

FDA Update

Tim Stenzel, MD, PhD
Director

Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health
U.S. Food and Drug Administration

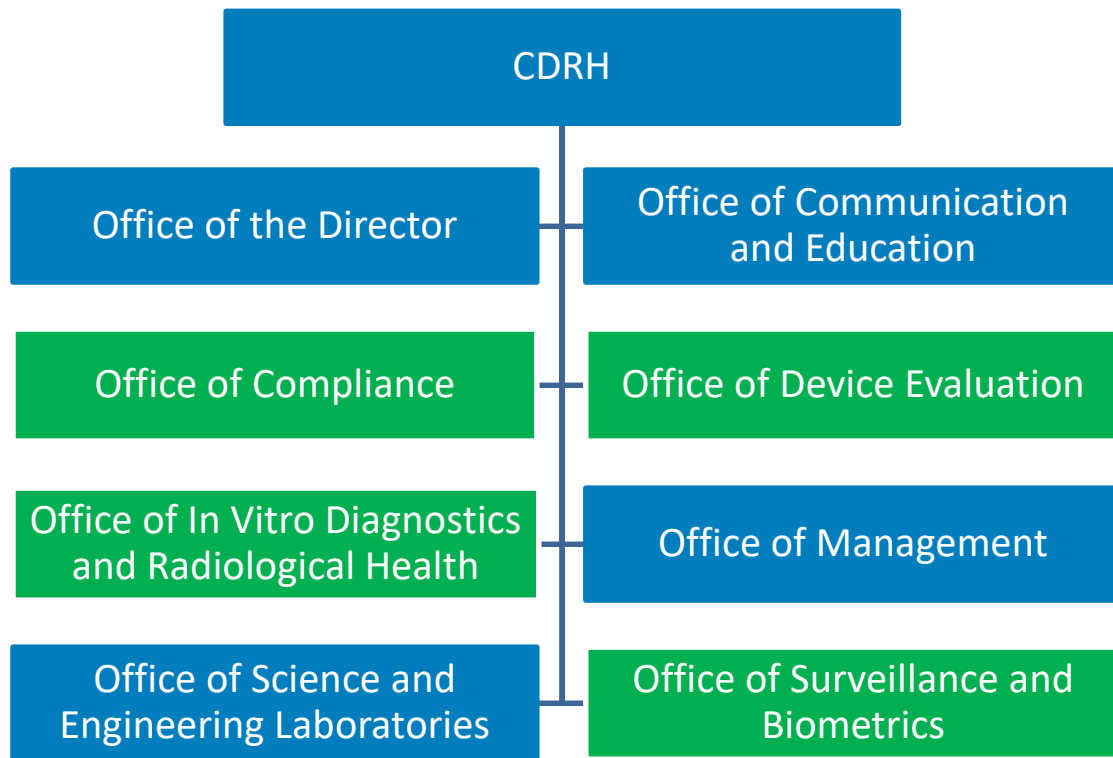
Today's Agenda:

- CDRH TPLC Reorganization & Staffing Changes
- Final Guidance Update
- Draft Guidance Update
- Breakthrough program is taking off
- CLIA Waiver Program improvements continue
- Current, Immediate, and Long-term priorities

