HL7’s 29th Annual Plenary Meeting
October 5, 2015 / 8:30 am – 12:30 pm

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FDA Chief Health Informatics Officer

@DrTaha_FDA

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openFDA lowers the barrier of entry for researchers and software developers of consumer and enterprise applications who want to use FDA’s publicly available data.
OpenFDA promotes data sharing, data access, and transparency in our regulatory and safety processes, and spurs innovative ideas for promoting public health.

http://open.fda.gov | open@fda.hhs.gov | @openfda
What is openFDA?

- Consumer-Focused Apps
- Open Data
- Open Source
- Open Community
What is openFDA?

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

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

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

http://open.fda.gov | open@fda.hhs.gov | @openfda
Most are difficult to use at scale required by business and science.
With openFDA

http://open.fda.gov | open@fda.hhs.gov | @openfda
Open Community Resources

http://open.fda.gov | open@fda.hhs.gov | @openfda
Open Community Resources

continuing our commitment to openness, new open source API code released on @github github.com/fda/openfda

FDA/openfda
openfda - openFDA is a research project to provide open APIs, raw data downloads, documentation and examples, and a developer community for an important collection of FDA public ...
github.com

FDA
Food and Drug Administration
The official GitHub page for the US Food and Drug Administration. Privacy Policy @ http://www.fda.gov/privacy

http://open.fda.gov | open@fda.hhs.gov | @openfda
<table>
<thead>
<tr>
<th>Product</th>
<th>Data</th>
<th>Timeframe</th>
<th># of records</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>Labeling</td>
<td>Current</td>
<td>67K</td>
</tr>
<tr>
<td></td>
<td>Adverse event reports</td>
<td>Since 2003</td>
<td>4.9M</td>
</tr>
<tr>
<td></td>
<td>Recalls</td>
<td>Since 2012</td>
<td>4K</td>
</tr>
<tr>
<td>Medical device</td>
<td>Classification</td>
<td>Current</td>
<td>6K</td>
</tr>
<tr>
<td></td>
<td>Registration &amp; Listing</td>
<td>Current</td>
<td>24K establishments &gt;100K devices</td>
</tr>
<tr>
<td></td>
<td>510(k)s (including de novos)</td>
<td>Since 1976</td>
<td>141K</td>
</tr>
<tr>
<td></td>
<td>PMAs (including supplements)</td>
<td>Since 1977</td>
<td>30K</td>
</tr>
<tr>
<td></td>
<td>Adverse event reports</td>
<td>Since 1991</td>
<td>4.2M</td>
</tr>
<tr>
<td></td>
<td>Recalls</td>
<td>Since 2002</td>
<td>9.5K</td>
</tr>
<tr>
<td>Food</td>
<td>Recalls</td>
<td>Since 2012</td>
<td>8.5K</td>
</tr>
</tbody>
</table>

#s as of October 2015
Welcome to openFDA!

There are a few things we need to make sure you’re aware of before you begin experimenting with the API and associated data.

⚠️ This API is not for clinical or production use. While we make every effort to ensure that data is validated, please assume all results are unvalidated. The openFDA API is Public Domain and registered in the Public Domain Dedication and License, Commons CC0.

⚠️ This API is in beta. Do not assume the data is accurate or complete. As we continue work, we may need to rework queries, or move to a new URL. You will see this message once a week throughout beta.

The openFDA team

Terms of Service

Last modified: May 22, 2014

The U.S. Food and Drug Administration ("FDA") offers some of its public data in machine-readable format through openFDA, a service located at https://open.fda.gov. Use of the data made available via openFDA is generally unrestricted (see "Data Rights and Usage"). However, the service through which we make that data available is offered subject to your acceptance of the terms and conditions contained herein as well as any relevant sections of the FDA Website Policies.

Scope

The service ("openFDA") through which you may access FDA public data is subject to these terms. Use of openFDA constitutes acceptance to this Agreement.

http://open.fda.gov | open@fda.hhs.gov | @openfda
Step 1 – Register for an API Key

1. Get your API key
   - Email address
   - Get API key

   We require API keys above a certain number of requests to manage load on the system, promote equitable access, and prevent abuse.
   Signing up for an API key means you agree to our terms of service.

2. Learn the basics
   - OpenFDA may be different from other APIs you’ve seen. Here are two tips.
     - To search for individual records:
       ```
       search = field : term
       ```
     - To count the number of records matching the unique values of a field, combine search with:
       ```
       &count = field.exact
       ```

   The API has powerful features, including timeseries generation. Learn more on the openFDA API basics page.

