The Office of the National Coordinator for Health Information Technology

Sync for Genes

Office of the National Coordinator for Health Information Technology (ONC)
Annual Meeting
December 1, 2017

Panelists and Agenda

- Tracy H. Okubo, PMP; Office of the National Coordinator for Health Information Technology (ONC) – Moderator
  - » Welcome and Introduction of Panelists
- Kevin Chaney, MGS; ONC
  - » Introduction to Sync for Genes, Background, and Importance
- Bradley Ozenberger, Ph.D; Program Director, All of Us Research Program, National Institute of Health (NIH)
  - » Introduction to *All of Research* Program, Background, and Importance
- Gil Alterovitz, Ph.D; Harvard Medical School, Boston Children's Hospital, and Massachusetts Institute of Technology
  - » Sync for Genes Phase 1 Overview and Approach
- Elaine Johanson; Director, Office of Health Informatics (Acting), U.S. Food and Drug Administration (FDA)
  - » Sync for Genes Phase 1 Pilot Participation Overview
- Kevin Chaney, MGS; ONC
  - » Sync for Genes Next Steps
- Q&A

The Office of the National Coordinator for Health Information Technology

Syncing Up: ONC's Role in Precision Medicine

Kevin Chaney, MGS
Office of the Chief Scientist
ONC Annual Meeting
December 1, 2017

Overview

- ONC's Mission
- Office of the Chief Scientist Overview
- Precision Medicine Initiative (PMI)
- ONC's Role in the PMI
- ONC PMI Activities

ONC Mission

Improve the health and well-being of individuals and communities through the use of technology and health information that is accessible when and where it matters most.

Office of the Chief Scientist (OCS) Overview

Responsible for:

- developing and evaluating ONC's overall scientific efforts and activities and, as necessary, develops, establishes, or recommends scientific policy to the National Coordinator; and
- identifying, tracking, and anticipating innovations in health care technology across the ONC organization.

The Precision Medicine Initiative

A federal effort launched in 2015

MISSION: To enable a new era of medicine through research, technology, and policies that empower patients, researchers, and providers to work together toward development of individualized care.

What is Precision Medicine?

Precision medicine is an emerging approach for disease treatment and prevention that takes into account individual variability in lifestyle, environment, and biological makeup.

It is a radical shift in how each of us can receive the best care possible based on our unique characteristics.

ONC Role in the Precision Medicine Initiative (PMI)

- Accelerate innovative collaboration around pilots and testing of standards that support health IT interoperability for research

- Adopt policies and standards to support privacy and security of cohort participant data

- Advance standards that support a participant-driven approach to patient data contribution

ONC PMI Activities

- **Sync for Science Pilot**
  - » Demonstrate the feasibility of open, standardized, API-based individual access to and donation of data for research
- **Sync for Science Application Programing Interface (API) Privacy and Security**
  - » Technical and administrative testing, analysis, and assessment of APIs developed under the S4S Pilot Project
- **Sync for Genes**
  - » Develop and pilot resources for standards for genomics information

https://beta.healthit.gov/topic/precision-medicine

All of Us Research Program

Brad Ozenberger, Program Director

December 1, 2017

@AllofUsResearch #JoinAllofUs

National Institutes of Health

All of Us Mission and Objectives

Nurture relationships

with one million or more participant partners, from all walks of life, for decades

Our mission

To accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care for all of us

Deliver the largest, richest biomedical dataset ever

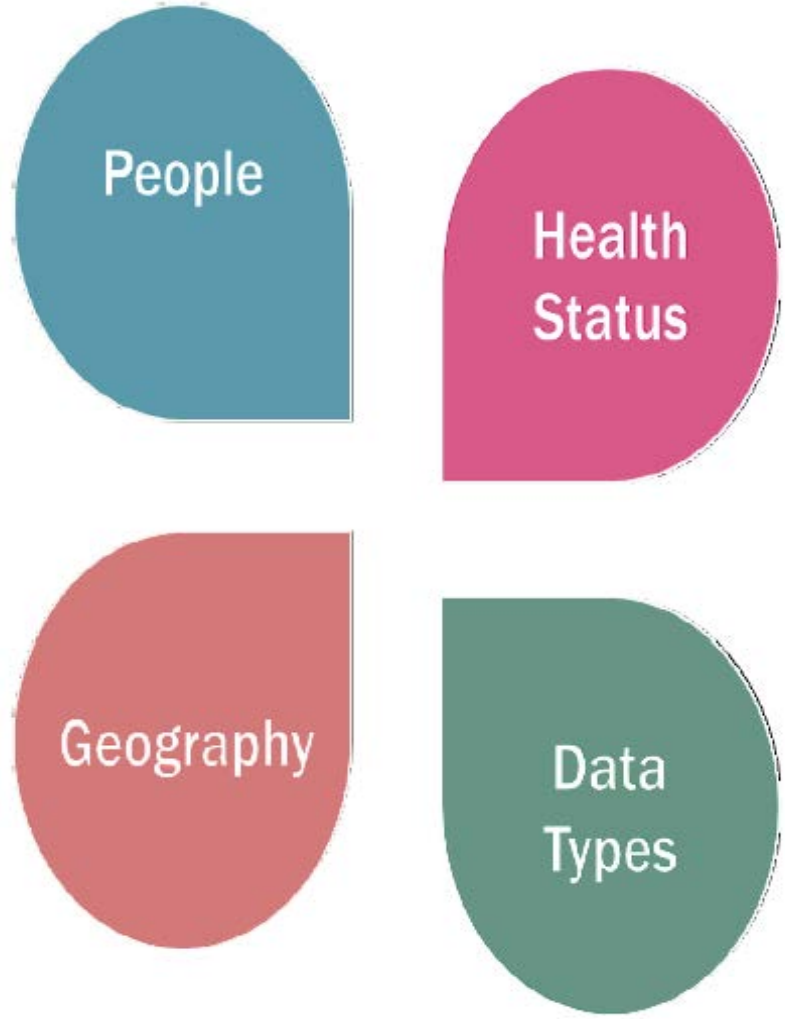
that is easy, safe, and free to access

Catalyze the robust ecosystem

of researchers and funders hungry to use and support it

A Transformational Approach to Diversity

Reflecting the country's rich diversity to produce meaningful health outcomes for communities historically underrepresented in biomedical research.



All of Us Research Program Data

The program will collect standardized data from sources that will include:

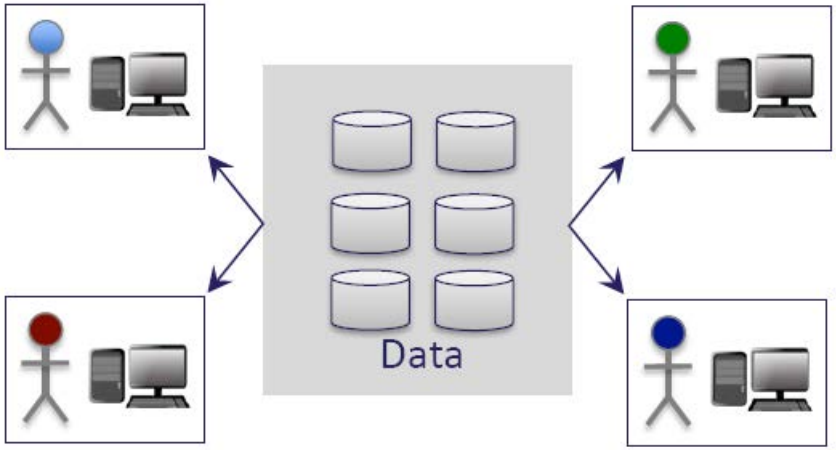
- Participant surveys
- Electronic health records
- Physical measurements
- Mobile/wearable technologies
- Geospatial/environmental data

Also will collect biosamples (blood and urine) and begin generating genomic data in 2018.

