FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DEVICES & RADIOLOGICAL HEALTH

CDRH Virtual Town Hall Series

Test Development and Validation During Public Health Emergencies

(#103 COVID-19)

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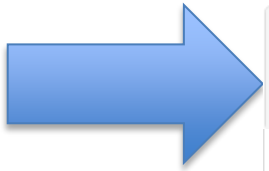

In Vitro Diagnostics - *(Updated 03/22/23)*
IVD Development, CLIA, and Virtual Town Hall Series

Series Number	Topic	Date	Materials
102	Monkeypox (mpox) and COVID-19	03/22/2023	Presentation Transcript Printable Slides
101	Monkeypox (mpox) and COVID-19	02/15/2023	Presentation Transcript Printable Slides
100	Monkeypox (mpox) and COVID-19	01/11/2023	Presentation Transcript Printable Slides
99	Monkeypox (mpox) and COVID-19	12/14/2022	Presentation Transcript
98	Monkeypox and COVID-19	11/30/2022	Presentation Transcript
97	Monkeypox	11/09/2022	Presentation Transcript
96	COVID-19 and Monkeypox	10/26/2022	Presentation Transcript
95	Monkeypox	10/12/2022	Presentation Transcript
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2021 and 2020 virtual town hall presentations and transcripts are archived and located in the Specialty Technical Topics section as: Coronavirus (COVID-19) Test Development and Validation Virtual Town Hall Series.

COVID-19 Transition Guidance Documents: IVD-specific Topics

COVID-19 IVD Transition – Agenda

- Overview of public health emergencies (PHEs) and related authorities
- Overview of COVID-19 Transition Guidances
- IVD-specific transition policies and recommendations

*These slides present high level discussion points. Please refer to the statute, regulations, and guidance documents for details and official policies.

Public Health Emergency Determinations

- **Public Health Emergency Determination under Public Health Service Act (PHS Act):**
  - Under section 319 of the PHS Act, the Department of Health and Human Services (HHS) Secretary can **issue a determination** that a "**public health emergency" (PHE) exists** (the "319 PHE declaration")
  - The 319 PHE declaration is in effect for **90 days** or until the Secretary declares the emergency no longer exists; it may be extended by the Secretary in 90-day increments
  - The 319 PHE declaration is **set to expire** on May 11, 2023
  - A 319 PHE declaration **does not enable FDA to issue EUAs**
- **Public Health Emergency Determination under the Federal Food, Drug, and Cosmetic Act (FD&C Act):**
  - Under **section 564** of the FD&C Act, the HHS Secretary can **determine that there is a public health emergency**, or **a significant potential for a public health emergency**, that affects, or has a significant potential to affect, national security or the health and security of United States citizens living abroad (the "564 determination")
  - A 564 determination is not time limited and continues until the HHS Secretary terminates it

EUA Issuance, Revision, and Revocation

- **Criteria for Issuance:**
  - Serious or life-threatening disease or condition caused by agent
  - Product "**may be effective**" to diagnose, prevent, or treat the condition (lower level of evidence than "effectiveness" standard)
  - Known and potential **benefits outweigh** known and potential risks
  - No adequate, approved, and available alternative; unavailable includes insufficient supplies of the approved alternative

- **Emergency Use Authorization (EUA) is temporary**
  - FDA will periodically review the circumstances and appropriateness of an EUA, including circumstances that might warrant **revision or revocation** of the EUA
  - FDA **may revoke** an EUA for the following circumstances:
    - The circumstances for its issuance no longer exist
    - The criteria for issuance are no longer met; and/or
    - Appropriate to protect the public health or safety

- **In general, an EUA will remain in effect for the duration of the EUA declaration under which it was issued, unless revoked**