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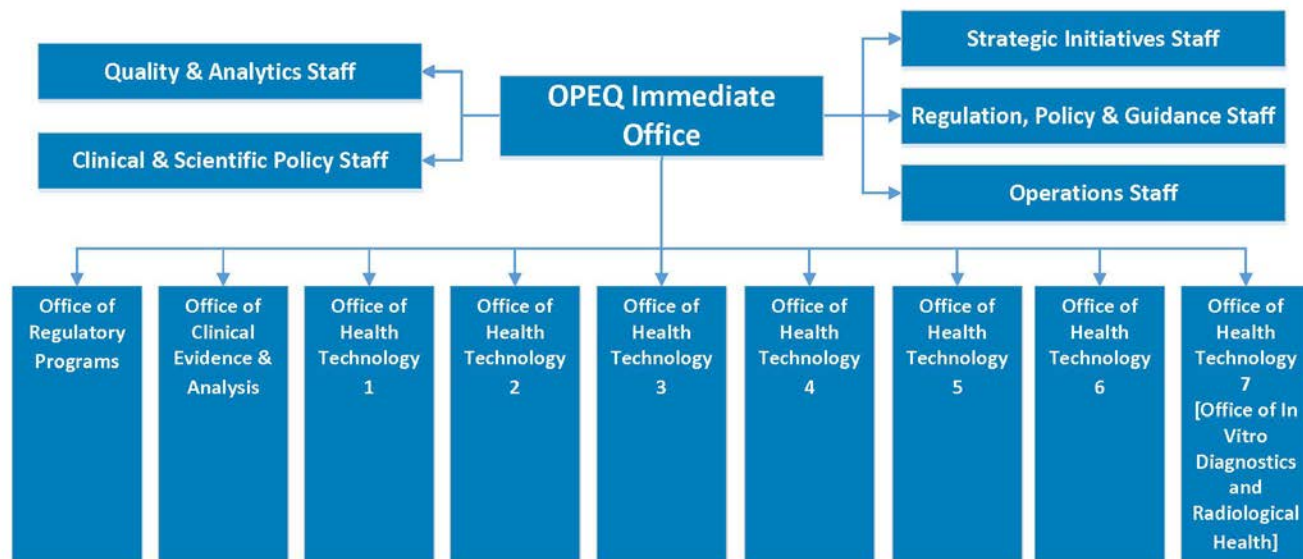
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CDRH is reorganizing to support a Total Product Life Cycle (TPLC) approach

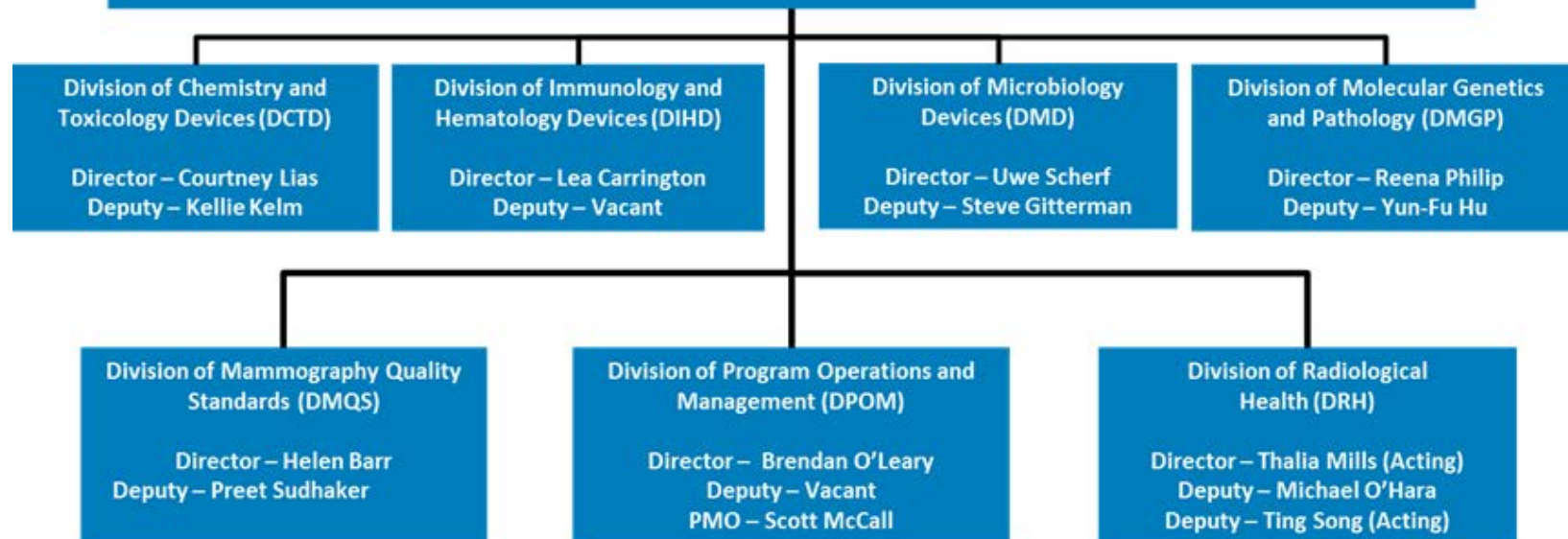


Future TPLC Super Office Design:

Office of Product Evaluation and Quality (OPEQ)