AOU centralizes data to enhance security and improve usefulness

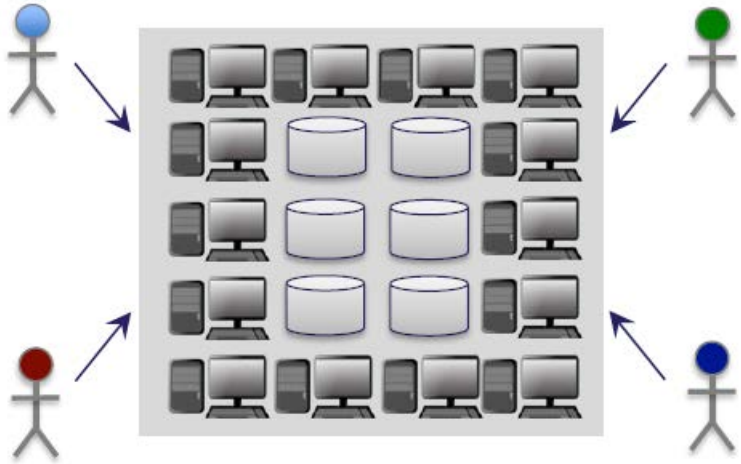
Traditional Approach

Bring data to researchers



AoU Approach

Bring researchers to the data



Problems

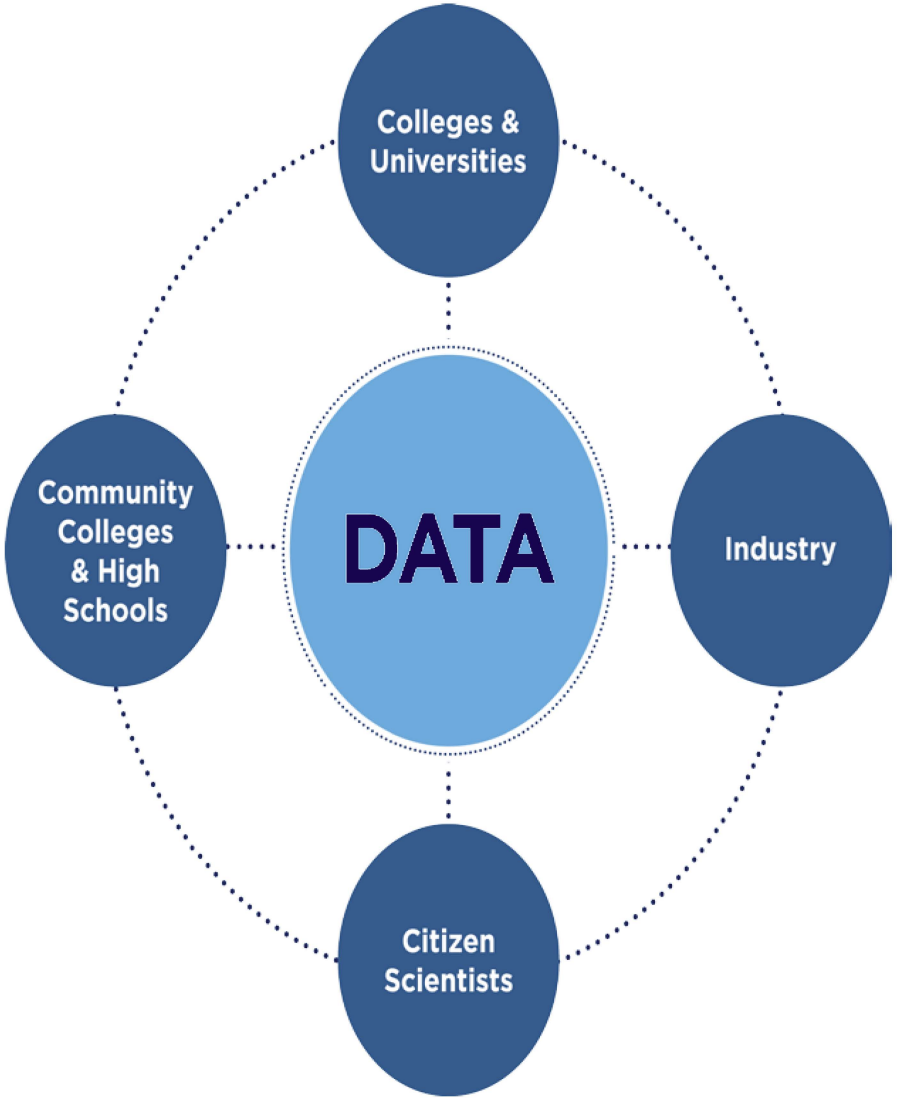
- *Data sharing = data copying*
- *Decreased security (data lots of places)*
- *Huge infrastructure needed*
- *Encourages siloed research*

Advantages

- *Improved security and auditing*
- *Increased accessibility to researchers*
- *Shared compute*
- *Facilitates collaboration*

A Transformational Approach to Data Access

- Data sharing will be a priority to both researchers and participants
- Participants will have access to study information and data about themselves
- Data collection will start small and will grow over time
- Privacy and security will adhere to the highest standards
- NIH will invest to level the playing field so diverse researchers can play



National Standard for Genomic Data in Clinical Care

Clinical Care

Research

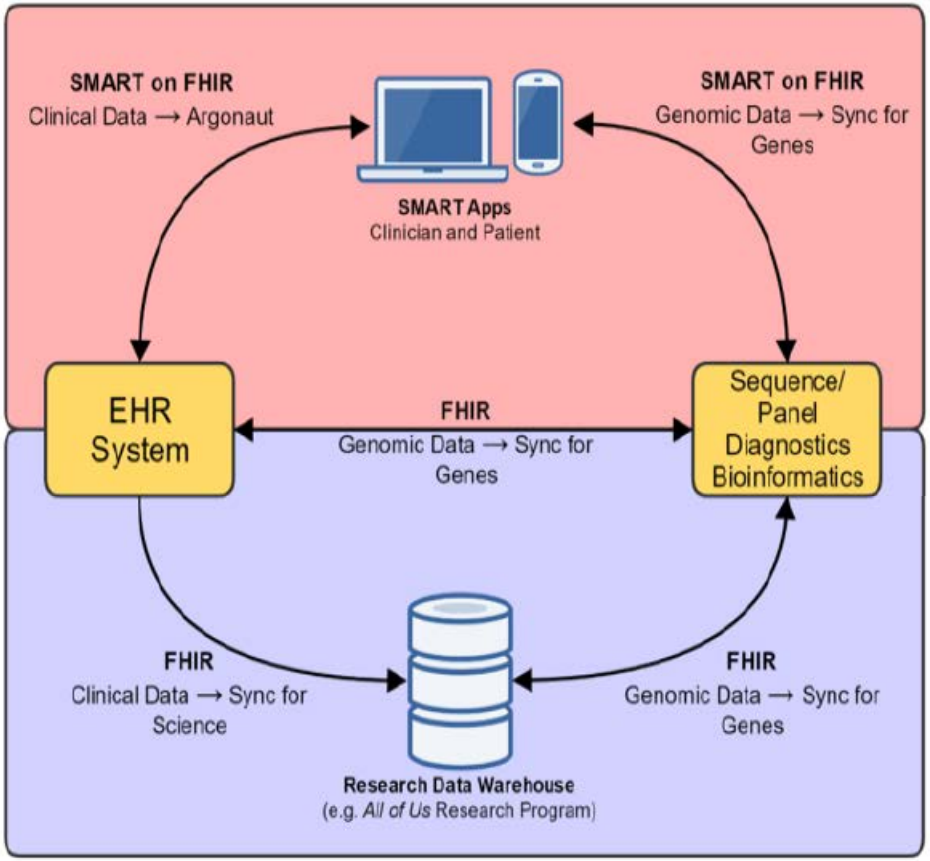
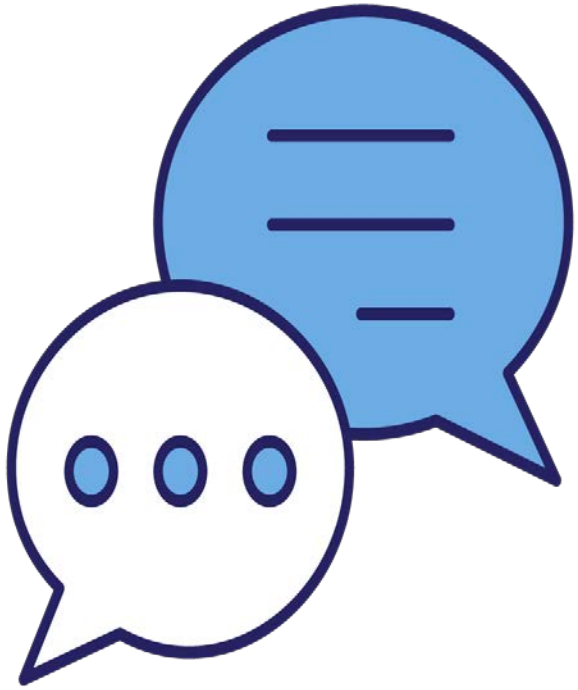


