#HL7

April2016 Taha Kass-Hout

Joint work with many colleagues at FDA, White House, NIH, and ONC

precisionFDA

precision.FDA.gov

FDA advancing precision medicine with precisionFDA:
a collaborative informatics community
to explore regulatory science

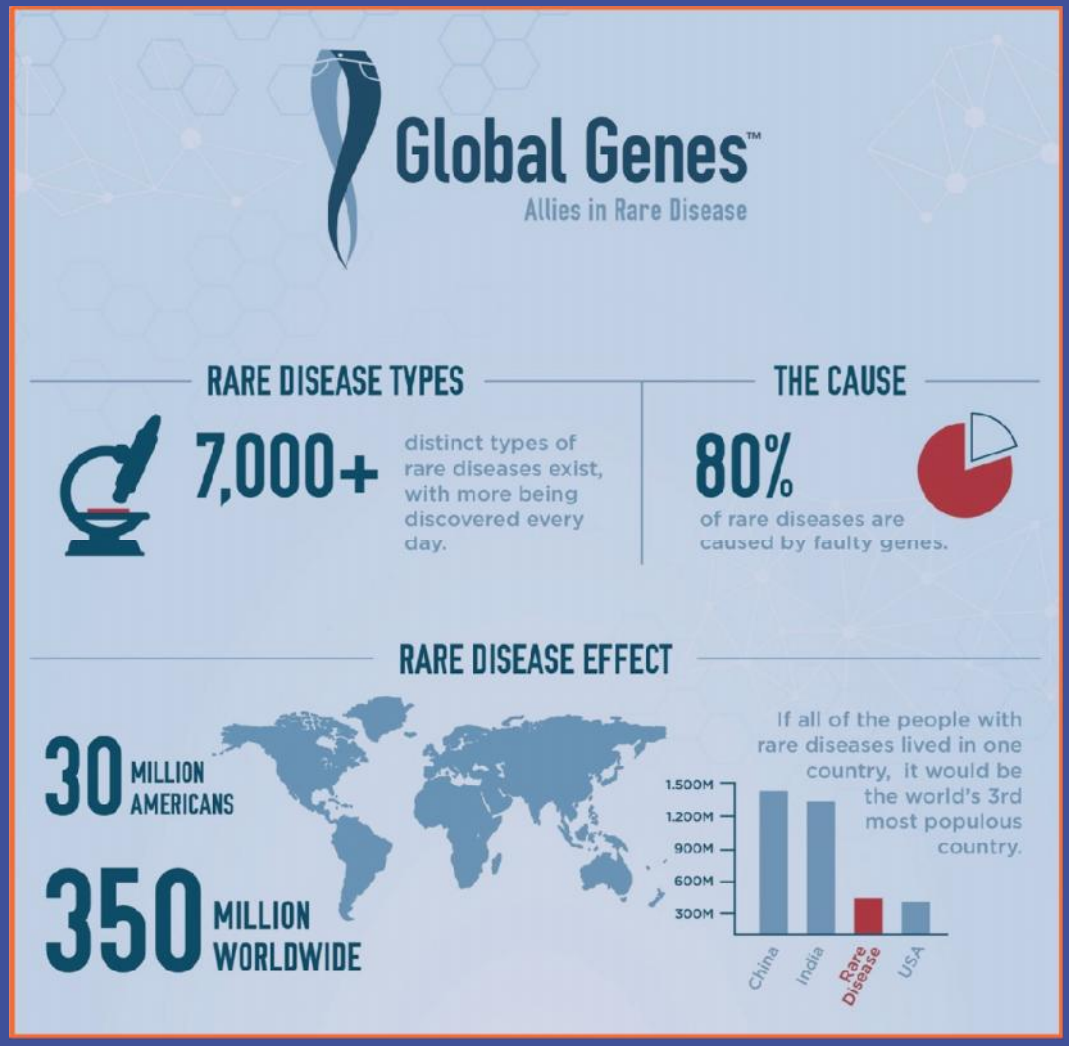
DNA

Gene

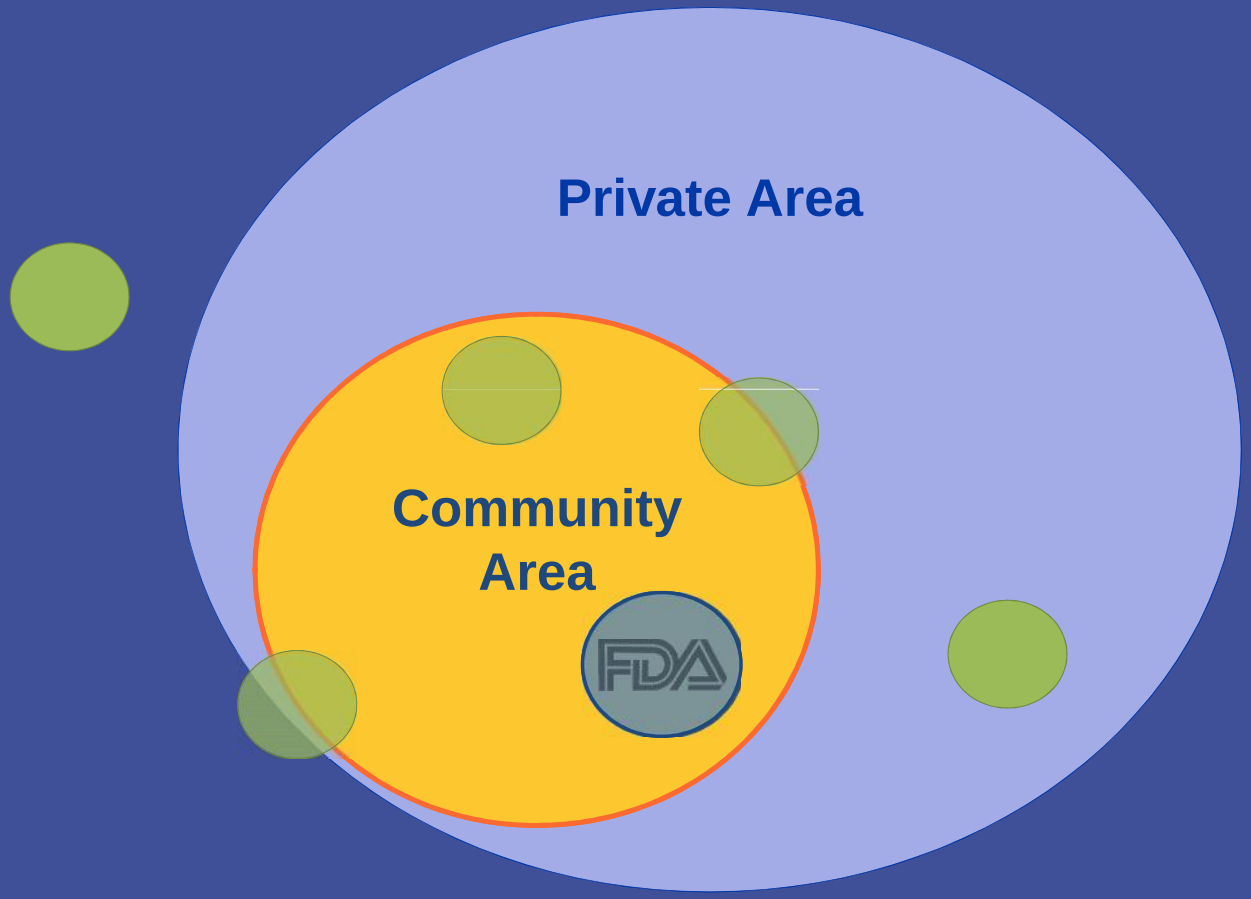
… AGCATCGATGCAGAAGATTACAAGACGATCCGCTC …

THE PRECISION MEDICINE INITIATIVE

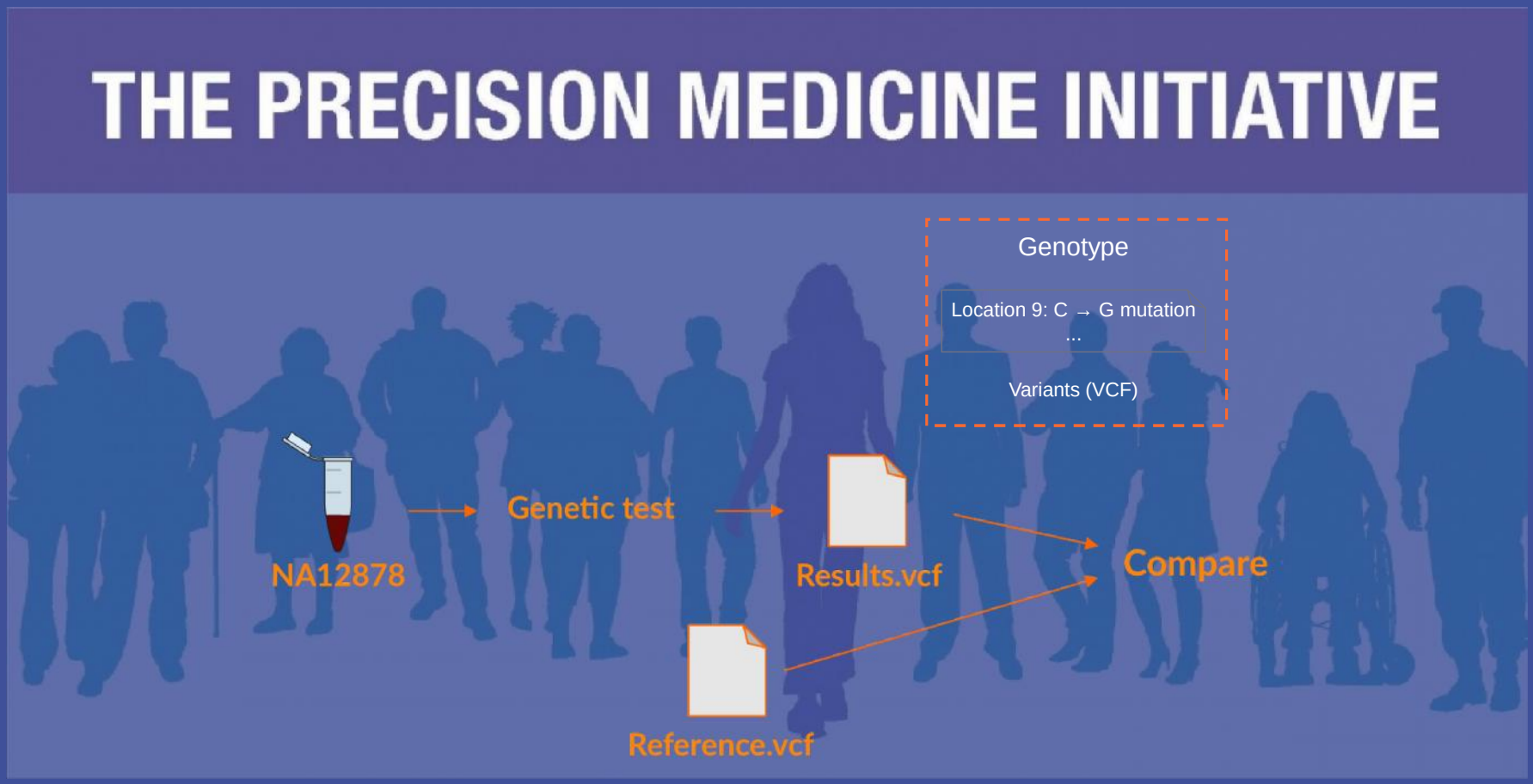
precisionFDA
precision.FDA.gov


Global Genes™
Allies in Rare Disease
RARE DISEASE TYPES
7,000+
distinct types of rare diseases exist, with more being discovered every day.
THE CAUSE
80%
of rare diseases are caused by faulty genes.
RARE DISEASE EFFECT
30 MILLION AMERICANS
350 MILLION WORLDWIDE
If all of the people with rare diseases lived in one country, it would be the world's 3rd most populous country.
1.500M
1.200M
900M
600M
300M
China
India
Rare Disease
USA

