# FDA Update: Office of In Vitro Diagnostics

Association of Medical Diagnostics Manufacturers (AMDM)
Fall Focus Meeting
October 19, 2023

Toby Lowe
Acting Deputy Director
Associate Director for Regulatory Programs
Office of In Vitro Diagnostics (OIVD/OHT7)

# OHT7: Office of In Vitro Diagnostics

Office Director: **Timothy Stenzel**
Deputy Office Directors: **Toby Lowe** (Acting), **Brittany Schuck, Ryan Lubert** (Acting)
Associate Director for Regulatory Programs: [Toby Lowe]
Chief Medical Officer & Associate Director for Medical Affairs: **Sara Brenner**

**Division of Program Operations and Management (DPOM)**

Division Director – **Amy Zale**
Deputy Division Director – Vacant

**Division of Chemistry and Toxicology Devices (DCTD)**

Division Director – **Marianela Perez-Torres** (Acting)
Deputy Division Director – **Paula Caposino** (Acting)

**Division of Immunology and Hematology Devices (DIHD)**

Division Director – **Lea Carrington**
Deputy Division Director – **Takeesha Taylor-Bell**

**Division of Microbiology Devices (DMD)**

Division Director – **Uwe Scherf**
Deputy Division Director – **Kristian Roth**

**Division of Molecular Genetics and Pathology (DMGP)**

Division Director – **Donna Roscoe** (Acting)
Deputy Division Director – [Donna Roscoe]

# OHT7: Device Types Reviewed by Division

## Division of Chemistry and Toxicology Devices

- Chemistry
- Toxicology
- Cardio-renal
- Diabetes

## Division of Immunology and Hematology Devices

- Hematology
- Immunology and Flow Cytometry

## Division of Microbiology Devices

- Viral Respiratory and HPV
- General Viral and Hepatitis
- General Bacterial and Antimicrobial
- Bacterial Respiratory and Medical Countermeasures

## Division of Molecular Genetics and Pathology

- Molecular Pathology and Cytology
- Molecular Genetics

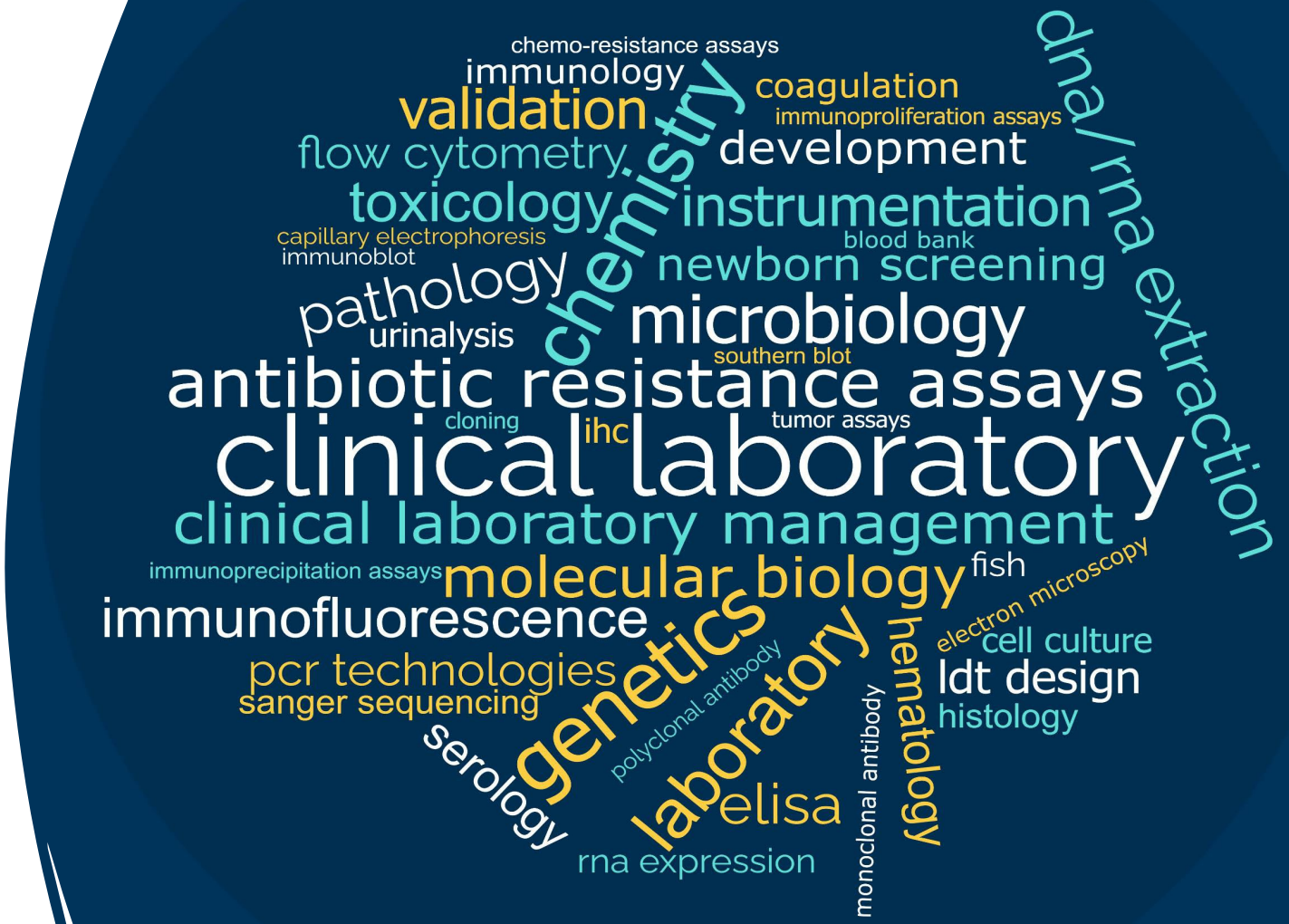
# OHT7 Staff Have a Wealth of Experience

