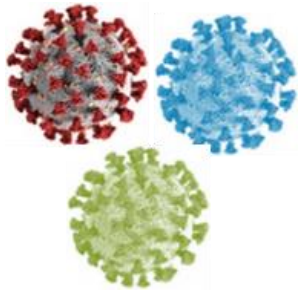


Conversion of a COVID-19 EUA to a 510(k)

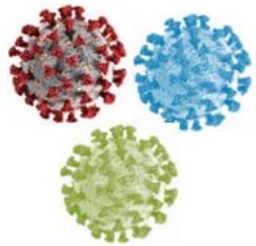
Tara Viviani, Senior Director Molecular Regulatory Affairs

20 April 2023

DiaSorin Molecular

The Beginning of a Pandemic

- WHO issued a global health emergency
- U.S. declared public health emergency in response to the COVID-19 outbreak
- FDA provided templates to guide developers and manufacturers
  - There was a need for rapid development
  - Minimal validation to demonstrate product was safe enough to help fill the need for diagnostics
- No IVDs available at the time



DiaSorin's Response to the Emergency

- The FDA Emergency Use Authorization (EUA) process was available for COVID-19 tests to accelerate the regulatory approval pathway

- DiaSorin Molecular had the capability to rapidly develop a molecular test for COVID-19 and had access to the BARDA funding to potentially defray a portion of development costs

- Interactive reviews and discussions with FDA/BARDA supported the development, validation and manufacturing for the COVID-19 test
  - Assay must be developed for use with an existing FDA-cleared molecular platform currently widely placed in U.S. healthcare settings (LIAISON MDX)
  - Original assay design based on minimizing risk of virus mutations in the variable region
  - Direct Triplex RT-PCR
  - Initially only NPS in UTM and then amend EUA for other claims, as needed
  - FDA recognized clinical samples were not available; therefore they did allow contrived samples for the EUA
  - Testing may be performed internally for EUA activity

Simplexa COVID-19 Direct EUA vs 510(k)

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EUA Strategy

- No Pre-Submission required
- Submit an EUA Interactive Review Template, Including:
  - Intended Use/Indications for Use
  - Summaries of:
  - Design/Operating Principles
  - Kit description
  - Manufacturing and Distribution plan
  - Reagent/Kit Stability plan
  - Sample Handling/Stability
  - Performance studies
  - Labeling
- Necessary studies include:
  - LoD for each sample type
  - LoD confirmation with FDA Reference Panel
  - Reactivity/Inclusivity
  - Cross Reactivity
  - Interfering Substances

510(k) Strategy

- Pre-Submission required
- FDA Guidance Documents available
- Submit Traditional 510(k) (*DeNovo* if no other cleared assays)
- Necessary studies include:
  - LoD for each sample type
  - LoD confirmation with FDA Reference Panel
  - Reactivity/Inclusivity
  - Cross Reactivity
  - Interfering Substances
  - *Reproducibility*
  - *Carry-Over Contamination*
  - *Reagent Stability*
  - *Open Use Stability*
  - *Sample Stability*
  - *Fresh vs Frozen Sample Stability*
  - *Matrix Equivalency*

Challenges

- Performing Analytical studies in real time (FDA requirements change)
- Availability of clinical samples
- Availability of enough raw materials to manufacture
- Labeling Revisions
- FDA staff turnover and file reassignments
- The unknown

Simplexa COVID-19 Direct EUA vs 510(k)

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EUA Claims

- Specimen types - NPS, NS,NW, BAL

- LoD NPS= 500 copies/mL
- LoD NS = 242 copies/mL
- LoD NW = 500 copies/mL
- LoD BAL = 1208 copies/mL

- Clinical Evaluation*
- N = 93 samples including contrived
- NPS = PPA 100%/NPA 100%
- NS = PPA 100%/NPA 100%
- NW = PPA 96.7%/NPA 100%
- BAL = PPA 100%/100%

* Established comparator used

510(k) Claims

- Specimen types – NPS and NS

- LoD NPS= 500 copies/mL
- LoD NS = 242 copies/mL

- Clinical Evaluation*
- N= 1,011 native samples(no contrived)
- NPS = PPA 98.4%/NPA 99.6%
- NS = PPA 98.0%/NPA 99.5%

*CRM consisted of 3 EUA approved NAAT assays

DiaSorin Molecular – COVID-19 Assays

Product	Simplexa™ COVID-19 Direct (K212147)	Simplexa™ COVID-19 & Flu A/B Direct (K220963)
Regulation	21 CFR 866.3981 - Device to detect and identify nucleic acid targets in respiratory specimens from microbial agents that cause the SARS-CoV-2 respiratory infection and other microbial agents when in a multi-target test	
Panel	MI - Microbiology	
Classification	Class II	
Product Code	QQX - Respiratory Specimen Nucleic Acid Sars-Cov-2 Test	QOF - Multi-Target Respiratory Specimen Nucleic Acid Test Including Sars-Cov-2 And Other Microbial Agents
Predicate	Biofire COVID-19 Test 2 (K211079) Submitted 04-12-2021, Cleared 11-01-2021	Biofire Respiratory Panel v 2.1 (DEN200031) Authorized 03/17/2021

Newsworthy Accomplishments

- Simplexa COVID-19 Direct was the 4th EUA product authorized by FDA

- Biofire Respiratory Panel 2.1 was the only cleared product at the time of submission
  - 2nd stand alone SARS-CoV-2 product cleared by FDA

QUESTIONS??

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