Recent Initiatives in Precision Medicine

PMC Policy Committee Meeting
February 20, 2018

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CDRH/OIR

Agenda

- Oncopanels
- 2018 Priorities in Precision Medicine
  - NGS Guidances
  - Codevelopment Guidance
  - Investigational IVDs
- CDRH Strategic Priorities

Oncopanels

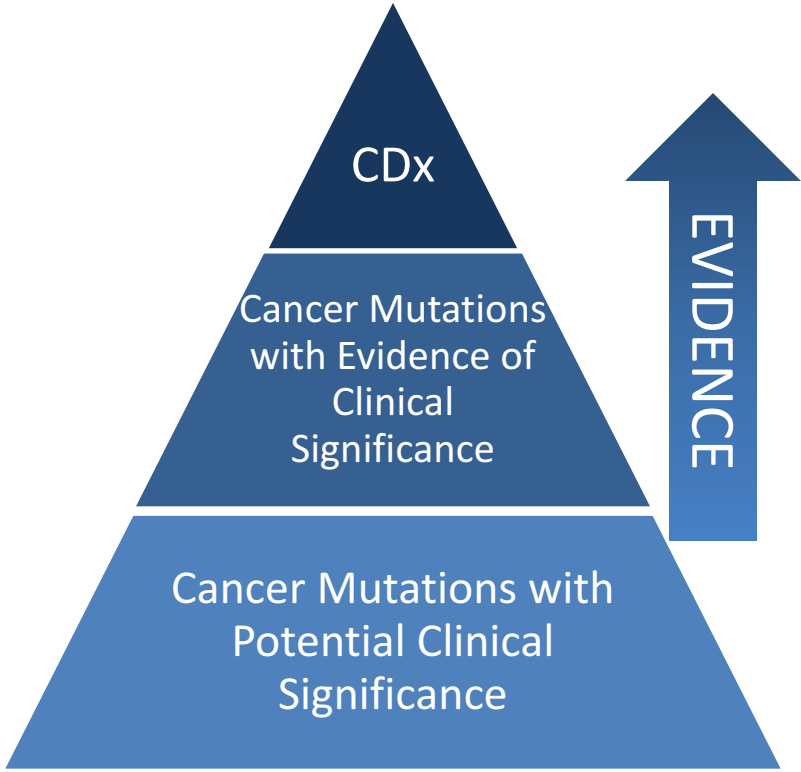
- 3 key authorizations in 2017
  - ThermoFisher's OncoMine Target Test Dx
    - Lung cancer panel
    - 3 CDx claims
    - 23 genes
  - MSK-IMPACT
    - Solid tumor panel
    - 468 genes + MSI
    - De Novo set up Class II pathway, potential 3rd party review
  - Foundation Medicine's F1CDx
    - Solid tumor panel
    - 15 CDx claims in 5 cancer types
    - 324 genes + MSI, TMB

Three Tiered Approach for Reporting Biomarkers in Oncopanels

Level 1 companion diagnostics: AV for each biomarker; CV established by clinical study or clinical concordance with a previous CDx

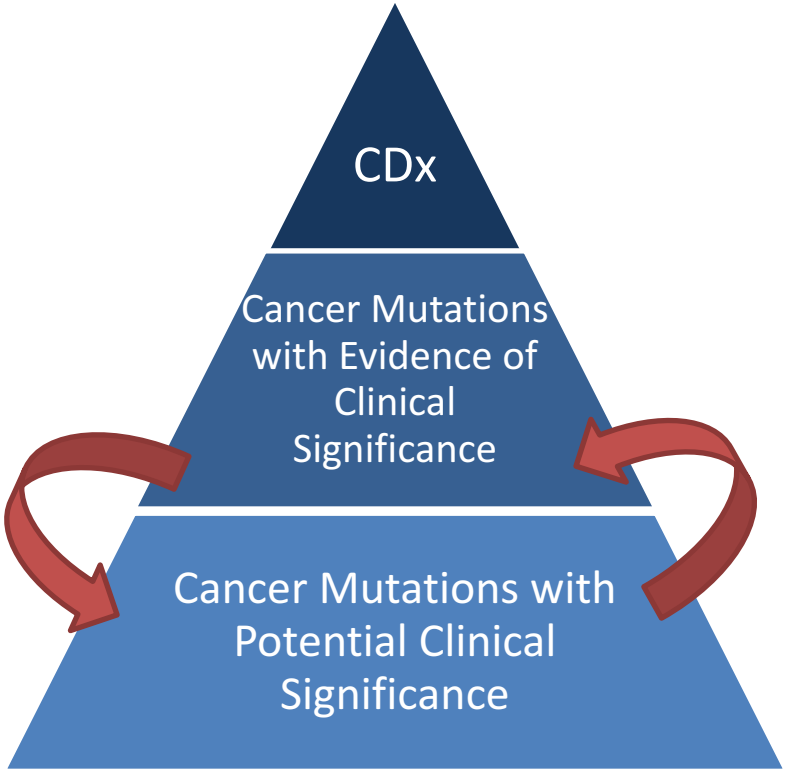
Level 2 biomarkers: AV either per biomarker or representative; CV established in professional guidelines, but **NOT** demonstrated with the test.