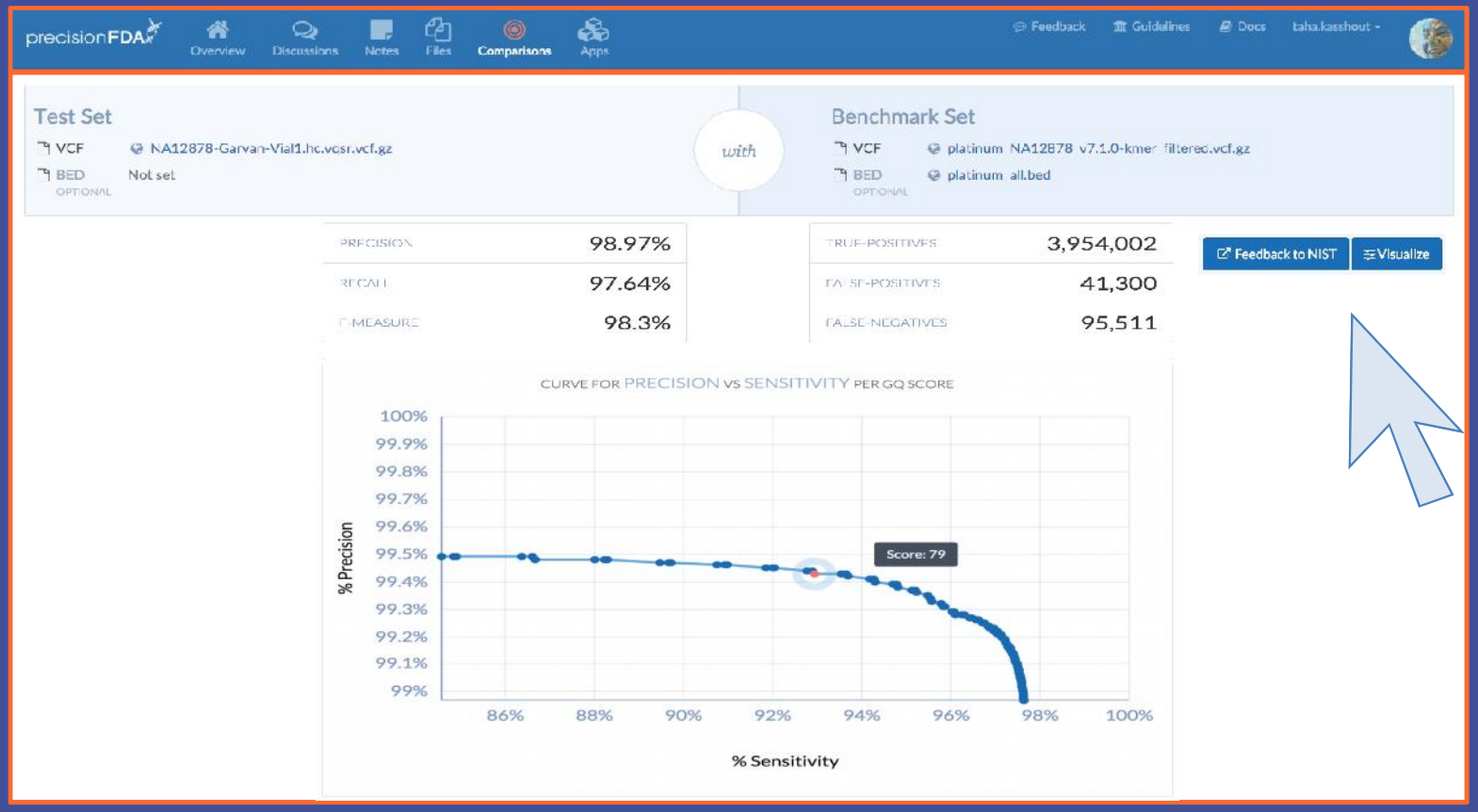
precisionFDA Eco-System



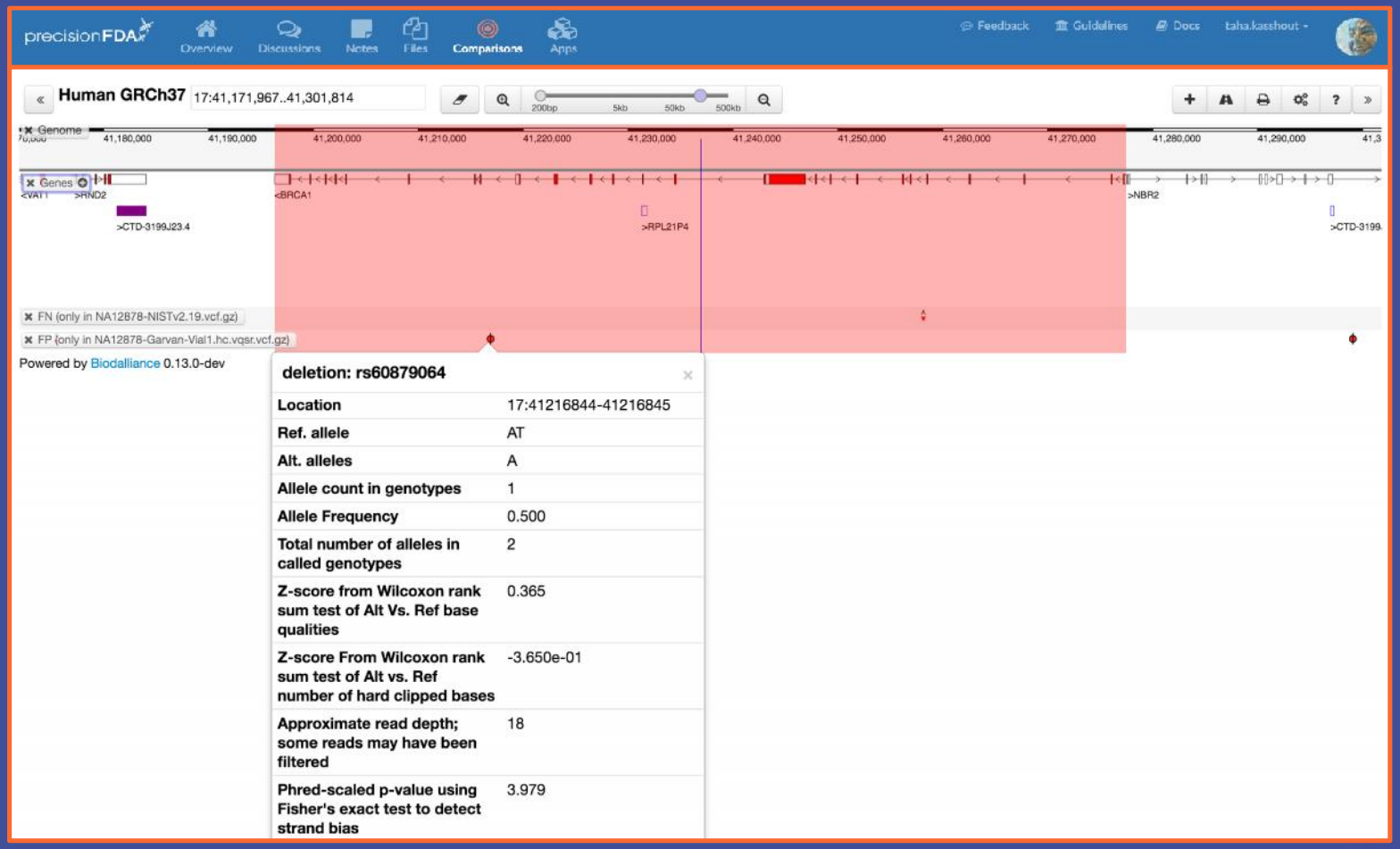
THE PRECISION MEDICINE INITIATIVE



Comparisons



Comparisons



FHIR Use Case

precisionFDA
precision.FDA.gov

FHIR®©

Quality Resource Extension

# of tp
# of fp
# of fn
Recall
Precision
f-score

Community Challenges

precisionFDA

Join the precisionFDA Consistency Challenge!

Join the FDA in engaging and improving DNA test results with the first community challenge. Learn more: precision.fda.gov.

President Obama's Precision Medicine Initiative envisions a day when an individual's medical care will be tailored in part based on their unique characteristics and genetic make-up.

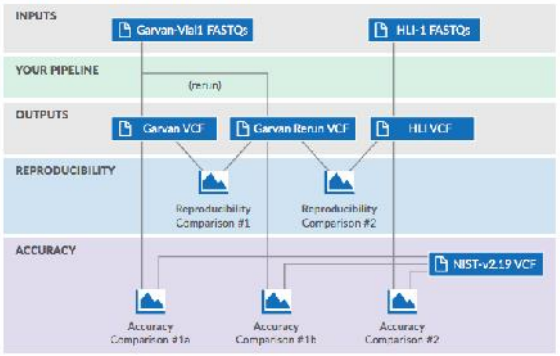
The goal of the FDA's first precisionFDA challenge is to engage the genomics community in advancing the quality standards in order to achieve more consistent results in the context of genetic tests (related to whole human genome sequencing), advancing the goal of better personalized care.

PrecisionFDA invites all innovators to take the challenge and assess their software on the supplied reference human datasets. Participation is voluntary, but instrumental in helping the community prepare for the coming genomic data revolution.

