

COVID-19 Rapid Response Impact Initiative | White Paper 9v2

The Mechanics of the COVID-19 Diagnostic Testing Supply Chain: Version 2.0

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Testing is an essential and fundamental component of any strategy to relieve aggressive social distancing measures, reopen the economy, and begin to return Americans to a more normal life. In the United States we are currently delivering approximately 1 million test results per week. To deliver a safe social opening by June 30, we need to deliver 5 million tests per day with results returned in 12-24 hours. The number of test results delivered will need to increase to 20 million per day by July 30 to fully re-mobilize the economy. Although such an effort will be expensive – it will cost about \$15 billion per month – it represents enormous savings compared to the \$350 billion monthly cost of our current collective quarantine. This paper begins to detail how America can boost and innovate its testing supply chain to reach the necessary level of daily testing. We argue that this can be achieved through a combination of scaling up existing approaches, small- and large-scale innovations, and 30 mega-labs established across the country to perform high throughput processing (1-3 million tests per day) with 12-24 hour turnaround. This would achieve the testing scale necessary to support targeted tracing and isolation strategies that will enable Americans to safely re-engage in normal life.

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01 Overview

Testing is an essential and fundamental component of any strategy to relieve aggressive social distancing measures, reopen the economy, and begin to return Americans to a more normal life. When combined with contact tracing, accurate test results guide decisions about who can circulate and who needs to be isolated or quarantined. They also provide macro information about where the virus may be more or less prevalent in certain communities. Evidence is mounting that many people infected with the coronavirus have minimal or no symptoms, making it essential that large numbers of seemingly healthy people be tested. The more reliable the test data, the more focused and targeted can be the interventions. Without sufficient test data, only the most expensive strategies like aggressive social distancing can protect our healthcare system capacity and, ultimately, our citizens.⁴

In the United States we are currently delivering approximately 1 million test results per week.⁵ The recipients of these tests are not distributed evenly across the country. For example, patients in New York State received approximately 150,000 test results last week, while those in Arkansas received approximately 5,500. Among other things, that is a function of the different levels and rate of infection in those two states. We need to test not only to diagnose people, but to help stop future infections. This means we must test seemingly healthy people too. To do that, we need to scale up to deliver a much larger number of tests all over the country.

To deliver a safe social opening by June 30, we need to deliver 5 million tests per day with results returned in 12-24 hours. The number of test results delivered will need to increase to 20 million per day by July 30 to fully re-mobilize the economy.⁶ Although such an effort will be expensive – it will cost about

⁴ This paper is focused on the supply chains for diagnostic rRT-PCR tests. Serology testing for SARS-COV-2 antibodies is beyond the scope of this paper.

⁵ COVID Tracking Project, <https://covidtracking.com/data>, consulted on April 19, 2020.

⁶ Siddarth and Weyl, “Why We Must Test Millions a Day,” https://ethics.harvard.edu/files/center-for-ethics/files/white_paper_6_testing_millions_final.pdf, consulted on April 20, 2020

<https://ethics.harvard.edu/covid-supply-chain>

Overview

\$15 billion per month – it represents enormous savings compared to the \$350 billion monthly cost of our current lockdown. It is also far less expensive than the cost incurred if we have to go into recurring lockdowns, as multiple waves of the virus strike in the fall/winter. Investment in this testing capacity not only will provide the infrastructure and processes necessary to withstand future waves of COVID-19, but it will also enable more effective and targeted responses to other contagious illnesses such as influenza, and protect the nation from future pandemics.

02 Current Testing Process and Supply Chain

The current testing procedure and supply chain is depicted on the left side of Figure 1.