Director	Timothy Stenzel
Deputy Dir. for New Product Evaluation	Donald St. Pierre
Deputy Dir. for Patient Safety and Product Quality	Scott Gonzalez (Acting)
Deputy Dir. for Personalized Medicine	Stayce Beck (Acting)
Deputy Dir. for Radiological Health	Robert Ochs
Associate Dir. for Programs and Performance	Elizabeth Hillebrenner
Associate Dir. for Strategic Initiatives	Toby Lowe (Acting)
Associate Dir. for Regulatory Counsel	Scott McFarland
Chief Medical Officer	Vacant
Chief Medical Officer for Radiological Health	Donald L. Miller



OIR by the numbers: We're proud of our talented, well-educated, and professional staff

About **290** Scientists & Engineers

>20 MDs

>150 PhDs

>40 Masters

CDRH by the numbers:

>90%

external customer
satisfaction rating

100%

of MDUFA 4 FDA-Days
Goals Met

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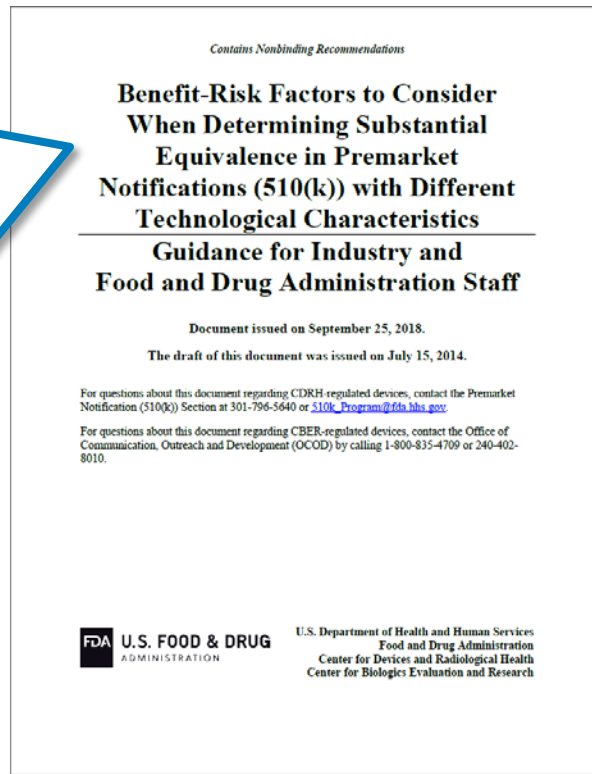
Final Guidances advance novel and risk-based regulatory approaches

- 1 Benefit-Risk for 510(k)
- 2 Voluntary Consensus Standards
- 3 LOINC Codes
- 4 NGS design, development and analytical validity
- 5 Genetic Variant Databases as sources of clinical evidence

New Benefit-Risk guidance has recommendations for diagnostics

For diagnostic devices specifically, benefit(s) in reference to the nature of the public health impact, could be based on a number of factors including:

- Identification of a specific disease;
- Provision of diagnosis at different stages of a disease;
- Prediction of future disease onset;
- Improvement of patient workflow;
- Increase in efficiency or examination;
- Provision of reproducible and quantifiable results contributing to the optimization of therapy and treatment; and
- Improvement of patient outcome (e.g., well-being, health status, safety of patients) by facilitating fewer missed diagnoses (or the right diagnosis the first time, hence the correct treatment plan) and/or identification of patients likely to respond to a given therapy and therefore enable treatment of the disease or reduce/prevent its spread, which can often be measured through the use of PROs.



FDA continues increased emphasis on standards, implementing *Cures* legislation

Contains Nonbinding Recommendations

Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices Guidance for Industry and Food and Drug Administration Staff

Document issued on September 14, 2018.

The draft of this document was issued on May 13, 2014.

This document supersedes "Guidance for Industry and FDA Staff; Recognition and Use of Consensus Standards," issued on September 17, 2007, "Frequently Asked Questions on Recognition of Consensus Standards," issued on September 17, 2007, and "Guidance for Industry and for FDA Staff: Use of Standards in Substantial Equivalence Determinations," issued on March 12, 2000.

For questions about this document regarding CDRH-regulated devices, contact the Office of the Center Director at 301-796-5900; or Scott Colburn at 301-796-6287 or by e-mail at scott.colburn@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.

"The use of consensus standards can increase predictability, streamline premarket review, provide clearer regulatory expectations, and facilitate market entry for safe and effective medical products."