AT A GLANCE

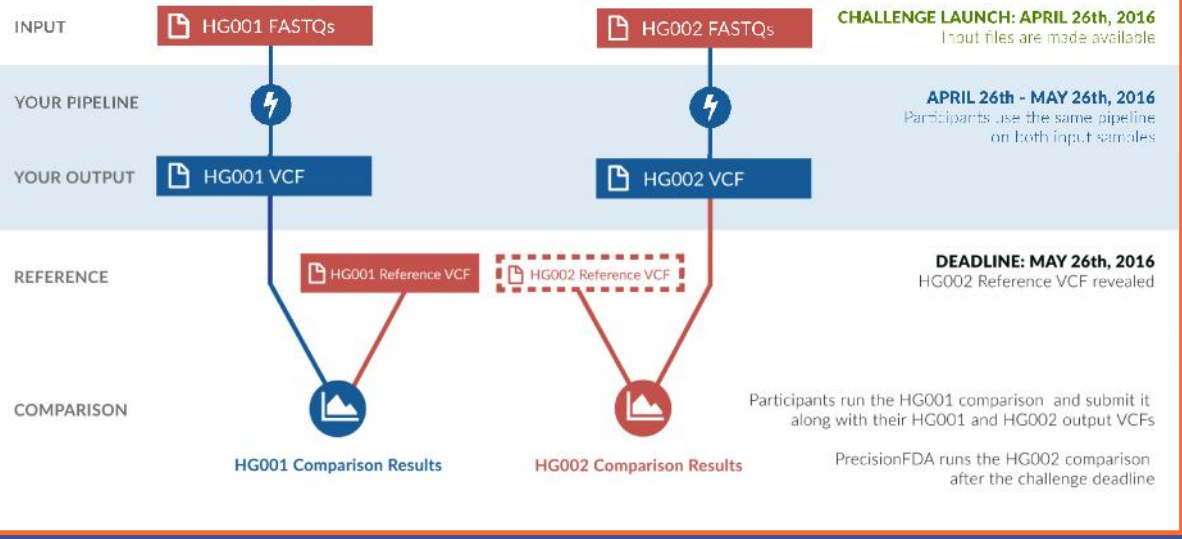
PrecisionFDA Consistency Challenge

February 25, 2016 through April 25, 2016

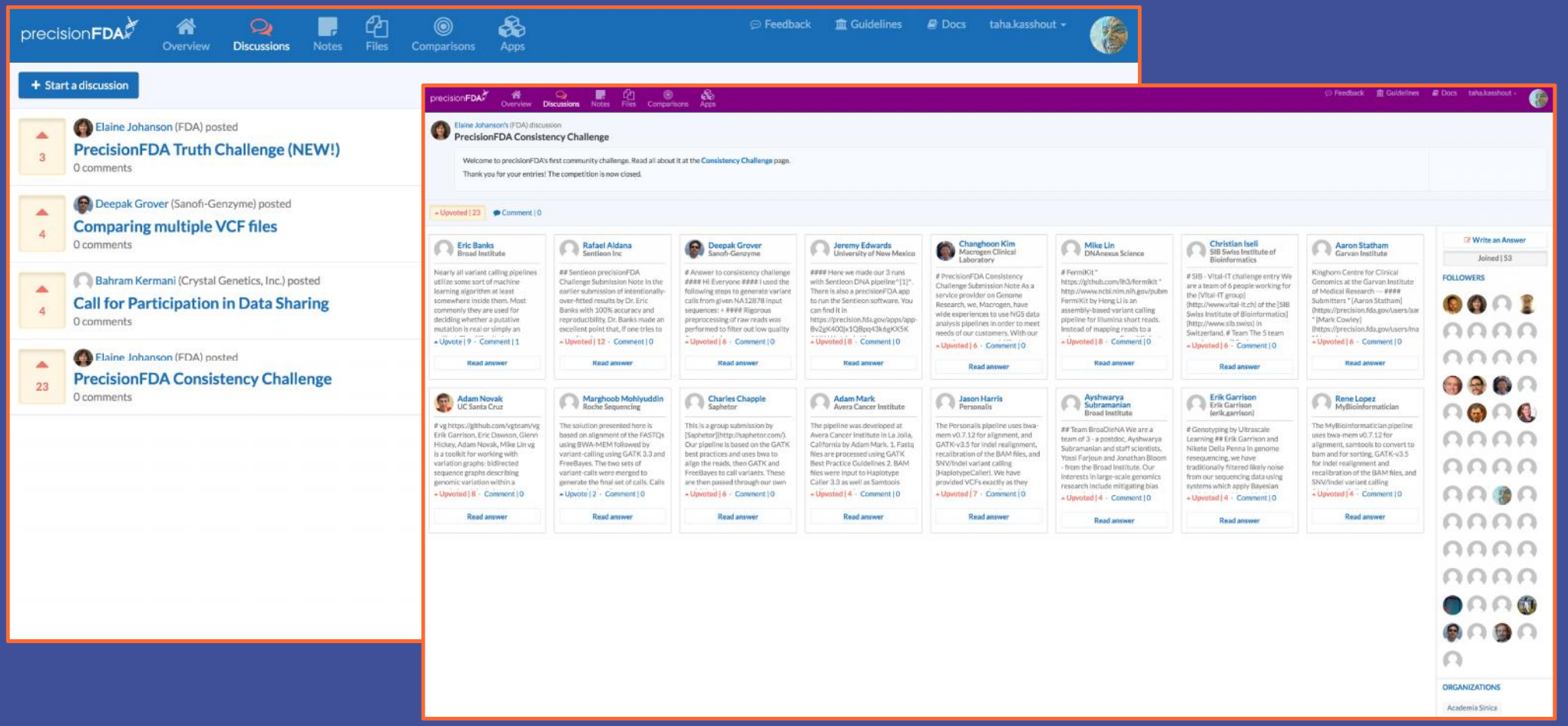


PrecisionFDA Truth Challenge

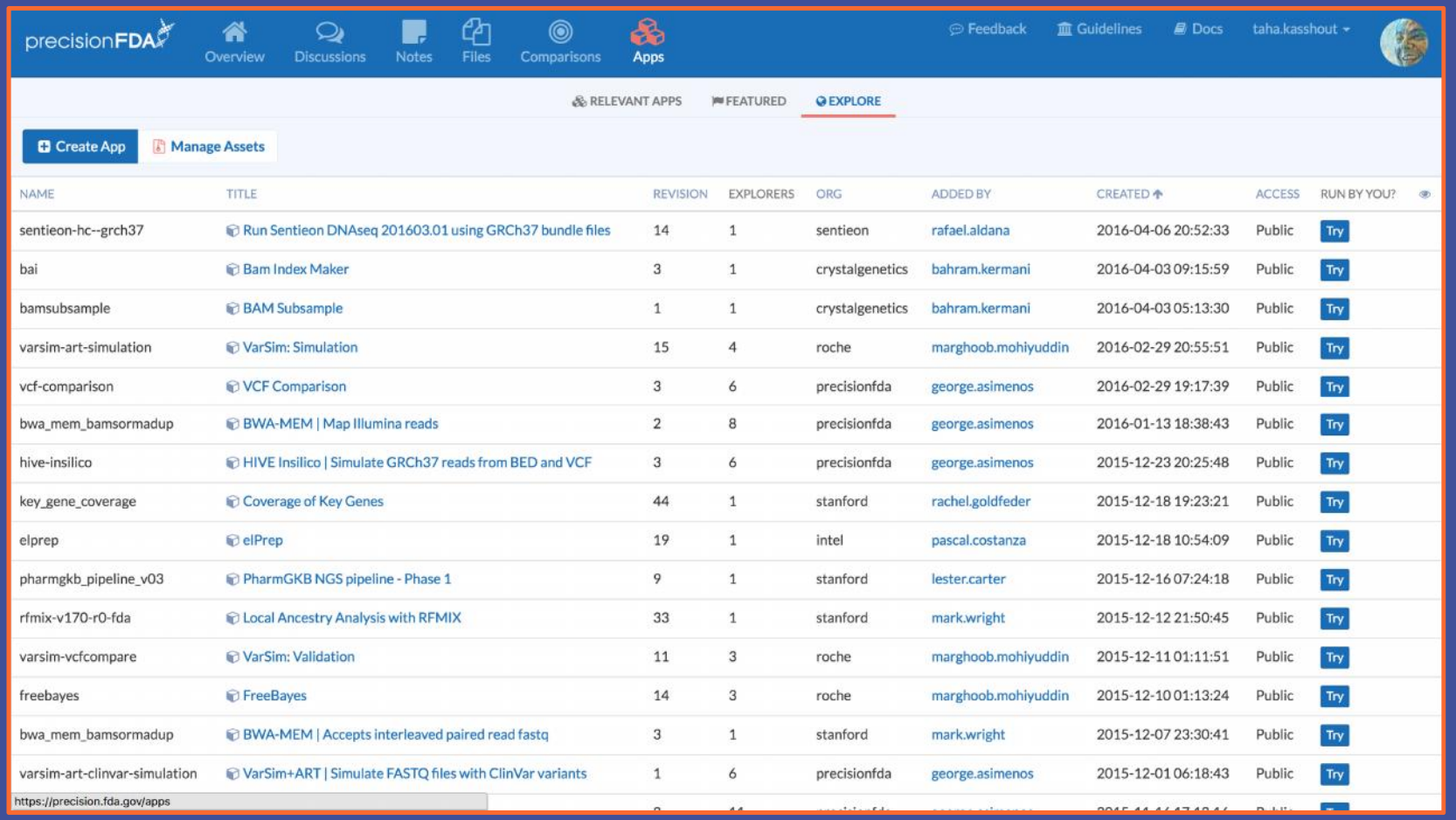
April 26, 2016 through May 26, 2016



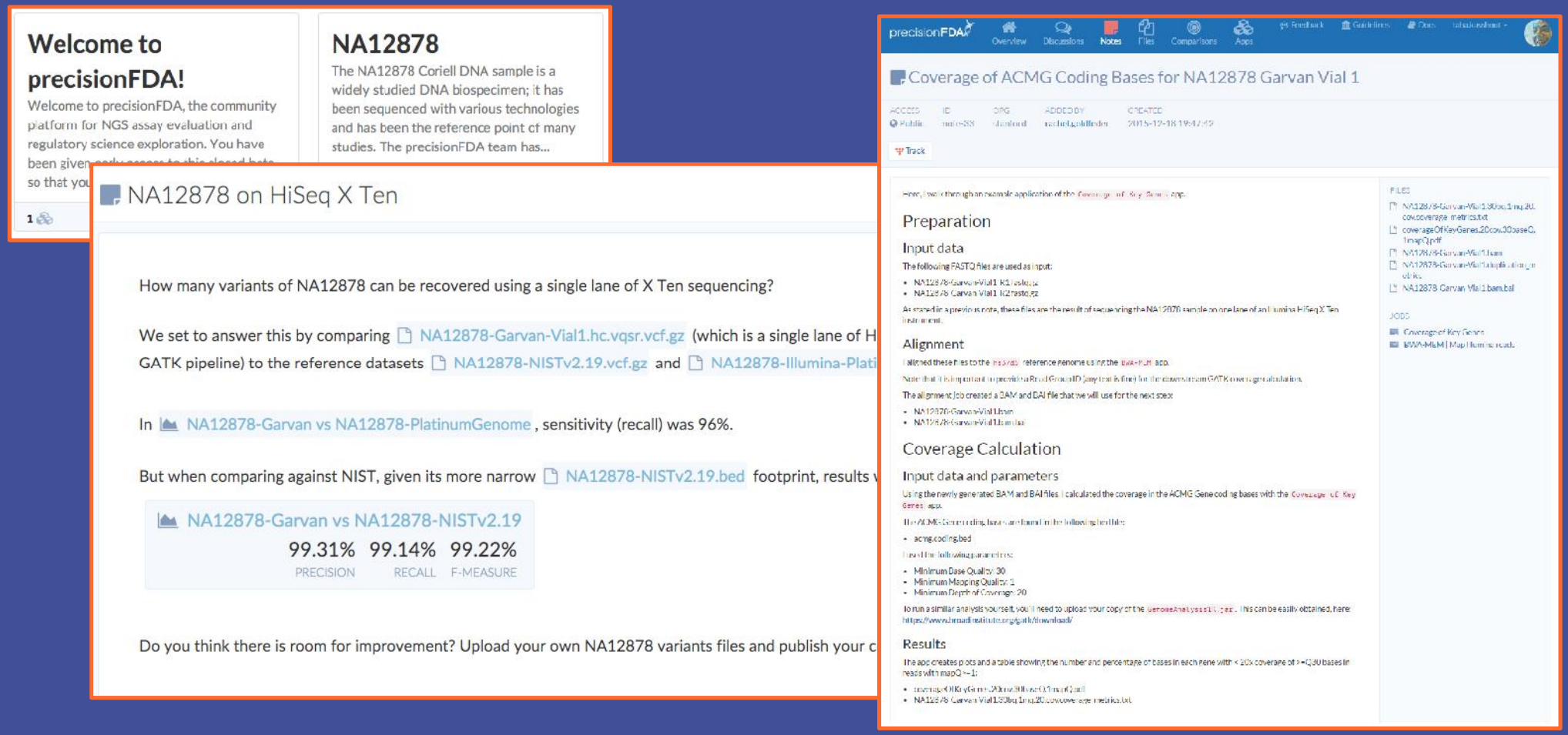
Discussions



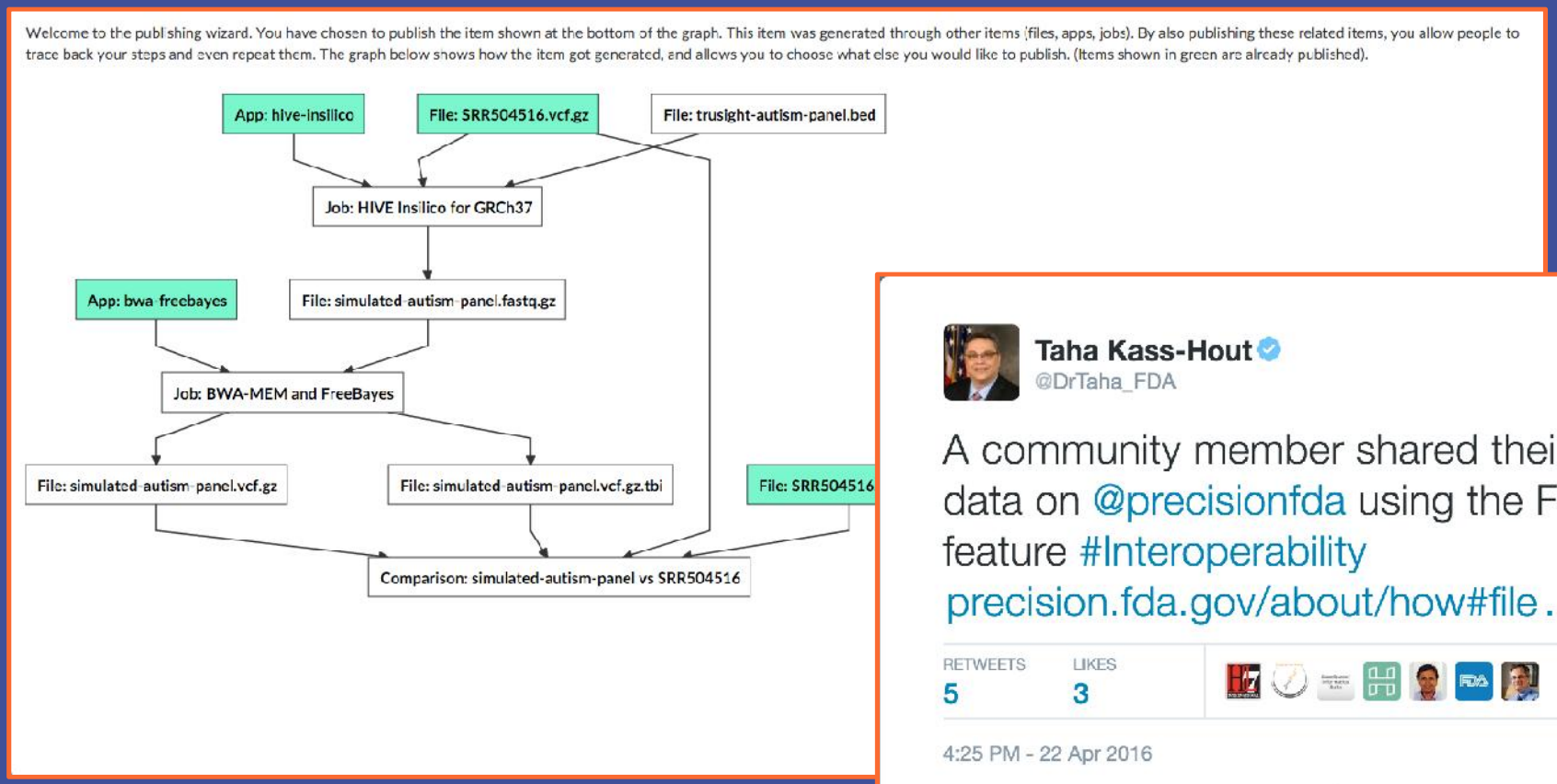
Apps


precisionFDA
Overview
Discussions
Notes
Files
Comparisons
Apps
Feedback
Guidelines
Docs
taha.kasshout
RELEVANT APPS
FEATURED
EXPLORE
Create App
Manage Assets
NAME | TITLE | REVISION | EXPLORERS | ORG | ADDED BY | CREATED | ACCESS | RUN BY YOU?
sentieon-hc--grch37 | Run Sentieon DNAseq 201603.01 using GRCh37 bundle files | 14 | 1 | sentieon | rafael.aldana | 2016-04-06 20:52:33 | Public | Try
bai | Bam Index Maker | 3 | 1 | crystalgenetics | bahram.kermani | 2016-04-03 09:15:59 | Public | Try
bamsubsample | BAM Subsample | 1 | 1 | crystalgenetics | bahram.kermani | 2016-04-03 05:13:30 | Public | Try
varsim-art-simulation | VarSim: Simulation | 15 | 4 | roche | marghoob.mohiyuddin | 2016-02-29 20:55:51 | Public | Try
vcf-comparison | VCF Comparison | 3 | 6 | precisionfda | george.asimenos | 2016-02-29 19:17:39 | Public | Try
bwa_mem_bamsormadup | BWA-MEM | Map Illumina reads | 2 | 8 | precisionfda | george.asimenos | 2016-01-13 18:38:43 | Public | Try
hive-insilico | HIVE Insilico | Simulate GRCh37 reads from BED and VCF | 3 | 6 | precisionfda | george.asimenos | 2015-12-23 20:25:48 | Public | Try
key_gene_coverage | Coverage of Key Genes | 44 | 1 | stanford | rachel.goldfeder | 2015-12-18 19:23:21 | Public | Try
elprep | elPrep | 19 | 1 | intel | pascal.costanza | 2015-12-18 10:54:09 | Public | Try
pharmgkb_pipeline_v03 | PharmGKB NGS pipeline - Phase 1 | 9 | 1 | stanford | lester.carter | 2015-12-16 07:24:18 | Public | Try
rfmix-v170-r0-fda | Local Ancestry Analysis with RFMIX | 33 | 1 | stanford | mark.wright | 2015-12-12 21:50:45 | Public | Try
varsim-vcfcompare | VarSim: Validation | 11 | 3 | roche | marghoob.mohiyuddin | 2015-12-11 01:11:51 | Public | Try
freebayes | FreeBayes | 14 | 3 | roche | marghoob.mohiyuddin | 2015-12-10 01:13:24 | Public | Try
bwa_mem_bamsormadup | BWA-MEM | Accepts interleaved paired read fastq | 3 | 1 | stanford | mark.wright | 2015-12-07 23:30:41 | Public | Try
varsim-art-clinvar-simulation | VarSim+ART | Simulate FASTQ files with ClinVar variants | 1 | 6 | precisionfda | george.asimenos | 2015-12-01 06:18:43 | Public | Try