over 300 highly motivated staff

widespread experience

various specialties

>96% customer satisfaction rating in 2022



# OHT7 Key Activities

### Premarket Activities

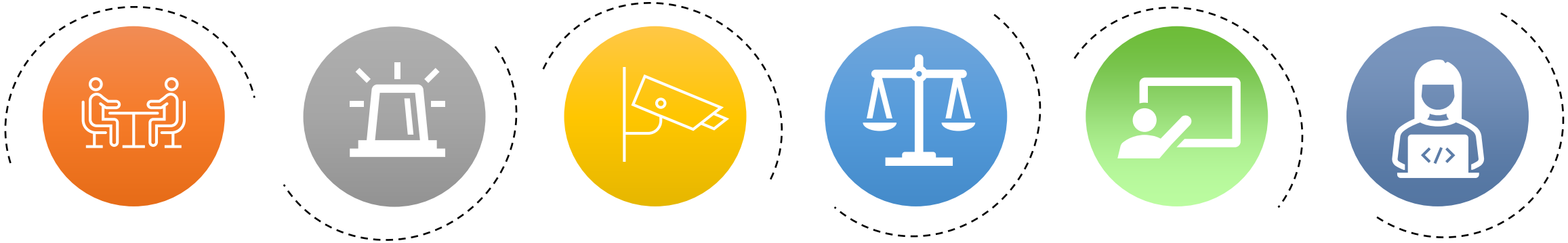
- PMA, 510(k), De novo request reviews
- Investigational Device Exemptions
- Humanitarian Device Exemptions
- Pre-submissions
- Breakthrough designation requests
- Premarket inspections
- CLIA waiver applications
- CLIA categorizations

### Postmarket Activities

- Monitoring and Surveillance
- Postmarket Inspections
- Postmarket Studies
- Recalls
- Compliance and Enforcement Actions
- Safety communications

### External Engagement & Outreach

- External training and engagement
- Public meetings
- Conferences
- Town Halls
- Inquiry responses



### Emergency Use

- Emergency Use Authorizations
- Cross-agency collaborations
- Stakeholder engagement, including Town Halls

