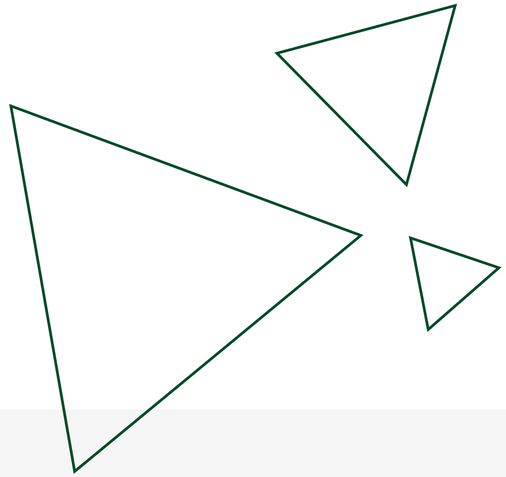
COVID-19 Laboratory Considerations and Strategy

An overview of the impact of Covid-19 on laboratories and recommendations to best prepare your organization



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COVID-19 Background

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Summary

The SARS CoV-2 pandemic has put strain on the clinical laboratory and In-Vitro Diagnostics (IVD) industries. Shortages of COVID-19 test kits. specimen collection supplies, and transport products have resulted in the supply chain not being able to keep pace. Each hotspot in the US will be on its own curve, because initial cases arrived at different times. This presentation is directed at laboratorians and hospital administrators to help them navigate the maze as they develop strategies for testing.

FDA & CDC

Using their Emergency Use Authorization (EUA) authority, the FDA has streamlined their approval process to facilitate the release of as many commercial kits as soon as possible, and have granted states CLIA authority over laboratory developed tests (LDTs) for COVID-19 without FDA oversight and approval.

In-Vitro Diagnostic Companies

Over 200 companies have investigated the EUA process; as of 3/30, 20+ vendors have been authorized by the FDA to sell kits; all of EUA approved assays are molecular amplified methods, with 2 designated Point of Care (POC). 42 companies have/will be introducing serology assays to identify previous exposure. Most of these assays were developed in Asia where Ab testing is more prevalent than MDx assays.

Clinical Laboratories

As of 3/30, over 100 US labs have begun testing for COVID-19; 50+ are listed on the FDA's website as running LDTs . Most labs cannot secure enough inventory to meet demand, and have been forced to improvise collection kits and transport media. Most large reference labs now offer testing, but turnaround times have not been optimal.