Level 3 biomarkers: AV by representative approach; CV validity not demonstrated either in professional guidelines or with the test, but suggestive based on clinical/biological evidence.



A Fluid Approach to Reporting within Levels 2 and 3

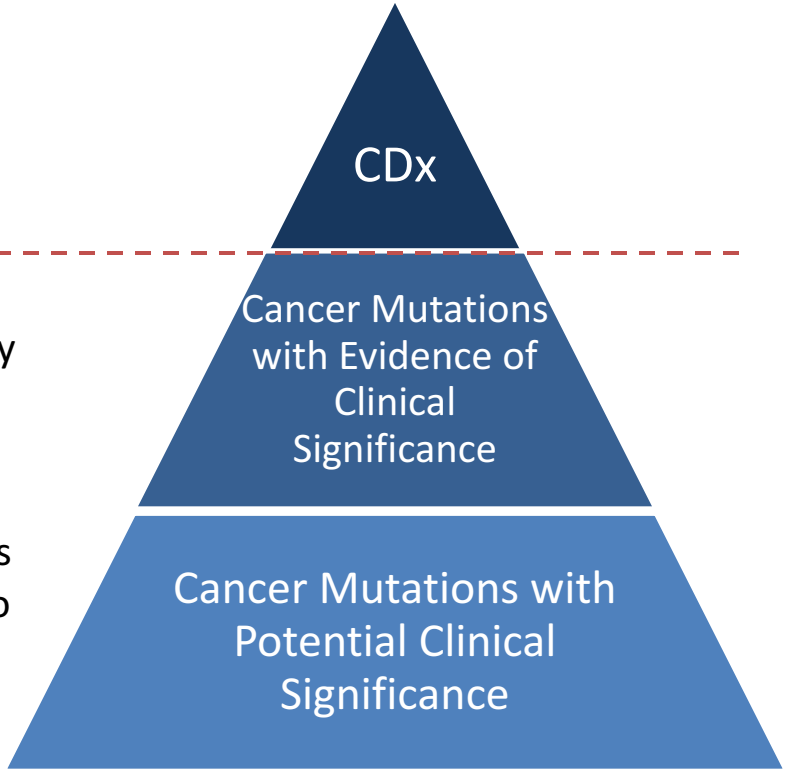
- Clinical evidence regarding mutations accumulates rapidly and may differ based on tumor type.
- Test developers need flexibility in how they report mutations.
- As clinical evidence develops, can move mutations from level 3 to level 2 provided the AV of the test reviewed and established via a submission



Pathways for FDA Clearance or Approval

- Premarket Application (FDA):
  - Appropriate for oncopanels with companion diagnostic claims
  - Can also make Level 2/3 claims

- 510(k) Pathway (FDA or 3rd Party):
  - For tumor profiling tests making Level 2/3 claims only
  - Can choose to submit 510(k) to FDA directly or elect to use an accredited FDA third-party reviewer (e.g., NYSDOH)
  - Test developers that want to submit their oncopanels for federal clearance through NYSDOH can request to have their NYSDOH package and review memo forwarded along to FDA
  - For 3rd party review, FDA has 30 days to make a determination follow receipt of package
  - For direct submission, FDA has 90 days to make determination