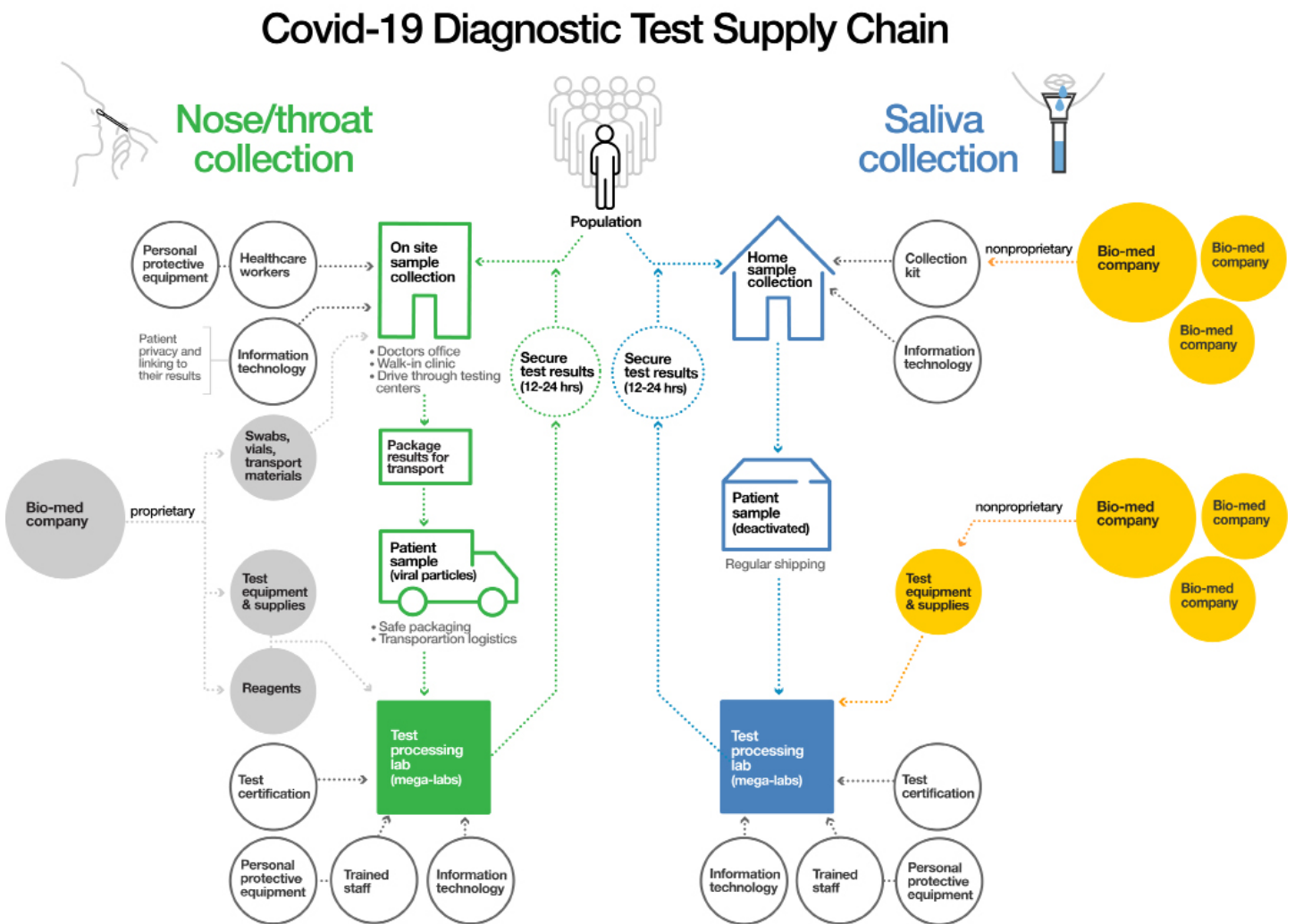


Figure 1.