Figure 1 Enabling a single national standard for clinical care and research via FHIR.
Source: G Alterovitz. "FHIR's Promise and Genomics," HL7 2016 Genomics Conference, 2016

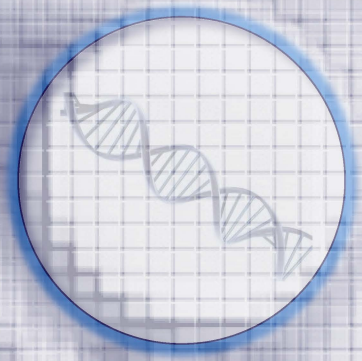
Questions?

Sign up for updates:
joinallofus.org

@AllofUsResearch
#JoinAllofUs



Sync for Genes



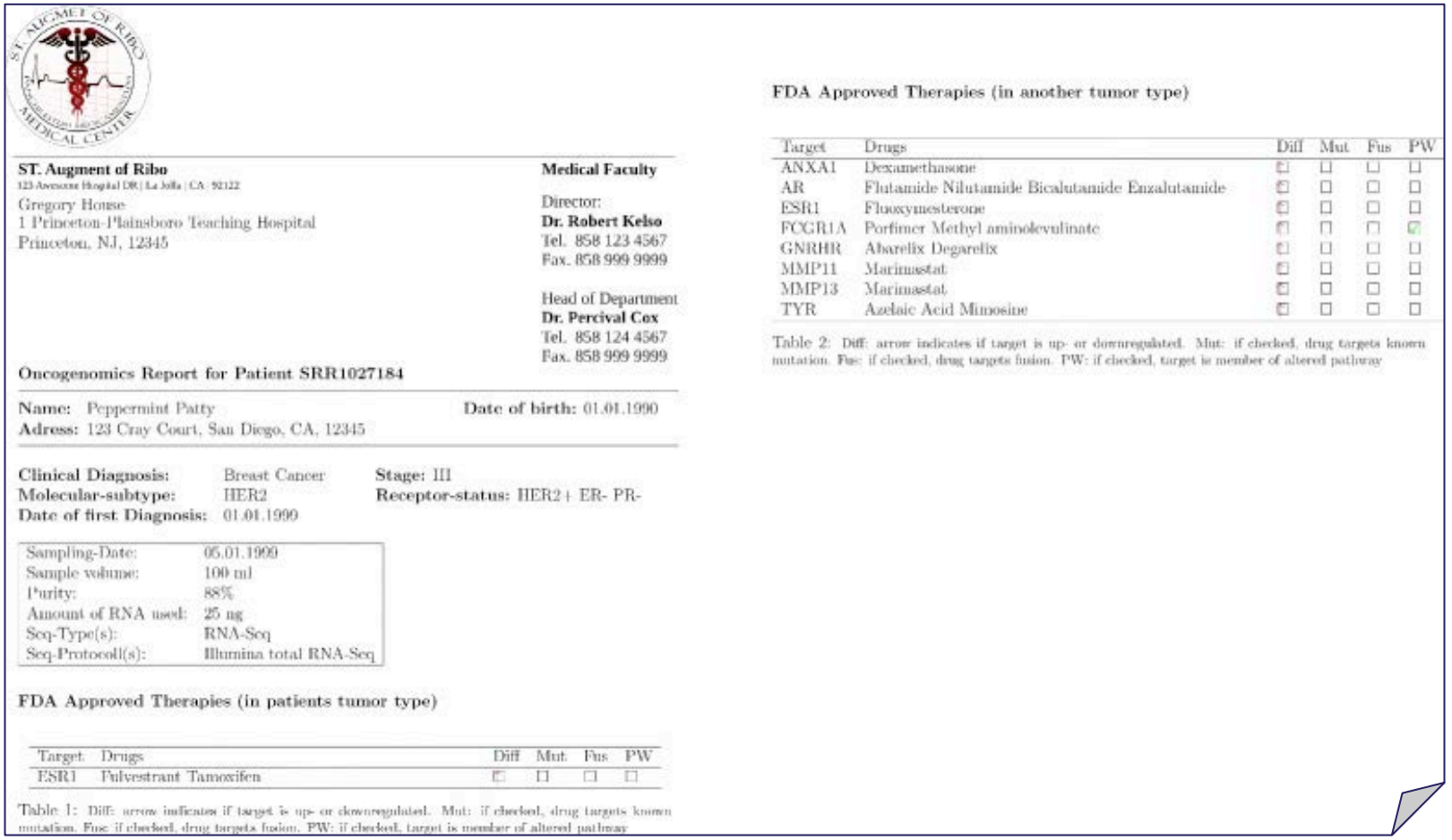
Gil Alterovitz, Ph.D.