### Guidance

- Issue new guidances
- Update existing guidances
- Training and webinars

### Program Development & Operations

- Internal training
- Performance tracking
- Data reporting

# FY 2023 OHT7 Premarket Review Progress

**~ 1621 Submissions:**

- ~90 PMAs and PMA Supplements
- ~300 510(k)s
- ~20 De Novos
- ~900 Pre-Submissions
- ~50 IDEs
- 1 CLIA Waiver by Application
- 15 Dual 510(k) and CLIA Waiver by Application
- ~80 EUAs

# YTD Office Highlights for 2023

- First de novo authorization for a preeclampsia risk assessment test, which had been designated as a breakthrough device (and helps address one of the unmet public health needs highlighted in the breakthrough device designation guidance)
- First de novo authorization of an in vitro diagnostic intended to aid in the assessment of risk of progressive kidney function decline in adult patients with Type 2 diabetes and existing chronic kidney disease
- Cleared two “mega submissions” which allow for the simultaneous antimicrobial susceptibility testing of a larger number of drugs and drug concentrations than previous cleared systems
- First De Novo authorization for a COVID-19 molecular testing at-home over-the-counter (OTC) use test
- First two SARS-CoV-2 serology tests for the qualitative detection of IgG antibodies to SARS-CoV-2 in human serum or plasma samples
- First adeno-associated virus (AAV) companion diagnostic IVD test to detect pre-existing antibodies to help health care providers identify patients who may benefit from receiving gene therapy to treat severe hemophilia A
- First commercially available rapid TBI biomarker laboratory-based blood test to evaluate concussions
- Clearance of four completely new insulin pumps – more than doubling the number of options patients have had for the last decade
- Clearance of an automated insulin dosing (AID) system that introduces a new paradigm in simplified user experience, expanding access to users who want a more hands-off approach to managing their insulin pump therapy
- Clearance of improved versions of iCGM sensors, which drops a prior restriction against use in AID systems.
- First de novo for a digital behavioral therapeutic to aid in the management of type 2 diabetes

# FDA Proposes Rule Aimed at Helping to Ensure Safety and Effectiveness of Laboratory Developed Tests

- The proposed rule seeks to amend the FDA's regulations to make explicit that IVDs are devices under the Federal Food, Drug, and Cosmetic Act, including when the manufacturer of the IVD is a laboratory.
- Along with this amendment, the FDA is proposing a policy under which the agency intends to provide greater oversight of LDTs, through a phaseout of its general enforcement discretion approach to LDTs.
- Submit comments to the docket: FDA-2023-N-2177


NATIONAL ARCHIVES

FEDERAL REGISTER

The Daily Journal of the United States Government

Proposed Rule

**Medical Devices; Laboratory Developed Tests**

A Proposed Rule by the Food and Drug Administration on 10/03/2023

This document has a comment period that ends in 55 days. (12/04/2023)

SUBMIT A FORMAL COMMENT

5 comments received. View posted comments

PUBLISHED DOCUMENT

**AGENCY:**

Food and Drug Administration, HHS.

**ACTION:**

Proposed rule.

**SUMMARY:**

The Food and Drug Administration (FDA, the Agency, or we) is proposing to amend its regulations to make explicit that in vitro diagnostic products (IVDs) are devices under the Federal Food, Drug, and Cosmetic Act (FD&C Act) including when the manufacturer of the IVD is a laboratory. In conjunction with this amendment, FDA is proposing a policy under which FDA intends to phase out its general enforcement discretion approach for laboratory developed tests

DOCUMENT DETAILS

Printed version:
PDF

Publication Date:
10/03/2023

Agencies:
Food and Drug Administration

Dates:
Either electronic or written comments on the proposed rule must be submitted by December 4, 2023.

Comments Close:
12/04/2023

Document Type:
Proposed Rule

[FDA News Release]

# Webinar on LDT Proposed Rule – October 31, 2023

**Webinar Details**

Registration is not necessary.

**Date:** October 31, 2023

**Time:** 1:00 PM - 2:00 PM ET

Please dial in 15 minutes before the start of the call to allow time to connect.

