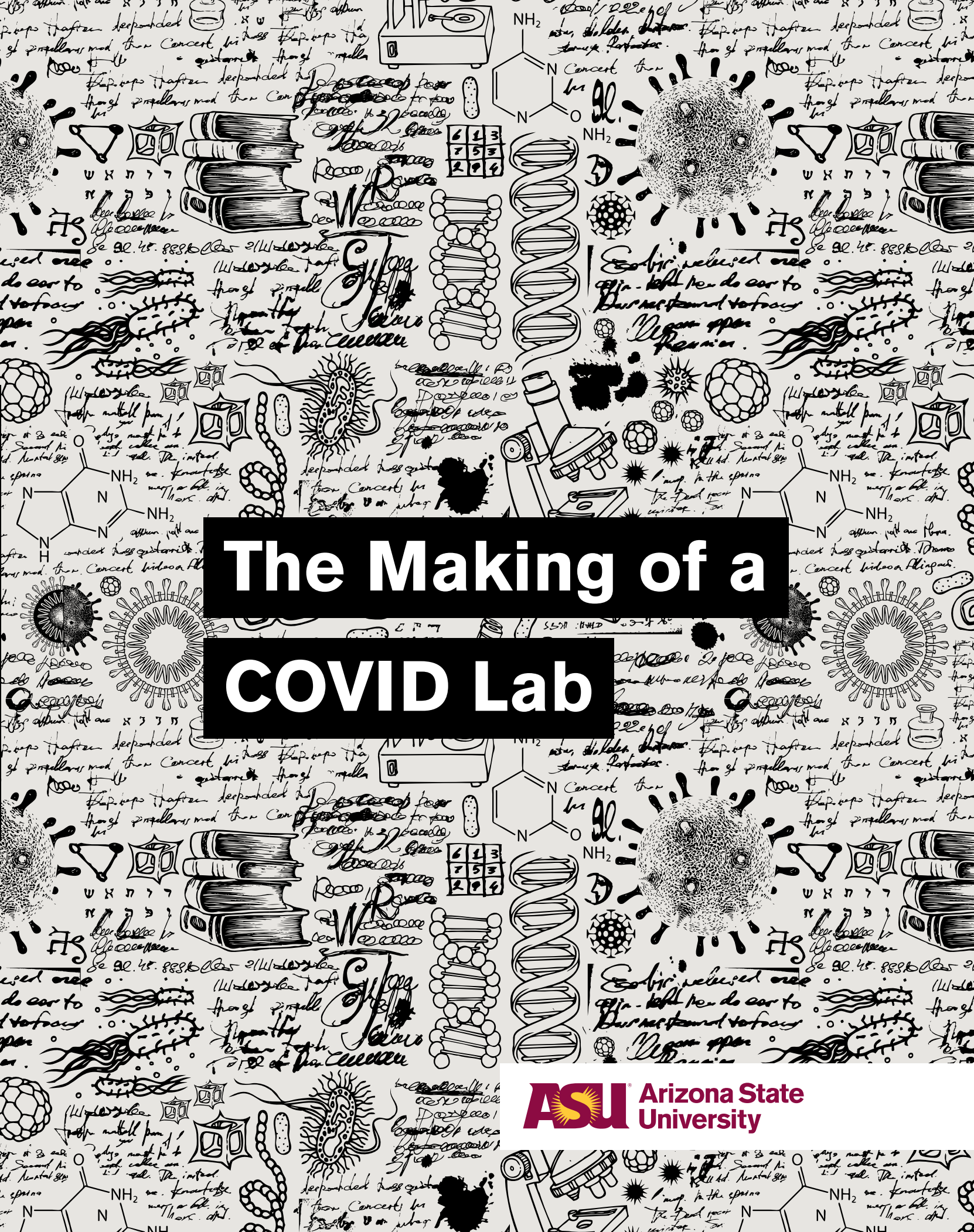


The Making of a COVID Lab

Arizona State University

Preface

This Project Report documents the accomplishments of an extraordinary group of students, faculty, and staff at the Arizona state University, who participated in a year-long, multidisciplinary, first-of-its-kind academic endeavor entitled “The Making of a COVID Lab.” The lab that is the focus of this project is the ASU Biodesign Clinical Testing Laboratory, known simply as the ABCTL.

“The Making of a COVID Lab” represents a multidisciplinary team honors project, the largest ever to be supported by the Barrett Honors College, comprised of 38 students who competed to enter the project in August 2020. The project was conceived and lead by Dr. Carolyn Compton, the Medical Director of the ABCTL, but was team-taught by expert faculty from more than seven different schools, colleges, and institutes across ASU including the School of Life Sciences, the Hugh Downs School of Communications, the Sidney Poitier New American Film School, the WP Carey School of Business, the Sandra Day O’Connor College of Law, the Ira A. Fulton Schools of Engineering, and the ASU Biodesign Institute.

The project comprises a detailed academic study of the critical aspects of the establishment, regulatory certification, expansion, and operation of a high-complexity, high-throughput clinical (medical) testing laboratory for the diagnosis of Sars-CoV-2 during

the COVID-19 pandemic. The process afforded students a once-in-a-lifetime learning opportunity. In designing the project, the ABCTL was deconstructed into key component elements falling under 6 specific domains: legal and regulatory issues, business operations, scientific and technical solutions, communications challenges, training and management requirements, and information technology solutions. The team of students working in each domain performed extensive research on a specific subtopic relevant to laboratory medicine, in general, and/or the ABCTL, in specific, to become the subject matter expert for the project. The 7th team of students, under the direction of experienced documentary film makers from the ASU faculty and staff were charged with creating a short documentary film intended for a general audience that told the story of the ABCTL, guided by the expertise of their colleagues on the project to assure the veracity of the film subject matter.

For two semesters, each team met weekly for an hour with Dr. Compton and their faculty leaders to discuss their research, and the entire project membership was convened once a month at an all-hands meeting for updates and progress reports from each team. At the end of the project, each student submitted a written thesis on their topic and defended their thesis in an oral presentation, as per Barrett requirements. Those theses form the individual chapters of tis Project Report.

The documentary film team produced an 18-minute film that was shown at a public event on April 22, 2021 and highlighted on a news segment on PBS. Following the film, the students conducted an open discussion and answered questions about their roles in the film development, the specific processes they carried out, and their scholarly studies on the artistic and technological aspects of documentary film making.

This project has established a new precedent for ASU and Barrett Honors College alike and is proudly documented herein. The subject of the project, the ABCTL itself, has established a new precedent for ASU in meeting the urgent need for diagnostic testing amidst the worst pandemic in a century despite having no prior experience in the practice of clinical laboratory medicine. It is hoped that the Report may serve as a roadmap for others in the future and stand as a testimony to the resilience, ingenuity, and altruism of ASU and its community of student, faculty and staff.

Project Director: Prof. Carolyn Compton, MD, PhD

Project Managers: Serena Christianson, EdD and Christopher Floyd, MEd

Business: Contracts; Billing; Quality Management Systems; Lean 6 Sigma; Scheduling; supply chains; inventory

Faculty Leader: Prof. Gene Schneller

Students

- Claire Agee
- Sam Cosgrove
- Corine English
- Kyle Mattson
- Kyle Qian

Communications: Internal/among groups, External/ website/customers, Patients, Public/website

Faculty Leader: Pauline Cheong

Students

- Van Dexter Calo
- Matt Nofi
- Courtney Raymond

Information Technology: data transmission; logistics and identification control; registration; barcoding; return of results (Point N Click™ system)

Faculty Leader: Prof. Sean Dudley

Students

- Mani Kandan
- Garrett Knox
- Michael Leung
- Jacob Schmit
- Sabrina Woo

Laboratory: qPCR; robotics; controls; analysis

Faculty Leader: Prof. Mitch Magee

Students

- Laura Anderson
- Scott Breshears
- Kajol Majhail
- Ellen Ruan
- Jennifer Smetanick

Law: CLIA (CMS), HIPAA (OCR), NPI (CMS), EUA (FDA); OSHA

Faculty Leaders: Prof. Adam Rigoni and Prof. Michael Stanford

Students

- Hale Anna Espinoza
- Marina Filipek
- Landon Jenkins
- Nathaniel Ross
- Madeline Salvatierra
- Osvin Serrano
- Alex Wakefield

Quality Management and Training: Specimen collection logistics, transport, specimen processing, stand operating procedures manuals, non-conforming events: CAPA plans, workflows and efficiencies, personnel proficiency testing

Faculty Leader: Prof. Dan McCarville

Students

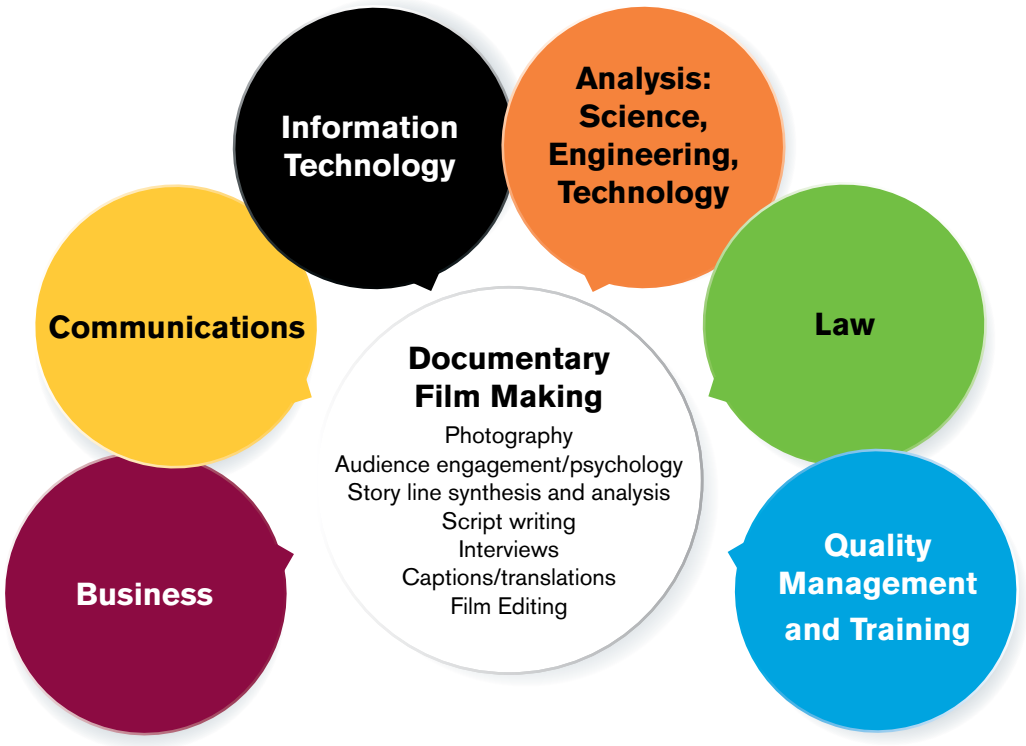
- Ishna Barwey
- Ashley Bruner
- William Hymer (Will)
- Abby Krell
- Gabriel Lewis
- Jack Myers
- Frankincense Ramesh
- Sage Reagan

Documentary Film: storyboarding; scriptwriting filming; animation

Faculty Leaders: Prof. Nita Blum

Students

- Sierra Bardfeld
- Joriel Cura
- Nikhil Dholaria
- Hannah Foote
- Tara Liu
- Julia Raymond
- Mahima Varghese



1 Business

Costing
Financing: reimbursement/billing
Purchasing: supply chains
Business plan: sustainability; scalability
Positions and personnel
Contracts with customer organizations
Direct-to-consumer models

2 Communications

Internal/among groups
External/website/customers
Patients
Public/website
Contact tracing
Apps for contact tracing

3 Information Technology

Patient registration
Analytical data capture/analysis/storage
HIPAA compliant systems
Bar coding and maintenance of identity
Inventory control
Return of results
WiFi issues to assure results returns

4 Analysis: Science, Engineering, Technology

Emergency Use Authorization
qPCR
Robotics
Test validation/controls
Pooled testing
Test interpretation: pos/neg/"invalid"
Safety

5 Law

21 CFR: CLIA (CMS)
FDA IVD regulation
EUA
HIPAA
NPI registration (CMS)
Reporting to state

6 Quality Management and Training

Specimen collection logistics
Transport
Specimen processing
Stand operating procedures manuals
Non-conforming events: CAPA plans
Workflows and efficiencies
Personnel proficiency testing

Introduction

Following its introduction into human subjects in China in the late fall of 2019, the Sars-CoV-2 virus spread rapidly around the world, creating the worst global pandemic in a century. The virus was highly contagious, and in a sizable subset of those infected, it produced a severe acute respiratory syndrome that was debilitating or lethal. The lack of protective immunity in the human population allowed the virus to spread rapidly, and the lack of effective treatments made it difficult-to-impossible to save those who became severely ill. Because as great as 40% of infected individuals were asymptomatic but fully capable of spreading the disease, the only way to identify the infected was through diagnostic testing for the virus. With testing, all infected individuals could be identified, alerted, isolated until no longer infectious, and treated when needed.

Disruption caused by COVID-19 was felt by organizations across all sectors, including educational institutions. Early in the pandemic there was great uncertainty regarding how or if Arizona State University could or should remain open. The University quickly decided to put classes online and encouraged students to return home in order to limit the spread of the virus on campus. For those living on campus, however, testing, case tracking and isolation of infected individuals was essential to keep the community safe.

Beyond ASU, the entire state of Arizona was severely affected by the pandemic. During a span of several weeks in 2020, Arizona led the nation in cases, hospitalizations and deaths. Commercial medical laboratories quickly became overwhelmed with the demand for testing, resulting in delays of 7-10 days for the return of test result. Critical services, such as electric power, were threatened by the inability to keep employees safe. Even healthcare workers themselves lacked access to necessary testing.

To meet the testing needs of this crisis, ASU mobilized its human, technical and financial resources to stand up a medical testing laboratory that met all federal regulatory requirements, could collect and test thousands of specimens a day, and return highly reliable test results to the patient within 36-38 hours. It was an effort that brought together huge numbers of volunteer faculty and students, working around the clock, to meet the need. It generated dozens of relationships with communities in need of testing support such as the homeless, Native Americans, and essential workers but also, with the support of the state government, offered the opportunity to be tested to any Arizonan free of charge. The ABCTL had one mission: to save as many lives as possible.

The creation of this laboratory was a multidisciplinary effort. The coordinated effort of multiple experts working across the domains of molecular laboratory technology, information technology, quality management, business, law, and communications. Each of these topic areas as they applied to the ABCTL was analyzed in depth by the student teams listed on the previous page as the focus of their thesis work for Barrett, The Honors College at ASU. This report, a compilation of their theses, details the requirements across academic domains to establish the ABCTL, a large-scale diagnostic clinical laboratory, in the midst of an ongoing pandemic. The success of the ABCTL is a testimony to ASU's designation as America's most innovative university.

Table of contents

Chapter 1

The Making of a COVID Lab

A Focus on Business Exploration

Authors: Claire Agee, Samuel Cosgrove, Corinne English, Kyle Mattson and Michael Qian

Submitted in fulfillment of requirements for the honors baccalaureate program of Barrett, The Honors College at Arizona State University

Thesis Director: Professor Carolyn Compton, School of Life Sciences

Faculty Leader, Business Group: Professor Eugene Schneller, W. P. Carey School of Business

August 2020 – May 2021

Introduction to Chapter 1

Early in the pandemic, Arizona State University (ASU) leadership recognized an opportunity to involve the Biodesign Institute in an effort to keep local communities safe. Equipped with capital investments (and expertise) in diagnostic testing, university president Michael Crow tasked Dr. Joshua LaBaer - the executive director of Biodesign - to begin mapping out the lab's logistic capabilities and operational plan. While initially testing using nasopharyngeal swabs, the ASU Biodesign Clinical Testing Laboratory (ABCTL) eventually developed a saliva-based COVID-19 test that was easier to collect and more resource-efficient for the lab. By maintaining rapid turnaround times for test results, the ABCTL has helped both the university population and local community operate safely. Lauded as a highly innovative testing site, the lab proved to be an essential asset as ASU, and the world, look to return to normalcy. The purpose of this chapter is to analyze the ABCTL's inception and development using multi-faceted approaches from the business realm. There are five topics discussed in this chapter:

- Section I – Stakeholder Theory and Analysis (Claire Agee),
- Section II – The Lab as a Business Within a University Environment (Samuel Cosgrove)
- Section III – An Operations Management Perspective (Corinne English)
- Section IV – An Analysis of its Upstream Supply Chain (Kyle Mattson)
- Section V – A Managerial Economic Perspective (Michael Qian)
- Section VI – Future Perspectives (All members of the Business Group)

Section I: Stakeholder Theory and Analysis

Author: Claire Agee

Background

As of Fall 2020, ASU students have become widely aware of the new testing lab available on the Tempe campus. With some residents on the Tempe campus frequenting the Sun Devil Hall and the Sun Devil Fitness center to get COVID-19 results every week, the COVID-19 saliva testing lab at the Biodesign Institute has become integral to the students at . However, the relations of the ASU Biodesign Covid-19 saliva testing lab range much farther than just the ASU students and faculty who utilize the program and the researchers who work there. The purpose of this volume is to flesh out these relationships and explore the stakeholder mapping of the ABCTL.

When the ASU COVID-19 response team was formed there was only one goal: to create a facility capable of offering testing to the students at ASU. Testing and the ability to manage a population at risk was recognized as integral to ASU's goal to remain open and sustainable during the pandemic. This has arguably made ASU the most important internal stakeholder to the clinical testing lab and its largest contributor. The response team was formed within ASU and originally, solely for ASU. Today, the reach of the ABCTL is spreading outside the University and is even offering testing to local communities and the State of Arizona.

To have made this venture possible there were sponsors, managers, and a push for better testing facilities from the public. All these factors worked to form this high-output lab that has to date tested more than 255,000 samples since its conception. There has been involvement of the government, international testing facilities, and competition from other labs that have played a large part in the development of the ABCTL. As COVID-19 changes business in the United States as we know it, it is with a mixture of implementing, mapping, and executing an efficient stakeholder management strategy that has truly allowed the ABCTL to flourish even under uncertain times. One can see this when looking at how the COVID-19 Biodesign Institute at ASU has thrived and used its stakeholders to its advantage over the course of the COVID-19 pandemic.

This section of Chapter 1 focuses on stakeholders associated with the lab and the efforts to engage and manage them for the good of the effort. It provides insight into the importance of stakeholder analysis and maps the internal and external stakeholders and their involvement. It is unique in its classification of stakeholders and distinguished between those faculty and staff who took on the effort to build the lab within ASU and those that require its services outside the organization. It explores the unique mission to accomplish the implicit goal to provide one of the foundations for sustaining the ASU community to carry on their work and, consequently, for the university to remain open and those hired to carry out critical functions. Lastly, it discusses the management of internal and external stakeholders.

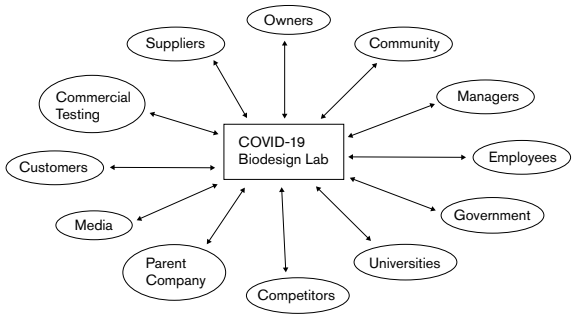
Stakeholder Analysis

As defined by the Stanford Research facility in 1963, "In a corporation, a stakeholder is a member of groups without whose support the organization would cease to exist," (Gomes, 2006). Stakeholders are integral to any business or corporation as without stakeholders a business simply cannot take off successfully or gain profitability. Some examples of obvious stakeholders include employees, customers, investors, and management. However, stakeholders vary much more than just these key participants and stretch out to include the government, suppliers, creditors, and often the entire community surrounding the enterprise. These numerous stakeholders can be looked at in greater detail by putting them into two categories – (1) internal stakeholders and (2) external stakeholders.

Stakeholder theory emphasizes the importance of analysis and management of stakeholders, both internal and external stakeholders alike (Blackburn, 2020). Stakeholder analysis on the other hand focuses on analyzing the role of a company in deeper ways than just profit margin and looks at topics such as social responsibility, business ethics, and values associated with managing stakeholders (Blackburn, 2020). Stakeholder theory also addresses larger issues such as the overall morals and values that go into managing an organization while attempting to optimize the relationships between stakeholder and corporations, ultimately increasing the effectiveness of the business.

It must be understood that enterprises exist in a dynamic environment, thus it is important to assess stakeholders existing in a constant state of change. Some relationship dynamics are constant, while others come and go. These relationships are ones that are maintained with the help of a detailed stakeholder mapping system that establishes need for stakeholder communications. Below is a current stakeholder map of the COVID-19 Biodesign lab based off "Stakeholder Analysis for Systems Thinking and Modelling," by Arun A. Elias and Robert Y. Cavana (Elias & Cavana, 2011).

These relationships will be explored deeper within the context of the ABCTL and sorted into categories of external and internal within this section. Mappings, both internal and external, will be based on the strategies in the literature (Stakeholder Analysis for Systems Thinking and Modelling, cited above from the Victoria University of Wellington (Elias & Cavana, 2011).



Mapping Internal and External Stakeholders and their Involvement

Internal Stakeholders Analysis

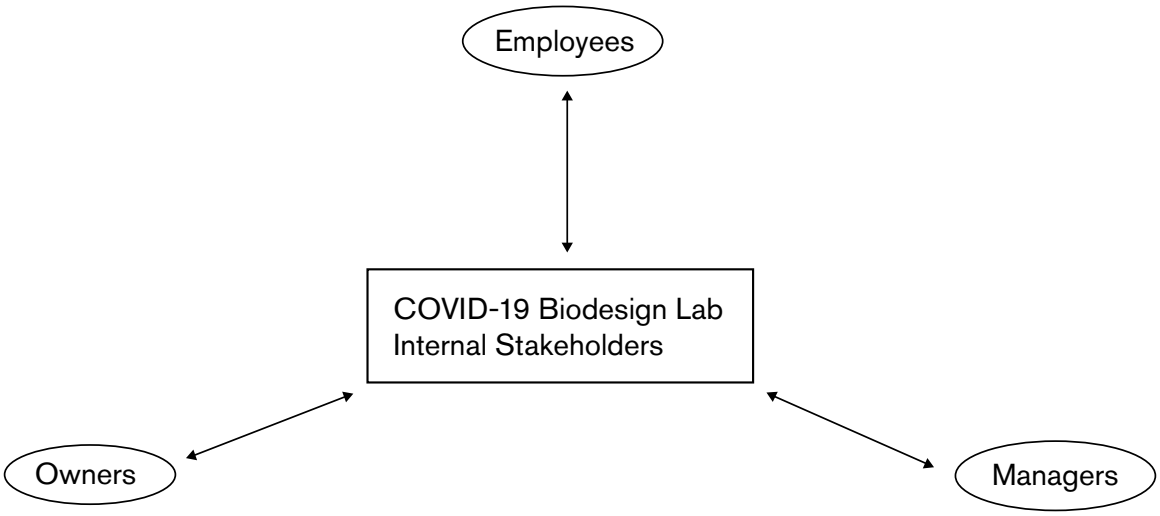
For the purpose of this analysis, internal stakeholders are defined as entities within a business such as employees, managers, the board of directors, and investors ("Introduction to Business", n.d)." Overall, internal stakeholders are simply those that are directly within an organization. These individuals are key to the success or failures of an enterprise, a few are the bosses, the investors, and the employees closest to the company. These people are considered the ones who keep the enterprise operating and who profit and generate revenue directly from the success of the enterprise. It is these innermost members of a company's stakeholder mapping that allows it to operate. These entities that are directly within the organization itself are often referred to as internal stakeholders.

In *Strategic Management*, R. Edward Freedman mulls over the attributions of the term "internal stakeholder" to being a blanket statement for any entity that is used "to refer to those internal groups who may appear to a particular manager to be much more troublesome than external groups (Freeman, 1984)." The word "troublesome" refers to the amount of gravity of the effect that internal stakeholders can give in comparison to external stakeholders. Internal stakeholders are those that can exert more influence and be exerted on with more impact than external stakeholders. In this way, stakeholder mappers often find internal stakeholders more troublesome or more helpful towards the corporation than their external counterparts. Internal stakeholders, if performing unwell, can greatly inhibit the enterprise. Alternatively, if internal stakeholders are performing splendidly, they can create vast amounts of profit. The close nature of the internal stakeholder to the corporation it is within makes these stakeholders easier to identify and find, but also the most important entities to analyze and manage closely. Below is a rudimentary mapping of the current internal stakeholders of the ABCTL.

As a next step, an internal stakeholder chart can be completed from this internal stakeholder mapping. The figure is displayed below.

Owners	Managers	Employees
Arizona State University	President Michael Crow	Lab Staff
Arizona Board of Regents	CEO, Dr. Joshua LaBaer	Clinical Testing Site Staff
	Medical Director, Dr. Carolyn Compton	Miscellaneous Staff
	Managers from the Knowledge Enterprise	
	Miscellaneous Professors Managers	

Starting with the owners of the ABCTL, there is no private owner and Arizona State University, and The Arizona Board of Regents are the technical proprietors of the entity. The entire Biodesign Institute is considered property of Arizona State University including the ABCTL and by extension is governed by the Arizona Board of Regents which oversees the State of Arizona's other public universities and is composed of twelve overseeing members. Looking at managers there is a much larger diversity of positions under one stakeholder category. All these positions will be differentiated below, starting with President Crow and the other types of managers in the chart including Dr. Joshua LaBaer and Dr. Carolyn Compton. This section will then end with an exploration of the employee internal stakeholders belong to the ABCTL.



The COVID-19 pandemic challenged colleges and universities across the US to bring students, faculty and staff back to campus. Michael Crow, the President of Arizona State University, spearheaded the initiative to bring back students in the Fall of 2020 following the great flight of residents from campus in the Spring of 2020. The Crow strategy included finding a way to instantiate a facility for the testing of students, staff, and faculty.

Taking advantage of the Biodesign Institute, President Crow began by asking key professors and researchers to find a way to get clinical testing to the University. Dr. Joshua LaBaer, Executive Director of the Biodesign Institute, had conversations with President Crow as they discussed how the facilities on hand could provide testing for everyone at Arizona State University. Coincidentally, Dr. LaBaer had just finished doing a separate project attempting to find ways of assessing the degree of radiation on individuals at the Biodesign Institute. After taking inventory, Dr. LaBaer found that the Institute had the people, instruments, and availability to transition the radiation lab into one for live specimen testing. After a means and a place were founded, the next task was to source the manpower.

Key Roles: In late February of 2020, Dr. LaBaer called together 7 people in his group who had unique expertise in software development, molecular biology, and several other fields to discuss how they could provide efficient testing to the entirety of the Arizona State University campus by Fall 2020. While one might look at stakeholders based on their employment status, it is noteworthy that a core group came together to take on a prodigious task – one that required special commitment, determination and in some instances personal sacrifice. Key roles included:

Dr. Joshua LaBaer

Dr. Carolyn Compton

Dr. Joe Miceli

Dr. Vel Murugan

Dr. Mitch Magee

Dr Neal Woodbury

Dr. Tamara Deuser

Dr. Joshua LaBaer is the current Executive Director of the Biodesign Institute and the creator of the COVID-19 response team. He is the head in regard to the creation and executive oversight of the ABCTL

Dr. Carolyn Compton, an anatomic and clinical pathologist, was chosen to be the Medical Director of the ABCTL about three weeks after the team was formed and would later become the organizer of the large-scale Barrett honors thesis team in the Summer of 2020. Dr. Compton is an MD, PhD pathologist who was chosen because of her vast experience and board certification in laboratory medicine and her active status as a physician in the State of Arizona. She is a professor at ASU in the School of Life Sciences.

Dr. Joe Miceli was chosen as he had a history of working in the DNASU plasmid repository as he oversaw the day-to-day workings of the technicians there. He had previously worked with Dr. LaBaer and was asked to cover the inventory and sample size collection side of the project.

Dr. Vel Murugan, a molecular biologist, had been leading a high intensity laboratory team dedicated to expression clones for storage and distribution by the DNASU plasmid repository lab. As the ABCTL instantiated itself in Fall 2020, Dr. Murugan worked on personally signing each released sample result to be returned back to patients.

Dr. Mitch Magee was assigned to help with supply chain of the ABCTL. He was chosen because of his extensive experience working with pathogens and live specimens and appointment at the Biodesign Institute.

Dr Neal Woodbury, Chief Science Officer of the Knowledge Enterprise, which is the parent company for the ABCTL, lent his support as someone in charge of advancing the research on the science efforts at Arizona State University.

Dr. Tamara Deuser, Chief Operations Officer of the Knowledge Enterprise, is mainly charged with the finances and outside contracts of the lab. She supports the more science-based executives of the lab such as Dr. Neal Woodbury and Dr. Joshua LaBaer by controlling the cash flows in and out of the lab and communicating with outside contractors.

As the Knowledge Enterprise Officers lent their support from the parent company of the Biodesign Institute to the COVID-19 testing laboratory, additional ASU professors continued to join the cause. The additional funding provided by the University and backing of the parent company allowed the operation to grow larger and take form in the late Summer. The team had been dedicated to meet every day and the idea for the implementation of a viable COVID-19 testing lab budded into fruition. Dr. Mitch Magee recalls that, "We had a meeting and as we started these eight o'clock calls… that we have had for about five months. We met every day at eight o'clock, Saturday, Sunday, Monday holidays July, the fourth all those days." In this way, the ASU COVID-19 response team was officially launched in late February to early March. The team was later successful in instantiating the testing lab that would welcome ASU students in the Fall of 2020.

When looking at the hierarchy of the lab it seems to be a confusing, disorienting ladder of unassigned control. Any one employee could be asked who the boss is and express complete honesty when responding about how they were not quite sure. The impromptu nature of the lab is a direct consequence from the necessity of the institute having to be implemented as soon as possible.

As a university-based lab, there are seemingly only two types of employees: salary and hourly. Most employees are hourly workers and do manual jobs such as moving saliva live samples to different testing machines. A smaller, more technical group of more experieced professionals that also commonly double as ASU professors, are salaried employees who work on specialized jobs such as signing off test results, procuring different equipment in the lab, and managing other workers. Each lab member does their own work independently or perhaps two or three team members, under the immediate supervision of a manager, without much attention to the hierarchy of the organization. In this way, the ABCTL is largely representative of a "flat organization" which is defined as "an organization structure with few or no levels of management between management and staff level employees. The flat organization supervises employees less while promoting their increased involvement in the decision-making process (Meehan, 2019)." Impromptu gathering, constant meetings, and daily communication are what keeps the lab together, not rigid hierarchy and business formality. The number of employees in the COVID-19 lab is small, but the line of communication is chaotic and ever-changing. What does keep the team together in this shaky ladder is the even shakier pandemic environment and the determination to provide stability to ASU.

The current employees of the ABCTL are no exception to the now main-stream intensity of the lab's work life. With the exception of salary workers who often double as professors, employees of the lab number around fifty and complete jobs such as working at the testing facility to funnel patients through the saliva system and moving samples to different testing machines in the ABCTL itself. Most of these hourly employees are found via advertisements towards recent graduates interested in working in a clinal lab who have had previous experience handling live specimens. These employees are usually paid fifteen to sixteen dollars hourly and sign up for up to eight hours of slots in an online system a day. Workers are encouraged to move quickly and efficiently so testing results can be brought back to patients as soon as possible. These more manual workers are usually comprised of young graduates from the fields of biology, chemistry, or anyone with background lab experience. However, The ABCTL has recently found itself subject to the competitive nature of finding new hands in a pandemic environment.

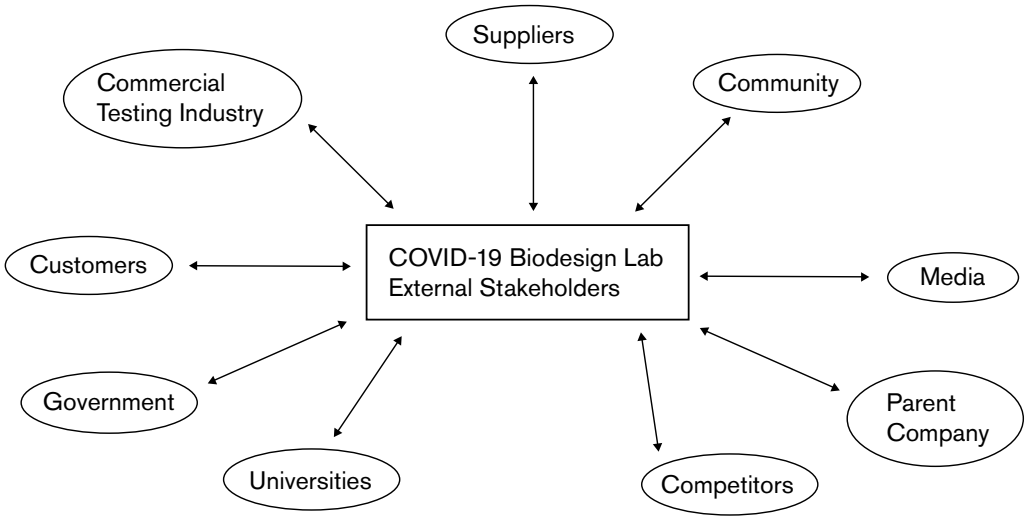
Starting hourly workers at the Biodesign Institute are often poached from other commercial labs and are attracted by the higher wages and vertical growth offered at these competitive corporations such as Sonora Quest and Paradigm labs. Additionally, the future of the ABCTL is largely unknown and young workers seek more instantiated and stable commercial labs over the newfound underdog of the market. On the other hand, salary workers are often much less likely to be poached.

Salary employees often work as professors at ASU and do not sign up for hourly slots. These employees work frequently and often over-zealously at their own pace. Higher level members in the lab do more analytical jobs in comparison to hourly workers including signing off testing results, re-testing inconclusive

results, and looking at ways to improve the supply chain of the lab. The very highest members of the lab include the medical director, Dr. Compton, the technical director of the ABCTL, Dr. Vel Murugan, leadership of ASU Knowledge Enterprise, the parent company of the Biodesign Institute, including Dr. Joshua LaBaer, Dr. Tamara Deuser, and Dr. Neal Woodbury. These members do highly analytical work and meet often to discuss the overall direction and future that the lab may face. As salary workers at the lab double as professors and add working and supervising to their already extremely busy schedule of teaching classes, their workload has become crushingly heavy. Dr. Vel Murugan has spoken about how many members of the lab continue to work this hard for the necessity of the community, not money. Amazingly, he himself has admitted that he works "anywhere from sixteen to twenty hours a day," (V. Murugan, digital interview, October 23, 2020).

External Stakeholder Analysis

The counterpart of internal stakeholders, external stakeholders, are defined as "those who do not directly work with a company but are affected somehow by the actions and outcomes of the business (Fernando, 2021)." This includes all stakeholder that are impacted by or influenced by an organization that are not within the organization itself. The below mapping is a rudimentary figure showing the current external stakeholders of the ABCTL.



As a next step, an external stakeholder chart can be completed from the above external stakeholder mapping. The figure is displayed below:

Customers	**Community**	**Competitors**
ASU Students Arizona State Staff Contracted Residents of Arizona	Local Community Arizona Community Community at Large	Sonora Quest Labs involved in any type of COVID-19 testing
Government	**Suppliers**	**Media**
DHHS: The Clinical Laboratory Improvements	Large medical supplies companies	Social Platforms
Universities	**Parent Company**	**Commercial Testing Industry**
ASU Colleges with a saliva testing program	Knowledge Enterprise	COVID-19 Testing Industry COVID-19 Vaccination Industry

Starting with a look into the parent company of the ABCTL, the ASU Knowledge Enterprise supports several interdisciplinary research institutes and initiatives. These supported ventures include the Interplanetary Initiative, the Institute for Social Science Research, and of course, the Biodesign Institute which houses the ABCTL. As an external stakeholder with extremely high influence and high impact to Knowledge Enterprise the ABCTL is managed incredibly closely. Recently, Knowledge Enterprise has been focusing a majority of its resources to keeping up and supporting the ABCTL in response to the pandemic. This includes the utilization of the COO and CFO of Knowledge Enterprise, Dr. Tamara Deuser and Dr. Neal Woodbury, towards assisting the subsidiary company.

When the COVID-19 response team was first in session there was one main goal that had to be overcome before creating an environment primed for live specimen testing. When any lab wants to work with clinical testing, they must first become CLIA (Clinical Laboratory Improvement Amendments) certified. CLIA are federal standards applicable to all U.S. facilities or sites that test human specimens for health assessments or to diagnose, prevent, or treat disease (*Clinical Laboratory Improvement Amendments* (CLIA), 2020). This made the government a very prominent and early external stakeholder to the ABCTL. After successfully passing inspection, the ABCTL was able to officially be established and begin preparation for testing incoming patients.

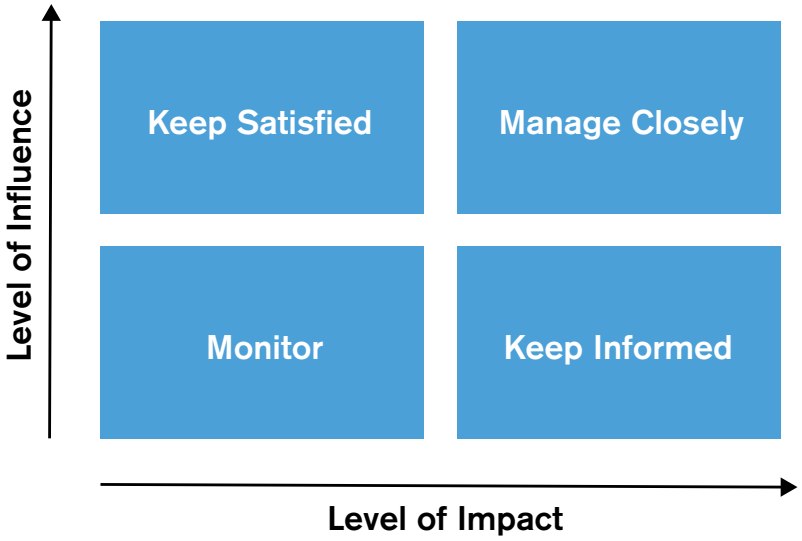
Delving into the customers of the ABCTL we can see that an overwhelming majority are ASU students. In the Spring of 2009, it was recorded that there were 50,397 students solely on the Tempe Campus. However, the ABCTL has recently increased its reach from the original goal of testing Arizona State staff and students to also offering tests to contracted clients and the residents of Arizona. In this way, the ABCTL now has the local community of Tempe and the community at large in Arizona as an external stakeholder to manage.

An underdog in the commercial testing industry, the ABCTL has been able to out-compete and under-price all commercial labs in Arizona. Notable competitors include Sonora Quest and other CLIA (Clinical Laboratory Improvement Amendments) certified labs that offers COVID- 19 testing. It is the ease of the saliva tube and the 48 hours turnaround time that has caused so much success for the ABCTL. Some notable suppliers out of several dozen include Digi-Key Corporation, Amazon Capital Services, and Fisher Scientific Co LLC who do business with the ABCTL frequently. These supplier relations are generally efficient as goods are received and paid for by the lab in a timely matter. The overall external relations of the ABCTL are friendly and non-threatening to the lab's success.

Managing Stakeholders

General Considerations

As stakeholders are often numerous and varied, stakeholder analysis requires a detailed mapping system to manage each entity. One way that companies manage their stakeholders is by listing names of entities, competing organizations, or prominent individuals and ranking their impact and influence. Impact is how much the organization's actions could affect the stakeholder while influence is how much the stakeholder could affect the organization (Sharma, 2010). The figure below pictures how the influence and impact of a stakeholder causes the organization to react.



Stakeholder Influence/Impact Matrix (Sharma, 2010)

Looking at the influence/ impact matrix, if stakeholders are deemed low impact and low influence, they should be continuously monitored and re-evaluated for importance over time. However, if stakeholders are deemed with high levels of impact and high levels of influence, they should be managed extremely closely in order to keep them well satisfied and well informed. By having a good mapping system, organizations are able to identify key stakeholders and build their stakeholder management efforts around the consequences and rewards perceived from their actions. In this way, stakeholder relations can be optimized and increase the effectiveness and profit of a company.

Managing University and Internal Stakeholders

As of Spring 2021, tens of thousands of students has visited the Biodesign COVID-19 drop-off saliva centers ("Devils Drop-Off") to get testing whether it was from their own volition or required by the University after being randomly selected for mandatory testing. Before the return of students on campus in Fall 2020 and the return of students to campus in Spring 2021, negative COVID-19 tests were required for admission. These new requirements have been met with slight controversy among students. The act of getting tested or selected for testing can be considered somewhat inconvenient, but it has been integral to keeping the campuses open and managing the university as a stakeholder. As of Fall 2020, "more than 2 out of 3 colleges with in-person classes either have no clear testing plan or are testing only students who are at risk (Nadworny & McMinn, 2020)." This is heavily correlated with how cases of COVID-19 in young adults in Fall 2020 were "up by 55% nationally between early August and early September, when many colleges opened for the semester (Nadworny & McMinn, 2020)." As 40% of cases are estimated to be asymptomatic, it is essential that Universities have quickfire testing available (Nadworny & McMinn, 2020). Students at Arizona State University also get additional benefits from the newfound saliva testing technology as it is widely considered to be much less painful than the traditional method of nasal swabbing.

As laboratory COVID-19 testing has found its way to ASU, it hasn't been just the students who have benefited from the opened campus. Professors and staff at ASU have been able to continue teaching their classes with the knowledge that testing is strictly mandatory for everyone. Some professors such as the salary workers in the COVID-19 lab have been able to research the virus itself and feel true meaning in their work as they continue to test students and prevent the spread. However, even professors outside of these more scientific roles at the Biodesign Institute have been able to continue teaching classes to students over zoom and even occasionally in person due to the existence of the clinical testing lab. In a survey published on "Inside Higher Ed", it was found that "more than 40 percent of survey respondents

considered leaving their jobs as a result of COVID-19's impact (Flaherty, 2020)." Just like students, teachers have found themselves shaken by the pandemic and the new movement towards online learning. However, with even the Professors themselves subjected to mandatory testing at the COVID-19 facility at ASU, the increased scope of testing has no doubt increased the safety of campus and made both teachers and students alike feel slightly more comfortable with the knowledge that they can virtually get a test whenever they want.

Managing External Stakeholders

As the ASU clinical testing lab has grown ever more active and efficient in testing for COVID-19, further external organizations have become contracted with the lab and become external stakeholders. The idea behind the attraction of outside companies looking to get contracted with the Biodesign lab at ASU is easy to understand. It was recently found by researchers from Memorial Sloan Kettering that "the saliva tests detected the virus' genetic material in saliva samples at similar rates as swabs that collected material through the mouth or nose. They were also stable for up to 24 hours when stored with ice packs or at room temperature (Murez, 2020)." Currently, saliva testing is the easiest and most efficient testing method and is regarded as much less painful than nasal swabs which require prodding the deepest parts of the nasal cavities. Additionally, the turnaround time for saliva samples being returned to patients is exponentially greater compared to nasal samples. With the capacity of the laboratory ever-increasing, outside companies have tried to reach out to the Biodesign Institute to get their own employees tested. This is mutually beneficial to both parties as the laboratory makes money from the tests it provides, and the corporations can continue to have work in person and in a safe environment. However, these relationships are not without their faults and offer many downsides to the contracted.

External stakeholders understand that their relationship with the ASU lab requires an understanding of the lab's mission to serve the ASU community. Around seven months down the line some partner organizations have their contract with the Biodesign Institute found in the hands of a procurement specialist belonging within the company. When an inside employee at a company that is partnered with the ASU's COVID-19 lab takes another look at the contract that had been previously approved they can tend to be confused as to how. Unlike a commercial lab, the lab at Arizona State University offers no guaranteed service, test quantity, or length of testing specifications. Dr. Tamara Deuser, the Chief Operations Officer at Knowledge Enterprise, often must sit down with these companies as the one in charge of contracts and explain why she agrees that these are natural things to expect in

a business deal, and why they are purposely not provided by her organization. "We're not a vendor, we came in during a critical time with a unique asset that we agreed to provide to you as a service to the community (T. Deuser, digital interview, November 3, 2020)." In this way, relations with contracted clients can be quite rocky as they believe they are entitled to the services a usual vendor would provide.

However, once the client truly understands that the Biodesign COVID-19 lab is not a vendor, but a service to the community, the stake of the lab becomes clear. Clients trade the safety found in most commercial lab contracts for the ease and affordability that the COVID-19 lab provides. As Tamara Deuser states if "President Crow decided tomorrow that everyone in the entire community is getting tested tomorrow. We can do that, but we'd have to shut everything else off (T. Deuser, digital interview, November 3, 2020)."

Influence of the ACBTL has stretched far beyond just ASU and the companies it currently contracts for. As the saliva testing strategy can test more students even more quickly with each coming advancement, the State of Arizona has offered several grants and subsidies to the lab. These grants were mostly to extend the lab's reach to citizens of Arizona and has succeeded in greatly increasing the number of people able to access consistent testing. As an external stakeholder to the ABCTL, Arizona has been extremely helpful by providing countless financial aid to the lab. However, the external stakeholder managing of the State of Arizona must be under constant evaluation. The ABCTL has been able to source this funding because of the need from the population. However, when the lab is no longer needed, the State of Arizona

will not be as willing to give money and grants as it is now, and additional methods of funding will need to be located.

The funding provided has allowed the ABCTL to greatly expand its reach. Beginning as just a saliva testing predominantly for students and employees at Arizona State University, the Biodesign Institute's influence has spread to the entire State of Arizona. In 2020 the State of Arizona recognized that Biodesign Institute's response to COVID-19 and awarded the Biodesign clinical testing laboratory with the Innovator of the Year Award, marking its processing of just over 255,000 tests (Kass & Koerth, 2020). The public is now able to choose areas around their place of residence and get saliva testing. Additionally, Universities outside of Arizona have started looking at ASU as an example of how to properly manage student welfare in a pandemic environment. Other colleges have followed suite in exploring saliva testing, like Yale and the University of South Carolina, to combat the spread of COVID-19 among college students. These universities gain the great benefits of saliva testing that are like Arizona State University's, twenty-four-hour result times and the ease of saliva testing in comparison to nasal swabs are just a few. Overall, it has been the reputations of colleges that is at stake. If there is no research of prevention methods done at a University in the middle of a pandemic environment, the college is often looked at as ineffective and behind the times. In this way, saliva testing has made innovative schools that have implemented it continue to make strides and to look good in the public eye.

The industry of commercial clinical testing in Arizona and even the United States has been thoroughly changed by the introduction of University saliva testing labs. Arizona State University at this time has faced other companies in the market of COVID-19 but considers none of them competitors and with good reason. The clinical testing lab at the Biodesign Institute can provide more saliva tests with quicker results than any other testing facility in Arizona. Other large suppliers of COVID-19 tests include the second largest Sonora Quest, which still relies on nasal swabs and can sometimes take up to ten days for patients to receive results. In contrast, the monopoly the Biodesign Institute has on the students at Arizona State University and its painless methods of saliva testing that guarantees results within twenty-four hours greatly outpaces these other options. To put it simply, currently no commercial testing facility is regarded.

Conclusion

The ABCTL has truly become an entity on which thousands depend. From the students at ASU, to the citizens of the state, the newfound saliva testing methods that have been able to rapid test thousands of individuals has become an example of innovation to even America. Arizona State University has famously prided itself on its patterns of innovation, and the Biodesign lab has been no exception to this trend. Pioneering the way and setting an example for other Universities and able to even out-compete long-standing commercial testing labs, the Biodesign Institute's clinical testing lab on the Tempe campus is the definition of evolution in a struggling, rigorous pandemic environment.

However, stakeholder analysis and the theory of stakeholder mapping agrees on one thing: stakeholder risk is ever changing. With the recent release of the COVID-19 vaccine to essential workers and high-risk individuals in late Fall 2020, the number of people relying on the clinical testing lab may dwindle. Only the future can tell what may happen to the ABCTL. Whether testing for COVID-19 will continue for years to come, whether the lab will convert its saliva tests to check for other diseases, or whether the COVID-19 clinical testing lab will branch off into a startup is all unknown. However, the stakeholder dynamic is ever changing and only time may tell who the stakeholders of the lab will be or continue to be in the future.

The main goals of the ABCTL team may have begun simply to find a way to become a CLIA (Clinical Laboratory Improvement Amendments act)-certified lab, as is required under federal law for medical testing, and start testing at the University. However, with the current success in founding a working, successful clinical testing lab for COVID-19, Dr. LaBaer looks towards an even brighter future of having ASU "generate tools to save lives." Recently, the Arizona State University laboratory has opened contracts for outside parties to be able to request testing in the State of Arizona.

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Section II: The Laboratory as a Business Within the University Environment

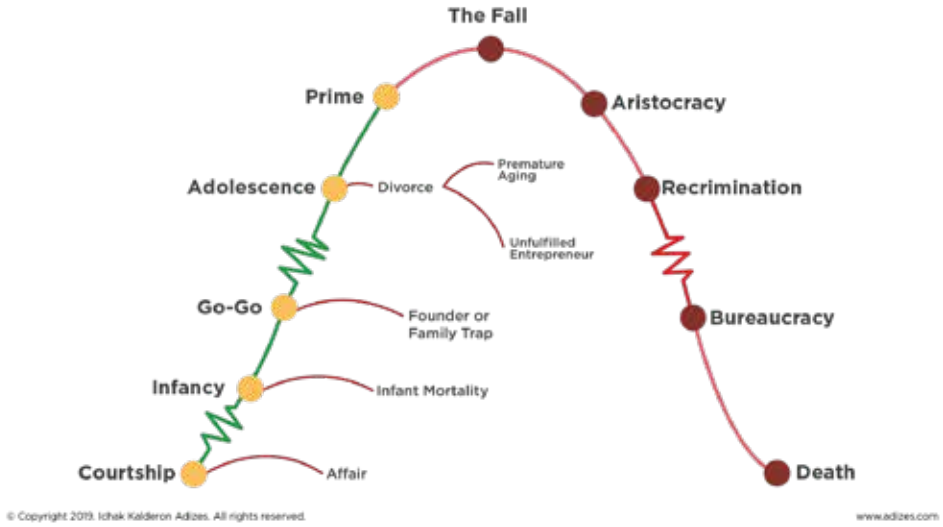
Author: Samuel Cosgrove

Background

While organizations often evolve in an "ad hoc" manner – following the intuitive decisions of founders, the idea of a business plan provides a framework for understanding how an organization originates, makes decisions, moves forward, and matures. The business plan can be the foundation that stabilizes an organization and unites team members around a common goal and strategy. Organizations have been observed to exist within the framework of a lifecycle-from being at a relatively infant stage, through intermediates stages and into maturity. The ASU Biodesign Clinical Testing Laboratory (ABCTL) displays this growth and transformation through its organization life cycle. Numerous studies and analyses have been conducted on organizational life cycles, with one being from Dr. Ichak Adizes, an experienced businessman.

Adizes explains how organizations go through ten stages in the business life cycle which are: "courtship, infancy, go-go, adolescence, prime, the fall, aristocracy, recrimination, bureaucracy, and death" These stages are scrutinized later in this section and are used to analyze the different life cycle stages of the laboratory. The Life Cycle stages and descriptions are shown below.

Life Cycle Stage	Description
Courtship	The initial development of the business.
Infancy	The initial period after the start of the business.
Go-Go	Fast-paced, commotion, early-growth
Adolescence	Starting to find its groove in the industry. Still developing.
Prime	The organization at its peak. The entity is popular, profitable, and competitive.
The Fall	When the organizations start to drop-off following its peak.
Aristocracy	Displays strength and accumulated success. However, shows little growth and loss of market share to competitors.
Recrimination	Questions, doubts, and internal problems hang over the organization's original purposes.
Bureaucracy	Self-centered administration. Operating and market challenges are characteristics of this stage.
Death	End of the organization. Closure, Sell-off, and Bankruptcy are common



Figures 1 and 2: Adizes Corporate Life Cycle Table and Model

As an enterprise within Arizona State University (ASU), the ASU Bio Design Lab and its operations mirror a business in many ways. From the formation of the lab, it has many similarities to a startup business. The lab has numerous similarities to a startup business in terms of its formation, business agility, supply chain, and other aspects.

The COVID-19 testing lab was established in the middle of a global pandemic. Because of this, lab personnel had to make many decisions quickly. Due to the rapid assembly of the laboratory, there was no formal business plan in set for the lab. One of the hallmarks of this laboratory is the rapid agility with which it moves. The lab develops its processes quickly and looks for ways to continuously innovate, which is consistent with Arizona State's proud moniker "#1 in innovation." For example, a look at the lab's coronavirus test has shown vast evolution within a year. When the lab began testing in spring 2020, it used the nasopharyngeal test for the Coronavirus. However, realizing the costly price of obtaining Personal Protective Equipment (PPE) and the need for quicker testing, the lab developed its signature saliva test in the summer. The saliva test provides numerous advantages over the nasal swab test. The America Society for Microbiology says that the saliva test is, "easy to collect, fewer collection supplies are required, and there are fewer steps in testing" (ASM). The advantages of the saliva test are further explained by Dr. Vel Murugan of the Biodesign laboratory, who mentions that the saliva samples are "faster and easier to collect." Also, saliva samples are the "perfect sample to collect due to the large number of aerosols humans produce", which are tested in COVID-19 (V. Murugan, Personal Communication, October 23, 2020). The saliva test does not require large amounts of nurses wearing PPE equipment to obtain samples. The saliva test proves to be more efficient and demonstrates the lab's improvement of its business processes. The lab took this test a step further by creating a third generation of testing that involves a smaller test tube size allowing for the quick removal of caps and more efficient testing. The different generations of coronavirus tests used by the laboratory are displayed in Figures 3-5:

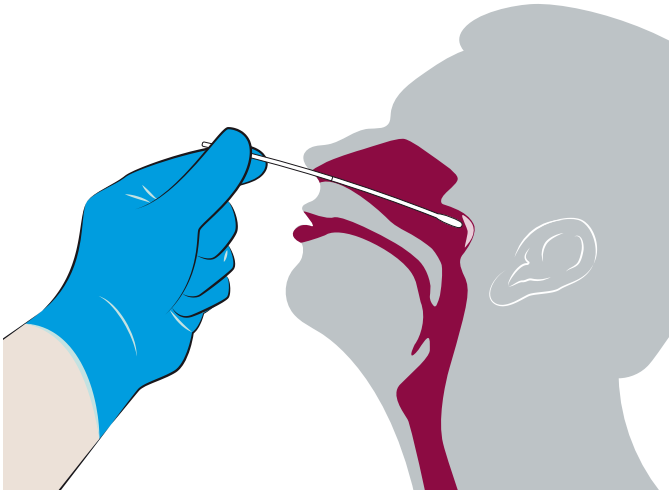


Figure 3: Nasal Swab Test. Figure 4: Original Saliva-Based COVID-19 Test. Figure 5: Updated Saliva-Based COVID-19 Test.

As there was great uncertainty about how long the COVID-19 pandemic would persist, it made a good deal of sense that the lab would be focused on short-term goals. The lab was focused more on short-term goals due to the necessity of a rapid response to the Coronavirus (COVID-19) pandemic. The lab needed a Big Hairy Audacious Goal (BHAG) that lab personnel could rally around. In an Investopedia article (2019) by William Kenton, he describes a BHAG as "A long-term goal that everyone in a company can understand and rally behind (Kenton).

Successful companies like NASA and Facebook all have BHAG's that unite their employees and help them work towards a common purpose. The Biodesign's overarching BHAG is to help save lives. The organization does not run for profit, but instead aims to curve the COVID-19 Pandemic through research and testing. Part of the early short-term goals for the lab consisted of focusing on meeting regulatory requirements and meeting the needs of vital community workers in Arizona. It gradually grew to expand its reach to include the public Arizona community and the Arizona State university student population. Another short-term goal for the laboratory consisted of creating organizational stability. With the rapid development of the early laboratory, it was able to create organizational stability early on through obtaining support from stable outside sources.

Initial support for the laboratory came from Arizona State University itself through the vision of President, Michael Crow. The work of the laboratory has been vital to Arizona State University conducting classes for the 2020-2021 academic year. In the words of Arizona State University President Michael Crow (2020), "We would not be moving forward (with students on campus) if we did not have confidence in our ASU team and our framework (*Office of the President*)." With the support of the university President, organizations in Arizona, and alliances throughout the world; the lab has now grown into being the premier COVID-19 testing center in Arizona and has performed over half a million tests to date at the publication of this volume. The lab is a pioneer in the saliva test industry as it became the first institution in the Western United States to produce an FDA-approved saliva test (LaBaer). The lab has had great success, which largely contributed to having the proper resources and personnel structure prior to the pandemic.

The lab grew out of an ongoing set of activities at ASU. The Bio Design Institute already conducted research and had many technological components in place prior to the Pandemic. Some of the labs cutting edge technology can be seen in Figures 6 and 7:

Figures 6 and 7: ASU Bio Design Technology

The presence of technology provided much of the early infrastructure and ability to meet the early stages for development of the lab. Referencing Adzes' life cycle model, having the proper technology in place allowed the laboratory to quickly progress through the "courtship, infancy, and go-go stages." These early stages are characterized by business formation, frantic growth, and meeting early challenges. The lab began in "courtship" when the laboratory saw a need for testing and began to look for ways to implement its processes. It was able to quickly transition to infancy, and then go-go with the help of the proper technology in place. The laboratory could quickly perform tests and get tests back to patients with the help of the proper technology in place. Despite having the right technology in place, it still had to obtain the proper testing materials and equipment. The difficulty in obtaining nasal swabs and PPE equipment is detailed later in page 22 of this literature.

The lab's existence, within a large university, also provided opportunities to meet needs that others would see as a barrier. These include:

- Establishing an organizational structure. Most businesses have a clear hierarchical structure with a CEO, CFO, and COO. However, the Bio Design Lab does not have these positions. Instead, the laboratory has directors, managers, and other positions. Some of the laboratory's leadership also hold positions in the larger organization that is the Office of Knowledge Enterprise Development (OKED).
- Developing a workforce. Originally the lab consisted of approximately seventy-seven people. The lab grew by creating a volunteer base to increase its employees. Lab Director, Dr. LaBaer reported that approximately two hours after an email was sent to prospective volunteers, over one hundred people volunteered to help with the efforts of the laboratory (J. LaBaer, personal communication, September 24, 2020). Looking at the organizational leaders of the laboratory, the laboratory differs compared to most businesses. There are numerous program directors, focused on overseeing the testing process from start to finish, and managers that work within both the ASU Knowledge Enterprise and the Bio Design Lab. Outside of the lab directors, the rest of the officials have their respective roles in their departments.
- A tradition of collaboration and inclusion. In another comparison to a typical business, the laboratory holds weekly meetings where updates about testing are given to lab officials. These meetings could be characterized as brainstorming, status, and operational meetings for businesses (Gregorio). However, these meetings' function more like staff meetings where Laboratory members give their input and advice.