We've clarified expectations for communicating LOINC codes for unapproved uses

- Upon receipt of an “...individual, unsolicited request...”
- “...where the manufacturer’s response provides the appropriate LOINC coding...”
- “FDA does not intend to consider that response as evidence of the firm’s intent that the product be used for unapproved or uncleared uses.”*

*** Read this guidance for full context.
It's only 8 pages long.**

Logical Observation Identifiers Names and Codes for *In Vitro* Diagnostic Tests

Guidance for Industry and Food and Drug Administration Staff

Document issued on June 15, 2018.

For questions about this document, contact the Digital Health Unit in the Office of the Center Director at (301) 796-6900 or email: DigitalHealth@fda.hhs.gov.



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

FDA believes innovative diagnostics merit innovative regulatory paradigms

Contains Nonbinding Recommendations

**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**

**Guidance for Stakeholders and
Food and Drug Administration Staff**

Document issued on April 13, 2018.

The draft of this document was issued on July 8, 2016.

For questions about this document concerning devices regulated by CDRH, contact Zivana Tezak at 301-796-6206 or Adam Berger at 240-402-1592 or by email at OIRPMGroup@fda.hhs.gov. For questions regarding this document as applied to devices regulated by CBER, contact the Office of Communication, Outreach and Development in CBER at 1-800-835-4709 or 240-402-8010 or by email at ocod@fda.hhs.gov.



U.S. Department of Health and Human Services
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“FDA’s vision is that NGS-based tests can be developed, validated, and offered for clinical use through a process that leverages appropriate standards, quality systems controls and community assessment of clinical validity to streamline the premarket review process.”

Genetic Variant Database Guidance advances innovative paradigm for showing clinical validity

“publicly accessible
databases of human genetic
variants can serve as sources
of valid scientific evidence to
support the clinical validity
of genotype-phenotype
relationships”

Use of Public Human Genetic Variant Databases to Support Clinical Validity for Genetic and Genomic-Based *In Vitro* Diagnostics

Guidance for Stakeholders and Food and Drug Administration Staff

Document issued on April 13, 2018.

The draft of this document was issued on July 8, 2016.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0850 (expires 03-31-2021).

See additional PRA statement in Section 7 of the guidance.

For questions about this document concerning devices regulated by CDRLH, contact Laura Koonitz at 301-796-7561 or CDRLH.Koonitz@fda.hhs.gov. For questions regarding this document as applied to devices regulated by CBER, contact the Office of Communication, Outreach and Development in CBER at 1-800-835-4709 or 240-402-8010 or by email at ocod@fda.hhs.gov.



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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- Introduction & Staffing Changes
- Final Guidance Update
- **Draft Guidance Update**
- Breakthrough program is taking off
- CLIA Waiver Program improvements continue
- Current, Immediate, and Long-term priorities

Comment and monitor Draft Guidances to help us set our future direction

The FDA logo, consisting of the letters "FDA" in white on a blue square background.A red rectangular stamp with a double border, tilted slightly, containing the word "DRAFT" in red, bold, italicized capital letters.

- 1 Special 510(k) program expansion
- 2 Recognition and Withdrawal of Standards
- 3 3rd Party Premarket Review Program
- 4 Consideration of Uncertainty in Benefit-Risk
- 5 Q-Submission Program
- 6 Multiple Functions

We've proposed expanding the Special 510(k) Program

Contains Nonbinding Recommendations
Draft – Not for Implementation

The Special 510(k) Program

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE
This draft guidance document is being distributed for comment purposes only.