COVID-19 Transition Guidances

- **Transition Plan for Medical Devices That Fall Within Enforcement Policies Issued During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency**
  - Referred to as the "Enforcement Policies Transition Guidance"
  - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/transition-plan-medical-devices-fall-within-enforcement-policies-issued-during-coronavirus-disease
- **Transition Plan for Medical Devices Issued Emergency Use Authorizations (EUAs) Related to Coronavirus Disease 2019 (COVID-19)**
  - Referred to as the "EUA Transition Guidance"
  - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/transition-plan-medical-devices-issued-emergency-use-authorizations-euas-related-coronavirus-disease
- **Collectively referred to as the "COVID-19 Transition Guidances"**

Webinar on COVID-19 Transition Guidances

- April 18, 2023 – FDA hosted a webinar for stakeholders interested in learning more about the COVID-19 Transition Guidances
  - Help prepare manufacturers and other stakeholders for the orderly and transparent transition to normal operations
  - Describe recommendations regarding submitting a marketing submission and the timeline for doing so
  - Provide examples to illustrate the transition policies and exemplify the 180-day transition period timeline
  - Answer your questions about the guidances on the COVID-19 transition plans

- The presentation, printable slides, and transcript will be available at CDRH Learn under "Specialty Technical Topics", sub-section "COVID-19 Transition Policy".
  - https://www.fda.gov/training-and-continuing-education/cdrh-learn

Enforcement Policies Transition Guidance

- Transition Plan for Medical Devices That Fall Within Enforcement Policies Issued During the COVID-19 PHE
  - Guidance applies to devices that fall within enforcement policies listed in the guidance*
    - Enforcement Policy for Remote Digital Pathology Devices During the COVID-19 PHE
    - Enforcement Policy for Modifications to FDA Cleared Molecular Influenza and RSV Tests During the COVID-19 PHE
    - Coagulation Systems for Measurement of Viscoelastic Properties: Enforcement Policy During the COVID-19 PHE (Revised)
    - Enforcement Policy for Viral Transport Media During the COVID-19 PHE (Revised)
  - Certain IVD-related guidances are **out of scope**
    - Policy for Coronavirus Disease-2019 Tests (Revised)
    - Policy for Evaluating Impact of Viral Mutations on COVID-19 Tests (Revised)

*This is not a complete list of enforcement policies listed in the guidance. See guidance for the complete list.

Enforcement Policies Transition Guidance: Implementation Date May 11, 2023

- **Prior to transition:**
  - **Begin preparation of any required marketing submission** with a **Transition Implementation Plan** if intending to continue distribution of devices after Phase 2
- **May 11, 2023, Phase 1 begins:**
  - Manufacturers should **follow 21 CFR Part 803** (adverse event reporting requirements)
- **August 9, 2023, Phase 2 begins:**
  - 90 days after the implementation date
  - Manufacturers should **follow 21 CFR Part 806** (reports of corrections and removals requirements)
  - **Register and list in accordance with 21 CFR Part 807 Subparts B-D** (registration and listing requirements) before the start of Phase 2 if the manufacturer intends to continue distribution of their devices after Phase 2
  - **Submit marketing submission to FDA** and have it accepted before the start of Phase 3 if the manufacturer intends to continue distribution of their devices after Phase 2
- **November 7, 2023, Phase 3 begins:**
  - 180 Days after implementation date
  - Guidances in List 1 are no longer in effect

EUA Transition Guidance

- Transition Plan for Medical Devices Issued EUAs Related to COVID-19
  - Guidance applies to **devices with EUAs** issued on basis of a COVID-19 EUA declaration
  - Does not apply to devices with EUAs that FDA chooses to revoke because the criteria in section 564(c) of the FD&C Act are no longer met or because other circumstances make such revocation appropriate to protect the public health or safety
  - 180-day advance notice(s) of termination of the EUA declarations pertaining to devices – **not yet announced**