Please click the link below to join the webinar:
https://fda.zoomgov.com/j/1601249212?pwd=UnlIbThyOXN2R3gvTGJveERxRXpUdz09

Passcode: k+S8kN

Please note: Participants who join the webinar using the Zoom webinar link above should use computer audio (listen through their computer speakers and speaking through computer microphone/headset).

*The dial-in information provided below is for participants who will be joining the webinar by phone only.*

- **U.S. Callers Dial:** 833-568-8864 (Toll Free)
  - For higher quality, dial a number based on your current location:
    - +1 669 254 5252 US (San Jose)
    - +1 646 828 7666 US (New York)
    - +1 646 964 1167 US (US Spanish Line)
    - +1 415 449 4000 US (US Spanish Line)
    - +1 551 285 1373 US
    - +1 669 216 1590 US (San Jose)
- **International Caller Dial:** Please check the international numbers available
- **Webinar ID:** 160 124 9212
- **Passcode:** 298020

- On October 31, 2023, the U.S. Food and Drug Administration (FDA) will host a webinar to provide information on the proposed rule regarding Laboratory Developed Tests or LDTs.
- https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/webinar-proposed-rule-medical-devices-laboratory-developed-tests-10312023
- During the webinar, the FDA will:
  - Provide an overview of the rulemaking proposal to amend the FDA's regulations to make explicit that in vitro diagnostic products (IVDs) are devices under the Federal Food, Drug, and Cosmetic Act including when the manufacturer of the IVD is a laboratory.
  - Describe the proposed phaseout of FDA's general enforcement discretion approach to LDTs.
  - Host a Q&A session based on questions that have been submitted prior to the webinar at CDRHWebinars@fda.hhs.gov. Questions will not be taken during the live webinar. All questions are due by October 23, 2023, to be considered for the discussion.

# CDRH's Efforts to Return to Normal

- Reauthorization of the Medical Device User Fee Amendments (MDUFA) authorizes FDA to collect user fees for the review of device applications for fiscal years 2023 through 2027
- CDRH is accepting and immediately initiating the review process for all new in vitro diagnostic (IVD) premarket submissions and pre-submissions in accordance with the performance goals established in the MDUFA V Commitment Letter
- COVID-19 Tests
  - Hundreds remain authorized under EUA
  - Many have received traditional marketing authorization
  - Developers are encouraged to seek traditional premarket clearance for most COVID-19 tests

# COVID-19 IVD EUAs Authorized as of October 12, 2023

296

## Molecular diagnostic tests

- 33 Pooling
- 68 Asymptomatic single use screening
- 6 Serial screening
- 25 Multi-analyte (i.e., SARS-CoV-2 + Influenza)
- 25 Point-of-care
- 73 Home collection
  - 16 Direct-to-consumer
  - 5 Multi-analyte
  - 14 Saliva home collection
- 21 Standalone home collection kits
- 3 Standalone saliva collection devices
- 1 Prescription at-home test
- 5 Over-the-counter (OTC) at-home tests

65

## Antigen diagnostic tests

- 59 Point-of-care
- 2 Prescription at-home tests
- 32 Over-the-counter (OTC) at-home tests
- 50 Serial Screening
- 3 Serial Testing
- 4 Multi-Analyte

83

## Serology and other immune response tests

- 13 Point-of-care
- 3 Neutralizing antibody tests
- 16 Semi-quantitative
- 1 Quantitative
- 1 Home collection

# At-Home OTC COVID-19 Diagnostic Tests and Expiration Date Extensions

- 37 OTC COVID-19 diagnostic tests authorized under EUA
- FDA web page provides information about Authorized At-Home OTC COVID-19 Diagnostic Tests including links to home use instructions for each test and information about updated expiration dates.
- On September 25, 2023, The Biden administration resumed offering free at-home Covid tests to American households at COVID.gov/test.