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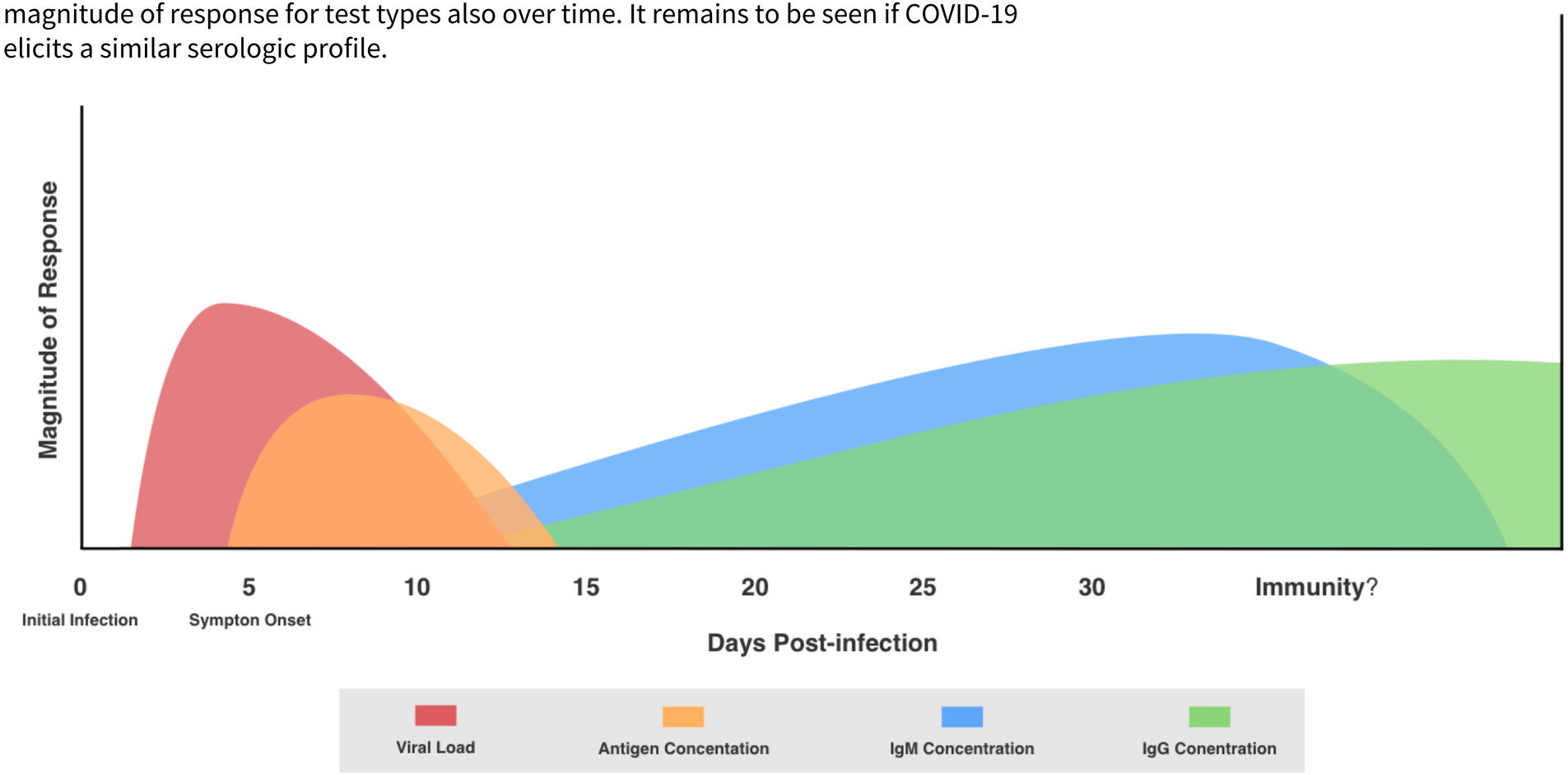
Typical Viral Serologic Profile

Different test types are effective at different time intervals post-infection. The magnitude of response for test types also over time. It remains to be seen if COVID-19 elicits a similar serologic profile.



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COVID-19
Impact on Lab

Decrease in non-COVID-19 Test Volumes

With physician offices transitioning to tele-medicine, fewer lab tests are being ordered, and patients are hesitant to visit patient service centers (PSCs). Labs must adjust their staffing models to meet changes in volume.

Increased Emphasis on COVID-19 Testing

Hospitals are balancing testing demands for their patients and health care providers with their laboratory's struggle to meet demand. Testing inpatients and health care providers have been prioritized over other requests.

Increased Dependence on IVD and Ref Lab Vendor Relationships

As IVD vendors transition from R&D to production, they are preferentially supporting existing customers, but even then with quotas on products.

New customers face long queues to order new equipment, without guaranteed reagent delivery. Consequently, labs are forced to contract with multiple vendors to ensure access to product as well as multiple reference labs as insurance against long turnaround times.

Reference Labs perform the bulk of testing in the US, albeit with huge variation in turnaround times (TAT) as they expand their test capacity.

Opportunity for Administrators to Work Closely with Labs to Develop a Plan

Hospital and laboratory executives need to meet regularly to communicate test strategies, especially with changes associated with patient flow and laboratory capacity.

Integrating multiple variables into a cohesive deliverable plan.

Health care systems need to consider a multi-vendor strategy targeting core lab and POC products to address institutional requirements, balancing acute needs without committing to undesirable obligations and compromising long term objectives.

