MRIGlobal

MAGELLAN SERIES

NAVIGATING SCIENTIFIC CHALLENGES

Confronting COVID-19

Pathway to EUA and 510(k) for COVID-19 Diagnostic Assays:
Key components and how to expedite FDA clearance

MRIGlobal Diagnostics Center of Excellence

- 10+ years experience with IVD Product Development and FDA Submissions
  - Design and Development
  - Feasibility Testing
  - Verification and Validation Testing
  - Reference Lab Testing
  - Stability Testing
  - 510(k) Submissions
  - CE Mark
  - Emergency Use Authorization (EUA)
  - Laboratory Developed Test (LDT)
- MRIGlobal Sponsored the FDA-Cleared BW agent diagnostic assays for use on the ABI 7500 Fast Dx – Cleared October 2019
- Testing for 20+ Commercial customers supporting FDA Clearance and CE Mark

ACCELERATE DIAGNOSTICS™ Nanosphere ThermoFisher SCIENTIFIC Cepheid® BIOFIRE DEFENSE BD DEPARTMENT OF DEFENSE UNITED STATES OF AMERICA BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY BARDA MEDICAL CBRN DEFENSE CONSORTIUM Prevent | Diagnose | Treat MCDC Medical CBRN Defense Consortium Prevent | Diagnose | Treat

What is an EUA and 510(k)?

EUA

The Emergency Use Authorization (EUA) authority allows FDA to rapidly respond to a public health emergency by allowing unapproved medical devices and products to be used during an emergency.
(Section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act))

- Provides an expedited pathway for diagnostics and therapeutics when there are no adequate, approved, and available alternatives.

510(k)

A 510(k) is a premarket submission made to FDA to demonstrate that the device to be marketed is as **safe and effective**, that is, substantially equivalent, to a legally marketed devices.
(Section 513(i)(1)(A) FD&C Act).

- Submitters must compare their device to one or more similar legally marketed “predicate” devices and make and support their substantial equivalence claims.
- The 510(k) process is substantially longer and requires more robust testing than the EUA process

Which Path to Take? EUA or 510(k)

When EUA:

- When a public health emergency requires new technologies to rapidly respond with therapeutics, diagnostics, or vaccines
- Note: On February 4, 2020 the Secretary of HHS declared an EUA for COVID-19

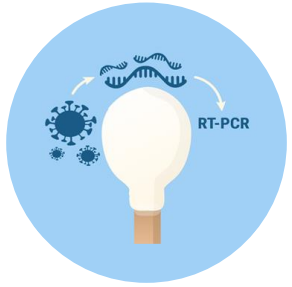
When 510(k):

- Medical products intended to be marketed in the US
- When intending to market a product after termination of an EUA authorization

(EUA termination occurs when HHS determines the circumstances no longer justify the EUA or if there is a change in the approval status of a specific product)

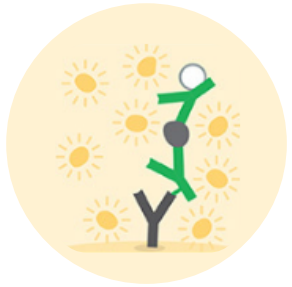
COVID-19 Diagnostics

Three Primary Types of COVID-19 Tests



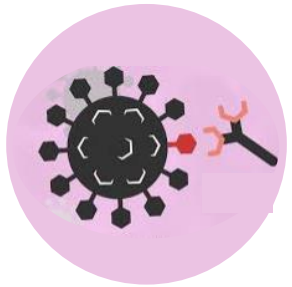
Molecular Tests

- Directly detect the COVID-19 causing virus SARS-Cov-2
- Detection is through the presence/absence of SARS-CoV-2 RNA
- Viral RNA is detected through RNA amplification (primarily RT-PCR)



Serology/Antibody Tests

- Detect viral exposure and immunity
- Detection is through presence/absence of human IgM, IgA (exposure) and IgG (immunity)
- Human antibodies are detected with Rapid Diagnostic Tests (RDTs) or ELISAs



