FDA Overview on Next Generation Sequencing (NGS) Testing

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Overview

- Regulatory Issues
- FDA Goals
- Current Guidance Documents
Regulatory Issues

- NGS tests often lack a specific intended use
  - Can’t predefine the results that will be obtained
  - Often don’t know the disease that will be diagnosed until the test is performed
  - Incidental findings
- Traditional requirements for review
  - Review each claim
  - Review modifications that affect the safety and effectiveness of a test
- *Differences in data volume and interpretation may warrant a new regulatory approach* that will ensure that patients and providers are able to make treatment decisions based on accurate test results
- Need to ensure that the information that patients receive from NGS tests is accurate and relevant to their condition (analytically and clinically valid)
FDA’s Goals

Optimize regulatory oversight of NGS tests to:

• Help to ensure the accuracy of genetic tests
• Develop approach suited to unique nature of NGS tests
• Adapt regulatory processes to encourage innovation while helping to ensure safety and effectiveness

Released two draft guidances for public comment in July 2016, finalized in April 2018
Purpose of the Guidances

• Anticipate and support the needs of rapidly-evolving NGS technologies
• Support reliable, accurate and understandable tests results
• Promote an efficient path to market for all test developers
  - Encourage the development and implementation of standards to assure test quality
  - Describe a regulatory pathway for NGS-based tests for certain uses
  - Recognize genetic databases for evidence on the clinical relevance of genetic variations
  - Based on open processes and accessibility
Guidance #1

Considerations for Design, Development, and Analytical Validation of Next Generation Sequencing (NGS) – Based In Vitro Diagnostics (IVDs) Intended to Aid in the Diagnosis of Suspected Germline Diseases

Analytical Standards Guidance

Recommendations

• Design
  - Indications for use
  - User needs
  - Components and methods
    - Understand and document technical limitations of NGS-based tests

• Performance characteristics and test quality metrics
  - Accuracy, precision
  - Read depth, completeness, performance thresholds

• Test Reports

Benefits

• Combines design and performance standard approaches
• Accommodates different test designs
• Can form the basis for future FDA-recognized standard(s) and/or special controls
Use of Public Human Genetic Variant Databases to Support Clinical Validity for Genetic and Genomic-Based In Vitro Diagnostics

Genetic Databases Guidance

- Recommendations for administrators of databases to demonstrate that the database can be considered a source of “valid scientific evidence”
- **Voluntary** database recognition pathway (similar to standards recognition)
- Evidence from databases could support the clinical validity of NGS-based tests
Benefits of Using Data from Genetic Databases

• Evidence generated by multiple parties

• Aggregated data provide a stronger evidence base (the current state of scientific knowledge)

• As clinical evidence improves, new interpretations could be supported
Guidances: Summary

- The approaches outlined in the FDA guidance documents are intended to:
  - Incentivize innovation
  - Assure the quality and reliability of NGS-based tests
  - Promote their adoption into clinical practice
  - Improve patient care
  - Advance precision medicine
Thank You