This section describes the purpose and goals of the Lab, provides an organization overview, and assesses the products and services that the firm offers. Provided is an Industry Analysis, Customer Analysis, and Market Analysis. The following sections are organized to depict the evolution of the laboratory between January 2020 and March 2021. Section 1- Foundational Framework, considers the laboratory during its early evolution. Strong emphasis is on developing a viable strategy, meeting the regulatory requirements, and assembling needed resources. Section 2-Growing Enterprise looks at the operations of the lab, the

consumer base for the laboratory, and the main products of the lab. Section 3-Future Outlook focuses on the future of the laboratory, possible opportunities for growth and expansion, and the possibility of developing new products and tests.

Foundational Framework of the ABCTL

The Biodesign's effort against COVID-19 began in January 2021 after an Arizona State University student traveling from Wuhan, China became the first Arizona resident to contract the Coronavirus (KTAR.com). Dr. LaBaer quickly assembled a team together to begin researching the virus and developing testing for COVID-19. Looking at the big picture for the laboratory, the team had to not only conduct research on the COVID-19 virus, but also solve a slew of operational issues and future problems. Startup businesses have many questions to answer during their formation, and this laboratory is no different.

Formation and Problems

The laboratory mirrors a startup business during its formation and development. As previously mentioned, the laboratory went through the typical courtship, infancy, and go-go periods. However, the laboratory differs from other businesses in its business agility. An article from a Villanova University publication defines business agility as "an organization's ability to adapt and respond to changes in external market conditions (Villanova University)." Because the lab was already not a large-scale testing entity beforehand, this allowed the laboratory to be flexible and its approach and outreach. Prior to COVID-19, the Bio Design Lab served as a traditional laboratory performing research for Arizona State University and conducting other functions. Its goals and decisions were less responsive to an evolving critical need, but instead geared towards research and development. However, once the global COVID-19 pandemic started, the Arizona community needed a solution for COVID-19 testing. At its origins, the laboratory faced many problems. Some of these problems are presented as following:

- Assembling a business plan/strategy
- Defining a coherent business/organizational structure
- Hiring lab personnel
- Obtaining Financial support
- Obtaining management support (advisers, service providers, university support, and others)
- Obtaining CLIA certification
- Organizing supply chain/value chain activities

Business Plan and Agility

First, the analysis of the lab's Foundational Framework looks at the Business plan/strategy of the laboratory. The lab differs from most businesses and other healthcare providers in that it did not have a set plan when it first started. Research from healthcare business plans shows that common sections included in a healthcare business plan are: Executive Summary, Services, Market Analysis Summary, and a Financial Plan ('The Laboratory Business Plan"). The lab did not develop a set plan with these sections. The lab could have benefitted if it had done so. A clear financial plan to determine suppliers would have helped the entity. Despite, not having a clear business plan the entity was able to thrive. This is because the lab is extremely agile. The adaptability and agility of an organization is important to its success and survival. As stated by ASU Knowledge Enterprise staff, Dr. Neal Woodbury, "speed is everything (N. Woodbury, Personal Communication, November 3, 2020)." Looking at the agility of the organization, it has many characteristics that mirror an agile business. An analysis done by McKinsey & Company can help to understand how the Biodesign institute fits the idea of an agile organization. Figure 8 shows the growth of companies in the modern era evolving to become agile organizations.

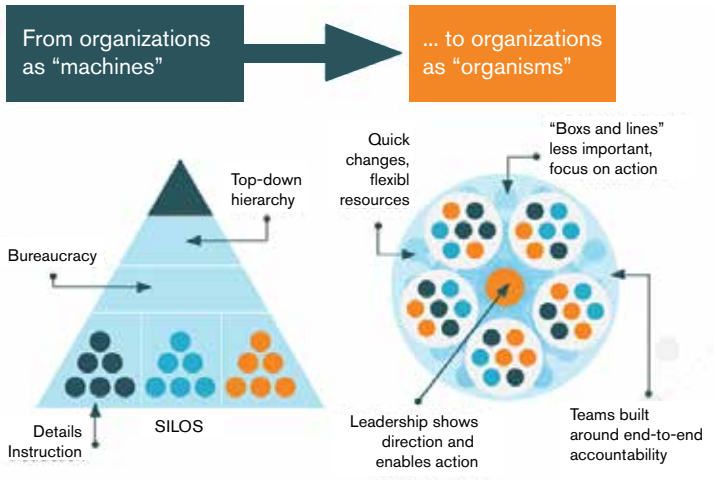


Figure 8: McKinsey & Company Business Agility

The laboratory does not have a Top-Down hierarchy. Instead, the lab has leaders that as pictured on the photo on the right relay vision and objectives for the team. In addition, the lab has cross- functional teams. The different teams in the laboratory attend weekly all hands meetings where they are able to provide input on the operations of the lab and voice their questions and concerns.

Another attribute of agile organizations that the laboratory displays are the Objectives and Key Results (OKR) goal system. According to *Felipe Castro.com*, "OKR is a simple, fast-cadence process that engages each team's perspective and creativity." This system has been used by successful companies such as Google, Spotify, LinkedIn, and others (*Felipe Castro.com*). This system allows employees to gather around a short-term goal with vision and clarity. The lab shows this when they move from existing research development projects to new projects.

Referencing the different generations of Coronavirus testing, the lab developed a new generation of testing in reaction to increasing efficiency and making stronger techniques and processes with the new data available to them. Their ability to innovate quickly has allowed them to help the Arizona community, and opened up doors for future growth and development. These actions demonstrate some of the benefits that come with being an agile business as listed by Product Plan, which include challenge management, competitive advantage, and cross-functional collaboration. The laboratory was able to quickly respond to the opportunity for COVID testing in the marketplace. It did not have to go through any bureaucratic hoops which organizations that are not agile are unable to do. The laboratory has demonstrated the ability to quickly adjust its trajectory in the testing market. It quickly flip-flopped from the nasal swab test to the saliva test for COVID. In addition, the laboratory established efficient cross-functional teams, which has allowed it to conduct its operations.

Pop-Up Business Aspects

The organization has some characteristics of pop-up businesses. Popup businesses take advantage of fleeting opportunities and aim to take advantage of new markets (Mccray). Pop-up businesses are fairly common in the state of Arizona. An AZ Family article (2020) details how pop- up businesses enter the market and test out their product to see if it's something that they would like to continue long-term (Campbell). The laboratory entered the testing market with the short-term goal of meeting an issue in the community. There was no large-scale future outlook for the laboratory in terms of what to do after the slowdown of the COVID-19 pandemic. Referencing Adzes' life cycle stages, the laboratory leap frogged past the courtship and infant stages, quickly jumping into the go-go stage. The laboratory swiftly began distributing tests to officials during initial testing. It did not have to spend large amounts of time in the courtship or infancy stages as it had the proper foundational framework in place. As pop-up organizations grow, they have the opportunity to pursue an offensive strategy.

The organization made decisions quickly and efficiently due to a race in time against the Coronavirus Pandemic. These quick decisions represent an offensive strategy for the organization. Dr. LaBaer, states that the laboratory went on the offensive against the virus as it wanted to seek out those that had the virus, and then get those people safely quarantined from the rest of the population. In addition, the laboratory displayed an offensive strategy through rapid research that aims to curb the influence of the virus. Another offensive strategy that the laboratory can pursue in the future involves moving to meet customer needs as a mobile organization. An article by *My Corporation* details how pop-up businesses have the mobility to go where their customers go (*My Corporation*). This successful practice has been demonstrated by companies in the retail industry. They look at their customers wants and where they are headed next. They then follow their customers and tailor their pop-ups to the desires of their customers. The laboratory may have an exciting future, yet one that has with many questions and unknowns. It is important for the lab to keep its customer and patient needs in minds for the future. They can potentially move from COVID-19 testing and "pop-up" to meet another testing need in the community. The lab operates on a problem solution basis. It mirrors the pop-up business analogy where companies meet a need and then close. The laboratory needs to decide on future services and goals if it does not want to follow the pattern of numerous pop-up businesses. It will need to be continually innovating and developing its processes. As COVID-19 continues to mutate and evolve, the laboratory will be able to continue testing for the near future. The lab staff understand this, and thus have to be adaptable in their response to the Pandemic. However, it will need to plan for different Scenarios, which is further discussed in the Scenario Planning section of the Future Outlook.

Organizational Structure

ASU Bio Design Lab has a unique organizational setup. The laboratory is part of the larger organization known as the ASU Knowledge Enterprise. According to the Enterprise website, The ASU Knowledge Enterprise (2021), "supports several interdisciplinary research institutes and initiatives" (ASU Knowledge Enterprise). The Knowledge Enterprise embarks on many signature ASU initiatives including the McCain Institute for International Leadership, LightWorks, NewSpace Initiative, The Biodesign Institute, and numerous others (ASU Knowledge Enterprise). Many of the lab personnel in the Bio Design lab are part of the ASU Knowledge Enterprise. The laboratory has no direct Chief Financial Officer (CFO) of the organization as most businesses do. Instead, the Finance Director of the laboratory is Tamara Deuser. She serves as the Chief Operating Officer (COO) for the Office of Knowledge and Enterprise Development.

Funding

No organization can exist without key financial resources. It is important to note how the lab receives its funding. The laboratory receives funding from the following sources:

- Grants from non-profit organizations
- University funds
- Funds from the State of Arizona

The laboratory receives most of its funding through grants and from nonprofit organizations. One of the main sources of funds is from the President of the university itself. President of Arizona State University, Michael Crow helps provide funding for the laboratory project. Due to the importance of the project, President Crow told lab personnel to focus on their work of the lab and the university would help to provide the necessary funding (LaBaer). Other sources of funding for the laboratory are non-profit organizations and the government. The Virginia G. Piper Charitable Trust which has provided approximately two million dollars for equipment, labs, reagents, and supplies (Biodesign-2020-Year- In-Review_ISSUU). Another source of funding comes from the Arizona Department of Health Services (AZDHS). In July 2020, Arizona State University and AZDHS reached a partnership worth approximately thirty million dollars that aimed at providing free Coronavirus testing for the state of Arizona.

Another key player for funding comes from the government. Back in March, to combat the coronavirus, Congress passed the Coronavirus Aid, Relief, and Economic Security (CARES) act, which provided over 178 billion dollars to hospitals and healthcare workers (HHS.gov). Through Arizona governor Doug Ducey, 5.2 million dollars was distributed to the ABCTL from the CARES act in March (Thorne). The lab benefited from another 12 million dollar investment from the governor in July. The lab receives large amount of grants and funding; however, these funds are not only designed to benefit the lab itself.

Not for Profit Status

The goal of the lab as a nonprofit institution is to remain revenue neutral. This differs from businesses that focus on generating revenue. The main thing to note is the different in the purposes between the two entities. The purpose of the ABCTL is to help the greater world through research and providing COVID-19 testing to the general public. There is no incentive for the laboratory to profit off of its customer base. In this aspect, the laboratory is different from other organizations such as hospitals. Hospitals provide care and services to their patients. However, hospitals charge fees to their clients. Once the lab determined their goals and organizational structure, the next step was to obtain the necessary qualifications and accreditations for the laboratory.

Accreditation

The laboratory had to obtain the necessary accreditations and certifications to start COVID-19 testing. The lab had to receive regulatory clearance through the Federal Drug Administration. In order to do this, the lab needed to obtain CLIA certification.

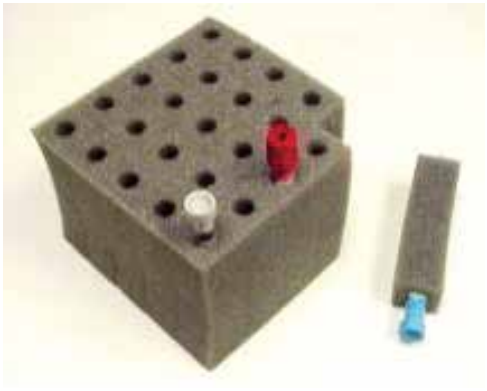
There are numerous components, competencies, and capabilities that a lab needs to obtain in order to be considered a COVID-19 testing laboratory including:

- Collecting, Handling, and Testing Clinical Specimens
- Conduct RT-PCR testing
- Obtain Clinical Laboratory Improvement Amendments (CLIA) certification
- Follow COVID-19 packaging under United Nations 3373guidleines (UN3373)
- Shipment of COVID-19 Specimens properly

Figure 9 contains the PCR testing machines. Figure 10 depicts the journey of a specimen and processes.

The laboratory had to take the necessary steps necessary to follow and meet the requirements listed above. When it comes to the collect, handling, and testing of clinical specimens, labs need to ensure that laboratory staff are trained on one set of standardized guidelines (CLIA). The next step for laboratories

to be considered COVID-19 institutions involves conducting RT-PCR testing (CLIA). RT-PCR testing is defined by the Federal Drug Administration as real-time reverse transcription polymerase chain reaction test for the qualitative detection of nucleic acid from SARS-CoV-2 in upper and lower respiratory specimens (Federal Drug Administration). The laboratory does this and has developed strategic processes along the way. The lab acquired the necessary competencies and capabilities to achieve CLIA status in April 2020.



Figures 10, 11, and 12 above show packaging used by laboratory to handle COVID-19 samples. Its CLIA status allows the lab to test humans and use their specimens for development purposes. COVID-19 testing facilities need to follow the proper COVID-19 packaging and shipment protocols effectively. CLIA requirements that specimens must be packaged in leak proof containers (CLIA). The laboratory these procedures, and the following figures are of packaging used by the laboratory to handle specimens. One of the aforementioned capabilities referred to labeling.

By obtaining the CLIA certification the laboratory was able to begin testing and help the community. The lab joins other accredited hospitals who strive to provide high quality care to its patients. In a JAMA Network article (2018), Ashish K. Jha, MD, mentions how hospitals with accreditation tend to provide better quality services than those who do not. In addition, Jha states that studies have shown that accredited institutions "are more likely to adhere to evidence-based process measures (Jha)." By taking the steps to meet CLIA requirements the laboratory is able to deliver quality services and safe care to its patients.

The Supply Chain Challenge

The next issue in this section focuses on the early problems that the laboratory faced in obtaining the materials needed for Supply Chain activities. After lab had conducted its research and obtained accreditations, it needed to obtain the materials and supplies needed to fully conduct its operations. The laboratory benefited from having some of the technology equipment already in place, however it needed to obtain the materials needed for value chain activities. An article from *The New England Journal of Medicine*, details how scores of institutions around the globe had trouble obtaining the necessary supplies to begin testing due to global shortages of personal protective equipment (PPE) (Griffeth). The lab faced this similar constraint and had to work hard to overcome the constraints that it faced. They had to build relationship with suppliers and find connections from across the globe. The lab also questioned how it would obtain testing samples. Dr. LaBaer mentions that at the beginning of testing, there were only two thousand nasopharyngeal swabs available in Arizona (LaBaer). The lab had to overcome this issue and did so through reaching out to the community.

This early chaos for the lab represented a growing pain for the lab in the infant stage of Adzes' life cycle stages. It had to work through the difficulties of not having the needed supplies. However, it demonstrated great resolve in working out relationships with suppliers and eventually obtaining the highly coveted nasal swabs. For further information about the Supply Chain about the laboratory please refer to Volume IV: An Analysis of its Upstream Supply Chain.

Demonstrating Agile Supply Chain Capabilities

As previously mentioned, the laboratory thrives on having quick business agility. The laboratory's Supply Chain capabilities are another example of business agility. This section looks at how the lab was able to procure supplies quickly that were necessary for testing. The lab had issues obtaining nasal swabs as it reached out tirelessly in the community. Joe Miceli, a key player in the procurement process for the lab mentions that the lab needed a third-party distributor in order to obtain the nasal swabs (J. Miceli, personal communication, October 24, 2020). In regard to obtaining PPE, the laboratory setup a donation drive where the research community could supply resources to the laboratory. A medical research article by *McKinsey & Company* suggests a strategy that the lab put to use. Authors of the article suggests universities partner with local laboratories to help with finding suppliers and improving processes. The laboratory has done this through working with the Arizona Department of Health Services. The lab partners with the organization to increase its funding, which expands the capacity of the laboratory to obtain the materials that it needs. The lab's funding help to offset the procurement costs that tons of relatable entities such as hospitals face. *Business Wire. com* details the issues faced in healthcare procurement which include limited control in price and hidden costs in healthcare procurement (*Business Wire.com*). The article also suggests that labs have the proper Health IT systems in place which can help to eliminate costs. The laboratory was not able to establish these systems at its origins, however as it grows into the future cutting down on procurement costs can help as it evolves into a growing enterprise.

Growing Enterprise

Customer/Market Base: High Early Need and Demand

Next in the analysis of the university lab as a startup involves looking at the customer base/market for the laboratory. When looking at obtaining customers early on in the beginning of an organization, companies in the infant stage are frequently challenged by the lack of customers and demand. However, this laboratory differed from most institutions in the infant stage as it had a large number of available customers who desperately need COVID-19 testing. The laboratory's main clients are the Arizona community. Specifically, the Arizona student population and residents of the surrounding Arizona area.

The ASU population has a risk for obtaining the virus with students being allowed to live on campus for the 2020-2021 academic school year. This population and the young adult population is at risk for the virus despite the virus being more mortal for the older population (Maragakis). In fact, a study by John Hopkins Medicine (2020), reports that of adults aged 18-34 who contracted COVID-19, "21% ended up in intensive care, 10% were placed on a breathing machine and 2.7% died (Maragakis)." These significant numbers worried scores of people in the Arizona community and beyond. In addition, an article by the Phoenix Business Journal mentions that, "People aged 20-44 make up 50% of all cases in the state" (Smith). Because of this statistic, it is vital that the lab conduct testing for this age demographic. In comparing the lab's consumer base to a typical for-profit business there are important distinctions to be made.

The consumers of the laboratory have few needs and preferences as their main need is to receive a COVID-test. The main criteria in evaluating which supplier to use for consumers is price and convenience. When looking at the consumer market, consumers have numerous preferences in regard to products. An example would be customer's preferences to designer cars. A Science Direct article details the importance of luxury car manufacturers who need to understand the customer requirements for a car such as speed, comfort, quality care, and tailor their services accordingly.

The main preferences for consumers in the COVID testing market are cost and quality of services. Looking at the lab as a business it has a large advantage over its numerous competitors that include Sonora Quest, Mayo Clinic, and others.

Strategic advantage

The lab has an advantage from these other institutions in that the services provided to the community are free of cost. Other institutions charge patients for receiving Coronavirus examinations and can have many burdensome issues for patients which include getting insurance companies involved and the coverage of healthcare plans. In addition, the laboratory holds an advantage over its competitors in regard to response time. The laboratory is able to return results back to patients within forty-eight hours. This quick response time for the laboratory represents its "ace in the hole" against other laboratories that have a response tine of a week. Another sector in which the lab thrives in and has an advantage over competitors is through its operations.

Operations of the Laboratory

The ABCTL thrives on an efficient operations system that allows its workflow processes to flow smoothly and provide effective services to its consumers. The laboratory is able to overcome constraint issues due to its effective operating workflow. An article by Health Leaders, emphasizes various strategies that can compete with disruptions with one of them being an effective "logistics command center" (Betbeze). The lab's "logistics command center" is located in the Biodesign Institute. The lab has an advantage over competitors in that it can testing results back to patients within 48 hours compared to other institutions which can take up to a week to get results back to patients. The lab's continuously expansion and innovation in testing capabilities allow its supply chain processes to flow quicker. For example, Joe Miceli stated that the development of the saliva test cut down costs related to PPE by seventy-five percent. With the continuous innovation of its supply chain, the lab mirrors businesses who utilize strategies such as Lean and Six Sigma to improve its efficiency. These efficient processes have given it an advantage over other healthcare providers in the industry.

Innovation and Advancement

The laboratory falls under the healthcare and non-profit industries. Despite, being a relatively infant organization, the laboratory has already made numerous innovations and has received national news coverage for its operations. With the development of the saliva test for COVID-19, the lab has demonstrated itself as an innovator in the industry. The laboratory has displayed the ability to keep up with the life cycle of the industry. The idea of the evolutionary industry life cycle known as "clock speed" comes from Massachusetts Institute of Technology (MIT) professor Charles Fine. Fine has written that "all advantage is temporary" (Fine). Because advantage is temporary, companies must be adaptable to change or face extinction. An example of how the ABCTL continues to be adaptable can be viewed in the developments of how the laboratory collects samples. Not only has the lab switched from the nasal swab test to the saliva test, but it has also improved its sample collection services evidenced through the new drop-off saliva test it offers. An article by *The State Press* explains how the test eliminates the need for in- person testing as patients can now pick up COVID-19 testing kits at locations across Arizona State University campuses (Dortch). Once an individual collects a sample, they simply drop their sample at one of the many testing sites (Dortch). The ABCTL followed the drop-off approach used by the University of Harvard. A *Harvard Gazette* article mentions how drop-off testing is "more flexible and convenient" for members of its community (Milkowski). The ABCTL has displayed its adaptability in seeking to improve its processes, while keeping up with other institutions in its industry.

It is helpful to look at another organization in the public enterprise that has displayed adaptability and innovation in the industry. For analysis purposes, the lab can be compared to the well-known brand Gatorade. Gatorade, established in 1965, was an innovator. The compay released a sports drink that gave athletes energy and electrolytes, which proved to be a great upgrade from the alternative hydration options at the time. The ABCTL became the first saliva testing institution in the Western United States. Going back to Gatorade as time went on other competitors developed products that began to compete with Gatorade. The saliva test for the laboratory has given them a leg up on competitors, however other institutions are closely following the laboratory, and developing methods and processes that challenge

the laboratory's prestigious rank. Gatorade knew the seriousness of its competition, and thus added a new product line known as the G-Series (Robertson). The ABCTL knows it will need to be innovative and has taken steps to begin developing the antibody test as previously mentioned, developing new tests, and expanding its research capabilities. These new ventures demonstrate the laboratory growing into the adolescence stage of Adzes' organizational life cycle. The laboratory is still developing new tests; however, it has found an established niche in the testing industry with the saliva test.

Future Outlook

What is the Future of the Lab in the Context of the Life Cycle Model?

The Future Outlook for the laboratory is a promising one. There are numerous routes and avenues that the laboratory can travel due to its strong leadership, available technology, and ready to use funding. Going back to Adzes' life cycle model, the laboratory can be currently slotted into the prime stage. The organization is at a good spot right now with its continuous innovation in testing and strong foundational framework. However, the laboratory will most likely transition into the stability and aristocracy stages as the COVID-19 pandemic slows down signifying a slowdown in success and market share. The most likely farthest stage the laboratory will enter is the recrimination stage where the lab's mission differs from the original purpose. The laboratory will not always be a hub buzzing with patients in the realm of the Coronavirus. It will need to develop new products and services to keep up with the change in times. With the continuous rise in COVID-19 vaccine production and distribution, this represents an industry that the laboratory can pursue. Dr. Neal Woodbury would like to see the Biodesign expand its testing capabilities.

He states that he would like to see testing capabilities for the flu. Woodbury explains how this is a new era of thinking about disease and would like to see the laboratory undertake endeavors to research and learn about various diseases. According to Woodbury, fifty thousand people a year die from pneumonia related viruses. The laboratory can be involved in the research and testing phases for years to come. It could be a research lab that quickly jumps into a testing facility for other viruses if needed. The organization's strong background makes it highly unlikely to ever enter the bureaucracy or death stages, with the recrimination stage the farthest that it will ever enter.

The laboratory originally started with its main aim to be COVID-19 testing facility. Most likely one day, the COVID-19 pandemic will greatly decrease in terms of cases. The laboratory will not be able to fulfill its original purposes of the recrimination stage. Instead, it will have to look for new testing and processes in which to develop. The lab is an unlikely candidate for bureaucracy or death due to its strong leadership background in place. Having the focus as a service organization, the laboratory does display any signs of bureaucratic entanglement. It would be surprising to see the lab diverge in any path that does not have serving the community and the ASU population as its main focus. There will, as discussed below, be a need to make decisions, understand different scenarios and prepare for the future. There are, however, options related to COVID-19 vaccination and research that the lab can further pursue.

Growth Distribution Curve

In addition to organizational life cycle stages, it is helpful to look at the distribution curve known as the S- Curve, which looks at the growth of organizations over time based on their dependence with numerous other variables. The diagram of the S-Curve is shown below in the following figure:

Figure 13: S-Curve distribution

The S-Curve distribution does not define growth as simply increasing profits and revenues, but instead places an emphasis on maintaining momentum with a mindset. Along the way, the organization faces numerous “inflection points” along the way, which are decisions that have the potential to either continue growth or stagnate (Barlow). The ABCTL has responded well to various “inflection points” so far in displaying its ability to continuously innovate its processes and be agile. In the middle of the S-Curve distribution figure is an innovation loop. Organizations need to constantly define, ideate, refine, and experiment throughout its life cycle. The lab has demonstrated these capabilities thus far and will need to continue them further into the future. Looking at the end of the S-Curve, the lab can either continue its forward momentum, face stagnation, or face obsolescence/no-growth. It is helpful to look at former rivals in the entertainment industry Netflix and Blockbuster. Pictured below is a graph comparing the growth adaptability between Blockbuster and Netflix:

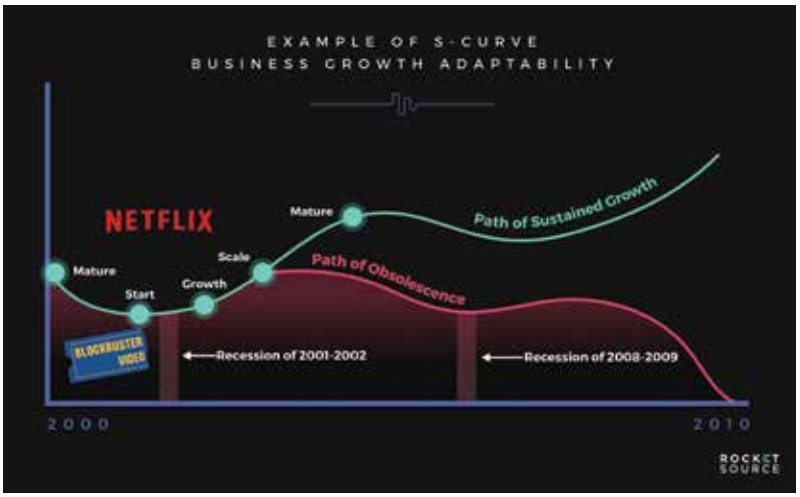


Figure 14: Growth Adaptability Comparison Between Netflix and Blockbuster

Netflix was able to sustain its growth and momentum into the future, while Blockbuster did not. Blockbuster experienced rapid growth in its early days as it thrived on an efficient barcode system that allowed it to track a substantially greater number of movies compared to its competitors. However, as time went on companies started to innovate and started to reach customers online (Ash). Blockbuster's brick-and-mortar store retail model proved to be largely inefficient compared to competitors and led to its demise (Ash). Looking further into the industry, private companies have nearly caught up to ABCTL's effectiveness and efficiency of testing, it might be time to leave COVID-19 testing up to the private sector. The laboratory will need to consider this scenario and others as well.

Scenario Planning

As previously mentioned, the laboratory has the opportunity to pursue numerous avenues and will need to consider various scenarios looking into the future. With all the change facing the laboratory looking into the future, it is of paramount importance for it utilize scenario planning. An article by Harvard Business Review details the importance of scenario planning and spotlights Shell Global, an organization that has scenario planning for great success in its operations (Wilkinson and Kupers). Scenario planning has numerous benefits as detailed by Germany's EBS Business School who explains "strategic foresight (scenario planning) efforts add value through an enhanced capacity to perceive change, an enhanced capacity to interpret and respond to change, influence on other actors, and an enhanced capacity for organizational learning (Wilkinson and Kupers).

The ABCTL should use scenario planning as it looks to find its identity in a post COVID-19 testing environment. When looking at how an organization should conduct scenario testing, Shell Global represents a strong example. Shell's scenario planning is not so much on predicting the future as it is focused on finding links between scenarios, and organizational processes such as: strategy making, innovation, risk management, public affairs, and leadership development (Wilkinson and Kupers). The lab can consider how COVID-19 will evolve; however, it should not be entirely concerned on predicting the future. It contrasts, the lab can consider the potential mutations of the Coronavirus and note the capabilities and processes it can develop to continue the survival of the organization. Jimmy Davidson, the Head Group of Planning for Shell form 1967-1976 makes a good argument when he explains, you can never identify all the forces at play. If you could, and see their interactions, then real prediction of the future would be simple." The lab needs to be aware of future scenarios, and when possible, takes steps to quantify numbers and amounts relevant to scenario planning. However, it could not spend its entirety predicting the future. It can instead plan for scenarios using agile framework to be adaptable to attack future opportunities and challenges that may arise. The ABCTL has a few options to choose from in moving forward as a business which we will now analyze in greater detail.

Antibody Testing

The ABCTL is in the process of developing an antibody test. In winter 2020, the laboratory received a 12.5 million multiyear subcontract from the Frederick National Laboratory for Cancer Research (FNL), to help further expand its testing capabilities and become part of the Serological Sciences Network, which is the United States largest endeavor to study patient's responses to COVID-19 (Caspermeyer). This grant will help with antibody testing as Dr. Joshua LaBaer states, "We hope to develop a simple, FDA-approved COVID-19 antibody test to detect for previous SARS-CoV2 exposure and to better understand a person's immune response to COVID-19 (Caspermeyer)." This development by the laboratory in expanding its laboratory testing demonstrates an initiative to innovation, which isa critical component of agile organizations. The laboratory jumped ahead in the COVID testing market back in the spring, however other institutions and laboratories are starting up and competing with the laboratory's services. The lab is trying to enter the Blue Ocean of laboratory testing by offering an FDA approved antibody test (Agile Planning Map). Doing so will help to expand the scope of the lab far into the future with the uncertainty of the COVID-19 pandemic.

Molecular Testing

A potential possibility for the laboratory to pursue is to expand its molecular testing capabilities. A *Modern Healthcare* article by Adam Bonislawski (2020) mentions how labs that did not previously have the ability to conduct molecular testing now do so with its expanded technological testing capabilities. Hopefully in the future, the world can experience a post COVID-19 environment. Institutions that have focused their energies on Coronavirus testing will need to look for ways in which it can expand its services. Molecular testing is a huge opportunity for the university as it already has the technology in place. An article by *Sunquest*, mentions for labs looking to grow in volume and complexity need a purposeful technology system that can help the laboratory with its testing prowess. The laboratory's increased testing capabilities in the future can help serve as an asset to the Arizona community. Despite the advantages provided by testing, the laboratory can decide to also pursue research and other works. The laboratory can function like a fire department. It can become a premier research institution, while also being ready to answer the call for an immediate to test the next wave of viruses in the future.

Conclusion

This section has demonstrated how the ABTL emerged and progressed through the early stages of the organizational life cycle and how its agility has provided for both speed and success. Key issues identified included organizational resolve, organizational structure, securing financing, supplies and legitimacy through accreditation. Looking at the future of the laboratory's supply chain it will need to be continually adaptable and agile as it carries on into the future. A scholarly article published in the Milbank Quarterly, mentions five key attributes for a competent national healthcare system which include: flexibility, transparency, persistence, global independence, and for the lab to be equitable (Handfield et. al.). The lab has already demonstrated its flexibility, persistence, and transparency during the pandemic. Assembled quickly, the lab has proven to be able to operate effectively given a short time frame. Lab personnel have been persistent, an example being Joe Miceli who went great lengths to obtain the nasal swabs that were necessary for the lab to conduct its supply chain operations in the early stages. Next, it's critical that the laboratory becomes more financially independent in the future. The laboratory will not always be able to obtain funds at will from the University president. Hopefully, the laboratory can improve its financial systems and supply chain processes to cut down on costs, which will allow it to have more funding for future endeavors.

The laboratory has proved to be great for the Arizona community and the healthcare industry. Developments by the laboratory have helped it receive national news coverage for its efforts. The development of the saliva test has greatly increased supply chain efficiency and decreased wait times for consumers all across Arizona. Although, the laboratory was assembled in a relatively short period of

time, having the proper leadership and technology in place has allowed it to prosper into the premier COVID-19 institution in Arizona and become a force in the healthcare industry. The laboratory has an opportunity to maintain its competitive advantage over other firms. In ohn Mullin's keys to org competitive advantage, he details how organizations with "superior organizational processes, capabilities, or resources" (Mullins), have an advantage over those who do not. The ABCTL will need to continue its roll of innovation in to beat competitors and serve its customers. The laboratory will not always be able to be filled with patients during a pandemic. It will need to develop multiple functional areas where it can be fully effective. Importantly, the laboratory could function as a research institution ready to answer the call when needed to provide testing services to the community. With the laboratory's goal being to save lives and a firm foundational framework in place, the laboratory should continue to thrive in its operations for years to come.

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Section III: An Operations Management Perspective

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Introduction

This section will describe and assess the operational risk management practices of ABCTL as an evolving, university-based laboratory in a COVID-19 era. The purpose of this volume is to depict the operational challenges ABCTL has had to overcome and how they continually mitigate operational risks using an operational risk management framework. This volume will provide a basis for best operating practices in a similar laboratory setting to minimize the potential for operational risks. I will compare the operational risk management practices of ABCTL to those suggested in literature over various topics including but not limited to certifications, clinical laboratory regulations, and potential operational risks across testing processes and staff.

To preface this section, it is important to note that ABCTL is constantly adapting to the status of the pandemic and needs of the state and university. Being a laboratory within Arizona State University, a university extremely focused on innovation, it is no surprise that the laboratory management staff is constantly looking for ways to improve and refine the processes involved in order to best serve the immediate needs of the community. Because of this, the operational processes and regulatory procedures are regularly changing. What started as a response to a university need has developed into a community-reliant, fully functional, business- like testing laboratory.

Operations Management and Operational Risk Management

Overview

Operations Management (OM) is a business function designated to oversee the transformation process of inputs into outputs. OM includes the transformation process enhancements dedicated to efficiency and effectiveness, involving heavy and frequent measurement and analysis of internal processes (McNamara). The accumulation of all of the transformation processes of inputs into outputs form an operational system that an operations manager is responsible to oversee and continually improve. Inputs include but are not limited to experience, funding, equipment, materials, and customer feedback that all proceed to form outputs, or high-quality products and services (McNamara).

This section discusses and analyzes ABCTL with an operational risk management framework, which is a function under OM focused on the quality and safety of internal processes with an intention of mitigating risk. For the purpose of this effort, the operational risk is defined as as the risk of loss resulting from inadequate or failed internal processes, people, systems, or external events. Internal processes in a laboratory setting can include internal transportation processes or hiring processes, the risks associated with staffing and human error is categorized under people, systems include the processes to transform inputs into desired outputs, and external events includes the risk of disruptions of testing due to supply chain failure (a common issue with procurement in laboratories during COVID-19). Operational risk management deals with uncovering and mitigating the risks that those processes, people, systems, or external events evoke.

In a laboratory environment it is extremely important to be diligent in operational risk management efforts. Samples containing insufficient volumes, errors with managing quality control, and the failure in reporting are all errors that can easily be resolved with an efficient operational risk management strategy within laboratories (Hammerling). Most errors (64.5%- 93%) in laboratory testing occur in the pre- and post- analytical phases of testing, so the errors are most frequently stemming from the organization's inconsistent and erroneous operational procedures and not with the test itself (Hammerling). ABCTL is tasked with sending out patient results of COVID-19 tests, either positive or negative, and if that were to

be incorrect there would be large consequences for the laboratory and the surrounding environment. If a test is truly negative but sent to the patient as positive, then there is a patient in quarantine for 14 days for no reason. On the other hand, if a test is positive but recorded as negative there could be a large spread of the virus to others surrounding the patient, harming more people.

The following sections include a discussion of "generic" operations management concepts and issues – those that are important across many organizations in different settings. These issues include Risk Mapping, Risk Metrics, and Quality Control vs. Operational Risk Management. These sections are followed by a focus on the testing laboratory setting where we consider the overall setting, the regulatory environment, especially CLIA, and HIPPA and issues related to data security and risk in the laboratory environment. We then consider the specific case of the ABCTL and its collection processes, risks, risk metrics and processes including collection, inventory control, and staffing. We are reflective of the fact that there are processes not under the direct control of the ABCTL – this is considered the outsourcing environment.

Risk Mapping

Successful operational risk management in a laboratory combines all best operating practices, as highlighted under regulatory guidelines, while maintaining a constant reevaluation of the processes that pose the most risks. It is important to first uncover the largest risks throughout the testing process through the development of a process map and identifying the steps that have the greatest potential for risk. A great operations risk management strategy ensures all processes, people, and systems throughout the phases of testing operate with the same intent and goal in mind while predicting and preventing risk from external events.

Risk mapping is one of the tools used to identify the specific steps that hold the key risk indicators (KRIs) in an operational business process (Scandizzo, 2005). Scandizzo states that "risk mapping is an analysis tool whereby risk exposures are linked to the relevant parts of the business process" (2005). Risk mapping is a systematic process that works to uncover what can go wrong at each step in the process. It attempts to pinpoint the root causes of error based on three main resources: people, processes, and systems. Within those main resources, risk mapping then uncovers which part of the organization was responsible for the failure and then the impact of the error (Scandizzo, 2005). KRI's are then identified through statistically measuring the probability of the risk occurring which then, if meaningful, are used to anticipate future areas of error (Scandizzo, 2005).

Although Scandizzo is referring to operational risk areas more prevalent in the banking industry, his argument uses the same risk drivers defined in operational risk management (people, process, technology, and external factors) to determine the business activities and processes that pose the greatest risk (2005). Additionally, Scandizzo uses a risk severity matrix with axis for likelihood and potential impact to place the KRIs into (2005). With each risk driver it is important to identify all risk factors that driver poses (ex: under the risk driver of People, the quantity of staff is a risk factor) (Scandizzo, 2005). Then their risks, the potential losses they could ensue, and the KRIs are determined. Keeping a watch on the KRIs, such as % of staffing needs met, allows for the constant oversight of the risk factor associated with the KRI (Scandizzo, 2005). This provides a substantial and quantifiable way to check on potential risks that have been identified in processes and potentially catch errors before they happen, like hiring more staff as soon as possible.

Risk Matrices

Errors in different steps in the processes can cause different levels of risk based on their frequency and likelihood of occurring. The combinations of different frequencies and likelihoods occurring can be combined into a Risk Matrix. Errors happening frequently but with minor impacts or changes to the processes are considered low risk. Errors that are not likely or unlikely to occur but with moderate impacts

are also low risk, along with errors that have a remote chance of occurring (<2%). Those with high-risk have a major to extreme consequence of occurring and are considered possible or likely to occur.

Figure 1 - Risk Matrix Template

In operational risk management the focus needs to be to first identify the high-risk errors, change the processes resulting in those errors, and then compare the results before and after to hopefully identify a change in its error category.

Quality Control vs. Operational Risk Management

Quality control is seemingly similar to operational risk management, especially through the lens of a laboratory setting, but quality control is most concerned with the internal processes and systems dedicated to transforming the test sample (input) into an accurate result sent to the patient (output). Quality control is most concerned with the transformation process that the test sample goes through and ensuring the result that is given to the patient is the correct result. On the other hand, operational risk management covers the entirety of the testing process, from the appointment setup to the disposal of the remaining sample and everything in between, including staff considerations. Although operational risk management and quality control have a few overlappings in their efforts in risk mitigation, operational risk management covers a broader range of areas for mitigation efforts than quality control does.

The Testing Laboratory Setting

Under Good Clinical Laboratory Practices (GCLP), twelve different operating procedures are outlined in an effort to minimize the potential areas for risk in a laboratory setting (Ezzelle et. al., 2008). “These procedures include those related to quality control, such as including a quality control program and assigning a quality manager, but they are not limited to only quality control sectors causing risks” (Ezzelle et. al., 2008). Other procedures of the GCLP outline the necessity of having proper training for laboratory staff and having a standard documented procedure for transporting and managing specimens which are, in contrast, operational risk mitigation efforts (Ezzelle et. al., 2008). Quality control specializes in mitigating errors and risks within the testing processes itself, including factors surrounding the machines and technology used to transform the test sample into a positive or negative result.

Operational Risk Management is focused on finding the areas of greatest concern through different techniques in order to mitigate the risk threats posed during operations. Successful operational risk management does this by constantly and continually asking questions about business processes to ensure they are operating under good practices. In a laboratory environment, it is important to ask questions like “how are we checking that the test sample is from the correct test subject” and “what are

the steps in place to make sure there is not any tampering done with the test sample." There are many areas for risk along a testing process, starting from when the test subject states that they do not have symptoms to the computer- generated results being checked by a qualified individual. The potentials for risk at each step in the processes have to be considered in order to mitigate the risks before they cause errors.

Operational risk management can provide a basis for laboratory quality control practices in order to highlight the key areas of caution for laboratory operations. Nichols argues that the first step in taking a risk management approach to quality control in laboratories is to create a process map (2011). The process map should include all steps of the testing process, including the pre-analytical, the analytical, and the post-analytical testing phases (Nichols, 2011). This is important in order to pin-point potential sources of error, keeping in mind that most errors in a testing process occur in the preanalytical or post-analytical phases (Nichols, 2011). It is suggested that laboratories use control processes, such as testing control samples frequently, on a regular basis in order to stay up to date on the status of processes and machine's results accuracy (Nichols, 2011). Viewing laboratory quality control through a risk management perspective allows operations personnel to be confident in their testing processes producing accurate results to patients.

Clinical laboratory testing is separated into three different processes: pre-analytical, analytical, and post-analytical. The highest percentage of errors (46-68.2%) are reported during the pre-analytical phase of testing, which includes the incorrect identification of the patient, the mislabeling of the sample, incorrect tube storage, etc. (Eliza and Mindora, 2015). 18.5-47% of the errors are due to the post-analytical process including the correct result being identified, the results going to the correct, etc. (Eliza and Mindora, 2015). The stage that is least likely to produce errors is in the analytical process itself, but if an error occurs in this process, it would include errors due to the reagents, equipment, internal control measures, or not following the procedures (Eliza and Mindora, 2015). It is inherent that laboratories evaluate their processes at each phase of testing to ensure they are mitigating the errors that have a higher probability of occurring.

The Regulatory Environment and Clinical Laboratory Testing

Overview

Considering how fast laboratories had to start operating during the COVID-19 outbreak, it is valuable to analyze laboratories now through an operational risk assessment. A survey conducted by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), a non-political organization tasked with setting a global standard and best practices for clinical laboratories, showed that in April 2020 most operating COVID-19 testing laboratories highlighted that "ensuring safety within the laboratory was an ongoing challenge. Reported operational challenges included managing the change in test demands and in operational processes, as well as needing to set up new diagnostic tests within a very short time" (Loh et al., 2020). Having to set up diagnostic testing systems and procedures in a rush is concerning for the safety and quality of testing laboratories if not properly operating. Rushing to operate can also result in laboratories not following the Good Clinical Laboratory Practices (GCLP) or other regulatory procedures properly. It is important to have designated personnel to cover certain areas of the laboratory's operations, such as someone to be a single point of contact for all document control. When starting up operations in a hurry, it is easy to overlook certain aspects of safety and documentation because of the dire need for operations.

Additionally, to having to set up laboratories quickly, the laboratories had to be operating in a regulatory environment. Thankfully, the U.S. Food and Drug Administration (FDA) during COVID-19 realized the importance of approving tests in a timely manner, but that is only the beginning of compiling with the important rules and regulations for testing laboratories. Clinical Laboratory Improvement Amendments act of 1988 (CLIA) is another crucial certificate for testing laboratories, although a more strenuous process.

CLIA covers all phases of the laboratory testing including the reporting out of test results (Centers for Medicare & Medicaid Services (CMS), 2014).

Abiding by CLIA is important for laboratories to ensure they are sending out reliable and accurate test results (Eliza and Mindora, 2015). During the pandemic, the Centers for Medicare and Medicaid Services (CMS) that runs CLIA temporarily loosened their restrictions on university-based labs giving results to patients ("Lab Testing FAQs", 2020). Before a laboratory's CLIA certification, the laboratories can only provide "presumptive positive or inconclusive test results" and refer them to take a test at a CLIA certified laboratory ("Lab Testing FAQs", 2020). ABCTL is operating as a university-based laboratory and was able to provide patient-specific results because the CMS reduced their enforcement of certifications of tests considered surveillance testing. CLIA guidelines enforce that laboratories are following the manufacturer instructions properly and is a baseline for laboratory safety and quality assurance ("Frequently Asked Questions (FAQs), CLIA Guidance During the COVID-19 Emergency", 2020). CLIA is a high standard of certification for laboratories to operate under because it provides the certification of the mitigation procedures combatting the common operational risks.

Health Insurance Portability and Accountability Act (HIPAA)

The Health Insurance Portability and Accountability Act (HIPAA) is another act enacted in 1996 in order to protect patients' privacy and security (CMS, 2014). HIPAA ensures that test results are securely reported back to the patients, considering both the privacy and security of that disclosure. Under privacy regulations, any personal identifiers, or protected health information (PHI), are not allowed to be disclosed to anyone but the patient (W. Lee and C. Lee, 2008). This includes but is not limited to the patient's address, telephone number, and name (W. Lee and C. Lee, 2008). On the other hand, information such as admission sequence number or charge number are considered deidentified health information and its disclosure is not restricted (W. Lee and C. Lee, 2008). It is inherent that testing laboratories operate in a HIPAA compliant manner as to not ensue and damage or loss to the university.

The laboratory's risk mitigation efforts also impact its customers: the staff, students, and general public that they serve. How to distribute test results safely and conveniently in a university setting is a large, impactful consideration. These HIPAA regulations put additional pressure on the Biodesign Institute, never before testing such a large portion of the population at a time. Fortunately, though, being attached to an institution, especially one as large as Arizona State University, means that there are already precedents in place for providing test results of any kind. The Biodesign Institute's adoption of ASU Health Center's PointnClick system was easy as it was already in use within the ASU Health Center and is reputable as a HIPAA compliant site.

This is also important for Arizona State's liability considerations when providing test results as if it were a primary health care provider. Most testing procedures end in the testing center notifying the primary healthcare provider of the results for them to share with their patients, but in the era of COVID-19 this has changed. Most people getting COVID tests go through independent testing centers, because of the need to isolate and the ease and speed of centralized testing. This means that testing centers are deemed liable for the accuracy of the results that they share with the patient. The Biodesign Institute has a designated individual, Dr. Carolyn Compton, named as the doctor for all test results they send out. She is responsible for all results being correctly sent out with the accurate result and to the correct patient (Compton, 2020). Paperwork had to be signed in order to relieve Dr. Compton of all liabilities in the case of harm ensuing from an inaccurate test result. This is low on the risk matrix because it is not a common occurrence, nor can it harm ABCTL due to the legal documents signed.

Data Security Risks

Especially now in the 21st century where receiving test results and storing patient information in a database is the easiest and fastest way to send and receive test results, it is important to analyze HIPAA and the role it plays in patient information security. The creation of HIPAA was aimed at protecting private

patient information, so patients feel comfortable disclosing information to their doctors (Annas, 2003). Even back in 2003, Annas points out that some computer experts at the time believe that "personal control of private information is an illusion in the computer age and that privacy is already dead." Now in 2021, the Internet of Things (IoT) plays a large role in daily life, and a much larger role than it had in 2003. Data security is a large concern withholding information in a patient portal and a failure of good data security can have many repercussions on both the healthcare provider and the patient.

In 2018 a new initiative, MyHealthEData, was announced with the intention of making patient health data more accessible to help individuals manage their health (Cohen & Mello, 2018). Especially considering the recent data breaches in sites like Facebook, data is never fully secure online which is concerning when storing confidential health data online (Cohen & Mello, 2018). The increase of data storage systems for healthcare and PHI questions HIPAA's validity and protection of patient privacy in this day and age. The failure of HIPAA in covering all health-related concerns (such as target advertising done through shared data between various types of companies) raises questions about the liability of data breaches of such electronic storage systems (Cohen & Mellow, 2018). Since HIPAA only applies to entities and not types of information, it is imperative to create a more encompassing set of rules regarding the spread of data that is relevant to patient health (Cohen & Mellow, 2018).

Despite the data security concerns over an Electronic Medical Record (EMR) system, there are some benefits that come with the ease of electronically sharing information. In a study conducted from May 2000 to September 2001 looking at the influenza vaccination rates in comparison to child asthma hospitalization showed that the EMR's streamlined system made it easier to see the correlation between vaccinations and decreased hospitalization rates (Martin, 2006 pg. 221). Using an EMR system is known to decrease pharmacy errors and costs while improving the care provided to patients (Martin, 2006, 225). In addition to decreasing pediatric asthma-related hospitalizations, EMR systems in clinical uses increase the quality of care provided to patients including those with diabetes showing decreased levels of key indicators after implementation (Martin, 2006, 225). Although data security is a major concern with implementing EMR systems globally, there are large benefits to storing patient information online with easy accessibility.

ASU's Biodesign Clinical Testing Laboratory (ABCTL)

Overview

Over five weeks the Business Group conducted interviews with six different individuals that all played a role in developing the ABCTL's operations in one way or another. We also took a 30-minute tour of the laboratory to see the operation first-hand, guided by two important lab personnel that we later interviewed. I have also personally taken over 20 COVID-19 tests through the Biodesign Institute over the past six month and have noticed something new about the process every time (due to changes in processes, the variation in staff's procedures, and my perception of different stages each round). After conducting primary research and developing outlines, I reviewed countless articles discussing the importance of operational risk management that led me to discover areas of potential risk in the ABCTL. For the next segment of this volume, I will discuss the five areas and processes I see within the ABCTL that pose the greatest operational risks that I have uncovered from all of the reviewed literature.

The first discussion focuses on the collection process, the operational risks associated with collecting test samples and what the best measures are in place in order to mitigate these risks. Second, I will look into the receiving process at the Biodesign Institute and how to ensure that the test samples are being safely received by staff and best reported under GCLP and CLIA guidelines. Third I will highlight the areas in the transformation process of the test sample that pose the greatest operational risk to the organization in terms of both processes, people, and systems.

The second discussion focuses on the inventory management processes in relation to best practices, including the systems in place tracking reagents expiration dates and comparing ABCTL to another COVID-19 testing site, Banner Health. My last area of scrutiny is covering the staffing risks throughout the laboratory and the implications a shortage of staff would have on the testing process. In conclusion of this volume, I will consider the potential operational risks that could arise under different potential global future outcomes and provide an analysis of the strategies that allowed ABCTL to mitigate their operational risks to the best of their abilities.

Collection Process

The internal test collection process is a relatively simple process with multiple steps designated to ensure the patient data is being accurately recorded into the system. Since this is the pre-analytical phase, it is important to ensure the correct procedures are being followed because of the large probability for error at this stage (Eliza et. al., 2015). At a high-level, the saliva PCR test is done by the patient spitting their saliva into a specimen vial and turning it in to volunteers at the testing center. Since this is a relatively simple procedure, it is easy to assume that there is not much room for error. In reality, the process requires both the working staff to be well-trained and following necessary confirmation procedures and the patient to be diligent and honest with their answers to the questions they are asked. Figure 2 below illustrates the testing process steps, starting with the subject booking an appointment online to a staff member checking the final test sample and the patient's date of birth and form of identification.

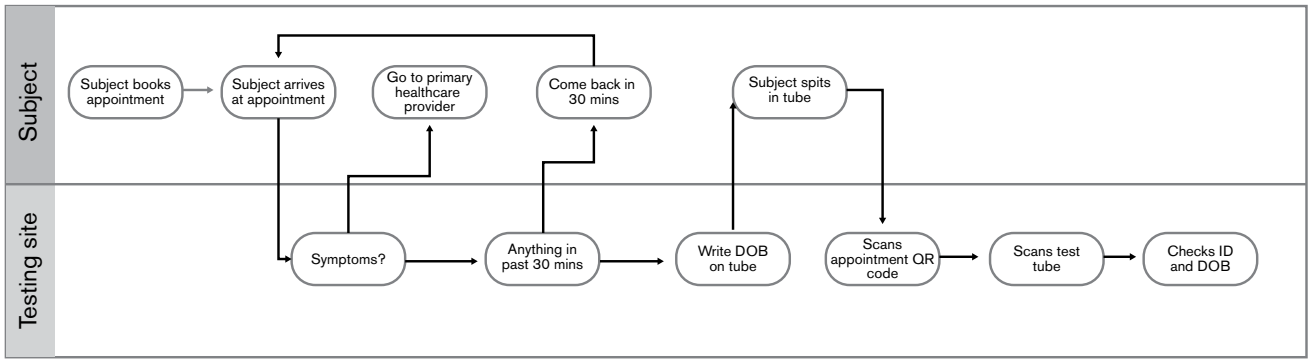

Figure 2 - Testing Process at ASU

The process starts with the subject booking their appointment online through the PointandClick portal which sends them a QR code that holds their personal information. The subject then arrives at their designated time and is asked two questions: "Are you experiencing any of the following symptoms?", and "Have you eaten or drank anything in the past 30 minutes? "These questions are necessary steps in the process as they are efforts to ensure quality control.

The saliva-based PCR test is most accurately transformed into positive or negative results if the subject has not had food, water, gum, or smoked/vaped in the past 30 minutes. As of recent, though, it has been found that the only real concern is with those who chew tobacco, so there is a low risk for an incorrect test result if the patient lies (Nelson, 2021). The subjects are next asked their date of birth and the staff member writes it on the specimen vial. Then they are told the instructions for the test, to use the straw to deposit saliva into the vial, to seal the cap tightly, and to wipe down everything after use.

After the subject follows these instructions in their assigned chair, they throw away the excess materials (the straw, straw wrappings, and wipe in a plastic bag) and go in line to turn in their vials. The staff member at this station inquires about the patients' relation to ASU (staff or student) because that correlates to the necessary health portal (HIPAA complaint for students) that they send the information in and out of. The staff then scans the data matrix symbol on the specimen vial and scans the patient's QR code, connecting the two together for the rest of the testing process. The staff is also responsible to

then confirm the date of birth labeled on the vial and check a photo ID to confirm the identity of the person dropping the vial off. This is in order to ensure the test results are tied to the correct vial that is tied to the correct patient portal of the correct individual. The staff then places the vial into a larger, Styrofoam cooler to be transported to the Biodesign Institute.

The first area that stands out as an area for potential operational risk throughout this process is the process's reliance on truthful patients when answering the staff's questions. If the patient says "no" to having symptoms when they are experiencing one or more symptoms there is an inherent risk of the potential spread of the virus to the staff members and volunteers and the other patients. This potential error would be considered a medium risk in the risk matrix because it is probable that students lie and potentially spread infections, but it is hard to confirm the exact moment of infection, so the outcome is uncritical. If the patient lies about eating or drinking in the past 30 minutes, there is less of an impact on the testing facility and Biodesign Institute as a whole. Either the staff catches the lie when inspecting the vial before placing it in the cooler or the test results produce an inaccurate result or cannot be read.

One effort in place as a partial effort in reducing operational risk is the use of specimen vials with data matrix symbols on them. ABCTL has gone through several phases of test tubes each with different forms of 1D and 2D codes on the vials. The first two phases included barcode stickers for scanning, but now ABCTL purchases vials with built in data matrix symbols (similar looking to QR codes) on the bottom of the test tube.

They made this switch because of the caps of the tube that coincide with decapper machines. This is not only efficient for the laboratory's operations because of the automation, but they are also safer in protecting private patient information and are more durable than stickers. Additionally, the 2D symbol on the vial is read differently than a 1D barcode is read. A 1D barcode reader is able to detect errors and prevent misreads, but it cannot fix the error it found (Barcode-Test, 2014). A 2D scanner, on the other hand, can both find the error and correct it if between 7-40% of the data matrix is damaged (Barcode-Test, 2014). The switch from tubes was initially due to the want to automate the decapping process but has added benefits in the protection of information and a greater coded durability.

It is important to note that the process to switch tubes in the midst of operations was not an easy process. ABCTL had made a contract with a tube manufacturer and had committed to buying over a million of the second-generation tubes with labels over 12 weeks (Deuser, 2020). Luckily for ABCTL the manufacturer was able to switch to the more efficient and durable tube six weeks in, but that is not always the case for smaller companies with less of a leverage over their suppliers (Deuser, 2020). The combination of the unique global situation and the need for ABCTL to continue supplying tests to the community made the safer innovation effort possible. In other cases, this could not have been able to have been accomplished, so although it did mitigate an operational risk not all operational risk management efforts can always be accomplished by all companies.

Outsourcing and Receiving

The testing process described above is specifically for the on-campus testing site at ASU and is different from the process ABCTL goes through in outsourcing their operations. Although the test itself is run in a similar manner, it is more difficult to regulate the collection procedure because in most cases ABCTL's staff is not responsible for running the operations. ABCTL, in the beginning of the pandemic, went into contractual agreements with nearby businesses for testing their employees on a regular basis (Deuser, 2020). Inherent risks are posed with outsourcing collections because ABCTL cannot ensure the quality of the test samples until they are at Biodesign Institute. Tamara Deuser, COO of Knowledge Enterprise, was able to mitigate the potential risks through her contract negotiation strategies, leaving the university free of any liability that could occur (2020). In a normal situation, ABCTL would not have had such favorable contract negotiation processes but due to the global state of emergency the balance between supply and demand had companies eager to partner with ABCTL and have access to regular testing facilities.

Under GCLP standards, the receiving process at the testing facility of all tests should have important procedures. “The establishment of a sound specimen chain of custody from collection through to reporting of test results is paramount in ensuring quality data” (Ezzelle et. al., 2008). Along with a chain of custody being established in order to ensure the quality of test specimens, other quality control measures such as the inspection of containers and the documentation of rejected/accepted criteria is necessary to have standardized testing procedures.