December 1, 2017

Contact: ga@alum.mit.edu

Genomics in the Clinical Setting

Reports …



ST. Augment of Ribo
123 Awesome Hospital DR | La Jolla | CA 92122

Gregory House
1 Princeton-Plainsboro Teaching Hospital
Princeton, NJ, 12345

Medical Faculty

Director:
Dr. Robert Kelso
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Head of Department
Dr. Percival Cox
Tel. 858 124 4567
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Oncogenomics Report for Patient SRR1027184

Name: Peppermint Patty **Date of birth:** 01.01.1990
Adress: 123 Cray Court, San Diego, CA, 12345

Clinical Diagnosis: Breast Cancer **Stage:** III
Molecular-subtype: HER2 **Receptor-status:** HER2+ ER- PR-
Date of first Diagnosis: 01.01.1999

Sampling-Date:	05.01.1999
Sample volume:	100 ml
Purity:	88%
Amount of RNA used:	25 ng
Seq-Type(s):	RNA-Seq
Seq-Protocoll(s):	Illumina total RNA-Seq

FDA Approved Therapies (in patients tumor type)

Target	Drugs	Diff	Mut	Fus	PW
ESR1	Fulvestrant Tamoxifen	☐	☐	☐	☐

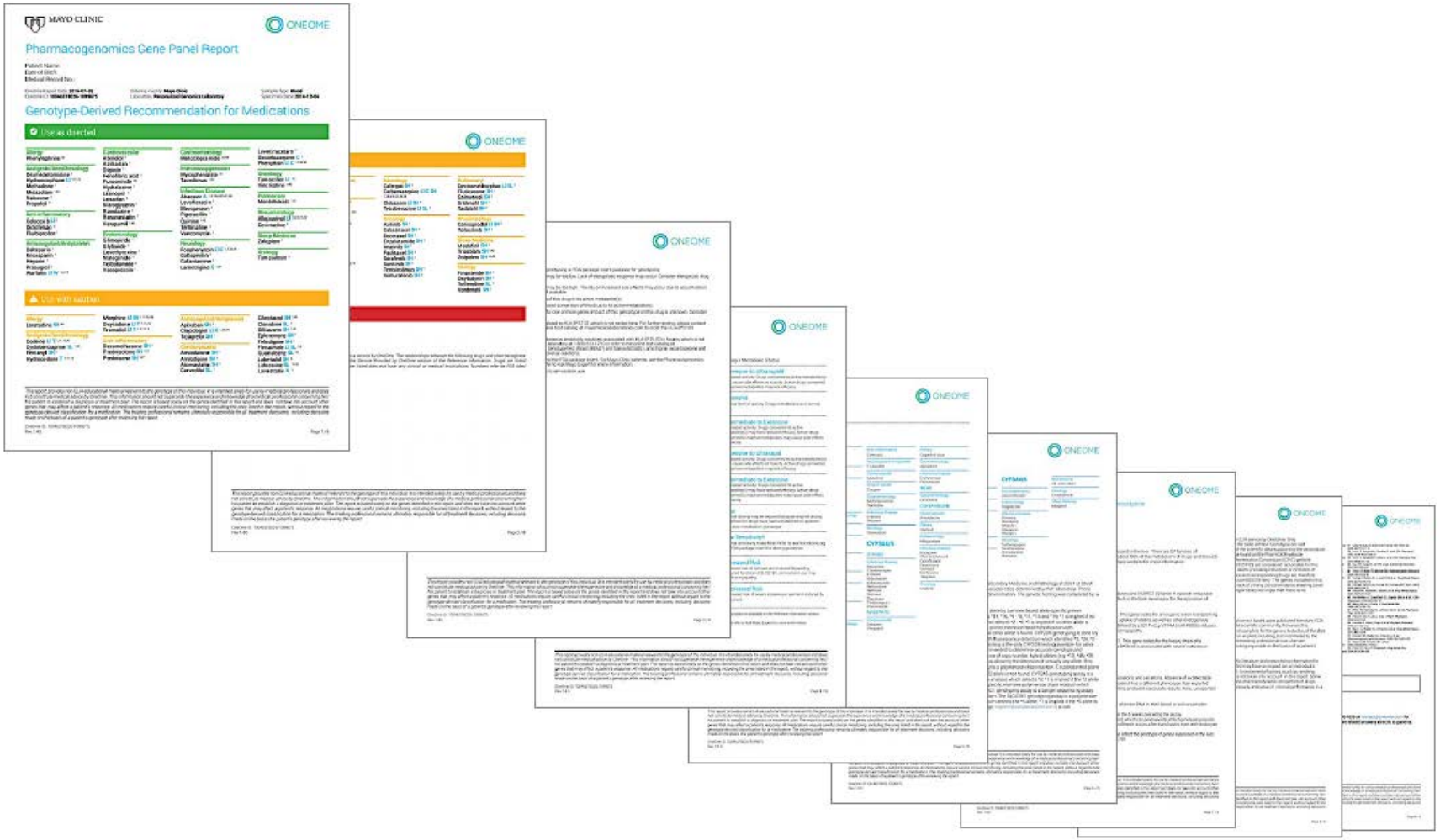
Table 1: Diff: arrow indicates if target is up- or downregulated. Mut: if checked, drug targets known mutation. Fus: if checked, drug targets fusion. PW: if checked, target is member of altered pathway

FDA Approved Therapies (in another tumor type)

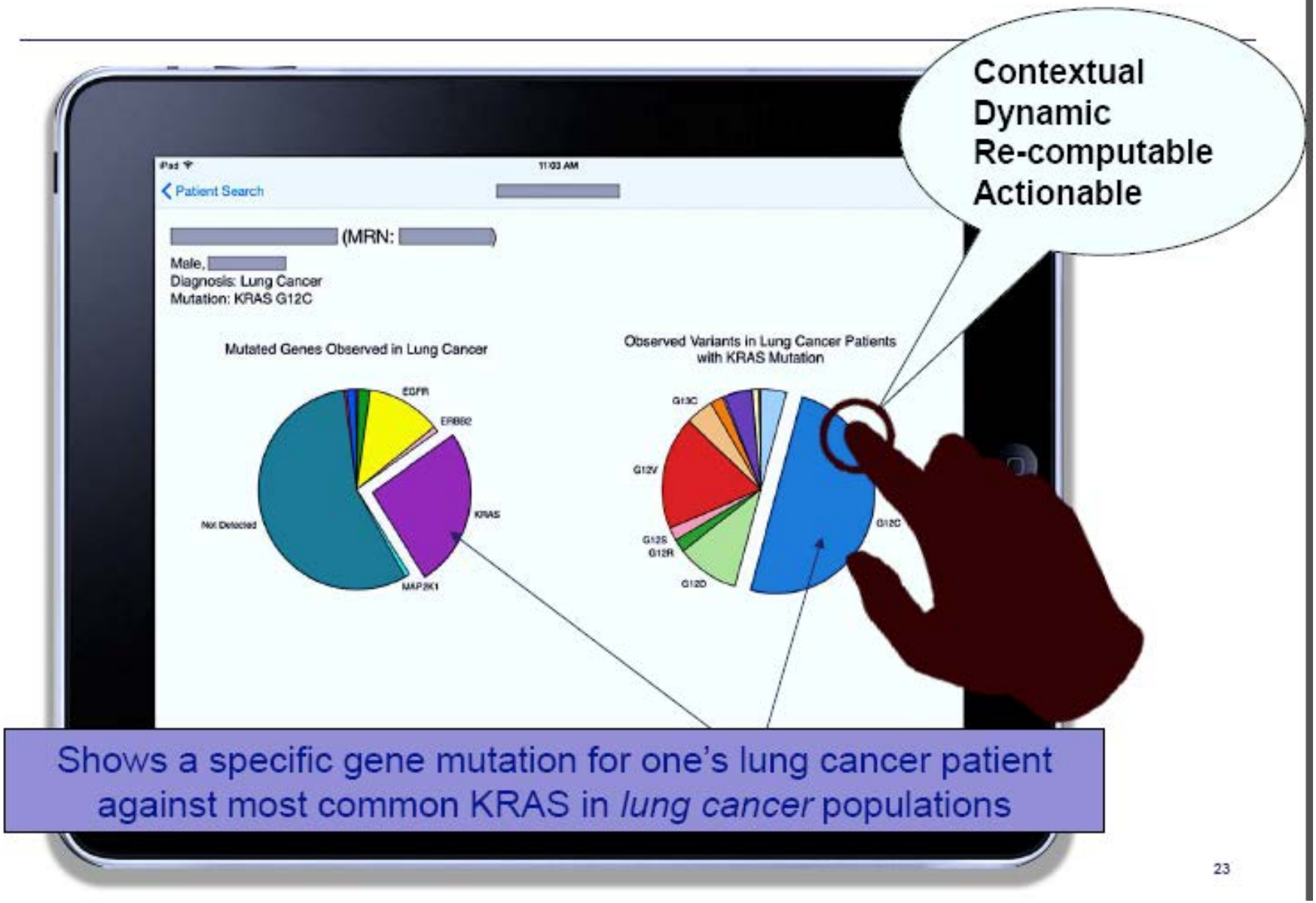
Target	Drugs	Diff	Mut	Fus	PW
ANXA1	Dexamethasone	☐	☐	☐	☐
AR	Flutamide Nilutamide Bicalutamide Enzalutamide	☐	☐	☐	☐
ESR1	Fluoxymesterone	☐	☐	☐	☐
FCGR1A	Porfimer Methyl aminolevulinate	☐	☐	☐	☑
GNRHR	Abarelix Degarelix	☐	☐	☐	☐
MMP11	Marimastat	☐	☐	☐	☐
MMP13	Marimastat	☐	☐	☐	☐
TYR	Azelaic Acid Minosine	☐	☐	☐	☐