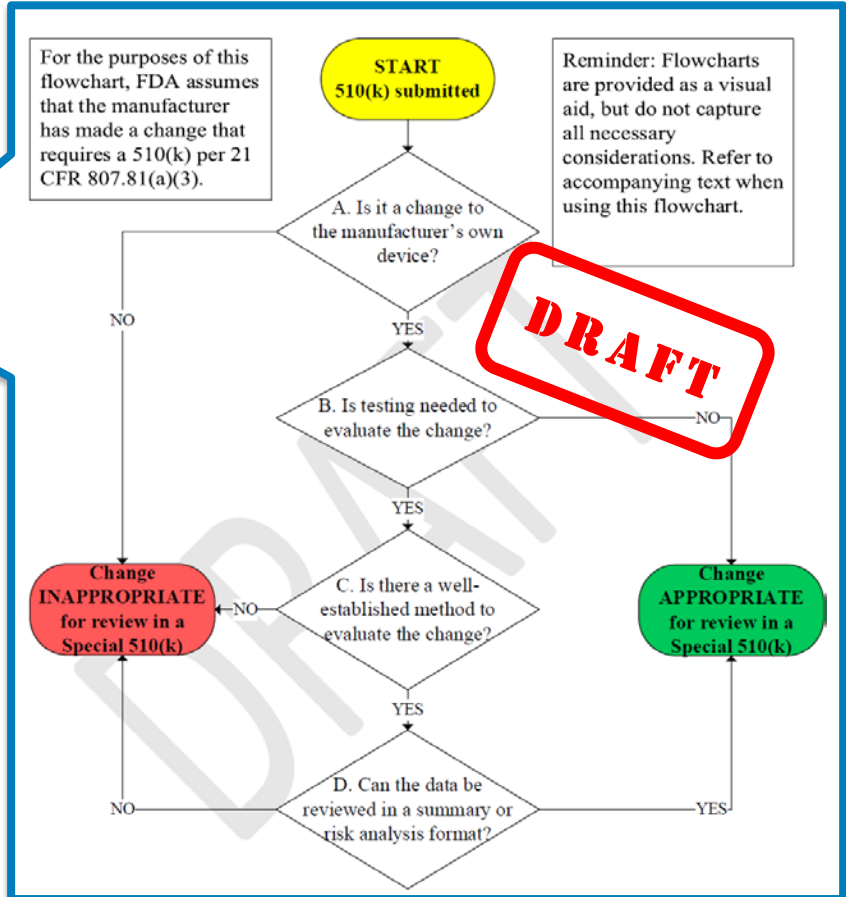
Document issued on September 28, 2018.

You should submit comments and suggestions regarding this draft document within 60 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 the 510(k) Staff at 301-796-5640. For questions regarding this document regarding CBER-regulated devices, contact the Office of Communication, Outreach and Development (OCOD) in CBER at 1-800-835-4709 or 240-402-8010 or by email at ocod@fda.hhs.gov.

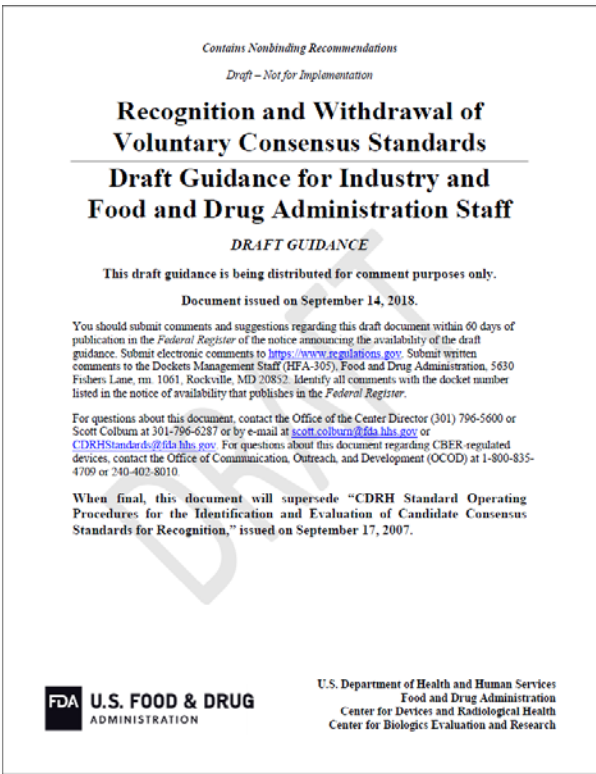
When final, this guidance will supersede the Special 510(k) policy in "The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications," issued on March 20, 1998.

FDA U.S. FOOD & DRUG ADMINISTRATION U.S. Department of Health and Human Services
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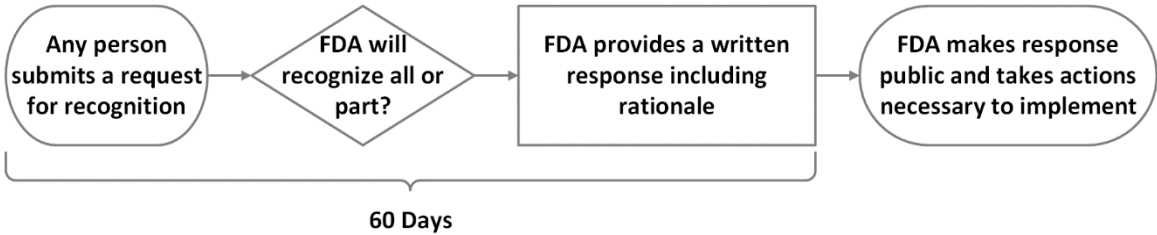