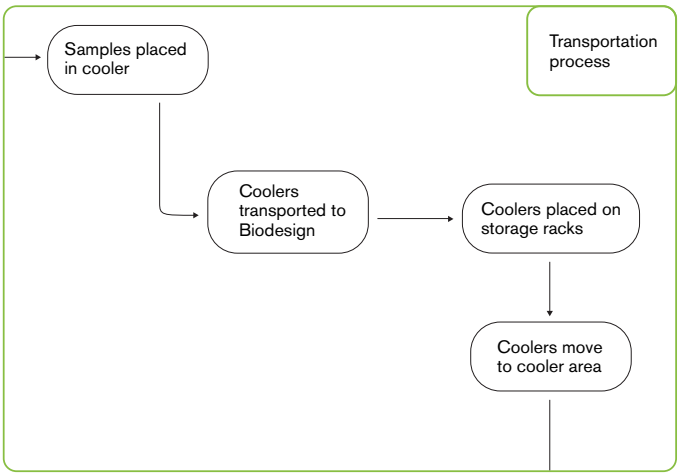

Figure 3 - Transportation Process of Test Samples to ABCTL

The coolers get transported to the Biodesign Institute to continue along the testing process. They are placed on shelves in the loading dock area of the Institute and are left for an average of 2-3 hours but up to 8-10 hours. There is a sign off of custody here and an additional one following the placement of the coolers in a cooling room before they move to the analytical phase of testing. These procedures are necessary in following CLIA guidelines and are a part of security and quality assurance throughout the process in order to minimize the potential for risk that the university could be responsible for.

Specimen Analysis

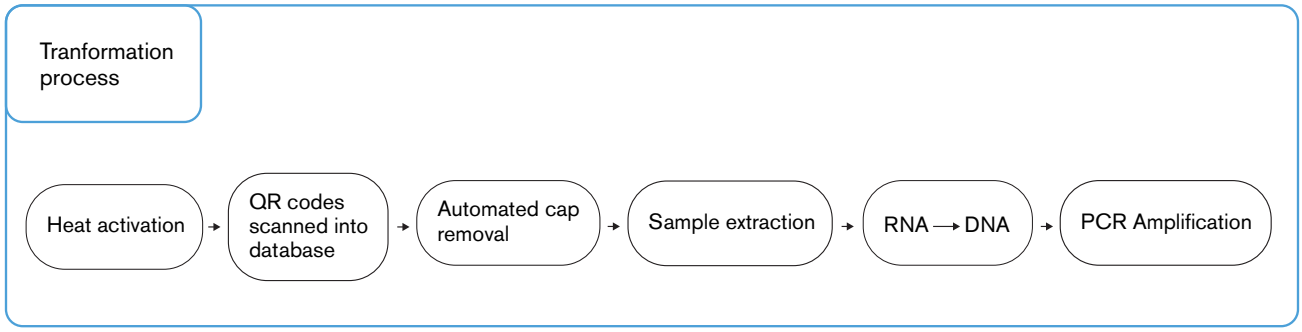

Figure 4 - ABCTL Transformation Process

The first step in the transformation process is heat activation, where the samples are placed in a room to be heated for one hour to kill the virus in the samples. This first step is important because it decreases the biosafety from a level three to a level two, meaning the staff who interact with the coolers and samples following the heat activation do not need to be in full PPE nor worried about catching the highly contagious virus. After this, the individual samples get hand-scanned into a database marking their reception into the laboratory and the start of the sample transformation. Because this is not an automated task, there is room for human error during the process. If a staff member misses scanning in a sample, the error will be caught in the post-analytical phase of testing.

The next steps are the automated cap removal process and the automatic extraction of the sample done by the Biomek i7. The decision to recently automate the cap removal process was a recent one mostly made with a consideration of the balance between speed, quality, and cost (Murugan, 2020). Implemented partially as a quality control measure, the automation of the process makes it much easier to identify any errors along the way, contrastingly to how human error is difficult to detect early on (Murugan, 2020).

The final transformation process is all done through machines and ends in a final output of results, either positive, negative, or invalid. This output is based on three genes and 2/3 of the genes have to be positive for the test to be considered positive. Before the results are sent to patients, they are all viewed by qualified individuals before the results are sent back to patients.

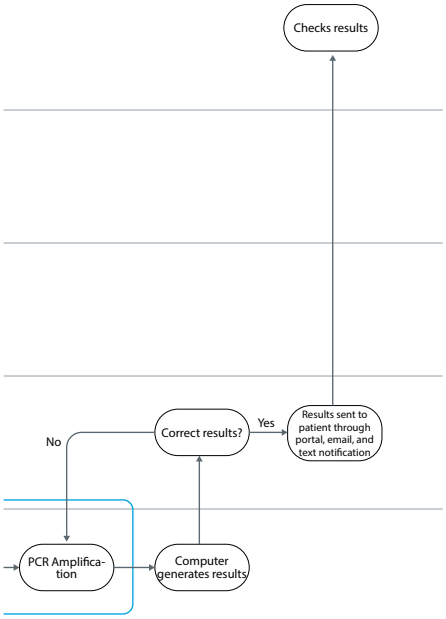

Figure 5 - ABCTL Distribution of Test Results

At the time of our interview with Vel Murugan on October 23rd, 2020 he was the only one who was qualified to verify every test result sent out and therefore had double checked every single test result sent from ABCTL. When asked about the objectivity of the test results, Murugan said that “99.9% of tests are not subjective and are very clear with a positive or negative outcome” (2020). The remaining 0.01% of tests that are undetermined are retested and at that point 99% will show clear results (Murugan, 2020). The operational risks that come about due to the systems in place are very low, since there is a low chance for error and a low frequency of the error actually occurring.

Inventory Control

Strict and detailed inventory control processes are also necessary in mitigating and managing the potential for operational risk. For the purpose of this volume inventory control is defined as a planned approach of determining what to order, when to order and how much to order and how much to stock so that costs associated with buying and storing are optimal without interrupting production and sales (McNamara). A part of inventory control that is especially prevalent in ABCTL during the COVID-era is the storing and tracking of all goods but especially the reagents.

ABCTL tracks their reagent inventory and expiration dates by inputting their dates into an Excel spreadsheet. The main issue that they see happen the most frequently is within the receipt of their reagents, where the expiration date is not listed for that case of reagents (Nelson, 2021). In that situation, the laboratory sets the expiration date as a year from the date of the arrival of that case as

is recommended (Nelson, 2021). There is a risk here for potentially using expired reagents, but it is minimized through the operating procedures.

Similarly, Banner Health also uses Excel spreadsheets to track their inventory levels of reagents (White, 2020). Although Excel is not a complex tracking system, before the pandemic they did not have a need for complex tracking procedures as they were never operating with such large capacities in the past (White, 2020). Now Banner Health is switching over to an Enterprise Resource Planning (ERP) system, not due to the increase in testing volume but because Banner Health as a whole is implementing it throughout and it requires cross functional support (White, 2020).

Another crucial part of tracking reagent in a proper system is to monitor the recalls. If each reagent is properly tracked in a database and in storage, when a recall of a reagent occurs it is much quicker to remove the expired reagent than if they are stored in an unorganized way. If reagents are stored together based on batch numbers, this adds to the quickness of the process and also the quality of the process. It is much easier to ensure you have removed all expired or recalled reagents if they are located in the same place because of the processes in place.

Another risk associated with inventory control is the wide availability of counterfeit tubes. In the beginning of ABCTL's procurement process, they encountered many instances of being offered counterfeit tubes to use in their operations (LaBaer, 2020). If the correct quality control measures are not in place to ensure that no counterfeit tubes were being purchased, there could be a large risk of loss to the university including providing inaccurate results and failure of product, both of which would cost ABCTL a substantial amount of money in a time of shortages of such supplies. Both the external events of the pandemic causing a large demand for tubes and the internal quality control measures in place are crucial in mitigating the potential for risk or loss.

There are also greater stockout risks associated with a testing laboratory operating during a pandemic. In the case of ABCTL, there were not as many cost and stocking considerations as there was the concern for not being able to produce the amount of tests that ASU students and staff, the community, and their customers demanded. The state of national emergency meant that normal business operations were not in place, therefore more necessary testing supplies could be purchased without a large consideration of storage space or costs. This is because of the potential operating risk, if ABCTL did not have enough supplies to test all parties reliant on tests they could break their contracts with companies and they would have the potential to impact the status of university classes being held in-person. In this case, the potential operational risks were large enough to outweigh the standard inventory control procedures that a testing laboratory would have.

The result of over-purchasing necessary items for testing has resulted in an excess of materials being stored in an unused conference room in the Biodesign Institute. ABCTL has to now manage the reverse logistics of ordering too many goods that it no longer uses in their testing process. This includes donating, returning, and potentially discarding the materials (Nelson, 2021). ABCTL, luckily not overwhelmingly concerned with money at this point, is losing a significant amount of money due to the unique purchasing process that disregarded the normal inventory control standards.

Staffing

The final sector of the ABCTL being assessed through an operational risk management framework in this volume is the staffing, or the framework of staffing as a key risk indicator. Staffing is considered one of if not the largest bottlenecks in the company, which is partially why the unscrewing of tube caps was automated (Murugan, 2020). The poaching of trained staff by other testing centers because of a high demand means that there is a fairly high turnover rate, which requires more training than would be required if there was not a frequent rotation of staff in the laboratory. These circumstances cause a few operational risks that have to be addressed.

The first of the potential operational risks is the potential for ABCTL to not be able to run their testing procedures at full capacity with a shortage of staff. At the end of October in 2020 the laboratory was running 4-5,000 tests a day with a goal of running up to 16,000 tests a day, but in order to do that the laboratory would have had to hire a third shift of employees to run the laboratory (Murugan, 2020). Similar to the risks ensued if they overuse test supplies, if they do not have enough staff to run the testing processes there is a risk of loss from their contracted customers and the reputation of the laboratory and ASU.

Another cause of a shortage of staff in ABCTL is the risk of infection among staff. This risk is properly mitigated by ABCTL by employing staff in shifts where individuals are only in contact with a minimal amount of other people. According to a global IFCC survey, this is a common technique that 46.6% of other surveyed testing laboratories have taken as a preventative measure during the pandemic (Loh et. al., 2020). Most commonly the staff is split into two or more teams that work shifts together in order to minimize the potential spread of the virus (Loh et. al., 2020). This measure also works to ensure that laboratory operations can still continue even with portions of the staff contracting the virus.

The final operational risk to be examined with processes failing due to people is the abundance and hard-to-detect nature of human error. Throughout all of the procedures mentioned prior as risk mitigation efforts during operational processes, they do not help reduce loss if all staff and employees are not diligent with following procedures in addition to being comprehensively trained. Human error is a large risk because it is not as easily identifiable as other risk factors are, so there is no telling how frequently they occur nor how they can best be mitigated without an internal investigation of the failed processes. This is also in accordance with the GCLP and CLIA guidelines, where Standard Operating Procedures (SOPs) must be written and available to staff (Ezzelle et. al., 2020). Additionally, training must be conducted every six months in order to ensure all staff are following the correct documented procedures as an effort to decrease the potential for error and risk (Ezzelle et. al., 2020).

Conclusion

Like previously mentioned, ABCTL is continually improving their operations. They are working towards mitigating the potential operational risks on a regular basis, most recently with hosting meetings to discuss the laboratory's potential for risk. Within their risk analysis using the risk matrix framework, they identified the greatest risk as the individual who is responsible for sending out the results to the patients, which is not even an element I covered in this volume.

Operational risk management includes a wide range of topics involved throughout processes and it is impossible for one individual to be able to uncover and understand all of the potential risks. ABCTL has a large group of individuals with a diverse range of backgrounds dedicated to continually improving the operations that allows them to properly analyze all phases of operations effectively.

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Section IV: An Analysis of its Upstream Supply Chain

Author: Kyle Mattson

Introduction

The ABCTL is one of the foremost Covid-19 diagnostic labs in the Southwest. The lab's goal is to meet the testing needs of ASU's students and faculty, as well as those of the Arizona community. The business group's goal has been to analyze the lab's development and evolution from a business perspective, and to find out as much as possible about its role in the future for the rest of the pandemic and beyond. Part of this goal has been examining the complex supply chain of this operation, which includes contracts logistics, sourcing, and day to day operations. Supply chain includes flows of products, information, human resources, and funds; this volume considers each of these areas.

The ABCTL, which has provided over 300,000 tests to the people of Arizona since its inception in early spring of 2020, will continue to provide testing throughout the remainder of the pandemic. This volume will discuss the evolution of the ABCTL through a supply chain lens with a special focus on essential upstream supply chain functions such as sourcing, procurement, operations, and contracting. This volume will discuss the various aspects of the lab with regards to its complex supply chain, including how materials and staff were procured and transported, as well as the technologies and strategies that are being used to support the lab. In addition, an important topic to be discussed is the lab's future, which can seem as uncertain as the future of the pandemic itself. The following sections focus on key supply chain flows including those of products, processes, people and information.

Procurement, according to *Healthcare and Supply Chain Management*, is the "planning and purchasing of components required to perform a service or create a product" (Ledlow et al., 2017). Procurement, also called sourcing, is an essential function of supply chain in that it involves a process of finding, securing, and contracting for materials and components that are needed to complete a final product. Strategic sourcing often requires outsourcing, which means ordering these said materials and components from an organization or location other than one's own. As the *Harvard Business Press* puts it, deciding what to outsource involves analyzing a firm's capabilities (Gottfredson 2005). This, in turn, involves determining which capabilities are core capabilities and which are not. Core capabilities are functions and processes that are easier to do and cost less money when done in-house. When looking at which capabilities could be outsourced, commonality and proprietary value must also be considered. Commonality and proprietary value mean the degree to which outside firms could perform a capability, and the value that is gained from your firm performing that capability, respectively. In other words, firms should consider outsourcing tasks with high commonality and a low proprietary value.

An example of outsourcing is the Xbox 360, a popular gaming console released in 2005 by Microsoft as a competitor to the already established Sony PlayStation console program. Microsoft listened to complaints about the original Xbox's size, appearance, and production. Learning from their mistakes, Microsoft outsourced processor production and console design to the most capable and advanced firms in those areas. In short, the Xbox 360 eventually outsold the PlayStation of the time. Strategically sourcing capabilities can increase a product's market power and sales by keeping functions with high proprietary value in-house and outsourcing other processes that can be done better and perhaps cheaper in another place (Hau et. al 2006).

Healthcare Sourcing and Procurement

Since the lab's inception, one of the greatest challenges has been the strategic sourcing of materials needed to efficiently operate. Strategic Sourcing, according to *HealthcareFacilitiesToday.com*, refers to procurement that "continuously improves and reevaluates the purchasing activities of a company" (Roach

2016). Whereas typically clinics, labs and other diagnostic and healthcare related enterprises rely on a small number of vendors for materials necessary to put together tests, etc., the pandemic-induced shortages have forced institutions to search for products elsewhere (FDA 2021).

In the healthcare industry, partnerships with suppliers create efficiently to outsource production and distribution of products. However, the Covid-19 Pandemic has drastically changed the way healthcare providers and commercial labs are doing business. This was emphasized in an interview that our team conducted with Rose White, a procurement specialist for Banner Health, which is a large healthcare provider in Arizona. Ms. White described how procurement was fairly simple pre-pandemic, save for the higher-than-average number of regulations and rules that needed to be followed industry wide. Each lab had one supplier for testing kits and materials that they could depend on. According to Ms. White, sole sourcing reduced complexity and ensured better quality by allowing more quality control resources to be utilized per supplier. Additionally, a single supplier meant a stronger, more personal relationship, which almost always translated to smoother negotiating and better business. However, a lean supply chain strategy with little buffering is prone to the risk of failure should an unforeseen increase in demand arise. Once the coronavirus started gaining steam and supplies started dwindling, providers like Banner Health struggled to find suppliers and vendors and started signing contracts with multiple suppliers to meet the demand for tests. Resource dependency became a central issue as commercial labs, who rely on swab, reagent etc., manufacturers for test kits scrambled to procure the resources they needed. The scarcity of lab supplies was accompanied by a worldwide shortage of Personal Protection Equipment (PPE), which was adapted to by strategic means. Simrit Sandhu, the Chief Supply Chain Officer for the Cleveland Clinic, explained in a blog post on the Clinic's website that the supply chain utilized internal and external intermediaries to source scarce PPE (Sandu 2020). Internal stakeholders, according to Sandhu, include partners within the Cleveland Clinic's supply chain such as Group Purchasing Organizations (GPOs), whereas external stakeholders refer to public sector agencies, as well as the government's national stockpile.

The role of the Strategic National Stockpile (SNS) is to "supplement state and local medical supplies and equipment during public health emergencies" (U.S. Dept. of Health and Human Services) Made up of 230 logistics, science, medical, and IT specialists, the SNS utilizes public and private sector parterships to distribute PPE, treatments, and other supplies and/or information during a disaster (U.S. Dept. of Health and Human Services). Non-disaster related activities include researching and stocking treatments and equipment so that the government may be better prepared to support the public in the event of a catastrophe. It has been reported that its failure to provide PPE and other needed supplies quickly contributed to the inability of health care providers to achieve a safe environment for themselves and for patients (Handfield, R., et al. 2020). According to (Handfield, R.), the Covid-19 crisis differed from other medical crises from a supply chain perspective because of the number of materials that became scarce. With the Ebola outbreak for example, only certain materials were in short supply, making it easier for manufacturers to ramp up production for that one specific area. On the other hand, the Covid-19 outbreak caused many different materials such as masks, treatments, equipment and of course materials necessary for viral testing to dwindle in supply, making it more difficult for any production to ramp up. Of course, Covid-19 is exponentially more widespread, which has only added to suppliers' inability to produce sufficient quantities (Handfield et. al 2020). In addition, the SNS was not ready to be utilized as it should have been. According to the same study by (Handfield et. Al), the SNS had no category strategies for items such as PPE, which is a product that lacks domestic suppliers in the first place and requires strategies for sourcing strategically. Subsequently, the stockpile relied heavily on overseas suppliers and was thus at the mercy of foreign regulations and restrictions which came into effect as the pandemic gained traction globally.

On top of the aforementioned reasons, the SNS's depletion in February of 2020 was also caused by its lack of forecasting and planning capabilities. Their inability to forecast was partly caused, as stated in the report, by hospitals' general lack of transparency and visibility into their own inventories. This made

forecasting even more difficult, which led to a lack of overall strategic and even tactical planning. In the end, the SNS essentially counted itself out early as providers scrambled to find alternate suppliers for devices, tests, reagents, and materials as these same items that were once plentiful became scarce. Sourcing and purchasing processes in the industry were altered, and longstanding methods, such as the use of GPOs, were strained. GPOs have proven to be quite the asset in the healthcare industry, their main benefit being purchasing materials for hospitals and clinics at wholesale prices, reducing costs of equipment/materials in some supply chain functions by over 90% (Schneller, 2009). According to The Value of Group Purchasing Organizations, "the "bottom-line" rationale for group purchasing is to achieve: (1) lower prices, (2) price protection, (3) improved quality control programs, (4) reduced contracting cost, and (5) monitoring market conditions" (Schneller 2009). Subsequently, GPOs have had an incredible impact on healthcare providers' bottom lines. Data from the Healthcare Supply Chain Association (HSCA) shows that GPOs save providers $55 billion annually, ad are expected to reduce healthcare costs by almost $1 trillion over the next ten years (Dobson Ph. D & DeVanzo Ph. D, MSW., et al., 2017). While some GPOs actually serve as suppliers, in most instances they develop contracts with distributors for materials that will go to clinics, hospitals, labs and other healthcare institutions.

Companies, regardless of size, have needed to adapt to direct sourcing for scarce goods during the pandemic. Brent Bolton, the Director of Supply Chain at the healthcare company Acumen, described to *Dark Daily*, a publication for clinical labs and pathology groups, that "large medical laboratory distributors are partnering with American manufacturers that generally don't create lab supplies—like Hewlett Packard, 3M, and Ford. Health systems can do the same'' (Bolton 2020). Larger manufacturers created supply sources that in pre-pandemic times would be found outside the United States or within smaller medical supplies companies. Corporations that traditionally manufacture anything from tape to automobiles stepped up to meet the sudden increase in demand proved useful in getting everything from PPE, masks, ventilators, and testing materials into the hands of healthcare providers. Bolton reports that his company has used a network of 3D printer companies to manufacture nasal swabs to be included in Covid-19 testing kits. However, as scarcity hits the market, fraudulent products and scams, especially counterfeit products like PPE, medication, and masks continue to pose a significant threat (Tucker 2021).

This is why Mr. Bolton suggests that all companies that must source products from multiple and/or unfamiliar vendors implement Lean Six Sigma programs to vet materials for quality. As a bottom line, while companies must ensure product quality, the sourcing strategies they use must be innovative and flexible. This may have served as a turning point going forward for the healthcare industry, because although dependency on one or two vendors worked outside the scope of a pandemic, such was not the case during a crisis such as this. The Biden administration's plans for supply chain integrity directly addresses this by first and foremost, bringing healthcare industry suppliers back to the United States (*joebiden.com,* 2020). President Biden has expressed concern over not only our lack of preparation for this pandemic but

U.S. dependency on foreign manufacturers of medication, treatments, equipment, masks and other goods that contributed to this lack of preparation. The Biden administration has pledged to use federal power to build a resilient American supply chain for critical goods by increasing manufacturing capacity, particularly capacity for what the administration classifies as "critical goods" such as medications, ventilators, semiconductors, and other equipment. The administration highlights how around seventy percent of ingredients used for medications come from abroad, and how implementation of the Defense Production Act (DPA) would create jobs making these critical goods (*joebiden.com, 2020*). President Trump leveraged the DPA in March and ordered automotive manufacturers to start manufacturing ventilators, a decision that according to the New York Times was applauded by some of President Trump's staunchest critics including Michigan governor Gretchen Whitmer (Youngs, Swanson 2020). In order to leverage the federal government, President Biden has promised to work closely with the private sector to write up long-term agreements that would eventually bring the United States to an acceptable disaster preparation level. Should the goals in the new administration's plan come into fruition, then sourcing products in the healthcare sector could be radically changed. Healthcare providers and labs could have more options and

could work to not only optimize their value chains, but also diversify them in methods that would better prepare them for sudden fluctuations in supply and demand.

Products and Materials

As Covid-19 gained traction around the world, nasal swab testing kits, critical to gathering material for testing, ran out, forcing long waiting times for shipments onto healthcare providers. In late Spring 2020, ASU developed a test based on saliva samples, which utilized straws, thus negating the need for nasal swabs. Reagents, which are supplied to the ABCTL by Thermo Fisher Scientific, are considered leverage items, and require supplier development tactics, as well as maintenance of supplier relationship in order to assure supply. This is because although leverage items typically have a high impact on the bottom line and can be slightly less difficult to source, it is important to maintain a healthy relationship with the supplier as to not underestimate assurance of supply. The most elusive item to source as of now is the tips, which are used by lab machinery to mix the reagents with the live samples before analysis. Tips, which are non-reusable and highly complex supply items, are also made by Thermo Fisher and several other scientific materials manufacturers. Unfortunately, supply has not been greatly assured, despite the use of a familiar supplier, namely one that is the single most qualified supplier of tips available. To combat this supply risk, ASU is looking into insourcing the production of tips, but for now continues to closely monitor tip supply and keep substantial amounts of inventory.

Significant sourcing challenges have represented hurdles to the lab's operations. As stated above, sourcing for the ABCTL's lab operation has been difficult due to the fact that the products for sample analysis come from different product lines within the same category. What makes strategic sourcing processes even more difficult is the lack of cohesiveness between suppliers and their own products. For example, the majority of both the machine tips and the reagents, two essential materials for sample analysis, have come from one supplier, Thermo Fisher Scientific. Thermo Fisher remains the main supplier because of Biodesign's strong relationship with the company and an assurance of supply early in the pandemic. In fact, ASU's Saliva test is based somewhat off of Thermo Fisher's Taqpath Covid-19 Combo Kit (T. Rosov (personal communication) March 22, 2021).

Tips, which are non-recyclable and more easily botched in manufacturing and/or damaged in logistical phases are at times more difficult to procure than reagents, which are typically less prone to post-production risk than tips. Given how these two products are in two different categories, despite sharing a main supplier, they have differing levels of supply complexity. However, they both have an equal level of "profit" impact. In other words, both products are equally as impactful in ensuring accurate testing results. The ideal supply strategy of any organization should include proper buffering/risk management, flexibility, optimization and reasonable pricing. Two goods from the same manufacturer but nonetheless with two different sourcing complexities require two different strategies while. The aspect that the ASU must keep constant between the two products is maintenance of a healthy relationship with the single supplier, Thermo Fisher.

Although Thermo Fisher remains the primary supplier for lab products in the ABCTL for the reasons discussed above, the lab realized the importance of avoiding the same mistake that left the healthcare industry unprepared for a pandemic in the first place: an excessively lean supply chain. According to Wendy Winslow, who is the lead laboratory manager at the Biodesign Institute, ABCTL has slightly diversified its supply chain. In addition to Thermo Fisher, the ABCTL has purchased lab supplies from Integrated DNA Technologies (IDT), VWR, Labcon, Beckman Coulter Diagnostics and Amazon (W. Winslow (personal communication) March 21-22, 2021). Thermos Fisher, Beckman Coulter, VWR and Labcon provided mainly tips, while IDT is an additional source of reagents and primers and Amazon is mainly used for supplies. These suppliers were classified more specifically as the lab grew into its increased capacity and role. According to Ms. Winslow, Thermos Fisher, Beckman Coulter, IDT and WVR had what the lab needed from the start, so orders were placed in order to secure as much material as

possible. Conversely, Labcon and Amazon were “used to avoid shortages with backup products” (W. Winslow (personal communication) March 21-22, 2021). Aside from the items mentioned previously, Thermo Fisher is a primary provider for other lab materials including gloves, deep well plates, and other chemicals. Materials supplied by other Major Lab Suppliers (MLS) include pipettes, ethanol, buckets, bleach, and laboratory freezers. Additionally, the sample collection tubes used by the ABCTL as well as the racks to store them on are both produced by Micronics Inc. and are distributed by NBS Scientific.

Implications for the ABCTL. Looking specifically at the ABCTL at its inception as a tool to combat the virus, the lab had already been equipped with the capabilities needed to run diagnostics, thus giving it a prime opportunity to take a role in the testing sphere. However, there were obviously some that the lab needed to source in order to properly operate in the capacity of a Covid-19 specific diagnostic laboratory. These items included reagents, swabs, and barcoded tubes; three items that made up the testing kits themselves, along with containers that were needed to transport the tests to and from the lab and PPE for volunteers at testing sites. In addition to physical materials, people were needed to work in the lab as technicians, researchers, and initially, drivers.

From the time that Biodesign introduced swab testing in February, swabs were some of the most coveted items in the world, and difficult to be found. Dr. Joseph Miceli runs the DNA repository at the Virginia C. Piper Center for Personalized Diagnostics and has served as the ABCTL’s central sourcing strategist. Although Dr. Joseph Miceli was able to source them through his contacts in the biomedical industry, they nonetheless were a challenge to secure.

With ABCTL becoming the first lab in the world to produce and run saliva diagnostics for Covid-19, 1.5 mL tubes and straws were the new items of choice for the test kits. Since these items, according to Miceli, were easily bought in large quantities, the lab was able to cut 75% of supply chain costs (Miceli, J. (2020, October 20th). Personal Interview). On top of that, there are always 80,000 test sample collection tubes in inventory as buffer stock. Aside from the test kits themselves, for which ASU is reimbursed by the State of Arizona, Miceli has repeatedly cited PPE and transport bins as crucial materials that were sourced from the inception of the effort. Bins were purchased by ABCTL staff at various Walmart locations and other big box stores across the Phoenix metropolitan area. Smaller, Tupperware-like containers, which are used to hold racks full of tubes containing live samples, were also procured from local stores across Phoenix. Many of the coolers were fitted with lock-type mechanisms to ensure the security of the samples inside.

As this was the most popular testing method around the globe, sourcing quickly became an issue. Dr. Joshua LaBaer and Dr. Joseph Miceli, ABCTL’s chief supply chain specialist respectively, both emphasized when interviewed by our team how swabs were by far the most difficult materials to source. That being said, Dr. Miceli has said repeatedly that his strategic sourcing of swabs and other materials came out of his personal connections within the healthcare industry, which he had developed over the years. The nasal swaps quickly became difficult to source in the spring of 2020, although supply increased in the fall of that year as major companies across North America and Europe such as Thermo Fisher Scientific, Luminex Corporation and DiaSorin increased capacity and ramped up production (MedGadget, 2020) However, although sourcing strategies involve planning, they also dictate flexibility as well. In late spring 2020, ABCTL transitioned from the traditional swab tests to saliva tests, and according to Dr. Miceli, this made a massive difference in terms of cost and procurement efficiency, even cutting supply chain costs by 75%. The procurement of items needed for saliva testing kits became much easier because most testing centers and labs around the world were still using swab tests. The new saliva test, which was first conceptualized by Yale University, was first put into practice by Arizona State University. This kit, which involves a participant simply spitting through a straw into a barcode-labeled plastic tube, allows more readily available materials to be purchased wholesale from fewer vendors.

Information Technology

An important note when discussing procurement of supplies in this lab's context is the addition of barcode labels on the tubes that are used in the tests. These labels, which are put on the tubes themselves, help the lab to track batches of test samples and efficiently return test results to the correct recipient. The system used by the ABCTL is similar to the process used by UPS, Amazon, and other package delivery entities. Just as a labeled package can be scanned at various points in the shipping process, the test samples can be scanned and therefore traced as well. This is helpful mainly for quality control, as it allows for whole batches to be inspected upon errors with one sample.

Track and trace technologies are a crucial implementation, as it improves accountability to the recipient. The main source of risk with barcodes is that since they are outsourced, an error on the part of the third party that prints them onto the tubes could mean invalidated samples and ultimately, retests for people whose samples were affected. Morgan Nelson explained during the ABCTL tour that at one point, the barcode manufacturer double-printed labels, then provided a blank batch. Mr. Nelson considers this risk very minimal and has expressed that the lab as a whole has not had many issues with third party suppliers and partners. The recent influx of cash from state grants and contracts has given the lab the ability to hold safety stock of 100,000 tests at all times. Although the Thermo Fisher Scientific reagent and the Micronics 1.5 mL tubes are not a problem to order, tips prove to be more difficult. The lab's development team is currently working in conjunction with Knowledge Enterprise to fix the problem by either manufacturing tips independently or finding a stable supplier.

Fraud and Counterfeit Products Challenging Supply

Fraud continues to pose a major issue in the healthcare products industry, and the coronavirus-induced shortages on masks, PPE and tests only exacerbated the flood of phony products that have hit the market (FDA 2021). Inauthentic materials pose grave risks for patients, and providers in the healthcare industry, especially while in the depths of a major pandemic. A faulty mask can expose the wearer and surrounding people to the viruses, and cheaply made test kits are unreliable, producing a higher rate of false negative and positive results (FDA, 2021). Therefore, a key measure of importance is fraud mitigation.

Since the virus-induced scarcity began, counterfeit items have entered the market in force. As recently as February of 2021, the FDA has released warnings of fraudulent Covid-19 treatments, tests, and other materials. Counterfeit treatments and products, according to the FDA, have been circulated by groups, people and organizations looking to make a quick buck off of the crisis (FDA 2021). The ABCTL's responsibility is to provide quality tests to the university and general community, a responsibility which mandates rigorous vetting of sourced products as much as possible, as well as quality control within the process itself. According to Morgan Nelson, a clinical quality and compliance specialist at the ABCTL, every batch of tests that's analyzed is checked for quality. At a throughput rate of 384 tests per hour and an estimated 750,000 tests analyzed to date, sourcing for the lab's manufacturing and quality within testing operations has been done with the utmost vigilance for substandard products. Since ABCTL already had some of the machines required to analyze tests, this was more of a focus with the test kits, especially after the transition to more common use materials such as straws. Mr. Nelson explained that the lab hasn't experienced fraudulent products but described one of the only instances of faulty materials where the third-party code manufacturer sent the ABCTL blank barcodes, which required a mere retest on the customer's end.

Human Resources

One of the first necessities of the lab's operation was its staffing process. The Biodesign Institute already had a sizable staff before the pandemic, with Dr. Joshua LaBaer as the director. However, after University President Dr. Michael Crow charged the lab with using its diagnostic ability to begin testing the ASU community, that number grew. In addition to the original staff of researchers, professors and students, staff and students alike began volunteering their service to the ABCTL. Morgan Nelson explained that once grants for other areas of research in Biodesign were halted because of the pandemic, the ABCTL commandeered their services for the lab's purposes. In Dr. LaBaer's words, the executive team grew from "seven to seventy in a month and a half" (LaBaer, J. (2020, September 29th). Personal Interview) Personal Interview. According to senior leadership at the lab, the process of sample analysis is mostly automated. However, people who work on the line are Biodesign employees. Volunteers are needed mostly for outside research and transportation of materials to testing locations. Dr. Miceli and Dr. LaBaer both touted their lack of need for staff when transporting test kits to contractors. When ABCTL first became operational, some of their initial customers were utility and healthcare companies. Dr. Miceli explained in our interview with him how laboratory staff began training employees of Salt River Project, Phoenix Children's Hospital and APS, among others, to transport tests to and from locations by themselves. By doing this, the need for drivers was eliminated in a lot of cases. Recently however, the ABCTL has since developed a new system for collecting samples on and around campus called Devil's Dropoff. Devils drop off gives ASU students, staff, and faculty the option to both pick up test kits and drop off their samples at locations around ASU's campuses. Biodesign staff collect samples once or twice every day as to not allow samples to expire. This system both decreases complexity and mitigates risk in the testing supply chain by allowing for less in-person testing centers to exist, therefore reducing the amount of people (staff, students, etc.) that are exposed to live, open-air Covid-19 samples. About 75% of the testing kits are packaged by Dirck's Logistics, an Arizona-based supply chain solutions company that also assists with transportation of test kits to testing sites around the state. The rest of the Devil's Dropoff kits are packaged by student workers in Biodesign, who pack a special sealable baggie with straws, tubes, and instructions. Students, faculty, and staff can log their test into their ASU health portal by typing in two codes that appear on their sample tube, and test results can be checked and managed through the Health Portal as well. These kits maintain the same twenty-four-to-forty-eight-hour result turnaround time, given that they are still comprised of the saliva test.

Funding and Capital

AAny entity needs money to get started, and the ABCTL is no different. Despite having much of the existing machinery and technology needed to support diagnostics and therefore virtually no overhead costs, the lab has received much needed capital from a variety of sources in order to expand their mission. At the helm of this massive funding operation has been ASU Knowledge Enterprise (OKED) Chief Operating Officer Tamara Deuser. Ms. Deuser, who our team interviewed in November of 2020, oversees spending and contract negotiating for the ABCTL, and handles disbursements of funds to and within the lab. To kick off operations, ASU Biodesign's ABCTL received a $2 million grant from the Virginia Piper Charitable Trust, of which Dr. Joshua LaBaer is a board member The Arizona Department of Health Services (ADHS) awarded ASU Biodesign $12.5 million dollars to operate the diagnostic testing facility, which will be used to cover testing and material expenses. ADHS, with their initial investment, bought up the lab's 100,000 test excess capacity before making their capital investment. Since then, the ADHS has made additional investments in the lab, which have been used for upgrades. The state of Arizona also pays the ABCTL $100 for each test that is manufactured, which covers the cost of each kit. The lab officially prices their tests at this same price point since $100 is the going Medicare rate, despite the fact that more expensive tests exist on the market. All in all, most of the funding that the lab receives comes from state and federal grants, as well as direct payments from contractors.

ASU Biodesign will not bill insurance companies for the tests, and there are now concerns that the laboratory may be "in the red" with regards to costs and expenses (LaBaer, J. (2020, September 29th). Personal Interview). ABCTL staff have been appreciative towards Dr. Crow's and the university administration's support and assurance during this time. Everyone that our team interviewed expressed extensive gratitude to the university as well as ASU Knowledge Enterprise for their flexibility.

Agility has been an important factor in attracting and sustaining funding. Ms. Deuser also elaborated on what she thought gave ASU an advantage in gaining contracts: Biodesign's adaptability. The switch from nasal swab testing to the "radically better" saliva test was a change that other organizations and providers have been wanting to make due to the fact that the saliva test was quicker, less intrusive, and cheaper. In fact, Dr. Miceli told our team that while a nasal swab kit cost $10.00, a saliva test costs $00.75. The significant difference in cost between the two tests is mainly due to the supplies needed; the nasal swab test simply required more materials that were already difficult to source (Miceli, J. (2020, October 22nd) Personal Interview).

The difference between our institution and other providers is that ASU had been able to pivot faster and execute the change. This has allowed us to shore up external partnerships with companies like Salt River Project and APS that have ended up subsidizing ASU's student testing operation. This general agility, according to Ms. Deuser, has been the result of existing automation structures. She explains that commercial labs' machines, although efficient for a certain kind of test, cannot be easily switched. Where Biodesign's testing and diagnostic machines could be switched easily from nasal swab to saliva analysis, other labs will have a harder time transitioning due to the fact that they have to be "re-validated" (Deuser, T. (2020, November 3rd) Personal Interview).

Partnerships have been critical to funding. Altogether, the ABCTL has over 30 partners that provide financial stability. In addition to funding from the state and other public domains, the lab has negotiated contracts with utility and healthcare companies around Arizona. Aside from getting accurate and timely testing to the ASU community, expanding the operation to essential utilities, power, electric and healthcare companies was a priority. As per these contracts, these companies pay cash for tests, rather than getting billed by insurance (Deuser, T. (2020, November 3rd) Personal Interview). To our team's knowledge, the most recent contract was negotiated with Phoenix Children's Hospital and gives the ABCTL the ability to efficiently test patients and staff in the network. As part of these agreements, which Ms. Deuser negotiates herself with the help of the university counsel, ASU incurs minimal risk, and liability for the university is avoided.

The relationship between funding and ABCTL's ability to become both efficient and productive is notable. Funding has been important to ABCTL's goals for automation to analyze test samples more efficiently. Support for technology funding initially came a $2 million grant from the Piper Foundation at the ABCTL's start. ADHS's initial capital investment allowed Dr. LaBaer and his team to automate an entire line of lab machines, setting the stage fora structured analysis process. An example of this is the lab's capping machine. Whereas previously lab staff would need to manually uncap each tube for analysis, the lab installed a machine to do the job, which saves time and labor by uncapping batches of samples at a time.

Operations and Logistics

A factor that differs from client to client and contract to contract is how the tests are delivered. Some clients, like the Arizona Department of Administration, request that ASU train their employees to transport kits to and from Biodesign. Others, however, opt for a hybrid system, in which Biodesign employees or volunteers transport and handle kits and samples to or from the testing location. Still, some organizations such as ADHS depend on the ABCTL to transport tests and samples to and from testing sites (Deuser, T. (2020, November 3rd) Personal Interview). As of now, the ABCTL outsources test kit and sample transportation to third party logistics providers such as UPS and Dirck's Logistics, which is particularly cost effective for the Devils Dropoff program. The kits include one straw, one sample collection tube,

one biohazard bag, one alcohol disinfectant wipe and a set of instructions for how to log your collection tube's barcode into the computer and view results. These items are assembled by student workers at the Biodesign Institute, put into batches, and packaged by Dirck's Logistics. Once they are complete and back in the ABCTL, they are shipped to the drop-off sites around campus next to the bins where they will eventually be picked up and analyzed. Samples coming from off-campus testing sites are stored immediately after collection in secured, labeled coolers before being brought back to the ABCTL to be heated up to seventy degrees Fahrenheit, mixed with reagents, analyzed, then disposed of. The Biodesgn Institute is using a large section of its infrastructure, including its loading and shipping dock, to ensure the most efficient transport of tests to and from the ASU Biodesign Covid Testing Lab.

Achieving Scale and Supply Chain Constraints

Dr. Neal Woodbury explained to our team how the ABCTL and OKED is in talks right now with "one partner" to further scale up testing (Woodbury, N. (2020, October 30th). Personal Interview). He made it clear that ASU does not want to give exclusive rights to any one person or organization so that this technology may be spread as far as needed for widespread testing to be accessed safely for as many people as possible. Dr. Woodbury's insight into partnerships, combined with ASU's existing aforementioned relationships with utilities and healthcare companies highlights the importance of cooperation and adaptation in these circumstances. However, it is unclear how long these existing contracts will last and when these companies and state agencies will cease to renew. Ms. Tamara Deuser, in her interview described OKED's methodology when negotiating contracts with organizations to receive tests. Ms. Deuser described the nature of the negotiations in which ASU needed to assure its own supply while negotiating with both suppliers of test materials, and contactors to whom the tests would be distributed to. Ms. Deuser noted how she made it known to its downstream contractors that due to supply volubility, the ABCTL could not guarantee a regular and precise number of test kits that would be delivered, and acknowledged the risks involved, including shortages (Deuser, T. , Personal Interview: November 3rd, 2020).

Conclusion

Supply chain excellence was critical to the lab's initiation, growth and plans for the future. The ABCTL was set up in short notice but still managed to enact a solid supply strategy amidst a difficult sourcing landscape. As previously mentioned in this volume, categorizing products according to profit impact and complexity to procure allowed the lab to source materials from various suppliers effectively as its capacity increased. Strategies such as buying materials from available suppliers in bulk at the start of its operation were central to the ABCTL's ability to meet and exceed the ASU community's and the state's testing requirements. Using multiple sources for certain lab materials while maintaining healthy relationships with suppliers has enhanced Biodesign's ability to prepare for shortages and other unforeseen supply challenges – an industry shortfall which was pushed out in the open amidst the pandemic. The University also did well to staff the ABCTL with knowledgeable and experienced staff who leveraged their combined abilities in research, business, and contracting areas to ensure the lab's material success.

Without supplies, testing cannot take place; described in this volume is an amazingly agile and resourceful organization. Supplies were identified, categorized, sourced, and procured with the utmost attention to risk and the unknown. The lab also developed systems like Devil's Dropoff to ensure access to ASU staff, students, and faculty, all while mitigating the risk of the virus spreading at in person testing sites on campus. All of this culminated in the ABCTL's successful operation.

From a supply chain perspective, the key to the lab's ongoing success in any capacity is the maintenance of its agility. The ABCTL utilized existing technology in Biodesign's facility to ramp up production of tests while also acquiring funding and equipment necessary to increase its capacity for production and sample analysis. If the lab, excluding factors of new location or purpose, could remain as operationally and financially agile as it has been, Biodesign could be successful in other fields as a laboratory.

The future of the ABCTL will likely be defined by heightened agility to maintain diagnostic abilities for both academic and emergency use. Dr. Compton and Dr. LaBaer, have indicated that they would like to eventually expand testing capabilities after the threat of Covid- 19 is sufficiently mitigated or destroyed altogether. Testing for other strains of Coronavirus, Influenza, and other diseases is a goal that the lab hopes to reach one day. Morgan Nelson noted that a goal of the lab is to continue to operate as part of ASU, not as a separate entity, and that the lab will continue to make use of the infrastructure it has developed due to the pandemic. Dr. Compton has expressed doubt as to whether the ABCTL, or whichever specialized lab takes its place, could operate in the current setting on Biodesign's Tempe campus location. Discussions have included the Health Futures Center (HFC) as a possible location candidate. The ASU building situated adjacent to the Mayo Clinic in Northeast Phoenix currently is set to house engineering, nursing, and health solutions functions, but could also provide machinery, space, and storage for a more continuous lab similar to the ABCTL. The lab should and likely will of course return to its academic purposes, while also remaining agile.

Agility is a marketable trait, especially given that the ABCTL's very existence proves this. While the demand for Covid-19 tests will inevitably fade, the lab should maintain the capability to meet the next challenge, whatever that may be. From a supply chain perspective, Tamara Deuser discussed that the model of testing for one condition, for extended periods of time, is not sustainable, and that the lab would need to diversify eventually if it intended to cover costs:

> Just the enterprise associated with going out and running public testing sites and having sample collection and doing that all over the state" ..."it's a major undertaking from a logistics perspective and again"..."it's what needed to be done, and we're happy to do it, but it's probably not something we should be doing for another two or three years, (Deuser, T. (2020, November 3rd) Personal Interview).

Ms. Deuser explains that testing for a condition can be more efficiently done in the region by branching out - adding that Biodesign has been negotiating with commercial labs in the area like Sonoran Quest and LabCorp to work together in the future. The main focus right now, however, is to provide testing until the need no longer exists.

Finally, as COVID-19 persists, sourcing of the tips that are used to mix reagents with the samples remains the top procurement challenge. It appears that innovation will continue, as the ABCTL is currently looking at developing tips independently in a major insourcing decision.

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Section V: A Managerial Economic Perspective

Author: Michael Qian

Introduction

This section examines the ABCTL from a managerial economic perspective. Through cost and asset analyses, not only can we compare the estimated costs of in-house testing to outsourcing, but we can also identify key assets that help the lab lower their operational costs. Incorporating both aggressive and conservative assumptions into our analysis, we can construct a fluid range of cost projections that considers the uncertainty of the pandemic and vaccine rollout. For the asset analysis, this volume identifies key intangible assets that help the ABCTL execute their long- term strategy and realize certain advantages in the local diagnostic market. In addition, we also highlight the instrumental changes and challenges to the lab's core assets (science and technology) to pinpoint improvements in the ABCTL's capital allocation strategies.

The Efficiency-Thoroughness-Tradeoff (ETTO) framework, developed by Erik Hollangel, is employed in our intangible asset analysis. In the context of the ABCTL, the ETTO framework serves as an upgraded version of the traditional cost-quality tradeoff because of the concept's consideration for safety repercussions. Within the ETTO framework, efficiency is achieved when the number of resources (time, money, workload, fatigue) used to satisfy an objective are minimalized (Hollnagel, 2012). Thoroughness, on the other hand, is realized only when the organization is confident that sufficient conditions exist for the activity to achieve its long-term objectives without unwanted side-effects (Hollnagel, 2012). If demands to productivity or performance are high, thoroughness is reduced until the productivity goals are met (Hollnagel, 2012). Similarly, if demands to safety are high, efficiency is reduced until the safety goals are met (Hollnagel, 2012). Since traditional organizations are often unable to be both effective and thorough at the same time given resource constraints and stakeholder pressures, people within the organization routinely make sacrifices between being effective and thorough (Hollnagel, 2012). As a result, the ETTO framework factors in numerous variables like cost, employee satisfaction, time and safety when determining optimal output and direction.

Cost Analysis

This section estimates the ABCTL's use of direct materials (DM), direct labor (DL), allocated overhead (AOH) and capital expenditures (Capex), we have determined that in all three cases (base, low and high), the costs of operating in-house were significantly lower than outsourcing testing needs at a fair market price. One of the foundation variables in this cost analysis was Total Tests Performed, which was calculated using a combination of current testing rate (provided by Dr. Vel Murugan in October 2020) and assumed forward testing rate to May 2021 (Murugan, 2020). Given the uncertainty of the virus and vaccine rollout, there remains significant volatility risk in testing demand, and subsequently output, so the low and high case both provide some margin of error.

Additionally, since the outsourcing projection uses the same $100/test ASU charges on their testing contracts with local companies, the outsource bar in Exhibit 3 is essentially the lab's total projected testing revenue through May 2021 - assuming ASU students and faculty were charged the same market rate. The lab's modified EBITDA (earnings before interest, taxes, depreciation, and amortization) can also be calculated by taking the difference between outsourcing costs and any one of the in-house cases in Exhibit 2, and EBITDA margin from dividing that difference by the outsource cost. Although cost optimization was not at the top of the ABCTL's agenda, this model provides a telling story of the lab's cost-efficient performance throughout the pandemic.

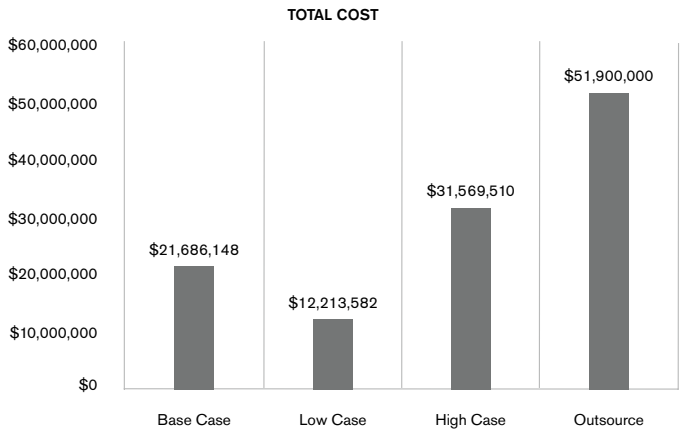
Formulas used to calculate each of the four cost components are shown below. The green variables are estimates based on interviews with Biodesign employees and various online resources. The blue variables are estimates without readily available baselines.

Direct Materials (DM)	→	Material Cost/Test x Total Tests Performed
Direct Labor (DL)	→	Allocated Salary Base x Salary Multiplier
Allocated Overhead (AOH)	→	Total DL Cost x (Indirect Cost Rate + Fringe Benefit Rate)
Capital Expenditures (Capex)	→	Equipment Unit Cost x Units Purchased

The cost analysis showed that perating in-house ended up being significantly cheaper than outsourcing testing needs.

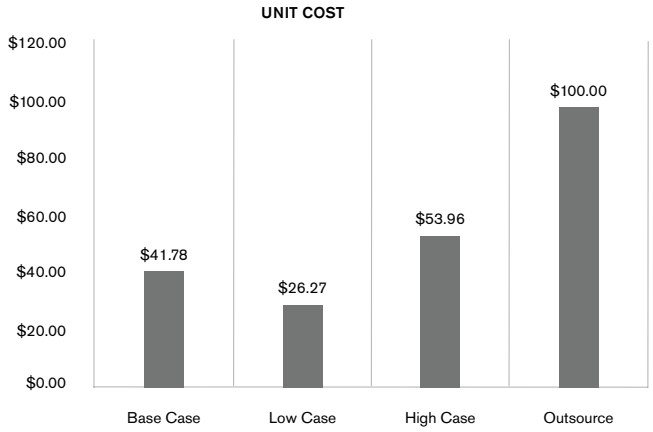
	Total Cost	Unit Cost
Base Case	$21,685,148	$41.78
Low Case	$12,213,582	$26.27
High Case	$31,569,510	$53.96
Outsource	$51,900,000	$100.00

The estimated costs incurred by the lab compared to the projected outsourcing costs are show below.



Total in-house testing costs vs. total outsourcing costs

In-house and outsourcing expenses from a unit cost perspective are shown below.



In-house testing cost/unit vs Outsourcing cost/unit

From a financial perspective, ASU made the correct decision to provide testing services in-house rather than outsourcing. According to our analysis, that decision prompted significant cost savings (anywhere from 46% to 73%) when compared to the $100/test "base rate." While there is already a significant discrepancy between in-house and outsourcing costs, that gap should widen with additional testing volume. Although marginal costs have not been tracked by Biodesign, it is fair to assume that given the growing presence of automated processes within the lab, the ABCTL is still in the early stages of the economies of scale. Once the lab successfully integrates all of their machines into the testing process, their unit costs should decrease exponentially. With a set amount of fixed costs (FC) coming from depreciation, utilities and certain salaries, the ABCTL's higher testing output and capabilities will decrease the lab's FC/unit. From a variable cost (VC) perspective, automation shifts the bulk of labor from humans to machines. With energy being significantly cheaper than wages, the ABCTL's VC/unit will also go down with each sample experiencing less contact with lab employees. As a result, under the assumption of consistent testing demand, the ABCTL's unit cost projections (and savings) look incredibly favorable moving forward.

Key Competencies and Advantages

Intangible Assets

Historically, ASU has been a university that leverages its size and funding to conduct groundbreaking scientific research. Although their focus has primarily been on molecular and cell biology, the Biodesign Institute - and its leadership team - have a long-standing reputation of devising innovative solutions to complex problems. In academia, common measures of high- quality research include: 1. Has it been peer reviewed, 2. Did a reputable scientific journal publish the work and 3. Where else has the research been referenced. Since 2010, tenured professors within the School of Life Sciences have contributed to large national projects like the GTEx Consortium to better understand gene expression and had peer-reviewed papers published by prestigious organizations like the National Cancer Institute. The simple pairing of scientific curiosity with institutional financing has supported the development of ASU's Biodesign Institute into one of the top research centers in the nation.

We consider the ABCTL as a subsidiary to the larger Biodesign Institute, which has primarily been a research entity rather than an operational lab. Yet they checked off all of the boxes needed to become a successful diagnostic laboratory. Before the onset of the pandemic, the ABCTL worked on a $40 million project with the Biomedical Advanced Research and Development Authority (BARDA) to assess the degree of radiation exposure in the context of a nuclear explosion. A key stipulation to that research grant

was that the ABCTL needed to perform 200,000 qPCR tests per week, meaning they needed to have the necessary testing equipment and processes mastered. Since they demonstrated the ability to perform large-scale testing through the BARDA project, when early information on Covid-19 came out, the ABCTL could set up their testing operations using the same machines and procedures. With a relevant track record in qPRC testing and grant-supported infrastructure, the ABCTL had all of the right ingredients to execute their transition to an operational lab.

University Status

With the ABCTL being classified as a university lab directly under Biodesign, they are afforded the distinct bonus of performing cash-generating activities while still receiving sizable funds from the university and government via grants. As a result, the ABCTL's predictable funding presents a significant competitive advantage over a traditional startup's reliance on seed money and equity financing to cover research and development expenses. This funding disparity becomes increasingly relevant when we factor in critical cost-quality trade-offs avoided by ABCTL.

Using the ETTO framework, traditional organizations need to optimize their resources to achieve desired production, employee satisfaction and high standards of safety. In the context of ETTO, "Efficiency focuses on producing more with existing human and technical resources'' while "Thoroughness implies that organizations and people invest more time… on creating resilient plans and courses of action" (Kontogiannis, 2019, p. 709). In practice, an organization would demonstrate efficiency by "Forcing people to undertake workarounds and shortcuts'' to recognize short-term value while the benefits of thoroughness "May be manifested only in the long term" (Kontogiannis, p. 709). Essentially, this principle states that with limited capital, organizations must compromise between meeting short-term obligations and building out your long-term strategy, all the while maintaining exceptional safety standards. However, because of the ABCTL's classification as a university lab, the absence of a cost constraint relieves them of the need to strike a balance between efficiency and thoroughness. In the short term, the lab is able to temporarily work around their key constraints to satisfy the testing demand from the university and outside contracts. For example, Dr. Murugan - the only person qualified to analyze sample results - has been placed in a situation where he needs to work 18+ hours/day to keep up with the volume sample inflow. This is a major human resources workaround. Despite that workload being unsustainable long-term, Dr. Murugan has been able to work efficiently through the long hours to meet short-term demand without compromising the ABCTL's high safety standards.

In that situation, a traditional lab startup would likely need to invest all of their resources to accommodate for short-term demand variability. Fortunately, the ABCTL still has enough capital to execute long-term initiatives like training additional employees to analyze sample results and investing in machinery to automate routine tasks. In a pandemic that forced smaller organizations to adopt cash conservation strategies, the well-funded ABCTL has a unique opportunity to both fulfill short-term obligations and build out long-term infrastructure.

Given the university's strong commitment to preserve the lab in the interest of public health, the ABCTL's status as an ASU entity primarily hedges any downside risk of insolvency. However, the ABCTL can also take advantage of legislative trends that have helped universities monetize their own intellectual property (IP). In 1980, the Bayh-Dole Act was passed in response to the heavy post-invention investments required by universities to bring the invention to market. Beforehand, academic institutions were not given a "Secure economic environment for the investment that converts ideas into reality," so universities were unwilling to "Support these costs [of invention] without some assurance of protection from competition" (Hall, 2010, p. 284). To encourage continued innovation from academia, the Bayh-Dole Act allowed "Institutions and grant recipients, such as universities, to hold the title to patents on inventions stemming from government-funded research" (Wilbur, 2019). With universities involved in IP ownership, the legislation enabled research institutions to license their invention rights to private sector partners for additional development and commercialization (Wilbur, 2019). For the ABCTL, their affiliation with

ASU not only secures the necessary funding to sustain operations, but it also grants them flexibility to negotiate licensing agreements (lump sum, royalties, etc.) through Skysong Innovations, ASU's invention management partner. In an industry where IP is king, the ABCTL's status as a university lab places them on a clearer path to profitability through 1. Diminished downside risk via government/university funding, 2. Heightened protections in the open market via patent ownership and 3. Additional monetization opportunities via licensing contracts. As a result, the ABCTL's ability to develop, own and profit off IP using funds not bearing financial covenants presents a key advantage in the open market.

People and Culture

Similar to a conventional start up, when the ABCTL first came together - it was a small group of seven people that had a vision for a value-added service. From their early meetings, the leadership team instilled a "can-do" collaborative culture that persevered through the upticks in testing operations. Connected through their shared mission of preserving public health, the ABCTL has constructed an agile team within their business model.

While the ABCTL is significantly smaller than many of their local competitors, their lower headcount allows them to maintain high levels of organizational connectivity and preserve a high-performing culture. Combined with the absence of any hiring pressures, the ABCTL team only brings in driven professionals whose values align with the lab's mission statement. Piecing together the work of many management researchers, the three-primary performance-enhancing motives were discovered to be:

Three primary motivating factors within organizations

- **Play** is when you are motivated by the work itself. You work because you enjoy it. A teacher at play enjoys the core activities of teaching — creating lesson plans, grading tests, or problem solving how to break through to each student. Play is our learning instinct, and it's tied to curiosity, experimentation, and exploring challenging problems.
- **Purpose** is when the direct outcome of the work fits your identity. You work because you value the work's impact. For example, a teacher driven by purpose values or identifies with the goal of educating and empowering children.
- **Potential** is when the outcome of the work benefits your identity. In other words, the work enhances your potential. For example, a teacher with potential may be doing his job because he eventually wants to become a principal.

(McGregor, 2020)

Given the lab's small workforce, additional responsibilities must be delegated to each team member in order to cover all of the functional areas. As a result, the increased workload satisfies the three motives and inspires employees to buy into the "can-do" culture.

For Play, the size of the organization allows each leader to focus on their specialty and develop comprehensive solutions to the lab's challenges. The original seven individuals that helped transform the ABCTL into an operational lab were all experts in different critical areas including software development, automation, and molecular biology (LaBaer, 2020). Each subject matter expert has been observed to operate within their own sphere while still being in conjunction with the overall organization. This is due to the ABCTL's egalitarian culture, which offers employees a space to nurture their curiosity and engage with the task at hand.

For Purpose, because the majority of the people involved with the ABCTL are Biodesign employees, they share the same mission as their parent entity: to innovate for the betterment of human health and communal safety ("Mission"). Comparatively, the primary goal of healthcare companies in corporate America is to increase shareholder value. While their stakeholders include the patients and communities they serve, public (and private) companies still bear the responsibility of generating substantial returns to

institutional and retail investors. As a result, aside from their social responsibility to improve the communal well-being, healthcare companies still have to focus on delivering financial results by improving top-line growth, maintaining margins, and minimizing cash burn. Transitioning back to the ABCTL, the university lab does not face such pressures from investors and can thus solely focus on their social mission. Combining that key distinction with the majority of wealth being reinvested into industry, we can infer that leaders within the ABCTL share the organization's sole purpose of keeping local communities safe and knowledgeable. The alignment between employee purpose and organizational goals helps keep the team motivated and willing to take on more responsibilities.

