Welcome to Today's FDA/CDRH Webinar

Thank you for your patience while we register all of today's participants.

If you have not connected to the audio portion of the webinar, please do so now:

Dial: 800-857-5170

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Conference Number: PW9346232

Next Generation Sequencing (NGS) Draft Guidances: Implications for Patients and Providers

David Litwack, Ph.D.
Laura Koontz, Ph.D.
Personalized Medicine Staff
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health
Food and Drug Administration

Objectives

- Provide context and an overview of the draft NGS guidances for patients and providers
- Discuss how the guidances would advance personalized medicine and improve patient care
- Provide background so that you can submit comments
- Answer your questions about the draft guidances

Agenda

- Introduction and background: FDA's role in the Precision Medicine Initiative
- Review analytical standards draft guidance
- Review genetic databases draft guidance
- Next steps
- Questions and answers

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White House Precision Medicine Initiative

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.

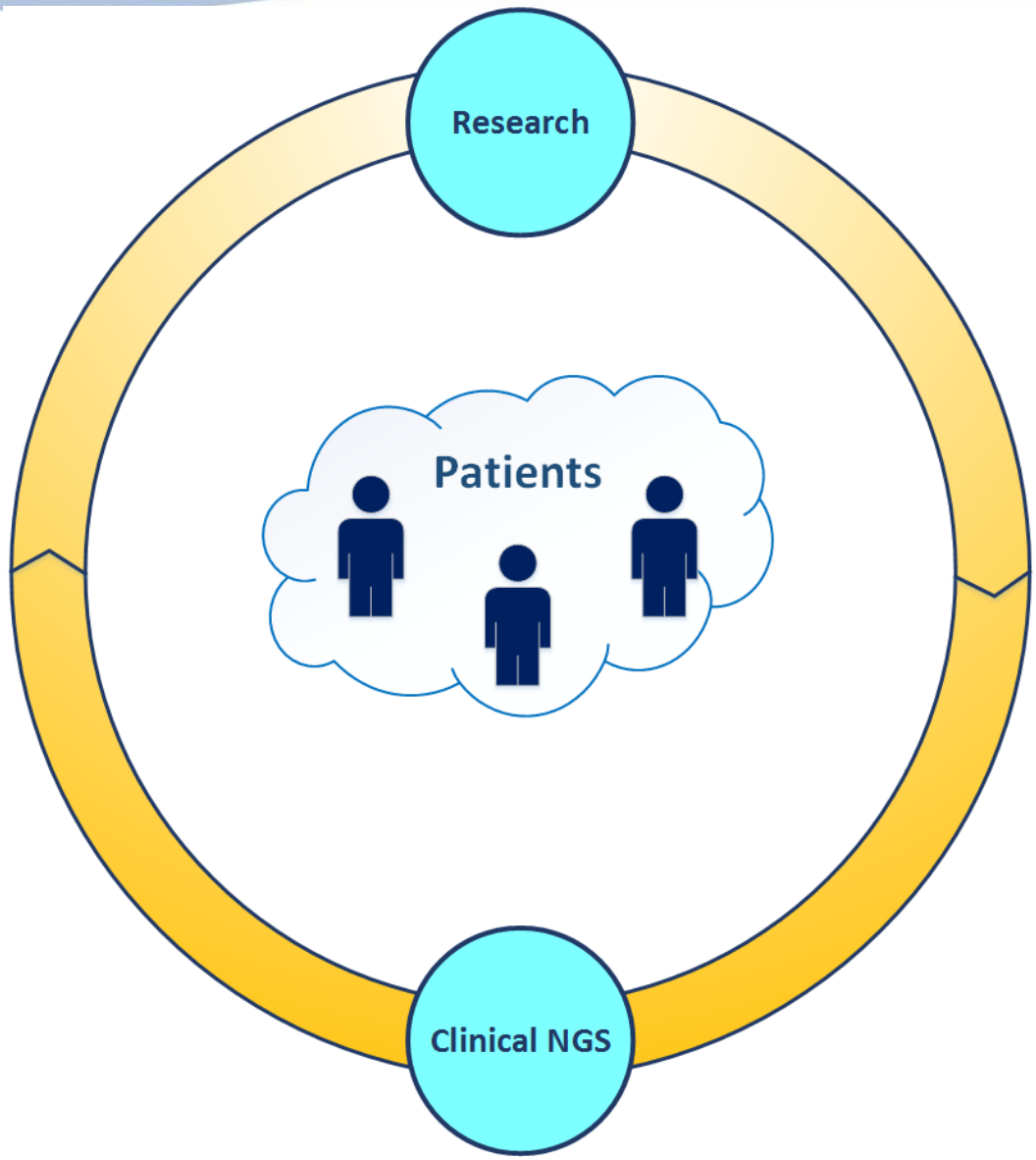
FDA's Role in PMI

Optimize regulatory oversight of Next Generation Sequencing tests

- 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

Purpose of the Draft 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


Research
Patients
Clinical NGS

Elements of FDA Premarket Review

- Analytical validity
  - Does the test correctly detect the analyte(s)?
  - How precise is the test?
  - What are limits of detection/measurement?
- Clinical validity
  - Does the test correctly identify the disease/condition?
  - What are the clinical sensitivity, specificity and predictive values?
  - Evidence must be scientifically valid
- Labeling
  - Are the directions clear? Is what you say about the test truthful and not misleading?
- Based on intended use of the test

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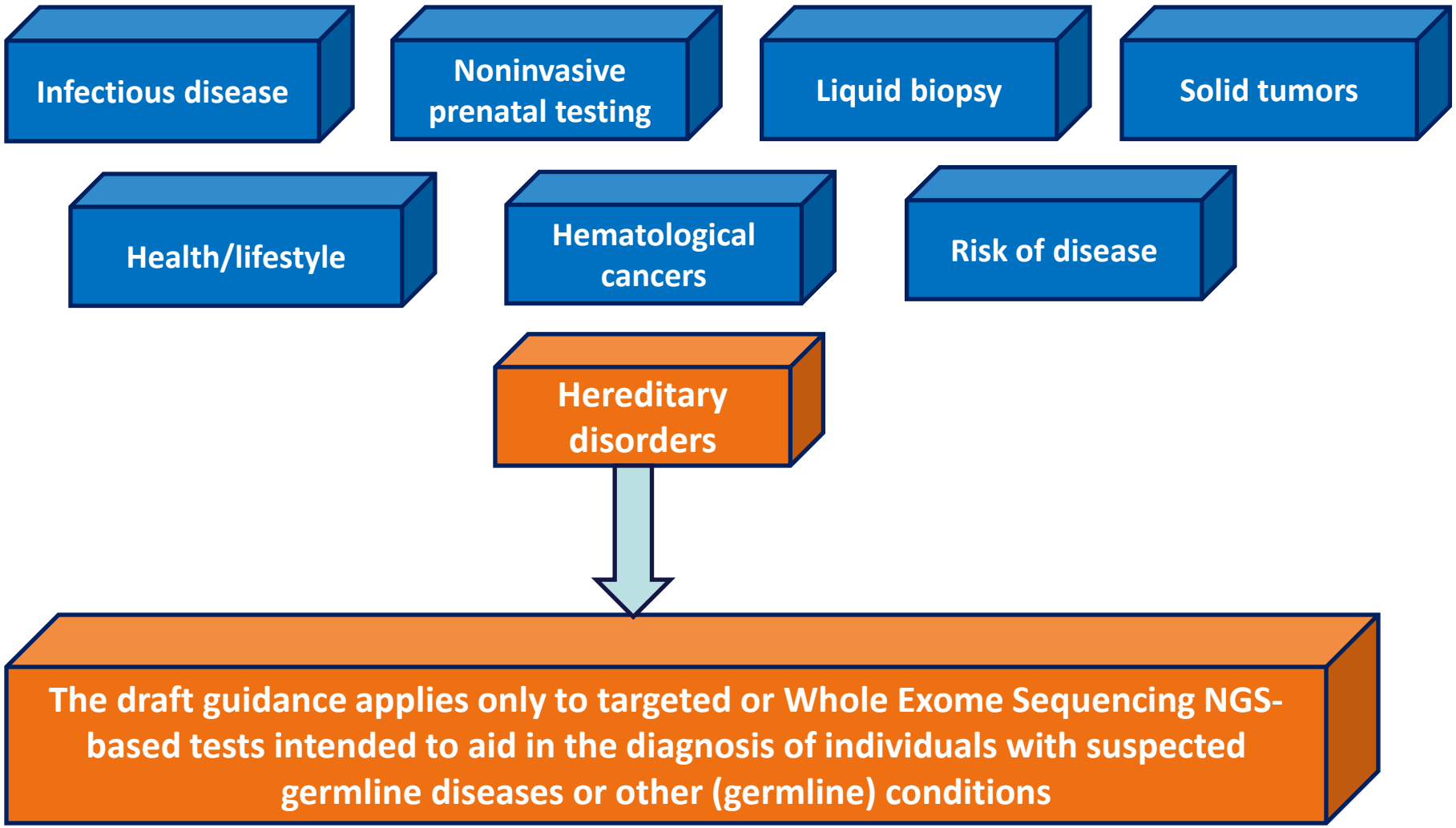
Use of Standards in FDA Regulatory Oversight of Next Generation Sequencing (NGS)-Based In Vitro Diagnostics (IVDs) Used for Diagnosing Germline Diseases