Draft guidance would improve transparency of standards recognition

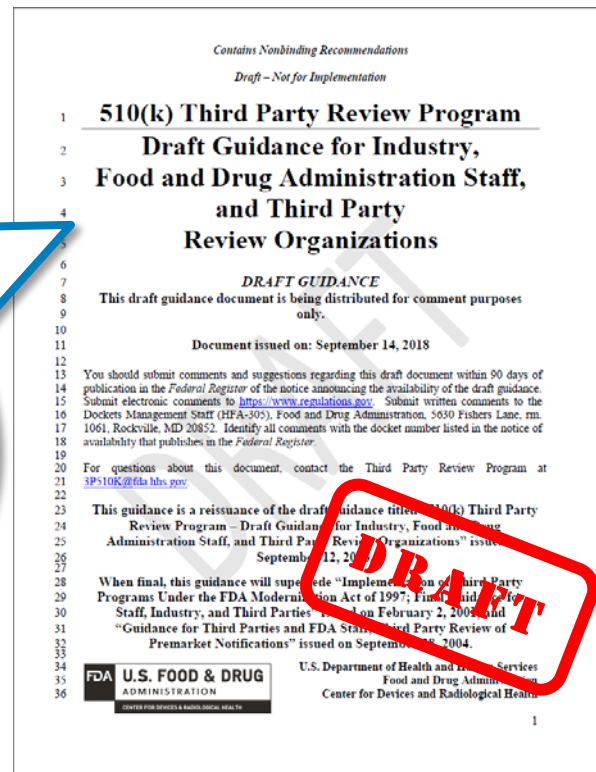


DRAFT



Proposed 3rd Party Review guidance adjusts clinical data restriction, reinvigorates program

“However, if a device type contains simple clinical data such as sample clinical images or tests using banked specimens, it may be eligible for 3P review. Most in vitro diagnostic (IVD) devices are eligible for 3P review...”



Draft “uncertainty” guidance describes possible postmarket data collection options

Contains Nonbinding Recommendations

Draft – Not for Implementation

Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on September 6, 2018.

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, contact the Office of the Center Director at 301-796-5900.



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

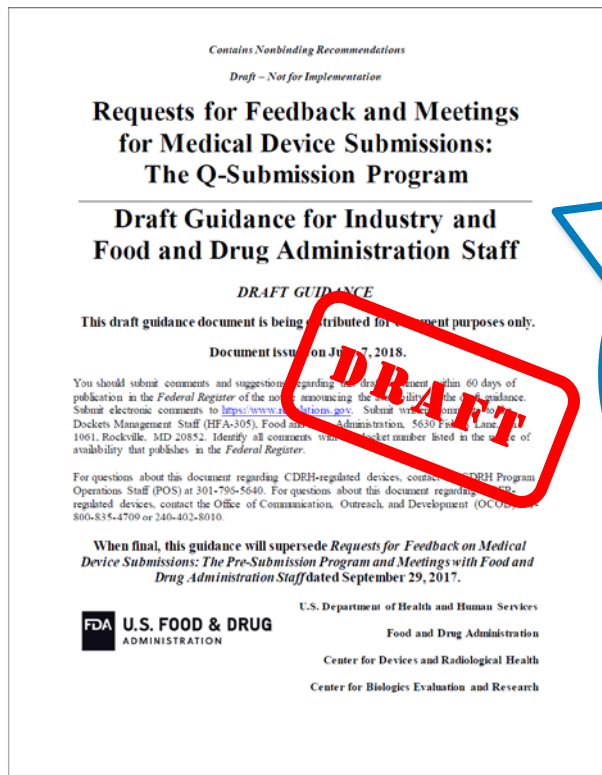
“FDA’s decisions operate in the context of a broader healthcare system...”