For Potential, the increased workload on current employees helps develop the necessary skills to move up in their respective fields. While the ABCTL may look drastically different a year from now, the experience of guiding and helping an organization navigate through muddy waters builds up key transferable skills to move up in academia. The opportunity to grow within (and possibly beyond) their role provides strong motivation for the ABCTL leaders to take on a larger workload.

Organizational Agility

Given the novel nature of Covid-19, healthcare organizations that can rapidly adjust to new information and economic conditions are presented an opportunity to capture additional market share during the pandemic. If a diagnostic lab remained rigid in their processes and strategy, a sudden increase in material costs (caused by heightened demand) could hinder their ability to honor commitments or take on new contracts. As a result, the ABCTL has been able to rapidly scale upwards during volatile times because of their focus on strategic commitment, environmental scanning and organizational leadership.

Although the ABCTL operates as a university entity, they still face the same open market pressures as private labs and thus require the same levels of strategic flexibility. With new Covid-19 developments each week and additional labs entering the testing market, the ABCTL must "Embrace continuous strategic change in order to remain relevant and to retain their competitive advantage" (Vaishnavi, 2019, p. 2376). For the ABCTL, that agility has been evidenced in their Monday morning meetings to discuss not only their current capabilities, but also any anticipated future changes. Through these weekly strategic meetings, the ABCTL leadership team quickly committed to key strategic shifts like saliva-based testing when they anticipated future shortages in nasopharyngeal swabs. The lab's willingness to strategically "zig when others zag" has allowed them to stay ahead of testing trends and maintain their operating efficiency.

For the ABCTL, while the science of their COVID-19 tests is a core competency, their comprehensive understanding of the testing market helps the lab adjust to new industry dynamics. Going beyond sample analysis, "Healthcare organizations must scan the external environment to understand the changes in legal, political, economic and competitive sectors" with the scan including "Competitors, customers, vendors, partners, supply-chain partners and government agencies" (Vaishnavi, 2019, p. 2376). Essentially, this states that in addition to a strong scientific research team, healthcare organizations also need operational experts with a heightened understanding of the industry. For the ABCTL, this is evidenced through their collaboration with the ASU Knowledge Enterprise to both negotiate testing contracts and maintain vendor/customer relationships. Having people outside of traditional R&D, the Knowledge Enterprise helps the ABCTL remain agile by conducting the necessary industry research and handling testing logistics so the lab can scale to meet demand.

Although we briefly mentioned the ABCTL's small headcount in the previous competency, its direct impact on the organizational structure helps keep the lab agile through strategic implementations. Research has suggested that in order to operate nimbly, "Top management should design the organizational structure in such a way that it would be a flattened or decentralized organization" (Vaishnavi, 2019, p. 2377). While a centralized organization may be more beneficial for larger companies, if we applied that hierarchy to the ABCTL, Dr. LaBaer - needing to sign off on every initiative - would have been a severe bottleneck during

the lab's inception. Rather, the delegation of power to multiple subject experts has allowed the ABCTL to quickly respond to challenges without constant workflow moving up the pyramid. As a result, the lab's decentralized structure has enabled them to take advantage of any short-lived opportunities that slower-moving, hierarchical healthcare organizations could not capitalize on.

Core Assets - Changes and Challenges

The changes within the lab's core assets are attributable to one major organizational decision: the shift away from nasopharyngeal swabs in favor of saliva-based testing. Capitalizing on their expertise in pathology and personalized diagnostics, the ABCTL leadership team pivoted away from the "gold standard of diagnostics'' to construct their own test using more attainable materials. Combining common materials with a simple testing procedure, the ABCTL's scientific advancements helped accelerate the lab's adoption of automated processes by increasing incoming input (saliva samples). Although the ABCTL has experienced exponential growth heading into 2021, the lab still faces key challenges with the evolution of the virus and healthcare solutions.

Scientific Innovation

For the ABCTL, switching from nasopharyngeal swabs to saliva-based testing was a key decision point in the lab's lifecycle. Anticipating major supply chain issues in traditional qPCR testing, the ABCTL pivoted towards a lesser known but equally effective diagnostic method.

This scientific change capitalized on the lab's ability to operate efficiently while allocating significant resources to back-end R&D. For example, when the ABCTL leadership team realized that demand for basic testing supplies were skyrocketing, they quickly began evaluating the efficacy of saliva samples heated at varying temperatures. Having developed the novel solution in late May, the ABCTL had an entire summer to purchase the necessary equipment and perfect their testing processes in anticipation for the wide-ranging fall migration of students back to campus. Combined with accurate forecasts of testing capabilities, the lab could also determine the additional volume from outside testing contracts they could take on. While rival diagnostic labs were competing for the same highly specialized nasal swabs and transport mediums, the ABCTL developed their own saliva-based PCR test using drinking straws and common test tubes. By using simpler front-end materials, the lab decreased their reliance on technical, single-use material suppliers like Becton and Quidel, and subsequently hedged their exposure to near- term supply shortages. With competing labs relying on the same dwindling supplies, the ABCTL's scientific advancements allow them to operate and scale independent of traditional resource constraints. Without compromising their accuracy or speed, the ABCTL's scientific innovation has helped them stay ahead of market trends and ramp-up testing operations.

While saliva-based samples have provided important benefits like comfort and convenience, the biggest improvement came in the transition from professionally administered to self-administered testing. Beforehand, medical professionals would need to stand out in a parking lot and collect samples one at a time from passengers in cars. That resource-intensive (labor, time and space) collection method was a major bottleneck in the ABCTL's operations.

When the lab switched over to saliva testing, their heightened capital efficiency allowed them to scale operations and meet testing demand. For example, whereas the complexity of nasopharyngeal swabs required medical professionals to be engaged throughout the entire testing process, the intuitive nature of saliva sampling allows those same employees to only handle the front-end (handing out testing kits) and back-end work (scanning and storing tubes) within that testing process. By delegating the time-consuming collection responsibilities to the consumer, the ABCTL is able to better utilize labor hours to funnel greater amounts of samples into the lab for analysis. Following the Lean Six Sigma methodology, the ABCTL's transition to saliva- based testing helped shift resources (primarily labor and time) to value-

added activities like sample testing and analysis. By focusing their efforts on the activities consumers pay for, the lab limits resource waste, increases total testing volume and maintains a rapid turnaround time - one of their primary KPIs (Gupta, 2018).

Just as viruses mutate and adapt over time, the diagnostic testing market also adjusts to new strains and developments. As a result, one challenge regarding the ABCTL's scientific innovation are the significant capital investments required to stay ahead of market trends. In traditional service companies, speed is money. For healthcare specifically, that concept becomes increasingly relevant when we factor in the contagious nature of Covid-19. With accuracy rarely in question given the FDA's strict approval guidelines based on statistical significance, the diagnostic lab that can quickly turnaround results will be awarded lucrative enterprise contracts. In the private sector, this principle is evidenced through OPKO Health's BioReference Laboratories securing exclusive testing contracts with the NFL, NBA, MLS and CDC.

Although BioReference is significantly smaller than traditional legacy players like Quest Diagnostics and Roche, their ability to reliably turnaround Covid-19 test results within 24-48 hours when larger labs sometimes took two weeks allowed them to gain market share and become an industry challenger. Similarly, the ABCTL's transition to saliva-based diagnostics has helped them turnaround test results within 48 hours when local labs required anywhere from a couple days to a week. However, following the market's never-ending demand for faster service, the diagnostic industry has gradually been shifting towards rapid point-of-care testing. Specifically, Abbott's BinaxNOW™ COVID-19 Ag Card - the $5 antigen test – demonstrated how quickly consumer preferences evolve to favor diagnostic tests that are fast, convenient and cheap ("Abbot's Fast" 2020). While ASU has received a $6 million state contract to construct a similar point-of-need device, substantial capital investments lie ahead for the commercialization of such a product. As a result, while the lab's scientific innovations to date have kept them ahead of industry, maintaining that scientific edge will come with a hefty price tag as large diagnostic companies usher in the future of Covid-19 (and diagnostic) testing.

Automation

While the lab has a track record of large-scale testing from their BARDA project, they still needed to add specific equipment to improve their operational efficiency. The leadership team quickly identified a need for additional Biomek i7 Automated Workstations to handle sampling and analysis responsibilities. Talking with Dr. Magee, each i7 machine costs approximately $160000, has a useful life of ~10 years and is still practical post-Covid for general diagnostic testing (Magee). The i7 purchases (along with other machinery) exhibit the ABCTL's core focus on open-source equipment - machines that can perform multiple functions. Whereas established labs might already have substantial pre-existing infrastructure that are one- dimensional in functionality, the ABCTL combined their "clean slate" with industry/academia expertise and sizable funding to build a flexible asset base that will continue to generate value post-Covid. This has allowed the lab to grow from a qPCR machine and Kingfisher to six i7 machines in addition to those aforementioned. When we toured the lab, Dr. Magee also mentioned that a rival lab recently purchased six i7 machines to boost their Covid-19 testing operations (Magee). Such market activity not only validates the lab's current philosophy on open-source equipment, but also confirms the leadership team's ability to identify and purchase key equipment before demand upticks.

Preanalytical, analytical, and postanalytical laboratory activities that may be automated

Preanalytical phase	Analytical phase	Postanalytical
Specimen receipt	Analyzer loading	Result reporting
Specimen accessioning	Specimen integrity checks	Recapping
Labeling	Testing	Specimen archiving
Sorting	Dilutional analysis	
Centrifugation	Result transmission	
Decapping	Speciment unloading	
Specimen quality inspection		
Aliquoting		
Specimen distribution		
Specimen retrieval		

Figure 6. Automatable activities within a traditional laboratory (Marzinkle, 2020)

Automatable laboratory activities traditionally include mundane physical tasks or basic binary analysis. While the i7 machines have automated many activities in the analytical phase, the ABCTL still has to delegate significant portions of the preanalytical phase to their workforce - primarily decapping and specimen retrieval. Without the necessary machinery to automate those steps, hourly employees within the lab have to decap each storage tube, extract a specific amount of sample, and recap the tube. This time-consuming process ultimately bottlenecked the entire operation because it was limiting input into the i7s. An anticipated change to solve that issue is the incorporation of a capper decapper into the lab, which will automate most preanalytical activities. In Dr. Magee's estimation, such automation could increase their throughput from their current 4000 to 5000 tests / day to 16000 tests / day (Magee, 2020).

As the lab looks to incorporate a new decapper machine to achieve heightened scale, questions arise regarding equipment integrations in the testing process. Following the 80% benchmark many laboratories use for automation decisions, "if 80% of specimen containers and handling activities can be standardized, improvements will be achieved with regard to overall labor and costs associated with specimen handling and processing" (Marzinkle, 2020, p. 240). In the case of the ABCTL, while the two machines (i7 and capper decapper) could theoretically automate close to 95% of handling and processing activities, significant implementation concerns still persist:

1. Are there any non-compatibility issues between manual and automated processes that would force suboptimal workarounds (Marzinkle, 2020)?
2. Is there any lack of familiarity with the proposed automation system (Marzinkle, 2020)?

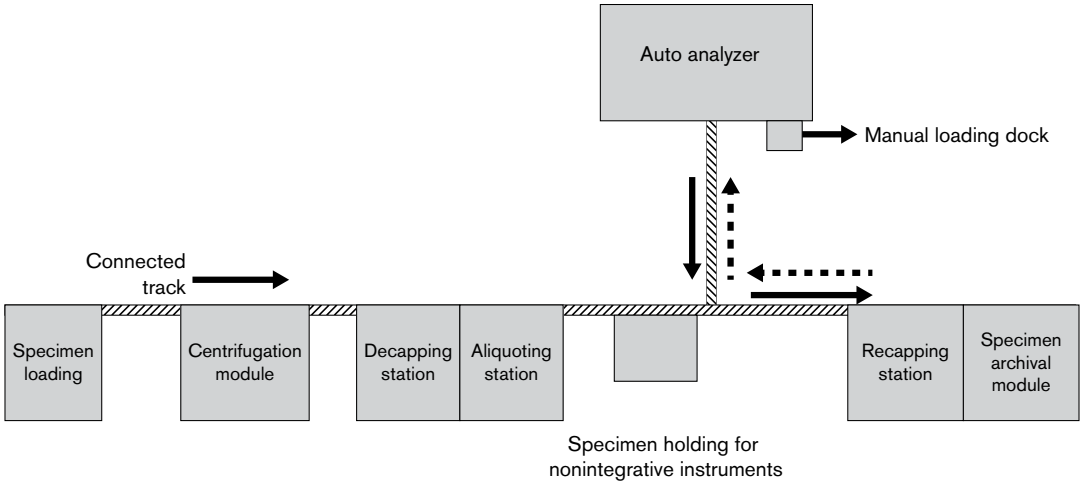


Figure 7 – Layout of complete automation within a laboratory setting (Marzinkle, 2020)

The diagram above depicts a centralized automation platform that consists of a single preanalytical line connected to multiple analytical instruments - similar to a fully automated assembly line for diagnostic testing (Marzinkle, 2020). Assuming the ABCTL decides against full automation given the mammoth capital investments (machines, lab redesign, etc.), partial automation requires employees that can work effectively with machinery throughout the testing process. While simple technological training can resolve a lack of familiarity, the integration of manual/automated processes require more pensive planning. For example, if there were issues within preanalytical equipment functionality, manual workflows would be required to sustain routine operations (Marzinkle, 2020). With such a workaround being extremely resource- inefficient, the ABCTL must ensure that sample tubes can seamlessly transition from the decapper to i7 machines to achieve maximum efficiency. If that becomes the norm, hourly lab employees would then be tasked with either preparing sample racks (specimen loading) or disposing waste (specimen archival module) with machines performing the time-intensive responsibilities in between. Although a connected track (depicted above) would be difficult to construct, with trained employees and minimal switches between manual and automated processes, the ABCTL can resolve any integration issues and achieve maximum output.

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Section VI: Future Perspectives

Authors: All members of the Business Group

As the numbers of Covid-19 cases decrease and more and more people receive vaccinations, the pandemic that has gripped the world for the past year will eventually fade away. With this consideration, the role of the ABCTL in the future remains uncertain. Our team, from talking with Dr. Carolyn Compton, has determined that the diagnostic testing for viruses and infectious diseases will eventually return in full to the private sector commercial labs. However, given this, there remains another set of routes for Biodesign to continue down. As of the time that this paper is being written, no concrete discussions have taken place regarding the future of this lab.

The world has learned a lot more about viruses and infectious diseases, notably coronaviruses, over the course of this pandemic. The ABCTL is no exception. The ABCTL has developed an efficient method of testing for the Covid-19 virus and has provided close to one million people with quick, accurate tests. The University has proven itself to be agile and adaptable, having set up the lab in the first palace, and having made necessary changes from nasal swab to saliva without interrupting the testing process significantly. The general consensus is that ASU must take this knowledge and ability and utilize it where appropriate in the future.

All companies follow a variation of the generic business life cycle. The stages include launch, growth, stake-out, maturity, and eventually decline. With the increasing availability of vaccines in Arizona, ABCTL is currently at its maturity stage which is an important stage in an organization's life cycle. Now is the time to decide the lab's next steps, whether that be moving forward and evolving or absolving ABCTL entirely. These decisions are made by businesses frequently when the time comes, but this is a new challenge Dr. Compton and other main stakeholders of the laboratory are faced with. It can be hard to let go of a successful business that effectively responded to a rapidly changing environment.

The launch cycle is initiated when a business is created due to a need in the environment for the product or service being offered. ABCTL originated out of the Biodesign Institute, using equipment and personnel that were already involved with the laboratory. This phase of the business cycle was short, as the need for ABCTL's services were dire, and were requested immediately by both the State of Arizona and ASU. The company launched before processes were fully flushed out because the need was so large for ABCTL right away. Large losses are known to occur in the launch phase due to product testing and development and ABCTL was no exception to this but was not set back. It can be useful to bring in a common distribution curve known as the J-Curve to analyze the initial stages of this start-up laboratory. Coined by Howard Love, the J-Curve gets at the idea of how start-ups often experience dips when they start-up.

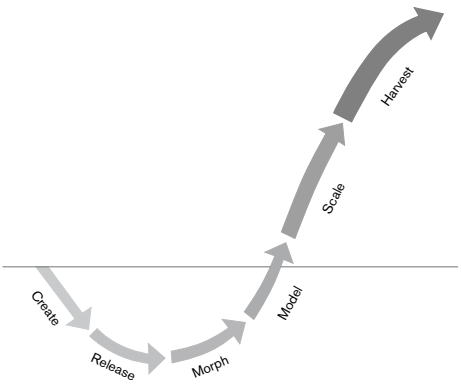

Figure 1: J-Curve Graph

The laboratory entered the COVID-19 testing market at the creation stage. It then released its product to the Arizona community. Although it occurred some early losses due to inefficiency with nasal swab testing, it hedged its loss significantly and experienced a smaller dip compared to most start-up organizations. The laboratory has grown into the morph, model, and scale stages.

Next came the growth phase, which started in August when classes started in the fall. On- campus students, faculty, and staff were getting tests and ABCTL needed to ramp up their testing process to fulfill the needs of the community. Along with the ASU community, ABCTL was tasked with helping out the state by providing testing for private companies and the public community. A grant was provided to help cover the costs of testing which helped ABCTL remain in business during this time. The growth phase lasted through November, as there was a spike in COVID-19 cases and therefore a larger demand for testing around Thanksgiving.

The shake-out phase is when a company is still experiencing an increase in sales/demand, but the rate of increase is declining. This can be due to more entrants in the market or due to a decrease in demand. By December of 2020, all companies in the private sector that wanted to provide COVID-19 testing were doing so. As students and staff left campus for winter break, testing demand declined in the immediate community. While the ABCTL saw another spike in demand following winter break in January, the influx in demand was short-winded and eventually slowed down to a steady, lower number of tests being run in February. The ABCTL is now at the maturity stage, a stage defined by a decrease in sales and the opportunity to reinvent themselves before a decline. Before the decline of a company happens, the maturity stage allows organizations to reposition themselves in the market, or potentially find a new market to enter based on the strengths and weaknesses of the company.

In addition to organizational life cycle stages, it can be helpful to look at the distribution curves of entities. A common distribution when analyzing continuous organization growth is the S-Curve. The distribution looks at organizational growth amid different areas along their journey. It is important for the ABCTL to know where it falls in regard to their place among growth distribution. The S-Curve looks at the growth of organizations over time based on their dependance with numerous other variables. The diagram of the S-Curve is shown below in the following figure:

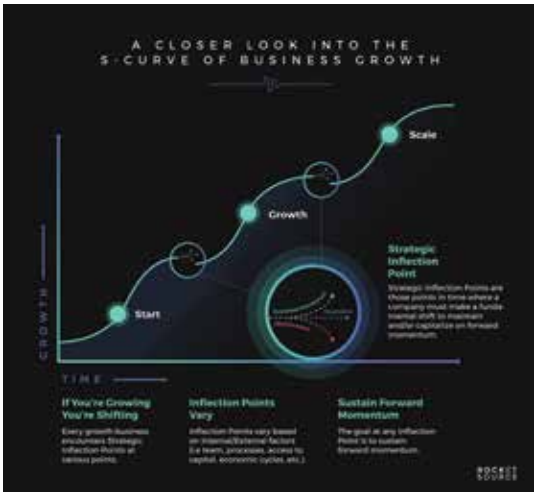

Figure 2: S-Curve Graph

As previously discussed in Volume II: The Laboratory as a Business Within the University Environment, the laboratory will need to sustain its growth going into the future. The laboratory has responded well so far to various “inflection points,” or important markers where an organization needs to act critically to sustain its growth. The laboratory has experienced great growth from the offset and has scaled its operations. However, with the rise of COVID vaccinations and the sharp decline in COVID-19 cases at ASU, the

laboratory is coming upon another inflection point where it will need to act critically. The Butterfly versus Dinosaur metaphor is helpful when looking at the future outlook of the laboratory. Will it continue to grow as a butterfly, or Will the laboratory face the possibility of extinction like the dinosaurs?

As previously mentioned, some options exist for the ABCTL to continue its operational functions in some capacity. Dr. Compton has expressed doubt that a diagnostic lab could continue to operate in the current location at Biodesign's complex on the Tempe campus.

However, the newly constructed Health Futures Center (HFC) in Northeast Phoenix could be the ABCTL's next home. According to bdcnetwork.com, the $80 million facility "is meant to bring together the university's College of Nursing and Health Innovation, College of Health Solutions, and the Ira A. Fulton Schools of Engineering, together with some shared programs of the Mayo Clinic (Barnes 2019)." This facility would provide the equipment, square footage, and overall capacity to run continued testing as the ABCTL is currently trying to run a clinical lab inside a non-clinical environment. While many may point to the new variants of the virus that are currently spreading, Dr. Compton pointed out that the lab has received grants to test for the original COVID-19 strain only and would need additional funding to begin testing for other strains. However, should the lab receive more funding and continue to test for other conditions, the HFC would be a welcome place to expand.

Another opportunity for the lab's continuity could be in niche testing environments, helping certain organizations test for certain conditions, and keeping track of people with known conditions over a period of time. For example, Columbia University keeps a registry of some people that are afflicted with celiac disease, a genetic autoimmune disorder that primarily affects the small intestine. With this, they keep track of the disease in patients on the register over a certain period of time and continue research into cures and treatments. As of recently, they have been encouraging clinicians to notify them of COVID-19 cases in celiac patients, so that they may expand their research and track how the coronavirus affects these specific types of patients. Dr. Compton explained to our team how ASU could possibly maintain a similar registry, and that this type of research could even likely be done in the current location. The final and perhaps the gloomiest option would entail the ABCTL's dissolution, and a return to Biodesign's normal research via grant funding. Senior leaders of the ABCTL and Knowledge Enterprise have expressed, nothing can be expanded without more funding. This funding would need to come from the federal and/ or state government through grants from the National Institutes of Health (NIH), and other public sector research organizations, or private funding.

This funding will inevitably dry up once the pandemic recedes and needs to be replaced by funding for other ventures as discussed above in order to continue in any direction. With that, the lab could go back to its normal research on a grant-by-grant basis, conducting antibody testing and COVID-19 testing as required.

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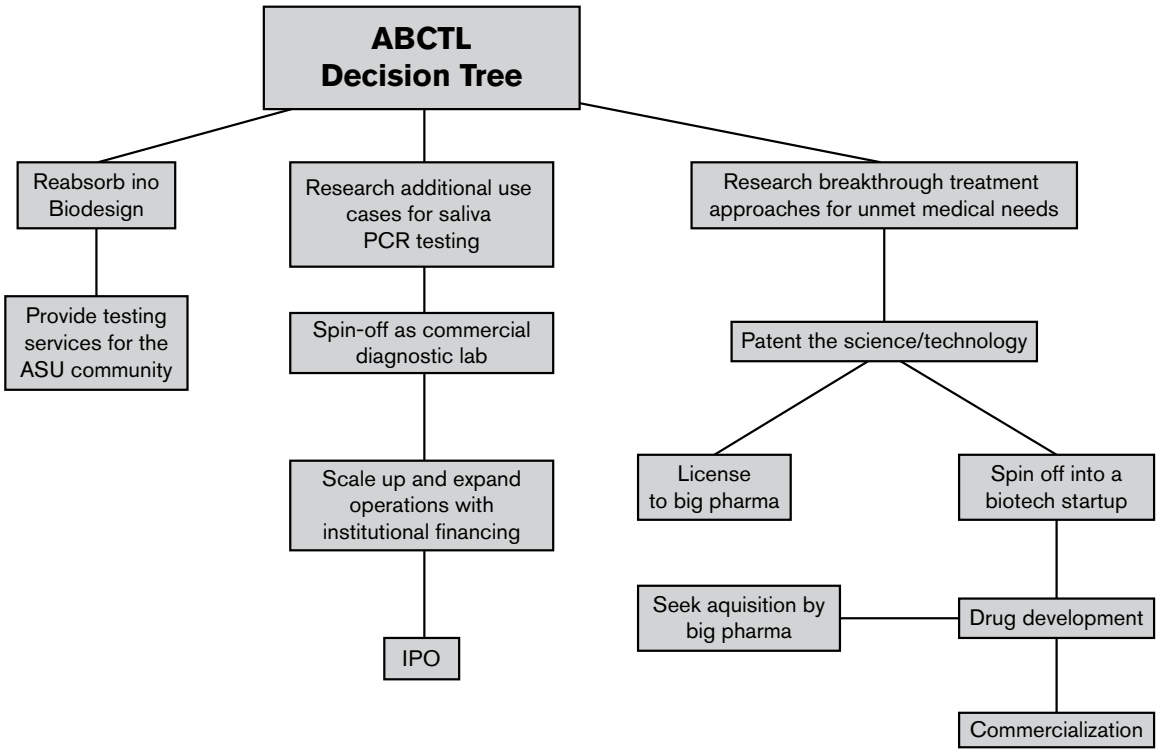
Direction for the Future



Chapter 2

The Making of a COVID Lab

A Focus on Intercultural, Organizational and Developmental Communication

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Submitted in fulfillment of requirements for the honors baccalaureate program of Barrett, The Honors College at Arizona State University

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Introduction to Chapter 2

The ASU Biodesign Clinical Testing Laboratory (ABCTL) was created to offer an accurate, less invasive, less labor intensive, and less resource draining public COVID-19 testing in Arizona. The goal of the Communications Group was to analyze and document the communication practices of the ABCTL, through a series of interviews and an analysis of media, both public and internal. In order to accomplish that goal, each member of the communications team chose to focus on an area they felt was crucial to the future emulation of the success and transformation of the ABCTL. These areas of specialization were: a) evolving best practices for COVID testing and intra-organizational communication, b) diffusion of innovations and influencing groups with relevant health information, and c) socio-cultural conditions and context of COVID communication and community partnerships.

The COVID-19 pandemic has fueled new communicative practices and innovations, affecting how various social groups communicate across many areas and disciplines. The theses of this group take on the ABCTL's efficacy of evolving communication practices in the areas of intra-organizational channels, patient-provider relationships, public media and cross-cultural community collaborations throughout a novel pandemic situation. By analyzing and documenting the specific areas of communication outlined above, the communications team contributes a vital piece to the greater group puzzle that is creating a blueprint for future organizations to transform their academic laboratories into viral testing laboratories, should the need arise.

The Covid-19 global pandemic is not only an unprecedented health crisis but for many, holds significant implications for human life and well-being. As such, a communication studies approach draws attention to the profound interactions that comprise and constitute co- occurring physical and social ills, as well as our response, including ASU's institutional efforts as exemplified in the case of the ABCTL.

While some popular understandings of communication center on the broadcast or transmission of messages from sender to receiver, this group honors project draws upon the multidimensional sub-fields of communication studies, including intercultural communication, organizational communication, and developmental communication.

In the research process, the communications group have discussed and applied a range of theories, including cultural humility, auto-communication, the diffusion of innovations, and viral transmediation. We have learned that the complexity of communication efforts related to ABCTL cannot be reduced to merely public relations communiques (as important as these are). Accordingly, we explored a wider network of social and mediated agents, communication contexts, as well as power dynamics that animate communicating and organizing in the everyday operations of the lab.

We thank the following individuals for their participation in this work as interviewees:

- Dr. Susan Pepin, the Managing Director of Health and Clinical Partnerships at Arizona State University
- Tamara Deuser, the Office of Knowledge Enterprise Development officer at Arizona State University

Section I: The Implicit Modification of the Patient-Physician Relationship to Reduce Medical Mistrust and Discriminatory Bias

Author: Van Dexter Calo

Background

Introduction

COVID-19 has made a global impact in all aspects of people's lives and led to an exponential increase of pressure in the healthcare systems around the world. Data has shown that African Americans are the most overrepresented among COVID-19 deaths as of August of 2020 (Milam, et al. 2020). Throughout March to mid-April, there have been 1,497 coronavirus discriminatory actions that have been reported against Asian Americans (Jeung and Nham, 2020). In addition, Asian American healthcare workers have also seen an increase of racial hostility and reported incidents from patients they serve. It is noticeable that there is a connection between both sides. The patient of color and medical professionals' perspective of a specific racial group both experiences the same theme of discriminatory biases and medical mistrust. It reflects a reciprocal relationship that simply depends on the context and individual. As a result, it is evident that there is a loss on both sides which can lead to even more issues beyond the pressures of a global pandemic.

This Section explores historical and recent cases that have eventually cultivated the varying ways in which biases are projected in modern-day medicine. It then shifts the focus on how the COVID-19 pandemic has impacted levels of trust within the medical profession. Also, the thesis features the discriminatory experiences from Asian American healthcare providers when engaging with patients as well as their private lives outside of the hospital in the midst of the global pandemic. This was done by doing a secondary content analysis of various forms of media in which Asian American healthcare workers spoke about their experiences and will highlight the common themes.

Ultimately, this was essentially tied to the work of the ABCTL. This Section examines the relevance of ABCTL indirectly modifying the patient-provider relationship in the time when the reciprocal discriminatory biases exist on both sides. Despite this modification, the Section still discusses communication practices when targeting disadvantaged communities of different socioeconomic and cultural backgrounds due to the known mistrust present. As a result, it examines the ABCTL's training process for the volunteers and explore their tailored interaction with each community in light of potential discriminatory biases linked to specific ethnic groups. Lastly, the thesis acknowledges the massive and impressive efforts of its innovative creation made available to Arizona, ASU students, and local community partners.

Health Equity

A critical component of any healthcare system is health equity which provides all the resources to a population regardless of the demographics. However, it is not black and white due to underlying mistrust and biases from both the healthcare provider and the community itself.

With the increased tensions and social pressures from both parties due to COVID-19, this practice holds much more significance than ever before. Therefore, establishing a partnership would be an essential step for ABCTL to alleviate some mistrust levels. A national study focuses on health equity's goal using a community-based participatory research (CBPR) conceptual model that determined how contextual and partnership practices were shown to be correlated with successful partnerships (Duran, 2019). The seven categories -- power-sharing, partnership capacity, bridging social capital, shared values, genuine community involvement, mutuality, and ethical management -- were applied to practices within the community partners (Duran, 2019).

The two most critical components relevant for ABCTL to consider would be power-sharing and shared values (Duran, 2019). The category of power-sharing is associated with short and immediate outcomes and how communities' interaction can eventually impact the program's image in the long run (Duran, 2019). Therefore, power-sharing allows for space to be open and emphasizes that their voices matter to ensure that historical and systematic medical mistrust problems among minority groups do not prevent them from achieving the partnership's purpose (Duran, 2019).

As a result, ABCTL has the responsibility to brand its services carefully in ways that do not appear to be controlling towards the community and instead provide opportunities for them to actively engage in improving the community's health in the end.

Furthermore, the category of shared values talks about the purpose of community partnerships. It is not a "business as usual" approach but is more focused on the immediate and overall composite outcomes as a result (Duran, 2019). In other words, the core reason was utilitarian-based (Duran, 2019).

This easily translates to the timely and innovative development of ABCTL. It created a resource open in order for the public to raise awareness of the global health crisis. ABCTL's branding to the communities must be tailored not only to the community they intend to work with but also the approach that will give them the image of being a helpful resource for the group rather than a business-centered act.

The following literature review is a good foundation that ABCTL should consider when planning how to approach and communicate to ensure the impact and goal are clear and, in a context, where the populations are comfortable participating. The 7 CBPR Conceptual model outlines a variety of directions and ways that working in these communities can impact the program or organization, and of course, the community itself (Duran, 2019). However, it is crucial to not only have a well-developed and established system in place. ABCTL must consider the range of gaining trust, having a full understanding of cultural context, and building opportunities for the community to contribute to providing insight into the progress for a successful partnership. With the higher rates of medical mistrust from the influx of information about the virus, ABCTL incorporating these traits would establish trust with community members and lead to an overall awareness of the significance of COVID-19 testing.

Cultural Humility

While health equity focuses on raising the level of trust, the concept of cultural humility concerns the issue of implicit discriminatory biases among both parties. Because ABCTL intends to work in disadvantaged groups, ABCTL's approach should consider the varying cultural factors that pertain to distinctive communities' health beliefs and practices. Regarding cultural humility, Foronda demonstrated that the attributes in the concept analysis study were openness, self- awareness, egoless, supportive interactions, self-reflection, and critique (Foronda, 2016).

Openness, in particular, takes the first step to explore the various ways in understanding the needs of a diverse population (Foronda, 2016). The other is self-awareness which is knowing one's values and image and how that translates to the way they are viewed by others (Foronda, 2016). Both of these attributes play a vital role in the practices that the ABCTL lab is involved in. Therefore, both of these attributes should be integrated as ABCTL begins to establish partnerships with diverse groups and communities.

Since the entire framework for cultural humility conveys a long-term impact, it may be a little tricky for ABCTL, but it is still very manageable if done well. In other words, researchers best summarized the definition as "incorporat[ing] a lifelong commitment to self-evaluation and critique, to redressing the power imbalances in the physician-patient dynamic, and to developing mutually beneficial and non-paternalistic partnerships with communities on behalf of individuals and defined populations" (Foronda, 2016).

The keyword here is "lifelong component," which does not easily translate to the work of ABCTL. The program is categorized as a short-term resource for the community partners and the duration of the pandemic. Therefore, based on this definition, it is expected that ABCTL would face some challenges and maybe lacking in their approach when the interaction comes. However, cultural humility more heavily relies on the healthcare workers' and volunteers' training process. Although the following literature review considered being reflective as more reasonable than being educated on cultural competence, the ABCTL should then pay close attention to the training process, approach when establishing community partners, and eventually, the on-site interaction with the members of the community.

The mention of physician-patient dynamic and community partnerships within the cultural humility definition highlights both the issues presented in the thesis. Considering the medical mistrust that has been ingrained in certain minority groups and the ongoing implicit or explicit discriminatory biases physicians have or may face themselves, ABCTL must take into account many factors. Therefore, ABCTL's image and branding when reaching out to African Americans and any other minority groups who may not feel confident with current medical practices must be consistent and clear. Furthermore, Asian Americans around the nation have been facing discrimination in all forms, and communities that ABCTL serves may have biases against one if they see an Asian volunteer on the site, for example. As a result, the following literature review leads to the idea that ABCTL must ensure a strategic and routine-like approach to establish consistency within their training and sample collection process to truly ensure that volunteers or community members are subject to forms of discrimination. As COVID-19 cases continue to rise around the United States and the world, there is not much flexibility regarding time and power to culturally maximize testing services. Considering the expectations among healthcare providers and, in particular, ABCTL volunteers for cultural humility are on a larger scale.

Medical Mistrust within the Black Community

Medical mistrust is defined as the "decreased likelihood of engaging in various health behaviors, including health utilization and preventive screening" (Williamson, 2019). Knowing that this has been present among specific communities for decades, ABCTL must consider this issue when planning to expand its services. A better understanding would stem from looking into the background and history to get a broader picture of the circumstance.

The Tuskegee Study of Untreated Syphilis in the African American Males set a prime example of how medical mistrust and discriminatory acts function. In Tuskegee, Alabama, and lasting for 40 years from 1932-1972, about 600 impoverished African American men were recruited to essentially study the natural course of syphilis (Alsan and Wanamaker, 2016). Various medical procedures were performed on the subjects, and they were discouraged from seeking medical services and denied treatment for any symptoms associated with the infection (Alsan and Wanamaker, 2016). When Jean Heller of the Associated Press disclosed the study, it was already too late as most of the subjects were dead from syphilis-related complications (Alsan and Wanamaker, 2016). Ever since, more figures like journalists, social scientists, and medical researchers began to identify Tuskegee as the main reason why Black people are now skeptical about being part of any public health-related events and clinical trials. As a result, it now has this detrimental impact on their health, specifically Black men (Alsan and Wanamaker, 2016). Overall, due to the Tuskegee study, African American men's relationship with medical establishments has set a wrong perception and further increased the medical mistrust in the community (Alsan and Wanamaker, 2016). This historical study is critical to consider as a reference to one of the well-known cases in how medical mistrust became among Black people in the United States.

ABCTL may be limited in time to study every detail that contributes to each community's mistrust levels. Nevertheless, this literature review sets the foundation to see how it all started. However, if ABCTL takes the time to understand its presence, that is already a step in the right direction.

The Impact of COVID-19 on African Americans' Medical Trust

The rise of COVID-19 has shone a light on African Americans' medical mistrust to a greater extent. This is where ABCTL must pay attention to the most because this will provide even more precise insight into how this mistrust level corresponds with the pandemic. The Kaiser Family Foundation (KFF) and The Undefeated released a new poll that revealed the mistrust of African Americans on the health care system in the U.S. compared to white people. The survey asked 1,769 adults with 777 African Americans from August to September (Washington, 2020). The recent numbers increased from 6 to 7 out of 10 Black people believed that they are unfairly treated, a 56% increase compared to a similar poll in 1999 (Washington, 2020). This recent poll also points out that 37% of Black mothers, 25% Black women, 15% black men, while only 7% white women and 4% of men report some form of racial-based mistreatment (Washington, 2020).

While this literature review would be relevant in a medical setting, this does not significantly apply to an institution like ABCTL. The laboratory's goal is to perform mass testing for the population it serves and, therefore, structures it in a way that almost disregards the conflicts that may arise from a much more direct patient-provider relationship.

Discriminatory Bias Against Asian Americans Post COVID-19

Because this thesis focuses on the patient-provider relationship and its relation to racial discrimination biases toward patients, it does not mean that healthcare providers are exempt from this. Racial biases against Asian Americans are now getting faced with severe discrimination. Because the reports do not disclose profession, this set of information is still highly relevant to understanding the severity of discrimination they face, which can apply to any Asian American healthcare provider. From March 19, 2020, to April 15, 2020, 1,497 reports of coronavirus-related discrimination were submitted on the CAA/A3PCON STOP AAPI HATE website. The types of discrimination range with 69.8% of the reports being verbal harassment, followed by 24% of shunning and even as violent as a physical assault that made up 8.5% and being coughed and spat on that made up 6.1% (Jeung and Nham, 2020). Out of all of the responses, it is also no surprise that 40% were Chinese. The state that had the most reports were California at 41.8%, followed by New York at 16.7%, which is also no surprise considering they were the significant hotspots for COVID-19 during those months as well as being the home to a majority of Asian Americans living in the United States (Jeung and Nham, 2020).

This literature review further strengthens the importance of having no patient-provider relationship presence on behalf of ABCTL. It shows the reciprocal relationship happening as a result of the pandemic. Although these acts are nothing new, it is notable to point out that both the Black community and Asian Americans are faced with discrimination at increasing levels. This then interprets the idea that a patient-provider relationship carries this potential for racial-based judgments. Therefore, ABCTL's best interest is to avoid any of this from happening with a consistent structure.

Analytical Framework and Findings

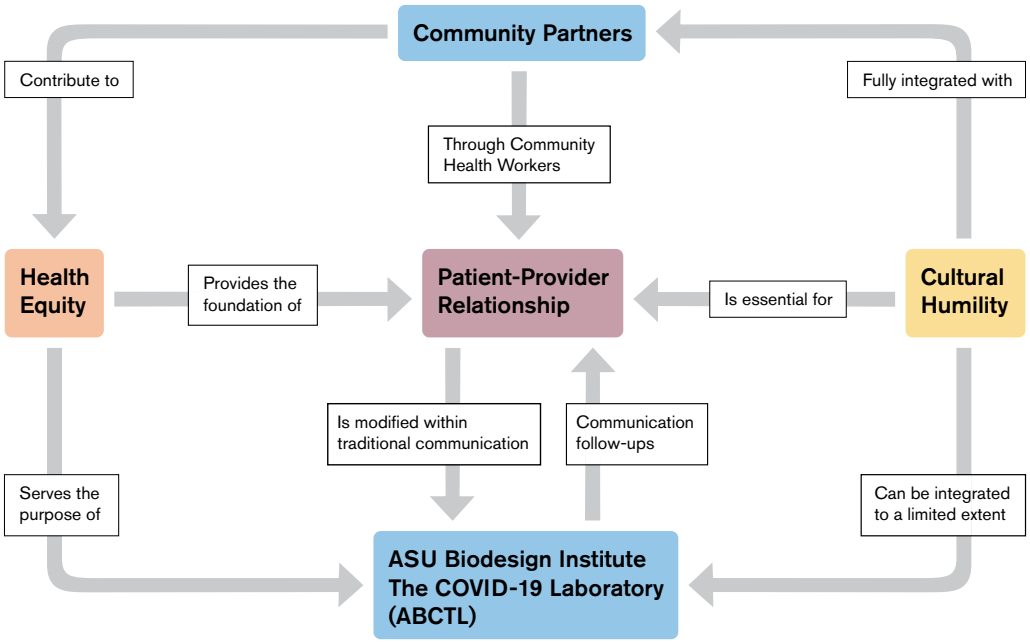

Figure 1: The concept map of communication methods of health equity and cultural humility in its contribution to a patient-provider relationship that relates to ABCTL's work

Secondary Content Analysis

A variety of forms in the media were used to highlight the discriminatory biases or acts against Asian American healthcare workers during their shifts in the hospital and their personal lives. The types of media were social media posts, TV interviews, and article interviews. A 3 to 4 sentence summary was written on that media that best focuses on the healthcare provider's biases. This was all taken into consideration, and a common theme or trend of the responses was determined.

ABCTL Training and Community Partnerships

Meetings were conducted with Dr. Susan Pepin, the Managing Director of Health and Clinical Partnerships at Arizona State University, and Tamara Deuser, the Office of Knowledge Enterprise Development officer at Arizona State University. The purpose of these meetings was to understand how the ABCTL works with regard to the training process and the development of expanding this to disadvantageous communities. The discussion that followed is the benefits of this partnership and its effects on non-typical patient-to-medical provider interaction.

Asian American Healthcare Workers

COVID-19 Related Social Media Posts, Interviews, and TV Appearances

Date Published	Author	Title	Summary
April 9, 2020	TIME	COVID-19: Asian-American Doctor On Being 'Both Celebrated And Villainized At The Same Time' | TIME	Dr. Chen Fu talked about being symbolized as a hero by his parents, but he notes that he is more worried about them and other Asian Americans right now. His mother's car was destroyed, and similar experiences arise from other close friends. He was even dressed in full scrubs only to be faced with racial slurs at the subway. Dr. Fu notes that kindness is what keeps him going through each and every day.
April 10, 2020	Dr. Christina Chen	"Asian doctors unite over COVID19 racism"	The video from Dr. Christina Chen's Instagram shows multiple doctors with signs of the racist phrases the doctors heard either working at the hospital or in their daily lives. For instance, @DrLifestyle101 on Instagram had "You're a disgusting filthy bat-eater" as her sign. It shows a montage of doctors showing their personal sides and ethnic origin emphasizing the diverse cultural background. The hashtags #ImNotAVirus and #HumanLikeYou are used to emphasize kindness and respect for the work they do every day.
April 14, 2020	Jacquelyn Corley	Boston Doctor Becomes Victim Of COVID-19 Racism. Here Is How We Should Respond	As Dr. Lucy Li, an anesthesia resident doctor at Massachusetts General Hospital (MGH), goes to work, she is assaulted by a threat asking why Chinese people are killing people and has never experienced instances ever since immigrating from China. There should be support for healthcare workers to reach out for help when faced with any form of racism or xenophobia. It is also critical that any acts of racism should be identified and called out immediately, minority representation is increased in the healthcare system, and everyone is responsible to go against xenophobic remarks even if it does not affect them directly.
April 21, 2020	Sojung Yi	I'm an Asian American doctor on the front lines of two wars: Coronavirus and racism	Patients are asking for different nurses and providers that are not Asian or from China. Dr. Sojung Yi talked about the President's impact of the term, Chinese virus, and emphasized the power hurtful words can have on physicians who are only trying to serve their patients.
April 24, 2020	Today Show	Threats Against Asian Americans Are On The Rise Amid Coronavirus Crisis	The news segment highlights the notably increasing hate crime against Asian Americans mentioning the NYPD reporting 11 hate crimes and taking into twitter a video emphasizing to call 911 if they fell victim to any acts like this. Dr. Chen Fu was featured to talk about his experience of getting called racial slur along with local Asian American residents being stabbed, yelled at, and hurtful messages left at their homes. Also, it mentioned nurses being rejected simply because they were of Asian descent and Trump was noted to always refer to the virus as the "Chinese Virus".

Date Published	Author	Title	Summary
April 24, 2020	CBS News	ER doctor worries about COVID-19 racism	Dr. Joan Cheng, an emergency physician at Markham Stouffville Hospital, reports having a Chinese patient that was a victim of a physical racial motivated assault. She talks about her fear of discrimination during her international travel when reports of the virus unfolded in January.
May 19, 2020	Allie Caren	Asian American health- care workers describe racist incidents | Voices from the Pandemic	Dr. Audrey Sue Cruz, a Filipino Internal Medicine physician, described a telemedicine phone appointment with a patient who asked where she's from and then blamed her "people" for causing the virus as well as noting that the patient usually does not see Asian doctors. Nurse practitioner, Hengky Lim, had been approached by a patient who refused to wear a mask, repeatedly coughed on his face shield, and blamed Lim's "people" for his sickness. Dr. Gem Manalo was encountered with racist comments against Chinese people for "eating bats" and general blame for the rise of COVID-19 while she was on the train.
May 26, 2020	GBH News	An Asian American Healthcare Worker Talks Dealing With Racism While Treating COVID- 19	Dr. Lucy Li. resident physician in Massachusetts General Hospital details her experience after her shift in which he encounters a man blaming her for killing people. She emphasizes the need to support others like the hospital sending out emails to everyone regarding the incident. Dr. Li also mentions that even though she is an anesthesia resident, the pandemic has changed her regular shifts to more time spent in COVID ICUs.
June 2020	ACP Hospitalist	Anti-Asian bias brought out by pandemic	Dr. Elisa I. Choi, MD, FACP, mentions an Asian encounter in which the patient was asked about his/her risk factors to getting COVID-19 and the response was that he/she was "surrounded by Asians". She has always emphasized that educating the patients about the false perspective of those of Asian descent encourages other physicians to keep on promoting inclusion and respect in their medical practices. Another doctor noted that a racism virus is also being fought during this time.
June 23, 2020	CNN	Dr. Wen: I've been told to 'go back to my own country'	Dr. Leana Wen, an Emergency Room Physician, talks about her experiences when speaking to the public about the virus in which she has been named as a "bat eater", to "go back to her country" and "her people" has caused this virus. She also points out her coworkers getting spit on and other discriminatory acts. She then points out that the country's leadership should talk about this issue and how, for instance, President Donald Trump's term for the virus has effects on the public's attention.

Communication Successes

Training

Dr. Pepin provided training materials of documents regarding sample packing transport instructions, directions on the process of running saliva testing sites, a step-by-step guide to wearing the personal protective equipment (PPE) properly, the disposal of hazardous waste, and appropriately storing N95 for reuse. To complete the training, the presentation needed to be reviewed. For instance, for the Health Insurance Portability and Accountability Act (HIPAA) Training, the quiz and confidentiality agreement were completed. Lastly, the site manager must report on ASU Career EDGE to verify the volunteer has completed training requirements.

When working with diverse groups of community partners, it was critical that ABCTL tailored the training material in the appropriate language and presented it in a format that the community healthcare workers can comprehend to the fullest. However, the materials, process, and logistics of testing must not be altered.

The instructions for wearing and disposing of the PPE were visually easy to read step-by- step guide with short descriptions. The accompanying PPE-related document was the guidelines for the reuse of N95 respirators. The document was a short word document that had a visual of how the N95 respirators should be stored and another visual supplement of the process of wearing and removing the mask. Then, the documents that followed were the guidelines of running the saliva testing sites either in an in-person facility or through a drive-thru site. The setup instructions were provided, and the procedure for both types of the site was provided along with a script and other roles and duties for other volunteers.

The script provided only four primary questions or a set of instructions. The first was to greet the participant, ask for identification for verification of their appointment, and follow directions to the website to register for one if they did not have an appointment. The second set of questions asked if they had any food, drink/water, smoke or chew, or gum within the last 30 minutes. If they responded “yes,” they were instructed to wait for the next 30 minutes. However, there should be a portion of the script that explains, in simple medical terminology, to the participant why the 30-minute period is critical to getting a good sample. That way, the participant can walk away with the comprehension of why it is essential rather than being told to simply wait. The next follow-up question was if they had their QR code ready with instructions on how to retrieve it if they did not have access to it already. Then, their date of birth was asked to be written on the test tube, and they were given the next set of instructions on how to proceed with collecting the sample into the test tube properly. Based on these simple questions, it is clear that the interaction is created to meet the testing site’s high demands and turnout quickly.

The last piece of the document was the packaging process of how the samples should be oriented to ensure the quality is maintained and delivered appropriately. There were also appealing visuals similar to the PPE document that shows the packaging instructions. This is an excellent supplement to add since it is clear and straightforward to understand the variety of community partners ABCTL intends to work with.

Community Partners

The ABCTL was created for the sole purpose of serving the ASU population but soon realized that the lab has the capability and the volume to branch out and be a more excellent service to the community (Deuser and Pepin, 2020). Since ABCTL is not a healthcare service, potential partnerships with clinical settings did not collaborate because the several modalities integrated into those medical establishments did not match with the ABCTL services to fit well together (Deuser and Pepin, 2020). Therefore, ABCTL successfully partnered with the Arizona Department of Health Services that helped ramp up the testing volume that ABCTL provided access to for the general public. From there, they have further reached out to several local organizations and specific communities to continue the expansion of free COVID-19 testing, especially towards disadvantaged groups.

Now, an important message that ABCTL has when it comes to its involvement with community partners is "we are not a hospital" (Deuser and Pepin, 2020). The facility explicitly states there is no physician-patient relationship, and that this lab does not serve as a clinical provider (Deuser and Pepin, 2020). As mentioned, the purpose of ABCTL was to start with the ASU population and take responsibility to test the general public because it is part of ASU's charter to be a service to the community (Deuser and Pepin, 2020). Another critical component to ABCTL's reputation is that it does not want to provide any clinical needs. Instead, the institution intends only to supply a large volume of tests for potential established healthcare retail that does want to be the face for COVID-19 services (Deuser and Pepin, 2020). When creating these partnerships, the requirement that ABCTL has to emphasize that testing- related services are solely ABCTL's responsibility (Deuser and Pepin, 2020). However, whether positive or negative, ABCTL includes descriptions of resources and extra information of what the results mean which is attached to the same page of the results. Specifically, if it is a positive result, there is more content added, such as directions for the quarantine [process as well as links to CDC website for specific directives. In addition, there are results that may be "invalid" and that is also followed up with directions to get a repeat test. Therefore, the communications within the patient and the provider, which is ABCTL and Dr. Carolyn Compton, are still present despite the absence of a face-to-face contact.

The City of Guadalupe

A prominent example of the work of ABCTL is their involvement in the city of Guadalupe. This town of 6,600 residents contained COVID-19 cases that were significantly impacting mostly Hispanic and Native American individuals. This could be due to the lack of knowledge in the severity of the virus or whether there was a local positive case. Promotoras, individuals who have close ties with the community that works to educate on health conditions, were recruited to help distribute food boxes, inform them about hygiene practices, and do so with little to zero contact. Due to residents being uncomfortable traveling to other testing sites, with the help of the Pascua Yaqui Tribe employees and ABCTL, they could bring testing to the community. As a result, a range of 1,000 to 1,500 people were reported to be tested in early September 2020.

It has also been noted that there is distrust in institutions that contributed to the difficulty of effectively communicating vital information. This was shown with the integral implementation of promotoras and having to bring a testing site to the town of Guadalupe despite having one only 2 miles away from the community due to residents being uncomfortable going there. With all of this in mind, a trend clearly shows that social and medical trust is a more significant barrier in this situation. This is an essential factor that institutions should consider when partnering with communities to provide any support. It is merely the fact that community health workers' deep connection with the residents has a much more significant impact, and it should be utilized to its most tremendous potential. It also noted that some residents in Guadalupe were embarrassed by getting COVID-19, but because of the shared stories from other residents that it is not something to hide is critical to spread the message that everyone is going through the same thing. As a result, institutions like ABCTL have the resources, money, and supplies to provide the testing materials, but their involvement must not go further. Community relationships, customs, traditions are deeply ingrained and should not be interfered in any matter. ABCTL contributed so much to Guadalupe regarding testing and was done so formally to meet the community's demand.

Conclusions

Modification of Patient-Physician Relationship: Health Equity

This section's focus is the relevance of ABCTL's implicit decision to modify the patient-provider relationship. Based on the known reciprocal relationship of mistrust and discriminatory biases on both sides, this modification allowed ABCTL to successfully fulfill its goal of reaching out to communities and providing mass-testing sites.

The first factor in their success was their intentions and branding. In other words, the institution was always straightforward with what it can only offer: mass testing to populations who need it. With this into account, the concept of health equity was accomplished. This is not only referring to their large and massive capability to run the test but also to the institution's decision to go to specific populations and ethnic groups that were disproportionately affected. Due to the unexpected, fast-paced, and severe nature of COVID-19, the goal was for immediate outcomes yet also engaging the community to increase that level of trust in the institution moving forward. As noted from Guadalupe residents' skepticism in going to another testing site, it was made clear that ABCTL carried the power-sharing concept to share a supportive image to the community members by recruiting community healthcare workers. In considering how ABCTL branded themselves as an institution, the patient-provider relationship was therefore modified to a great extent since it was not the typical interaction in a medical setting, but communications that led to and the ones that follow still hold the principles of the relationships. As a result, this provided the possibility to fulfill their intentions successfully.

Modification of Patient-Physician Relationship: Cultural Humility

Just because the patient-provider relationship was altered on behalf of ABCTL does not mean that this concept was not fulfilled. Community healthcare workers took control of the idea of the "patient-provider relationship" although, of course, no medical treatment nor diagnoses were performed. Regardless, their work has increased this level of trust from community members. ABCTL must rely on community health workers to carry a long-term connection with the residents to be their support system throughout the pandemic. Now, this is critical to point out the difference between the two. ABCTL was a new and innovative institution, while the community healthcare workers have been with that population for some time. Therefore, the level of trust is not altered in any form within this exchange.

Because ABCTL knew that they could not provide any follow-up treatment, leaving the community only with testing will not ultimately bring the change that the community needs, which is when community health workers step in. ABCTL was the first step that the community needed, but it was only intended for short-term purposes. However, this should not be mistaken as a disadvantage of the institution since this was the goal ever since the launch of the service. Since this thesis focuses on the reciprocal relationship that results from mistrust and discriminatory biases from both sides, ABCTL gave the community health workers the platform to aid in completing that role within the patient provider relationship. The success of this was due to ABCTL knowing their place of where they stand with the community.

Additionally, the patient-provider relationship's modification addresses the barrier of the power imbalances between both parties, as noted from the cultural humility definition. This was observed in the training process for the volunteers. While the documents have varied for different communities and populations, such as being translated in a different language, the overall routine dialogue was intended to be consistent. The four sets of questions asked were expected only to last less than 5 minutes per participant. As a result, ABCTL opens an opportunity to provide clinical testing without any other factors accompanying a typical medical facility visit. In other words, it alters social viewpoints from both the patient and provider and leads to a conclusion that potential medical mistrust or discriminatory biases were reduced.

Furthermore, cultural humility is a lifelong commitment that the medical provider must develop and improve throughout his or her time in this field. However, it does take away this level of training available for the volunteers. While the quick testing process limits any culturally aware procedures, it would still help integrate this in the training when serving underserved populations or communities. Nevertheless, ABCTL has been launched to contribute to the global health crises, but the training structure does limit the volunteers' chances to strengthen their cultural humility perspectives.

On the other hand, the community healthcare workers have been trained enough to grasp the concept of cultural humility and its long-term component to be able to apply it to their service. In fact, they already have close ties with the residents, and their presence was already a reassurance to many in the community when information about COVID-19 was still unclear. Self-awareness and openness are the most important here. Because these individuals are part of the community themselves or have worked with them before the pandemic began, it was not a trait that needed to be implemented at the start of their training.

Modification of Patient-Physician Relationship: Reducing Mistrust and Potential Biases

Consequently, what connects all of these factors is that modification of this patient- provider relationship was the best approach for ABCTL in times like this. Increasing tensions among the physicians themselves, especially Asian Americans, were at an all-time high. The ongoing medical mistrust among minorities, especially African Americans, had contributed to their vulnerability to getting the virus. Considering this disproportionate rate, there needed a system to provide high demand for testing but with little to zero resemblance to a typical medical visit. ABCTL's innovative testing allowed for both factors to happen. The training requirements and systematic approach to each participant closed the door for any potential connection. In other words, the routine, fast-paced, and straightforward instructions from booking appointments to leaving the testing site altered the concept of a typical patient-provider relationship. However, ABCTL was strong in their communication efforts as they continued to provide guidance when results of the tests arrived. Although the aspect of having a face to face or direct contact was not possible, the relationship between both parties is still present, but simply more efficient to accommodate the demands of mass testing.

Lastly, in times of high demand, pressure on the healthcare system, and the ongoing increase of COVID-19 cases as the year 2020 comes to an end, being perfect was not the purpose. Instead, the goal of the lab of mass testing was the priority at the moment. This system simultaneously implicitly reduced the reciprocal discriminatory biases and mistrust that affect both the provider and patient.

Future Forecast

It is not enough to only acknowledge the ABCTL contribution to the ASU student population. Most importantly, the ABCTL supported the various diverse communities in Arizona. The magnitude of the number of tests conducted has undoubtedly raised awareness of COVID-19 by providing this service open for the public and for free. Moving forward, ABCTL should continue making community partners and finding approaches to expand and increase its efficiency as an institution. Because ABCTL plans to continue making community partners, the institution must ensure that the program does everything in its power to provide its services in those communities in critical need to fulfill the concept of health equity. Regarding cultural humility, ABTCL should continue altering their approaches in culturally sensitive ways to appropriate measures according to their partners. However, to maintain the concept of modifying the patient-provider relationships, ABCTL must lean on community healthcare workers' work to continue addressing health concerns and follow-ups if needed.

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Section II: Analyzing Communication Strategies Used to Promote the ASU Biodesign institute's Saliva-based Covid-19 PCR Diagnostic Test

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Background

This Section discusses the communications strategies used to promote the adoption of the saliva-based COVID-19 diagnostic test developed by the ABCTL. It examines what constitutes successful adoption of health innovations as well as some of the factors that contributed to the success of the lab's efforts. The investigation reviews communication materials and strategies through the lens of Diffusion of Innovations by Everett Rogers. It identifies what messages were targeted at which social groups and where they were appropriate and effective.