3. Meet the data
   - Use this page’s interactive queries to learn the endpoint, and take advantage of the field-by-field reference.
   - Ask questions and give feedback where other developers can benefit from the discussion:
     - Ask questions on StackExchange (tag with openfda)
     - Log bugs or suggest improvements on GitHub

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<table>
<thead>
<tr>
<th>Authentication method</th>
<th>Per minute limit</th>
<th>Per day limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>No API Key</td>
<td>40 requests per minute (per IP Address)</td>
<td>1000 requests per day (per IP Address)</td>
</tr>
<tr>
<td>API Key</td>
<td>240 requests per minute (per key)</td>
<td>120000 requests per day (per key)</td>
</tr>
</tbody>
</table>

http://open.fda.gov | open@fda.hhs.gov | @openfda
Step 2 – Learn The APIs

API: Drug event

Search: records reported by the public

Count: Patient(s) reactions

Adverse drug event reports since 2004

This is the openFDA API endpoint for adverse drug events. An adverse event is submitted to the FDA to report any undesirable experience associated with the use of a drug, including serious drug side effects, product use errors, product quality problems, and therapeutic failures.

Reporting of adverse events by healthcare professionals and consumers is voluntary in the United States. Increases in the total number of adverse events are likely caused by improved reporting. News, enforcement actions, and other phenomena can also spur reporting.

What API query produced these results?

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

receivedate: [20040101+TO+20150101]+AND+missing_companyumb

count=receivedate
Step 2 – Learn The APIs

About
How records are organized
Data downloads

Anatomy of a response
Meta
Results

Field-by-field reference
Event
Source
Device
Identification
Use of device
Manufacturer
Patient
Report text
Reporter-dependent fields
By user facility/importer
Name and address
Suspect device manufacturer
By device manufacturer
Corrective or remedial action
Contact
By any manufacturer
Keys and flags

Devices API reference

Adverse events

Source

These fields describe the source and initial reporter of the adverse event report.

report_source_code

string

Source of the adverse event report. Possible values:

Manufacturer report
Voluntary report
User facility report
Distributor report

health_professional

string

Whether the initial reporter was a health professional (e.g. physician, pharmacist, nurse, etc.) or not.

Y = The initial reporter is a health professional.
N = The initial reporter is not a health professional.
Step 3 – Meet the Data

Query: URL

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

Results: Disclaimer

{},
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

ETL

Joins | Identifiers

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

http://open.fda.gov | open@fda.hhs.gov | @openfda
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.

```json
openfda:
  unii: [
    "75J73V1629"
  ],
  spl_id: [
    "86e3103c-9d8b-4693-b5db-3fd62330c754"
  ],
  product_ndc: [
    "0004-1963",
    "0004-1964"
  ],
  substance_name: [
    "CEFTRIAXONE SODIUM"
  ]
```
Harmonization – Adverse Events

Join key is NDA/ANDA (application number) and medicinal products
Harmonization – Enforcement Reports

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: 25675 The Old Road #138, Newhall, CA 91321. The dates of distribution are between June 2011 – Aug 2012 in the quantities mentioned above.
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.
Core technologies of any given openFDA API request

Core technologies for preparing and loading the data for the API

API Management
first EHR integration
bit.ly/1ndB3jf
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

<table>
<thead>
<tr>
<th># of Cases</th>
<th>% of Cases: Primary Drug</th>
<th>% of Cases: Serious</th>
</tr>
</thead>
<tbody>
<tr>
<td>27,717</td>
<td>37.1%</td>
<td>93.5%</td>
</tr>
</tbody>
</table>

Gabapentin Fair Price

The fair price for this drug is: $14

PER PRESCRIPTION

Research/Clinical Trials

The following research reports and clinical studies cover the latest findings on Gabapentin.

