Speaker Introduction

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Sr. Executive with more than 25 years of experience in pharmaceutical clinical research processes, standards and technologies.
Conflict of Interest

Wayne Kubick, BA, MBA
Receives salary from HL7
Extremely minor stockholder with Oracle, Inc.
Has no real or apparent conflicts of interest to report.
Agenda

• The current state of the pharmaceutical industry
• Biopharma use of EHR clinical data
• What FHIR can mean for Biopharma
  – Clinical trial planning and management
  – Clinical trial data management
  – Regulatory and safety
• Setting clinical research on FHIR
Learning Objectives

• Use real-world evidence from healthcare to inform program and trial design, support pragmatic and other research trials and improve pharmacovigilance and regulatory review

• Recognize the benefits of using FHIR to improve the clinical trial data collection process from clinical sites and patients

• Discuss how SMART on FHIR can bring more patients and patient data to research and improve availability of research data to patients.
Potential Benefits Realized

- Reduced stress of redundant data entry & mapping
- Patient Data More Available for Research
- Automated e-Consent; Personal Health Data Access
- >25% reduction in clinical data management costs
Pharmaceutical Costs Under Fire

$86M spent by pharma to defeat Prop 61 in California
Typically 6 or more transformations of data (red arrows), increasing cost and risk of error

Very difficult to trace back to source

Risk of nuance lost when transcribing to CRFs and SAS v5 Transport file format
Healthcare and Pharma Clinical Research: Separate Worlds

HL7 Vision: A world in which everyone can securely access and use the right health data when and where they need it.
What's Changed

The American Recovery and Reinvestment Act of 2009

$17.2 Billion in Medicare and Medicaid incentives designed to facilitate widespread implementation of certified EHR systems in physician practices and hospitals.

MACRA

2017: Two Pathways for Payments

- Alternative Payment Models
- Merit-Based Incentive Payment System

What you do in 2017 will impact your pay in 2019

Use of Electronic Health Record Data in Clinical Investigations

Guidance for Industry

US Food and Drug Administration - Califf: Leveraging Real World Evidence is 'Top Programmatic Priority' for FDA
- The Common Clinical Data Set includes key health data that should be exchanged using specified vocabulary standards and code sets as applicable.

<table>
<thead>
<tr>
<th>Patient name</th>
<th>Lab values/results</th>
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<tbody>
<tr>
<td>Sex</td>
<td>Vital signs</td>
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<tr>
<td>Date of birth</td>
<td>Procedures</td>
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<td>Race</td>
<td>Care team members</td>
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<td>Ethnicity</td>
<td>Immunizations</td>
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<tr>
<td>Preferred language</td>
<td>Unique device identifiers for implantable devices</td>
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<tr>
<td>Problems</td>
<td>Assessment and plan of treatment</td>
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<td>Medications</td>
<td>Goals</td>
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<td>Medication allergies</td>
<td>Health concerns</td>
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<td>Lab tests</td>
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**ONC Interoperability Roadmap Goal**

2015-2017
Send, receive, find and use a common clinical data set to improve health and health care quality.
The Fundamentals of FHIR

- A next generation **standards framework & platform**, built on 30 years of HL7 experience, designed for implementation

- Advanced RESTful Services technology platform (used by Facebook, Twitter…)
  - Can Create, Read, Update and Mark Deletion

- Content based on Resources: essential modular information components easily assembled into working systems.