The Section examines the communication strategies that were used to highlight the innovation and advantages of the saliva-based COVID-19 test versus the nasopharyngeal (NP) swab test that was most commonly used prior to the introduction of the saliva test.

Additionally, this Section discusses the effectiveness of these strategies in communicating the advantages and offers suggestions for improvement if necessary.

Analytical Framework and Findings

In order to provide answers to the research question, establishing terms through literature review is critical. The communication strategies employed by the BioDesign lab will be examined through the lens of Everett Rogers's theory on *Diffusion of Innovations*; his theory attempts to explain why technologies or innovations spread through specific populations and why others do not. There are four main elements of the diffusion of innovations theory, first "the innovation, the communication channels, time, and social system"(Rogers, 2003, pg.11). In the following literature review, these terms will be defined. Additionally, this research aims to establish the efficacy of the BioDesign lab's communication efforts and offer suggested improvements for future campaigns.

The first term in need of clarity is diffusion. Rogers defines diffusion as "the process in which an innovation is communicated through certain channels over time among the members of a social system"(Rogers 2003, pg.5). Unfortunately, this definition brings more questions than answers, albeit a technical pandora's box. It begs the question of what an innovation is, and subsequently, what is the specific innovation is being investigated in this paper.

Rogers defines innovations as a new idea, or object, or practice. He goes on to discuss that the actual novelty of the innovation is relatively unimportant as long as the item appears to be new or is perceived as new. That caveat, though rather interesting, is currently believed to be inconsequential to this analysis. The particular innovation being discussed in this Section is the polymerase chain reaction test to detect SARS- CoV-2 genetic material in saliva samples, developed at the ABCTL. This innovation would fit the new object or practice parameters for Roger's definition of innovation. The particulars to why this test was very innovative will be discussed later, but in short, the test was simpler and easier to administer, as well as safer for all involved.

The term that requires an operational definition is communication. Rogers describes communications as participants that create or share information to reach a mutual understanding (Rogers, 2003 pg. 5). This definition implies that communication is not a one- party system. In the methods, the parties will be

identified. Additionally, the understanding that is trying to be reached will be parsed out by examining the Biodesign lab's messaging.

Recalling the four elements of diffusion of innovations, the remaining two undefined terms are the communication channel and the social systems. A communication channel, as described by Rogers, can be broken down into three main categories, mass media, interpersonal, and interactive media. Mass media being what was familiar to most until recently, television, newspaper, radio. Interpersonal communication is when one person communicates with another person. Rogers infers interpersonal communication to be the most effective at increasing adoption. Lastly, interactive media, which we might call social media, in which individuals can interact with organizations (Rogers, 2003, pg.18)

The last major term to be clarified to frame the examination of the ABCTL's diffusion of innovations is the social system. A social system is described in Diffusion of Innovations as a group of connected people participating in group problem solving to accomplish a common goal(Rogers, 2003, pg.37). This definition could not fit our scenario more perfectly, being that the world was working together to survive the COVID-19 epidemic with the least number of casualties. The population this research is concerned with is much smaller than the people of the world, but it gives an excellent framework to progress forward.

Communications at the ABCTL

Research for this section was performed to answer a series of questions, as discussed below.

First, what communication strategies were used to highlight the innovation and advantages of the Saliva-based COVID-19 test developed at ASU versus the nasopharyngeal test that was most commonly used previously to the introduction of the saliva test?

To answer this question, it was necessary to define the terms and the lens I would be using to investigate this question. Now that the terms have been defined and the lens has been set. The next step is to answer the first part of the research question. In that, I will examine various communications and messages used by the Biodesign Lab. In these communications, I will examine the messaging to see if appropriate for the targeted demographic or social system.

Second, how would the Biodesign lab team communicate the differences between the saliva-based test from the NP swab test. I initially thought it would be in everyone's best interest if the public were pushed towards the simpler and safer saliva-based test in favor of the painful and hazardous NP swab test. Joshua LaBaer, executive director of the Biodesign Institute, gave an explanation of the differences between the two tests in an interview with ASU News, the saliva test sample can be collected by the customer, and the NP swab test must be collected by an additional trained person. The method of collection using the nose swab can trigger a sneeze or cough, which could spread respiratory droplets, thus making the collection of the NP swab test more hazardous than the saliva test. The administrator of the saliva test does not have to wear as much P.P.E., which eliminates sourcing of P.P.E. issues, and the chain of advantages could go on infinitum (ASU News, 2020).

Upon reading countless press releases and news articles as well as the Biodesign Labs social media pages, no communications were found that cast the nasopharyngeal test in a negative light. It was communicated that the saliva-based test was an improvement but never was put in a light that cast doubt on the NP swab test. I believe that the communications regarding nasopharyngeal tests were never negative in an attempt to not steer people from receiving any kind of COVID-19 diagnostic test. This lack of negative press would fit the objective laid out by Dr. LaBaer for frequent testing as never to steer anyone away from a test, regardless of the method (ASU News). This narrative of frequent testing was found only in the live interviews by Dr. LaBaer and did not appear in the print communications or in the interactive media messages.

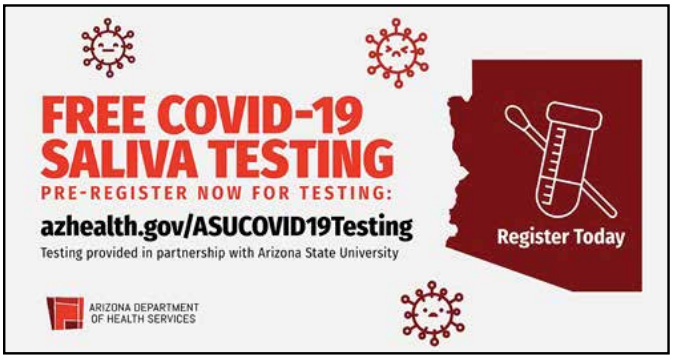
The fact that this message of frequent testing was left out of many communications is unfortunate because it is so important, as shown by academic sources. In an article by Francois Berthiaume in the March 2021 edition of Nano Life, he explains there is a direct correlation between testing frequency and decreased rates of COVID-19. He states that once-weekly testing lowers rates of infection 20%-40% from the baseline, and twice-weekly testing reduces infection rates by 95% (Berthiaume, 2021).

Additionally, a paper by Christensen et al., outlines that the presence of testing can cause citizens to live in a more cautious way, avoiding risky behaviors likely to cause a spread of COVID-19. It is unknown if there is a relationship between the frequency of testing and the level of caution, but it would be safe to say there is not a negative relationship. In light of those conclusions, it would appear that the most important messages were communicated through online news media interviews and articles. These channels of communications would fall more towards the mass media spectrum. Rogers defines the channels as mass media, interpersonal and interactive. Though with today's technology, people have the ability to leave comments and the like on online newspaper articles and re-uploaded YouTube news videos, I have chosen to treat them as closer to mass media than interactive media such as Twitter, Instagram, and other social media platforms.

Though it was worth noting that the message about frequent testing was left out of the interactive media communications, this may have not affected rates of adoption. In the May 2017 edition of Mass Communication & Society, an article was published titled "Seeking Out and Avoiding the News Media: Young Adults' Proposed Strategies for Obtaining Current Events Information" it was found that young adults perceived print news and network television as being the least helpful for obtaining information regarding current events. Consequently, for those 65 and above placed great trust and devoted more time to seeking out news from these channels. Whether intentional or not, this may have a positive effect, reaching the more vulnerable populations, 65 and above, with this more critical info. In the climate of the COVID- 19 pandemic, increasing adoption by diffusion of innovations is critical, so applying appropriate strategies to create understanding amongst social systems is important. As discussed in the December 1985 issue of Journal of Consumer Research in the article "The Elderly Consumer and Adoption of Technologies" the elderly consumer, as being defined as 65 and above, are the last to adopt new ideas, practices, or innovations. In the lens of the diffusion of innovations, this would put them into the late majority or laggard category. This means, according to Rogers, that much if not all uncertainty will need to be removed for people in the social systems and adoption strata to use the saliva-based test (Rogers, 2003 pg. 284). Intentional or not, the team at the ABCTL did an excellent job of allocating the correct communication resources towards this particular demographic. The extra time to explain the process and the ease of use in the promotional materials that were distributed via mass media were surely worth the extra effort to increase adoption amongst the late majority and laggard population, which primarily would consist of older to elderly peoples.

In stark contrast to the messages and communications distributed via mass media, the messages distributed by interactive media were much simpler.

Biodesign Twitter account sample. (Twitter, 2020)



This infographic is repeated many times on the ASU Biodesign social media platforms. It has now been pinned to the group's Twitter page. This means that this image will stay at the top of the page and will be the first image that is seen when someone navigates to the Biodesign Twitter page. The message consists of four main components, the cost, the product, the URL, and the call to action. The cost is free. The product is the Saliva test. The URL is how to register. The call-to-action states that people should register today. The cost is important for multiple reasons, Rogers would say that the cost is not so important to the Innovators and Early Adopters (Rogers, 2003, pg.282), but the cost is very important for other reasons. The specific population that is immediately being addressed is the Arizona State University community, most of which is made up of students. Students have often been understood to not have as much disposable income as other socioeconomic groups. For this reason, the inclusion of the test being no-cost is very important. Secondly, the message plainly states what is being promoted, the saliva- based COVID- 19 test. This may seem plain and not attractive enough as an advertisement, but for the innovator and early adopter, it is plenty.

These social systems will be familiar with the NP swab test, and the statement of a saliva test will signal to them that it is innovative. The innovator may take the test merely because it is cutting edge as the early adopter may take the test to gain the respect of their peers (Roger, 2003, pg.283). A side-note for the interested observer, in the graphic advertising the Saliva-based COVID-19 test, there is a piece of clip art with the saliva tube and a NP swab, not that most would notice, but spending enough time looking at the graphic I did notice. This infographic is a great choice as well for creating understanding amongst these social systems because, as shown by the authors of a 2017 article "Infographic Utility in Accelerating Better Health Communication," the authors specifically address why infographics are preferable for spreading information for public health campaigns. As the article describes, an infographic is ideal for communicating information in a public health campaign because it makes otherwise complex topics easy to digest. Most of the information that was conveyed in Dr. LaBaer's news interviews and other videos was conveyed in an infographic that can be seen and understood in seconds. After analyzing this infographic, I can say with confidence that it will appropriately convey its message of promoting registration for the innovative saliva COVID-19 diagnostic test to the targeted demographics of young people and otherwise innovators and early adopters.

Conclusion

The purpose of this research was to investigate what communication strategies were used to highlight the innovation and advantages of the Saliva-based COVID-19 test developed at ASU versus the nasopharyngeal test that was most commonly used previously to the introduction of the saliva test? I believe that I have performed that investigation and am ready to draw conclusions. Firstly, the two main communication channels used to convey the existence of and increase adoption of the saliva-based COVID-19 test were mass media and interactive media. The Lab used appropriate messaging styles in the mass media realm, such as news interviews and articles, to most effectively increase understanding amongst the targeted populations, the elderly, or other otherwise late majority and laggards. The lab team prioritized the messaging of simplicity and ease of use to reduce uncertainty for these populations. The lab also used appropriate messages and communication styles on their interactive media pages, such as Twitter and Instagram. In these communication channels, the Lab prioritized efficiency in communication to cater to the already innovation-biased innovators and early adopters.

Dr. LaBaer said in his interview with ASU News that he wanted testing to be an intervention as well as a screening tool. It is inferred by LaBaer's statement that more tests being done is a marker of success in reaching this goal. Looking at the COVID-19 diagnostic test reporting data from several sources, I can begin to draw some conclusions, or at a minimum, observe some potential relationships. The Arizona Department of health services reports that as of March 2021, 3,984,375 COVID-19 diagnostic tests have been administered(AZDHS, 2021). As of March 2021, The ASU Biodesign Institute reports processing 752,496 COVID-19 tests. Using this data, the Biodesign Institute has been responsible for about 19%

of the total number of COVID-19 tests in Arizona since the beginning of the COVID-19 pandemic. To add context to that statistic, the student body and faculty of ASU in Arizona is around 115,000(Wikipedia, 2021). The population of the state is Arizona is about 7 million. This means that ASU's student body and staff make up about 1.5% of the state of Arizona's population. This means that either everyone at ASU has been tested multiple times or ASU has tested many more people outside its walls than within them, or both of these things can be true. ASU could have tested its community many times over and still administer many tests to the Arizona community as a whole. The Biodesign Lab's COVID-19 testing initiative does not have an official mission statement, but I believe I can parse one from the overview webpage. The webpage states that the Lab sprang into action to protect our community. I believe if they were speaking about the ASU community, they have accomplished that goal and surpassed it. I see no need to make additional considerations for improvements. Job well done ASU Biodesign Institute.

In regard to future forecasting and adoption of the ABCTL model by other organizations some additional considerations should be taken into account. An analysis of the broader culture when considering which messaging should be used is important. The ABTCL was broadcasting to an individualistic culture in the U.S. but other cultures may be more collectivist and a more collectivist messaging may be more effective. An example of this would be Vietnam's superhero style messaging where citizens who followed COVID related guidelines were held up as heroes by the state media. This messaging proved to be profoundly effective in a collectivist culture like the one found in Vietnam (Three Rules for Coronavirus Communication). An additional success of the messaging used in Vietnam was the use of more viral style messaging to create memetic engagement. A viral tik-tok dance video was created to demonstrate the WHO recommendations for hand washing. I believe a similar approach would be very effective amongst a younger population as it would allow young people to spread the message to each other. This type of interpersonal communication has been by Rogers to be one of the most effective communication strategies. A suggestion for future replications of the ABCTL model would be to conduct focus groups covering multiple demographic groups. These focus groups could confirm that the messaging would be effective within the demographic groups as well address some concerns with overcoming the digital divide by using appropriate channels for various groups.

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Section III: Staying on Top of Evolving Best Practices for Testing and Organizational Communication

Author: Courtney Raymond

Background

The ABCTL is ASU's COVID-19 response laboratory. The ABCTL was created to provide Arizona with rapid, public testing. It was the first lab to offer public saliva testing for identification of COVID-19 in the western US (Overview, 2021). Saliva testing was chosen as the primary method of identification because it is "accurate, less invasive, less labor intensive and requires fewer medical personnel [than nasal swabbing]." The need for minimal labor and medical personnel were especially important for providing widely available testing to the public. The total number of tests performed by the ABCTL as of March 22, 2021 was 752,496 and the average turnaround time for an individual test was 16.99 hours (Critical Trends, 2021).

The COVID-19 pandemic caused every individual to change their way of life. For some people, it was a small change. However, for others, it was monumental. In the United States alone, more than 568,000 people have died as of March 2021 (US COVID Deaths).

The definition of COVID-19, according to Oxford Languages is "an acute respiratory illness in humans caused by a coronavirus, capable of producing severe symptoms and in some cases death, especially in older people and those with underlying health conditions. It was originally identified in China in 2019 and became pandemic in 2020."

SARS-CoV-2, more commonly known as COVID-19, is an RNA virus with three major factors that make it especially dangerous. It has high morbidity and mortality, reported to be ten times worse than the seasonal flu. The virus is primarily airborne transmitted, via droplets and aerosols. Peak infectivity was measured to occur when the infected individual is pre-symptomatic, and roughly 40% of infected individuals will never show symptoms. (ABCTL.Basics, 2020)

Intra-Organizational Communication

Intra-organizational communication is crucial for the success of a large project such as the ABCTL. However, it is often the source of significant error in healthcare related settings (Pirnejad et al., 2008) and this is only made worse by the communication challenges caused by the need to limit on site personnel due to COVID-19. There was a greater importance for asynchronous communication such as email and direct messaging. There was also the new terrain of virtual zoom meetings and conferences. In order for the ABCTL to succeed given the unique circumstances for a research lab, it was necessary to put measures into place both before the project began and as it grew that supported successful interpersonal communication. Some of these important factors were: holding regular meetings, having predefined clear team roles, and fostering interpersonal relationships.

Best Practices and Their Communication

The definition of best practices research is taken from Mold and Gregory (2003), "refers to a systematic process used to identify, describe, combine, and disseminate effective and efficient clinical and/or management strategies developed and refined by practicing clinicians". The ABCTL had a wide variety of experienced experts working together, following this process, to stay on top of the ever-evolving best practices for COVID-19 diagnosis.

Insight into the evolution of ABCTL best practices for testing and intra-organizational communication was done through multiple methods. The first was attending the large group meetings for the students and faculty of this multidisciplinary thesis pro ect . Additionally, a review of media published by the ABCTL media team and greater ASU media was done. An interview of Joshua LaBear was reviewed, as well as the "Pressers" that ASU held weekly throughout the duration of the ABCTL development.

Each review covered an important aspect of the lab's communication on testing protocols. The literature review documents the types and methods of testing offered by the ABCTL. The interview review documents the organization of the lab and high-level faculty/staff. The presser review documents consistent updates on internal progress as well as the protocol for the pressers themselves.

Testing Methodologies

PCR (RT-PCR, qPCR or molecular) Test

This is the type of COVID-19 testing that has been offered at the ABCTL throughout the pandemic, beginning in March 2020. PCR testing is a highly-accurate type of molecular test that was deployed by the ABCTL for the diagnosis of SARS CoV-2 viral infection.. A PCR test can detect genetic material from the coronavirus from a nasal swab, nasopharyngeal swab or saliva sample.from an infected person. The testing performed at the ABCTL at first utilized naso-pharygeal swabs but evolved to the use of mire easily acquired saliva samples. Results from tests of this kind at ASU can be returned to patients within 48 hours.

Because of the virus's long incubation time and that it takes several days for enough of the virus to accumulate in the body, some of the patients tested a short time from the point of exposure have a negative result despite being infected. For this reason, the ABCTL recommended that patients without symptoms wait up to five days after exposure to get tested. On the other hand, if a patient tests positive, it can be assumed that this result is reflective of the patient's infection status at the time of testing. This is because PCR testing is not likely to return a false positive result. (Types of COVID-19 Tests, 2021).

Antibody (Serology) Test

This type of test is not yet offered at the ABCTL. However, there is planning underway for these to be offered in the future. Antibody testing can tell a patient if they previously had COVID-19 but cannot be used as a diagnostic test. According to the page Types of COVID-19 Tests (2021), "This blood test detects antibodies to the coronavirus. Antibodies are proteins your body produces to help fight off future infections." Results from antibody serology testing are typically returned to patients in one to three days.

Antibodies for COVID-19 can take between one to three weeks to develop and become detectable in the blood. Currently, it is unknown how the presence of antibodies affects the likelihood of infection.

It is possible for a patient to have a false negative result if they take the test too soon after recovering from COVID-19. It is also important to note that it is currently unknown how long COVID-19 antibodies last in the body, so a patient may return a negative result after previously testing positive for COVID-19 antibodies. It is also possible for current methods of COVID-19 antibody testing to cross-react with other coronavirus antibodies and produce a false positive. (Types of COVID-19 Tests, 2021)

Methods for Test Specimen Collection

There are currently three methods for specimen collection at the ABCTL. For all methods, a patient begins by visiting their ASU patient portal online. From their patient portal, patients who select that they wish to receive a saliva sample COVID-19 test receive the following instructions (Patient Health Portal, 2021):

Pre-appointment requirements

Hydration will help you accumulate saliva. Hydrate up to 30 minutes before your start.

1. Rinse your mouth with plain water for 20-30 seconds and spit it out 30 minutes before your appointment.
2. After mouth rinsing, do not eat, drink - even water - smoke, vape or chew gum for 30 minutes before your appointment.

On-site appointment process

1. Please arrive at your scheduled appointment time.
2. Wear a protective face cover. Either a cloth or surgical mask is acceptable.
3. Maintain social distancing if you are in a space with others.
4. Have a water bottle handy for post-appointment hydration.

Patients who are participating in the Devils' Drop Off home test service receive the following, alternate instructions at the point of selecting that they wish to receive a test (Patient Health Portal, 2021):

No appointment required. Simply pick up a kit from an on-campus location and collect and drop off your saliva sample. Prior to dropping off your saliva sample, the barcodes on your sample tube must be registered below.

All in person patients must select an ASU location for their test. Testing locations are available depending on whether a patient has active COVID-19 symptoms or not. Patients can either select a drive through option or a walk-in option and choose a date for their test. For patients who select the drive through option, the process is as follows:

1. Arrive at the location selected for check in (remain in car for the entire duration)
2. Receive the tube and straw for saliva collection
3. Patients are then directed to a parking spot for saliva collection
4. Salivate into the collection tube via the provided straw, then cap the tube
5. Provide date of birth and name to receive identifying marker for tube
6. Scan unique barcode located in the patient health portal
7. Hand over the sample to ASU employee

For patients who select the walk-in option, the process is nearly identical. The exception is that instead of collecting their saliva sample in their car, patients are directed to a room with a screen playing a video of food that helps increase salivation. Once the sample has been collected, it is then transported to the ABCTL lab in accordance with health regulations and tested for COVID-19 RNA. All of the employees at the testing locations wear appropriate personal protective equipment, including masks.

The Devils' Drop Off program is a home collection for saliva specimens. These tests are performed without supervision, at whatever time is convenient to the patient. This subjects them to a higher user error than that for the in-person testing. The process is as follows:

1. Obtain a prescription for an at home test kit
2. Activate the unique sample identifier
3. Use the tube and straw for saliva collection
4. Salivate into the collection tube via the provided straw, then cap the tube
5. Drop the sample off in a collection bin at designated campus locations

The samples are transported to the ABCTL lab and the same saliva PCR test is performed at the lab as for in-person patients.

The Evolution of Organizational Communication

An interview of Dr. Joshua LaBaer was conducted by the Business Group, along with Dr. Carolyn Compton. The information provided in the interview is supported by additional information to provide appropriate context. to the evolution of communications within the ABCTL. Dr. LaBaer explained the timeline of the ABCTL project to be, on a broad scale, as follows (Dr. LaBaer Interview, 2020):

Mid-Spring Semester

A small group of people were called together in Dr. LaBaer to meet 7 days a week to discuss the possibility of transforming the existing Biodesign lab into the ABCTL that we now have. A specific agenda was created for these meetings, which contained the most important topics. The agenda would continue to be used for future leadership meetings.

Late-Spring/Early-Summer Semester

Arizona state allocated funds for general population testing. The core team was making weekly calls to address locating and sourcing supplies. The necessary supplies that had been difficult to obtain were being made at the ABCTL lab itself.

Late-Summer/Fall Semester onwards

The lab was operational with the needed testing supplies, but development towards further efficiency and testing volume continued. The core team members appointed by Dr. LaBaer continue meeting on a weekly basis regarding the status and progress of the lab.

There are three people at the highest level of leadership for the ABCTL, Dr. Carolyn Compton, Dr. Joshua LaBaer, and Dr. Vel Murugan. Dr. LaBaer introduces himself, as well as mentions the other leaders at the lab and their importance in his interview. Each plays a vital role in ensuring that the lab runs smoothly and that the smaller teams under their supervision complete the duties assigned to them.

Dr. Compton is the Medical Director for the lab. She is a Professor in the School of Life Sciences at ASU and a Professor of laboratory medicine and pathology at Mayo Clinic. Dr. Compton specializes in pathology, and is board certified in both anatomic pathology and clinical pathology. She is the Chief Medical Officer of the National Biomarker Development Alliance (Team, 2021).

Dr. LaBaer is the Laboratory Director for the lab. He is a leading researcher in cancer and personalized medicine, as well as the Executive Director for the Biodesign Institute at ASU (appointed in 2017). It was Dr. LaBaer's academic research lab that was transformed into the ABCTL viral testing facility that it currently is (Team, 2021).

Dr. Murugan is the Program and Technical Director for the lab. He is a leading molecular biologist, whose expertise in diagnostic test development was critical to the development of an RNA biomarker-based high-throughput ARad radiation biodosimetry test. Dr. Murugan is an Associate Research Professor at the Biodesign Virginia G. Piper Center for Personalized Diagnostics (Team, 2021).

Presser Review

The purpose of the pressers, weekly news conferences led by Dr. LaBaer, was to give reporters and other attendees the chance to ask questions of the ABCTL and receive the most up- to-date answers on a weekly basis. The pressers also served as a way to mark and review consistent updates on internal progress. These were held via Zoom meeting, as meeting in person was not advisable during the pandemic.

Each presser began with Dr. LaBaer providing updates on general state trends, laboratory news, and policy effects on cases. He would then answer questions from those in attendance. Attendees were asked to introduce themselves prior to asking their question. When the allotted time was up, or there were no further questions, the presser would end. Each presser was recorded by an ASU staff member (ABCTL Pressers, nd.).

These pressers are an excellent example of the weekly meetings that were held across the different ABCTL teams and provided a structure to ensure that the public had access to accurate information from the lab. It also provided the lab with the opportunity to clarify any current issues related to the updated testing processes and trends.

ABCTL Communication

Intra-organizational communication was critical throughout the process of creating and running the ABCTL. This could be seen in the process for collecting saliva samples, which requires an orchestrated effort from those collecting samples, conducting tests, and returning results to the patients. From the initial idea and discussions of what the lab could become, to the ABCTL as it is at the time of this writing, the group closest to Dr. LaBaer was meeting daily to weekly. As the project progressed, further groups were formed, and more collaboration was required. Additional methods of communication that are not immediately obvious include regular emails, text messages, and cell phone calls. Due to the unique nature of the pandemic, it was necessary for the groups to communicate in the very new terrain of Zoom.

The ABCTL, and broader ASU, did an excellent job of publishing regular updates to their website pages related to the lab and COVID-19. As new types of testing evolved, the lab put out information to the ASU community and the public that kept them updated. The ABCTL stayed on top of the evolving standards for COVID-19 testing and ensured accurate results over several semesters time.

The highest level of leadership, Dr. Carolyn Compton, Dr. Joshua LaBaer, and Dr. Vel Murugan, made the entire project possible by maintaining their areas of expertise and the teams that they were in charge of. They saw the necessity of assigning further levels of leadership and responsibility along the way to ensure a steady intra-organizational flow of information.

By giving interviews and pressers, the members of the ABCTL team ensured that the correct information was being released to the public. These regular meetings gave the public the ability to trust the ABCTL to provide accurate and up-to-date information, as well as to answer the questions of those who did not have the opportunity to work directly with COVID-19 related projects.

Conclusion

This section documents the intra-organizational communication channels and the ABCTL's efforts to stay on top of the ever-evolving best practices for testing. A review from several different sources, both ABCTL specific and from broader ASU, provided insight into the types and methods of testing, timeline and organization of the lab, important leadership personnel, and how the ABCTL managed the public and external communication from the internal perspective. It is hoped that the information contained in this thesis and those of other group members will be able to provide a blueprint for future organizations to streamline the process that ASU pioneered when the BioDesign institute transformed their academic research lab into a viral testing lab for COVID-19.

The ABCTL will continue evolving as the pandemic continues. New methods of testing will be created and implemented, such as antibody serology testing. The United States is currently in the process of vaccination against the COVID-19 virus, and it is entirely possible that the ABCTL will become a site for vaccination. If that were to occur, then additional protocols and teams would need to be put into place.

Future recommendations for any organization using the ABCTL theses projects as a blueprint for the transformation of their research lab to a viral testing facility includes review of additional literature created after the publication of these theses, especially literature that may center around updated policies and vaccination protocols.

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Chapter 3

The Making of a COVID Lab

A Focus on Information Technology

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Introduction to Chapter 3

Information technology (IT) was identified as one of the six essential facets of the Arizona Biodesign Clinical Testing Laboratory (ABCTL.) IT enabled the development, operation, and regulatory compliance of the ABCTL and continues to be a fundamental necessity for its existence. One Section of this Chapter covers the background of clinical laboratory automation and details the automated laboratory workflow to perform ABCTL's COVID-19 diagnostic testing. Another discusses the usability and efficiency of key information technology systems of the ABCTL. Other Sections explains the role of quality control and data management within ABCTL's use of information technology ad the importance of data modeling and best practices when responding to future public health emergencies. The Chapter focuses on how ABCTL's IT capabilities were modified to meet virus testing demands for the public, to specifically educate other universities and institutions for future public health crises. Eventually, our findings will be included in ABCTL's documentary produced by ASU's Cronkite School of Journalism and in a lab-wide report.

Each member of the IT Group was assigned a topic in the IT space as it applies to medical diagnostic laboratories: Clinical laboratory automation and the ABCTL's associated workflow; System usability and efficiency; Data workflow, integrity, and quality control; Data modeling, visualizations, top-to-bottom of statistics between ASU and partners.

The flow of the group topics is generally as follows: By automating a system's mechanisms and infrastructure with automated lab equipment, the system becomes more usable. If a system is made more accurate and efficient, it can achieve higher throughput. Eventually, that system becomes a more usable system, especially if it has high adaptability and integrity. So, once a system is automated where necessary, it becomes more usable to the institution or organization that it serves. By understanding the workflows and infrastructure of the data, institutions can manipulate their data into making new decisions.

The IT Group began their research into four focus areas by examining high-level COVID-related topics in the IT space. For this team's focus area, group interviews with Epidemiologists, clinical faculty members, and doctoral students who developed ABCTL's data modeling and visualization systems were essential. Based on findings within those resources, this defense will make recommendations on the approach ASU took when building infrastructure in response to COVID-19 and how future institutions can add on top of the team's findings within ABCTL for future emergency health responses.

Keywords: COVID-19, Information Technology, Arizona, Automation, Usability, User E perience, Data Workflow, Data Modeling

List of Interview Participants

- Dr. Carolyn Compton, MD, PhD
  Sean Dudley, BS, PhD(c) Ian Shoemaker
  Alma Douglas, BS
- Morgan Nelson, MS
  Kevin Tinnin, MS
- Dr. Timothy Lant, MS, PhD
  Tamara Deuser, BA, MBA
- Michael Fiacco
  Valerie Harris, PhD(c)
- Kajol Majhail, BS
  Amit Sharma

Section I: Data and Decisions

Author: Mani Kandan

Background

Only a few of the several interviews the IT Group conducted during the pro ect was relevant to the area of data and decisions. Specifically, three interviewees—Sean Dudley, Tamara Deuser, and Dr. Timothy Lant—were the most relevant.

The relationship between data and decisions is that of a missing link – how do institutions go from simply having data to making (new/er) decisions? This defense argues that is done by utilizing data modeling and data visualizations. Within data modeling, there were several focus areas, and those are discussed in more in depth within the Findings and Recommendations sections below.

Analytical Framework and Findings

To be clear, this section will not be chronicling a historical review of what happened throughout ABCTL's crusade against COVID-19. This section is structured as advice for future groups, with specific IT considerations towards data modeling and decision-making. It will tell the story of ABCTL through this IT perspective through ten pieces of advice: five findings and five recommendations. The Findings section will focus on five areas: early activation, secure storage, the structure of data models, model to media transparency, and prior responses. The Recommendations section will focus on five areas: multidisciplinary needs, workload management, frequent findings sharing, apolitical stance, and future planning.

5 Findings

Finding #1: Early Activation

As cases were being discovered in late 2019 in the Hubei province of China, findings were being tracked by researchers around the world. By late January 2020, Dr. Michael Crow (Arizona State University's President) activated the initial COVID-19 response (S. Dudley, personal communication, 2020). Early activation of response efforts was vital to begin a process that yielded a better, collective understanding of the problem. The sooner a response is formed, the sooner planning can begin. Especially in the case of infectious and contagious diseases, local and international media outlets must be heavily monitored for developments in disease spread.

Specifically, Dr. Lant mentioned how the vast majority of medical researchers and epidemiologists monitor the site medRxiv.org for pre-published research (Lant, 2021). This website is predominantly used for sharing results of medical studies before the research has been peer-reviewed. Afterward, the real process begins, and the theme of "the multidisciplinarian" becomes more prevalent.

It is important to understand that public health crises are rarely, if ever, handled by medical professionals and researchers alone. As the world has experienced globalization and technologization, further understanding and appreciation have grown around multidisciplinary approaches. Hence, the effort to bring different responses together was pivotal: AZ state and health department responses, ASU's response, and the statewide testing program. ASU's development of the first testing program had three components: understand the range of requirements, begin contact tracing of early cases, and build epidemiology infrastructure. Hence, the effort of bringing together individuals of different disciplines is not only pivotal, but also innovative.

Finding #2: Secure Storage

The I.T. infrastructure that would be built and used throughout the remainder of ABCTL's operation would be predicated on ASU's already existing HIPAA-compliant secure storage (Lant, 2021). As a research university with a longstanding relationship with medical research labs and Mayo Clinic, this would be a stroke of good luck. Data would be posted every day through Point and Click systems. The data from this location would eventually become public after processing and serve as the most fundamental aspect of tracking COVID-19 through ASU's campuses and Arizona's general population. Other university and institutional compute and storage centers should be used for identification and personal information of faculty, employees, and students. ASU used the University Technology Office's (UTO) for more confidential information.

Finding #3: Structure of the Data Models

The data models built by the epidemiologists and mathematicians at ASU began by following the structure of a Dynamic Systems Model (DSM) (Lant, 2021). This kind of model is used to "describe and predict interactions over time between multiple components of a phenomenon" (Irving & Zheng, 2017). At a minimum, the model must be able to compute the Susceptible, Infectious, or Recovered populations. This kind of model is known as a SIR model. The SIR model is used for tracking disease spread (Moore & Smith, n.d.), and variations on the three letters can identify variant forms of Epidemiological compartmental models. In Figure 1 below, an example DSM/SIR(D) model is shown (Ibarra-Vega, 2020) where multiple factors can filter into determining the sizes of the susceptible, infected, recovered, and dead (D) populations. Those factors can also be specified through auxiliary and state variables like hospital capacity, lockdown length, and number of lockdowns. A SIRD model, like Figure 1, can output piecewise functions in Figure 2 to project the size of the infected population through the severity of a lockdown or the number of lockdowns (Ibarra-Vega, 2020).

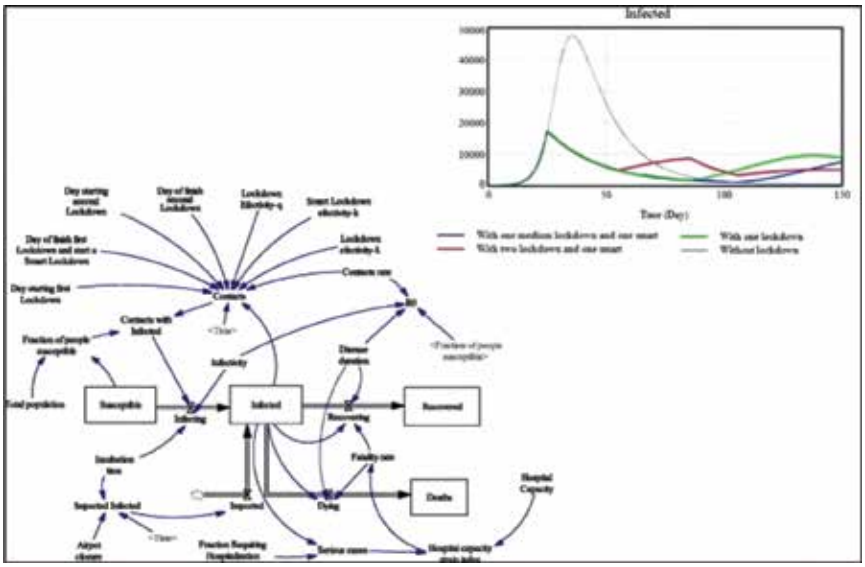


Figure 1 (Bottom Left) and 2 (Top Right). Ibarra-Vega, D. (2020). Example of COVID-19 SIRD model. From NCBI US National Library of Medicine National Institutes of Health. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7175877/. Copyright 2020 by Elsevier B.V.

The model that ASU built was a SEIRD model (and shared on medRxiv), but it also included a transmission model for measuring the speed of transmission based on contacts and their behaviors to model the size of the Exposed population (E) (Gel et al., 2020, p. 3). Colloquially, this was denoted as Ro (initial/basic reproduction number) and Rt (Rate of current effective reproduction), and one of the most tracked measures of how contagious COVID-19 was in different areas of the world (Simoneaux & Shafer,

2020). Models are also needed to track time relationships, indicators and signals for sick or health groups, but most importantly, what-if analyses.

In the past, data modeling was used to provide the early steps to finding an answer to the problem. However, as medical research and epidemiology saw massive technologization, data modeling became a tool to answer problems rather than only functioning as a preliminary measure. ASU's data modeling during COVID-19 focused on answering questions like, "Do we need more external hospital staff?" and "Do we have more external refrigerated capacities for corpses if mortuaries are running low on their internal capacities?".

Finding #4: Model to Media Transparency

Data models must be accompanied by transparency; they alone do not keep the general public at ease-- notwithstanding governments and institutions who prefer secrecy during public health crises (Lant, 2021). Several interviewees consistently mentioned throughout the I.T. team's research process that transparency was an early priority, especially given the nature of COVID-19's early history while in Wuhan. Prior to COVID-19, there was very little existing infrastructure and relationships within Arizona's media circle that supported the dissemination of scientific information and research; however, through the relationships built between ASU, ABCTL, Dr. LaBaer, and Arizona media, efforts like daily reporting and weekly model updates became easier. Several measures were taken on the communications and public relations side of ABCTL. Weekly meetings were conducted through a centralized person; for ABCTL, this was Dr. Joshua LaBaer. During the formative stages of the pandemic, there will be a necessity to present a united front on behalf of your organization's pandemic response faculty. It is important to align with the press on initiatives like the importance of frequent and rapid testing for at-risk populations/demographics.

Finding #5: Prior Responses

Although not nearly at the scale of the COVID-19 pandemic, the H1N1 pandemic in 2009 and the 2014 Ebola epidemic began to form the initial building blocks for ASU's response to COVID-19. However, it is important to understand the role of data modeling in these earlier health crises to learn how to develop an institution's capabilities for new public health emergencies. As Dr. Lant had mentioned in the early part of the team's interview with him, prior to COVID-19, data modeling was used to plan responses-- not to predict or solve them (Lant, 2021). However, there was more communication with the federal government during these efforts, almost making the efforts taken in 2009 and 2014 seem like overkill in 2020/1. With regard to the Ebola epidemic, it was the later health emergency with only two cases contracted in America and four total cases first diagnosed in America (CDC, 2017). Although it was touted as a threat to American public health, it was severely overrated. Models were created, and projections were released to media outlets. That type of response laid the foundation for the quick work made early on when modeling COVID-19.

5 Recommendations

Recommendation #1: "The Multidisciplinarian"

Earlier, it was discussed that a reoccurring theme would be "the multidisciplinarian" because of the vitality the collaboration between different disciplines within ABCTL would be to the success of ASU's COVID-19 response. The same degree to which mathematicians, medical researchers, clinicians, laboratory ethicists, lawyers, early-stage business professionals, data scientists, computer scientists, and public relations had to intertwine within ABCTL to make it successful, the same had to occur within the Barrett Honors thesis group documenting the transformation of a lab within ASU's Biodesign Center for Personalized Diagnostics into ABCTL.

Business:	**Communications:**	**Management and Training:**
Costing Financing: reimbursement/billing Purchasing: supply chains Business plan: sustainability; scalability Positions and personnel Contract with customer organizations Direct-to-consumer models	Internal/among groups External/website/customers Patients Public/website Contact tracing Apps for contact tracing	Specimen collection logistics Transport Specimen processing Stand operating procedures manuals Non-conforming events: CAPA plans Workflows and efficiencies Personnel proficiency testing
Information Technology: Patient registration Analytical data capture/analysis/ storage HIPAA compliant systems Bar coding and maintenance identity Inventory control Return of results WiFi issues to assure results return	**Law**: 21 CFR: CLIA CMS) FDA IVD regulation EUA HIPAA NPI registration (CMS) Reporting to state	**Analysis: Science, Engineering, Technology** Emergency Use Authorization qPCR Robotics Test validation/controls Pooled testing Test interpretation: pos/ neg/"invalid" Safety

Figure 3. Compton, C. & Christianson, S. (2020). Delegation of ABCTL areas to Barrett students. From Personal Correspondence. Retrieved from ASU email account. The Barrett thesis group studying ABCTL was split into six different teams: Business, Communications, Management and Training, Information Technology, Law, and (Lab Team).

Analysis: Science, Engineering, Technology (see Figure 3). Although having multiple perspectives and diversity in thought and execution are benefits themselves, the biggest one must be better workload management.

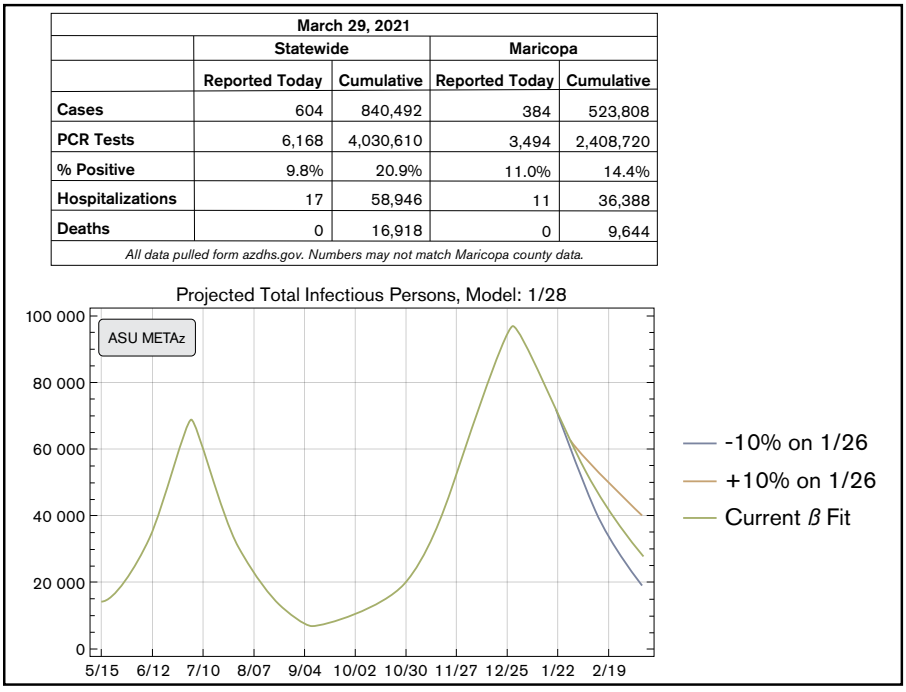
Recommendation #2: Workload Management

One of the most common areas of improvement given by several of the faculty members was workload management (Deuser & Dudley, 2021). Several factors resulted in overworking and inadequate overload management, such as the high rate of infection and transmission, very high demand for development of testing centers, and a relatively small ratio of the size of the ABCTL team to the size of the population served. Recommendations received in the area of workload suggested that the best solution when working within an institution or academic setting is to expand the search for more help. Oftentimes, just the ability to depend on additional volunteers or faculty can alleviate bottlenecks within the group when initially responding to a public health emergency. Deuser (2021) even recommends that more technical groups should limit their focus to five tasks at a time and filter by priority. Since technical teams tend to be overloaded with asks from several different groups of stakeholders, being able to prioritize and filter down to five focusable tasks can decrease the amount of stress experienced from being overwhelmed.

Ideally, workload management should be occurring at all levels of a pandemic response, even at the data modeling perspective in a different sense. As previously mentioned by multiple interviewees, modeling can be used as a means of workload management when developing metrics to predict how long an epidemic or pandemic will last. This attributes itself to the phrase that when responding to a pandemic, institutions are running a marathon—not a sprint.

Recommendation #3: Share findings consistently and frequently

Common critiques given by those who are outside of involved organizations, when responding to emergencies of most kinds, oftentimes is that there is not enough communication with members of the public who are outside of the system. In recent years, anti-establishment and anti-system sentiments have become more prevalent. Regardless of the origin of these sentiments, they must be accounted for. It is understandable, after all, that conspiracy cultivates within secrecy. If sentiments of this nature go unchecked, the veracity and strength of public institutions can be easily diminished. It becomes imperative to non-invasively collect data from those who are the targets of whatever emergency is present. For COVID-19, ASU decided to embed a daily health survey within the university's informational mobile app. The answers to this survey helped alert officials involved in contact tracing and identify at-risk students and faculty. Initially, this may cause frustration for the recipients; however, it can begin to develop an understanding, or assurance, that the public is now "involved" with the solution and/or tracking of a problem. Findings must also be shared with external stakeholders and local governments (municipal and state). With the case of data models and epidemiological data, situation and modeling updates were separately developed and disseminated by Dr. Lant's team on a monthly to bimonthly basis (see Figure 4 for March 29, 2020 COVID update, and Figure 5 for January 28, 2020 Modeling update).



March 29, 2021				
	Statewide		Maricopa	
	Reported Today	Cumulative	Reported Today	Cumulative
Cases	604	840,492	384	523,808
PCR Tests	6,168	4,030,610	3,494	2,408,720
% Positive	9.8%	20.9%	11.0%	14.4%
Hospitalizations	17	58,946	11	36,388
Deaths	0	16,918	0	9,644

All data pulled form azdhs.gov. Numbers may not match Maricopa county data.

Figure 4 (Top). Lant et al. (2020). Excerpted Chart from Bi-Monthly modeling report/update. From Arizona State University. Retrieved from https://eoss.asu.edu/sites/default/files/2021.03.29-COVIDUpdate.pdf. Copyright 2020 by Arizona Board of Regents. Figure 5 (Bottom). Gel et al. (2020). Excerpted Chart from Bi-Monthly modeling report/update. From Arizona State University. Retrieved from https://ewscripps.brightspotcdn.com/b1/fb/2011cdf24d2a9b401cbc342ba378/2021.01.28.model-adhs-final.pdf. Copyright 2020 by Arizona Board of Regents.

At these levels of government, relationships must be developed so that government officials and health department officials can understand the importance of the data modeling from institutions responding to health crises. For example, Dr. Lant discussed the process of reporting that occurred between ASU and the Arizona Department of Health Services (DHS) and noted that daily meetings were held between the two organizations (Lant, 2021). However, disruptions are likely to occur for political reasons.

Recommendation #4: Remain Apolitical

One of the largest disruptions to Arizona's response to COVID-19 was Governor Ducey's decision to cut off and retire the ASU/ABCTL team that was reporting and meeting daily with the Arizona DHS

on May 4, 2020 (Roberts, May 6, 2020). After working realistically for only two months, the governor's office's move towards ASU's epidemiologists had been made as a political gesture immediately preceding President's Trump May 5 visit to Arizona. Despite this setback, the media was able to rally behind the relationship formed between Dr. LaBaer, ABCTL, and Arizona media outlets (see section II (B) (4)). After experiencing this outcry, Governor Ducey reinstated the scientists he had "fired". Just three days after the May 4th press conference, Governor Ducey publicly reinstated his partnership with 23 scientists from ASU and the University of Arizona (Roberts, May 8, 2020). Expect setbacks from governments and parent or governing institutions but remain open to change. Oftentimes, disagreements will be resolved quickly if enough public and media outrage is voiced. In a similar vein, data models that are shared during public health emergencies must remain apolitical: they cannot be politicized or biased by excluding or exaggerating data points.

Conclusion and Future Forecast Recommendation #5: Plan for the Future

Tamara Deuser was one of the most influential people with regard to how ABCTL was led. From the get- go, Deuser understood that she and the rest of ABCTL would have to be thinking 12-18 months ahead (Deuser, 2021). As it would turn out, this would be the relative length of the COVID-19 pandemic before mass vaccination efforts. In order to reach the point of figuring out how to plan almost two years in advance, institutions will have to be "flying the plane as [they] are building it". The best way to ensure a new institution is future-proofing itself against future emergencies and disasters is by always asking, "how can [the organization] be of more assistance?" That question led ABCTL's operation in the Tempe/ Phoenix area of Arizona to be broadened and developed into a statewide operation. In the early months, ABCTL was focused on monitoring COVID-19 cases and testing within Maricopa County—the largest county by urban population in Arizona. However, rural counties and less populous areas were being underserved. As a result of the relationship forged between ASU/ABCTL and Arizona DHS, ABCTL began running operations in rural areas and other counties. Especially for institutions and universities that have multiple locations and campuses within their state, this can be very implementable. Broadening the scope of impact of the organization can provide much more utility during a public health crisis when resources are already stressed thin.

Dr. Timothy Lant emphatically states that policy goals need to change. After experiencing the brunt of being told that the pandemic was over when the data was showing the complete opposite, Dr. Lant's perspective is a necessity to share (Lant, 2021). For the next public health crisis, organizations and governments need to mobilize quicker responses, establish testing sites quicker, and develop contact tracing through social networks. All of this needs to occur around the country, but especially in highly mobile and congested populations like cities and colleges.

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Section II: Data Workflow, Integrity and Quality Control

Author: Garrett Knox

Background on Federal Regulations

As a portion of the I.T report, this chapter focuses on the data workflow of Covid-19 data involved in ABCTL operations. This includes a focus on ensuring quality of data throughout the data workflow from test collection to lab processing and patient result delivery. Data in the workflow must be secure, traceable, and in compliance with patient privacy regulations.

HIPAA Compliance

To illustrate the ways that the ABCTL has maintained the previously mentioned federal guidelines, it is important to understand what said guidelines are.

The first legal requirement of note is the ABCTL must be compliant with the Health Insurance Portability and Accountability Act (HIPAA). The ABCTL is designated as a HIPAA complaint entity because it is a research institution that is also electronically transmitting health information. The privacy rule of HIPAA means that the ABCTL must protect all "individually identifiable health information" (Health and Human Services, (HHS.gov)). This includes any demographic data that relates to an individual's health conditions, care, treatments, and payments as well as any individual identifiers such as name, address, birth date, social security number etc. To overcome this, de-identified health information data must be used.

CLIA Certification

The ABCTL was also required to be Clinical Laboratory Improvement Amendments (CLIA) certified. CLIA regulates laboratory testing and requires clinical laboratories to be certified by the Center for Medicare and Medicaid Services (CMS). There are multiple variations of CLIA certificates based on the kind of tests conducted, however laboratories must be CLIA certified before receiving any human samples for testing, which was a requirement before the ABCTL could implement Covid-19 testing early in the pandemic.

CDC Controls

In addition to abiding by HIPAA and CLIA, the ABCTL must also consider the extensive list of information required by the Center of Disease Control (CDC) and state health departments regarding Covid-19 testing. According to federal law, the ABCTL is required to securely deliver data to the CDC that includes the following (CDC (CDC.gov)):

1. Test ordered – use harmonized LOINC codes provided by CDC Device Identifier
2. Test result – use appropriate LOINC and SNOMED codes, as defined by the Laboratory.
3. In Vitro Diagnostics (LIVD) Test Code Mapping for SARS-CoV-2 Tests provided by CDC.
4. Test Result date (date format)
5. Accession #/Specimen ID
6. Patient age
7. Patient race
8. Patient ethnicity
9. Patient sex
10. Patient residence zip code
11. Patient residence county

12. Ordering provider name and NPI (as applicable)
13. Ordering provider zip
14. Performing facility name and/or CLIA number, if known
15. Performing facility zip code
16. Specimen Source - use appropriate LOINC, SNOMED-CT, or SPM4 codes, or equivalently detailed alternative codes
17. Date test ordered (date format)
18. Date specimen collected (date format)

Additionally, the ABCTL is required to securely deliver the following information to state authorities (8):

1. Patient name (Last name, First name, Middle Initial)
2. Patient street address
3. Patient phone number with area code
4. Patient date of birth
5. Ordering provider address
6. Ordering provider phone number

The CDC also requires that all data transmission should occur electronically using Health Level 7 electronic laboratory reporting implementation guides when possible, as well as that clinical and point of care testing facilities using electronic health records use electronic case reporting (eCR) standards to report laboratory testing data (CDC.gov). While this regulatory summation is by no means a comprehensive overview, it provides clear understanding of the complexity of regulatory and privacy requirements placed on the testing data that the ABCTL handles daily and the challenge and importance of keeping said data unidentifiable in connection to the patient.

Analytical Framework and Findings on Important Systems for Data Management within the ABCTL

LIMS System

The ABCTL utilizes a Laboratory Information Management System (LIMS), which allows one to manage samples and associated data. Using LIMS allows for the automation of workflows, integration of instruments, and the management of samples and associated information. This helps improve quality control and data validity by producing reliable results more quickly and tracking data from different sequencing runs over time. The functionality of a LIMS can be divided into five processing phases in the laboratory: (1) Reception and logging of sample and associated data, (2) scheduling, assignment, and tracking of the sample, (3) quality control and processing linked to the sample and inventory and equipment that is used, (4) storage of data, (5) verification, approval, and accumulation of sample data for reporting or analysis. In the context of the ABCTL, this process can be described as: (1) Covid testing collection and instrument integration, (2) determination of raw results, (3) preprocessing stage, (4) post processing stage done by the lab director to verify sample test results, (5) entry into the Point & Click system with automatic transfers of results.

Point and Click

The Point and Click (PNC) system is a system that was reconfigured to fit the needs of ABCTL in facilitating their Covid-19 testing response. The original system was never perfectly fit for the needs of the ABCTL, and thus there has been a need for great change and adaptation over time. PNC is a cloud-based system, which means any changes impact everyone who uses PNC. On the data integrity front, this

presents a security risk as making changes could open potential impacts on other users as well. Despite some issues with PNC, there are useful benefits that help the ABCTL meet quality control, privacy, and regulatory requirements. For example, PNC has agency capabilities, meaning that users are gathered into agencies which are subdivisions of the system that only has information relevant to the user. PNC is also able to separate student data into the health services PNC system where they are assigned a health provider from ASU, which is different from what is available for the public. To maintain quality control of the data in the PNC, when anomalies are found a root cause analysis is done to figure out the reason and fix it as quickly as possible. Additionally, PNC is the means through which testing results are sent to the correct person after final approval by the lab director. Text and email notifications are given to people to tell them the result, however one must be aware of potential issues that may occur, such as when T-Mobile blocked messages from certain users based on their settings (3). In such a complex data system it is crucial to ensure that problems are identified and dealt with as soon as possible.

Quality Controls in Early Covid-19 Testing

The ABCTL was one of the first major institutions in Arizona capable of implementing testing in the beginnings of the Covid-19 pandemic in Spring of 2020. Testing operations were much slower in the early days compared to the present. Initially, testing was done through nasal swabbing with clinical staff in full PPE. At the testing site was a site manager who oversaw quality control and ensured that regulations were being met. The former system had a lot of opportunity for information hand off, as someone would first read out the test code out loud, before someone behind them would type it into a computer. This took many minutes for each individual. These manual inputs led to big quality control issues from information handoff, as it was easy to make mistakes in noisy environments while wearing full PPE in the sun. The data integrity issues that stemmed from this system had to be addressed, and this began with the transition to saliva testing and led to the system of Covid-19 testing that is used today.

Quality Controls in Covid-19 Testing Today

Today testing sites are mapped out entirely to streamline the process. Individuals can walk or drive in, spit into the saliva testing vial, and return home, which makes the biohazard risk much lower. To address data validity concerns from the previously mentioned system, QR codes were implemented that included all the relevant information and reduced data inconsistencies. There were also two secondary verifications that were added, date of birth as well as checking if the lab orders volume was the same as the sample volume. This was greatly beneficial, as the lab only had the sample code and date of birth associated with the testing sample, in compliance with HIPAA.

Testing site collectors must be careful to ensure that all the necessary and needed data required by the CDC and State are collected from individuals when they are tested. For example, people will on occasion submit a false date of birth, which presents a data integrity problem where demographics cannot be verified, and at-risk groups cannot be identified (8). This has made date of birth and photo verification by testing site staff when accepting a sample crucial. To ensure safe delivery to the lab, samples are checked for proper packaging upon arrival at the lab. Additionally, the ABCTL has a sample tracking system in the lab, so that it is known that the deidentified health information is matched correctly to the right patient when results are delivered, which requires a computer and human verification (Nelson). Maintaining patient identity is the number one priority, and this is achieved through Point & Click, QR codes, and physical labels.

Quality Control and Security through the Laboratory Data Workflow

Arrival at the ABCTL

When testing samples are being transported to the ABCTL there is a chain of custody paperwork that goes with them, which lists the samples in transit which tells the laboratory how many samples to expect and ensures that they arrive. If the chain of custody paperwork fails, the electronic health records (EHR)

are cross checked to ensure that every patient record that was scanned is pushed out so there are no samples that are accidentally left behind (Nelson). To make sure the quality of the sample is assured, coolers carrying samples are disinfected before shipping to the lab, and staff handle samples with full PPE while temperatures are tracked in the sample's Styrofoam packaging (Nelson). The samples arrive at a loading dock and are brought into an Intake and Heat Deactivation facility, where staff ensure the samples are valid with no leaks, openings, or warming. Testing samples are scanned into the EHR system two times with two additional final verifications. HIPAA complaint de-identified information is uploaded into the ABCTL database, where nothing is connected back to the patient except through their randomly generated ID that links back to them.

Laboratory Testing Stage within the ABCTL

Vials are put into groups of 376 samples, where test tubes are pulled from the rack and are double checked to ensure that the QR codes physically match the vials. The samples are put into a quantitative polymerase chain reaction or qPCR testing machine, which produces a graph showing levels of gene expression. If gene expression passes a certain threshold the sample is typically positive (Harris). These results are not always definitive however, and thus a lab director is responsible for reviewing each result and to make a final verdict on whether it is positive or negative. This is a crucial step for ensuring the quality of the testing data, as it verifies the results determined by the testing machine. From this stage the testing results are uploaded in the EHR and Point & Click systems and subsequently distributed to the correct individuals.

Further Quality Assurance Steps and Processes within ABCTL

Ensuring quality control and data integrity involves multiple other processes that do not directly interact with the testing sample as well. The quality assurance team of the ABCTL has constructed three groups (pre-analytic, analytic, and post analytic), to evaluate every step of the process and anticipate and respond to any problems that arise and reduce the likelihood of the problem occurring. This is called a failure mode and effects analysis (FMEA), and although typically done for one process at a time, there are complexity and timing restraints that require the quality team to group everyone together (Nelson). There are additional audits of admin access to EHR to ensure that those that can see patient records are properly authorized under state and federal regulations.

There are bottlenecks that must be identified and remedied to ensure quality control and the smooth transfer of data throughout the system. For example, samples typically arrive in bulk rather than a steady stream, which can slow data processing as the upload time to EHR can take roughly 1 second/sample (Nelson). Some bottlenecks are necessary however, such as the verifications that must be done for each set of samples by a lab director. Training must also be monitored to ensure people are aware of proper regulations and data handling procedures.