Table 2: Diff: arrow indicates if target is up- or downregulated. Mut: if checked, drug targets known mutation. Fus: if checked, drug targets fusion. PW: if checked, target is member of altered pathway

… even detailed ones …



… cannot do this!



Warner & Alterovitz, JAMIA 2016

```
{
   "$schema": "http://json-schema.org/draft-
04/schema#",

   "definitions": {
    "variant": {
       "type": "object",
       "properties": {
        "seq_id": {"$ref": "#/definitions/sha512_20"},
        "span": {"$ref": "#/definitions/span"},
        "alt": {"$ref": "#/definitions/sequence"}
       },
       "required": ["seq_id", "span", "alt"]
    },

    "sequence": {
       "type": "string",
       "pattern": "^[A-Z]$"
    },

    "sha512_20": {
       "type": "string",
       "pattern": "^[0-9abcdef]$",
       "minLength": 20,
       "maxLength": 128,
    }
   }
}
```

Standards-based Structured data

Proposed Solution

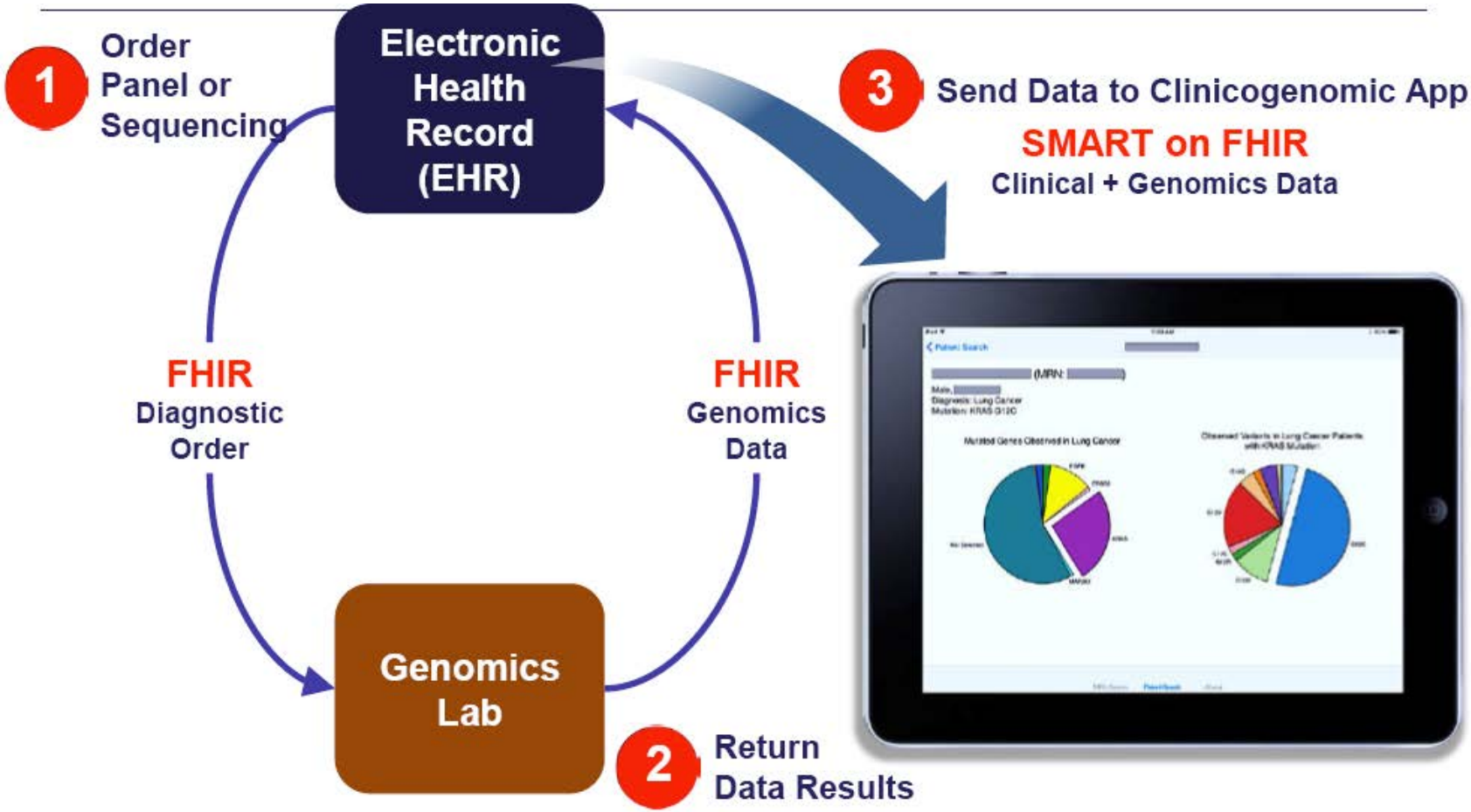
Deliver structured genomic data

Use resource-based data model

Adopt a modern, web-savvy application programming interface (API)