Conducting a test to determine whether a person is confirmed positive for COVID-19 requires that a sample be collected with a nasal swab by a medical health worker wearing personal protective equipment (PPE). These samples must be collected at a specially protected facility, which may be a doctor’s office, a walk-in clinic, or increasingly at drive through testing centers. In all cases, a safe and protected

Current Testing Process and Supply Chain

area must be provided since those being tested may be infected. In addition to needing adequate safe space for processing patients, there are several kinds of resources needed at these test collection facilities that can constrain test collection volume: swabs; vials; packaging for collecting, storing, and shipping samples; healthcare professionals to collect the samples; and personal protective equipment to protect healthcare workers from infection. Once a sample is collected, because it is a level 3 bio-hazard, it must be handled and shipped in accordance with regulations to protect those handling the shipment and the public.

When the sample is received at an FDA certified processing lab, it is tested for presence of the virus. Potential capacity constraints at the processing lab include: the number of test devices/platforms and the rate of throughput of those devices; the number of laboratory staff to process test samples; personal protective equipment for the staff; safe space available for the work, and the supply of reagents necessary to extract and purify the RNA from the sample for testing. Secure information technology must be in place to ensure that test results can be communicated back to the referring healthcare professional accurately while ensuring patient privacy.

This supply chain and associated processes for COVID-19 testing are overlaid on an existing industry and marketplace for biomedical testing. There are many private equipment and test providers, labs, medical supplies providers, transport agencies, and so on, that are engaged in commercial activity to serve that marketplace. Most deliver products using proprietary technologies, processes, and materials. Companies provide inputs through interdependent links in this supply chain, which are enormously complex and are normally aligned through market forces. This competitive free market, which has many benefits for producers, consumers, and society at large, cannot produce maximum output over very short time periods. To maximize output within the timeframe imposed by this pandemic, these companies need to receive demand signals and financial assurances to de-risk necessary capital

Current Testing Process and Supply Chain

investments, while the overall process must be coordinated and monitored to ensure that obstacles to production and delivery are overcome to meet societal needs. This role can be overseen by a Pandemic Testing Board.⁷

⁷ Akin to the War Production Board created in World War II, the Pandemic Testing Board would be established by the Federal Government with strong but narrow powers to invest in the infrastructure and provide the coordination necessary to meet test throughput goals. See “The best way out of this pandemic is to massively scale up testing. Here’s how to do it,” Danielle S. Allen, Washington Post, April 10, 2020.

<https://ethics.harvard.edu/covid-supply-chain>

03 **Scaling Existing Test Capacity** (achieving the first 2 million tests per day)

Meeting the desired testing throughput will require federal and state intervention to help existing companies better align their outputs and inputs to accelerate the completion rate of COVID-19 tests. From channel checks with major commercial labs (beyond LabCorp, Quest, BioReference, etc), it is clear that latent capacity exists, provided there is a sufficient demand signal to expand, a better means to coordinate with demand, and where the economics are rational, for these players to make fixed cost investments. We believe that better coordination of the supply chains associated with the test process can deliver an order of magnitude more test results with better organization and clear demand assurances. The first responsibility of the Pandemic Testing Board would be to provide that necessary leadership and guidance.

Acting on this guidance will require overcoming some CDC regulations, accelerating the production of the materials for test kits, and modernizing processing labs to increase throughput. The current limiting factors on sample collection include the volume of swab production and PPE production. Both swab and PPE production could be addressed by repurposing idle plant capacity; in the textile industry in the first instance, and in plants in Puerto Rico in the second instance. A broader survey of available capacity should be done. It is likely that once one set of constraints are overcome, new constraints will emerge, and it would be the responsibility of the PTB to respond and adjust to those situations as necessary.

Improvements in Sample Collection

The three options for collecting samples are: doctor's offices and urgent care facilities; newly established testing sites (e.g. drive thru sites); and test kits that can be used at home. The first two collection modes require setting up separate spaces for infection control as well as trained healthcare workers with personal protective equipment to collect patient samples. Mayors and county health officials are

Scaling Existing Test Capacity (achieving the first 2 million tests per day)

Improvements in Sample Collection

already assessing how their states can ramp up testing locations. A key component for ramp up would be a Health Reserves Corp, working alongside the national guard, that could remobilize the unemployed for employment in this industry.