Quality control staff are on occasion additionally tasked with monitoring testing sites, where issues may be reported afterwards, or staff could step in to reestablish quality and ensure testing data is secured.

Conclusion

The ABCTL faces many requirements for ensuring quality control, data integrity, security, privacy, accessibility, and HIPAA and other regulatory compliance. In a complex system that involves getting testing data from a patient, through the lab, and results back into the hands of a patient, protecting patient anonymity and verifying integrity of test results are of utmost priority. Multiple quality checks are taken throughout each stage of the testing sample's journey, and each one is crucial for ensuring that testing data provided both to the patient and the state and federal governments are correct. Quality control teams must identify, predict, and address active or potential problems in any part of the system and work to minimize bottlenecks to ensure the smooth flow of testing results. The assurance of accurate, secure, private, and compliant data may not be the ABCTL's most technically challenging aspect, it is integral to

ensuring that the ABCTL can perform at maximum efficiency with minimal errors. Quality control steps along the way allow there to be faith and confidence in the end sample result data that is given to the recipient.

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Section III: System Usability

Author: Michael Leung

Background

The ABCTL was created and launched in an extremely unique, dynamic context, and many of its components reflect this. The ABCTL's information technology (IT) department is one of the most representative examples, as its systems frequently undergo customizations, fixes, or even reconstruction altogether in order to meet the lab's and clients' increasing, diverse needs. A primary component of this is the electronic health records (EHR) system within the ABCTL. At its core, an EHR system is "a longitudinal electronic record of patient health information generated by one or more encounters in any care delivery setting" (Menachemi & Collum, 2011). In a clinical testing laboratory, an EHR is critical in that it is responsible for managing patient data, allowing essential lab faculty members to access and mobilize health information. In the context of the ABCTL, the EHR is particularly essential for communication with patients, relaying test results back to them in a timely and clear manner. It is essential that the system is simple to access and operate and has clear, standardized procedures to reinforce an efficient workflow for demanding productivity. In this regard, the ABCTL has made great strides to improve its EHR system and other IT systems since its initial implementation at launch.

Two key concepts throughout this chapter are user interface (UI) and user experience (UX). In general, UI refers to "a system and a user interacting with each other through commands or techniques to operate the system, input data, and use the contents," and these systems can range from "computers, mobile devices, games, etc., to application programs and content usage" (Joo, 2017). Put simply, a UI is the user's tool and means of interacting with a system, which can be as simple as the buttons to press on a smartphone application or the pages and tabs a customer navigates through while shopping online.

A well-designed UI is essential both in everyday technology and from a business standpoint because it optimizes the interactions between the system and its user, allowing the user to get the most beneficial use out of the system. In regard to the ABCTL and its systems, there are UIs across the lab, such as the interfaces laboratory staff members use to transfer and access test results and other data, as well as the patient portal for clients and partners to view their results. Considering the monumental number of samples the lab receives on a regular basis, the lab must maintain a streamlined and efficient workflow, and well-designed UIs are vital to success in this regard. This, in essence, contributes to the quality of the UX, which is defined as the "overall experience related to the perception (emotion and thought), reaction, and behavior that a user feels and thinks through his or her direct or indirect use of a system" (Joo, 2017). Quality UXs of both the administrative data systems and the end-user interfaces are essential for providing a smooth and efficient experience with the ABCTL's COVID-19 testing, while maintaining accuracy of communication and test results.

In general, if a system does not have a well-designed UI, then the user simply cannot use the system to its fullest. Worse, users could encounter issues with the system that could make it unusable altogether, which may result in users' needs not being met and possibly them becoming averse to using the system. For example, a smartphone could have the latest and most advanced hardware, but if its corresponding software has a poor UI design and is difficult to use, then it does not matter how great the smartphone's hardware is. It is simply not a user-friendly product, and customers will eventually shy away from it because it may not be able to perform desired functions. Shifting this to the ABCTL's context, it is imperative that patients and clients who are involved with its COVID-19 testing are able to use and interact with key systems, such as the patient portal for signing up for appointments and viewing test results. The ABCTL could have the best laboratory equipment available and boast an incredibly fast turnaround time; however, if the patient has difficulty with setting up appointments, or with accessing

or understanding their test results, then these aforementioned workflow feats would have been accomplished in vain.

While UIs are an important aspect of usability, it is imperative to note that there are many other aspects beyond interfaces that contribute to this as well, including but not limited to means of increasing the frequency of interactions with systems in general or increasing the overall functionality of a system. The term "usability" essentially refers to features or aspects that allow the user to get the most effective and optimized use out of a given system to perform desired functions or receive a service. The broad diversity of this topic will be evident in future sections in this chapter, which will provide additional context and a number of examples that highlight the many different factors that contribute to a better-quality UX. It is important to discuss the concept of UIs as a prominent facet of usability, and also as a means of recognizing and understanding that there are many different and equally important ways to improve the usability of systems besides interfaces. Thus, acknowledging the importance of a quality design and its subsequent implementation helps with understanding the basics and general idea of improving system usability in a number of other contexts that are also essential to the ABCTL.

Furthering this idea, system usability is just as vital regarding ABCTL staff and administrative personnel operating their systems from the back end, including but not limited to making changes to the EHR system, using key lab interfaces to push data along the lab workstream, and managing test results. Sean Dudley, the head of the ABCTL IT department (2021), emphasizes the importance of this: "Data accuracy is also usability...that is the end goal of usability: [quality, accurate] information." This adds another essential dimension to usability. As important as efficiency of workflow and data management is, the accuracy of the data is the top priority. Especially in a medical, healthcare setting, accurate data and effective communication is critical, as the information provided to patients can greatly impact their lives. Thus, from the back-end (administrative) perspective, it is important to improve systems and interfaces in ways that allow for more effective data management and communication. Considering the importance of a system's usability, the ABCTL also prioritizes administrative usability in order to provide efficient and accurate testing services for such a large patient population.

This section will provide a detailed overview of the various UIs and UXs of the ABCTL's technological systems, including its EHR system and other systems that pertain to lab production workflow and data flow. The ABCTL's systems are constantly changing as well to reflect the lab's efforts to meet dynamic needs, whether it be due to system enhancements, fixes, etc. Through interviews with subject matter experts within the ABCTL, valuable insight was obtained regarding diverse perspectives of operating and making changes to these various systems, as well as personal anecdotes about the UX in a number of contexts. The usability of systems and interfaces was considered from both the administrative and end-user perspectives as a more holistic overview. This chapter will present in detail several key IT systems involved in the lab, as well as major changes the ABCTL made in the past to improve the usability of these systems, such as enhancements or fixes to address urgent issues. All of this is presented with an overarching emphasis on prioritizing the usability, effectiveness, and practicality of these systems in the context of a refined, yet constantly evolving clinical testing laboratory.

The Evolution of ABCTL IT Systems

The Electronic Health Records (EHR) System of the ABCTL

During the early days of the ABCTL around the time of its initial launch, the E system in usewas not easy to use or understand, and this problem prompted a search for improvements to its overall usability. Insights into this process were obtained through extended conversations and interviews with ABCTL's lead technology architect, Kevin Tinnin

The EHR's first version was what Tinnin called "glorified spreadsheets" of data. Essentially, patient data and test results were collected in spreadsheets. Although this may seem like a simple format of storing

data, this EHR was very complicated in actuality due to the many obstacles to accessing this data. For instance, accessing the spreadsheets required a specialized virtual private network (VPN), specific HIPAA credentials, and virtual desktop infrastructure (VDI). Additionally, the shared folder with the data was not in an obvious location, requiring time and effort to find it once logged in. Tinnin (2021) notes, "That process was cumbersome. It was difficult." Oftentimes, the aforementioned parts of the EHR would run into issues. For instance, the VPN, VDI, or mapping of the shared drive would not work properly, causing the entire system to require immediate attention. To make it even more complex, passwords in this system were required to be reset every 90 days, causing log-in issues after every routine reset. Based on these aspects, it is evident that this system was not user-friendly. According to Tinnin (2021), "This system was not going to work long term...It is fine for a lab-type setup or research-type setup, [but] it was not going to work in scale." As the ABCTL aimed to become equipped and able to handle a massive uptake in COVID-19 test samples, a new EHR was needed.

Point and Click: A Lasting Solution to the EHR

In June of 2020, set to move on from the nonideal EHR system, the ABCTL partnered with Point and Click Solutions, the "leading Electronic Health Records/Practice Management System (EHR/PMS) provider for university health and counseling" (Point and Click, 2021). The system provided by Point and Click (PNC) is a complete EHR system, meaning that it can provide the necessary features for the ABCTL's logistic needs for COVID-19 testing and data management. The ABCTL adopted PNC's default stock system, and also worked with the developers at PNC to customize the system to their needs. This system proved to be an effective solution to the previous IT-related issues prior to its implementation. With routine communication between the ABCTL and the PNC CEO and developers throughout their partnership, changes were also made to the EHR over time to enhance its features and capabilities, while constantly working to improve its usability.

The following section is an in-depth overview of the ABCTL's PNC system, which is still in effective use today. Aspects and customizations of the system will be discussed with an emphasis on the user experience from both the back-end (administrative) perspective, as well as the end-user (patients') perspective. This section will not only provide a better understanding of PNC as an effective EHR system, but it will also demonstrate the importance of usability of this system, highlighting key features that contribute to a better UX and more efficient and accurate data management.

Overview of Point and Click

Starting with the back-end experience of PNC, one of its primary functions is to schedule COVID-19 testing appointments on the page called "PncSchedule." Although there are numerous testing sites across Arizona that are affiliated with the ABCTL, PNC manages to list them out in a chart with a scrollable view, also displaying each site's availability. To improve the UI and ease of viewability, the schedule exhibits colored blocks to display the relative availability of time intervals throughout each day. In order of increasing availability, the blocks will be colored red (little to no available appointments), orange, yellow, or green (many available appointments). According to Tinnin (2021), "this [interface] is what the majority of our schedulers use to keep tabs on [whether] we need to increase capacity, or close down some sites." This allows schedulers to quickly determine sites' general availability, influencing decisions that help employees' efforts and resources to be allocated effectively at collection sites where needed the most. Hence, viewing the schedule as color-coordinated time blocks contributes to an improved UI, a theme that will be seen throughout PNC.

In regard to patient registration for COVID-19 testing, there are two main ways of adding patients to the system to offer practical versatility. The first way is the most standard, which simply involves the patient registering themselves through the main patient portal of PNC. To help with better organization of patient information in the database, agencies were established and defined. Tinnin (2021) generally defines agencies as any group of people (organizations) throughout the valley partnered with the ABCTL for

COVID-19 testing, such as employees of a specific company. The purpose of agencies is to provide a logical way of categorizing people for practical and organized data management and sharing in the future. The ABCTL provides agency codes for patients to enter, if applicable, so that they can be sorted under a specific agency upon registering. The second way is through imported patient lists, where agencies can provide the ABCTL with a list of their employees, prompting the system to automatically create new accounts for each employee listed. Once the accounts are created, the registered individuals must log in to claim their premade account, and then they may begin scheduling their appointments. This method essentially allows for quick, automated registrations of relatively large numbers of people. Registration is a critical step in the beginning of the testing process, making it critical that the ABCTL makes this process straightforward, able to be done effectively in bulk, and beneficial for better-sorted patient test results down the line.

The activity dashboard is essentially the command center for PNC, displaying and providing useful information regarding test sample results in particular. Obtainable by a few clicks of a button, the results can be sorted and displayed based on a multitude of categories, including: number of positive/negative/inconclusive results, COVID-19 tests by date, test volume by location, test volume by ordering provider, test volume by location by agency, late test results by agency, still pending test results by agency, resources by agency, and appointments by agency (Tinnin, 2021). All of this data can be displayed in the form of charts and graphs, allowing for easy visualization and evaluation of the data collected. Having this data is not only useful for tracking the coronavirus within the area, but it is also beneficial to share to other agencies for health and safety reasons. Being able to provide testing data specific to agencies allows them to make better informed decisions on courses of action that are safe for their employees amid the pandemic.

Within PNC, admin users can access a wide variety of diagnostic information of the system through a page called “PncReport.” This page is dedicated to running and providing data reports, which are obtained by running scripts of code that act as the messengers who retrieve the data. When lab test results are obtained during the lab workflow, they are uploaded to a database; to retrieve data from this, a back-end user must run a report. These reports and queries (requests for data) in the ABCTL’s system are written in Structured Query Language (SQL), a language that is more ideal for managing data in greater volumes. To run reports in a way that is much easier to understand than lines of code, the SQL reports within PNC are displayed in the form of a graphic user interface (GUI), which refers to an interface that is ideally easier to understand and interact with. In general, the data retrieved as a result of the reports is typically shown in some kind of graphic or table for easy viewability.

For instance, a popular report that is often run is one regarding Devil’s Drop-Off, the ABCTL’s new take-home COVID-19 saliva testing kit. For useful diagnostic information, Tinnin wrote a customized SQL query that requests data on how many of these kits have been activated within a certain period of time. Once this report is run, a simple table is displayed, showing the various ASU-affiliated groups, and the number of corresponding activated kits next to each one listed. This system of running reports is effective because although SQL queries are running in the background, non-IT executive personnel interested in the data can primarily interact with and view GUIs with data that are presented. This is one of the most important parts of PNC, as reports can be customized to provide all sorts of data contained in the EHR database. For even more convenient use, IT administrators such as Tinnin publish reports on this page in folders, allowing other administrative users to easily access and run these reports on demand. As Tinnin (2021) often emphasizes, “The goal is to streamline [data management] as much as possible.” As seen in PncReport, the way the IT department went about this was to simplify and publish SQL reports in GUIs for both easy access and more pleasant viewability.

“PncAdmin” is the main interface on the back end that allows administrative users to customize and set up the various lab orders, appointments, and results management. Here it is important to recall that not

only can usability refer to interfaces and systems, but it can also refer to data management. From an administrative standpoint, there is a logical order of organization that is seen in the ABCTL's COVID-19 testing data to contribute to its system's usability. The ABCTL first established organization at the agency level, using agencies as a logical way of sorting patients among the thousands in total. Individuals knowing which agency they belong to is beneficial because it allows the system to direct them to the facilities where they are likely to be tested at based on proximity. This leads to the next two layers of organization: facilities and locations. To make it easier and clearer for patients to choose where to get tested, it would have been beneficial to list each and every facility upfront on the patient portal. However, since the ABCTL was unsure of how successful each testing site was going to be near the time of its initial launch, the concept of blanket facilities was utilized. Blanket facilities refer to the idea that several locations (which can be logically grouped together by location) can be defined under one overarching label, such as "Arizona State University." As a result, each blanket facility contains a set of testing sites to choose from. For instance, the ASU blanket facility contains Sun Devil Hall and Lot 59, locations that might be the most convenient for individuals selecting this blanket facility. This added level of organization effectively gives the ABCTL more flexibility in that it can add or remove locations from blanket facilities as it sees fit. This, in essence, gives the back-end users an easier time when it comes to modifying these testing sites.

Organization was then narrowed down to the **provider** level. Under normal circumstances, if a patient is registering in a typical EHR system, he or she would simply view the providers who are available at a given location, and then book an appointment. However, in the context of the ABCTL and COVID-19 testing, this traditional procedure is not the case, mainly due to the fact that allocating providers is vastly different. For example, at testing sites with drive-thru lanes, each lane is literally labeled as a "provider" for patients to book an appointment with to generalize this selection process. As a result, the provider, in this unique case, is the collection site staff member who is scanning the patient's sample tube. According to Tinnin (2021), "The goal was to basically try and make it as generalized as possible, and then we would keep track of who's actually scanning through the users."

At the **user** level, the narrowest level of organization, the staff members at the collection sites who are actively accessioning samples are tied to the individual samples that they scan. These implemented levels of organization within the ABCTL's version of PNC allow back-end users to have an easier time accessing test sample data throughout the testing and lab processes. Most importantly, this organization allows the ABCTL more flexibility in their planning on the administration side, as seen in the testing locations and providers. Since there was much uncertainty regarding planning and managing a massive increase in testing volume, the flexibility and generalizations were essential in the systems' usability while the ABCTL was adapting as needed.

There are also miscellaneous yet essential components of the back end of the ABCTL's version of PNC. Most notably, PncConfig is essentially the typical "settings" page in an application where admin users can make both large and trivial changes to interfaces across the system. The ABCTL has made customizations to this page to improve its usability for both the back-end and front-end users. Tinnin (2021) states that "since [PncConfig] is web-based, [the IT team has] taken that settings file and put it into kind of a GUI-based [interface]," which allows the IT team to more easily and quickly select files pertaining to the system to modify and customize. For example, if administrators wanted to rebrand Devil's Drop-Off saliva kits with a new name from the end user's perspective, within PncConfig they could click on the "OpenCommunicator" file, then select the "Home Kit" file, where they can directly modify the display name for Devil's Drop-Off. This example is representative of how the IT can effectively and routinely customize UIs ad hoc via PncConfig. "The idea that we have the ability to go in and make those sorts of changes is absolutely fantastic, and you do not really get that with an out-of-the-box solution. This has really been customized and tailored to what we're trying to accomplish here at ASU" (Tinnin, 2021). The implementation of GUIs within PncConfig makes the customization process even easier, as this settings page is simple to navigate and operate.

In retrospect of all the diverse features and functions of PNC, it is evident that PNC has been a healthy solution for the ABCTL's EHR system and more. What is impressive about this system is not only the abundance of capabilities in terms of testing and data management, but also its ability to be customized to fit the ABCTL's goals and needs. This system is being operated and used on a daily basis by many different types of users, making its usability essential to a quality UX in diverse contexts. On top of this, especially closer towards the ABCTL's earlier days, there were a lot of adaptations and urgent improvements that were necessities at the time. PNC contributed to this ease of customization, allowing the ABCTL to quickly make administrative changes on the fly, whether it be managing collection sites, monitoring patient registration, establishing new agencies, and more.

Mass Tester App: An Extension of Point and Click

As an extension of the PNC system, the ABCTL features an application used to sign in patients and scan their sample test tubes at each collection site. Commonly known as the "Mass Tester App," this is the application that collection site staff members interact with on a daily basis. This section will provide an overview of the Mass Tester App, discussing its components, as well as customizations and enhancements made to address its usability. The following information was obtained through extended conversations and interviews with Kevin Tinnin and Alma Douglas, an experienced front-line support and ABCTL collection site manager who has been with the lab since the early days.

The UI of the Mass Tester App is simple yet effective, contributing to its straightforward UX among collection site staff members. The main interface is shown on the following page in Figure 1:

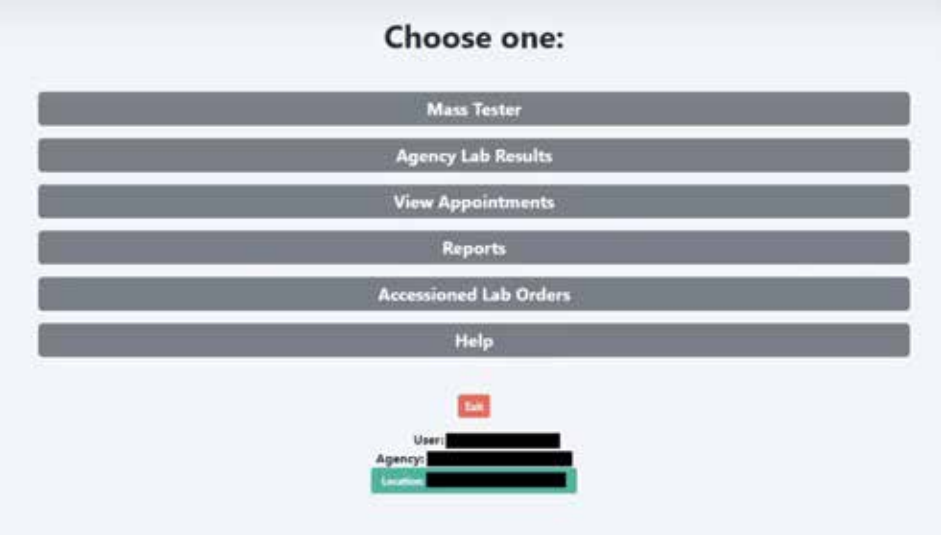

Figure 1. Tinnin, K. (2021). Main Interface of the Mass Tester App. The main menu of the Mass Tester App consists of just a few buttons, each with a specific function that pertains to COVID-19 testing, appointments, and data management. From Point and Click.

There are six main buttons that make up almost all of the UI's display: Mass Tester, Agency Lab Results, View Appointments, Reports, Accessioned Lab Orders, and Help. With few but essential features and buttons to select, the Mass Tester App is a quality example of a user-friendly interface. It is important to note that all of these buttons and features were not available at its initial launch. These features were added over time, as the ABCTL recognized the need for each. According to Douglas (2021), "When [the ABCTL] first started, it was just the Mass Tester button...but as time went on, we realized that we needed to give partners access to their report unit [and] access to their appointments...so we worked with PNC and they were able to create these additional tabs to create these [corresponding] functions." As partners and outside agencies requested more and more useful information from the ABCTL, the lab decided that the Mass Tester App would be the best interface to add these functions to.

Past Hotfixes, Customizations, and Enhancements to Point and Click

The ABCTL made modifications and enhancements to its system periodically, either as they saw fit, or as they ran into critical system issues. In general, the business team is in charge of setting the work priorities for the IT team, as they oversee requests from partners, and evaluate the overall productivity of the lab and areas for improvement. The relationship and continuous communication between the business and IT teams is essential for planning, implementing, and evaluating changes made to systems across the lab. The two teams meet on a regular basis and discuss their backlog, a list of all the changes and enhancements to the system that are either desired or already in progress. With the business team's help, they rank these items in order of priority. Tinnin (2021) notes, "It's eye-opening to find the things that I think are important from an IT perspective and the things that [the business team] thinks are important from a business perspective. They don't always match up." In these cases, the business team's input takes precedence more often than not, because maintaining working partnerships and optimizing its service are top priorities for the ABCTL. As a result, many of the IT team's desired work items fall to a lower priority on the list and may even sit on the backlog indefinitely.

Tamara Deuser, Chief Operating Officer of the ABCTL, discusses these priorities with the IT team, as her business team is a primary point of contact for inquiries regarding system modifications. According to Deuser (2021), "We get a lot of requests, and most of them are very narrow and focused on a particular partner or piece of the work stream." A hypothetical example Deuser provided is the perspective of Carolyn Compton, MD, PhD, the ABCTL's medical director. Responsible for reviewing and acknowledging test results in the EHR, her job is absolutely critical to the workflow, and her requests will likely center around improvements to the usability of the interfaces she uses. At the same time, there can be specific requests from other partners, such as agencies requesting custom reporting, which will be discussed in later sections. An essential principle in usability is the system's ability to meet the needs of the user, and as this list grew, Deuser (2021) admits that there came challenges with having to balance these requests and choosing which to prioritize. In regard to the overall UX of the ABCTL's systems, it is imperative to be aware of these logistical challenges behind the scenes, since this decision-making process heavily influences which aspects of usability get improved.

On another note, a key aspect of the ABCTL and the usability of its interfaces is the clarity and readability of their design. This is of utmost importance in regard to communication of test results to patients. The primary component of this is the test results page that is displayed to patients in their portal. Since the page contains a plethora of data and information (e.g., patient information, test results and their explanations, performing laboratory information, etc.), it is often difficult for patients to locate on the page their test results, the piece of information they care most about. The test result ("positive," "negative," or "inconclusive") was essentially buried in a mass of plain black text, as seen in Figure 2 on the following page.

Figure 2. Tinnin, K. (2021). The original version of the COVID-19 test results page. This image was edited to circle the test result in red. The word that indicates the test result, "negative" in this case, is somewhat lost and hidden in the large black and white body in the middle of the page. From Point and Click.

The ABCTL received numerous comments from patients that the results were difficult to locate, or that they could not interpret nor understand their results based on the information provided. Additionally, there were sometimes issues with identification labels in even earlier iterations of this page that resulted in patients having difficulty getting their test results approved when needed, as seen in work, air travel, etc. These issues, along with the large number of complaints, prompted the ABCTL to find a solution. When it comes to these kinds of system improvements, Tinnin (2021) emphasizes that "these changes come from and go through a number of people." First, the IT team and PNC CEO and developers meet to discuss the technological possibilities regarding changing the page's design. Additionally, the lab managers are consulted, in order to make sure that the medical and scientific information on the page is concise, understandable, and accurate. Lastly, the business team is consulted so that they can ultimately make sure that the IT team's technological solution is actually meeting the users' needs from a communication standpoint. The final result and most recent iteration of this page now has the test result stand out more and easier to locate, as shown below in Figure 3:

Figure 3. Tinnin, K. (2021). The latest version of the COVID-19 test results page. The "negative" test result is clearly indicated in large text and inside a colored box to help with clarity and readability, while still maintaining necessary information included in the original version. From Point and Click.

According to Tinnin (2021), "[Although] it looks small here, this was actually a huge project that took us a solid month of development because we had to rewrite this [generated PDF] on the fly." Not only does this design change highlight the ABCTL's commitment to a better UX including readability and clarity, but it also shows the demanding nature of the back-end work that is required for changes as such. This example further emphasizes the importance of usability. Regardless of how well the ABCTL performs COVID-19 testing, it is meaningless if the lab results cannot be effectively communicated to the patients. Additionally, bringing awareness to this change is essential, as communication and user interactions via interfaces are vital aspects of a testing laboratory that might not be as noticeable at first glance.

Additionally, to improve readability from the end-users' perspective, language support was added. As the ABCTL expanded its testing across the state, the lab aimed to translate key interfaces to languages that were popular throughout these areas. Before translating, the ABCTL had to determine which languages to translate to. Sean Dudley was tasked with this, and he obtained relevant census data by searching through a public, federal website. According to Dudley (2021), languages were highly considered to be translated if three or more percent of the target population spoke it. Ultimately, the languages that are provided on the front-end view are English, Spanish, Navajo, and Tagalog, while languages like German just missed the cut. All in all, language support is an essential aspect to UX, as it simply allows a more diverse population to effectively use the ABCTL's system.

Additionally, there are instances where users encounter errors in the system on the front end, which may cause hindrances in usability or efficiency. A critical issue that is representative of the ABCTL's priority of helping the workflow is the patients' registration of Devil's Drop-Off kits. When students pick up and activate kits, many times they would not wait for the interface to refresh the page, meaning that the registration process did not fully complete on the back end. Because of this, if a student were to mistakenly click the registration button again before the registration officially finished processing, the interface would give an error message saying that the kit had already been activated and cannot be used as a result.

According to Tinnin, there were several ways to go about solving this issue. To come up with initial ideas, the team looked to other businesses who might have run into similar issues in the past. For example, Ticketmaster, a popular company that distributes tickets for events, circumvents the issue that the ABCTL was experiencing by displaying a message to the user to not touch their smartphone screen for 60 seconds while the transaction is processing. This was an example of a possible idea that the ABCTL IT team was able to pull inspiration from in order to improve their own interfaces. The final solution that was ultimately implemented was that when the activation button is clicked, the button command in the back end is deactivated, meaning that if the user were to click it additional times while the system was processing the registration, these extra clicks would be ignored and not registered. This solution in particular is especially beneficial to the UI, as its implementation was discreet in that it did not impact the end user experience nor workflow, while still addressing the issue at hand. This aspect of implementing fixes and patches is paramount in the context of a clinical testing lab that must be able to maintain and optimize its workflow at such a high level. Focusing on implementing back-end changes that does not noticeably hinder the UI helps to mitigate any trouble and confusion that might arise after the update.

Lastly but importantly, there were usability-related issues that can be attributed to slow loading times. Most notably, this was an issue within the EHR. To fully understand the nature and cause of this issue, it is important to first understand the workflow of the lab and how patient and sample testing data is tracked in general. At collection sites, manifests are created, which essentially tell the testing laboratory how many collected samples are coming from that specific site. In this manifest, the ID numbers on the tubes are also listed, for further identification and tracking once in the lab. Although the lab receives all this information from the manifests, it does not actually have any patient data, and therefore cannot put a patient name to each test tube. This reconnection of patients and their test results actually occurs in PNC, once this data is pushed to the EHR. Tinnin (2021) claims that "this push was actually processing

about one result per second," referring to the process of "ingesting the result" and "generating the report." Considering this very slow process, the IT team did some investigation on the cause of this and found that a data table within the database was not clearing itself out the way that it was expected to. Basically, at midnight every night, the table was supposed to automatically clear itself unless directed otherwise. However, due to the way the system was configured at the time, the system was mistakenly constantly preventing the table from clearing itself. Thus, the IT team reconfigured this section so that the table could function as expected. This fix increased the processing rate by roughly a factor of eight. For reference to the typical workflow, Tinnin (2021) states, "Normally it took about an hour...and now that we're automating Dr. Compton's acknowledgement [of results], from the lab sending the results it literally takes about five minutes for 3000 people to get the notification that the results are ready." This solution greatly enhanced the UX of the EHR, with drastically quicker loading times that contribute to more efficient usability and data transfer.

Enhancements to the Mass Tester App

In regard to customizations, the Mass Tester App has also undergone key changes to help with usability and features for outside agencies. Early on in the ABCTL's lifespan, agencies increasingly wanted lab result data and other statistics of their particular patient population, such as appointment data. These agencies would reach out to the ABCTL via email requesting for this data, so the IT team had to email this data on a regular basis. This became a tedious and nearly impossible task, based on the high volume of testing and demand. To address this, the IT team created and added the "Reports" button to the Mass Tester App, which essentially allows agencies to run custom reports specific to their agency. As mentioned earlier, this feature was implemented in the Mass Tester App and not the true back end of PNC due to practical and security reasons. Tinnin (2021) adds, "many of the agencies who were requesting this testing data and reports did not actually participate in the mass testing themselves at collection sites," meaning that it is not necessary to give these agencies access to the full back end of PNC. Additionally, this feature allowed the ABCTL to segregate the reports by agency, to ensure that when a specific agency accesses this reporting on the Mass Tester App, only their relevant reports will be displayed. Not only is this vital for data security and privacy, but it also makes it more straightforward and easier for agencies to directly access the desired data. All in all, this button creation was a key addition that added to the usability of the Mass Tester App from the front-end (user's) perspective, marking a milestone for data sharing.

The implementation of custom agency reporting in the Mass Tester demonstrates the differences in priority and how usability of the system is improved for partners. From a business standpoint, custom reports in the "Reports" button are a practical feature, because it allows agencies to have easy and direct access to their population's testing data. However, according to Tinnin (2021), from an IT perspective, this implementation was not a priority because there are simply other ways for these agencies to obtain this information, such as simply surveying their employees for testing statistics. However, since this feature was in such high demand, the IT team pushed this to the top of their priority list at the time, putting their other tasks on hold until this new method of custom reporting was implemented.

Additionally, there were a number of functional enhancements that were added to the Mass Tester App, and many of these were to help with its versatility in regard to registering and signing in patients. The ABCTL quickly noticed early on that a number of patients preferred to come to collection sites to get tested without an appointment scheduled in advance. To address this new issue, the IT team decided to work on a solution that can successfully and quickly register patients in this exact scenario. According to Tinnin (2021), this added feature "worked well for people that were coming to get tested for the very first time and just showed up without an appointment." This eventually led to the accommodation of "full walk-in appointments," which is a feature on the app that can immediately create an account for and sign in a patient at a collection site. According to Tinnin (2021), the next iterative update of this would be to have a patient QR code that can be printed out through the patient portal. With this special code, all

patients would have to do is present it at the collection site and have it scanned to officially register as a walk-in patient. By implementing this series of updates, the Mass Tester App has become much more accommodating for different patient registration scenarios. Not only does it make it easier for patients to choose how they want to register and make appointments, but it also allows collection site staff members to easily handle a wide variety of patient sign-ins with simple clicks of a button. Thus, these customizations and enhancements only improve the UX for both the back-end and front-end users.

With the constant customizations to the Mass Tester App, there were also system issues that users encountered firsthand along the way. An example of this is an issue that the lab ran into, where the data system indicated that it was supposed to contain several tubes with the same identification number, which in reality, is not supposed to be possible. After some investigation, it was discovered that collection site staff members sometimes did not refresh the page after every barcode scan of a sample tube, so that barcode got scanned into the system multiple times. Although this is a simple mistake, it can have critical consequences later on in the lab. However, there was an easy solution to fix this. The IT team created an error reporting system, where the Mass Tester App would send out an error message to the user scanning the tubes if a second barcode with the same identification information was scanned within a three-month period. This safety net feature essentially eliminated the possibility of scanning the same QR code multiple times. After this fix was implemented, it was also clearly communicated to the collection site staff. This was a vital step, allowing the staff to quickly understand the situation, and to avoid being confused or flustered at the sight of the new error message if it appears. The connection between the Mass Tester App and PNC allows usability fixes like these to be more easily implemented, allowing for effective patchwork and enhancements to a system that vitally needs to be able to quickly adapt and change on the fly as needed.

Miscellaneous Enhancements

The ABCTL aimed to improve users' interactions with the ABCTL's systems by increasing communication with users through text messaging. However, sometimes there were issues regarding these messages, causing extended investigations to find the source of the issues. For instance, usually, the system will send out a text reminder to patients 30 minutes before their appointment. At one point, it was discovered that this function was not working properly, so the IT team had to go into the back end of PNC and examine the overview of the SMS and text message transmissions page. They ultimately discovered that T-Mobile, one of the most popular cell phone providers, was flagging the ABCTL's text reminders as spam, since the ABCTL began to send out so many of the same message in such a relatively short time. Tinnin (2021) says that finding the sources of these issues "takes a lot of detective work," suggesting that hearing about and encountering issues can come from a number of different sources, whether it be by word of mouth, or listed in the back end. Thus, situations like these should be carefully considered moving forward, as issues that limit patient interactions with the system can sometimes go unnoticed, but still hinder the usability of the system.

On the subject of patient communication, it is important to note how the ABCTL utilized its systems to effectively monitor patients' usage of the system. The IT team decided to keep the results in the portal, rather than individually sending them out to patients. By doing this, they are able to track whether patients have logged into the portal to view their results. According to Tinnin (2021), more often than not, roughly 10 percent of the total patient population with the ABCTL did not open their results at all. This is obviously not ideal, as the COVID-19 test is essentially useless for the patient if they do not ever check their test results. To help mitigate this issue, the ABCTL began to send out an additional wave of text reminders to patients who had not checked their results more than 24 hours after they were released. This, in addition to monitoring of patient portal activity, helped to decrease the portion of patients who did not check their results to a mere three percent of the total population, a substantial improvement. Decreasing this percentage only helps to increase interactions with the system, and consequently overall safety regarding being aware of who has COVID-19.

Usability Within the Lab Workflow

Throughout the sampling lifecycle of a COVID-19 test sample at the ABCTL, there are a number of interfaces that are involved with handling samples and contributing test results to both the lab information management system (LIMS) and EHR. Conversations with lab director Vel Murugan, PhD, and lab manager Valerie Harris, graduate student, provided insight regarding this area of the workflow. A process that underwent interface changes is the lab directors' review and verification of saliva test results that come from the QuantStudio Dx Real-Time PCR Instrument, the ABCTL's machine that utilizes a polymerase chain reaction (PCR) test to detect the presence of SARS-CoV-2, the strain of coronavirus that causes COVID-19.

This is a very tedious and timely process for the lab directors, as they must review each and every result one at a time. When looking at each individual test result, the lab directors look for specific aspects to determine the validity of the result, namely the cycle threshold (Ct) value. For instance, Dr. Murugan (2021) confirms results as negative if they do not have an associated Ct value, as a rule of thumb. To determine positive or inconclusive results, the lab director must look at the Ct value for a given sample, as well as the overall "amplification curve" of the graph, to determine if a test sample is truly positive. Specific details regarding the biochemistry behind this test will not be discussed, but the key takeaway is that the lab directors undergo a timely yet vital procedure. Harris (2020) emphasizes, "We have to remember that these are people's lives we are dealing with, you do not want to accidentally give someone a positive result because it will have a major impact on their life...so every single positive result, I verify with my eyes, sitting here, clicking through every result on my computer." Especially considering the immense increase in testing volume, like many aspects in the lab, adapting to scale was paramount.

Relatively early in the ABCTL's lifespan, an interface and database unofficially called "COVID DB'' was implemented to streamline this process of verifying test results.

COVID DB's key feature and function is that it automatically classifies test results to be positive, negative, or inconclusive, prior to reaching the lab directors to be reviewed. The general interface is shown in Figure 4:

Figure 4. Murugan, V. (2021). The interface of COVID DB. COVID-19 test results can be filtered and accessed by selecting the radio button of the desired test result category. The user (lab director) can also view COVID-19 test results within specific time frames by modifying the "Select Date qPCR Plate was Uploaded" parameters. From ABCTL information technology.

This makes the review process much easier for the lab directors. Since the database has already classified each sample and grouped them together, the lab director can easily review the negative results, quickly confirming that there is an "N/A" label in the Ct value for each, since there is no Ct value associated with negative results, as mentioned earlier. Now, with the remaining positive and inconclusive

results, the lab directors perform the same procedure as they did before the implementation of COVID DB. While the tedious task still remains for safety reasons, the overall process is much faster because the negative results, the most abundant ones, can be more quickly reviewed. This drastically decreases the time it takes to review batches of samples, not only streamlining the process and making the lab directors' job run more smoothly, but it also contributes to more accurate and confident reviews of results.

Past Enhancements to the Streamlining Interface

Additionally, the interface is equipped with safety nets and points of additional confirmation that ensure that the correct data is being uploaded and shared with the lab directors. These features essentially improve the UX of the system by preventing crucial data errors from occurring, which can go undetected and potentially lead to significant issues in later steps in the workflow. A primary example of this is during the PCR tests. For every batch of samples, a lab technician is responsible for uploading a data file to the QuantStudio Dx to inform the machine of which patient identification number belongs to which sample. This presents an opportunity for human error, since technicians can upload an incorrect file, or forget to upload one altogether. As a result, the test results would be transferred to the database without any patient identification.

This is, of course, a serious issue, but the interface plays a role in counteracting this. As part of its function to classify and group positive, negative, and inconclusive results together, it has been designed to reject test results that do not have any patient identification. Additionally, this security feature also prevents duplicate patient identification information from being uploaded, because that simply should not be allowed. Being able to prevent errors that can slow or stop the workflow is critical for the lab and contributes to a better UX in that regard. Potential errors like these, especially human error, may be common, but COVID DB is a primary example of addressing them to improve the workflow and mitigate user errors with the interfaces.

Critical IT Dependencies for the ABCTL

The usability of IT systems and interfaces across the ABCTL is undoubtedly an essential aspect that is vital to the lab's success. In other areas of the technological side of the lab, factors such as improved lab equipment, increased automation, and customized data systems have played a critical role in advancing the efficiency of the lab. While this is greatly beneficial in terms of turnaround time and processing larger quantities of samples at faster rates, it is important to remember that these feats would essentially be pointless if users and patients are unable to effectively perform key tasks pertaining to the overall COVID-19 testing process, such as setting up appointments or accessing and understanding their test results. In other words, it is essential to prioritize individuals having a quality UX on the front end of these IT systems so that they are able to receive the ABCTL's testing service in an efficient and straightforward manner. Additionally, data accuracy and ease of communication are top priorities throughout the ABCTL, and key modifications and customizations to the usability of systems in both the back and front ends have allowed for advancements in this regard. The ABCTL's past and continued optimization of data management, communication, and system maintenance through fixes and enhancements to the overall usability of its essential systems is an immense accomplishment that might not be as recognized as other areas of the lab but is absolutely vital to the lab's overarching productivity goals.

Looking at the ABCTL from a business perspective in terms of a clinical testing laboratory providing a service (COVID-19 testing) to patients, usability of IT systems is a necessity, as it allows patients and users to get the most effective use out of the systems they interact with to contribute to a relatively simple and smooth overall testing process. In the back end, a quality UX allows administrative users to maintain data accuracy and continue to improve technological aspects of the workstream while adapting to the

increased efficiency and sample volume of the lab. On a similar note, on the front end it is important that users are able to perform simple yet vital steps of the testing process with ease. In essence, usability is a diverse and constant priority that encompasses a wide range of the lab's essential processes, allowing the ABCTL to perform at the high level it currently attains. An invaluable component of this is the ability to provide its patients and partners a pleasant experience with clinical testing while accurately communicating and delivering the information they care about the most in this context: COVID-19 test results.

Conclusion

In retrospect, the ABCTL is an incredible and unique initiative that has displayed ASU's innovation at its best to help combat the COVID-19 pandemic. Deuser (2021) states it best: "the way that the ABCTL was born was an emergency." To be able to transform an academic research lab into a certified clinical testing lab in a matter of months is a remarkable feat that required many different aspects of the lab to operate in sync at a high level. There are many characteristics of the lab that are critical to its success, but its ability to adapt to new standards and needs is arguably the most important. The IT department is a major contributor to this ability, allowing the lab to meet the usability needs of both administrative and front-end users.

A key takeaway from learning from the ABCTL is to truly recognize and understand the importance of system usability as a vital component of the lab. With such a large-scale, ambitious project like the ABCTL, there are many opportunities for customization. Although this is an added benefit, it is imperative to ensure that these customizations are made with the end objective in mind: to provide COVID-19 testing in an efficient and accurate manner as a means of contributing to public health amid a deadly virus. Technology is an indispensable tool in accomplishing this and must be treated as such moving forward by valuing its usability and its ability to function smoothly and properly, features that should not be taken for granted. The reality of the concept of a quality user experience is that it is difficult to create the best, most optimized technological product the first time around to fully satisfy users. For that reason, numerous attempts and modifications such as enhancements and hotfixes are critical to this process, which also entails being receptive, responsive, and flexible when it comes to addressing feedback from a wide range of users of the ABCTL's systems. With this in mind, as a means of moving forward and potentially planning for future pandemic responses, it is imperative to recognize and analyze the ABCTL's many firsthand experiences regarding processes of trial and error, resulting usability improvements, and most importantly, responses to issues and the ever-growing needs of users and partners. These paramount factors continue to refine the ABCTL as an effective and efficient COVID-19 testing facility.

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Section IV: Automation

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Background

Clinical laboratories, facilities that perform tests on clinical specimens to obtain information about a patient, are a keystone in medical decision-making. They are essential for diagnosis, screening,prevention, treatment, and disease monitoring (Plebani, 2015). The clinical laboratory has been a nexus of technological evolution in the past few decades due to a shortage of qualified laboratory personnel,a focus on reducing costs in the healthcare system, and commitment to high-quality services (Ward et al., 1994). The greatest innovation of all, automation—the technique whereby a machine operates with reduced human interaction—has been a driving force of progress in modern clinical laboratories. Generally, clinical laboratory automation refers to the automation of a laboratory procedure or technique by use of an analytical instrument with minimal involvement of an analyst or laboratory technician (Hawker et al., 2017). However, clinical laboratory automation can also apply to non-testing or non-analytical processes, a development that has occurred only in the past two decades (Hawker et al., 2017). Currently, the global laboratory automation market size is valued at $4.8 billion as of 2018 and is projected to reach $8.4 billion by 2026 (Gill & Sumant, 2019).

With the increased availability of automated instruments and systems, clinical laboratories have experienced a variety of benefits. Labs are able to handle larger workloads without comparable increases in staff and face a reduction in the errors and variability of lab analysis by eliminating repetitive tasks (Hawker et al., 2017). Additionally, the ability to reproduce results with little variability through automation led to a significant improvement in the quality of laboratory tests (Hawker et al., 2017). Overall, automation has become an almost mandatory means of eliminating errors, improving quality, and reducing costs, and improving turnaround time. Now, in response to the COVID-19 pandemic, clinical laboratories and the use of automation are essential to providing patients and public health officials with expedient information about COVID-19 infection.

In Arizona, local clinical laboratories were hoping a low-cost COVID-19 diagnostic test would emerge and were hesitant to scale, basing their decisions on the market at the beginning of the pandemic (S. Dudley, personal communication, 2020). Additionally, local clinical labs had designated instruments for specific tests which then led to supply chain issues as testing grew in popularity and necessity around the globe (LaBaer, 2020). Due to these reasons, there was a vacuum for large-scale and high-throughput COVID-19 testing in Arizona.

In February 2020, President Michael Crow of Arizona State University (ASU) promoted the transformation of Dr. Joshua LaBaer's academic laboratory into a medical reference laboratory for the COVID-19 pandemic. The laboratory, located in the Biodesign Center for Personalized Diagnostics, was renamed the ASU Biodesign Clinical Testing Laboratory (ABCTL) and the university repurposed its entire platform to detect coronavirus infection in samples from individuals with the suspected virus. This drastic transformation spurred continuous changes to the underlying technological systems as the lab rapidly scaled up to meet testing demands. The rate of change was extreme, and many systems were under constant enhancement to meet user requirements and yield diagnostic test results in 24-48 hours. Given the unique circumstances of the lab, this chapter will cover the typical planning and implementation process for automation in the clinical laboratory space, the decision making for automation within ABCTL, and finally the current lab testing workflow with emphasis on prior process improvements.

Analytical Framework and Findings

Planning for Clinical Laboratory Automation

There are multiple ways to manage an automation project, but typically, a clinical laboratory develops a plan that addresses the needs of the entire organization (Kost, 1996). Laboratories must determine the type of services to offer and create a plan to achieve those goals through automation (Kost, 1996). Justification for automation implementation can be achieved by reducing turnaround time without incurring additional expense, reducing staffing costs or reagent costs, increasing test quality, and improving worker safety (Kost, 1996).

Environment Assessment

The first step to a strategic plan for automation implementation or expansion is addressing any internal or external factors that may affect the clinical laboratory environment. A strategic plan for automation should be derived from the vision of the parent organization, as undergoing rapid structural changes without the proper direction can be quite costly. Decisions affecting services, renovations, equipment purchases, and automation should be done in the context of a total organizational plan. An environmental assessment should also consist of any external factors like regulations, reimbursement policies, staffing, and the general healthcare environment (Kost, 1996). By analyzing the impact of internal and external environmental forces on each clinical laboratory operation, the vision of the organization should be developed enough to begin a blueprint for the lab's desired state (Kost, 1996).

Workflow Analysis

Once the mission of the laboratory has been established, there must be an audit of the laboratory workflow to gather laboratory requirements—mapping the current laboratory workflow from patient sample collection through to the reporting of results. The audit requires a comprehensive workflow analysis of all preanalytic, analytic, and postanalytic steps and is integral to recognize steps that are bottlenecks, a waste of labor, or are prone to error and should be considered for automation (Hawker et al., 2017). Time metrics can be a useful tool in this process to find bottlenecks or time wasters (Hawker et al., 2017). Types of workflow mapping include outlining the process of material flows or specimen transfer, the process flow, data flow diagrams at different grains of detail, and a workload map (*The Future of Laboratory Automation*, 2014). The three sections of lab workflow—preanalytic, analytic, and postanalytic — should be considered more in-depth when auditing the lab workflow for better strategic planning.

Preanalytic Phase

The preanalytical phase comprises all functions performed prior to instrument analysis. This generally includes operations in the specimen processing area like specimen ordering, sample collection, identification, transportation, centrifugation, aliquoting, and sorting (Ward et al., 1994). Time-based metrics can be used to audit the preanalytical phase, including time spent for computer entry, aliquoting, sample waiting, identification, and assuring specimen integrity (Perrotta et al., 2020). It has been previously shown that a majority of lab errors occur in the preanalytical phase, like inadequate sample quality, patient identification errors, and inappropriate containers (Hammerling, 2012). Recently, there have been significant progress in automating preanalytical activities to reduce errors in the process (Hawker, 2017).

Analytical Phase

Analyzers have seen major advancements in clinical laboratory automation and are the largest percentage of the automated instrument market (Kost, 1996). Analytic operations are all functions performed by an instrument, or analyzer, to produce test results (Ward et al., 1994). Analyzers can identify samples, perform tests, and report results with improved efficiency, reproducibility, and throughput when compared to their manual laboratory counterpart (Hawker, 2017). An analyzer is engineered based on the specific

laboratory test, testing environment, manufacturer hardware design, and laboratory information system required (Hawker, 2017). Thus, choosing appropriate equipment to enhance laboratory automation is based on the needs of the laboratory and instrument capabilities (Kost, 1996).

For strategic automation planning, there should be a focus on key analyzer characteristics like test volume, processing time and handling time, ease of use, and reagent system. Throughput, or the number of samples analyzed per unit time, is the most important feature to consider in an instrument (Chapman, 2003). Decision-making for this feature depends on the lab environment, for example, a commercial or hospital setting, and the known test volume for peak periods (Kost, 1996). The right automated system can improve lab throughput by increasing the batch size of a run, i.e., the number of samples analyzed at once, or decreasing the turnaround time, i.e., the time spent to process each sample or run (Hawker, 2017). Additionally, specimen processing time, the time from sampling to result is an important factor for lab productivity.

Reagents, substances used in an analysis, are a major cost component for determining instrument usability. Instrument manufacturers determine whether an automated analyzer or system will be "open" or "closed" in regard to the reagent compatibility (Armbruster et al., 2014). An open automated system allows a user to change parameters for the assay as well as obtain reagents and consumable supplies from alternative vendors. A closed automated system requires the owner to commit to purchasing only reagents and supplies from the instrument's manufacturer while other reagents cannot be used. The restrictions on a closed analyzer can be based on proprietary licensing, technical restrictions of reagents, reagent size and shape, and software compatibility (Hawker, 2017). Some advantages for a closed automation system are the convenience of dealing with a single vendor, minimal reagent preparation, improved reagent stability, and calibration stability, although a closed system may have higher operational costs due to a lack of competition (Hawker, 2017). Open systems have the benefits of increased flexibility, decreased costs, and the ability to optimize assay performance through customization (Hawker, 2017). Disadvantages of an open automation system include additional regulatory requirements for in-house developed tests or reagents and increased manual reagent preparation (Hawker, 2017). The key considerations for choosing an open or closed automation system are labor, skill level, and cost of the specific facility (Kost, 1996).

Postanalytic Phase

Postanalytic operations within a clinical laboratory include all functions performed after an analyzer reports its results. These functions include the reviewing of results, acknowledgement for retest, result reporting, transportation, storage, and clinical action (Ward et al., 1994). A significant number of errors can occur during this phase, such as incorrect interpretations of diagnostic results, incorrect data entry, and failure to report results (Hammerling, 2012). Result reporting is an integral factor for clinical laboratory automation, as lengthened turnaround time can undermine the success or improvement of any preceding step (Kost, 1996). Automation for result review can occur with the implementation of a rules-based expert system software. This software can automatically release results and alert analysts of problematic results (Hawker, 2017).

Implementatio

Workflow mapping thus enables the laboratory to better identify what steps should be considered for automation. Implementation is the final, critical step in strategic planning for clinical laboratory automation. This step requires a detailed plan that identifies lab resources, recognizes feasibility, initiates process change, necessitates communication between all stakeholders, and plans for reevaluation.

After the laboratory's existing workflow has been mapped and its requirements have been identified, alternative solutions are considered. The first key consideration of implementation is identifying alternative solutions in the laboratory workflow for potential areas of reengineering. Improving poor processes should happen prior to the introduction of automation in the workflow, as automating the solution will just reiterate

poor performance and could be more costly (Hawker et al., 2017). Considering this, automation is not the solution to all steps in the workflow; a small low-cost reengineering project may have more impact on performance and productivity than an expensive automated replacement (T*he Future of Laboratory Automation*, 2014). Any solution, alternative or automated, that is selected for the laboratory should be emphasized on process control and process improvement. Eliminating unnecessary steps or non-value-added processes can prevent rework caused by systemic errors (Kost, 1996).

Environment Assessment

The COVID-19 pandemic was a global public health challenge with shortages of available tests, limited testing sites, and a surge of rising cases. The Arizona State University Biodesign Clinical Testing Lab (ABCTL) was created with a mission to serve the local community, repurposing a research facility into an established diagnostic laboratory during a crisis. The lab was able to use their existing expertise in molecular testing, diagnostics, robotics, and regulatory knowledge to produce a high-throughput diagnostic testing pipeline for detecting SARS-CoV-2.

Arizona State University (ASU) was poised to meet the challenge of the pandemic, ranked sixth in the nation for research expenditures in public institutions, the public university had the resources and leadership to respond to the pandemic (ASU Knowledge Enterprise, 2021). ASU President Michael Crow approached the leader of the Center for Personalized Diagnostics at ASU, Dr. Joshua LaBaer, to transform his research facility into a clinical testing laboratory to serve ASU students and the Arizona community during the crisis. Dr. LaBaer was able to repurpose existing equipment and personnel from a prior project with the US Department of Defense's Biomedical Advanced Research and Development Authority (ASU Research Project, 2018). The defense project was focused on developing tests to rapidly measure radiation exposure in a population in the event of a nuclear emergency, using real-time polymerase chain reaction and automation (ASU Research Project, 2018). Through this project, LaBaer had the equipment, faculty experts, and the knowledge to transition to COVID-19 testing.

Converting a research facility into a medical testing laboratory with expediency would present multiple challenges including state and federal regulations, supply-chain difficulties, and extended service to the general public of Arizona. To undertake this monumental task, specialized teams were created for sample procurement, virus testing, automation, database tracking, participant portal, contact tracing, regulatory clearance, communications, and partnerships (ABCTL, 2020). ASU Knowledge Enterprise, the ASU center for research and economic development, was incorporated to address the economic logistics of laboratory development. The leadership of President Crow, ASU Knowledge Enterprise, and Dr. LaBaer would provide influencing decisions for the direction of the lab.

State and federal regulations were a key feature in decision-making for creating the rapid SARS-CoV-2 test implementation. In February 2020, the Secretary of Health and Human Services declared that current circumstances justified the development of in vitro diagnostics for COVID-19 (U.S. Centers for Medicare & Medicaid Services, 2020). The US Food and Drug Administration (FDA) subsequently issued the Emergency Use Authorization (EUA) for the development of COVID-19 diagnostic tests from authorized public health laboratories (FDA, 2021). With these latest federal developments, ABCTL was able to develop a federally approved and validated diagnostic test under the EUA for immediate implementation. Timeliness during the pandemic also allowed local regulatory approvals like the International Building Code (IBC) for the development of the new testing facility and Institutional Review Board (IRB) for biomedical research to be fast-tracked (ABCTL, 2020). Federal licensing procedures under the Centers for Medicare & Medicaid Services' Clinical Laboratory Improvement Act (CLIA) were a huge undertaking for the laboratory. The CLIA program regulates all clinical laboratories in the United States to ensure high-quality laboratory testing (U.S. Centers for Medicare & Medicaid Services, n.d.). Dr. Carolyn Compton, a trained clinical pathologist and current medical director for ABCTL, was chosen to guarantee that the lab

adhered to CLIA standards. Requisitioning and results reporting were developed in compliance with CLIA and the Health Insurance Portability and Accountability Act (HIPAA).

As a newfound clinical testing laboratory with high throughput and full regulatory oversight, organizations were eager to partner with ABCTL. In its initial stages, ABCTL was focused on essential workers and vulnerable populations, creating partnerships with over a dozen organizations. Internal partnerships with ASU Health Services and University Housing were integral for testing the student population and informing university-wide decision-making.

Notable partnerships like the Arizona Department of Health Services and Arizona Department of Administration were developed to expand public testing across the state (Arizona Board of Regents, 2020). Partnerships with various organizations could influence leadership decision-making as ABCTL became beholden to multiple stakeholders. The downstream effects of the growing organization would later impact decision-making for automation.

Decision Making for ABCTL

Lab Costs

Typically, clinical laboratories are managed with cost-effectiveness in mind and ABCTL is no exception. However, in regular clinical laboratories, potential profits and the use of cost-benefit analyses are the driving focus of lab creation. For ABCTL, profitability was an afterthought; instead, the mission to serve the public was the forethought, allowing for extreme flexibility in determining lab costs. In its initial phase, lab costs were centered on the technical needs for diagnostic testing, creation of the facility, and operations from collection to result reporting. After the process was cemented, the lab focused on profitability and then scalability, even at the likelihood of lowered profits, to ensure the laboratory operations were sustainable at scale.

Initial disregard to lab profitability was also due to the favorable monetary situation of the university prior to the creation of ABCTL. A subset of $210 million from the Arizona Board of Regent's Technology and Research Initiative Fund allowed the ASU Biodesign Institute to grow substantially and leverage that initial investment into additional funding (Arizona Board of Regents, 2020). Strong monetary support allowed for the creation of the Biodesign Virginia G. Piper Center for Personalized Diagnostics, and thus by proxy, ABCTL. The movement to kickstart ASU's COVID-19 testing lab was directly funded by the Virginia G. Piper Charitable Trust for $2 million dollars and the lab was able to grow substantially from then on through partnerships and revenue (Caspermeyer, 2020)

Lab revenue has been a unique situation, but it has allowed the lab to cover the costs of automation and equipment. The ABCTL is a public entity funded by the state and public money, thus it is required by law that the institution cannot compete with private enterprise (Arizona State Legislature, n.d.). Typically for a university, research laboratories are grant-funded or there is a cost-reimbursement arrangement with the government. Since there are private entities offering COVID-19 testing in the market, the ABCTL cannot undercut testing prices; instead, it must keep it at a competitive price point due to its position as a public institution (Deuser, 2021). The ABCTL's ability to charge more than the cost of testing is a primarily unique situation to the lab in comparison to other academic operations. A benefit to this is that the lab's revenue has been able to supplement general university funding, which has suffered substantially from tackling the COVID-19 pandemic (Deuser, 2021). The lab's unique situation allows for revenue to exceed the cost of keeping testing operations afloat and provides stability for addressing the challenge of supply chain during a pandemic (Deuser, 2021).

In fact, current testing operations are running at substantially lowered costs compared to other testing laboratories in the state. The total cost to process a sample for ABCTL is approximately 40% of the average cost for other established clinical laboratories due to a variety of factors (I. Shoemaker, personal

communication, March 12, 2021). By leveraging long-term relationships with vendors, the lab was able to purchase equipment at favorable prices, as well as prioritize their needs to the manufacturer (I. Shoemaker, personal communication, February 3, 2021). With a limited time to scale, the lab was submitting orders for equipment faster than the manufacturer could create them, even obtaining and automated sample labeler built specifically for the lab (I. Shoemaker, personal communication, February 3, 2021). The clinical testing laboratory has also been able to purchase Beckman Coulter robotics as soon as they are available with an additional bonus of academic discounts (I. Shoemaker, personal communication, February 3, 2021). Overall, the cost of all equipment to process samples in current ABCTL operations has been estimated at $2.8 million with increased savings in regard to reagent and consumable costs (I. Shoemaker, personal communication, March 12, 2021). For example, the lab has been able to use 2.27 tips per sample, where the industry average is 6.3, because the lab reuses tips to pipette the same samples at appropriate places in the workflow process (I. Shoemaker, personal communication, March 12, 2021). The lowered costs for testing were extremely beneficial for university funding and sustainability for testing and ultimately derived from the initial decision to keep an open automated system.