Antigen Tests

- Directly detect the COVID-19 causing virus SARS-Cov-2
- Detection is through the presence/absence of SARS-CoV-2 nucleocapsid protein
- Viral protein is detected with lateral flow immunofluorescent assays

Studies Required for an EUA

- Varies by test type and user environment but for molecular diagnostics as an example:

MDx EUA

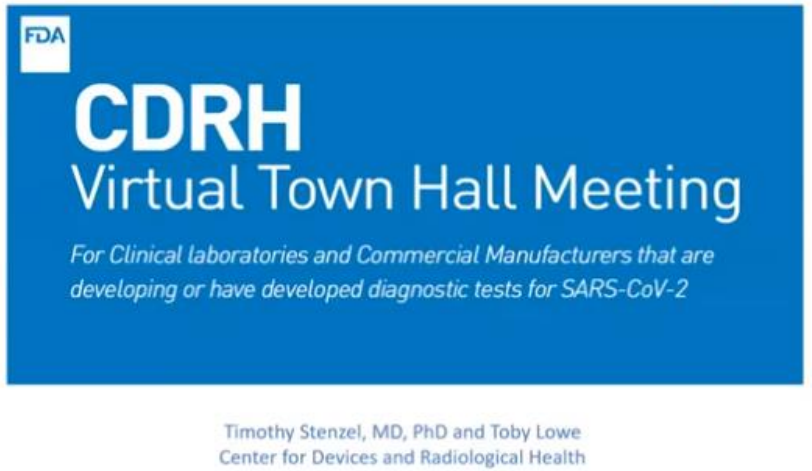
- Limit of Detection → Sensitivity in all claimed matrices
- Cross-reactivity → Mostly *in silico*
- Inclusivity → Mostly *in silico*
- Clinical Agreement → **MUST** use real clinical samples
- Usability studies → For self collected samples unless right of reference is made available
- Sample stability → Simulated shipping, worst case conditions
- Lay user studies → If intended use is Point of Care (PoC) Often combined with Clinical Agreement

Engaging with FDA for an EUA

- Pre-EUA

- General EUA inbox - Responses quick CDRH-EUA-Templates@fda.hhs.gov

- Weekly town hall meetings- interactive



- After submit an EUA, assigned a reviewer within 2 weeks
  - Large backlog now and can take weeks - months for EUA
  - FDA has stated interested in prioritizing POC and high throughput solutions, as well as direct antigen tests
  - You can start testing / distribution while you wait for your EUA