# Final COVID-19 Transition Guidances

- On March 27, 2023, CDRH issued two guidance documents to assist with transition plans for medical devices that were issued EUAs or fall within certain enforcement policies issued to support the response to the COVID-19 pandemic
  - *Transition Plan for Medical Devices Issued Emergency Use Authorizations (EUAs) Related to Coronavirus Disease 2019 (COVID-19)*
    - Referred to as "EUA Transition Guidance"
  - *Transition Plan for Medical Devices That Fall Within Enforcement Policies Issued During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency*
    - Referred to as "Enforcement Policies Transition Guidance"
    - FDA's Policy for Coronavirus Disease-2019 Tests (Revised) and Policy for Evaluating Impact of Viral Mutations on COVID-19 Tests (Revised) are outside scope

*This slide presents high level discussion points. Please refer to the guidance documents for the details and official policies.

# COVID-19 Transition Highlights

## PHE and EUA Declarations

- The Public Health Emergency declared under Section 319 of the Public Health Service Act ended on May 11, 2023.
- The determination and declarations under Section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) remain in effect.
  - For each EUA declaration, FDA will publish advance notice of termination in the Federal Register, **180 days** before termination of the EUA declaration and associated EUAs.

## COVID-19 Transition Guidances

- Outline the FDA's general recommendations to transition from certain policies adopted and operations implemented during the COVID-19 pandemic to normal operations, including the FDA's recommendations for:
  - Developing a transition implementation plan for in vitro diagnostics (IVDs) with an EUA
  - Submitting an IVD marketing submission
  - Taking other actions with respect to these IVDs
  - Additional information related to test developers and COVID-19 tests.

# Traditional Marketing Authorization for COVID-19 Tests

## COVID-19 Tests Granted Traditional Marketing Authorization by the FDA

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The FDA has been working with COVID-19 test developers seeking to pursue marketing authorization through the traditional premarket review pathways, which will allow these tests to continue to be used beyond the time allowed by emergency use authorization. This page lists COVID-19 tests that have received traditional marketing authorization. See the Marketing Your Device page for more information about the traditional premarket review and authorization process.

### Background

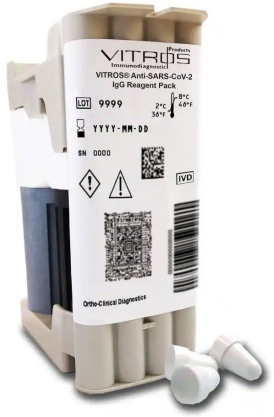
Initially, COVID-19 tests were only available under emergency use authorization (EUA). Since the Secretary's 564 declaration related to in vitro diagnostic tests for COVID-19, on February 4, 2020, the FDA has granted EUAs for many COVID-19 tests. Tests with an active EUA can continue to be used as long as they are available and not expired. The FDA has also issued a guidance document with a Transition Plan for Medical Devices Issued EUAs Related to COVID-19 and encourages EUA holders to pursue traditional marketing authorization. Visit the COVID-19 Test EUA page for more information about these EUAs.

New webpage provides information on tests with de novo and 510(k):

https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/covid-19-tests-granted-traditional-marketing-authorization-fda

# The 510(k) Pathway is Available for Most COVID-19 Tests


cue


Multiple marketing authorizations have been granted using the De Novo review pathway, a regulatory pathway for low-to moderate-risk devices of a new type:

- **BioFire Respiratory Panel 2.1 (RP2.1):** First COVID-19 molecular diagnostic test. *Granted March 17, 2021*
- **Quidel Sofia 2 SARS Antigen+ FIA:** First COVID-19 antigen test. *Granted March 8, 2023*
- **VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Test and Anti-SARS-CoV-2 IgG Test:** First COVID-19 serology tests. *Granted May 5, 2023*
- **Cue COVID-19 Molecular Test:** First over-the-counter (OTC) test for COVID-19 to be granted marketing authorization using a traditional premarket review pathway and the first ever at-home test authorized using a traditional premarket review pathway for any respiratory illness. *Granted June 6, 2023*

# CDRH: Center Initiatives

- Customer Collaboration Portal (CDRH Portal)
- Electronic Submission Template And Resource (eSTAR)
- Predetermined Change Control Plans
- Cybersecurity in Medical Devices
- Breakthrough Devices Program
- Medical Devices Intended for Use in the Home