2018 Priorities in PM

Finalization of NGS Guidances

- July 2016 – Two draft guidances published:
  - "Use of Public Human Genetic Variant Databases to Support Clinical Validity for Next Generation Sequencing (NGS)-Based In Vitro Diagnostics"
  - "Use of Standards in FDA Regulatory Oversight of Next Generation Sequencing (NGS)-Based *In Vitro* Diagnostics (IVDs) Used for Diagnosing Germline Diseases"

2018 Priorities in PM

Finalization of NGS Guidances

Database Guidance overview:

- Scope: publicly accessible databases of genetic variants
- 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

2018 Priorities in PM

Finalization of NGS Guidances

Analytical Guidance overview:

- Scope: germline WES or panels
- Makes a series of technical recommendations for how NGS-test developers can design and validate their tests
- Accommodates different test designs, components, indications, etc.
- Can form the basis for future FDA-recognized standard(s) and/or special controls
- Discusses potential for an expedited path to market for tests that meet these standards

2018 Priorities in PM

Finalization of NGS Guidances

- Database Guidance
  - 261 public comments from 38 organizations and individuals.
  - Commenters were generally supportive
  - Requests to expand the scope:
  - Clarify what is meant by “publicly accessible”
  - Discuss how proprietary databases can leverage this guidance document
- Analytical Guidance
  - 350 public comments from 38 organizations and individuals
  - Commenters were generally supportive
  - Requests for clarification on technical recommendations
  - Request to remove specific thresholds for analytical performance

2018 Priorities in PM

Finalization of Codevelopment Guidance

- GOAL: to support obtaining contemporaneous marketing authorization
- July 2016: "Principles for Codevelopment of an In Vitro Companion Diagnostic Device with a Therapeutic Product" draft guidance published
- Intended to be a "How To" for Codevelopment
  - described points to consider in both therapeutic and diagnostic development programs
  - described FDA preferences for certain elements
  - does not prescribe any particular development pathway

2018 Priorities in PM

Finalization of Codevelopment Guidance

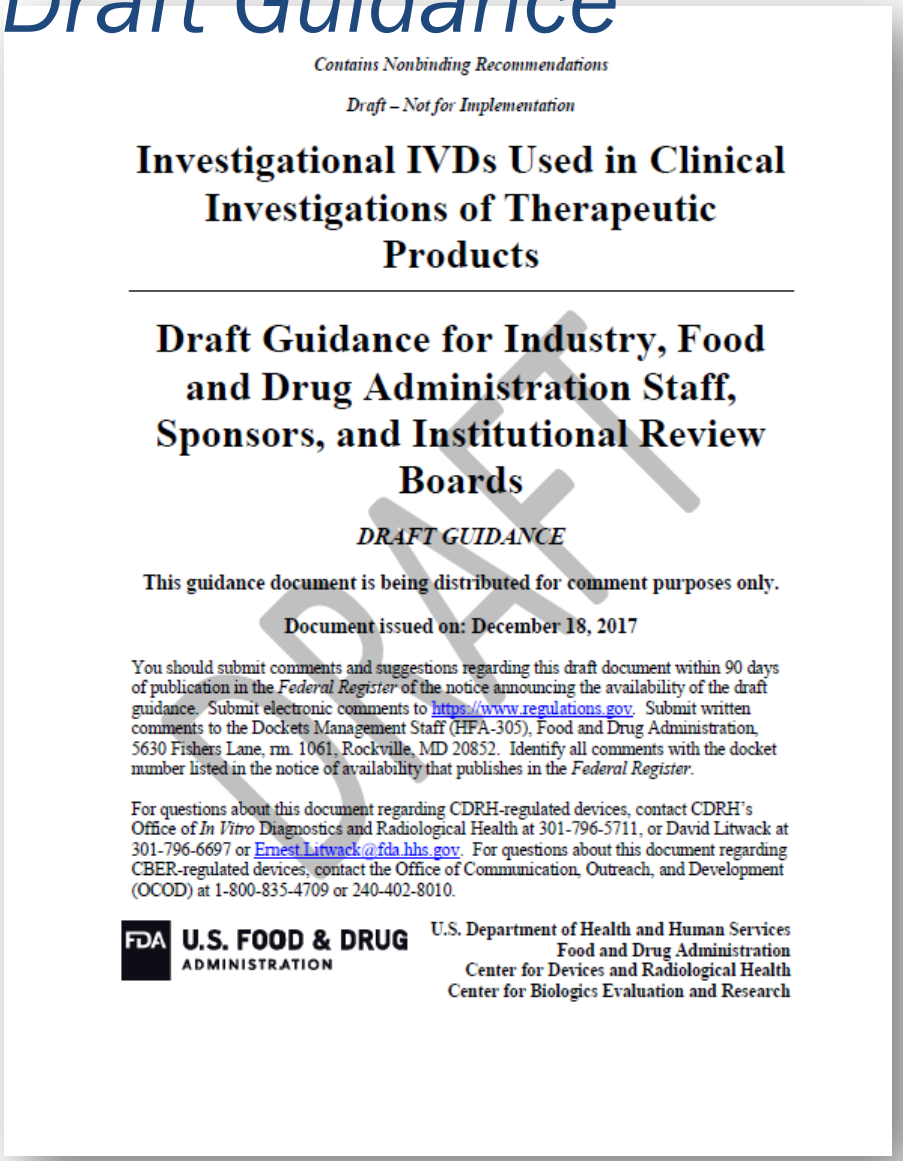
- 290 Comments received from 13 organizations
- Overarching themes:
  - Provide information regarding complementary diagnostics
  - Additional details requested on various validation strategies, trial designs, labeling, follow on CDx, etc.
  - Request for guidance on investigational IVDs
  - Request for better coordination between Centers
  - Requests for clarification on terminology, etc