- Flexible outputs: messages, documents, data, services
# FHIR Resources

Smallest logically discrete unit of transaction “of interest” to healthcare

<table>
<thead>
<tr>
<th>Clinical Reasoning</th>
<th>Decision Support, Clinical Quality Measures</th>
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<tbody>
<tr>
<td><strong>Clinical</strong></td>
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<td>Allergy, Problem</td>
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<td>etc</td>
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<td><strong>Diagnostics</strong></td>
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<td>Observation,</td>
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<td>Report, Request</td>
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<td>etc</td>
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<td><strong>Medications</strong></td>
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<td>Order, Dispense,</td>
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<td>Administration,</td>
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<td>Statement etc</td>
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<td><strong>Workflow</strong></td>
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<td>Task, Subscription</td>
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<td>etc</td>
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<td><strong>Financial</strong></td>
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<tr>
<td>Claim, EligibilityRequest etc</td>
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<table>
<thead>
<tr>
<th>Administration</th>
<th>Patient, Practitioner, Device, Organization, Location, Healthcare Service</th>
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<tbody>
<tr>
<td><strong>Implementer Support</strong></td>
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<td>Downloads Common Use Cases Testing</td>
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<td><strong>Security &amp; Privacy</strong></td>
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<td><strong>Conformance</strong></td>
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<td>StructureDefn Conformance Profiling</td>
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<td><strong>Terminology</strong></td>
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<td>CodeSystem ValueSet ConceptMap Terminology Svc</td>
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<td><strong>Ontology</strong></td>
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<td>RDF todo</td>
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| Foundation | Base Documentation, XML, JSON, REST API + Search, Data Types, Extensions |

[Diagram showing various categories and subcategories related to FHIR Resources]
Principles of FHIR

- Data resides at the **source of truth**
- **APIs** access data: *pull* what you need, instead of taking what’s *pushed*
- Focus on **implementers**
- Include rigorous **semantics**
- Design for the common **80%**; extensions for the rest
- Off-the-shelf **security and authorization**
- **Speed, scalability**
- Human **readable**, ease of understanding
- Open source, **freely** available for all.
The *FHIR Maturity Model* allows developers to assess the stability of FHIR components and realize the value of FHIR as it evolves.
What FHIR Can Mean for BioPharma

- Make healthcare data more consistent and more available for clinical research, safety, epidemiology, health economics, outcomes research …
  - Research in the broader sense for pharma R&D, government, healthcare and academia
- Opportunities to improve efficiency of clinical trials, shorten timelines, reduce costs
- Open new pathways to improve interactions with clinicians, payers and patients
Clinical Study Planning & Management

- Use FHIR API to evaluate feasibility of protocol eligibility criteria – and interact with patients
- Identify potential investigators and subjects for clinical trials
- A better way to manage e-Consent
- Clinical Decision Support - Potentially provide a window into protocol execution to prevent critical protocol violations that could compromise quality/usability of study data
The Costs of Protocol Complexity

Amendments reduce number of patients, but at high cost, longer study times

Nearly half of all substantial amendments are deemed avoidable

- The most frequent changes stemming from amendments are associated with modifications and revisions to study volunteer demographics and eligibility criteria.
- The total median direct cost to implement a substantial amendment for Phase II and Phase III protocols is $141,000 and $535,000, respectively.
1. EHR triggers a CDS hook

2. CDS Cards (displayed in EHR) & CDS Decisions (automatically applied)

3. User reads, runs apps, and decides.

4. Source: Josh Mandel

- Information card:
  - $200 per month (patient pays $30)

- Suggestion card:
  - Try HCTZ as first-line
  - Switch to HCTZ

- App link card:
  - Managing hypertension?
  - Launch JNC 8 Rx Pro

Source: Josh Mandel
Clinical Trial Data Use Cases

• Use FHIR API to pull EHR source data to pre-populate EDC CRFs
• Use FHIR API to apply study database changes to update EHR (sync with EDC)
• Collect patient-originated data (eCOA, ePRO, symptoms) for EHR or EDC with SMART-on-FHIR
• Capture and use genetic information to support precision medicine with SMART-on-FHIR
• Make study data more available to patients and EHRs after study ends
Potential Future Study Data Flow Using FHIR

- Orders, Results, Notes
- eForms
- Aggregate Study DB
- SDTM Views
- Analysis Views & Models (Sentinel, OMOP...)
- FDA Review

Coordinator

EHR

HL7 C-CDA
CCD Document & Form Archive

Discrepancy Mgmt

External Data Feeds
SMART on FHIR Genomics Apps

1. Order Genetics Labs
2. Return Genetics Labs Results
3. Present & Contextualize Genetics Labs Results

Source: Gil Alterovitz
DB (Diabetes Bear) EMR App
Alterovitz & Yang

Precision Cancer Medicine (PCM) App
Warner & Alterovitz

Genomics Advisor App
Alterovitz & Zhang

Pediatric growth chart – innovative parent’s view

- Custom view optimized for communication with parents and child
- Visually project height in terms of parent’s height
- Print copy for parents, or email via portal