# Customer Collaboration Portal (CDRH Portal)

- Submission hub for CDRH-led premarket submission types for internal and external stakeholders
- Online progress tracker dashboard displays near real-time submission status for Pre-Submissions and 510(k) submissions (traditional, special, and abbreviated 510(k)s)
- The CDRH Portal cannot receive files that are:
  - larger than 4GB
  - PDFs with an attachment larger than 1GB
  - To submit electronic files that exceed the technical limitations, you can mail the electronic version of your submission to the CDRH Document Control Center (DCC)

Send and Track Medical Device Premarket Submissions Online: CDRH Portal

# eSTAR
# electronic Submission Template And Resource

- As of October 1, 2023, all 510(k) submissions, *unless exempted**, must be submitted electronically using eSTAR
- Pre-Submissions, Premarket approval (PMA), and De Novo requests submitted using eSTAR remain voluntary until further notice.
- Dynamic PDF template for assembling submission
  - eSTAR is a submission preparation template, NOT a new type of 510(k)
- Guides the medical device applicant through the process of preparing a comprehensive medical device submission
  - Contains automation, guides, integrated databases, policies and procedures in a single package
- Modeled after the SMART review template used by review staff

Electronic Submission Template for Medical Device 510(k) Submissions: Guidance for Industry and FDA Staff

*See Section VI.A. Waivers and Exemptions from Electronic Submission Requirements of Electronic Submission Template for Medical Device 510(k) Submissions guidance

# Predetermined Change Control Plans

## CDRH Issues Draft Guidance on Predetermined Change Control Plans for Artificial Intelligence/Machine Learning-Enabled Medical Devices

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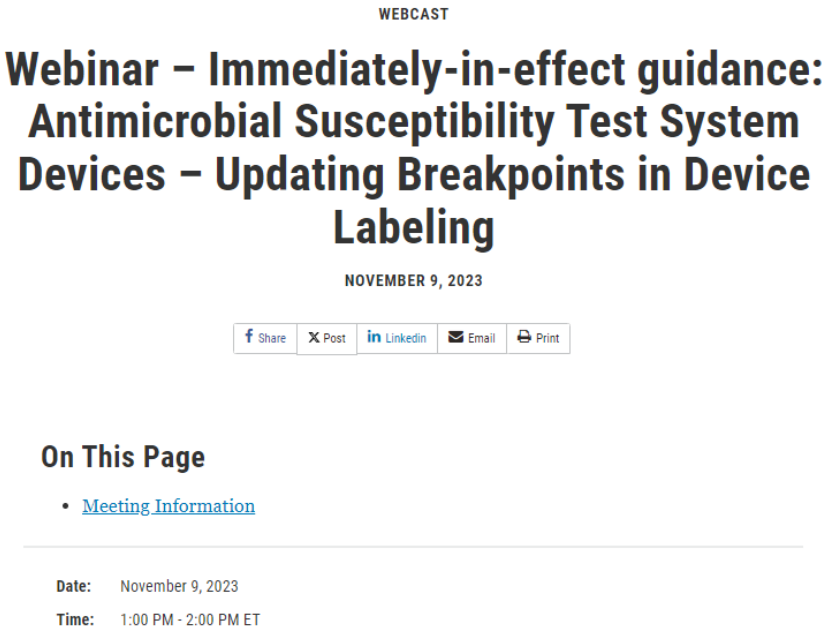
FOR IMMEDIATE RELEASE

March 30, 2023

*The following is attributed to Brendan O'Leary, Deputy Director*
*Center of Excellence in the FDA's Center for Devices and Rad*

Digital health technologies are playing an increasingly significant ro
our health and daily lives, and Artificial Intelligence and Machine Le
powering important advancements in this field. The FDA has alread
than 500 AI/ML-enabled medical devices, and more are under deve
that these innovative devices are safe and effective, and that they ca
potential to help people, is central to the FDA's public health missio

Today, the FDA is publishing a draft guidance, "**Marketing Subm**
**Recommendations for a Predetermined Change Control Pl**
**Intelligence/Machine Learning (AI/ML)-Enabled Device S**
This draft guidance proposes a science-based approach to ensuring
devices can be safely, effectively, and rapidly modified, updated, and
to new data.