Summary: Confidence levels and differences in sample size of premarket study

Scenario	Confidence level for both sensitivity and specificity	Number of subjects with target condition present	Study size for prevalence=20%	Postmarket data collection in light of the greater uncertainty
Case 1: Conventional Uncertainty	95%	120	600	Not applicable
Case 2: Greater Uncertainty, Modest Postmarket Data Collection	90%	80	400	Modest postmarket data collection as a condition of approval Flag postmarket data collection on FDA’s website

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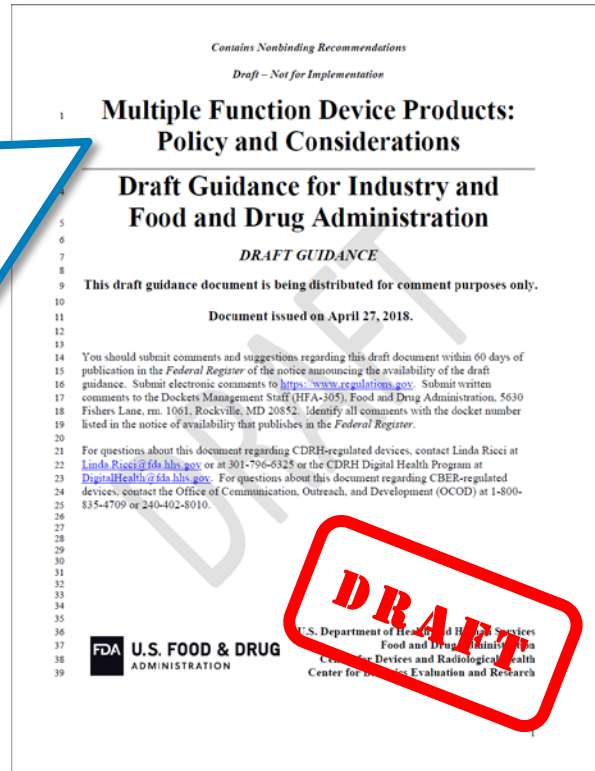
Draft Q-Sub guidance would clarify differences between pre-sub, SIMs



Pre-Subs help improve predictability about what information is appropriate to support a marketing application before you spend precious resources on testing

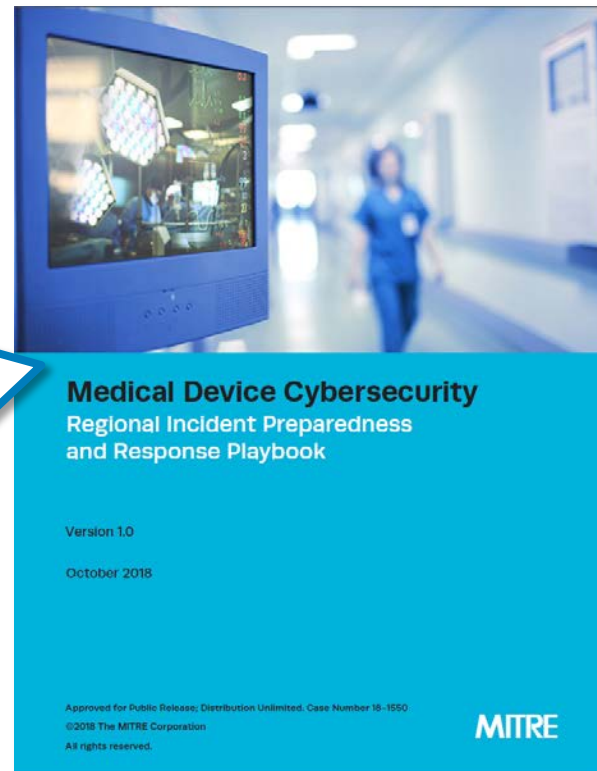
Draft Multiple Function guidance would clarify a key *Cures* provision

- “Architecture decisions early in the design cycle can facilitate optimal separation and support segregation necessary for risk control.”
- “The higher the degree of separation, the easier it is to independently review... the device function-under-review.”
- “In the premarket review of a device function-under-review, FDA may assess the impact of other functions on the device function-under-review.”



MITRE Cybersecurity Playbook* mentions manufacturers' role >40 times

“Through planning and practice, as well as support from and collaboration with manufacturers and regional and national partners, HDOs can be well positioned to manage medical device cybersecurity incidents.”



* Not guidance.