EUA Transition Guidance: 180-Day Advance Notice of Termination

- **Prior to advance notice of termination:**
  - **Comply** with the terms of the devices' respective EUAs
  - **Plan** post-EUA regulatory and disposition strategies
  - **Begin preparation of any required marketing submission** with a **Transition Implementation Plan** if intending to continue distribution of devices after EUA termination
  - Consider **initiating discussions with the Agency** (for example, Pre-Submissions)
- **90-day period after advance notice of termination:**
  - Manufacturers that intend to continue distribution of their devices after EUA termination and that have unique compliance considerations regarding QS requirements may **request an exemption or variance** from a device QS requirement
- **180-day period between advance notice of termination and the EUA termination date:**
  - **Continue to comply** with the terms of the devices' respective EUAs
  - **Submit marketing submission to FDA** with a **Transition Implementation Plan** and have it accepted before the EUA termination date if intending to continue distribution of devices after EUA termination
- **EUA termination date:**
  - 180 days after advance notice of termination; EUAs issued under that EUA declaration will be **terminated**
  - **Enforcement policy** for **devices with marketing submission under review** by FDA
  - **Discontinue distribution** on EUA termination date **if no marketing submission** or on date of **negative decision on marketing submission** (or date manufacturer withdraws or fails to provide a complete response)
  - **Enforcement policy** for **already distributed devices**

EUA Transition Guidance: Leveraging Real-World Data

- CDRH is committed to using fit-for-purpose **real-world evidence (RWE) for regulatory decision-making**, including using RWE to support the transition from EUA to traditional marketing authorization
  - National Evaluation System for Health Technologies (NEST) Implementation Cases
    - Analysis of point-of-care COVID-19 diagnostic test data, including data from lateral flow assays and laboratory tests
- **Data derived from real-world sources may be submitted in support of a marketing submission or CLIA Waiver by Application**
  - Various real-world data sources may be available from the **use of devices under EUA or enforcement policies**
  - Guidance: Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices
  - **Engage FDA**:
    - Discuss your approach with the review division
    - Submit a pre-submission to address specific questions on how real-world data can be used to support your premarket submission

EUA Transition Guidance: Additional Considerations – CLIA

- Authorization for use in specific settings, specified in an EUA, is effective only while the relevant EUA declaration is in effect
- CLIA categorization typically determined by FDA after clearance or approval of a marketing submission:
  - Prior to CLIA categorization, an IVD is considered to be high complexity and, under CLIA, use of that test is limited to CLIA-certified laboratories that meet the requirements to perform tests of high complexity
  - Moderate complexity categorizations – tests will be categorized immediately following FDA's final action on marketing submission
  - Waived categorizations – Dual 510(k)/CLIA Waiver by Application pathway (or Dual De Novo/CLIA Waiver)
  - Home use – if marketing submission cleared, approved, or authorized for home use, test will be waived by regulation, without the need for a CLIA Waiver by Application
- Enforcement policy for devices with marketing submission under review by FDA
  - For IVDs authorized under an EUA for use in high complexity, moderate complexity, and waived settings, at this time, FDA does not intend to object to the continued distribution and use of such tests consistent with the policy described in the guidance and in a manner consistent with the EUA that was in effect prior to the EUA termination date
  - Laboratories using such tests should consider whether CLIA requirements administered by the Centers for Medicare & Medicaid Services (CMS) may apply.

See Section V.B.(3) of EUA Transition guidance for full details of policy.

EUA Transition Guidance: Devices Not Distributed after EUA Termination Date

For manufacturers of EUA-authorized devices that do NOT intend to continue distributing beyond the EUA termination date, FDA does not intend to object to the disposition and use of already distributed devices (i.e., FDA does not intend to request market removal) where:

- Single-use, non-life-supporting/non-life-sustaining devices, including IVDs, that were distributed before the EUA termination date are used by the end user prior to the product expiration date, as applicable

- For IVDs authorized under an EUA for use in high complexity, moderate complexity, and waived settings that were already distributed before the EUA termination date, at this time, FDA does not intend to object to the continued use of such tests prior to the product expiration date in a manner consistent with the EUA that was in effect prior to the EUA termination date
- Laboratories using such tests should consider whether CLIA requirements administered by the CMS may apply

See Section V.C. of EUA Transition guidance for full details of policy.