https://precision.fda.gov/apps

Notes

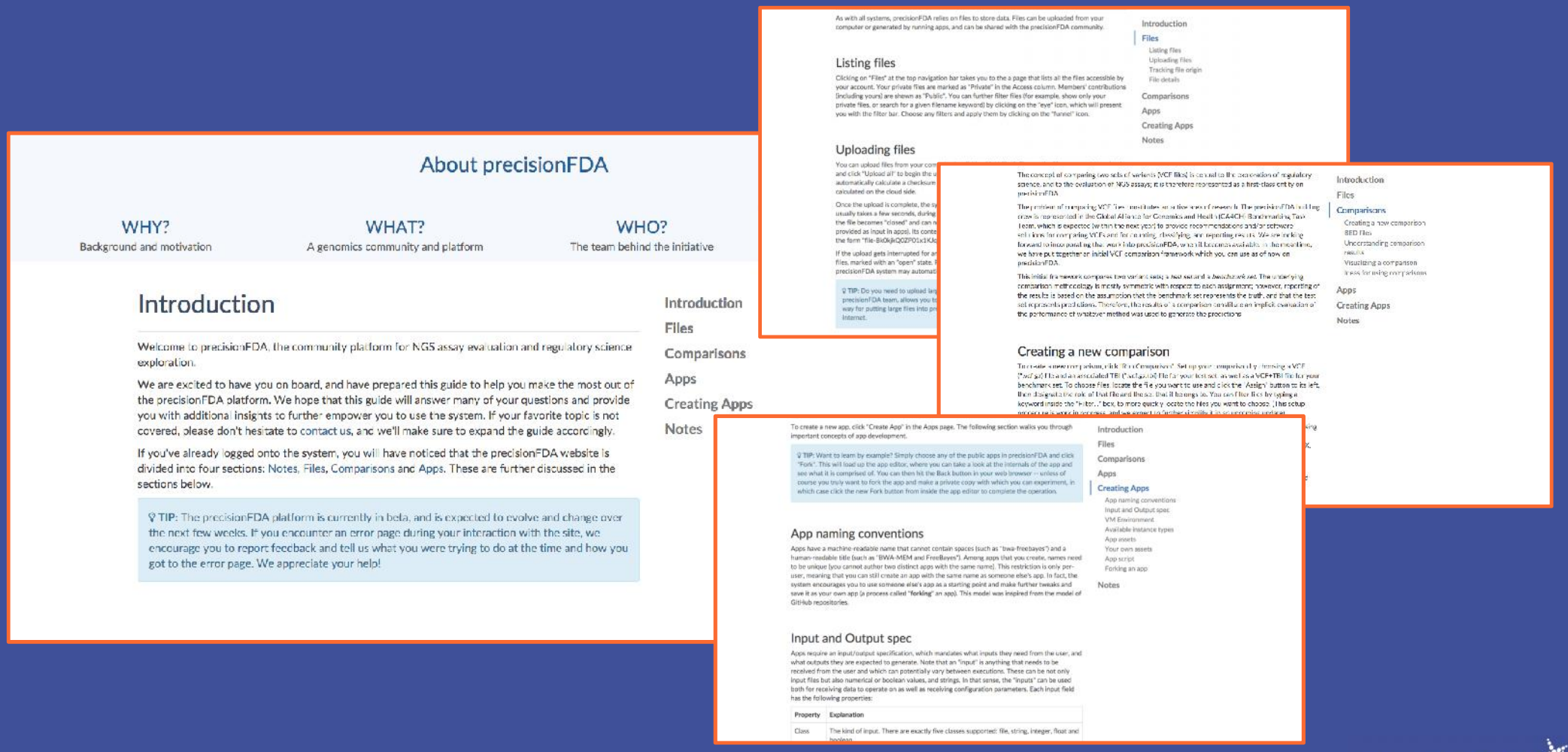

Welcome to precisionFDA!
Welcome to precisionFDA, the community platform for NGS assay evaluation and regulatory science exploration. You have been given early access to this closed beta so that you
NA12878
The NA12878 Coriell DNA sample is a widely studied DNA biospecimen; it has been sequenced with various technologies and has been the reference point of many studies. The precisionFDA team has...
NA12878 on HiSeq X Ten
How many variants of NA12878 can be recovered using a single lane of X Ten sequencing?
We set to answer this by comparing NA12878-Garvan-Vial1.hc.vqsr.vcf.gz (which is a single lane of H
GATK pipeline) to the reference datasets NA12878-NISTv2.19.vcf.gz and NA12878-Illumina-Plati
In NA12878-Garvan vs NA12878-PlatinumGenome, sensitivity (recall) was 96%.
But when comparing against NIST, given its more narrow NA12878-NISTv2.19.bed footprint, results
NA12878-Garvan vs NA12878-NISTv2.19
99.31% PRECISION
99.14% RECALL
99.22% F-MEASURE
Do you think there is room for improvement? Upload your own NA12878 variants files and publish your c
precisionFDA
Overview
Discussions
Notes
Files
Comparisons
Apps
Coverage of ACMG Coding Bases for NA12878 Garvan Vial 1
Track
Preparation
Input data
Alignment
Coverage Calculation
Input data and parameters
Results
FILES
JOBS

Sharing


Welcome to the publishing wizard. You have chosen to publish the item shown at the bottom of the graph. This item was generated through other items (files, apps, jobs). By also publishing these related items, you allow people to trace back your steps and even repeat them. The graph below shows how the item got generated, and allows you to choose what else you would like to publish. (Items shown in green are already published).
App: hive-insilico
File: SRR504516.vcf.gz
File: truslight-autism-panel.bed
Job: HIVE Insilico for GRCh37
App: bwa-freebayes
File: simulated-autism-panel.fastq.gz
Job: BWA-MEM and FreeBayes
File: simulated-autism-panel.vcf.gz
File: simulated-autism-panel.vcf.gz.tbi
File: SRR504516
Comparison: simulated-autism-panel vs SRR504516

Taha Kass-Hout
@DrTaha_FDA
A community member shared their @BaseSpace data on @precisionfda using the Fetch from URL feature #Interoperability precision.fda.gov/about/how#file…
RETWEETS
5
LIKES
3
4:25 PM - 22 Apr 2016