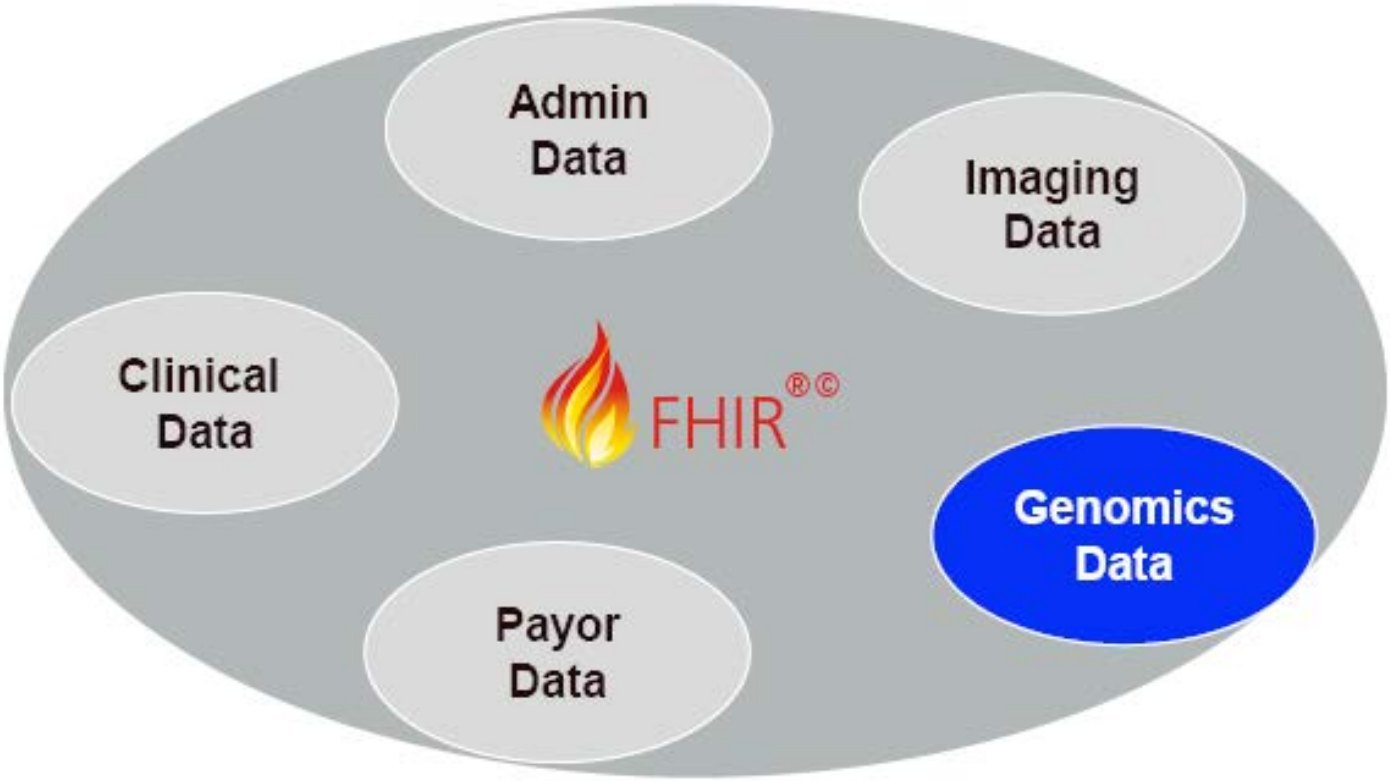
An open industry standard

Genomics data cycle



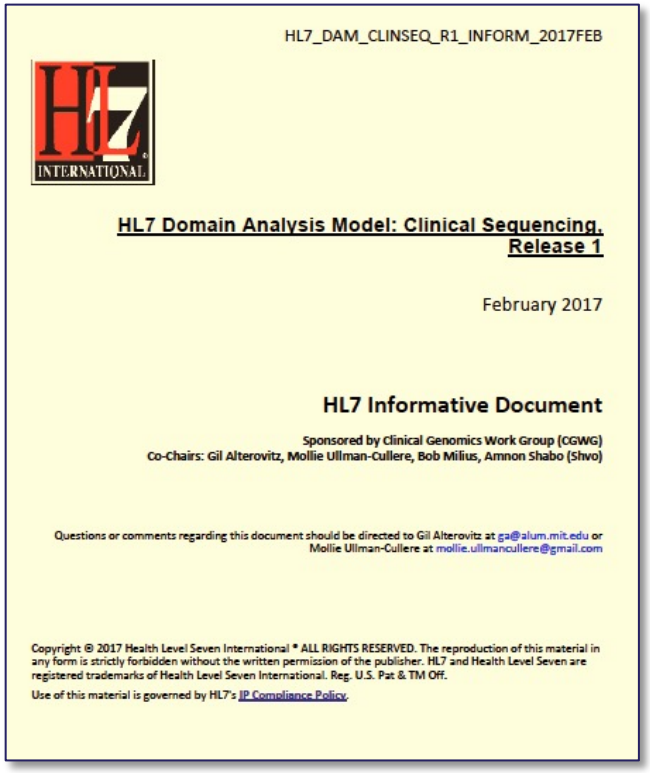
Warner & Alterovitz, JAMIA 2016

An Encompassing Standard?



http://hl7.org/fhir/2017Jan/index.html

There are many use cases...



HL7_DAM_CLINSEQ_R1_INFORM_2017FEB

HL7 INTERNATIONAL

HL7 Domain Analysis Model: Clinical Sequencing, Release 1

February 2017

HL7 Informative Document

Sponsored by Clinical Genomics Work Group (CGWG)
Co-Chairs: Gil Alterovitz, Mollie Ullman-Cullere, Bob Milius, Amnon Shabo (Shvo)

Questions or comments regarding this document should be directed to Gil Alterovitz at ga@alum.mit.edu or Mollie Ullman-Cullere at mollie.ullmancullere@gmail.com

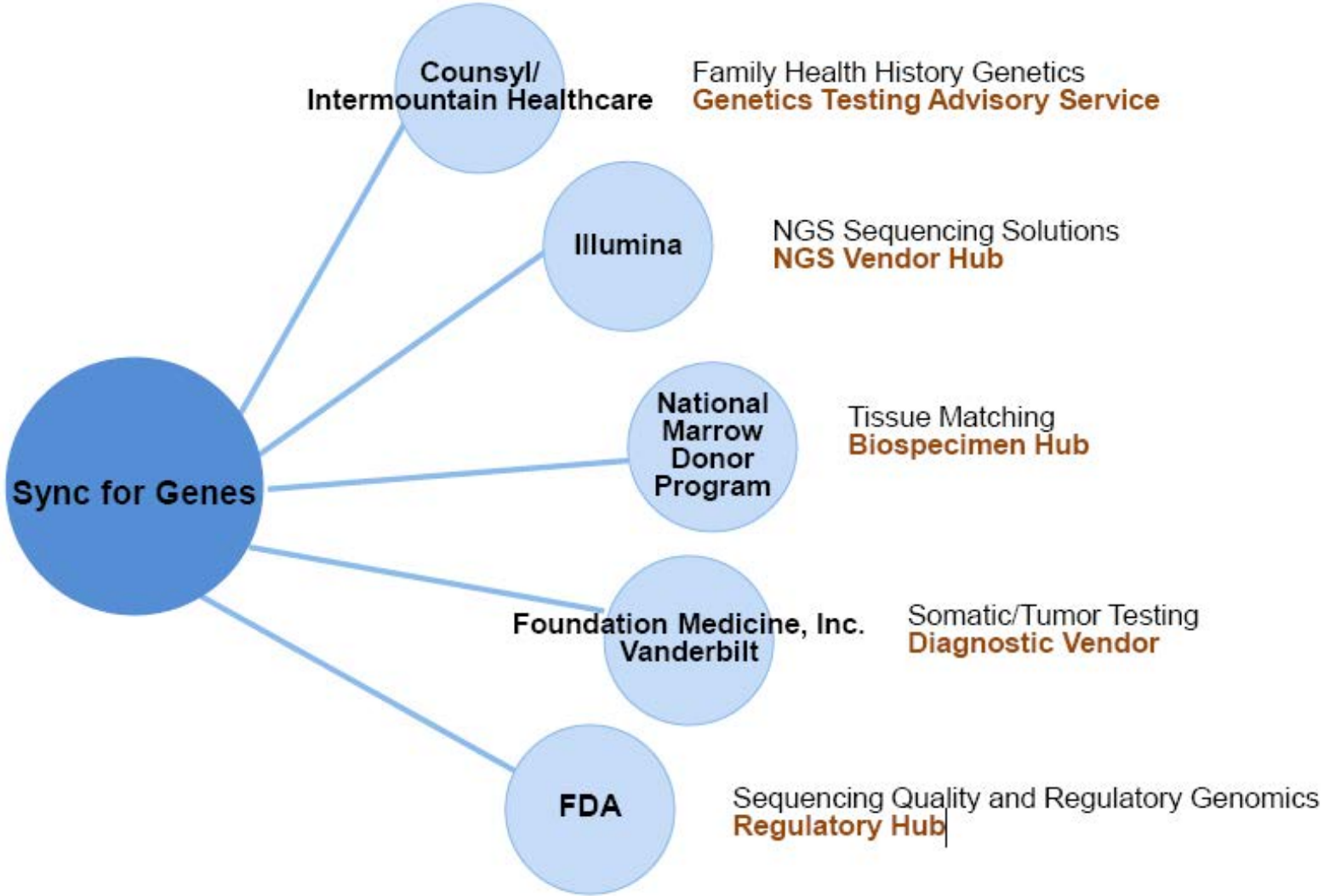
Specimen Identification + Germline testing for biomarkers/mutations (usually inherited) + Tumor testing for biomarkers/mutations (somatic / tumor specific) + Pediatric Testing + Prenatal Testing + Infectious Disease Testing + Emerging Specimen scenarios + Microbiome analysis of the patient + Free-cell cell-free circulating tumor DNA (ctDNA) + Cell-free fetal DNA (cffDNA) + Clinical Sequencing – Germline Testing + Description of Primary Clinical Sequence Workflow – Germline Testing + Alternative Germline Workflows + Alternative Flow 1: Chart Review + Alternative Flow 2: New Genetic Knowledge + Alternative Flow 3: New Clinical Indication + Cancer Profiling – Somatic Testing + Description of Primary Clinical Sequence Workflow – Somatic Testing + Alternative Workflows – Somatic Testing + Alternate Workflow 1: Referral + Alternate Workflow 2: Pathologist Ordered Testing + Decision Making Tools – Family History and Drug Dosage Calculators + Public Health Reporting + Description of Public Health Reporting Scenario + Cancer Registry workflow + Clinical and Research Data Warehouses + Cytogenetic Marker identification via sequencing + Pharmacogenomics + Description of Scenario + Pharmacogenomics – Somatic Profiling + Pharmacogenomics – Germline + Primary Germline Pharmacogenomics Germline Testing Workflow + Alternate Germline Pharmacogenom Workflow – Pharmacist Involvement + State & R ional Health formati xchanges (HIE) + Human leukocyte antigen (HLA) T + + Background on NMDP + HML and HL7 + (from Sep 2016) + Bone Marrow Repo Preimplantation Testing + Fetal Testing – C Prenatal Testing + Newborn Screenin Alternative Research-Based Newborn Screenin me a Targeted Panel Testing + Public Health Testing – Mic al