2018 Priorities in PM

Investigational IVDs Draft Guidance

- Clarifies that IVDs used in clinical investigations are subject to the IDE regulation.
- Assists sponsors and IRBs in determining the risks of the use of an investigational IVD.
- Defines the responsibilities of sponsors and IRBs in complying with the IDE regulations
- Provides FDA's recommendations and requirements for submitting an IDE application, when required.

Comment period closes on March 19, 2018



Contains Nonbinding Recommendations

Draft – Not for Implementation

Investigational IVDs Used in Clinical Investigations of Therapeutic Products

Draft Guidance for Industry, Food and Drug Administration Staff, Sponsors, and Institutional Review Boards

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Document issued on: December 18, 2017

You should submit comments and suggestions regarding this draft document within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions about this document regarding CDRH-regulated devices, contact CDRH's Office of *In Vitro* Diagnostics and Radiological Health at 301-796-5711, or David Litwack at 301-796-6697 or Ernest.Litwack@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

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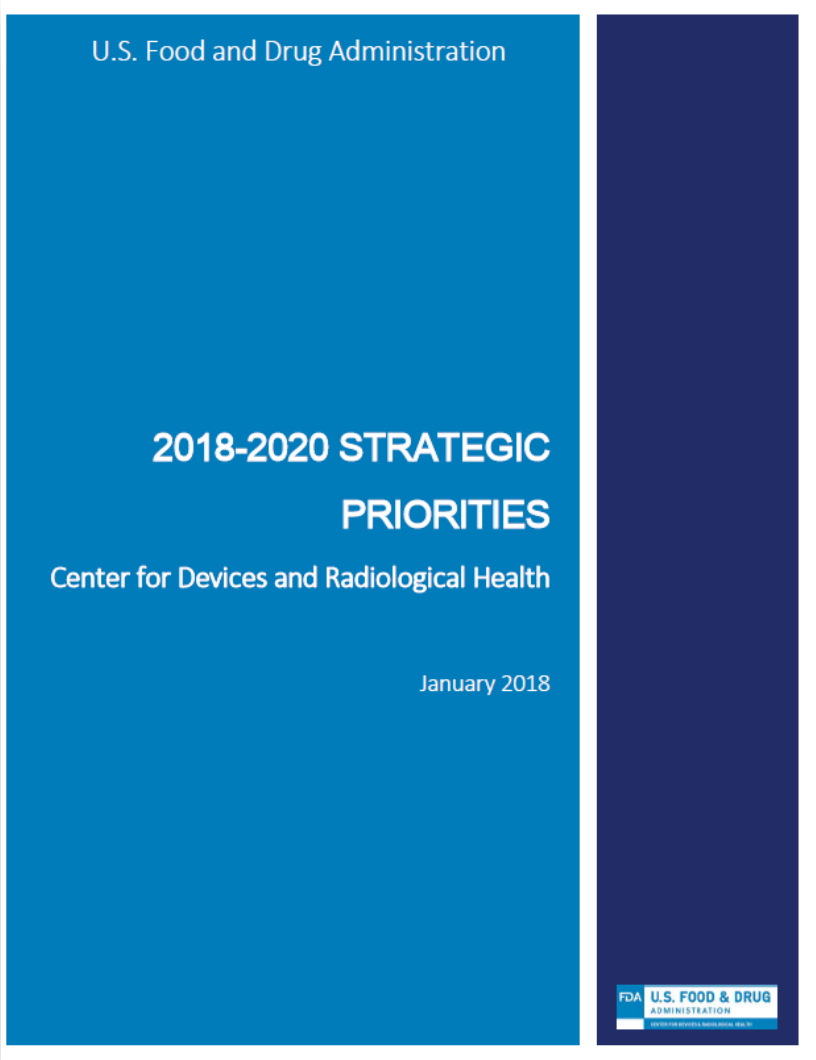
CDRH Strategic Priorities