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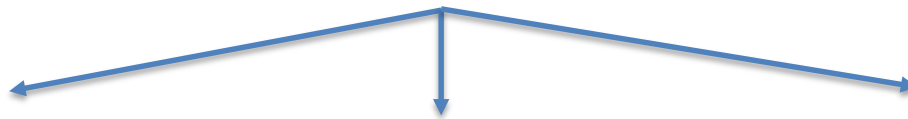
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More breakthrough diagnostics are coming to market through FDA

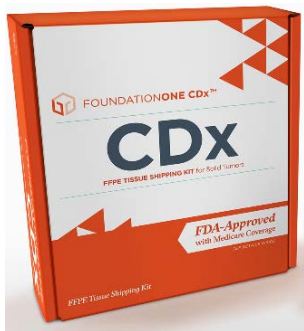
- >95 designated devices
 - 29 diagnostics
- 8 devices authorized to market
 - 4 PMAs approved
 - 2 510(k)s cleared
 - 2 De Novos granted



Early successes in breakthrough IVDs authorized to market include:



FoundationOne CDx



- 1st breakthrough to market
- 1st pan cancer CDx oncopanel

Banyan Brain Trauma Indicator



- 1st breakthrough De Novo to market
- 1st Blood test for TBI

More to come....

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We're reissuing revised CLIA Waiver guidances in draft before finalizing

Contains Nonbinding Recommendations

Draft – Not for Implementation

Select Updates for Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.
Document issued on November 29, 2017.

You should submit comments and suggestions regarding this draft document within 60 days of

Contains Nonbinding Recommendations

Draft – Not for Implementation

Recommendations for Dual 510(k) and CLIA Waiver by Application Studies

Draft Guidance for Industry and Food and Drug Administration Staff

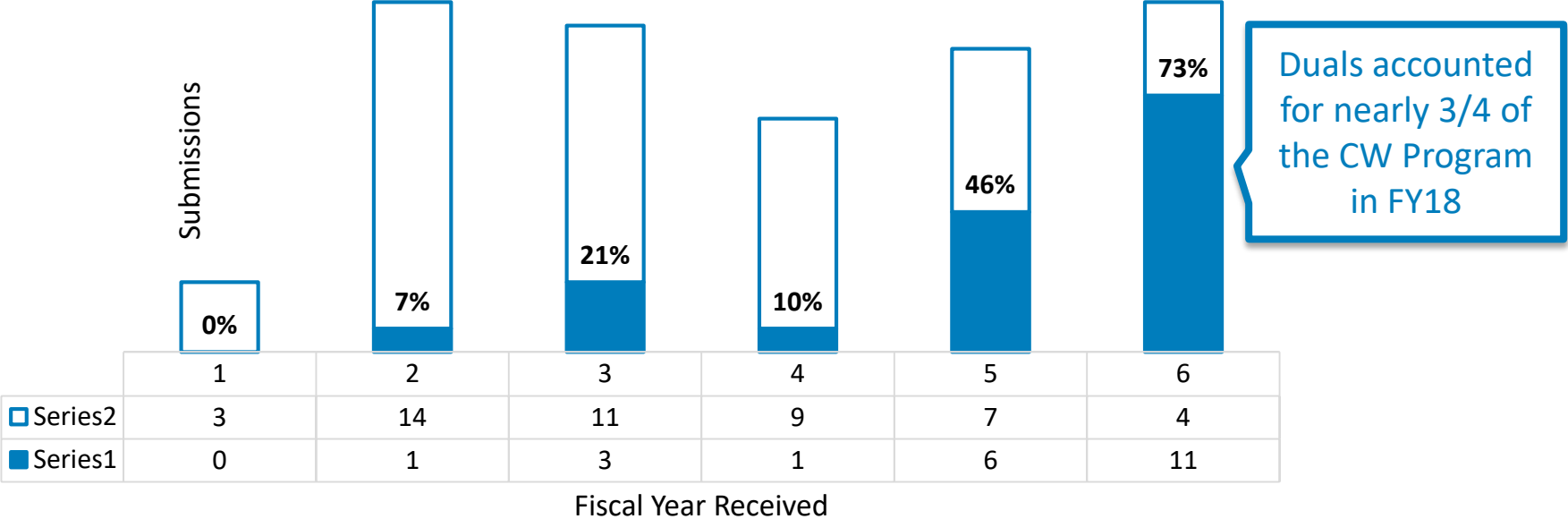
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Dual CWs eclipsed standalone CWs as the preferred waiver pathway in FY18



CLIA Waiver Decision Summaries:
<https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm578178.htm>

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Current, immediate, and long-term priorities

- 2018-2020 CDRH Strategic Priorities
 - Employee Engagement, Opportunity, and Success
 - Simplicity
 - Collaborative Communities
- OPEQ Reorganization
- Continue to Advance Personalized Medicine

Questions?

oir-policy@fda.hhs.gov