Published Feb 2017

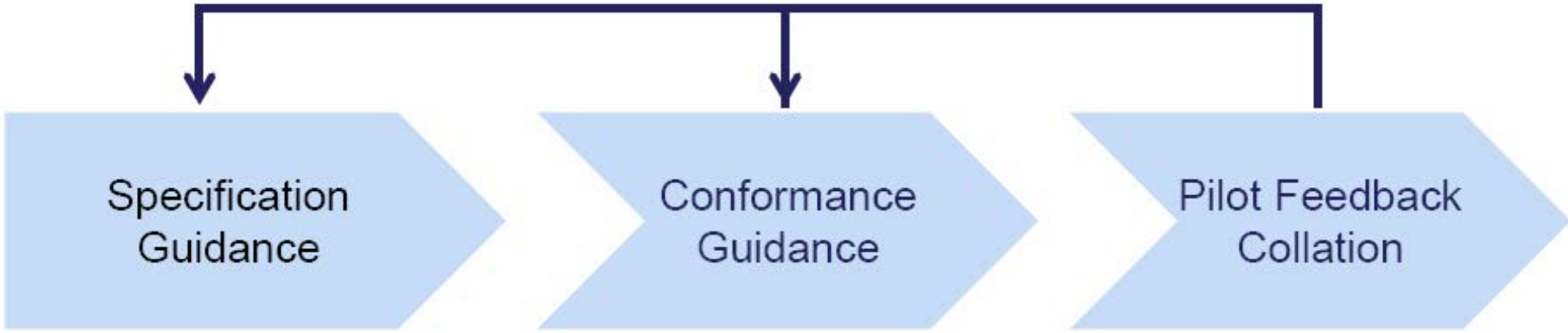
Sync for Genes

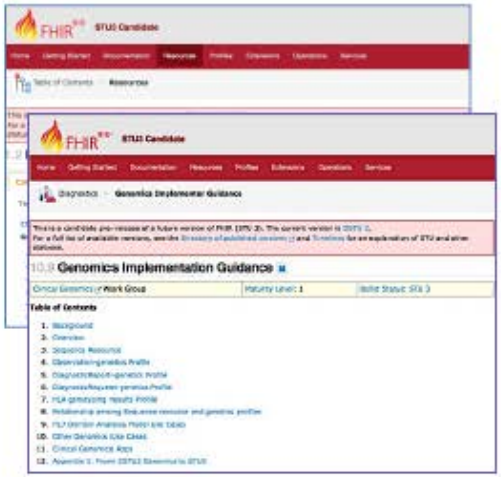
Sync for Genes Pilots' Timeline

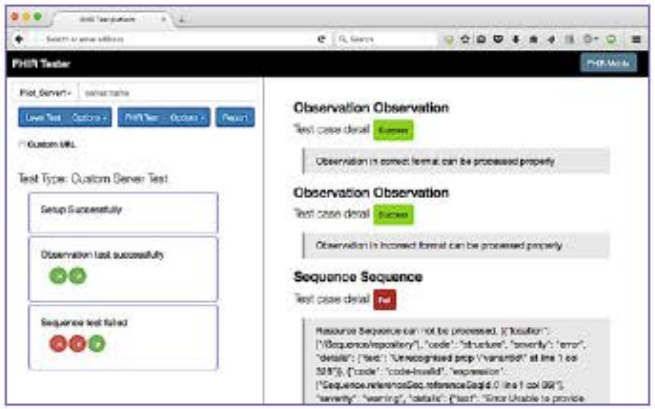
National Sync for Genes Pilots



Coordinate Pilot Implementations







Utilize Feedback

Conformance Guidance Site

Pilot Feedback Collation

Dissemination

Global Alliance for Genomics & Health

Recommendations

- Created list of standard development process recommendations
- Enhanced FHIR Profiles
  - http://build.fhir.org/genomics

