precisionFDA
precision.FDA.gov

OVERVIEW

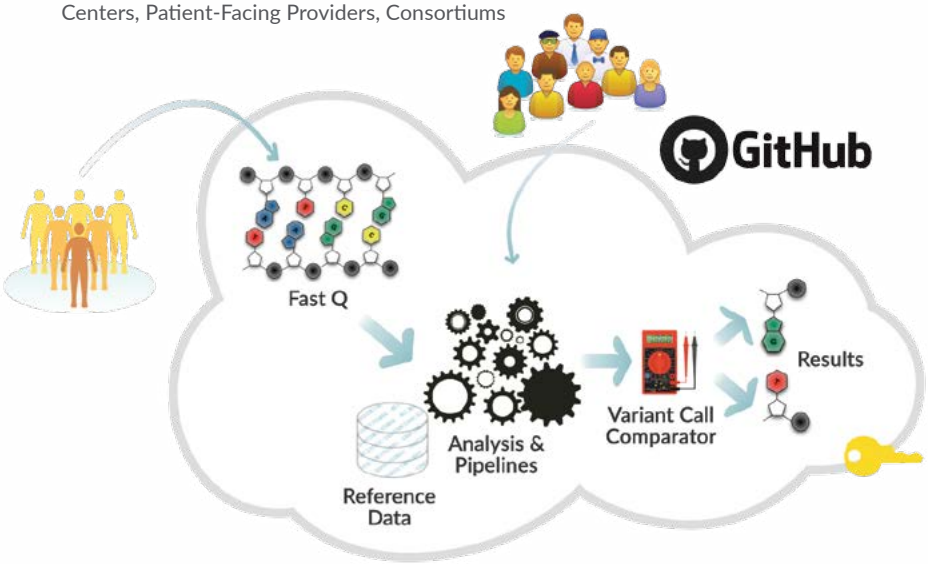
As part of the White House's Precision Medicine Initiative, the FDA took a new approach in advancing precision medicine by enabling a collaborative community and supporting informatics platform: precisionFDA.

As a crowd-sourced, cloud-based platform, precisionFDA provides an environment where the community can test, pilot, and benchmark new approaches to validating their next-generation sequencing (NGS) analysis pipelines. PrecisionFDA offers community members a secure and independent work area where, at their discretion, their bioinformatics tools or data can be kept private or shared with the precisionFDA participants.

VISION

The vision is to provide the genomics community with a cloud-based platform where participants can access and share datasets, analysis pipelines, and bioinformatics tools, in order to benchmark their approaches and advance regulatory science.

1. A workplace offering processing resources for development, testing, execution, and sharing of genomic analysis pipelines and data.
2. A comparison framework to compare the variant call results of NGS analysis workflows.
3. A community created around open source NGS analysis pipelines, related tools and reference data to crowdsource these and make more usable for clinical purposes.



SUMMARY

MISSION
Develop a crowd-sourced, cloud-based platform to advance regulatory science around NGS-based analytic tools and datasets.

WEBSITE
precision.fda.gov

CHALLENGE
Determine the best, currently available, approach to assessing the accuracy & reproducibility of NGS analytic pipelines.

SOLUTION
WORKPLACE to run analysis tools & access reference data.

COMPARISON framework to compare results.

COMMUNITY to publish & share datasets, tools & techniques.

COMMUNITY MEMBERS
NGS-based test providers

Standards-making bodies

Pharmaceutical & Biotechnology Companies

Healthcare providers

Academic medical centers

Research consortia

COMMUNITY APPLICATIONS
Call comparator

Read mapping and variant calling pipelines

Synthetic dataset simulators

REFERENCE DATASETS
Integrated callsets from NIST/Genome-in-a-Bottle and Platinum Genomes

Sequencing data from selected samples (NA12878, CHM1, etc.)

Security and Privacy
HIPAA/HITECH, CAP, ISO27001
Uniquely identified and immutable data
Version-controlled applications

ANALYTIC BENCHMARKING

PrecisionFDA is designed to provide test developers with flexible methods for independently evaluating the accuracy and reproducibility of NGS analysis workflows and diagnostic tests. Simplified example models presented below:

Reproducibility (Example at the VCF level)

Is the variant calling file (VCF) result reproducible? PrecisionFDA allows researchers to run multiple analyses on the same sample and compare the results (VCFs).

Accuracy

Does the VCF result contain errors? Researchers are able to run their tests on a reference sample (e.g. NA12878 NIST/GIAB*) where ground truth is known, and compare the result to the reference result to determine sensitivity (TP / (TP+FN)), positive predictive value (TP / (TP+FP)), and generate a ROC-curve.

Location 9: C → G mutation
Location 15: A → C mutation
...

File with variants (VCF)

Test results said...	But the patient in reality had...	Classification
Location 9: C → G mutation	(nothing)	Type I Error (False Positive)
(nothing)	Location 13: G → T mutation	Type II Error (False Negative)
Location 15: A → C mutation	Location 15: A → C mutation	Correct (True Positive)

*www.nist.gov | www.genomeinabottle.org

"PrecisionFDA is a new platform for evaluating bioinformatics workflows and is an integral part of the FDA's work in building a strong community contributing to a standards-based approach for ensuring the accuracy of genetic tests incorporating NGS-based technologies."

Taha A. Kass-Hout, MD, MS, Chief Health Informatics Officer, FDA

Result Classification

REFERENCE SAMPLE USE CASE

A researcher would use a widely accepted reference sample, such as NA12878, as part of the assessment of the genetic test. The resultant VCF would be compared to the ground truth reference VCF provided by the NIST/GIAB Consortium.