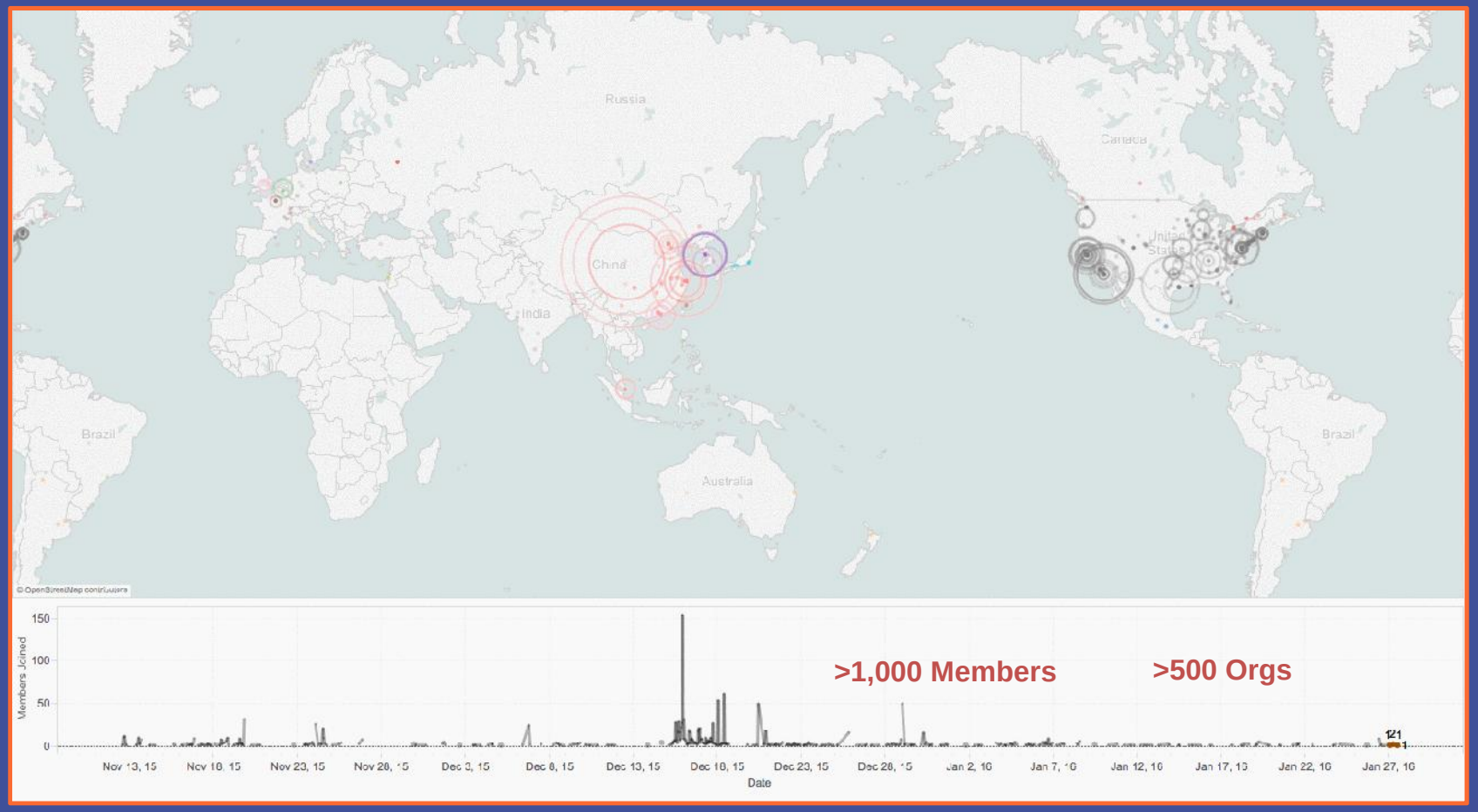
Documentation



FierceBiotechIT

FDA hits tight timeline for start of precisionFDA open beta

December 21, 2015 | By Nick Paul Taylor



PERSPECTIVE

REGULATORY SCIENCE

A research roadmap for next-generation sequencing informatics

Russ B. Altman,[1]* Snehit Prabhu,[2] Arend Sidow,[3] Justin M. Zook,[4,11] Rachel Goldfeder,[5] David Litwack,[6] Euan Ashley,[7] George Asimenos,[8] Carlos D. Bustamante,[2] Katherine Donigan,[6] Kathleen M. Giacomini,[9] Elaine Johansen,[6] Natalia Khuri,[10] Eunice Lee,[6] Xueying Sharon Liang,[6] Marc Salit,[4,10,11] Omar Serang,[8] Zivana Tezak,[6] Dennis P. Wall,[12] Elizabeth Mansfield,[6] Taha Kass-Hout[6]

Next-generation sequencing technologies are fueling a wave of new diagnostic tests. Progress on a key set of nine research challenge areas will help generate the knowledge required to advance effectively these diagnostics to the clinic.

The Precision Medicine Initiative (PMI) is a U.S. national effort "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" (*1*). One goal is to bring about the routine use of next-generation precision diagnostics to benefit individuals and public health. Central to the introduction of safe and effective new precision diagnostic technologies is an adequate understanding of how well they perform. Through the PMI, the U.S. Food and Drug Administration (FDA) is seeking to address this issue by providing dynamic, flexible, and well-balanced regulation of precision diagnostics. Because these complex technologies pose new challenges in understanding their likely benefits and their limits in terms of accuracy, precision, and clinical validity, FDA is advancing a robust research agenda in regulatory science. New knowledge gained from this agenda will inform the next generation of regulation for precision medicine.

The UCSF-Stanford Center for Excellence in Regulatory Science & Innovation (CERSI) hosted a series of meetings in September 2015 that included a public workshop and discussions on identifying key activities needed to evaluate the clinical implications of next-generation nucleic acid sequencing (NGS). Here we summarize the ideas and directions that were proposed and put forth a working "roadmap" for NGS evaluation, as a possible exemplar of how many other new next-generation diagnostics may be understood.

[1]Bioengineering, Genetics, and Medicine, Stanford University, Stanford, CA 94305, USA. [2]Biomedical Data Science and Genetics, Stanford University, Stanford, CA 94305, USA. [3]Pathology and Genetics, Stanford University, Stanford, CA 94305, USA. [4]Material Measurement Laboratory, National Institute of Standards and Technology, Gaithersburg, MD 20899, USA. [5]Biomedical Informatics, Stanford University, Stanford, CA 94305, USA. [6]Food and Drug Administration, Silver Spring, MD 20993, USA. [7]Medicine, Genetics, and Pathology, Stanford University, Stanford, CA 94305, USA. [8]DNAnexus, Mountain View, CA 94040, USA. [9]Bioengineering and Therapeutic Sciences, University of California at San Francisco, San Francisco, CA 94143, USA. [10]Bioengineering, Stanford University, Stanford, CA 94305, USA. [11]Material Measurement Laboratory, National Institute of Standards and Technology, Stanford University, Stanford, CA 94305, USA. [12]Systems Medicine and Psychiatry, Stanford University, Stanford, CA 94305, USA.
*Corresponding author. E-mail: russ.altman@stanford.edu

CREDIT: P. SOUZA/THE WHITE HOUSE

Sharing the stage with a DNA double helix, U.S. President Barack Obama discusses the Precision Medicine Initiative.

DEFINING THE TASK

Technological breakthroughs have recently led to DNA sequencing methods that can generate the raw data necessary for determining nearly the entire genome sequence of any individual. Eventually, these developments are likely to culminate in the routine sequencing of patients' genomes. In the meantime, there will be several years during which the process of DNA sequence determination remains challenging and in which cost-, quality-, and goal-driven tradeoffs result in a large diversity of testing strategies. In this Perspective, we lay out the technological challenges that are slowing the routine clinical use of a new generation of genetic tests and propose questions that regulatory science should address to arrive at a flexible yet robust regulatory framework that results in maximum benefit for patients.

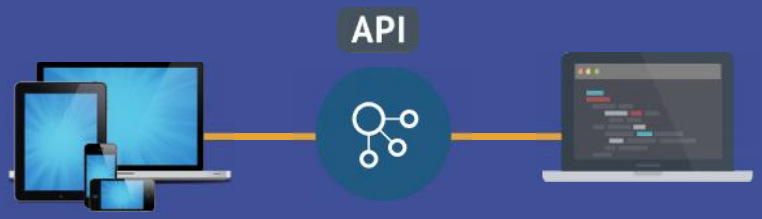
As part of its PMI effort, FDA seeks to undertake and support regulatory science research that will enhance our understanding of NGS test products and their development and validation, as well as how the results of such tests are best communicated in an evolving health care environment.

A centerpiece of this effort is precisionFDA, a research and development portal that will allow community members to better understand, develop, and improve existing and new bioinformatics approaches for processing the vast amount of genomic data that is collected using NGS technology. precisionFDA is a public, cloud-based platform developed by FDA and its contractor DNAnexus that hosts shared tools, crowdsourced testing, and community challenges, to improve and share

precisionFDA
precision.FDA.gov

openFDA
open.fda.gov

Got Side Effects? We have an (App) API for that!



Interoperability

**Application Programming Interface (API) provides an easy way for a software application to access, query, or update source data*

A unified set of open-source APIs for FDA drug, device, and food data

Available APIs

Product	Data	Timeframe	# of records
Drug	Labeling	Current	>74K
	Adverse event reports	Since 2003	>6M
	Recalls	Since 2012	>5K
Medical device	Classification	Current	>6K
	Registration & Listing	Current	>24K establishments >100K devices
	510(k)s (including de novos)	Since 1976	>143.5K
	PMAs (including supplements)	Since 1977	>31.6K
	Adverse event reports	Since 1991	>4.7M
	Recalls	Since 2002	>9.5K
Food	Recalls	Since 2012	>9.6K

Query: URL

https://api.fda.gov/drug/event.json?search=receivedate:[20040101+TO+20150101]+AND+_missing_:companynumb&count=receivedate

Results: Disclaimer

Results: JSON Format

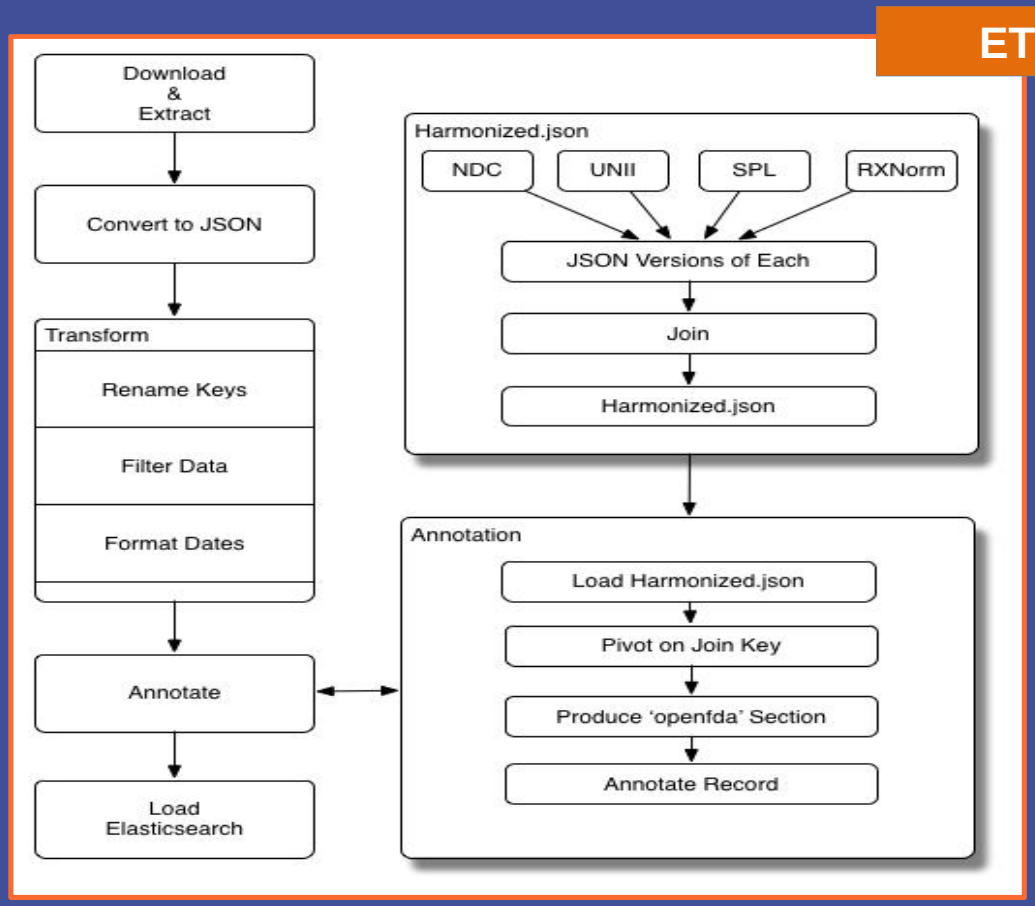

```
{
  meta: {
    disclaimer: "openFDA is a beta research project and not for clinical use. While we make every effort to ensure that data is accurate, you should assume all results are unvalidated.",
    license: "http://open.fda.gov/license",
    last_updated: "2014-08-06"
  },
  results: [
    {
      time: "20040102",
      count: 83
    },
    {
      time: "20040104",
      count: 53
    },
```

Harmonization

Joins | Identifiers

- National Drug Code
- Unique Ingredient Identification
- Structured Product Labelling
- RxNorm links drug terminologies.