The capacity of sample collections sites could also be increased by improvements in website and app support for identifying testing locations. A website/app could allow for individuals to provide information on their symptoms, risks, and exposures with an authorization (i.e., a QR code) that would provide direction on where to get tested along with a fast-pass prioritization for the appropriate testing provider. The highest risk exposures would get prioritized for test supply that is most proximate to the individual (e.g., a drive-through site with a Point-of-Care system) while lower-risk exposures would get routed to less immediate test channels (e.g., self-administered home test kit). More often than not, the system should direct someone to a testing channel that is not embedded in the healthcare system (e.g., ER/hospital, clinic). The third mode, do-at-home kits, imposes the least demand on personnel and infrastructure and should be a high priority for the FDA. These test kits would require a sample collection protocol using lower nasal and/or throat swabs that can be safely transported at ambient temperature.

Improvements in Sample Analysis and Test Processing

In addition to the constraints on test delivery imposed by the collection of patient samples, there are also constraints that emerge in the evaluation of patient samples in the processing labs. Innovations to increase the throughput rate of existing labs should be pursued, particularly those that would favor lab structures with generic robots and plates that can be easily adapted. Innovative lab designs can then be cloned and replicated. New capacity of this type is already coming online. A good example of the elements and pace for establishing a new high throughput lab can be found in this account of the Broad's rapid transformation: <https://news.harvard.edu/gazette/story/2020/03/broad-institute-races-to-enable-coronavirus-testing/> With prior experience analyzing 250,000 samples a day for the Human

<https://ethics.harvard.edu/covid-supply-chain>

Scaling Existing Test Capacity (achieving the first 2 million tests per day) ***Improvements in Sample Analysis and Test Processing***

Genome Project, the Broad is a model of the kind of lab that could be developed for mega sample processing (“mega-labs”) and that could supplement existing capacity to rapidly accelerate the rate of test analysis. These mega-labs can be either existing labs with footprint to grow, or greenfield labs that are set up near population centers.

Another promising area of innovation would be to eliminate the need for RNA purification. Various labs are working on this now but there is not sufficient demand to justify the capital investment. This would be an important innovation because lack of sufficient supplies of reagents is the most commonly cited constraint preventing increased testing throughput.

It is important to recognize that due to transportation challenges to some areas, it will also be valuable to increase the number of devices like the Abbott ID Now machines (now capable of a rapid result COVID-19 test) in the field. Although these machines have low throughput, they would be an important component in the overall system by reducing shipping latencies for testing in rural locations. Rapid in-clinic antigen test devices, like the one recently announced by Bosch to operate on the Vivalytic platform, may also play a valuable role in decreasing test result latency.

Other key components of the test processing systems that would need to be part of an industrial ramp up include: production of collection kits and test tubes; improved transportation logistics to reduce shipping times, including the possibility of making the virus inactive so that it need not be handled/shipped as a biohazard; barcoding, security, and communication systems and protocol that ensure accuracy but protect patient privacy; and technology necessary to certify testing status.

In addition to these steps to address supply backlogs and invest in innovative processing technologies, a monitoring system should be developed that provides visibility into the availability of specific test

Scaling Existing Test Capacity (achieving the first 2 million tests per day) ***Improvements in Sample Analysis and Test Processing***

centers/locations/services along with estimated wait times. Every capable COVID sample collection site and test processing lab should be mandated to provide near-real-time data on capacity, utilization, and forward visibility for supply-demand management. This dynamic matching of supply with demand is critical to overcome the supply chain bottlenecks of the current paradigm of lab testing in healthcare, which is not designed for the kind of high-speed routing of tests to a federation of lab vendors essential to meet the current challenge.

04 Mechanics of Massively Scaling Up Testing – Aiming for 100 million Tests per Day

Massively scaling up testing will require breakthroughs both in sample collection and processing technologies and approaches. We highlighted some of the processing innovations possible at labs through the work of places like the Broad Institute, but the single most impactful innovation would be to change the way that samples are collected from patients. The current process of collecting samples with nasal swabs is invasive and can be difficult to administer, leading to errors in collection. It also introduces multiple chokepoints in the process, including the availability of safe testing sites, swabs, healthcare personnel, and personal protective equipment.