WEBCAST

## Webinar – Immediately-in-effect guidance: Antimicrobial Susceptibility Test System Devices – Updating Breakpoints in Device Labeling

NOVEMBER 9, 2023

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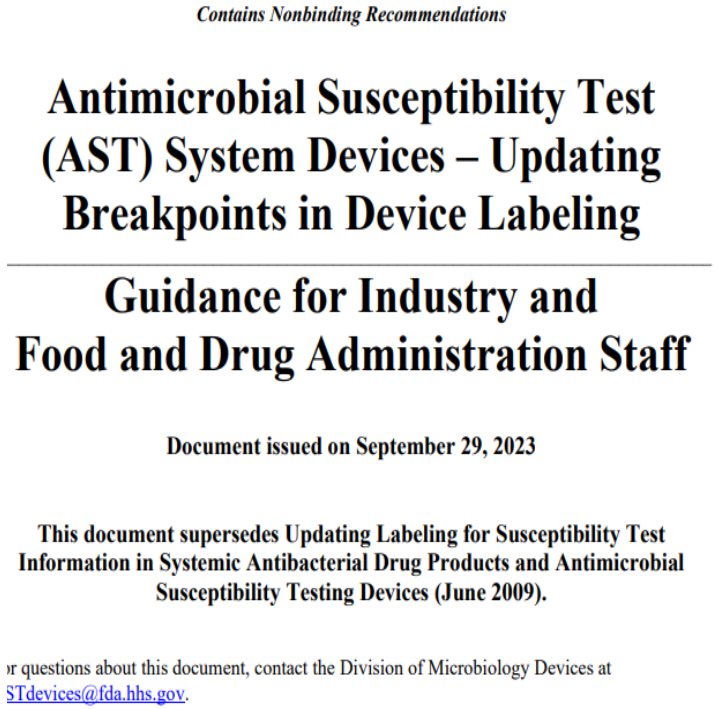
On This Page

- Meeting Information

**Date:** November 9, 2023

**Time:** 1:00 PM - 2:00 PM ET



*Contains Nonbinding Recommendations*

## Antimicrobial Susceptibility Test (AST) System Devices – Updating Breakpoints in Device Labeling

### Guidance for Industry and Food and Drug Administration Staff

**Document issued on September 29, 2023**

**This document supersedes Updating Labeling for Susceptibility Test Information in Systemic Antibacterial Drug Products and Antimicrobial Susceptibility Testing Devices (June 2009).**

r questions about this document, contact the Division of Microbiology Devices at STdevices@fda.hhs.gov.

[Webinar – Immediately-in-effect guidance: Antimicrobial Susceptibility Test System Devices – Updating Breakpoints in Device Labeling - 11/09/2023 | FDA]

# Final Guidance: Cybersecurity in Medical Devices

- Issued September 27, 2023
- Provides FDA's recommendations to industry regarding cybersecurity device design, labeling, and the documentation that FDA recommends be included in premarket submissions for devices with cybersecurity risk.
- These recommendations are intended to promote consistency, facilitate efficient premarket review, and help ensure that marketed medical devices are sufficiently resilient to cybersecurity threats.




Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions

# Breakthrough Devices Program: Updated Final Guidance

A voluntary program for certain medical devices that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions.

- The goal is to provide patients and health care providers with timely access to these medical devices by speeding up their development, assessment, and review, while preserving the statutory standards for premarket approval, 510(k) clearance, and De Novo marketing authorization.
- A ***Breakthrough Designation Request*** (via Q-sub) for a device can be sent at any time before sending a marketing submission.
- Inclusion in the Program is based on meeting statutory criteria
  - We communicate a final decision on the designation request within 60 days
- Reflects our commitment to device innovation and protecting the public health.

**September 14, 2023**

**Updates to the final guidance issued to:**

- Clarify how the Breakthrough Devices Program may apply to certain medical devices that promote health equity.
- Clarify considerations in designating devices, including eligible devices that may support innovation of new and existing technologies that address inequities.
- Clarify that the Breakthrough Devices Program may be available for certain non-addictive medical products to treat pain or addiction—consistent with the FDA's obligations under the SUPPORT Act.
- Clarify how the FDA discloses the Breakthrough status of designated devices once they receive marketing authorization.