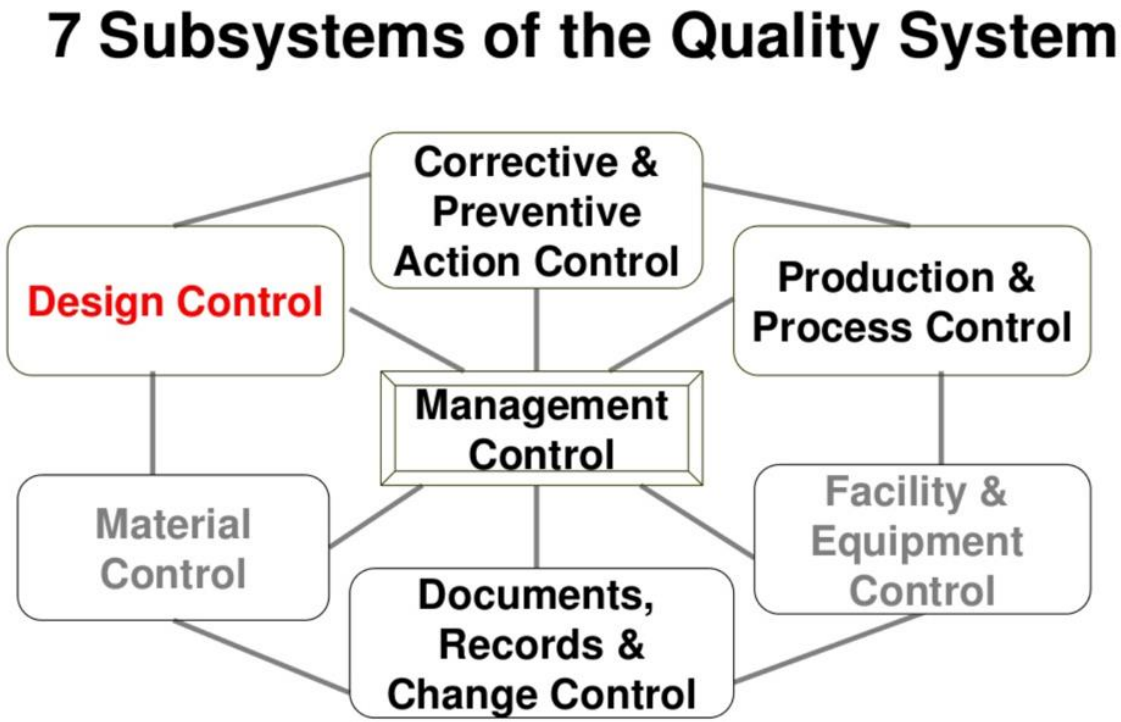
Moving from EUA to 510(k)

What to expect when moving from EUA to 510(k)?

- Expectation that companies that get an EUA will eventually pursue a full 510(k)
- Testing needed to support 510(k) much more rigorous, with more and larger studies required
- Quality Management System and design control requirements under 21 CFR 820 and ISO 13485 must be met for 510(k)

Think about the intended use statement for the EUA, and does it make sense for your 510(k)

- Additional sample types, other use environments, CLIA complexity



Engaging FDA for a 510(k)

Presubmission process

- Submit a formal presubmission package which includes draft intended use, device description, synopses of study designs
- Will receive written FDA feedback within 90 days
- Can request a meeting or telecon with the FDA in the presub if desired
  - VERY little time to prepare for this meeting
- Can submit supplements to a presubmission, and several rounds of discussion may be required for very novel devices (ex. *de novo*)

- Presubmissions for anything non-SARS-CoV-2 are being delayed

Studies Required for a 510(k)

- Varies by test type and user environment but for molecular diagnostics as an example:

MDx EUA

- Limit of Detection
- Cross-reactivity
- Inclusivity
- Clinical Agreement
- Usability studies
- Sample stability
- Lay user studies

MDx 510(k)

- Analytical Sensitivity → Multi-day, multi-lot, more replicates
- Cross-reactivity → More testing, both wet lab and *in silico*
- Inclusivity → More testing, both wet lab and *in silico*
- Interfering Substances → Exogenous and endogenous
- Linearity → If quantitative
- Real-time and accelerated stability
- Sample stability
- Open bottle stability
- Repeatability → Typically 20 days
- Reproducibility → 3 sites, 3x5x5
- Clinical Validation → Must larger multi-site with most samples being prospectively collected
- Usability and Flex studies
- Lay user studies

Open Discussion Q/A

Frequently Asked Questions

Is an EUA required for the testing I want to perform?

How do I find out what I need to do to secure a 510(k) clearance?

If I have an EUA can I get a 510(k)?

What do I need to do to get an EUA for my LDT?

What testing do I need to do to get an EUA?

How long does it take to get an EUA or 510(k)?

How do I start a clinical evaluation study?

What are the challenges and limitations of an EUA?

What are the challenges and limitations of a 510(k)?

Resources

Coronavirus Disease 2019 (COVID-19) Emergency Use Authorizations for Medical Devices

https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices

In Vitro Diagnostics EUAs for SARS-CoV-2 (COVID-19)

https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas

FAQs on Testing for SARS-CoV-2

https://www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-testing-sars-cov-2

The science you expect.
The people you know.

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