Evaluation Criteria for Automation Implementation

It was determined by leadership from the very beginning that the automation for ABCTL was going to be "open" for a variety of reasons. A defining factor was the supply chain issues that were occurring across the globe, affecting testing laboratories that were beholden to their closed instruments and premade testing kits (Woolston, 2021). Building an open automated system from the start allowed extreme flexibility and ability to redesign the system at a moment's notice. For example, the lab began with nasopharyngeal swabs to test for COVID-19 and later pivoted towards saliva testing to overcome obstacles with swabs (LaBaer, 2020). The open automated system allowed the ABCTL to consistently deliver testing results without having to stop their workflow from lack of reagent availability or other supplies for their automated instruments (LaBaer, 2020). There was also the benefit of using automated instrumentation and its increased likelihood for purchase availability and lack of competition, like Beckman Coulter liquid handling robots, that other labs were not usually using to test for COVID-19 (I. Shoemaker, personal communication, February 3, 2021). However, with an open automation platform, the ABCTL required additional staffing in comparison to other all-in-one diagnostic instruments (I. Shoemaker, personal communication, March 12, 2021).

The specific evaluation for automation implementation is highly dependent on the focus of the lab, as mentioned prior, but the general idea for implementation within the ABCTL is similar to the typical thought process. Improved turnaround time was paramount for automation evaluation, as it usually is when planning for automation, but it was further emphasized due to the emergency of the situation (C. Compton, personal communication, September 1, 2020). The principal lab systems automation engineer, Ian Shoemaker, was also concerned with process fidelity, meaning the extent to which automation will actually realize gains in the laboratory workflow. As said prior, re-evaluating alternative solutions to the laboratory workflow is crucial in automation implementation and some automated systems may be slower overall due to increased handling of nonconformance alerts (I. Shoemaker, personal communication, February 3, 2021). Similar to typical clinical automation, Shoemaker identified points in the laboratory process that are highly repetitive for lab personnel or may have a higher likelihood for human mistakes at larger testing scales (personal communication, March 12, 2021). Critical transfers, the act of moving liquid in precise volumes, were the specified steps of focus in the laboratory process for ABCTL. Robots were ideal to guarantee sample tracking and precise measurements during these steps and non-critical transfers were relegated to the technicians (I. Shoemaker, personal communication, February 3, 2021).

Evaluation for Instruments

Automation implementation cannot occur without a strict evaluation of the robotics or instruments that perform the process. For the ABCTL, the first step in evaluation is that the instrument is an open system and thus can be tailored or integrated into their existing open automation (I. Shoemaker, personal communication, February 3, 2021). This is also to assure that the instrument can be flexible regarding changing leadership decisions or project scope (I. Shoemaker, personal communication, March 12, 2021). The next step is determining that the instrument is designed to perform the lab's specific process in the workflow and meet the minimum feasibility criteria for that process. Considering the extremely short time period, the instrument must be able to meet current goals like 20,000 samples a week, as well as be flexible in growth to meet future goals like 100,000 samples in a few months. During this thought process, the automation engineer for ABCTL must be able to anticipate leadership and ensure that the proper equipment is in place to meet those goals (I. Shoemaker, personal communication, February 3, 2021). Additionally, identifying the feasibility of the instrument prior to contacting the manufacturer allows the buying process to be shortened, a significant importance when considering the time constraints of the pandemic (I. Shoemaker, personal communication, February 3, 2021). Then the ABCTL engineer checks the pedigree of the company, unless the instrument is created by a manufacturer with a pre-existing relationship with ABCTL. The lifetime cost of ownership is then identified alongside current funding outlooks for the ABCTL. Ensuring a secure supply-chain and the usefulness of the technology in the upcoming years is required since instruments are bought for the long-term. The length of this entire thought process is heavily dependent on the initial cost; for example, a $5,000 barcode scanner is decided upon faster than a $600,000 liquid handler. But once the system criteria have been evaluated, the lab creates a request for proposal and the buying process is initiated.

ABCTL Workflow

Overview

Considering that the ABCTL came from a prior established research project, workflow mapping was not done as part of the development process—it was done ad hoc, or when needed. The expert lab personnel were familiar with polymerase chain reaction (PCR) workflow used for the testing process and had knowledge of scaling through the BARDA project. Instead, workflow mapping was used as an internal tool to create actionable policy and report laboratory metrics to funding agencies, the general public, and other scientific collaborators (I. Shoemaker, personal communication, March 12, 2021). Currently, the theoretical 24/7 capability of ABCTL is approximately 14,000 samples a day (I. Shoemaker, personal communication, March 12, 2021). Reaching this capacity occurred through incremental automation implementation and continues to improve.

Reverse Transcription Quantitative Polymerase Chain Reaction (RT-qPCR)

SARS-CoV-2 is a single-stranded RNA virus that can be detected through a molecular biology technique called RT-qPCR (FDA, 2020). The COVID-19 RT-qPCR diagnostic test quantitatively determines if a respiratory specimen, such as saliva, contains the SARS-CoV-2 genetic material and thus if a patient has been infected with the disease (FDA, 2020). The process of the RT-qPCR test starts with the extraction of viral RNA from a sample. Then the RNA is reverse transcribed into complementary DNA (cDNA) using an enzyme called reverse transcriptase (Neidler, n.d.). This DNA is then amplified by a repeated process of denaturing the nucleic acids, annealing the DNA strands with primers, and then elongating the DNA strands through Taq polymerase. The use of fluorescent labels to collect DNA data as PCR progresses allows for quantitative analysis (Neidler, n.d.). The ABCTL was granted an EUA by the FDA for creating its own protocol for the RT-qPCR test and improvements have been made incrementally to automate the test and increase sample throughput.

Table 1: Sample Processing Workflow

Extract RNA	RT-qPCR	Analyze Data	Data Reporting
Automated RNA extraction in 96-deep-well plates by a KingFisher Flex	Automated RT-qPCR plate set up by a Beckman Coulter™ liquid handling robot into a Taqman 384-well plate. qPCR using Applied Biosystems™ QuantStudio Dx	Custom LIMS software from US Department of Defense's BARDA and further customized by ABCTL	LIMS data transfer to PnC that sends reports out to partner agencies and contacts participants by text message or email.

Note. This table describes the basic phases of sample processing and its associated instruments that comprise the ABCTL's COVID-19 diagnostic test.

Point and Click (PNC) and Laboratory Information Management System (LIMS)

To support the logistics of test ordering, sample collection, sample identification, sample tracking, and result reporting, the ABCTL used a pre-existing electronic health record (EHR) provider called Point and Click Solutions and a custom LIMS system to integrate into their open automated system with regards to lowered costs and HIPAA compliance.

At first, there was a custom EHR built for the lab at its start, however, they quickly pivoted toward PNC as a commercial end-to-end solution due to its advanced capabilities and the company's pre-existing relationship with ASU Health Services (Deuser, 2021). The CEO of PNC, David Tan, also expressed interest in partnering with ABCTL to customize the pre-built system into a solution for mass testing operations during the crisis (S. Dudley, personal communication, 2020). Currently, PNC has the capability to create the schedules for appointments at all the collection sites, ability for participants to create their own appointment through a patient portal, a custom mass tester application for staff to use at collection sites, built-in test sample accessioning, population metric reporting, specialized report generating for individual partner agencies, result reviewing, and result reporting through text message and email (Tinnin, 2021). A custom Application Programming Interface (API) allows a manifest, or data report, of the expected sample numbers from a collection site to be sent from PNC and retrieved by the lab's LIMS (Tinnin, 2021).

The LIMS was initially created through the BARDA project and further customized by ABCTL to ensure efficient sample tracking and HIPAA compliance. The LIMS is constituted of a HIPAA-compliant database, a custom implementation built by ASU data scientists and programmers to accommodate data logistics and transfers within the laboratory (I. Shoemaker, personal communication, March 12, 2021). Additionally, de-identified patient barcodes are used within the LIMS at all times, reducing the likelihood for patient privacy issues (S. Dudley, personal communication, 2020). For detailed sample tracking, the LIMS uses a watchdog software called DART (Data Acquisition and Reporting Tool) created by Beckman Coulter. This program monitors all activity of sample manipulation on the lab's robotics and transforms them into readable reports for analyst verification. Once the test analysis is done, the LIMS returns de-identified barcoded results through another custom API to be extracted by PNC for data reporting. Within this step, lab results are connected to their counterpart patient record through barcode matching and the participant finally receives their diagnostic test result.

Preanalytic Phase: Collection Sites

Key Process Improvements

A significant bottleneck at the start of ABCTL testing was the ability to obtain samples at an efficient rate. Nasopharyngeal swabs were swiftly replaced by saliva samples to overcome this challenge, reduce staffing, and increase staff safety (Adaptable team brings hope to Arizonans during pandemic, 2020). Initial sample collection also faced major changes with the development of specific saliva instructions for both participants and clinical staff to guarantee samples were of good quality to improve upstream sample processing (I. Shoemaker, personal communication, March 12, 2021). Sample transport was improved, albeit not automated with robotics, by standardizing shipping conditions and sample handling (I. Shoemaker, personal communication, March 12, 2021). The implementation of Devils' drop-off, a process whereby a participant picks up a saliva sample kit and then drops it off at a designated location on ASU campus, was also an improvement to decrease the need for staffing and scheduled appointments (S. Dudley, personal communication, 2020).

Workflow Description

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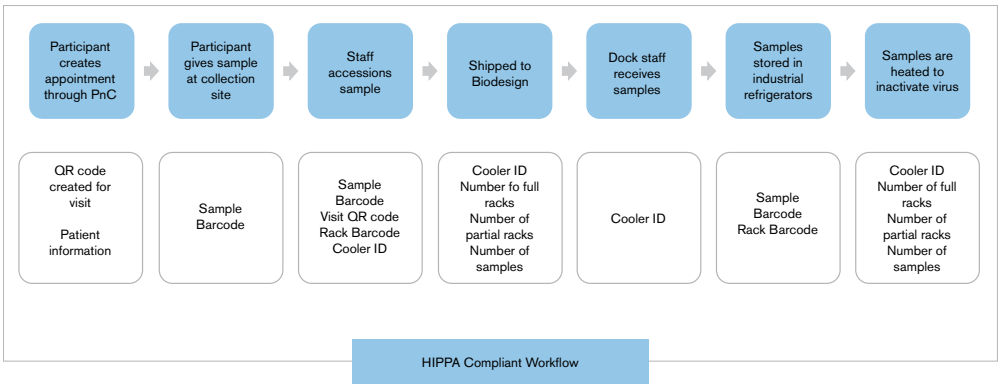
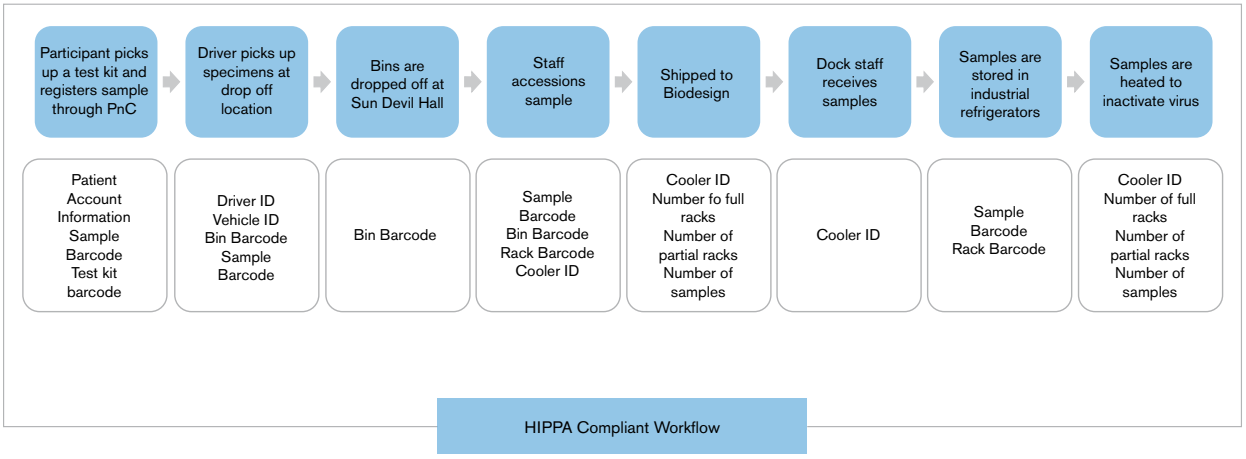
To safely store the collected samples, disinfected, portable styrofoam coolers are packed with absorbent material, ice packs, and leakproof plastic containers (M. Nelson, personal communication, December 18, 2020). The tubes, now with live participant samples, are then racked and sealed inside a secondary container to be transported back to the clinical testing lab (M. Nelson, personal communication, December 18, 2020). During transport, the tubes are monitored for temperature changes with an attached thermometer in each cooler for quality control purposes (M. Nelson, personal communication, December 18, 2020). Additionally, to ensure each sample is accounted for, chain of custody paperwork is required with the filled coolers during the shipping process (M. Nelson, personal communication, December 18, 2020).

Diagram 1



Sample Handoff from Collection Site

Diagram 2



Sample Handoff from Devils' Drop-off

Table 2 Necessary Lab Equipment

Step	Items
Sample Acquisition	▪ Saliva in a 5mL Micronics tube labeled with a Sci-Print™ VX2 labeler ▪ HeraTherm™ Incubator IMH180 at 65C for an hour
Accessioning	Beckman Coulter™ Biomek i7 Automated Workstation

Note. This table describes the preanalytic phases and its associated instrumentation after a sample is collected at the ABCTL.

Preanalytic Phase: Sample Acquisition

Key Process Improvements

Sample tubes were changed throughout ABCTL development for supply chain reasons and improved automation with barcode identifiers, with current automated systems using Micronics 5mL tubes (V. Harris, personal communication, October 23, 2020). Sample storage also improved with the implementation of specialty refrigeration and industrial refrigerators to guarantee sample stability and quality for later processing (I. Shoemaker, personal communication, March 12, 2021). For increased throughput, additional incubators were purchased (K. Majhail, personal communication, March 11, 2021).

Workflow Description

A VX2 labeler robot creates individual labels for the Micronics 5ml tubes that will eventually contain the saliva sample (M. Nelson, personal communication, December 18, 2020). Once the tubes return with live saliva samples, they are taken to the loading dock at Biodesign Institute (V. Harris, personal communication, October 23, 2020). The lab can verify the incoming sample numbers with a list of sample information generated from each collection site through PNC, ensuring that the exact number of expected samples has arrived (M. Nelson, personal communication, December 18, 2020). If there are discrepancies, the lab team uses PNC to verify that all patient records that have been scanned have actually been sent out from the collection site (M. Nelson, personal communication, December 18, 2020). This is a quality control process that minimizes the possibility that samples are accidentally unaccounted for at any step of transit (M. Nelson, personal communication, December 18, 2020).

Samples are brought to the “Intake and Heat Inactivation Facility”, a suite of rooms under biocontainment where the tubes are processed (V. Harris, personal communication, October 23, 2020). A team of ABCTL employees in the appropriate PPE unpackage the samples from the coolers and ascertain if all the samples are valid, i.e., lids screwed on, no leaks, correct temperature (V. Harris, personal communication, October 23, 2020). The specimens are manually scanned by the intake team to produce a file with locations of each sample in a rack (I. Shoemaker, personal communication, February 3, 2021). Then samples are immediately stored within specialty refrigeration (K. Majhail, personal communication, March 11, 2021). When the samples are ready to be processed, they are heated at 65C for an hour in the HeraTherm Incubator IMH180 to neutralize the live SARS-CoV-2 virus (V. Harris, personal communication, October 23, 2020). Once they are at a lesser bio-safety hazard, employees at the processing facility will then check the samples for empty specimen tubes, foreign objects within a sample, and sample quality (K. Majhail, personal communication, March 11, 2021).

Preanalytic Phase: Accessioning

Key Process Improvements

A major automation improvement was the implementation of the Brooks Life Sciences FluidX IntelliXcap™ 24-Format Screw Cap Tube Rack Decapper/Capper and the Brooks Life Sciences FluidX Perception™ HD Whole Rack Reader integrated within the Beckman Coulter™ Biomek i7 Automated Workstation. Prior to this automation, lab technicians had to manually uncap and recap every patient specimen and then manually accession every tube (V. Harris, personal communication, October 23, 2020). Earlier in the lab’s testing process, an older model, Beckman Coulter™ Biomek FXP Laboratory Workstation, was used as a task-targeted implementation to aliquot samples from tube to well-plate (K. Majhail, personal communication, March 11, 2021). Later, this older model was replaced by its newer flagship model, Biomek i7, for this task, improving automated workflow (I. Shoemaker, personal communication, February 3, 2021). To increase testing capacity and throughput, ABCTL also purchased additional Biomek i7s (Deuser, 2021).

Workflow Description

A batch of up to 94 saliva specimens is placed within the Biomek i7 and automatically accessioned into the LIMS by the Whole Rack Reader (I. Shoemaker, personal communication, February 3, 2021). Still within the Biomek i7, the Decapper/Capper uncaps a rack of tubes and the Biomek i7 liquid handler robot aliquots 200µL of each specimen into a 96-well deepwell extraction plate (I. Shoemaker, personal communication, February 3, 2021).

Although a major improvement to the preanalytic workflow, the Decapper/Capper had initial problems with implementation. The most critical problem was that the robot did not fail-safe (I. Shoemaker, personal communication, February 3, 2021). The robot would eject a problem sample from a rack without decapping or recapping them, as it did not have a way to deal with individual failures. This issue was quickly solved with firmware changes (I.

Shoemaker, personal communication, February 3, 2021). Another challenge occurred when a sample was not fully decapped by the machine and instead was lifted up from the rack by its cap (I. Shoemaker, personal communication, February 3, 2021). The solution to this challenge was engineering the robot to lift the caps about 5 to 10 millimeters and then moving the rack forward to knock off any tubes stuck to their caps (I. Shoemaker, personal communication, February 3, 2021).

Table 3 Analytical Lab Equipment

Step	Items
RNA Extraction	Thermo Fisher MagMAX Viral/Pathogen Nucleic Acid Isolation Kit using KingFisher™ Flex Purification System, standalone on lab bench
Assemble qPCR	Beckman Coulter™ Biomek i7 Automated Workstation
Run qPCR	Thermo Fisher™ TaqPath RT-PCR COVID-19 Kit and Applied Biosystems™ QuantStudio Dx Real-Time PCR Instrument

Note. This table describes the analytic phases and its associated robotics to perform the quantitative polymerase chain reaction diagnostic test for COVID-19 at ABCTL.

Analytic Phase: RNA Extraction

Key Process Improvements

To increase testing capacity and throughput, ABCTL purchased additional KingFisher Flex systems (Deuser, 2021).

Workflow Description

Every extraction plate contains one negative extraction control, one positive extraction control, and an internal control of MS2 phage to monitor RNA extraction. A positive control is composed of DNA representing a specific gene of SARS-CoV-2 and verifies that the assay is performing as intended. A negative control has no extracted nucleic acid and monitors for any cross-contamination that occurs during the RT-PCR process. An internal control, MS2 phage, is needed to verify that nucleic acid is present in every sample and is added to every sample (Viracor Eurofins Clinical Diagnostics, 2020).

The Biomek FXP uses the MagMAX™ Viral/Pathogen Nucleic Acid Isolation Kit to add 5µL of Proteinase K to each sample well, 200µL of nuclease-free water to the negative control well, 5µL of MS2 Phage control to each sample well and the negative control well, and a 275µL of bead mixture to each sample well in the 96-well extraction plate.

Once the extraction plate is mixed with the reagents, it is placed within a KingFisher™ Flex Purification System. The KingFisher Flex uses additional reagents from the MagMAX™ Viral/Pathogen Nucleic Acid Isolation Kit and extracts RNA from each patient sample. After the run is complete, a 96-well elution plate with 50µL of eluted RNA sample in each well is produced.

Analytic Phase: Assemble qPCR

Key Process Improvements

Earlier in ABCTL diagnostic testing workflow, the Biomek FXP was used to aliquot samples from four 96-well plates to a combined 384-well plate (K. Majhail, personal communication, March 11, 2021). Later, this older model was replaced by its newer flagship model for this task, Biomek i7 (K. Majhail, personal communication, March 11, 2021).

Workflow Description

Following RNA extraction, the Biomek i7 Automated Workstation performs RT-qPCR reaction setup using Thermo Fisher's TaqPath RT-PCR COVID-19 Kit by consolidating four 96-well elution plates into one

384-well plate with RT-qPCR mix. After the Biomek i7 adds positive and negative PCR controls, the 384-well plate is moved to a QuantStudio Dx Real-Time PCR Instrument for RNA detection.

Analytic Phase: Perform qPCR

Workflow Description

Purified nucleic acid is reverse transcribed into cDNA and PCR amplified using the TaqPath™ RT-PCR COVID-19 Kit and the Applied Biosystems™ QuantStudio Fast Dx.

Real-Time PCR instrument. Probes anneal to three specific SARS-CoV-2 target sequences for ORF1ab, N Protein and S Protein Genes (ABCTL, 2020). The probe is hydrolyzed during primer extension and amplification and the severing of the probe results in an amplification-dependent increase in fluorescence (Neidler, n.d.). Thus, the fluorescence signal from the qPCR reaction is proportional to the amount of the probe target sequence, or SARS-CoV-2 viral genome, present in the sample and reflected as a graph in QuantStudio Dx.

Image 1 QuantStudio Dx qPCR Graph Results

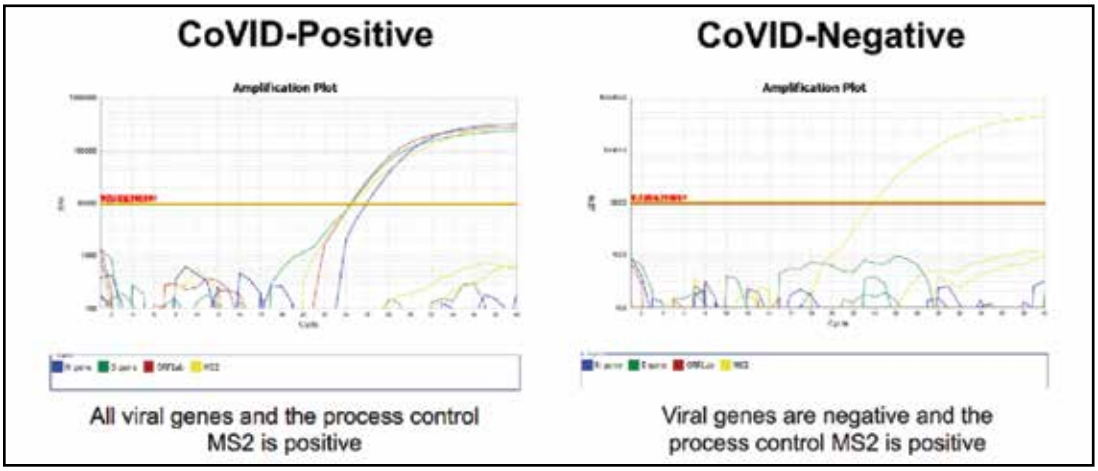


Image 1. Example of the quantitative graph from a qPCR analyzer. Image taken from ABCTL 2020 Presentation. Retrieved from https://chs.asu.edu/sites/default/files/asu_biodesign_clinical_testing_laboratory_rev20200417_up l20200518.pdf.

Throughout the assay, information is constantly being sent to the LIMS. Samples are accessioned by the Biomek i7 and securely transferred to the LIMS within a HIPAA-compliant database. The sample location information from the Biomek i7 384-well plate is extracted from the LIMS to the QuantStudio Dx, which then uses the Biomek i7 descriptive information to run the qPCR analysis and display results.

Postanalytic Phase

Key Process Improvements

DART software tracks and creates timestamped barcodes of the sample throughout the test workflow, allowing for improved quality control measures as well as a process improvement for result reviewing and retesting (I. Shoemaker, personal communication, March 12, 2021). For example, if a test result is invalid, then analysts can check testing metrics and ensure the assay is producing the correct data at certain process checkpoints. Automatic report generating within PNC for partners to see their population testing metrics was also an improvement to automatic result reporting (A. Douglas, personal communication, January 28, 2021).

Workflow Description

The lab director or manager manually interprets the results from QuantStudio Dx and can approve its result interpretation, assign the robot a different action, enter a comment about the test results, or retest a sample (M. Fiacco, personal communication, February 4, 2021). If the internal control, MS2 phage, is not present from the analysis, this marks the test as invalid, as there may be an issue with the sample or a mistake during analysis. If the internal control is present but the SARS-CoV-2 targets are not found during the assay, then the result is reported as negative. When only one SARS-CoV-2 target is quantified at high abundance, the test is considered inconclusive and will need to be retested. A high amount of viral genome found for two or more targets is considered a positive result for the viral disease.

Once test results are approved by the lab scientist, it is extracted through an API by PNC for data reporting. Within PNC, the ABCTL medical director must manually approve testing results, as they are legally responsible for the result validity and ensuring the proper result is sent to the correct patient (C. Compton, personal communication, September 1, 2020). Centers for Disease Control and Prevention, CLIA, and state reporting requirements are all automatically adhered to within PNC (C. Compton, personal communication, September 1, 2020). Participants receive a secure report on their result through text messaging or email, instructions for further action, and automatic contact tracing if a positive result is affiliated with ASU (C. Compton, personal communication, September 1, 2020). After the testing process is finished, the lab autoclaves all the samples to neutralize all remaining material in the sample and a third-party vendor disposes of the used tubes (M. Nelson, personal communication, December 18, 2020).

Lab Workflow Conclusion

The workflow for ABCTL's diagnostic testing has been incrementally automated for high throughput and faster turnaround time, although it can still be improved. The automation engineer, Ian Shoemaker, wishes to split future attention for process improvement at 60% preanalytical, 30% postanalytical, 10% analytical (I. Shoemaker, personal communication, March 12, 2021). The reasoning for this is that the preanalytical phase is more error-prone and at times cannot be resolved when a specimen has arrived for analysis (I. Shoemaker, personal communication, March 12, 2021). Ideas for continuous process improvement are ever-flowing and will be prioritized on the needs of the lab as it continues to face the COVID-19 pandemic.

Conclusion

The COVID-19 pandemic has spurred massive changes for the clinical laboratory space. Clinical laboratories, already a keystone in healthcare, have proven their worth tenfold during this crisis. However, it has also revealed the lack of preparedness for clinical laboratories to face any drastic changes, supply chain issues, or increased scaling to their testing operations. The development of ABCTL was a rapid transformation, diverging from typical clinical laboratory planning, and created from the serendipitous circumstances of funding and expertise at ASU.

From the outset, the ABCTL had to solve immediate problems, evolving their laboratory vision to fit the particular needs of the community and the public health department. Automation decisions were considered to be the best course of action that were possible at that time, especially considering that the COVID-19 pandemic disrupted normal laboratory services. Transferring the development knowledge of ABCTL for other crisis situations may be unrealistic if there are a different set of challenges to solve. However, its forefront mission to serve the community with altruism first and then successfully introduce profitability may fundamentally shift the profit-based enterprise of existing institutions.

Section IV: References

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Chapter 3: Appendix

Automation Defense Presentation

The Making of a COVID-19 Testing Laboratory

Automation within a SARS-CoV-2 Clinical Testing Laboratory

Arizona State University

Sabrina Woo | Barrett, the Honors College
Carolyn Compton, MD, PhD | ASU School of Life Sciences
Sean Dudley | ASU Knowledge Enterprise
April 5th, 2021

Agenda

- Background
- ABCTL Development
- Decision Making for Automation
- Automated Workflow
- Conclusion

Background

- Novel coronavirus SARS-CoV-2 became a global health emergency, aka COVID-19 pandemic
- Causes acute respiratory syndrome
- Transmission through cough, sneeze, or contact transmission through mucous membranes
- Large-scale testing important:
  - asymptomatic cases
  - high rates of transmission

Background

- COVID-19 pandemic in Arizona
- Vacuum for COVID-19 testing in Arizona
- ASU Biodesign Clinical Testing Laboratory (ABCTL)

Purpose

- To document the ABCTL's response to the pandemic
- Information Technology: **Automation,** Usability, Data Security, Data Decisions
- Part of a larger work: Laboratory, Business, Communications, Law, and Quality Management
- Documentary

Name	ABCTL Role
Sean Dudley	Assistant Vice President and Chief Research Information Officer for the Research Technology Office at Knowledge Enterprise
Ian Shoemaker	Principal lab systems automation engineer
Alma Douglas	COVID Operations Team Lead
Morgan Nelson	Head of quality management
Dr. Amit Sharma	Scientific software engineer
Kevin Tinnin	Technology architect
Timothy Lant	Lead epidemiologist and Director of Program Development for ASU Knowledge Enterprise
Tamara Deuser	Vice President and Chief Operating Officer for ASU Knowledge Enterprise
Michael Fiacco	IT Manager for the Center of Personalized Diagnostics
Dr. Carolyn Compton	Medical director
Dr. Valerie Harris	Lab manager
Kajol Majhail	Lab technician

ABCTL Development

Environment Assessment

- Mission to serve the local community
- US Department of Defense's Biomedical Advanced Research and Development Authority (BARDA)
- Federal and State Regulations

Point and Click (PnC)

- PnC as a commercial solution
- PnC capabilities

Lab Information Management System (LIMS)

- Initially created through the BARDA
- Ensure efficient sample tracking and HIPAA compliance
- De-identified patient barcodes

Decision Making for Automation

Lab Costs

- Typical: Clinical laboratories and cost-effectiveness
- Initial disregard to lab profitability -> Serve the public
- Monetary situation of ASU
- Lab revenue

Evaluation for Automation Implementation

- Open automated system
- Improved turnaround time
- Process fidelity
- Repetitive Processes

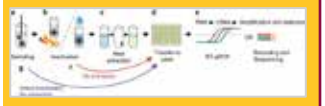
Evaluation for Instruments

1. Open system
2. Designed to perform lab process and meet the minimum feasibility criteria
3. Pedigree of the company
4. The lifetime cost of ownership

Automated Workflow

RT-qPCR

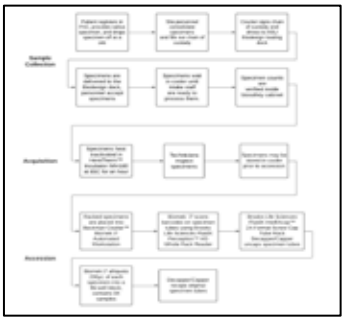
- The COVID-19 RT-qPCR diagnostic test
- RNA extraction -> complementary DNA (cDNA) -> qPCR
- Denaturing, Annealing, Elongating
- Quantitative analysis through fluorescent primers



Smyrlaki et al., 2020

Preanalytic

Comprises all functions performed prior to instrument analysis

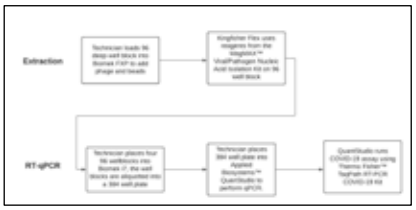


Preanalytic

Step	Process Improvements
Sample Collection	• Nasopharyngeal swabs to saliva samples • Specific saliva instructions • Improved sample transport • Devil's Drop Off
Sample Acquisition	• Sample tube changes • Improved sample storage • More incubators
Accession	• Brooks Life Sciences FluidX IntelliXcap™ 24-Format Screw Cap Tube Rack Decapper/Capper • Brooks Life Sciences FluidX Perception™ HD Whole Rack Reader integrated within the Biomek i7 • Beckman Coulter™ Biomek FXP Laboratory Workstation to Biomek i7 • Additional Biomek i7s

Analytic

All functions performed by an instrument to produce test results

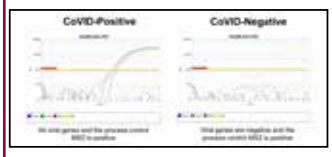


Analytic

Step	Process Improvements
RNA Extraction	• Additional KingFisher Flex systems
Assemble qPCR	• Biomek FXP replaced by Biomek i7
Run qPCR	• Additional QuantStudio machines

Postanalytic

All functions performed after an analyzer reports its results



ABCTL, 2020

Postanalytic

- Biomek i7 software tracks and creates timestamped barcodes of the sample throughout the test workflow
- Automatic report generating within PnC

Conclusion

Conclusion

- Automation engineer: future process improvement at 60% preanalytical, 30% postanalytical, 10% analytical
- Automation is a necessity

Acknowledgments

Questions

Usability Defense Presentation

The Making of ASU Biodesign Clinical Testing Laboratory (ABCTL):
The User Experience of Interfaces and Systems of the ABCTL

Michael Leung | Barrett, The Honors College
Carolyn Compton, MD, PhD | ASU School of Life Sciences
Sean Dudley | ASU Knowledge Enterprise
April 5, 2021

Agenda

- Background
- What is "user experience?"
- Overview of usability across IT systems
  - With examples
- Hotfixes, enhancements, and customizations
  - With examples
- Acknowledgements

Background

- The ABCTL is a traditional research lab transformed into a SARS-CoV-2 clinical testing lab
- Information technology (IT) systems were essential for its success
- Systems are always undergoing changes, even to this day!

IT Team Focus Areas

- Automation
- Usability
- Data Security
- Data and Decisions

What is "User Experience?"

- All the interactions between a user and systems
- "Usability" is something that we, as consumers, often take for granted!

Why is this important?

https://www.apple.com/

Important Topics

- Overview of the ABCTL's IT systems
  - Highlighting aspects/features contributing to usability
- Back end vs. Front end
  - Back end = admin users
  - Front end = end users (the ones who get COVID-19 tested)
- User experience refers to many different aspects of IT systems!

Point and Click (PNC): A Lasting Solution to the EHR

Components:

- Complete Electronic Health Records (EHR)
- Mass Tester App

Point and Click Website

https://www.pointandclicksolutions.com/

Back-end View of Point and Click

PncSchedule: Admin View

https://www.pointandclicksolutions.com/

PncReport

Screenshot courtesy of Kevin Tinnin

Devil's Drop-Off Report

Screenshot courtesy of Kevin Tinnin

Results of the Report

Screenshot courtesy of Kevin Tinnin

Queries are published in folders for easy access

Screenshot courtesy of Kevin Tinnin

Usability within the Lab Workstream

- The lab managers' role = verify sample test results that come from the machine tester
- Very tedious! They reviewed them one by one…
- Solution: a database that automatically categorizes and sorts results

The Lab Managers' Interface

Screenshot courtesy of Dr. Vel Murugan, PhD

Hotfixes, Enhancements, and Customizations

Improving the User Experience

- The ABCTL had to and continues to adapt to the ever-growing needs of its "users"
- There is an abundance of ways to improve the user experience/system usability

Key Aspects of Beneficial Modifications

Types of modifications:

- Usability issues that suddenly occur and require immediate attention
- Other modifications are discussed and planned over time

Test Results Page (Old Version)

Problem: Test result is difficult to locate, and hard to interpret.

Screenshot courtesy of Kevin Tinnin

Test Results Page (Old Version)

Problem: Test result is difficult to locate, and hard to interpret.

Screenshot courtesy of Kevin Tinnin

Test Results Page (New Version)

Screenshot courtesy of Kevin Tinnin

Side-by-Side View

Screenshots courtesy of Kevin Tinnin

Other Notable Modifications

- Language support
- Improving/fixing text notification system
- Fixing registration/scanning issues
  - Mass Tester App
  - Devil's Drop-Off
- Slow loading times with pushing data to the EHR

Closing Thoughts

- One of the ABCTL's most important qualities: adaptability on the fly
- Hotfixes/enhancements/customizations often go unnoticed from the end user's perspective
- To improve the ABCTL, we need to pay attention to the users' experiences of its systems, as well as understand the trial and error process that has shaped the ABCTL

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Thank you!

Questions?

Data Workflow Defense Presentation

The Making of ASU Biodesign Clinical Testing Laboratory (ABCTL):
Data Workflow, Integrity, and Quality Control

Arizona State University

Garrett Knox | Business Data Analytics, B.S.
Carolyn Compton, MD, PhD | ASU School of Life Sciences
Sean Dudley, MS | ASU Office of Knowledge Enterprise Development
April 5th, 2021

Topics of Focus

- Background on ABCTL
- Data security regulations
- Systems for facilitating data workflow
- Early challenges in test collection
- Steps taken remedy these challenges
- Data integrity in lab environment
- Recommendations and Conclusion

Background on the ABCTL

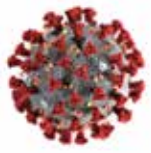
Pre-Covid

- Founded in 2003 as a research facility
- Directive to conduct research on health, sustainability, and security

ASU's Biodesign Institute

Transitional Period

- In the early stages of the Covid-19 pandemic, the ABCTL transitioned into a clinical laboratory
- Goal of facilitating Covid-19 testing
- IT challenge of ensuring data integrity compliant with federal and state regulations



Covid-19 Virus

Patient Data Regulations

HIPAA Compliance

- **The ABCTL must ensure all patient data is in compliance with the Health Insurance Portability and Accountability Act (HIPAA)**

- This includes any data related to
  - Health conditions
  - Care
  - Treatments
  - Payments
- Personal identifies such as
  - Name
  - Address
  - Birth date
  - Social security number
  - Among others

CDC Requirements

- **At the beginning of the pandemic, the CDC established a set of requirements listing the health and testing data needed to be reported.**

- This includes, but is not limited to
  - Test ordered
  - Test results
  - Result date
  - Patient
    - Age
    - Race
    - Ethnicity
    - Sex
    - Zip Code
- Personally identifiable information also required by the AZ Department of Health Services.

The IT Challenge

- How to transition to a clinical laboratory while shifting IT systems for regulatory compliance in data workflow?
- Adjusting existing systems and implementing new systems
- Ensure integrity of data each step along the data workflow

Diagram of data workflow process

Key Systems of Data Management

LIMS

- The ABCTL Laboratory Information Management System (LIMS) allows for managing samples and associated data
- Helps to improve data integrity in the data workflow
  - Production of reliable results quickly
  - Tracking information from different sequencing runs over time

Data workflow through LIMS

1. Reception and logging of sample and associated data
2. Scheduling, assignment, tracking of sample
3. Quality control and processing
4. Storage of data
5. Verification, approval, and accumulation of data for reporting

- As it applies to the ABCTL, the process can briefly be described as

1. Covid testing site collection
2. Transport of sample to the ABCTL
3. Quality checking and entry into systems processing
4. Receival and initial storage of test result
5. Verification from lab director and distribution through PnC

Point and Click (PnC)

- PnC is a custom system reconfigured to fit the needs of ABCTL data handling
- Was never a perfect fit and needed improvements over time
- PnC is the means through which testing results are sent to the correct individual after final approval by the lab director

Pros and Cons of PnC in terms of data workflow and integrity

- Cons
  - Cloud based system means that there are security risks that making a change could have cascading effects
  - Difficult to improve when nearly always active

- Pros
  - Agency capabilities allow for subdivisions of the system to include only relevant data to the user
  - Capacity to separate student health results from health results going to the public to pair students with ASU health providers

Data Integrity and QC in Test Collection

Initial Quality Control Challenges

- As one of the first major institutions in Arizona to be capable of Covid-19 testing, the ABCTL had to learn on the fly
- Was extensive opportunity for information handoff
  - First person reads test code
  - Second person enters it into the computer
- People would falsify or erroneously enter date of birth or phone numbers
- Represented a data integrity issue at the very start of the data workflow, including potentially mixing or missing patient data

Improvements that have been made

- Saliva testing offered massive benefits for data integrity, since it reduced the need for fully PPE staff to facilitate testing
- QR codes were implemented with all the relevant information to a vial
- Two secondary verifications were established
  - Date of birth
  - Ensuring lab orders volume was the same as sample orders volume

An ABCTL Saliva Test

Improvements made continued...

- Requirement of date of birth and photo ID verification
- Samples are checked for proper packaging upon arrival at the ABCTL
- Lab implemented sample tracking system ensures that de-identified health information is matched to the right patient
  - Requires both a computer and human verification before result delivery
- Maintaining the data integrity and connections to patient identity information is the top priority!

Data Integrity and QC in Laboratory Process

QC and Data Integrity Upon Lab Arrival

- Chain of custody paperwork
  - If this fails, the EHR is cross checked to verify that each patient record that was scanned is pushed out
    - Ensures no patient record is left behind
- Staff validate there is no leaks, openings, or warmings
- Samples are scanned into the EHR system twice with two additional final verifications
- HIPAA complaint de-identified information is upload into the ABCTL
  - Randomly generated ID links back to patient

QC and Data Integrity within the Lab

- Vials are put into groups of 376, where they are pulled from the rack and double checked once again
  - Ensuring the QR codes physically match the vials
  - Birthdate utilized as a secondary backup identifier
- Samples are entered into a qPCR testing machine which produces a graph of results
  - Lab director personally verifies each result and makes final verdict on if it is positive or negative
- From this stage results are uploaded to PnC and securely delivered to individuals

Example QR Code

Additional Quality Control measures

- ABCTL quality assurance team evaluates every step of the process
  - Anticipate and respond to any problems that arise
  - Reduce likelihood of problem occurring
- Failure mode and effects analysis (FMEA) is typically done for one process at a time
  - complexities require the quality team to focus on all aspects of the data workflow simultaneously

Diagram describing typical FMEA

Additional Quality Control Measures Continued...

- Audits of admin access to EHR to ensure that patient records are properly authorized under state and federal regulations
- Identifications of bottlenecks that slow data workflow
- Additional trainings ensuring people are aware of regulations and data handling procedures

Insights and Recommendations

Takeaways

- HIPAA, CDC, and other regulations on data integrity and privacy add significant complications to the ABCTL data workflow
- Three major stages along the data workflow
  - Administering and labeling tests
  - Transporting said samples from testing sites and to individuals
  - Maintaining data integrity in the lab
- Additional challenges of ensuring vial is secured and not corrupted or misplaced at any stage of the dataflow
  - As soon as a sample is comprised the testing data is useless
- All three stages must work together

Recommendations and Conclusion

- The ABCTL should continue to strive to search for and identify areas of issue and remedy them as soon as possible
- To improve the ABCTL, it must make every effort to add further quality control and data integrity checkpoints along the data workflow, but also keep in mind how said checkpoints may effect lab efficiency or create bottlenecks
- Overall the ABCTL has greatly improved the integrity of its data workflow overtime compared to the start of the Covid-19 Pandemic

Acknowledgements and Thanks

Thank you to all the experts who have helped myself and my IT Team group mates in creating this project and sharing their expertise including the following individuals:

Dr. Carolyn Compton, MD, PhD, Sean Dudley, Morgan Nelson, Alma Douglas, Valarie Harris, Ian Shoemaker, Amit Sharma, Kevin Tinnin, Timothy Lant, Michael Fiacco, Kajol Majhail, Tamara Deuser, Serena Christianson

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Thank you!

Questions?

Data and Decisions Defense Presentation

The Making of ASU Biodesign Clinical Testing Laboratory (ABCTL):
I.T. Role: Data and Decisions

Arizona State University

Mani Kandan | Computer Science, B.S.
Carolyn Compton, MD, PhD | ASU School of Life Sciences
Sean Dudley | ASU Office of Knowledge Enterprise Development
April 5, 2021

1

Agenda

- ABCTL Background
- IT Team Background
- My Focus Area
- Findings and Recommendations
- Acknowledgements

 2

ABCTL Background

 3

ABCTL Formation

- ASU BioDesign Center for Personalized Diagnostics
- Coronavirus causes Repurposing
  - Rapid nasopharyngeal and saliva testing
- Repurposing causes changes in 6 areas
  - Business
  - Communications
  - Quality Management
  - Law
  - Clinical Analysis
  - Information Technology

 4

IT Team Background

 5

IT Team Focus Areas

- Automation
- Usability
- Data Workflow
- Data and Decisions

 6

My Focus Area

 7

Data and Decisions

- How do we go from having data to making decisions?
  - Modeling and Visualization
- Interview Sources

Sean Dudley

Tamara Deuser

Dr. Tim Lant

 8

Advice, not an Archive

- 5 Findings
  - Early Activation
  - Secure Storage
  - Data Model Structure
  - Model to Media Transparency
  - Prior Responses
- 5 Recommendations
  - Multidisciplinarian
  - Workload Management
  - Sharing Model Findings
  - Remain Apolitical
  - Future Planning

9

Findings and Recommendations

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Finding #1/5: Early Activation

- COVID-19 cases discovered in late 2019.
- Epidemiologists and researchers monitor medRxiv.org
- 1-2 months after discovery, ASU President activates initial response.
  - Research
  - Planning
  - Multidisciplinarian
- Bridge efforts early on
  - State response, health department, ASU response, and statewide testing.

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Finding #2/5: Secure Storage

- (Pre-existing) HIPAA-compliant storage
  - Testing
  - Lab results
  - Inter/Intra ABCTL data pathways
- Separate secure storage for unique identifiers
  - Student, Faculty, Staff, Employee confidential identifiers
- Data posted daily through Point and Click systems

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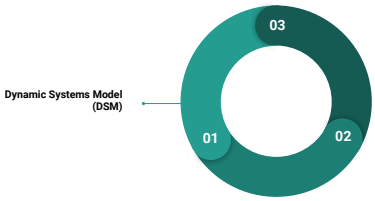
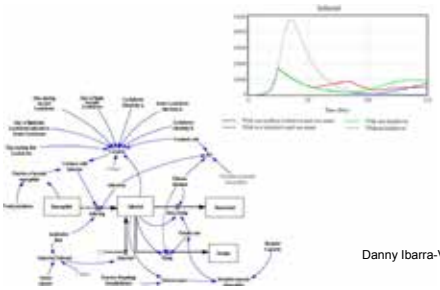
Finding #3/5 Data Model Structure



13

Example DSM for COVID-19 and Lockdowns



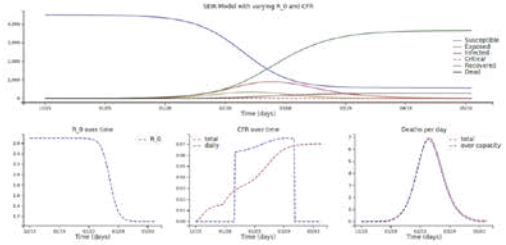
Danny Ibarra-Vega, 2020

14

Finding #3/5 Data Model Structure

15

Example S(E)IR(D) for COVID-19 Predictions



Henri Froese, 2020

16

Finding #3/5 Data Model Structure

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Finding #4/5: Model to Media Transparency

- Conspiracy cultivates with secrecy.
- Data allows for transparency
  - Allows for media allyship
    - Increase publicity for initiatives like testing
- Centralize institutional efforts through 1 speaker.
  - Daily Gov. Cuomo meetings for NY COVID-19 response
  - Weekly model updates
- Present a united front

ASU, Oberhaus 2020

18

Finding #5/5: Prior Responses

- Learn from prior responses
  - H1N1
  - Ebola
  - MERS
  - HIV/AIDS
- Data modeling has grown from allowing us to ask questions, to answering questions we haven't asked yet.

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Recommendation #1/5: Multidisciplinarian

- Collaborate early
- ABCTL's 6 areas

Christianson, Dr. Compton

20

Recommendation #2/5: Workload Management

- Faculty from across disciplines feeds into larger workforce/response.
- IT has many asks, consider enforcing a top-5 priorities approach
- A response with health/workload management outweighs a faster response.

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Recommendation #3/5: Share Model Findings

- Develop a culture of sharing. This includes people outside of the response.
  - ASU implemented mobile daily health checks.
- Consistent and frequent sharing of data:
  - Daily meetings between institution and state response leaders.
- Assume disruptions will occur; therefore, remain model-based.

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Recommendation #4/5: Remain Apolitical

- Politicization of public health crises is a given.
- Remain open to remedying relationships.
- Health and informed relationships with media put your institution in the public's favor.
- Depend on unbiased data and modeling.

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Recommendation #5/5: Plan for the Future

- Plan 12-18 months ahead when responding
- Accept you will be "flying the plane while building it"
- How do we future-proof?
  - "How can we be of more assistance?"
- Policy goals need to change
  - Quicker planned responses
  - Keep infrastructure intact
  - Contact tracing models

24

Chapter 4

The Making of a COVID Lab

A Focus on Laboratory Practices and Considerations

Authors: Laura Anderson, Scott Breshears, Kajol Majhail , Ellen Ruan and Jennifer Smetanick

Submitted in fulfillment of requirements for the honors baccalaureate program of Barrett, The Honors College at Arizona State University

Thesis Director: Professor Carolyn Compton, School of Life Sciences

Faculty Leader, Laboratory Group: Professor Mitch Magee, School of Life Sciences

August 2020 – May 2021

Introduction to Chapter 4

The creation of a clinical testing laboratory requires an interdisciplinary effort. This section evaluates the laboratory practices and science behind the ABCTL including: saliva preanalytics, robotics and automation, reverse transcriptase quantitative polymerase chain reaction (RT-qPCR), SalivaDirect, and antibody testing. Saliva has become the testing medium of choice due to its non-invasive and easy collection of considerable quantities of viral RNA (necessary for a PCR diagnostic test). Automation is required in order to rapidly and accurately process the number of tests demanded. The ABCTL utilizes RT-qPCR to detect SARS-CoV-2 in the saliva samples and is currently implementing another protocol (SalivaDirect) which removes the need for RNA extraction. Antibody testing, a future goal for the ABCTL, is performed to assess immune status after infection or vaccination. As of April 2021, there have been over 130 million recorded cases of COVID-19 globally, with the United States taking the lead with approximately 31.5 million cases. Developing highly accurate and timely diagnostics has been an important need of our country that the ABCTL has had tremendous success in delivering.

The ABCTL began in March 2020 after the severe acute respiratory syndrome, coronavirus 2 (SARS-CoV-2 began spreading throughout the world. ASU worked towards implementing its own efficient way of testing for the virus, in order to assist the university but also keep the communities around it safe. By developing its own strategy for COVID-19 testing, ASU was on the forefront of research by developing new ways to test for the virus. Initially, the lab used nasopharyngeal swabs to collect samples and RT-qPCR, or reverse transcription polymerase chain reaction, to match the components of the sample to a portion of the SARS-CoV-2 genome. Supply shortages caused by the scale of testing required during a worldwide pandemic led to the testing method to evolve as problems arose. In response to the nasopharyngeal swab shortage, saliva was identified as an alternative that performed just as well while being an easier test to collect and analyze.

Currently, the ABCTL is implementing a method called SalivaDirect which builds upon saliva collection and skips the nucleic acid extraction and purification. Not only did this method require fewer resources required, but more individuals were able to get tested at faster rates. The ABCTL is also developing antibody testing because of its importance in policy decisions and the development of therapeutics. In the future, the ABCTL will continue to adapt to the ever- changing needs of the community in regard to the unprecedented COVID-19 pandemic. The research collected throughout the past year following the breakout of the COVID-19 pandemic reflects the impressive strategy ASU has created to keep its communities safe, while continuously working towards improving not only the testing sites and functions, but also the ways in which an institution approaches and manages an unfortunate impact on diverse communities.

Section I: The Academic Response to the COVID-19 Pandemic - qPCR, Saliva Testing, and Lab Workflow

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Background of SARS-CoV-2

History of the Pandemic

On March 11th, 2020, the World Health Organization (WHO) deemed the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for the 2019 novel coronavirus (COVID-19) outbreak, could be characterized as a worldwide pandemic (WHO, 2020a). The initial cases of COVID-19 began in late December of 2019 in the Hubei province of China as a cluster of atypical pneumonia cases. Beginning in January 2020 and progressing into March, more cases of transmission appeared in countries across the globe as the World Health Organization continued its daily briefings. On January 26th, Arizona documented its first case of COVID-19 linked to a student at ASU, which was also the fifth case in the United States (Vandell, 2020). It was determined that much of the spread of SARS- CoV-2 was a result of human-to-human transmission during international travel. As of March 1st, 2021, there have been over 117 million confirmed cases worldwide and almost 2.59 million deaths from COVID-19 (WHO, 2020b).

SARS-CoV-2 Structure and Infection

The SARS-CoV-2 virus is part of a larger family of coronaviruses, all of which are named after the solar corona appearance they possess when viewed under an electron microscope (Esakandari et al., 2020; Singhal, 2020). This appearance is due to the spike (s) type I transmembrane fusion glycoprotein (~150 kDa) within the viral envelope, which plays a crucial role in penetrating host cells and developing the initial infection stages. In addition to the S protein, there are three other major structural proteins: the membrane (M) protein, envelope (E) protein, and the nucleocapsid (N) protein (see Fig. 1, Appendix). The M protein (~25-30 kDa) is the most abundant structural protein and helps determine the shape of the viral envelope. The E protein (~8- 12 kDa) is an integral membrane protein primarily expressed during infection of a cell; while only a minority of the produced protein is incorporated into the viral envelope, a majority of the protein assists in CoV assembly and budding within the site of intracellular trafficking inside the infected cell (Rabaan et al., 2020; Schoeman & Fielding, 2019). Both the M and E proteins make up the viral envelope and interact to generate the release of SARS coronavirus-like particles. The N protein (~50 kDa) enters the host cell while bound to the virus RNA genome to facilitate its replication and assist in viral assembly (Zeng et al., 2020).

When an aerosol droplet containing a SARS-CoV-2 viral particle is inhaled by an individual, the virus attaches itself to the inner lining of the nose and throat. Particularly in the nose, mucosal cells are rich in a cell-surface receptor known as angiotensin-converting enzyme 2 (ACE2); this receptor normally helps regulate blood pressure in the body, but the virus uses it as a method of entering the cell (Huang, Yang, Xu, Xu, & Liu, 2020; Wadman et al., 2020). The S protein binds to this receptor, promoting TM protease serine 2 (TMPRSS2) on the host cell membrane to activate the S protein and allow the virus to enter the cell. Once inside of a cell, the virus releases its RNA to replicate, transcribe, and translate more structural proteins to produce more viral particles. These newly-assembled viruses then go on to other portions of the body to replicate and shed back into the individual's environment using the host's produced aerosols while talking, breathing, or coughing.

One especially dangerous area of infection are the alveoli of the lungs, which are also rich in ACE2 receptors. The alveoli are responsible for transferring oxygen from the lungs into the capillaries, but an immune response to the viral infection disrupts this process (Wadman et al., 2020). The recruitment of

chemokines and more immune cells to attack the virus-infected cells and leave behind a layer of fluid and dead cells, generating the characteristics seen in individuals with pneumonia. In serious cases, this infection of the lungs can lead to the development of complications such as Acute Respiratory Distress Syndrome (ARDS), which results in an excess amount of carbon dioxide in the blood due to a degradation in the efficiency of the lungs (American Lung Association Scientific and Medical Editorial Review Panel, 2020; Wadman et al., 2020).

SARS-CoV-2 presents a wide variety of symptoms in patients with COVID-19. Cases of the COVID-19 disease range from asymptomatic individuals, who are frequently unaware of their infection, to severe illness that requires hospitalization. Symptoms vary between individuals and can include fever, cough, loss of taste or smell, difficulty breathing, fatigue, and body aches (Centers for Disease Control and Prevention, 2020d). Once inside of the body, the virus can cause other complications such as conjunctivitis, cardiac inflammation, pneumonia, lung scarring, cytokine storms, damage to blood vessels, as well as issues with the liver and kidneys. According to the Mayo Clinic, there is also a correlation between COVID-19 infection and increased strokes, seizures, and Guillain-Barre syndrome; it may also increase the risk of developing Parkinson's and Alzheimer's disease (Mayo Clinic, 2020).

The virus has proven difficult to treat for several reasons: it resides in both the upper respiratory tract and the lungs, symptoms do not often appear until it has already been transmitted to other hosts, and it can remain suspended in areas with poor ventilation for extended periods of time (ASU Biodesign Clinical Testing Laboratory, 2020c; Centers for Disease Control and Prevention, 2020c). Not only does the method of infection make the virus hard to treat, but factors such as healthcare staff shortages, medical equipment supplies, and hospital capacities have also hindered the ability to treat infected individuals. To reduce the harmful effects of these limitations and ensure that the virus spreads as minimally as possible, testing has become exponentially more accessible to the public in countries all over the globe. There are multiple methods of diagnosing patients with the virus, including reverse transcription polymerase chain reaction (RT-qPCR), CT scans, and loop-mediated isothermal amplification (LAMP) tests. Another form of testing for a SARS-CoV-2 retrospect infection is antibody testing. These tests are utilized to determine whether or not an individual has been infected by the virus in the past but are not used in the early diagnosis process. Antibodies such as IgG start to develop at least two weeks after exposure, and so typically these tests are given to individuals who suspect they were infected but have not had any new symptoms in the previous 10 days (Laboratory Corporation of America, 2020). There are a few rare cases in which someone previously infected with SARS-CoV-2 was reinfected with the virus, but most current research suggests that individuals do have a certain degree of immunity for at least 3 months following their initial infection (Centers for Disease Control and Prevention, 2020a).

Origin of the ASU Biodesign Clinical Testing Laboratory

Research surrounding the virus became more important than ever as countries began to shut down, expediting the process of genomic sequencing, generating virus tests, and increasing contact tracing between cases to slow the spread of SARS-CoV-2 and diminish the effects of COVID-19. In mid-March of 2020, ASU transformed one of its research labs into the ABCTL headed by Dr. Joshua L. LaBaer, Dr.

Carolyn Compton, and Dr. Vel Murugan. The ABCTL is a federally certified medical testing laboratory for COVID testing and the first location in Arizona to offer a saliva-based diagnostic test (ABCTL, 2020a). The transformation of an academic research lab into a center for medical testing of hundreds of ASU personnel, volunteers, community members, and consultants helped fight the spread of COVID-19. It was a bold and an unprecedented initiative at ASU. For the lab to start public operations, new methods were developed to collect biospecimens for testing, robotics were incorporated into the workflow to expedite analysis of samples, and the laboratory operated under the requirements of the federal Health Information Portability and Accountability Act (HIPAA) to safeguard the personal health information linked to those tested. In addition, the ABCTL established 100 testing sites throughout Arizona and Four Corners, available to both the public and specific communities. To date, results from the saliva tests have matched

100% with reference clinical laboratories. The laboratory initially functioned 24 hours a day, 7 days a week to meet the high testing needs of the surrounding community, but now operates during more limited work hours. The lab continues to provide a turnaround time from sampling to results in about 24-48 hours. As of September 2021, the ABCTL had processed over one million SARS-CoV-2 tests and achieved full accreditation through the College of American Pathologists, the highest bar for laboratory quality (ASU, 2020).