Testing Objectives

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Overview

COVID-19 testing objectives will change as the disease progresses. The earliest stages will focus on testing for infectivity to help triage patients, and back-track exposure to determine the scope of isolation for specific populations. As the disease progresses, in addition to patient triage, testing for Antibodies to COVID-19 will help identify patients who have been exposed and resolved their infection, especially to support health care providers to re-enter patient care. Late-phase requirements will integrate COVID-19 testing into respiratory viral panels.

Disease Progression Phases

Acute-phase (March-June?)

For immediate-term the goal of testing is to identify, triage, isolate, and remediate cases. Testing will be expanded beyond the core lab to include POC platforms that will provide test results while patients wait. Begin community screening initiatives.

Mid-phase (July-October)

The middle phase represents an expansion of testing from triage to assess convalescence and immunity, especially for health care providers who have been exposed and want to get back to patient care.

Late-phase (November+)

As the disease transitions from an acute pandemic to seasonal management, COVID-19 testing will be integrated into respiratory viral panels that already detect Influenza (Flu A/B) and Respiratory Syncytial Virus (RSV).

COVID-19
Testing Options

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Laboratory Test Types

Molecular (MDx) RNA

Modular (core lab)-mid/high volume
Semi-automated modules sequentially extracting, amplifying, and then detecting viral load.

Integrated (core lab or POC)-low/mid volume
Cartridge based integrated test packs run on automated platforms.

Immunoassay (IA) Serology-Ag, Ab

Automated (core lab)-mid/high volume
Ag and Ab serology assays run on track based IA platforms; anticipate vendors will introduce kits over next 1-2 months (May-June).

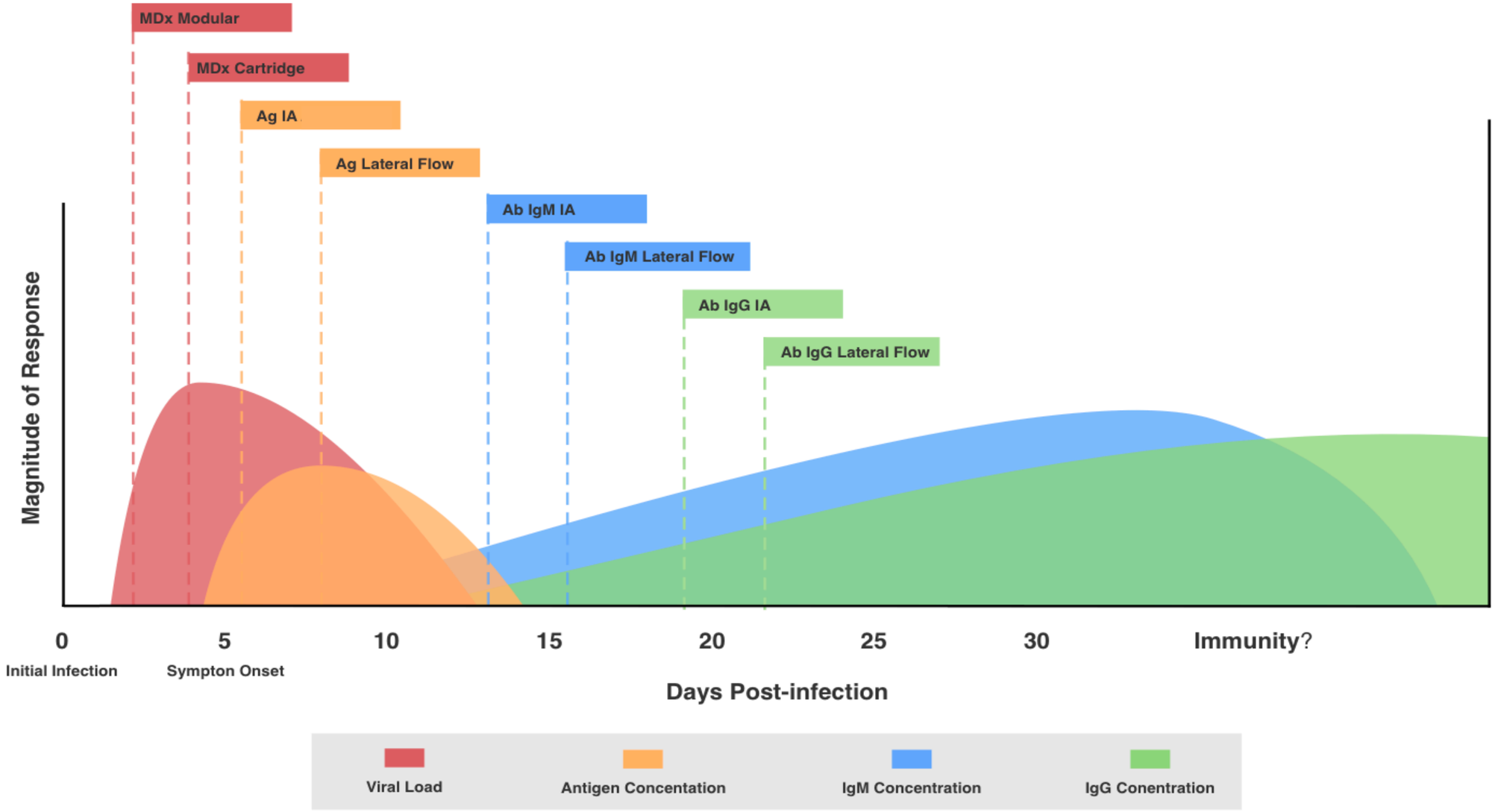
Integrated (POC)-low volume
Handheld devices targeting Ab and possibly Ag. Decentralized results wirelessly connected to EMR.