Diagnostic Tests in the Age of Precision Medicine

Conventional Diagnostics	NGS-Based Diagnostics
Number of analytes: one or a few	*Number of analytes:* undefined (could be millions)
Analytical validation: Review of the performance of each analyte for each test in premarket submissions	*Analytical validation:* Process-based approach to assure adequate performance over all possible analytes

Scope of the Analytical Standards Draft Guidance



Analytical Standards Draft 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

Analytical Standards Draft Guidance

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

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Use of Public Human Genetic Variant Databases to Support Clinical Validity for Next Generation Sequencing (NGS)-Based In Vitro Diagnostics

Diagnostic Tests in the Age of Precision Medicine

Conventional Diagnostics	NGS-Based Diagnostics
Number of analytes: usually one, maybe a few	*Number of analytes:* undefined (could be millions)
Evidence source used for premarket submissions: Sponsor led clinical studies	*Evidence source used for premarket submissions:* Need for crowd-sourced data

Harnessing the Power of Public Genetic Variant Databases

Harnessing the Power of Public Genetic Variant Databases

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

Genetic Databases Draft 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

FDA Recognition of Genetic Databases

- Database administrator submits request for recognition (voluntary)
- FDA reviews database policies and procedures
- Recognized database periodically reviewed by FDA to maintain recognition

Use of Database Assertions from FDA-Recognized Genetic Databases

- Intended to ultimately allow for patients and providers to receive complete information, based upon valid scientific evidence
- Assertions (statements) about a variant can include descriptors such as responder, non-responder, pathogenic, benign, likely pathogenic, likely benign and variant of unknown significance
- Assertions that a particular genotype-phenotype association is clinically valid should generally involve multiple lines of evidence and should identify a primary source of scientific evidence

Summary

- This guidance would help to enable patients and providers to receive results about a variety of genetic variants, provided they are supported by adequate evidence within the database
- These guidances are intended to incentivize innovation, assure the quality and reliability of NGS-based tests and promote adoption of NGS-based tests into clinical practice
- This approach is intended to improve patient care and advance precision medicine

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Next Steps

- Public discussion of draft guidances
  - 90 day open comment period
  - Upcoming public workshop
- FDA analysis of public input and incorporation of appropriate revisions into final guidances
- Publication of final guidances
- Long term: potentially expand to additional intended uses of NGS tests

Please Submit Comments

- Analytical standards draft guidance
  - https://www.regulations.gov/docket?D=FDA-2016-D-1270
- Federal Register notice
  - https://www.federalregister.gov/articles/2016/07/08/2016-16201/guidance-for-industry-use-of-standards-in-the-food-and-drug-administrations-regulatory-oversight-of
- Databases draft guidance
  - https://www.regulations.gov/docket?D=FDA-2016-D-1233
- Federal Register notice
  - https://www.federalregister.gov/articles/2016/07/08/2016-16200/use-of-public-human-genetic-variant-databases-to-support-clinical-validity-for-next-generation

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Questions?

Email us at: PMI@fda.hhs.gov
FDA Precision Medicine Web site:
http://www.fda.gov/ScienceResearch/SpecialTopics/PrecisionMedicine/default.htm

Slide Presentation, Transcript and Webinar Recording will be available at:

http://www.fda.gov/training/cdrhlearn

Under the heading “In Vitro Diagnostics (IVD)"