Summary

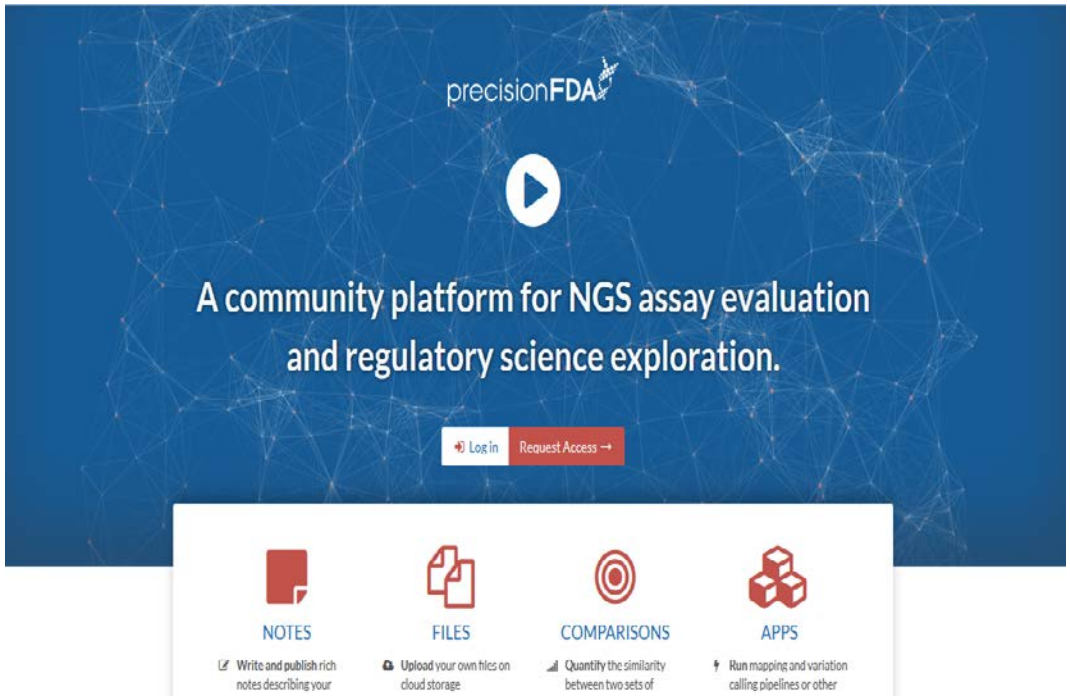
- Solve a real clinical point-of-care need
- Augment FHIR to handle genomics data
- FHIR genomics being piloted nationally
- Create a universal, modern health data standard

PrecisionFDA and the Sync for Genes Pilot

Elaine Johanson
Director, Office of Health Informatics (Acting)
Office of the Chief Scientist
Office of Health Informatics
U.S. Food and Drug Administration
Tel: 301-796-7315, 410-925-7279
elaine.johanson@fda.hhs.gov

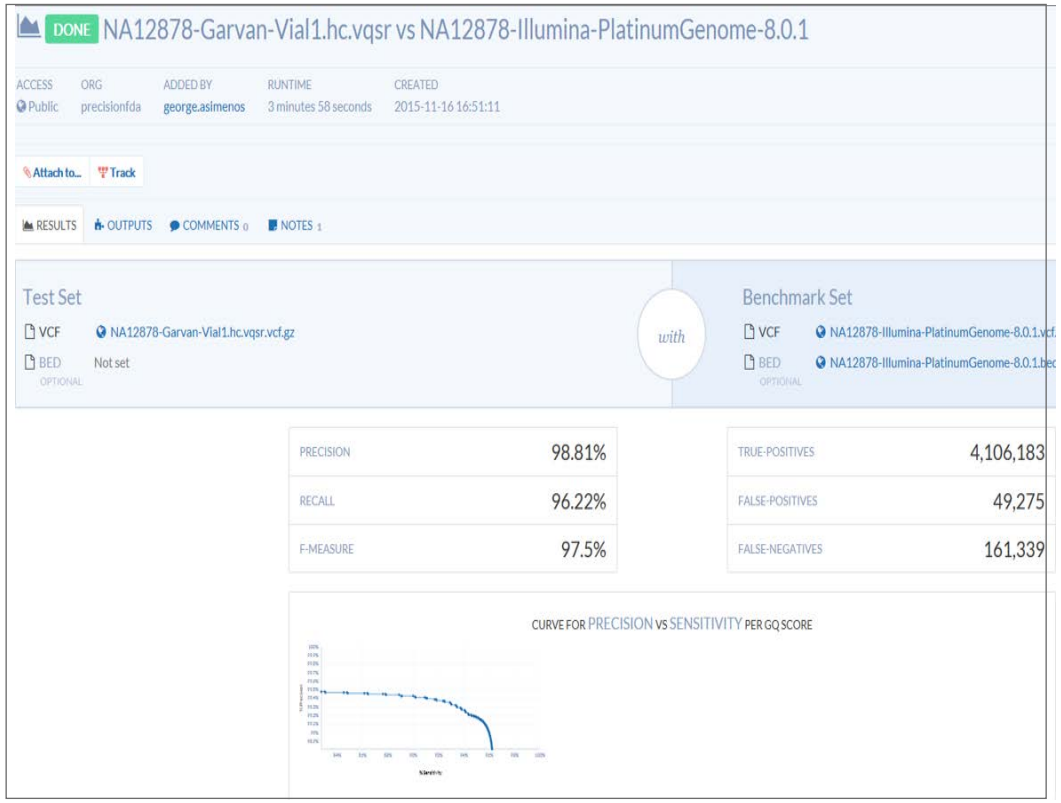
precisionFDA

A Next Generation Sequencing (NGS) collaboration platform that provides…



- An integrated VCF Comparator
- Access to Experts
- Public Challenges
- A Genomics Workspace
- Discussion Areas
- File Storage & Sharing
- A Library of NGS Tools & Applications
- Ability to “dockerize” applications for ease of use, transportability and consistency in performance across platforms

Comparing Files with Gene Sequence Variations on precisionFDA



- The "comparisons" feature of precisionFDA uses vcfeval 3.5.1.
- With the comparison tool integrated into precisionFDA, a test data set (provided by the user) and a benchmark set (representing the “truth”) can be analyzed across specific regions of the genome.

The Comparison Tool and

What we did as part of the Sync for Genes pilot…

1. Informed the FHIR standard (sequence resource) as it relates to comparisons of vcf files (FHIR format was modified to be able to represent precisionFDA comparisons). The full sequence resource is at: http://www.hl7.org/fhir/sequence.html
2. Utilizing the specification, changed the precisionFDA code to be able to output FHIR sequence resource objects. A portion of the comparison shown on the previous page on precisionFDA is show to the right when exported to FHIR…


```
{
  "resourceType": "Sequence",
  "type": "dna",
  "coordinateSystem": 1,
  "identifier": [
    {
      "system": "https://precision.fda.gov/fhir/Sequence/",
      "value": "comparison-1"
    }
  ],
  "quality": [
    {
      "type": "unknown",
      "standardSequence": {
        "coding": [
          {
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            "code": "file-Bk50Qg00qVbP6bvjpkXXVQfQ",
            "display": "NA12878-Illumina-PlatinumGenome-8.0.1.vcf.gz"
          },
          {
            "system": "https://precision.fda.gov/files",
            "code": "file-Bk50Qg00qVb6ZPJGgkFkJpj0",
            "display": "NA12878-Illumina-PlatinumGenome-8.0.1.bed"
          }
        ]
      },
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      },
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          98,
          97,
```

The Comparison Tool and (cont.)

What is available…

The results from hundreds of comparisons on PrecisionFDA are available publicly in a JSON format in accordance with the FHIR spec at https://precision.fda.gov/fhir/sequence

Possible Future steps…

Include a new version of the comparison tool that will allow multiple vcf comparisons against a benchmark.
Develop a tool that demonstrates consumption and rendering of the comparison data.

Thank You!

For additional questions after this meeting, please email…
Precisionfda@fda.hhs.gov

Next Steps

- Report and Blog post available from:
  - » https://www.healthit.gov/sites/default/files/sync_for_genes_report_november_2017.pdf
  - » https://www.healthit.gov/buzz-blog/precision-medicine/genes-fhir-advances-standardizing-genomics-hl7-fhir/

- ONC will continue its role as a coordinator and collaborator with NIH to advance the underlying standards necessary to support precision medicine and the *All of Us* Research Program

Stay Tuned . . .

Questions?

The Office of the National Coordinator for Health Information Technology

Thank You!

@ONC_HealthIT

HHSONC

HealthIT.gov