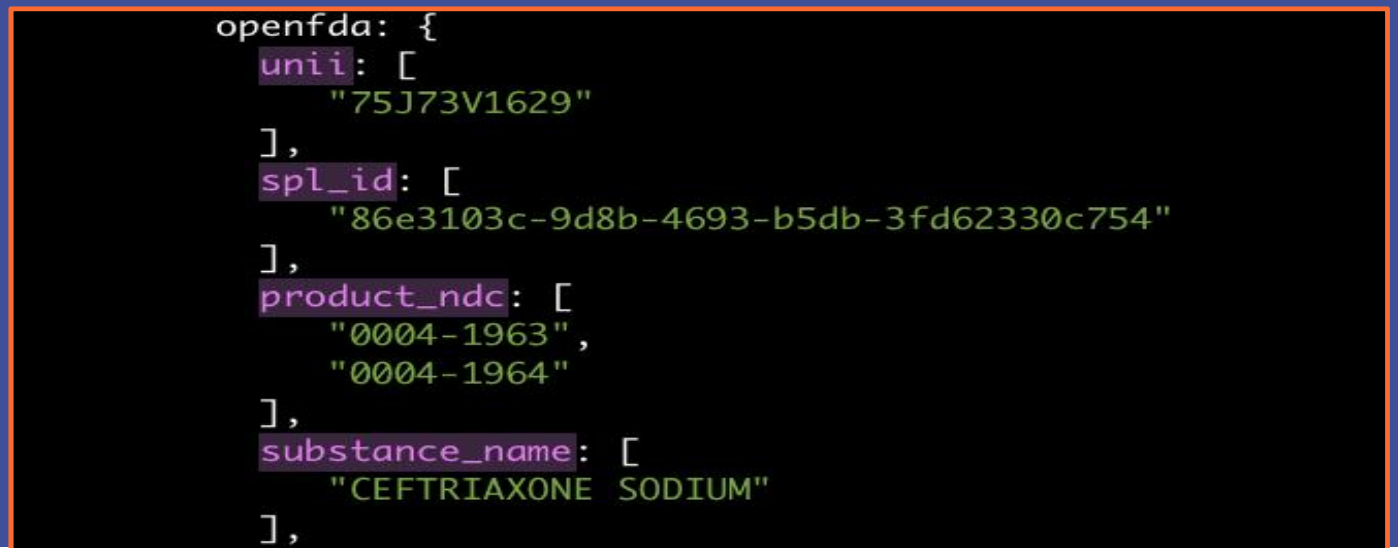
ETL



Harmonization

NDC and SPL datasets contribute the openFDA fields that we add to adverse events and recalls records that mention ≥1 drug

Contains identifiers such as brand name, generic name, SPL SetID, SPL ID, NDC, NDA, UNII, Drug Class and many more

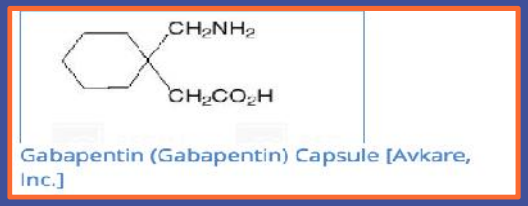


Harmonization – Adverse Events


```
{
    drugcharacterization: "2",
    medicinalproduct: "ROCEPHIN",
    openfda: {
        unii: [
            "75J73V1629"
        ],
        spl_id: [
            "86e3103c-9d8b-4693-b5db-3fd62330c754"
        ],
        product_ndc: [
            "0004-1963",
            "0004-1964"
        ],
        substance_name: [
            "CEFTRIAXONE SODIUM"
        ],
        rxcui: [
            "204871",
            "105212"
        ],
        spl_set_id: [
            "9467f6c9-3e59-45c6-a1be-77200f2d4554"
        ],
        product_type: [
            "HUMAN PRESCRIPTION DRUG"
        ],
        pharm_class_cs: [
            "Cephalosporins [Chemical/Ingredient]"
        ],
```


Join key is NDA/ANDA (application number) and medicinal products

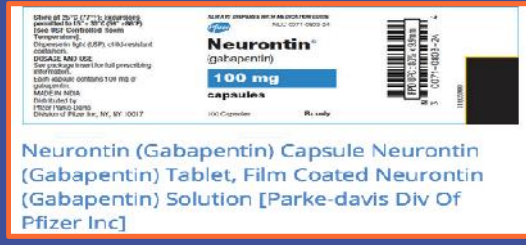
Harmonization – Enforcement Reports



Gabapentin (Gabapentin) Capsule [Avkare, Inc.]

Neurontin (Gabapentin) Capsule [Remedyrepack Inc.]

Gabapentin (Gabapentin) Capsule [Pharmaceutica North America, Inc.]



Neurontin (Gabapentin) Capsule Neurontin (Gabapentin) Tablet, Film Coated Neurontin (Gabapentin) Solution [Parke-davis Div Of Pfizer Inc]

PAXIL CR (Paroxetine HCL) Controlled-Release Tablets 25 mg, 30-count bottle, Rx only, Manufactured by GlaxoSmithKline, RTP, NC 27709, Manufactured for Apotex Corp., Weston, FL 33328, NDC 60505-3669-3

NDC Code

NDC 0049-2710-30

Free-text fields requiring structure

UPC code #'s FA02-90GM, FA02-180GM, and FA02-270GM

UPC Code(s)

The PREBIOTIC FORMULA was distributed in three sizes (90 gram, 180 gram, and 270 grams). UPC code #'s FA02-90GM, FA02-180GM, and FA02-270GM respectively. It is a berry flavored powder in a white plastic screw off container and contains a scooper. It is distributed by Eco-Health, Inc. and contains the following address on the label. 25876 The Old Road #158, Newhall, CA 91321. The dates of distribution are between June 2011 - Aug 2012 in the quantities mentioned above.

For Drugs

- NDC Code
- UPC Code
- FDA Application
- Brand Name
- Dosage Form
- Generic Name
- Manufacturer Name
- Drug Type
- Route Of Administration
- Active Ingredient
- Pharmacologic Class
- Mechanism of Action
- Chemical Structure
- Functional Activity
- UNII Code
- RxNorm Identifier

{"logo":"API Evangelist"}

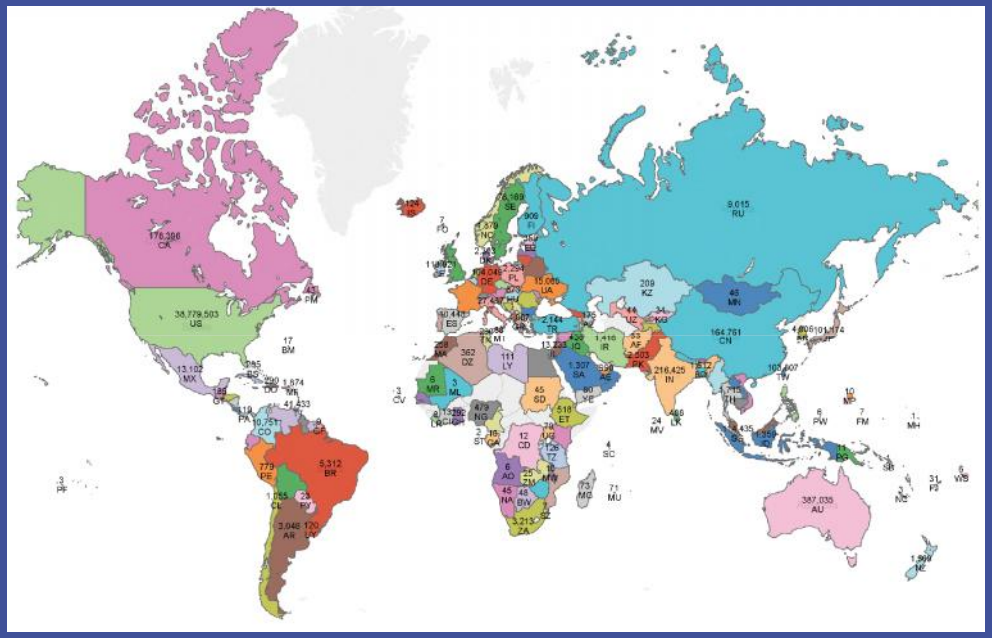
Another Strong API Implementation In Federal Government With OpenFDA

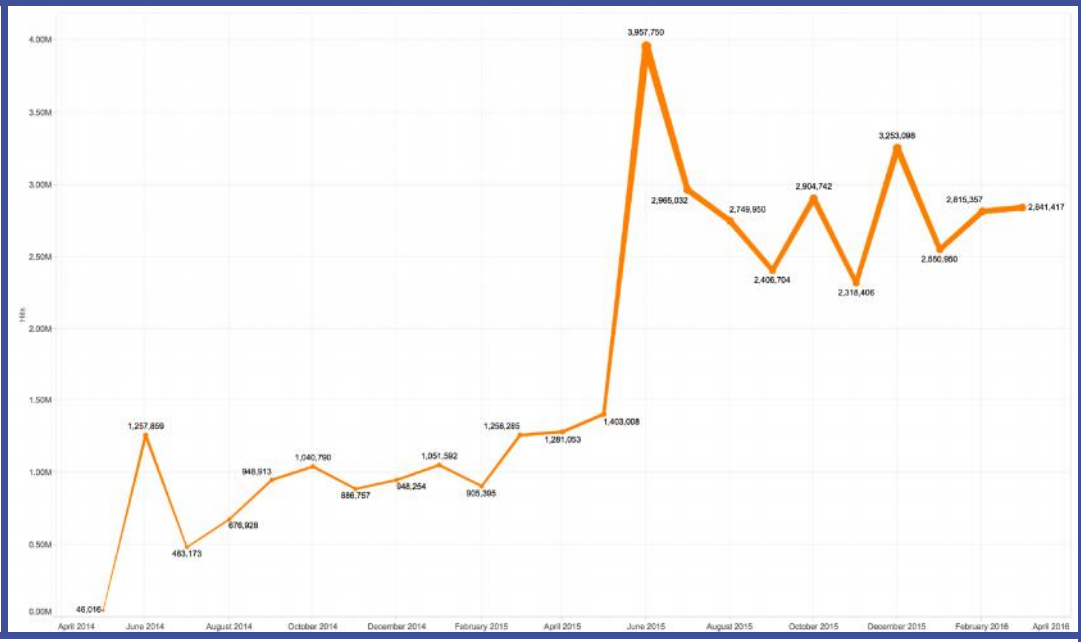
04 Jun 2014

I am really impressed with the quality of API deployments coming out of the federal government recently. I wrote about the **FBOpen API from 18F** a couple months ago, and the latest is the **OpenFDA API from the Food & Drug Administration**. I've been watching the rollout of the API from behind the scenes for a while now, but with all my travel and speaking I haven't had time to write about or participate, but now that they've officially launch publicly, I wanted to help showcase what they've been up to at the FDA.