Fortunately, a potentially transformative approach is on the horizon. On April 13, the FDA awarded RUCDR Infinite Biologics an emergency use authorization (EUA) for a saliva kit coronavirus test that can be self-administered. Other labs and companies are working on similar approaches. Not only does this sample collection kit make it possible for a patient to easily provide a sample from home, but the virus is also deactivated in the collection kit so that it is not a biohazard, allowing the sample to be shipped through normal means.

The wide availability of effective saliva collection kits to test for SARS-COV-2 would be a transformative innovation. It would eliminate many of the supply chokepoints, reduce errors in sample collection, and greatly simplify the testing process. It would also make it possible for test samples to be collected accurately and reliably by other entities that have a vested interest in maintaining safe local environments, such as schools or employers. This would create multiple points of leverage for accelerating the number of tests that could be administered to the population.

The right side of figure 1 depicts the supply chain for saliva test delivery.

Mechanics of Massively Scaling Up Testing – Aiming for 100 million Tests per Day

Obviously, a key capacity constraint will immediately emerge; namely, the rate of production of these saliva collection kits and the materials and equipment to test them. Fortunately, the technology used to create these kits is non-proprietary, and RUCDR Infinite Biologics is making the technology available to other companies to deploy.

If such a non-proprietary solution proves effective and reliable, the government could choose to favor such non-proprietary solutions in its establishment of mega-labs. These mega-labs could be the rallying point for creating new capacity; using the latest technologies, a single mega-lab should be capable of handling >1 million PCR tests/day. Defining the specifications for these mega-labs should be done in consultation with key equipment and reagent suppliers (e.g., Roche and Thermo Fisher), who could then bid to supply their newest machines and dedicate increasing reagent supply to these non-proprietary testing methods. Entities like the Lawrence Berkeley National Lab could also play a valuable role in the mix. Standing up approximately 30 mega-labs across the country to perform high throughput processing (1-3 million tests per day) with 12-24 hour turnaround would achieve the testing scale necessary to support targeted tracing and isolation strategies that will enable Americans to safely re-engage in normal life.

05 Appendix

Existing Firms and Products

This website has a list of all tests available – however, most manufactures haven't given detailed commentary. Many of the commercial players would probably comment on earnings. For example Quest said they can do 45k/day now. https://www.finddx.org/covid-19/pipeline/?section=molecular-%20assays#diag_ta

Current State of Supplies

Swabs & PPE: Sample collection has been a choke point for increasing testing throughput in the United States, in part due to a shortage of swabs from the two manufacturers (Copan, Puritan). There are only ~6M /week nasal swabs being made now (1M from Puritan and 5M from Copan) and that needs to increase significantly to meet any goals. FDA has a list of alternatives due to shortages, but we don't know much about their supply:

Nasopharyngeal:

- Puritan: 25-3316-H, 25-3316-U, 25-3317-H, 25-3317-U, 25-3318-H, 25-3318-U, 25-3319-H, 25-3319-U, 25-3320-H, 25-3320-U, 25-3320-H EMB 80, 25-3320-U EMB 80, 25-3320-H EMB 100, 25-3320-U EMB 100, 25-1406 1PF 50ff, 25-800 1PD 50**, and 25-800 1PD ALUM 50**
- Copan: 503CS01, 518CS01, 501CS01, and 502CS01
- BD: 220252 and 220251
- DHI/Quidel: 503CS01.DHI
- Fisher Healthcare : 23600952, 23600956 and 23600950

Further Detail

Current State of Supplies

Oropharyngeal:

- Puritan: 25-1506 1PF SOLIDf, 25-1506 1PF 100f, 25-3206-H, 25-3206-U, 25-3706-H, 25-806 1PD** and 25-806 1PD BT**
- Copan: 502CS01, 519CS01, 164KS01** and 175KS01**
- BD: 220250
- Fisher Healthcare: 23600950, 23600957 and 1490650**

Mid-Turbinate:

- Copan: 56380CS01, 56750CS01, 56780CS01

Anterior Nares:

- Puritan: 25-3206-H, 25-3206-U, 25-3706-H, 25-1506 1PF 100f , 25-1506 1PF solid f, 25-1506 1PF BTf, 25-1506 1PF TT MCf, 25-1506 2PF BT f, 25-1406 1PF BT***f
- Copan: 502CS01, 519CS01
- BD: 220144f, 220145 f, 220250
- DHI/Quidel: 20103f
- Fisher Healthcare: 23600950, 23600957

f Foam swab

** Polyester swab

Additionally, swabs may be provided with transport media as identified below.

Further Detail

Transport Media

VTM/UTM remains the preferred transport media. Examples of universal transport media for viruses and molecular transport media are listed here. All of the products listed below include a nasopharyngeal (NP) flocked swab unless noted otherwise.

- Copan: 305C, 307C, 360C and 519CS01*
- Puritan: UT-367, UT-317, UT-302*, UT-366** and UT-300***
- Hardy/Healthlink: 330CHL
- BD: 220526, 220527, 220528*, 220529, 220531
- DHI/Quidel: 330C***
- Fisher Healthcare: 23001718, 23600952, 23600956, 23600950 and 23600957*
- PrimeStore MTM: LH-1-02 and LH-1-03***

* flocked oropharyngeal swab

** Polyester swab

*** no swab

In the absence of VTM/UTM, alternative transport media can be used to collect and transport patient samples for molecular RT-PCR SARS-CoV-2 assays. These recommendations apply to swab-based specimen collection by healthcare providers (HCP), and to anterior nares (nasal) and mid-turbinate specimen collection onsite by self-collection. The best available evidence indicates that these transport media will stabilize the SARS-CoV-2 RNA without meaningful degradation.

Further Detail

Transport Media

Labs can create their own viral transport media. Refer to [CDC's SOP#: DSR-052-01: Preparation of Viral Transport Media](#). Specimens can be stored for up to 72 hours at 4°C.

Liquid Amies media may be used for viral transport when universal transport media is not available. Specimens can be stored in liquid Amies media for up to 72 hours at 4°C. All of the products listed below include a nasopharyngeal (NP) flocked swab unless noted otherwise.

- Copan: 481C, 482C 480C* and 480CFA*
- Puritan: LA-117, LA-116-H and LA-100***
- BD: 220246, 220532 and 220245*
- ThermoFisher: R723481, R723482 and R723480*
- Hardy/Healthlink: 481C, 482C 480C* and 480CFA*
- VWR: 89136-656, 89136-658, 89136-654* and 76181-494*
- Fisher Healthcare: 23600901, 23600902, 23600900* and 23600905*

* flocked oropharyngeal swab

*** no swab

Other solutions may also be used for viral transport when universal transport media is not available. FDA recommends use of phosphate buffered saline (PBS), including molecular grade PBS when available, and other similar formulations including Delbecco's PBS, to collect and transport samples for molecular RT-PCR SARS-CoV-2 assays. If PBS is not available, normal saline may be used. FDA believes that a sterile glass or plastic vial containing between 1mL and 3mL of PBS or normal saline is appropriate. Specimens can be stored up to 72 hours at 4°C. All the products listed below are examples of 1-3 mL of normal saline distributed in a vial without a swab.

<https://ethics.harvard.edu/covid-supply-chain>

Further Detail

Transport Media

- ThermoFisher: R064430, R064432, R064434, R064436 and R064438
- Hardy/Healthlink: D185, K248, R45 and R55
- Edge Biologicals: T-0625 and T-0110f

There is limited data available on test performance with specimens which have been frozen in any transport media; therefore, specimen stability should be investigated if freezing is necessary.