Lateral Flow Serology-Ab

Visually or instrument read manually performed POC Antibody assays targeting low volume settings. ~42 vendors have informed the FDA that they will be bringing kits to market, primarily in a self-contained cartridge that qualitatively measures IgM and IgG Antibodies to COVID-19. Assay performance specifications may not be equivalent to IA platforms, and there have been reports of poor performance using kits made in Asia.

Serologic Testing Options

Time to test for different methodologies are based on typical serologic profile.



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Testing Considerations

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Validation Requirements

MDx

Limit of Detection (LOD)
Clinical Evaluation (30 reactive, 30 non-reactive)
Inclusivity (100% across all published SARS-CoV-2 sequences)
Cross-reactivity

Antigen Assays

Analytical Sensitivity (LOD)
Analytical Specificity (Cross Reactivity)
Microbial Interference
Clinical Agreement Study

Serologic (Antibody) Assays

Cross-reactivity/Analytical Specificity
Class Specificity
Clinical Agreement Study

Off-Label Use

If an EUA approved assay SOP is modified, the FDA recommends a “bridging study” in lieu of a full validation.

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Specimen Collection and Transport Requirements

IFU Approved Types for Specimen Collection

- Nasopharyngeal (NP)-(preferred specimen)
- Oropharyngeal (OP)
- Nasal Swab (NS)*
- Nasal Turbinate (NMT)
- Sputum
- Nasal Wash (NW)

Unapproved specimen type is “off-label” use, and is considered a LDT

** FDA has determined NS is an acceptable alternative to NP, and has approved home self-collection*

Specimen Transport

- Viral transport media (VTM)
- Universal transport media (UTM)
- Saline (emergency use if other media NA). Note-may be considered off-label

Specimen Application

- Depending on the IFU, specimens can either be applied directly to a cartridge (POC) or eluted to a a viral transport media (VTM and/or UTM).

Testing Considerations

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Operational Requirements

Equipment Platform
Pre-existing: leverage current IVD relationships

New: Does placement on queue require conditional PO?

Does platform choice synch with long term plans?

Quality
Sensitivity (LOD): positivity in disease
Specificity (interferents): negativity in health

Turnaround Time (TAT)
Does TAT meet clinical objectives?

Cost
Equipment (Capex, Service)
Reagents ($/test vs. $/total patient encounter)

Portability
Core Lab vs. POC (cart based or hand-held)

Result Connectivity
Wireless interface to EMR

Recommended Strategy

Phase I

Contract with 2+ reference labs (ideally those with pre-existing interfaces) to address fluctuations in TAT as crisis evolves. Monitor TAT daily, and re-direct specimens as necessary to minimize report delays.