Community

>7,600 registered API users





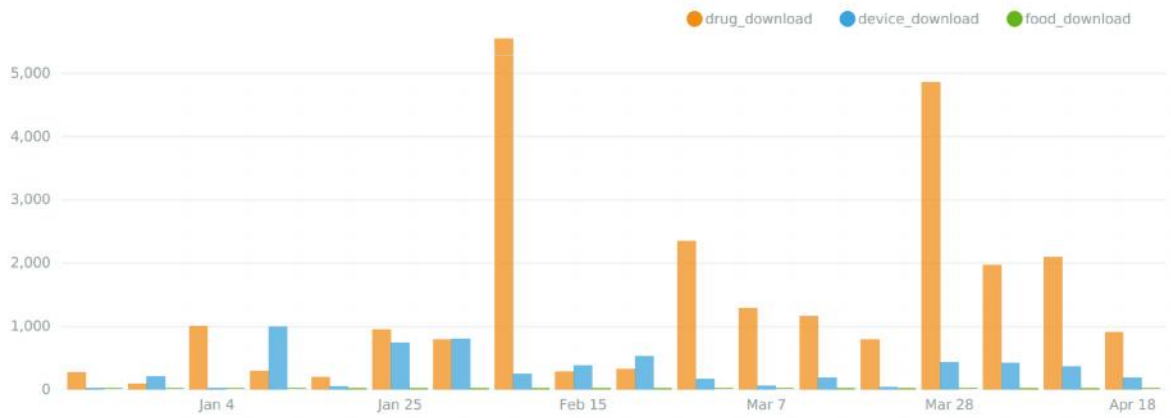
41,924,767	1,140	236,355	105ms
hits	unique users	unique ip addresses	average response time

Total File Downloads By Center Results

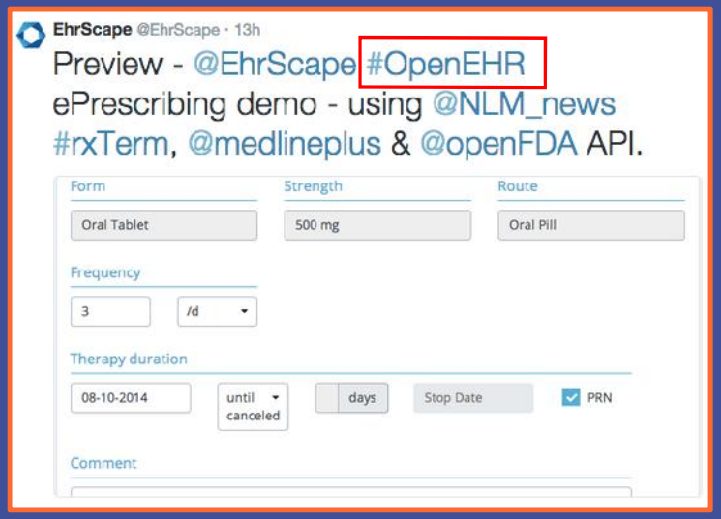
center	total
drug	24711
device	5848
food	241
data	159

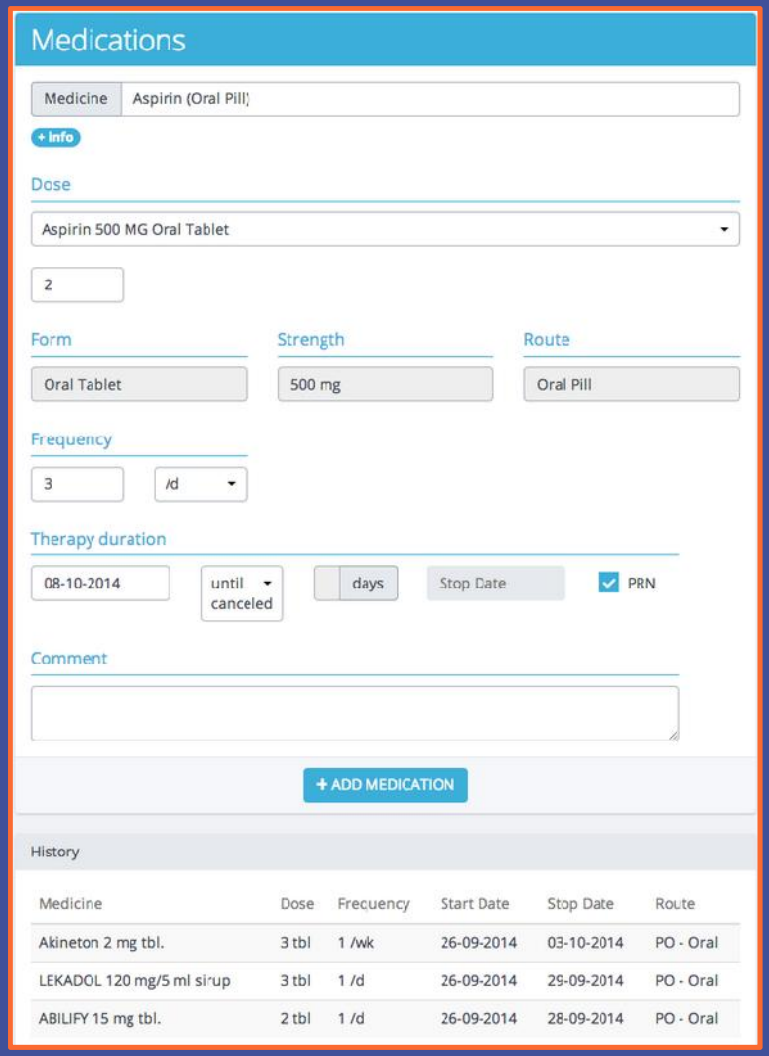
>30K Downloads in 3.5 Months

Downloads by Center and Week

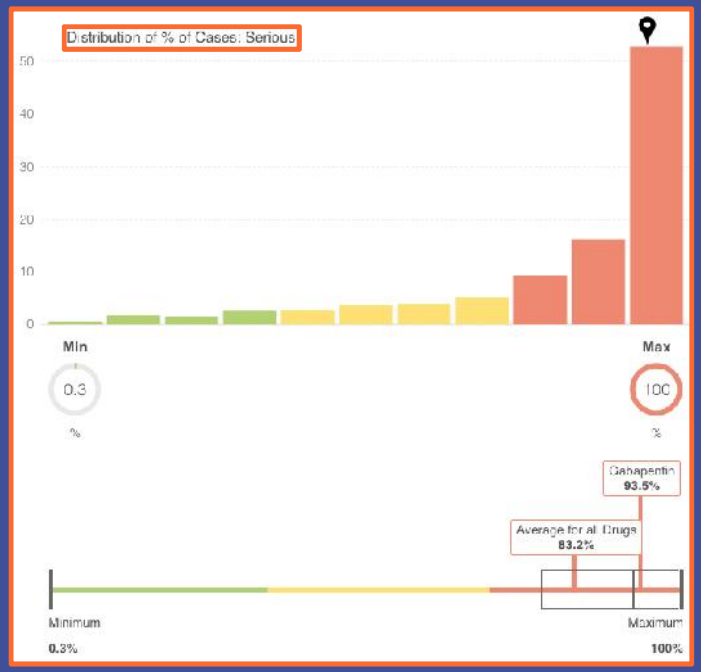


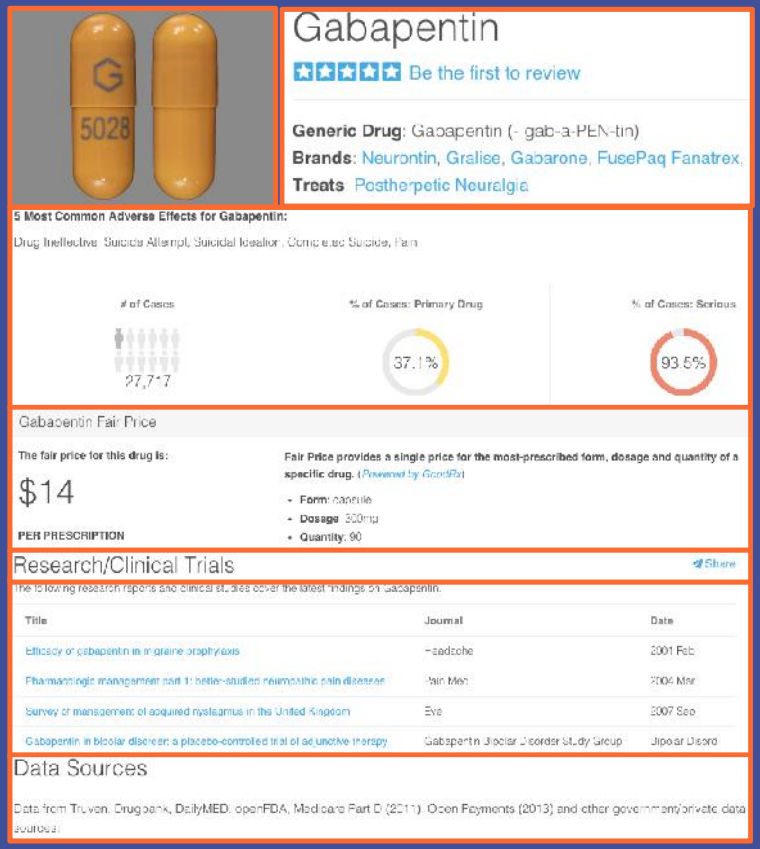
Sample App


EhrScape @EhrScape · 13h
Preview - @EhrScape #OpenEHR
ePrescribing demo - using @NLM_news
#rxTerm, @medlineplus & @openFDA API.
Form
Oral Tablet
Strength
500 mg
Route
Oral Pill
Frequency
3
/d
Therapy duration
08-10-2014
until canceled
days
Stop Date
PRN
Comment

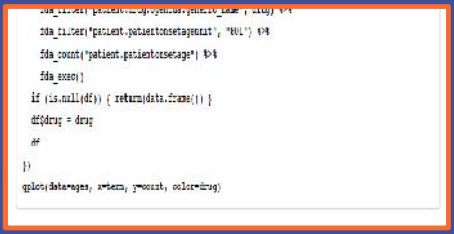

Medications
Medicine
Aspirin (Oral Pill)
+ info
Dose
Aspirin 500 MG Oral Tablet
2
Form
Oral Tablet
Strength
500 mg
Route
Oral Pill
Frequency
3
/d
Therapy duration
08-10-2014
until canceled
days
Stop Date
PRN
Comment
+ ADD MEDICATION
History
Medicine
Dose
Frecuency
Start Date
Stop Date
Route
Akineton 2 mg tbl.
3 tbl
1 /wk
26-09-2014
03-10-2014
PO - Oral
LEKADOL 120 mg/5 ml sirup
3 tbl
1 /d
26-09-2014
29-09-2014
PO - Oral
ABILIFY 15 mg tbl.
2 tbl
1 /d
26-09-2014
28-09-2014
PO - Oral

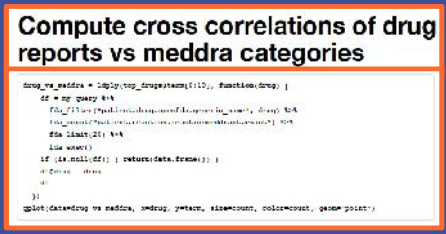
Sample App

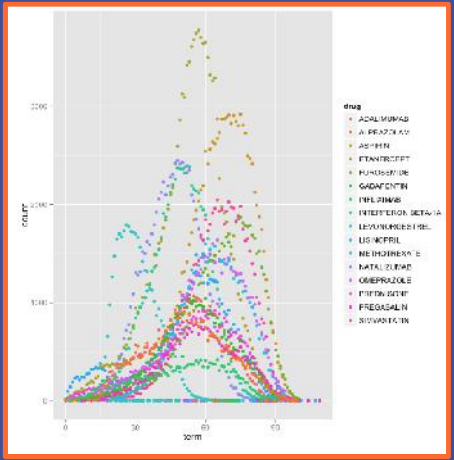

Distribution of % of Cases: Serious
50
40
30
20
10
0
Min
0.3
%
Max
100
%
Gabapentin
93.5%
Average for all Drugs
83.2%
Minimum
0.3%
Maximum
100%

