querying are being tested
• Incredible value-add opportunity to use FHIR as a unifying element connecting clinical and research interests in genomics
Looking Forward…

• SMART on FHIR-powered cloud-based servers with patient apps
  • App stores enable patients to customize experience based on needs
  • Patient ability to control information sharing in real-time for clinical/genomic information.

• Apps that enable patients and providers to “collaborate” on care
  • Screens built for provider-patient engagement

• Apps designed for genomic care coordination
  • Patient control of information/sharing
Incremental Adoption of FHIR Genomics

- Genetics Lab Test Results
  - + Additional Genetic Information
  - + Context
  - + Location/Quality Information
  - + Whole Sequence/Reads

- Observation
  - + Codes
  - Observation IG Genetics Profiles
  - + Family History/Other Resource Profiles
  - MolecularSequence Resource
  - + Repository Reads

Traditional Labs

NGS Labs
Thank You!

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