Phase II

Evaluate commercially available (core lab based) EUA kits, preferably on platforms lab presently uses. Contract with 2 vendors to ensure adequate supply of reagents.

Phase III

Evaluate commercially available (POC) EUA kits as they become available. Contract with 1-2 vendors to ensure adequate supply of reagents. Consider both MDx and Ag/Ab based platforms (preferably 1 of each, ideally single platform) to address testing requirements for both infectivity/triage and immunity.

Phase IV

Evaluate respiratory viral panel test options to prepare for fall/winter seasonal requirements; determine if COVID-19 will be requested by medical staff, and if so, if it will be included by vendor.

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Key Points

Ensure new IVD contracts dovetail with long term platform strategy

Communicate daily with hospital admin to ensure timely support for Capex and Opex resources

Communicate with medical leadership to inform them of changing environment and to keep pace with their test objectives

Leverage vendor relationships to ensure support is available and reagent quotas are met

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Future Considerations

Antigen Testing

Will Antigen test sensitivity and performance be clinically equivalent to Molecular amplified techniques?

If so, will lower cost higher throughput IA platforms be the platform of choice to provide a full patient disease profile from infectivity (Ag) to immunity (Ab)?

Quantitative Testing

Viral Load or Antigen: Does quantitative value correlate to disease progression and stratify risk?

Antibody Titer: Will high titers identify patients to target blood collection for immune Ab therapy?

Seasonal Viral Panel

Will SARS CoV-2 recur seasonally, and if so how will it be integrated into seasonal viral respiratory panels?

Current: Flu A/B, RSV

Future?: Flu A/B, RSV, COVID-19 (Ag, Ab)

COVID-19 Strategy Hotline

Get your COVID-19 Response Questions Answered by NMG Experts

We have been working with our clients on the challenges their labs face as COVID-19 progresses. What are yours? Send us your questions at: covid19@nicholsmanagementgroup.com

Stay Tuned for Insights and Strategies

Our team of experts will be sharing a series of articles with insights to empower your lab in the uncertain days ahead. We are all in this together. Our posts will cover the impact of COVID-19 on overall test volumes, turnaround time (TAT), costs, equipment considerations, and more.

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We're Here.

Get in touch and learn more about positioning your lab to best navigate this uncertain time.

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FDA/CDC/CMS Guidance

February 4th, 2020

HHS determined that there is a public health emergency and that circumstances justify the authorization of emergency use (EUA) of In-vitro diagnostics (IVD) for detection and/or diagnosis of novel coronavirus (nCoV).

February 29th, 2020

FDA Issues New Policy to Help Expedite Availability of Diagnostics

March 16th, 2020

FDA Provides More Regulatory Relief During Outbreak, Continues to Help Expedite Availability of Diagnostics

-- States to take responsibility for tests developed and used by labs in their states

--Agency does not intend to object to commercial manufacturers distributing and labs using new commercially developed tests prior to the FDA granting an EUA (15 day window)

--FDA does not intend to object to the distribution and use of serology tests to identify antibodies to SARS-CoV-2 where the test has been validated, notification is provided to the FDA, and warning statements are included with the tests

March 20th, 2020

FDA Alerts Consumers About Unauthorized Fraudulent COVID-19 Test Kits (for home use)

March 24th, 2020

Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons for Coronavirus Disease

Allowance for self- or healthcare worker-collected nasal (NS), nasal turbinate (NT) or oropharyngeal (OP) swabs as an acceptable specimen type if nasopharyngeal (NP) swab is not possible

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Antibody Test Disclaimer

Tests have not been reviewed by FDA

Negative results do not rule out COVID-19 Infection

Particularly in those who have been in contact with the virus. Follow-up testing with a molecular diagnostic should be considered to rule out infection in these individuals.

Results from Antibody Testing Should Not Be Used as the Sole Basis to Diagnose

Nor exclude SARS CoV-2 infection or to inform infection status.

Positive Results may be due to Past or Present Infection with non-SARS CoV-2 Coronavirus Strains

Could be due to coronavirus HKU1, NL63, OC43, or 229E or past or present infection with SARS virus (no. 6)