Breakthrough Devices Program
Guidance for Industry and Food and Drug Administration Staff

# Breakthrough IVD Devices

**>169** designated **IVD** devices

**18 IVD** devices authorized to market

- **6** PMAs approved
- **4** 510(k)s cleared
- **8** De Novos granted


*as of October 18, 2023

# Advancing Health Equity: Home Use Devices

CDRH is committed to facilitating access to medical devices designed to be safe and effective when used outside of traditional clinical settings, for example, medical devices intended for use in the home

Medical devices intended for consumer use have unique design and validation considerations

**Come talk to us, using our pre-submission program.**
**Submit novel devices that meet the breakthrough device designation criteria to the breakthrough program**

# Design Considerations for Home Use Devices

**Factors to consider while designing and developing a device for home use to minimize unique risks**

**Environmental Considerations** - When designing a home use device, you should account for the range of environments in which it might be stored, transported, and used

- Location
- Contaminants
- Water Supply
- Temperature
- Dampness and Humidity
- Atmospheric Pressure Changes
- Air flow
- Fluid Exposure
- Storage

**User Considerations** - Home users can have a large range of physical, sensory, and cognitive capabilities and disabilities, and emotional differences that should be considered in your home use device design

- Physical
- Sensory/Perceptual
- Cognitive
- Emotional

**Design Considerations**– When establishing design controls for home use devices, you should take into account considerations related to device performance and user needs in the home environment

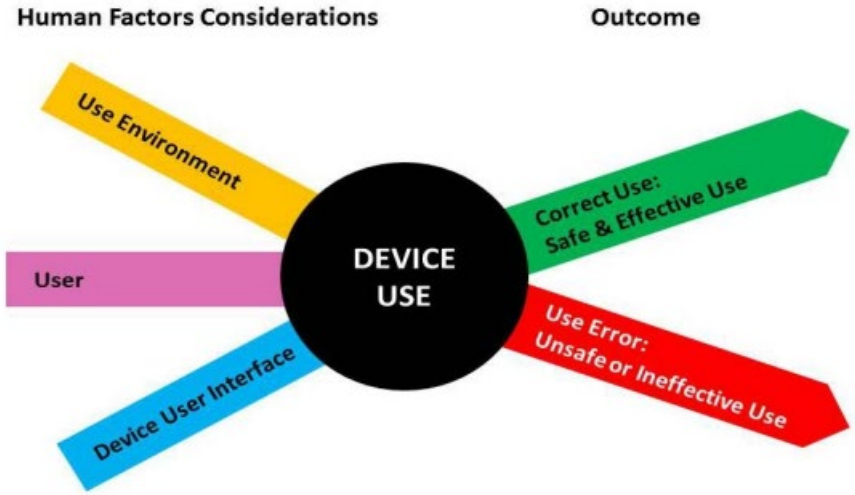
- Lock-out Mechanisms
- Maintenance
- Calibration
- Mechanical
- Electrical Issues

FDA Guidance: Design Considerations for Devices Intended for Home Use

# Validation Considerations for IVDs for Home and Consumer Use

Additional validation testing is conducted for IVDs for consumer use:

- Data submitted to demonstrate that the IVDs are safe and effective in the hands of lay users (including sample collection)
- Studies are performed to evaluate how well lay users can understand the instructions without prompting, perform a self-test (and/or collect a sample), and obtain an accurate result
- For IVDs where results are provided directly to lay users, lay user ability to understand the results of the test result is also evaluated
- Flex studies to demonstrate insensitivity to environmental or usage variation, as needed



# IVDs for Home and Consumer Use

- Pregnancy tests
- Drugs of abuse tests (e.g., morphine, benzodiazepine, methadone, amphetamine)
- Genetic Health Risk Test System
- Cancer Predisposition Test System
- Pharmacogenetic Assessment Test System
- Continuous glucose monitors
- Automated insulin dosing systems
- Glucose meters
- PT/INR monitors
- Infectious disease tests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