1. Employee Engagement, Opportunity and Success
2. Simplicity
3. Collaborative Communities



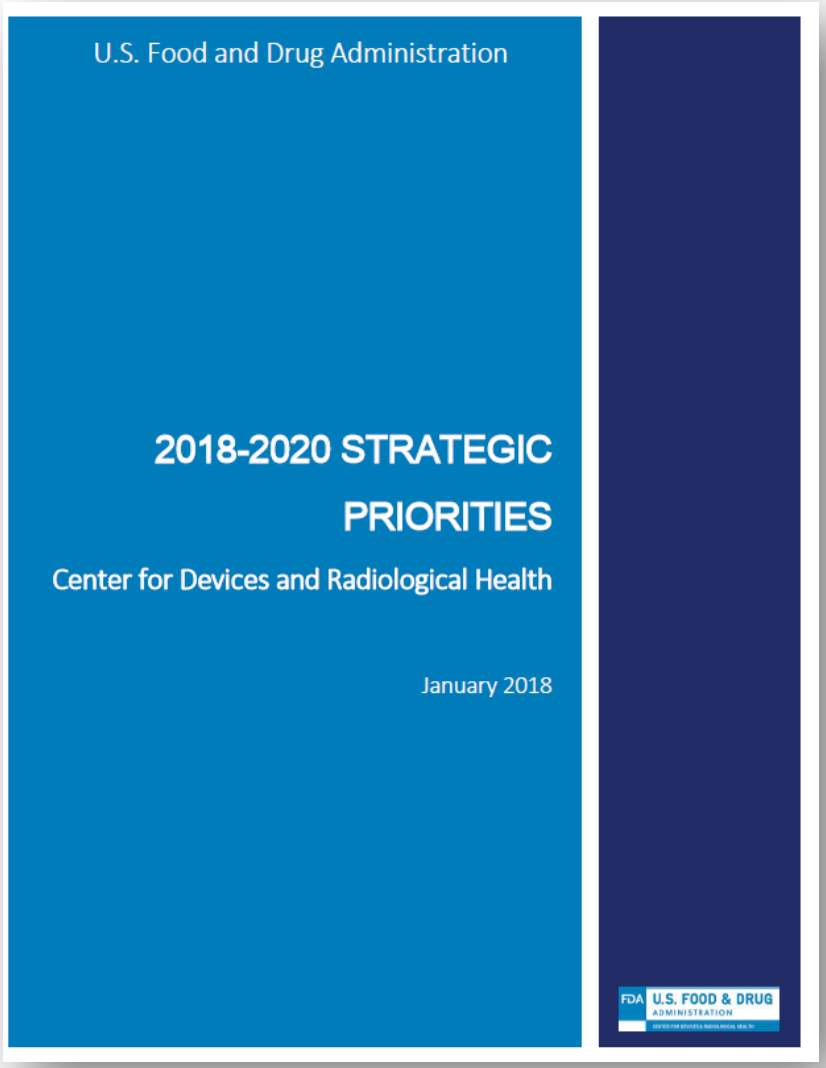
https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/UCM592693.pdf

CDRH Strategic Priorities

Collaborative Communities

The hallmark of a Collaborative Community is a continuing forum where public and private sector members proactively work together to solve both shared problems and problems unique to other members in an environment of trust and openness, where participants feel safe and respected to communicate their concerns.

- Goal to create 10 new Collaborative Communities by 2020.



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Questions?

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