<table>
<thead>
<tr>
<th>Title</th>
<th>Journal</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy of gabapentin in migraine prophylaxis</td>
<td>Headache</td>
<td>2001 Feb</td>
</tr>
<tr>
<td>Pharmacologic management part 1: better-studied neuropathic pain diseases</td>
<td>Pain Med</td>
<td>2004 Mar</td>
</tr>
<tr>
<td>Survey of management of acquired nystagmus in the United Kingdom</td>
<td>Eye</td>
<td>2007 Sep</td>
</tr>
<tr>
<td>Gabapentin in bipolar disorder: a placebo-controlled trial of adjunctive therapy</td>
<td>Gabapentin Bipolar Disorder Study Group</td>
<td>Bipolar Disord</td>
</tr>
</tbody>
</table>

Data Sources

Data from Truven, Drugbank, DailyMED, openFDA, Medicare Part D (2011), Open Payments (2013) and other government/private data sources.
see how men & women get different drug side effects gendereDreactions.com - a @GenderMedKI and @TheThinkTrain project using @openFDA data

@emberjs web app created in 4 days in association with @GenderMedKI and @openFDA to showcase drug side effects.
gendereDreactions.com
demonstration apps

gsa requirement

Boxed warning

WARNING: RISK OF SERIOUS CARDIOVASCULAR and GASTROINTESTINAL EVENTS

- WARNING: CARDIOVASCULAR and GASTROINTESTINAL RISKS

- See full prescribing information for complete boxed warning.

Cardiovascular Risk • NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. (5.1) • Meloxicam is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (4.2, 5.1) Gastrointestinal Risk • NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events. (5.2) Cardiovascular Risk • Nonsteroidal anti-inflammatory drugs (NSAIDs) may cause an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk (see Warnings and Precautions (5.1)). • Meloxicam is...
An open source R library for interfacing directly with openFDA APIs has been adopted by the rOpenHealth project. 

[GitHub Link](github.com/ropenhealth/openfda)
Coming soon…

open.fda.gov/analytics

Developed in a few weeks by an FDA bioinformaticist:
Jonathan (Jay) Levine, PhD
A natural question is what types of adverse events have been reported for a particular drug? However, this could be rephrased as what types of adverse events were more often reported in the same reports as that particular drug.

a drug that is associated with a side effect may in fact not be causing the side effect.

Association ≠ Causation
... AGCATCGATGCAGAAGATTACAAGACGATCCGCTC ...
Genes

... AGCATCGATGCAGAAGATTACAAGACGATCCGCTC ...
We are all unique

AGCATCGATGCA
reference

AGCATCGATGCA
George

AGCATCGATGCA
Elaine

AGCATCGATGCA
Taha
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.
Benchmarking

Genotype

Location 9: C → G mutation
...

File with variants (VCF)

Predicted Outcome

"You are at risk for cystic fibrosis."

Report

Analytical Benchmark

Clinical Benchmark
What is precisionFDA?

A community platform for NGS assay evaluation, and regulatory science exploration

Website (precision.fda.gov)
Get invited, sign up, log in

* Regulatory Science is the science of developing tools, standards, and approaches to assess safety, efficacy, quality, and performance
July 2015
Start defining initial use case(s)

October 2015
APIs, Wiki, initial standard pipelines (e.g., GiaB), apps, and security

December 2015
Beta launch with initial use case(s)

March 2016
Hardened environment

September 2016
Public code-a-thon

Beta Release Timeline
Initial use cases

Assess **reproducibility** of a test

Assess **accuracy** using reference samples

Assess **agreement** with other methods

Assess test **performance** on synthetic data
Test Validation Summary Results

<table>
<thead>
<tr>
<th>Summary of Results</th>
<th>Precision</th>
<th>Recall</th>
<th>F-Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>99.28%</td>
<td>99.09%</td>
<td>99.18%</td>
</tr>
</tbody>
</table>

Your Variant

- NIST GiAB 2.19

Reference Variant

- GfVN Whole-Genome Test

Actions

Details
false positives
false negatives
Add New or Update Existing Results

- Update existing: GRVN / Whole-Genome Test
- Add new
- Compare vs. NIST / GiAB 2.19

OK
Apps

+ **Mapping**
  + BWA-MEM
  + ISAAC

+ **Variation Calling**
  + FreeBayes
  + ISAAC

+ **Simulation tools**
  + BAMSurgeon
  + ART
  + HIVE InSilico
Reference data

+ **VCFs**
  + NIST Genome-in-a-Bottle (NA12878)
  + Illumina Platinum Genomes (NA12877, NA12878)
  + Baylor Lupski Genome

+ **FASTQs**
  + Illumina Platinum Genomes (Pedigree 1463)
  + Garvan NA12878 (PCR-free, v2.5 X Ten flowcell)
  + Baylor Lupski Genome
Architecture

Website browsing

User's browser

API calls

Cloud

(Data, Permissions)

(Data, Permissions)

(Metadata)

Preauth URLs for upload/download
The main goal is to build a strong \textit{(and self-correcting)} community…
Close-Beta Phase

Corporate 21

Government 9

Academia 6
Thank YOU!