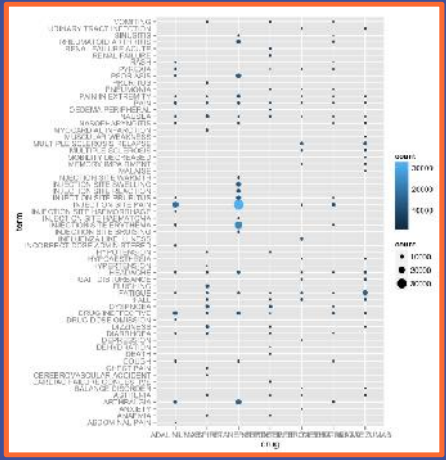

Gabapentin
Be the first to review
Generic Drug: Gabapentin (- gab-a-PEN-tin)
Brands: Neurontin, Gralise, Gabarone, FusePaq Fanatrex
Treats: Postherpetic Neuralgia
5 Most Common Adverse Effects for Gabapentin:
Drug Ineffective, Suicide Attempt, Suicidal Ideation, Completed Suicide, Pain
# of Cases
27,717
% of Cases: Primary Drug
37.1%
% of Cases: Serious
93.5%
Gabapentin Fair Price
The fair price for this drug is:
$14
PER PRESCRIPTION
Fair Price provides a single price for the most-prescribed form, dosage and quantity of a specific drug.
Form: capsule
Dosage: 300mg
Quantity: 90
Research/Clinical Trials
Share
Title
Journal
Date
Data Sources

Connecting with Data Scientists and Researchers





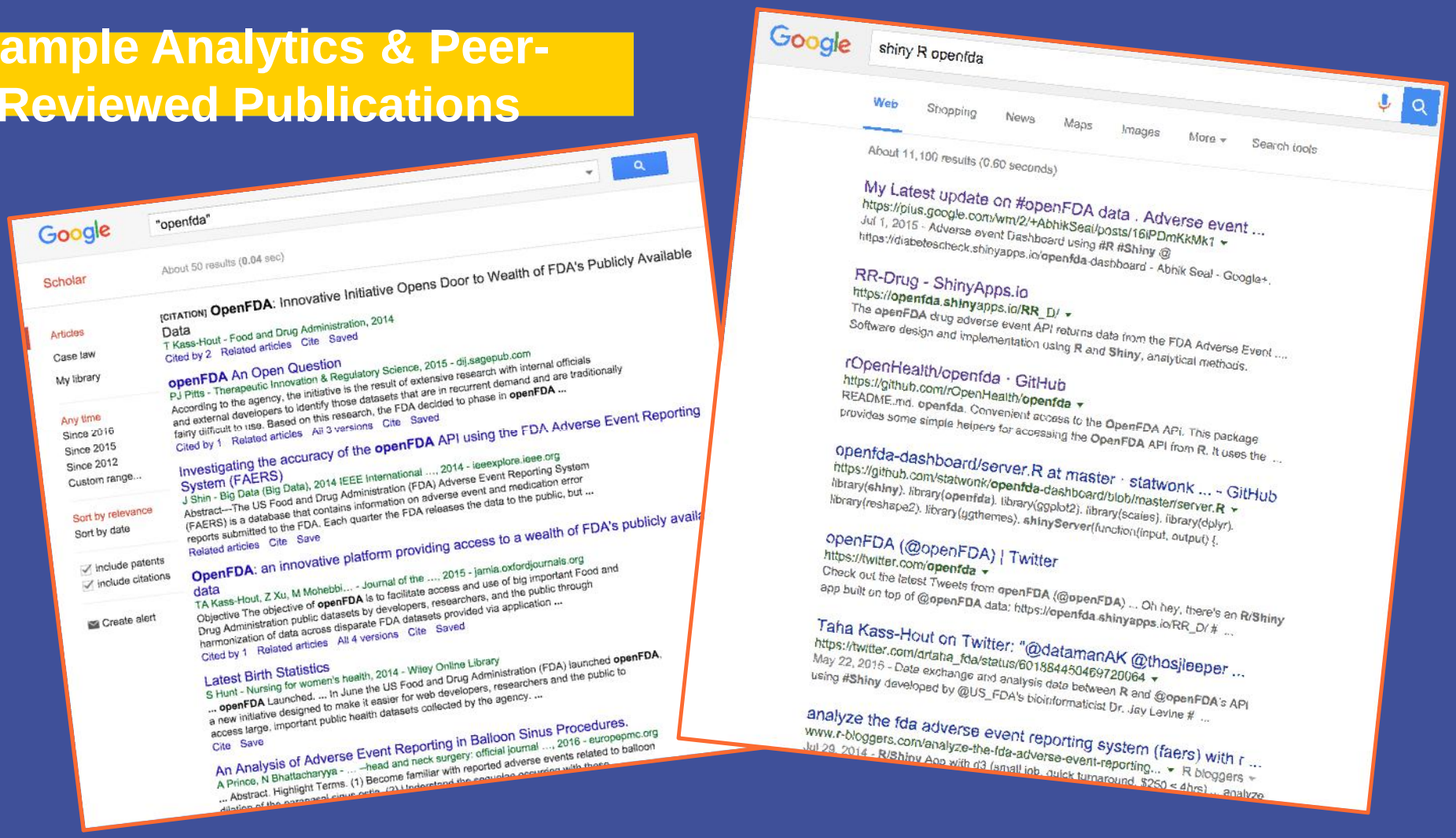




An open source R library for interfacing directly with openFDA APIs has been adopted by the rOpenHealth project

github.com/ropenhealth/openfda

Sample Analytics & Peer-Reviewed Publications



Thank you!


LETTUCE
Canada, Chile, Dominican Republic, Mexico, Peru, USA
CUCUMBERS
Canada, Honduras, India, Mexico, Spain, USA
FETA CHEESE
Canada, Denmark, Egypt, Germany, Greece, Israel, Italy, Turkey, UK, USA
VINAIGRETTE
Argentina, Brazil, Canada, Chile, China, France, Germany, Greece, India, Indonesia, Italy, Mexico, Morocco, Peru, Portugal, Spain, Thailand, Tunisia, Turkey, USA, Vietnam
The Well-Traveled Salad.
Do You Know Where Your Food Has Been?
As consumers, many of us fail to recognize that even our domestic and local food supplies are part of a global network. The daily activity of consuming food directly links our health as humans to the health of crops and produce, food animals, and the environments in which they are produced.
OLIVES
Greece, Israel, Mexico, Spain, USA
SPROUTS
Argentina, Australia, Bangladesh, Canada, China, Egypt, France, India, Morocco, Nepal, Pakistan, South Africa, Spain, Turkey, USA
CROUTONS
Argentina, Australia, Brazil, Canada, China, France, India, Mexico, Netherlands, Poland, Russia, Switzerland, Uruguay, USA, Vietnam
TOMATOES
Canada, Dominican Republic, Holland, Israel, Italy, Mexico, USA
ONIONS
Canada, China, Germany, India, USA
MANDARIN ORANGES
Israel, Mexico, Morocco, South Africa, Spain
A "One Health" approach to food safety—bringing together expertise and resources from the clinical, veterinary, wildlife health, and ecology communities—has the potential to reveal the sources, pathways, and factors driving the outbreaks of foodborne illness and possibly prevent them from occurring in the first place.
NOTE: Countries are listed in alphabetical order and not by volume of export.
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Illnesses

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Jury Verdicts: Guilty, Guilty, and Guilty in PCA Criminal T

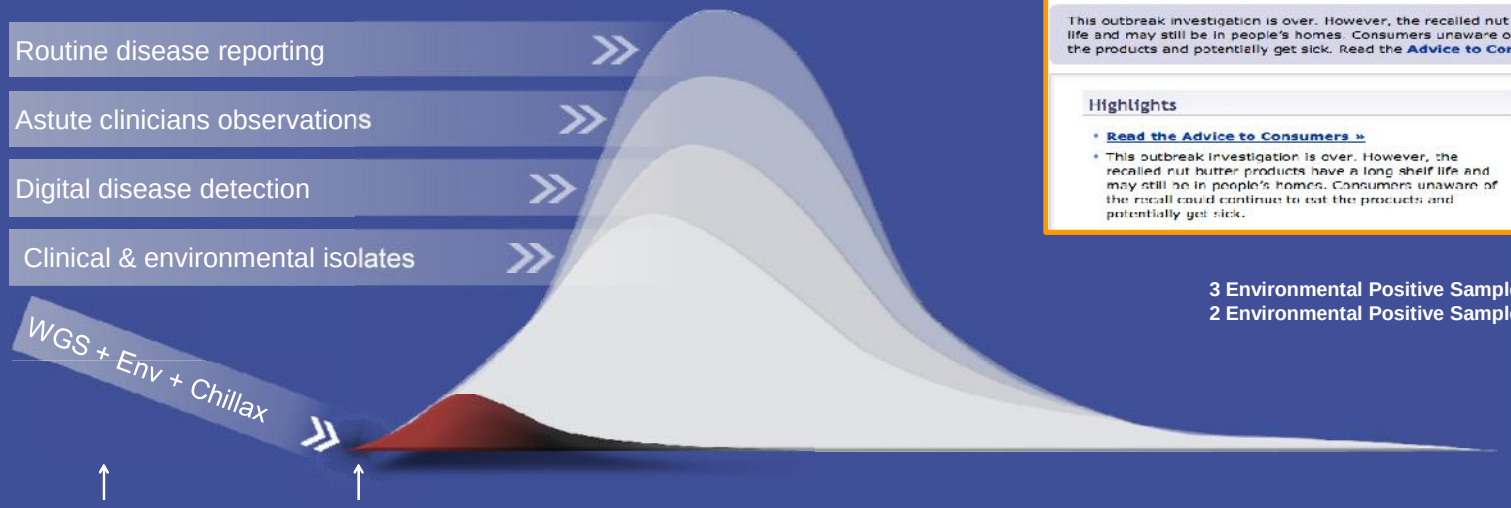
Y DAN FLYNN | SEPTEMBER 19, 2014

ormer Peanut Corporation of America
wner Stewart Parnell, his brother and
ne-time peanut broker, Michael Parnell, and
Mary Wilkerson, former quality control
anager at the company's Blakely, GA, plant,
ere all found guilty today by a federal jury in
lbany, GA.

entencing will come later. Announcement of
he jury verdicts brought an emotional
utburst from the two Parnell families, while
tewart Parnell, age 60, simply put his head
own.

arnell, former chief executive of the now-defunct company with plants in three states producing peanu
nd peanut paste used for its own products and as an ingredient in almost 4,000 others, was convicted b
2-member jury for his role in a deadly Salmonella outbreak that began almost six years ago.

he government accused Parnell, his brother, and the quality control manager of a mammoth conspiracy
nvolved fraud, wire fraud, obstruction of justice, and knowingly introducing both adulterated and misbr



Food enters commerce

Source of contamination identified from few cases

Multistate Outbreak of *Salmonella* Braenderup Infections Linked to Nut Butter Manufactured by nSpired Natural Foods, Inc. (Final Update)

Posted October 16, 2014 4:30 PM ET

This outbreak investigation is over. However, the recalled nut butter products have a long shelf life and may still be in people's homes. Consumers unaware of the recall could continue to eat the products and potentially get sick. Read the **Advice to Consumers**.

Highlights

- **Read the Advice to Consumers »**
- This outbreak investigation is over. However, the recalled nut butter products have a long shelf life and may still be in people's homes. Consumers unaware of the recall could continue to eat the products and potentially get sick.

At a Glance:

- **Case Count: 6**
- **States: 5**
- **Deaths: 0**
- **Hospitalizations: 1**
- **Recall: Yes**

3 Environmental Positive Samples by FDA in 2/2014
2 Environmental Positive Samples by FDA in 7/2014

6 Clinical isolates (5 States)