EUA Transition Guidance: Laboratory Developed Tests (LDTs)

- A laboratory developed test (LDT) is a type of IVD that is designed, manufactured, and used within a single site laboratory certified under CLIA that meets the requirements to perform tests of high complexity
- For LDTs in general, FDA has generally exercised enforcement discretion, meaning that FDA generally does not exercise its authority to enforce the regulatory requirements for these devices, although it maintains that authority
- FDA has not applied this general enforcement discretion approach to, among other LDTs, those used for declared emergencies under section 564 of the FD&C Act
- As such, following termination of the EUA declaration for COVID-19 IVDs, FDA intends to have the same enforcement approach for COVID-19 LDTs as it does for other LDTs

EUA Transition Guidance: IVD Example

Hypothetical example using July 1 of Year 1 as hypothetical advance notice of termination, and January 1 of Year 2 as hypothetical EUA termination date:

A molecular diagnostic test kit manufactured by a commercial manufacturer was issued an individual EUA for the qualitative detection of nucleic acid from SARS-CoV-2 in upper and lower respiratory specimens in authorized laboratories:

- **July 1/Year 1** – **Advanced notice of termination** of the EUA declaration is published
- **October 1/Year 1** – Manufacturer **submits marketing submission** and is accepted by FDA
- **January 1/Year 2** – EUA declaration **terminated**, EUA for device no longer in effect
  - FDA **does not intend to object continued distribution** of the device (with EUA-authorized labeling) before FDA takes a final action on the marketing submission

EUA Transition Guidance: IVD Example Resolution

- **February 20/Year 2 – Positive Decision**
  - FDA and manufacturer engage on manufacturer's **Transition Implementation Plan to address already distributed devices**; manufacturer **does not update device labeling for already distributed devices**
  - The manufacturer **updates the device labeling for devices that are in production** and **those in its possession** in accordance with the FDA-cleared version of the molecular diagnostic test kit
  - Manufacturer **continues to submit adverse event** reports
- **March 1/Year 2 – Negative Decision**
  - FDA and the manufacturer engage on the manufacturer's **Transition Implementation Plan to address already distributed devices**
  - Manufacturer **continues to submit adverse event reports**, even after cessation of distribution

Previously Emailed Questions

Resources for COVID-19 Test Development and Validation

How to Receive Updates/Alerts and Ask Questions by Email:

- To receive CDRH IVD update/alert emails, subscribe to the In Vitro Diagnostics Mailing List: www.fda.gov/about-fda/center-devices-and-radiological-health/subscribe-cdrh-mailing-lists
- For questions about COVID-19 IVD EUAs, email: COVID19DX@fda.hhs.gov
- For questions about laboratory data harmonization for COVID-19 testing, email: SHIELD-LabCodes@fda.hhs.gov

Where to Find Information:

- In Vitro Diagnostics EUAs: www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas
- Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency: www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised
- FAQs on Testing for SARS-CoV-2 *(Includes: Notifications and Emergency Use Authorizations, At-Home COVID-19 Diagnostic Tests, Test Development and Review, Test Uses, Testing Supplies, and COVID-19 Related Test Data and Reporting)*: www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-testing-sars-cov-2
- Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program: www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program
- NIH Independent Test Assessment Program (ITAP): www.nibib.nih.gov/covid-19/radx-tech-program/ITAP

Let’s Take Your Live Questions

- **To Ask a Question:**
  1. Raise your hand in Zoom 

  2. Moderator will announce your name and invite you to ask your question
  3. Unmute yourself when prompted in Zoom to ask your question

- **When Asking a Question:**
  4. Announce your first, last, and business name
  5. Ask one question only
  6. No questions about specific submissions

- **After Question is Answered:**
  7. Mute yourself and lower your hand
  8. If you have more questions - raise your hand again

Thanks for Joining Today!

- **Presentation, Slides and Transcript will be available at:**
  - CDRH Learn: www.fda.gov/Training/CDRHLearn
    - Section “Specialty Technical Topics”
    - Sub-Section “Public Health Emergencies”

- **If you have additional questions about COVID-19:**
  - Email: CDRH-EUA-Templates@fda.hhs.gov

- **Upcoming Webinars:**
  - www.fda.gov/CDRHWebinar


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