Source: Josh Mandel

Kimberly Revis is obese at 44.9kg (99lb).
Compared to her last weight assessment, she is more obese.
The healthy weight for her age and height is 22.0kg — 37.3kg (48lb. 8oz. — 82lb 4oz.).
Regulatory & Safety Use Cases

• Access to multiple EHR data sources through FHIR API for product safety signal detection and exploration

• Use of FHIR API for pragmatic trials

• Closely monitor responses to new product rollouts – and give early indication of serious adverse events – real-time Risk Evaluation and Mitigation Strategies

• Allow reviewers of new drug applications to drill down into the details of the patient EHR record when exploring serious adverse events
Pragmatic Clinical Trials

Study Design
- EHR-informed estimates of eligible patients/events
- Simple inclusion/exclusion criteria
- Quality-by-design directed by regulatory Guiding Principles

Sites
- Site networks linked by electronic document exchange
- Standardized contracting across network
- Central IRB or collaborative IRB agreements

Enrollment Process
- Eligible patient identification via EHR
- Real-time 'trial alerts' embedded in EHR
- Group recruitment models vs patients 'owned' by primary MD
- Special screening and enrollment clinics
- Online e-consent with comprehension questions

Efficient Trial Conduct
- Risk-based site monitoring
- Streamlined serious adverse event (SAE) reporting
- Technology to facilitate trial tracking

Source: Eric D. Peterson, MD, Duke
Trigger examples: influenza order, blood culture order, sputum culture order, CXR order

(ESP) Safety or Clinical data

Smart on FHIR API
Clinical Data Element Profile for Severe Acute Respiratory Infection data elements

Secure Data Broker
HHS & Booz Allen Hamilton
Data Aggregated & De-identified

Geolocation, case and site reporting, resource deployment overlay

Clinical Registry case level and patient level

Source: Skip Francis, FDA
Information Exchange and Data Transformation (INFORMED)

A holistic approach to oncology regulatory science and big data analytics

Real world data working group

Sponsor

Formal submission

Regulatory

Direct

Real world biometrics, omics, social media

CDISC

Clinical trials

New data pipelines

Data exchange/visualization/analytics*

Data exported for further analysis if needed

Source: Sean Khozin, FDA

*Technology and software development
DoF: FDA CDRH NEST

National Evaluation System for health Technology
to more efficiently generate better evidence for medical device evaluation and regulatory decision-making. A national evaluation system would generate evidence across the total product lifecycle of medical devices by strategically and systematically leveraging real-world evidence, and applying advanced analytics to data tailored to the unique data needs and innovation cycles of medical devices.

FHIR, Big Data to Support FDA Medical Device Development Network

Interoperable data standards, including FHIR, will form the basis for the FDA's new big data sharing community focused on streamlining medical device development.

NOTE: FDA CDRH 2017 Strategic Priority
Source: Todd Cooper
Forums for Clinical Research on FHIR

• Biopharma track at HL7 Partners in Interoperability
• Clinical Research track at FHIR Connectathons
• Collaboration with TransCelerate Biopharma eSource Team on proof of concept projects
• Biopharma stream on chat.fhir.org
• More to come
How to Get There: Lighting the FHIR

• Formal engagement from regulators and the biopharma community to flesh out use cases and requirements and engage resources and plan strategies for change management

• Formal assessment of availability, consistency, quality, and suitability for Clinical Trials of EHR clinical data accessible through FHIR APIs – perhaps by emulating or collaborating with Project Argonaut

• Development/Clarification of policies on consent, privacy, access for clinical data for research purposes using FHIR APIs (at workgroup meetings)

• Alignment with CDISC data representations (working with CDISC, TransCelerate Biopharma, government, academia, others) regarding RCTs for product approval

• Work with FDA and industry to define and pilot defined regulatory use cases for Real World Evidence and eSource

• Formal development of FHIR Implementation Guides (via HL7 workgroups).
Potential Benefits Summary

Reduced stress of redundant data entry & mapping

Patient Data More Available for Research

Automated e-Consent; Personal Health Data Access

>25% reduction in clinical data management costs

FHIR can unleash a wealth of opportunities for medical product manufacturers to access and repurpose healthcare data for streamlining multiple forms of research, increasing patient engagement, and improving patient safety.
Questions

Setting Clinical Research on FHIR

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