Reverse Transcriptase-quantitative Polymerase Chain Reaction (RT-qPCR) Testing

RT-qPCR Technology

RT-qPCR tests use a sample from an individual and match the components of the sample to a portion of the SARS-CoV-2 genome. Small manufactured sequences of the viral genome, known as primers, are the blueprints that code for certain proteins; an example would be a primer for the sequence in SARS-CoV-2 that is responsible for creating the S protein. During the RT- qPCR, a mix of primers, dNTPs, reverse transcriptase, and DNA polymerase are combined with the provided sample and used to make cDNA and then amplify it (ThermoFisher Scientific, n.d.). During the three-step process of the PCR — denaturation, annealing, and extension — the amount of cDNA made doubles after each cycle depending on whether or not the virus has replicated inside of the individual who provided the sample. If there are viral nucleic acids present in the collected sample, the primers will bind to the cDNA generated from the viral RNA and replicate it during the PCR process. If the sample does not contain any viral nucleic acids, the primers will not have anything to bind to and will thus not display amplification.

The amplification of the cDNA is measured in real-time with the use of fluorescent probes and a fluorometer as the PCR thermal cycler runs. Each of these fluorescent probes are specific for the different SARS-CoV-2 genomic regions targeted in the assay. During the PCR process, Taq polymerase degrades the probe and causes the reporter dye to separate from the quencher dye, generating a fluorescent signal. Fluorescence intensity is increased as more reporter dye molecules are cleaved from the probes and this intensity is recorded by the PCR thermal cycler (ThermoFisher Scientific, 2020a). RT-qPCRs are used in diagnostics with the use of a cycle threshold, or Ct value. This value is predetermined from the amplification baseline to ensure that a sample can be designated as positive or negative; typically, the amplification of 2 or more primers above their Ct value would signify that the sample is positive and possesses viral nucleic acids (ASU Biodesign Clinical Testing Laboratory, 2020c; Mollaei, Afshar, Kalantar-Neyestanaki, Fazlalipour, & Aflatoonian, 2020). Using multiple primers ensures that a combination of detections can be made to a sample so that the diagnosis is not mistakenly designated positive or negative. MS2, which is used as an additional gene in some RT-qPCRs, determines the validity of the results by acting as an internal control. If there is inadequate amplification of MS2 above the Ct value, the sample is deemed invalid due to a sample quality issue, incorrect cycle conditions, primer degradation, or failure of the DNA polymerase during amplification (ASU Biodesign Clinical Testing Laboratory, 2020c).

Primer Creation For SARS-CoV-2

Many different versions of the COVID-19 diagnostic testing use multiplex real-time RT- PCR tests. To determine what sequences to target in the SARS-CoV-2 genome, research was done on the specificity and sensitivity of multiple target gene sequences (Mollaei et al., 2020). In a paper published by Mollaei et al., the target genes ORF1ab, S, E, N, and the viral RNA polymerase enzyme (RdRp) were selected for primer designing and testing in two commercially available RT- PCR kits (Mollaei et al., 2020). The results of the RT-PCR for each primer returned as outlined in Figure 2, Appendix.

It was determined that the N gene was the most positive in the RT-PCR, which makes it one of the most abundant genes in SARS-CoV-2 infection. The E gene was determined to be the least positive during infection. Additionally, the ORF1ab gene target produced a positive predictive value of 100%, as well as a

false negative rate of only 4%, making it a preferred region for coronavirus detection in qPCR diagnostics. By using the OFR1ab and N gene targets simultaneously, the possibility of obtaining a false negative result is decreased. While the S gene target did not have the worst diagnostic results, the combination of the S gene with other targets greatly increases the predictive values and decreases the chance of false positives and negatives. Mollaei et al., recommend using a combination of the N, RdRp, and ORF1 primers to obtain the most accurate diagnostic results (Mollaei et al., 2020).

In addition to increasing the accuracy of the test results, the combination of these primers also allows for the detection of different strains of the virus during testing. One of these variants is the B.1.1.7 lineage, first detected in southeastern England in September of 2020. There were 17 mutations found in this variant, including a mutation in the receptor binding domain of the spike protein at position 501, potentially causing the variant to bind more tightly to cells (Centers for Disease Control and Prevention, 2020b; Robert Bollinger & Stuart Ray, 2021). Another variant of concern, the B.1.351 lineage, has multiple mutations in the spike protein (K417N, E484K, N501Y) and is associated with binding more tightly to human cells as well as invading some kinds of antibodies (Centers for Disease Control and Prevention, 2020b, p. 19; Corum & Zimmer, n.d.). Similar to the mutations found in B.1.351, the P.1 variant emerged in late 2020 in Brazil with the K417N, E484K, N501Y mutations (Centers for Disease Control and Prevention, 2020b; Corum & Zimmer, n.d.). All of these mutations have the potential to negatively impact the accuracy of diagnostic testing results if multiple primers are not used in conjunction; for example, using a test that only detects the presence of the S gene and the N gene on a sample From someone infected with a B.1.351 SARS-CoV-2 variant would result in a false positive test because of the non-specificity of the S gene target. The genes chosen by Mollaei et al. have yet to be seen in widespread mutations of the virus and are largely conserved in the variations, making them excellent targets for accurate diagnostic testing.

Transition to Saliva Sample Testing in the ABCTL

In early March, ASU began testing using NP swabs and the same methods of RT-qPCR (Dr. Joshua LaBaer, 2020). However, when shortages of medical swabs and transfer medium to use for this type of sample collection arose quickly all around the world, the ABCTL switched to collecting samples via saliva samples. This allowed for easier collection of samples, a decrease in the amount of PPE required of the collection staff, the permission for use of trained volunteers rather than only registered nurses, and a larger number of undiluted samples for testing. In terms of using saliva in conjunction with the TaqPath™ COVID-19 Combo Kit, the results are comparable, if not superior, to using nasopharyngeal swab samples (Wyllie, Fournier, Casanovas- Massana, Campbell, Tokuyama, Vijayakumar, Geng, et al., 2020). This is because saliva samples do not need to be diluted; the sample received from an NP swab must be diluted in a transfer medium, which ultimately increases the possibility of a false negative due to insufficient amounts of viral genome for the sample volume. Additionally, variation in the NP sampling methods is an additional source of false-negative possibility, which requires a specific technique for sampling. According to Wyllie et al., it was found that NP swabs had a greater variation in the human RNase P Ct values in comparison to the saliva samples when collected both from inpatients by health care workers and collected from the health care workers themselves (Wyllie, Fournier, Casanovas-Massana, Campbell, Tokuyama, Vijayakumar, Warren, et al., 2020). In addition, Wyllie et al. demonstrated that saliva samples were positive at a higher percentage up to 10 days after the COVID-19 diagnosis in comparison to samples from NP swabs. From 1 to 5 days after the diagnosis, 81% of the saliva samples were positive while only 71% of the NP swab samples were positive (Wyllie, Fournier, Casanovas-Massana, Campbell, Tokuyama, Vijayakumar, Warren, et al., 2020). However, it has been shown that testing too early — up to 5 days after exposure — with either type of test could result in a false negative (Arizona State University, n.d.). Using saliva samples in the RT-qPCR process ultimately makes it easier for samples to be collected, analyzed, and confirmed.

Use of the FDA-Authoruzed TaqPath™ COVID-19 Combo Kit for COVID Testing

The ABCTL uses the TaqPath™ COVID-19 Combo Kit in its saliva sample diagnostic testing. This kit is a multiplex real-time RT-PCR test intended for the qualitative detection of nucleic acid from SARS-CoV-2 (ThermoFisher Scientific, 2020a). This kit uses the combination of ORF1ab gene (which encodes polyproteins PP1ab and PP1a), N gene, and S gene primers for the identification of SARS-CoV-2 RNA. These gene sequences are targeted in this kit due to lower mutation entropy and higher specificity for this particular coronavirus. There is also an MS2 phage control present in the provided kit materials for the verification of effective nucleic acid extraction. The probes provided in this kit attach to three target sequences located between the three forward and reverse primers for the ORF1ab, N, and S genes. The evaluation of samples can be determined as positive or negative by the guidelines in Figure 3, Appendix Section I.

Multiple SARS-CoV-2 targets must be above the Ct value for the sample to be deemed as a presumptive positive. If there is no detection of any SARS-CoV-2 targets and no detection of MS2, the results of the test are inconclusive for a possible error in sample quality (ThermoFisher Scientific, 2020a). MS2 can be either positive or negative in a presumptive positive sample as there is still replication of multiple SARS-CoV-2 targets during the RT-PCR, but it is rare to receive a negative MS2 control result in a positive sample. False-negative results are more common than false-positive results, resulting from improper sample collection, degradation of viral RNA during the collection process, mutations in the SARS-CoV-2 genome, or inadequate following of instructions. False-positives mainly result from avenues such as cross-contamination or specimen mix-up.

This RT-PCR kit was analyzed for performance by determining the limit of detection, (LoD), interfering substances, cross-reactivity, and a clinical evaluation of confirming the test results (ThermoFisher Scientific, 2020b, 2020a). The lowest SARS-CoV-2 viral concentration that could be detected using this test with bronchoalveolar lavage and nasopharyngeal swab samples were 250 genome copy equivalents per milliliter of specimen (GCE/mL), or 10 GCE/reaction. In terms of reactivity, the TaqPath™ COVID-19 Combo Kit ORF1ab, S, and N gene targets are 100% homologous to >99.99% of known SARS-CoV-2 isolates in GISAID and 100% of known isolates in GenBank databases. The one exception to this was with EPI_ISL_407084; there was only 95.6% homology at position 7 from the 5' end on the reverse primer, but this mismatch does not affect the test performance (ThermoFisher Scientific, 2020a). When testing the impact of interfering substances — mucin, blood, nasal sprays, antibiotics, allergy medicine, etc. — there were no false-positive results observed in any of the samples or variance of concentrations (ThermoFisher Scientific, 2020a). Forty-three different organisms were used in testing the cross-reactivity of the TaqPath™ COVID-19 Combo Kit target sequence primers. Among them, *Neisseria elongata* had ≥80% homology with the forward N gene primer and 36% homology with the reverse N gene primer. However, the reverse N gene primer and the probe show low homology with *N. elongata*, meaning that there is a very low risk of a false positive from this organism as all three assay components — forward primer, reverse primer, and probe — must have high homology to generate a signal.

Finally, a clinical evaluation of TaqPath™ COVID-19 RT-PCR Kit was performed using 60 specimens of both nasopharyngeal swabs (NP) and bronchoalveolar lavage (BAL). Thirty of each specimen type were contrived positive samples and the remaining thirty were negative samples. Samples were spiked with known concentrations of SARS-CoV-2 viral RNA to test the LoD in the sample types and the resulting Ct values for each target. All 60 positive samples returned positive (2 samples were initially inconclusive but returned positive after retesting) and all 60 negative samples returned negative (1 sample was initially inconclusive but returned negative after retesting) (ThermoFisher Scientific, 2020a).

Despite its accuracy in diagnostic testing, The FDA sent out a warning on January 8th, 2021 regarding the impact of this test in regard to the genetic variants of SARS-CoV-2 becoming more widespread across various areas of the world (U.S. Food and Drug Administration, 2021). It was noted that one of the three targets — the S gene — had significantly reduced the test's sensitivity due to the mutations found in the

emerging variants of concern. However, since the test is designed to detect multiple genetic targets, it was deemed that the overall test sensitivity and accuracy should not be impacted. Additionally, a drop in S gene feedback from a sample while using this test for diagnosis could provide researchers with valuable information regarding whether or not certain variants have become more prominent in the surrounding community; If the number of tests returning with a positive result for the ORF1ab and N genes and a negative result for the S gene increases, it is recommended that labs should characterize the specimen to determine if there is an increased risk of transmission in the community due to an increase in more transmissible variants such as B.1.1.7.

Workflow in the ABCTL

Volunteer Training and Biosafety

Saliva samples for SARS-CoV-2 testing are handled with standard precautions as if the sample contains a transmissible infectious agent. These precautions combine features of universal precautions and body substance isolation to ensure the safety of all employees and participants. This includes wearing PPE according to the position of the employee and risk assessment, avoiding contact with all potentially infectious body substances, and using good hand hygiene and cough etiquette practices. High-touch surfaces at the testing facility are disinfected at least every 2 hours, and the outsides of the sample collection tube are disinfected after retrieved from the sample provider.

Any personnel that could come into contact with a positive COVID-19 individual or sample must undergo specific training programs that are required of their position. However, all testing site staff — including site managers, check-in station personnel, triage station personnel, and sample collection personnel — must complete the ASU COVID-19 Saliva Testing Sites Training course and HIPAA training for covered entities. Additional onsite training is also provided to personnel based on their respective positions via the site manager.

Criteria for Sample Rejection

To ensure that all saliva samples collected will effectively process in the PCR reaction and can be transported by the robotics, specimens are inspected at the site of collection. Samples are acceptable if they are viscous, without excessive debris, and are either translucent or slightly cloudy (ASU Biodesign Clinical Testing Laboratory, 2020b). This sample is collected from the saliva of the participant from the front of their mouth, ensuring that no mucus or phlegm is incorporated into the sample. The sample must also be between the minimum and maximum fill lines on the provided collection tube, which is approximately 2-3 mL (ASU Biodesign Clinical Testing Laboratory, 2020b). Inadequate samples — those containing a milky or opaque color, large amounts of debris, phlegm/mucus, or an incorrect amount of sample — are rejected at the testing site so participants can submit an acceptable sample. If a sample is deemed acceptable at the testing site but does not meet the requirements for an acceptable sample, it may return as an inconclusive test result in the laboratory. This could be for several reasons, such as an inability for the robotics or laboratory employees to extract an adequate amount of saliva to be processed, or if all primers and the internal MS2 control return with no amplification after RT-qPCR.

Collection of Samples

In addition to taking precautionary measures of human-to-human spread in testing facilities, samples are handled so that there is no potential spread of disease or contamination from the potentially infectious material (OPIM) (ASU Biodesign Clinical Testing Laboratory, 2020b). After undergoing a quality check, samples are stored at a temperature of 59-77 degrees Fahrenheit to prevent degradation of potential viral RNA. The transport containers are labeled with biohazard stickers and contact information of the responsible party, and samples are packed into a secondary transport container such as a leak-proof biological shipping bag by personnel wearing full PPE. Furthermore, sample counts are verified by two staff members, the outside of the secondary sample container is wiped down with a disinfectant, and then

the transport cooler is locked with a lock or zip tie once the samples are placed inside. Quality samples are transported to the laboratory for isolation and testing.

Lab Workflow and Sample Processing

When a sample is received from an individual at the ABCTL, it is heat-inactivated at 65° Celsius for 30 minutes to kill any active virus particles (ASU Biodesign Clinical Testing Laboratory, 2020c). The QC labels are then checked and arranged before 200 µL of each sample are placed into a Kingfisher deep well-block before the RNA is extracted using the MagMAX™ Viral/Pathogen Nucleic Acid Isolation Kit in the KingFisher Flex system. Samples are eluted and then Purified nucleic acid is reverse transcribed into cDNA and PCR amplified using the TaqPath™ RT-PCR COVID-19 Kit and the Applied Biosystems™ QuantStudio Fast Dx Real- Time PCR instrument (ASU Biodesign Clinical Testing Laboratory, 2020c).

The LoD for this assay in a saliva medium is 100% sensitive for samples containing 200 virus particles per sample. As outlined in Figure 3, two or more of the SARS-CoV-2 targets must be amplified above the Ct value for the sample to be deemed as positive. The positive sample in Figure 4, Appendix consists of all three SARS-CoV-2 targets above the Ct value as well as the MS2 control. Negative samples will only present the MS2 control as positive after amplification.

To speed up the process of testing, pooled testing is used on large quantities of samples (see Fig. 5, Appendix). Using a total of 96 different samples, portions from 8 different samples are combined into one tube and tested as a single batch. If this batch leads to a negative result, then it can be inferred that all 8 samples which were pooled together are negative. If the batch is deemed as positive, then individual samples from the positive-pool are tested to identify the positive individual. The process cuts down on the time needed to test the samples as well as the number of individual samples needed to be performed.

Future of the ABCTL

Devil's Drop-Off

Saliva samples were initially collected in designated testing sites, where ASU personnel and volunteers would guide individuals through the check-in, collection, and sample return areas in the testing center. However, in the spring semester of 2021, a program known as Devil's Drop- off was created For ASU students, faculty, and staff. This program allows individuals to pick up a testing kit, collect their sample in a private location, and drop it off at one of the designated drop- off locations (Arizona State University, 2021). Once a sample kit is obtained, the individual must register their kit using the unique barcode on each collection tube through the individual's online health portal. The individual then has 24 hours to collect and deposit the sample at one of the on- campus drop-off bins. This form of saliva collection does not require appointments, nor does it require testing site personnel and the use of PPE. Ultimately, this process saves on volunteer time, availability to run testing sites, and streamlines the process for collecting samples.

SalivaDirect

The ABCTL is also transitioning into using SalivaDirect, a protocol developed by the Yale School of Public Health (see Fig. 6, Appendix). This protocol removes the need for RNA extraction; it instead uses proteinase K and heat treatment to inactivate the virus and provide an alternative to the extraction step with minimal decrease in nucleic acid detection sensitivity (Vogels et al., 2021). This process is beneficial in SARS-CoV-2 diagnostic testing in labs across the globe, as there have been worldwide shortages of the supplies needed to process the nucleic acid extraction step in RT-qPCR testing. Additionally, it provides more flexibility to labs as it is not a kit, but instead a protocol that can be adapted to the reagents and equipment already available in the lab performing the testing.

Future Directions

At the beginning of the pandemic, the ABCTL operated on a 24/7 basis to meet the dire testing needs of the community. As time has progressed, however, that need is no longer as immediate, and the lab has scaled back on its hours of operation significantly. While the world and scientific community are still fighting this pandemic, it will eventually come to an end. The future directions of the ABCTL are still up in the air, but some plans are currently in the works. The lab would like to expand its Devil's Drop-off method of sample collection to school districts around Arizona, allowing for wider availability of SARS- CoV-2 testing for schools that need it as they start transitioning into an in-person learning mode once again. Furthermore, once the pandemic is largely concluded, the lab will expand into other areas of testing both related and unrelated to COVID-19. Antibody testing might be provided to the public as vaccinations are steadily becoming more available. Additionally, SARS-CoV-2 testing will operate on a level yet to be decided, as it is currently unknown whether future mutations of SARS-CoV-2 will be problematic for vaccine efficacy and full protection. Testing will help ensure that cases remain minimal and help detect whether or not the current vaccines are suited to protect against other variations of the virus. Finally, the ABCTL is planning to expand into other types of microbial and virus-testing, such as providing flu testing to distinguish cases of influenza from SARS-CoV-2.

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Section I: Appendix

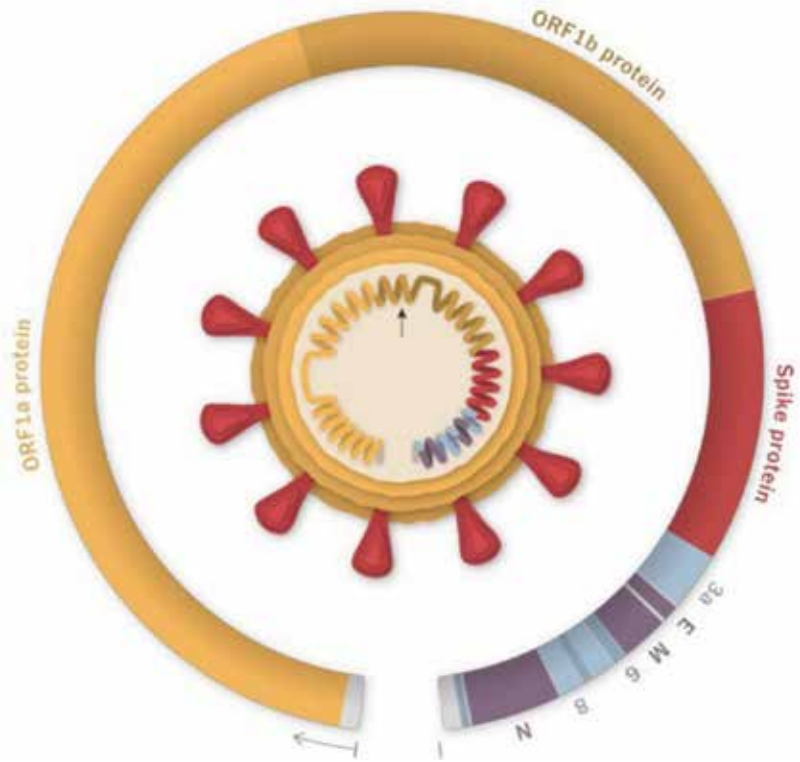

Figure 1. Diagram of the Coronavirus Genome (Corum & Zimmer, n.d.)

Analysis tests	Target Genes				
	RdRp	N	E	S	ORF1ab
% Sensitivity	95.7	96.6	66.7	85.7	96.0
% Specificity	88.9	100.0	66.7	50.0	100.0
% Positive Predictive Value (PPV)	95.7	100.0	88.9	96.0	100.0
% Negative Predictive Value (NPV)	88.9	50.0	33.3	20.0	83.3
False Negative Rate (FNR)	4.3	3.4	33.3	14.3	4.0
Fall out, False Positive Rate (FPR)	11.1	0.0	33.3	50.0	0.0
False Discovery Rate (FDR)	4.3	0.0	11.1	4.0	0.0
False Omission Rate (FOR)	11.1	50.0	66.7	80.0	16.7
Threat Score, Critical Success Index (CSI)	91.7	96.6	61.5	82.8	96.0
% Accuracy	47.0	31.3	29.3	27.3	40.7

Figure 2. Comparison Results of In-House RT-PCR by Newly Designed Primers (Mollaei et al., 2020)

ORF1ab	N gene	Sgene	MS2	Status	Result	Action
NEG	NEG	NEG	NEG	Invalid	NA	Repeat test. If the repeat result remains invalid, consider collecting a new specimen.
NEG	NEG	NEG	POS	Valid	SARS-CoV-2 Not Detected	Report results to healthcare provider. Consider testing for other viruses
Only one SARS-CoV-2 target = POS			POS or NEG	Valid	SARS-CoV-2 inconclusive[1]	Repeat test. If the repeat result remains inconclusive, contact CDC immediately for instructions for transfer of the specimen to CDC for additional testing and guidance.
Two or more SARS-CoV-2 targets = POS			POS or NEG	Valid	Presumptive Positive SARS-CoV-2	Report results to healthcare provider and CDC. Contact CDC immediately for instructions for transfer of the specimen to CDC for additional testing and guidance.

[1] Samples with a result of SARS-CoV-2 inconclusive shall be retested one time.

Figure 3. TaqPath™ COVID-19 Combo Kit Diagnostic Result Guidelines (ThermoFisher Scientific, 2020a)

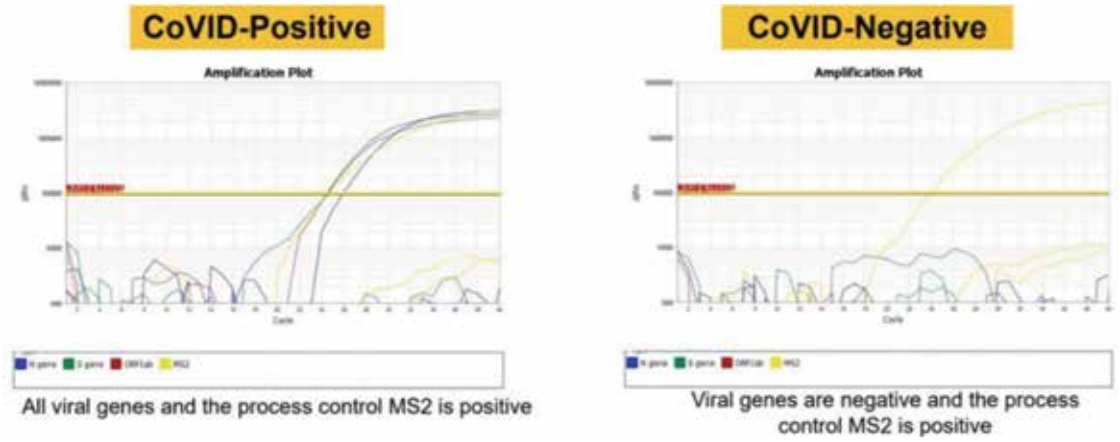

Figure 4. Amplification Plot of SARS-CoV-2 Positive and Negative Samples(ASU Biodesign Clinical Testing Laboratory, 2020c)

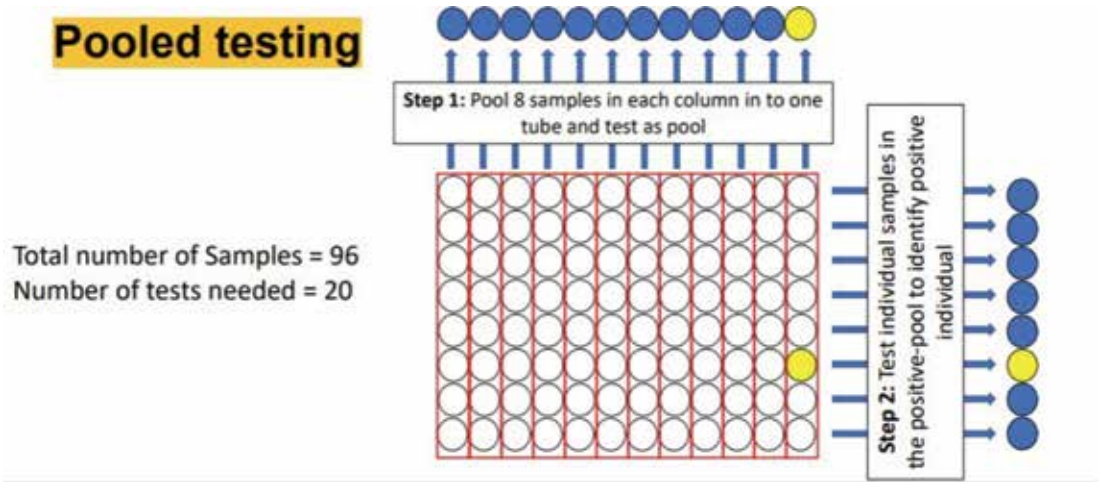

Figure 5. Process of Pooled Testing Performed by the ABCTL(ASU Biodesign Clinical Testing Laboratory, 2020c)

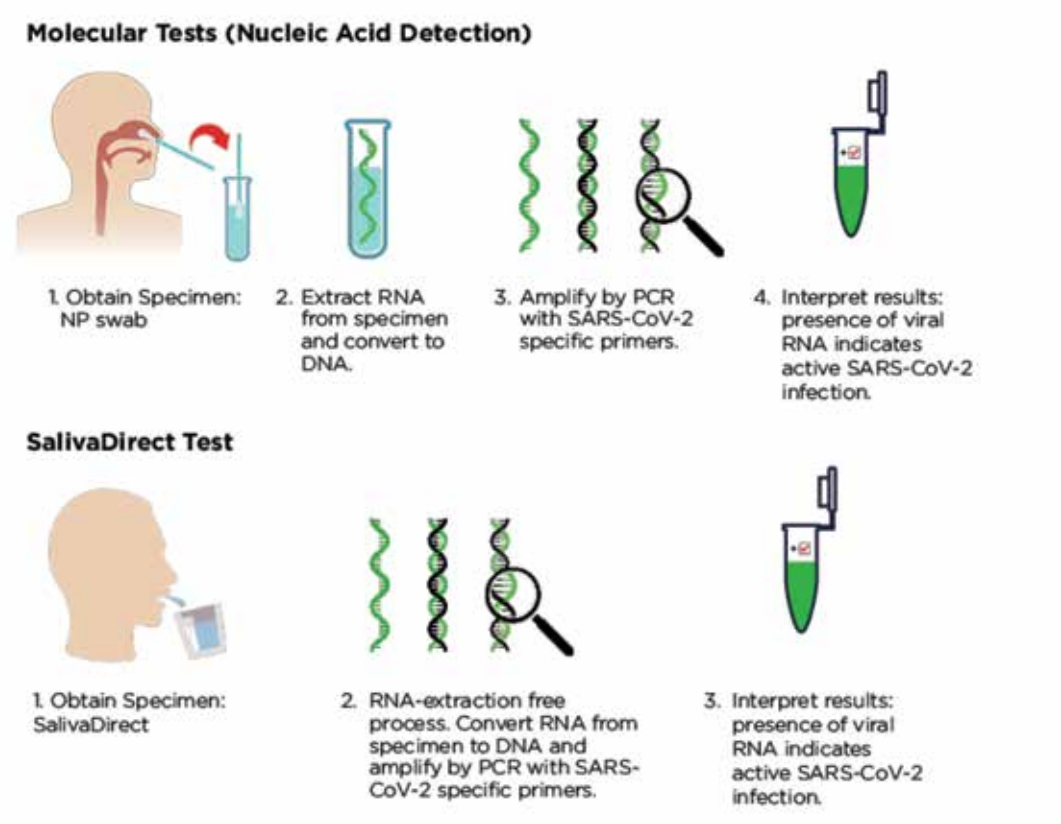

Figure 6. Comparison of COVID-19 Molecular Tests using Nasopharyngeal (NP) specimen collection and SalivaDirect collection (American Society for Microbiology's Clinical and Public Health Microbiology Committee, Subcommittee on Laboratory Practices, 2020)

Section II: SalivaDirect: A New Standard for an Epidemic

Author: Scott Breshears

Background

In the beginning of 2020, the standard of testing was the CDC approved quantitative reverse transcription polymerase chain reaction (RT-qPCR), which had standardized processes and materials designed for accuracy not for efficiency or conservation of materials. This consisted of multiple steps including: collection of a sample by nasopharyngeal swab, then nucleic acid extraction and purification, and finally RT-qPCR (Centers for Disease Control and Prevention et al., 2020). The process proved to be highly effective and repeatable which is why it was considered the initial gold standard. The limitations of this standard arose as a result of the constraints of volume, time, and material, caused by the worldwide epidemic. This process was time consuming, expensive, required large amounts of specialized equipment and chemicals, which produced a small fraction of the results required for large population testing (Wokniak et al., 2020).

To conduct testing on the scale required, high throughput automation is needed, which consists of even more specialized, complicated, and expensive equipment. This meant that high throughput RT-qPCR testing was not abundant, and was only found at large testing labs or labs that were conducting research that required it. Dr. LaBaer's laboratory group was fulfilling a Biomedical Advanced Research and Development Authority (BARDA) contract conducting research to try and identify biomarkers for exposure to radioactivity, which required the lab to be able to conduct high throughput PCR testing. By March 2020, with an already established high throughput PCR process, the ASU Biodesign Clinical Testing Lab (ABCTL) was formed for the clinical testing for SARS-CoV-2 and quickly became the largest testing site in Arizona.

As the year progressed, COVID-19 new cases grew and so did the required number of tests. Unlike the virus, testing facilities are heavily resource dependent, and as facilities worldwide tried to increase tests per day to combat the growth of new cases, these required resources depleted rapidly (Brown et al., 2020). The use of these resources was greater than the rate of production which created an inevitable supply chain disaster. This supply disaster was identified very early in the year, which unofficially launched a worldwide effort of scientific innovation. Unlike most scientific innovations of the past, where time and resources were abundant and failure was merely a lesson, this was the antithesis of that. What the scientific community was asked to do more closely resembled a soldier's decision-making process in war, where resources are limited, time is a finite resource, failure could result in serious harm or death, and sometimes there are no good options, only better bad options. Agencies like the FDA, that historically were very strict regulators became permissive and acted as a centralized database for promising, crude (relative to the standard), solutions to the problem (U.S. Food and Drug Administration et al., 2020). In this database, or the emergency use authorization database, hundreds of entities submitted possible promising solutions to the problem.

As the ABCTL began to scale, the pressure of supply shortages quickly followed first in the form of nasopharyngeal (NP) swabs then soon after nucleic acid extraction and purification kits (Fomsgaard et al., 2020). Due to the lack of diversity of reliable testing, these pressures were not isolated and were felt in labs across the world. The lack of diversity created the problem but also aided the solution by presenting a more refined and focused problem to solve. This also created a dynamic of one problem for many labs, which allowed more people to work the problem, which theoretically produced a solution faster. In the scope of the ABCTL, both of these issues were solved by the same entity, The Department of Epidemiology of Microbial Diseases, at the Yale School of Public Health which had found saliva as an

effective, if not superior, alternative to NP swab collection which was published in a paper on April 22, 2020 (Wyllie et al., 2020). Then about five months later, published another protocol that integrated the saliva collection method and added a simplified method of nucleic acid isolation and called it SalivaDirect (Vogels et al., 2020). This was published on September 28th, 2020, and soon after, the ABCTL began conducting their own validation of the protocol, and once validated, completely transitioning the lab to it.

Methodology Using SalivaDirect

Sample Collection

The ABCTL started its initial testing following the CDC approved RT-qPCR protocol, and even with the high throughput RT-qPCR machines, still were not producing enough results required for population testing. The ABCTL began to scale up testing through increased testing capacity as well as trying to increase efficiency of the processes already in place. One of the first major problems identified was with the collection of samples by NP swabs. Considered the standard for diagnosing respiratory viruses, NP swabs were associated with a decrease in test sensitivity during the early stages of the infection, relative to other respiratory viruses (Vogels et al., 2020). It also required trained medical personnel, who were in short supply as a result of mass hospitalizations. Of the people who were available, in the process of collecting the NP swabs, the irritation caused from the invasive nature of a NP sample, would often induce coughing and sneezing which significantly increased the collector's exposure to SARS-CoV-2. The secondary effect was that the collectors improperly collected the samples by not inserting the swab deep enough in the nasal passage which resulted in false negatives.

On top of all of these problems, there was also a global shortage of NP swabs and personal protective equipment which presented as the most consequential. Of all the potential alternatives to NP swab, saliva was identified as one of the most promising alternative collection methods (Vogels et al., 2020). Saliva offered a solution to the supply shortages, could be self- administered, and seamlessly integrated into the already established diagnostic workflow. This allowed for the elimination of the requirement for registered nurses and the need for personal protective equipment since samples could now be collected by the individual under the supervision of a volunteer. There was also the added benefit of increased stability at room temperature and did not require buffers to stabilize SARS-CoV-2. Saliva offered all these benefits without having to sacrifice sensitivity for determining the presence of the SARS-CoV-2 virus. Once saliva was determined as a realistic alternative to NP swabs, the ABCTL quickly began testing it. Upon the analytic and clinical validation of saliva collection, ABCTL had become the first lab in Arizona to transition to this collection method.

SalivaDirect Extraction Free Method

As the epidemic progressed and SARS-CoV-2 was continuing to rapidly spread around the world, labs, including the ABCTL, were continuously trying to scale up the number of tests they could conduct per day. This resulted in global shortages of the specialized chemicals required for nucleic acid extraction and purification (Fomsgaard et al., 2020). Unlike the saliva solution to the NP swab shortage, the solution to the impending chemical shortage was not evident and the diversity of possible solutions was much greater. With most labs using a similar diagnostic workflow, the solution ideally would have the ability to produce RNA that could be amplified in the PCR process and be plugged into the already established workflow. Prior to, and early in the Covid-19 epidemic, a handful of scientists predicted the chemical shortages associated with the scale of testing a global epidemic required and had tested potential simplifications of parts of the PCR process. These were conducted on a very small scale with different pathogens, which meant they were possibilities, not solutions. Of these studies a few had shown that it is possible to completely omit the nucleic acid extraction and purification and still be able to amplify the RNA. Instead of extracting and purifying the RNA they would just lyse the cell and then amplify the RNA in lysates directly, calling it direct RT-qPCR (Mallmann et al., 2020).

Using the studies of direct RT-qPCR, researchers at Yale created the SalivaDirect protocol, which uses proteinase K and heat inactivation to lyse the cell and inhibit RNase and use that solution for the follow-on amplification (Fig.2). Contrasting the standard RNA isolation and purification, this protocol uses one 96 well plate, one specialized chemical, and requires significantly less specialized equipment.

This process begins with creating a mix of proteinase K and MS2 control which is then added into the 96 well plate. Controls are added to their specific wells and samples are added to the rest. If there are bubbles present, centrifuge briefly to remove, then seal the 96-well plate and incubate at 95oC for five minutes in a thermal cycler. The RNA is now ready for amplification. In total this process takes about 20 minutes (Shoemaker et al., 2020).

The CDC Standard Nucleic Acid Extraction and Purification

The simple elegance of the SalivaDirect extraction free method is only fully appreciated when coupled with an understanding of the previous CDC standard. The purification of RNA from samples, via the CDC standard, consisted of four-steps and required five separate 96 well plates: three wash plates, an elution plate, and a sample plate (Thermo Fisher Scientific et al., 2020). Before testing the five plates required preparation: one wash plate was prefilled with a wash buffer, two wash plates were prefilled with an 80% ethanol solution, the elution plate was prefilled with an elution solution, and the sample plate was filled with a combination of: a bead binding mix, Proteinase K, and a MS2 phage control. The process of preparing the sample, if preparing one plate, and only accounting for the physical act of filling the plates, not machine set up, would take approximately 32 minutes and would require five different chemical solutions.

Once these plates have been prepared, they are then loaded into a Kingfisher Flex System that would conduct the RNA extraction and purification. This would consist of first mixing the 96- sample plate solution with 96 consumable plastic tip combs, which aids the proteinase K in lysing the cell. The proteinase K also degrades nucleases which are responsible for the degradation of RNA (Mallmann et al., 2020). Once the cells have been lysed, the beads from the bead binding mix bind to the RNA, by pre-designed addition of complementary functional groups to the surface of the beads (Somerville et al., 2020). This allows for the RNA to be the only thing extracted from this solution of chemicals and biomolecules. The machine can then move the RNA through the different plates via the magnetic beads. The hollow tip of the plastic tip combs allows room for a magnetic rod that attracts the RNA bound magnetic beads. The RNA is then transferred to the first wash solution, the magnetic rod is retracted, releasing the magnetic beads and RNA, then the plastic tip mixes the wash and magnetic beads. The magnetic rod is reinserted to the plastic comb tip, which retracts the magnetic beads, and is then transferred to the second wash well. This process is repeated for the final two wash wells and is transferred into the elution solution. The elution buffer is the final step, as it breaks the binding interactions between the beads and RNA resulting in purified RNA. This process takes a total of approximately 25 minutes, resulting in a conservative 57 minutes required for RNA isolation and purification (Thermo Fisher Scientific et al., 2020). Consumed in this time were: 4 96 well plates, 96 plastic tip combs, five specialized chemical solutions, and pipette tips.

The RT-qPCR Test for SARS-CoV-2

Overview

To understand how RNA is used to identify SARS-CoV-2 requires an understanding of the central dogma, RNA, and viruses. The central dogma is the fundamental biological process that takes the information coded in your DNA and converts it into proteins that are the foundation for all biological processes. DNA is broken into genes that are the protein specific production instructions, where each gene is used to create specific proteins. For example, the enzymes used to facilitate this process or the proteins that make up your blood cells. A gene is one section of one strand of the double strand helix in DNA that codes

for one protein. This process occurs in two distinct steps: the first being transcription and the second being translation. In transcription, the main player is RNA polymerase which opens the DNA helix at the gene and synthesizes a messenger RNA (mRNA) strand that is complementary to the target gene, with the only difference being the nucleotide thymine in DNA is transcribed to uracil in mRNA. At the end of the gene is a termination sequence that results in the mRNA being separated from the RNA polymerase. This all occurs in the nucleus of eukaryotic cells and once the mRNA is synthesized, is the end of the transcription process. The mRNA then works its way out of the nucleus where translation will then occur via ribosomes. A ribosome binds to the start of the mRNA sequence and using the unique nucleotide sequence, produces a peptide chain that will fold into a specific protein with a specific task. A virus does not have the biological machinery to create the proteins required, so they inject their RNA into cells and use the cell's machinery to produce new viral cells, using the viral RNA, that then go infect other cells via the same method. Viral RNA is composed of genes unique to the virus that are used to confirm a human's infection with the virus. In the case of SARS-CoV-2, it's RNA is a positive sensed, single strand RNA, which means that the RNA strand is the strand used to code the proteins, not the complementary strand (Liu et al., 2020).

This is why the isolation of RNA is so important, because by degrading the RNA before being able to test for its presence could lead to false negative results. Once the RNA is isolated it then goes through the process that is used to identify it called RT-qPCR, which begins with a process called reverse transcription (It is worth noting that the reverse transcription and PCR process are done in a single tube with all materials added at the same time, even though they are described as two different steps). This process requires the isolated RNA, a reverse transcriptase enzyme, a gene specific primer, a gene specific probe, and deoxynucleotide triphosphate (dNTP). The dNTP are the building blocks for the cDNA and consist of four different types representing the four different base pairs: adenine (dATP), cytosine (dCTP), guanine (dGTP), and thymine (dTTP). Unlike the transcription process that uses DNA to create mRNA via RNA polymerase, reverse transcription uses a reverse transcriptase enzyme to use the viral RNA to create complementary DNA (cDNA) that can then be amplified in the PCR process. The reverse transcriptase enzyme uses the primer to only create cDNA of the unique genes that are used to identify SARS-CoV-2, which are the N gene, S gene, and ORF1 gene. The reverse transcriptase then extends the primer creating complementary base pairs resulting in cDNA containing the target gene of the specific primer. Once the cDNA is created it is amplified by the PCR process using DNA polymerase. Amplification begins by first denaturing the cDNA, using heat, which splits the double helix structure into two strands. Then the target primers are annealed, or attached, to the beginning of the gene that they are designed to amplify. The DNA polymerase extends from the primer making cDNA from each strand, doubling the cDNA present. Each PCR round is called a cycle and each cycle doubles the amount of cDNA. The DNA is quantified through fluorescent signals that are released from probes that attach to specific sequences on the target genes, and when the cDNA is synthesized, the polymerase cleaves the probe releasing the fluorescence signal (Fig.3). Each probe has a unique fluorescence signal which allows for the differentiation of the genes present. With each cycle more fluorescence signals are released, and it is this signal that is used to diagnose the viral infection.

Results Using NP Swab vs. Saliva Samples

To test the diagnostic performance of the two collection methods for SARS-CoV-2, the researchers from Yale collected samples from a cohort of 44 COVID-19 inpatients. The participants were chosen with the intent to represent patients with severe COVID-19, with 31 of the 44 tested within the severe range. Severe patients in this study were defined as, "19 (43%) requiring intensive care, 10 (23%) requiring mechanical ventilation, and 2 (5%) deceased as of April 5th, 2020." (Wyllie et al., 2020) Of this cohort, 121 total samples were collected, the saliva via patient self-collection and the nasopharyngeal swabs collected by healthcare workers. From all the positive samples collected, the geometric mean concentration was five times higher in saliva then in nasopharyngeal swabs. Also, worth noting that eight positive samples only came back positive via saliva test while only three came back positive only for the nasopharyngeal swabs.

SalivaDirect Clinical Validation (RNA Extraction Comparison)

When the Yale researchers first published the SalivaDirect procedure, they were required to first conduct a clinical validation that compared the new test to the test authorized at the time. In the clinical validation of SalivaDirect the ThermoFisher proteinase K, Thermo Fisher TaqPath RT-qPCR kit, and Bio-Rad CFX96 were used and compared to the authorized ThermoFisher TaqPath COVID-19 combo kit (the same kit being used by the ABCTL). A total of 67 paired nasopharyngeal swabs and saliva samples were tested, with 37 positive paired and 30 negative paired samples, collected from patients and health care workers at Yale-New Haven Hospital. When directly comparing the two methods there was a positive agreement of 97.1% (Fig.5A) and 100% negative agreement (Fig.5B). SalivaDirect showed higher Ct values for the N1 gene (mean difference of 5.0 Ct), that were attributed to the nucleic acid extraction free method and using different thermocycler instruments (Vogels et al., 2020).

SalivaDirect Multi-Vender Limit of Detection

With one of the SalivaDirect goals being to limit supply chain limitations, three different vendors were both validated via limit of detection using the SalivaDirect method: AmericanBio, ThermoFisher Scientific, and New England Biolabs. This was done by taking the saliva from a COVID-19 positive patient with a viral concentration of 3.7 x 104 copies/µL and spiking the saliva from healthy health care workers. This allowed the different vendors to be directly compared under the exact same conditions while also establishing a limit of detection of the SalivaDirect method. A twofold dilution series of 400, 200, 100, 50, 25, 12, and 6 was used to validate the reagents and instruments. Once a preliminary limit was determined, it was then confirmed using 20 additional replicated and required 19/20 detection (Fig.6a-c). The limit of detection for the three proteinase K from different vendors resulted in a limit of detection of 6 SARS-CoV-2 copies/µL. This also suggests that the vendor of proteinase K does not affect results.

Following this, to determine the limit of detection, the RT-qPCR kits from each vendor were compared. Each kit had its kit specific thermocycler programs, but to make SalivaDirect truly universal, a standardized thermocycler program was created. After testing all three vendors it was determined that the Bio-Rad kit had a limit of detection of 6 SARS-CoV-2 copies/µL, which was the lowest, and ThermoFisher had the highest of 12 SARS-CoV-2 copies/µL. This suggests that RT-qPCR kits can affect the sensitivity of the SalivaDirect method.

Finally, the thermocyclers from ThermoFisher (Applied Biosystems (ABI) 750 Fast, ABI 7500 Fast DX) and Bio-Rad (CFX96) were compared using proteinase K and RT-qPCR kit from ThermoFisher (the highest limit of detection) (Fig.6g-i). It was determined that CFX96 and ABI 7500 Fast DX had similar limits of detection of 12 SARS-CoV-2 copies/µL while ABI 7500 Fast had the lowest limit of detection of 6 SARS-CoV-2 copies/µL. After all these tests it was determined that the limit of detection across all vendors was 6-12 SARS-CoV-2 copies/µL (Vogels et al., 2020).

Discussion

In the beginning of 2020, as COVID-19 turned from an outbreak to an epidemic, the world was caught off guard. It exposed flaws in our government's preparedness for such an event, and as a result the burden of finding solutions was put on researchers and laboratories alike. The ABCTL's impact in the Arizona communities is unparalleled and critical both at the start of the epidemic as well as today. Through the tireless work and dedication of the staff organic to Dr. LaBaer's group, as well as the new staff as a result of covid, the ABCTL has been able to ramp up number of tests per day and has become the foundation of the Arizona COVID- 19 response. Through a decentralized, undefined, borderless, scientific community, a sustained COVID-19 response was provided, which is best exemplified by SalivaDirect. As labs like the ABCTL began identifying problems, solutions were found to fit the epidemic's unique requirements of low cost, simple, repeatable, using the least amount of materials possible. It began with a plethora of issues with the collection method, with the most dangerous one being shortages of nasopharyngeal swabs. The researchers at Yale were able to provide a solution that not only matched the nasopharyngeal

swab method but outperformed it in many aspects including concentration of viral load. Through a small cohort, they were able to create an epidemic friendly collection process, saliva, that accounted for limiting the amount of material used as well as not using chemicals or materials that are highly specialized. It is a solution that is elegant in its simplicity. This same elegance was seen in the same Yale researcher's solution to the impending supply shortages of nucleic acid isolation and purification kits. The contrast of the SalivaDirect method and the old nucleic acid isolation and purification kits, is a microcosm of the scientific community pre and post COVID-19. The old nucleic acid isolation and purification kits are the gold standard and were designed with no regard for the economy of materials, simplicity, price, or even accessibility. It is the gold standard in a limitless world. In our current reality, its utility was as short lived as the availability of the long list of materials it required. The solution of SalivaDirect, although not unanimously better like saliva was to nasopharyngeal swabs, during an epidemic it was the best option available. By skipping the extraction and purification step entirely, they were able to eliminate the need for multiple specialized chemicals, and very expensive and specialized lab machines, and reduce the overall material requirement. This cut the cost of the test, lowered the time a test took, and its relative simplicity made it more available at a very minimal cost to accuracy. They also took the extra step of validating multiple vendors and tested them interchangeably so that if one of the companies were to run into production issues, other companies could be confidently relied on.

Currently it appears that we are on the mend and there is cautious optimism that we will see the end of this epidemic by this summer. Should we see that come to fruition, COVID-19 needs to be a wakeup call to countries all over the world to the very realistic and devastating effects of an epidemic and it should act as a catalyst for international change in how we should prepare for a similar event going forward. Although it might not be common knowledge, it was on the selfless shoulders of researchers, like those at Yale, and laboratories, like the ABCTL, that we are approaching a potential end of this epidemic.

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Section II: Appendix

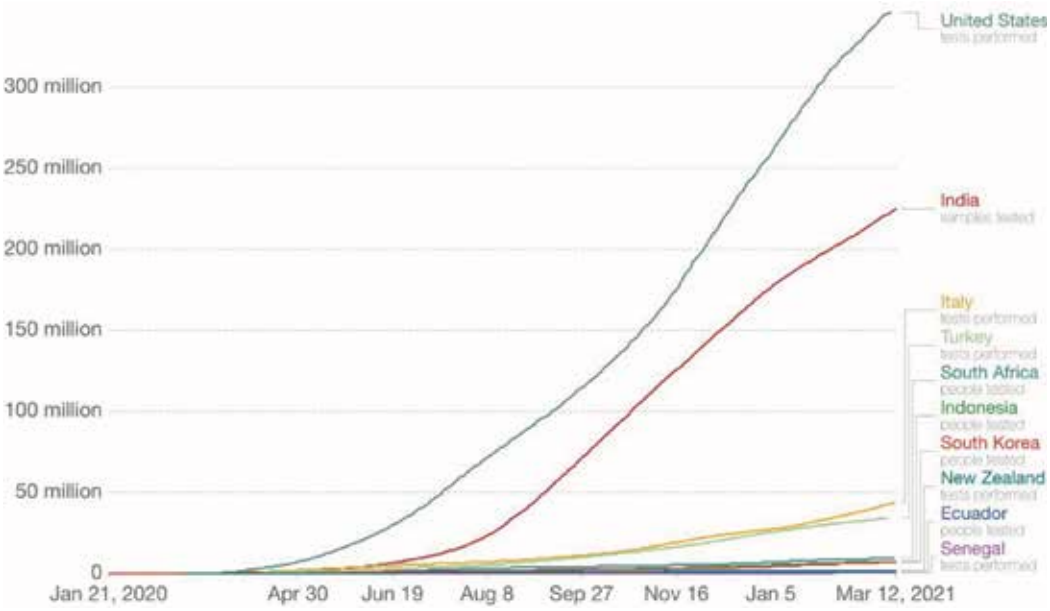

Figure 1: Total number of COVID-19 Tests, January 21, 2020-March 12, 2021. This graph depicts the increase in the number COVID-19 tests over the span of 2020 that led to the depletion of the supplies needed to run these tests. (Source: Official sources collated by Our World in Data OurWorldInData.org/coronavirus)

Figure 2: SalivaDirect Overview. Schematic overview of SalivaDirect workflow depicting the main steps of mixing saliva with proteinase K, heat inactivation, and dual plex RT-qPCR testing. (Source: Yale School of Public Health: SalivaDirectTM Publichealth.yale.edu/salivadirect) Figure created by Biorender.com.

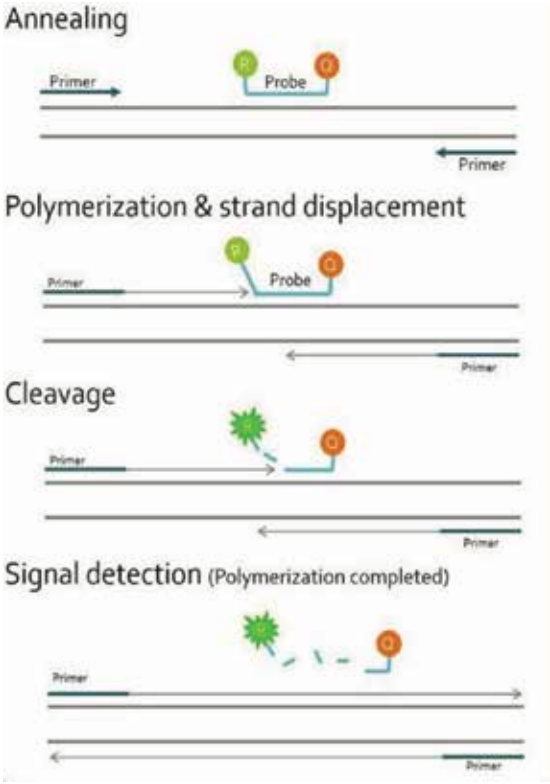

Figure 3: Quantifiable Florescence of RT-qPCR. The gene specific probe contains the fluorescence that is used to confirm the presence of that gene. Only when the probe binds to that gene, and is subsequently cleaved by the polymerase, is the fluorescence released and detectable. (Source: SMOBIO Technology, Inc. Smobio.com/faq-real-time-pcr)

	44 Total Participants
Gender (male)	23 (53%)
Age Range (years)	23-92 (mean=61)
ICU on admission	6 (14%)
ICU during hospital stay	19 (43%)
Mechanical ventilation	10 (23%)
Deceased (as of April 5th, 2020)	2 (5%)
Total samples collected	121

Table 1: Cohort Demographics. Source: Saliva is more sensitive for SARS-CoV-2 detection in COVID-19 patients than nasopharyngeal swabs https://doi.org/10.1101/2020.04.16.20067835

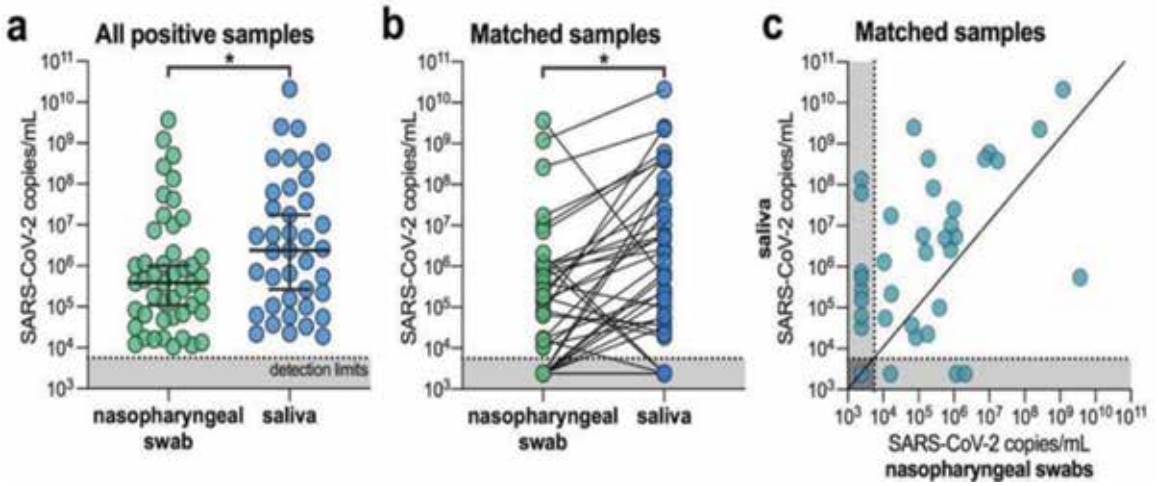

Figure 4: SARS-CoV-2 Titers in Saliva than Nasopharyngeal Swabs from Hospital Inpatients. (a) Bars represent the median and 95% CI. Yale's detection limit for SARS-CoV-2 using the US CDC "N1" assay is at cycle threshold 38, which corresponds to 5,610 virus copies/mL of sample (shown as dotted line and grey area). (b) Patient matched samples (n = 38) (c) Patient matched samples (n = 38) are also represented on a scatter plot. (Source: Saliva is more sensitive for SARS-CoV-2 detection in COVID-19 patients than nasopharyngeal swabs https://doi.org/10.1101/2020.04.16.20067835)

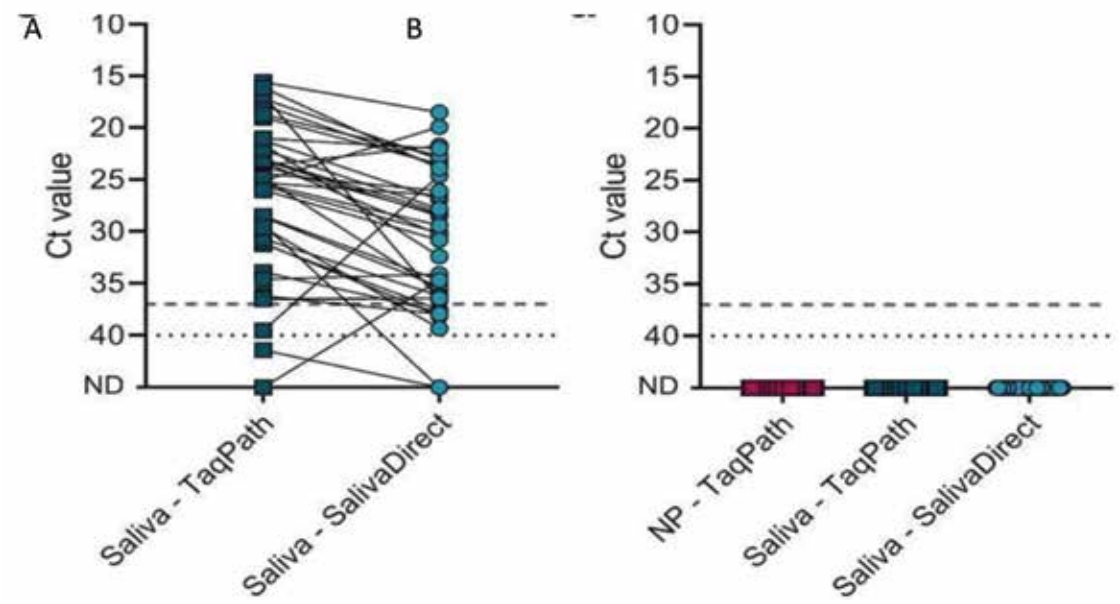

Figure 5: SalivaDirect Compared to Nucleic Acid Extraction and Purification. (A) Comparison of saliva tested with TaqPath COVID-19 combo kit and SalivaDirect again shows that SalivaDirect showed 97% positive agreement. Median N1 Ct values were 5.0 Ct higher for SalivaDirect (Wilcoxon; $P < 0.001$). (B) 30 paired nasopharyngeal swabs and saliva specimens tested negative with both the TaqPath COVID-19 combo kit and SalivaDirect. Shown are average Ct values for N, S, and ORF1ab for the TaqPath combo kit and N1 Ct values for SalivaDirect. The dashed line indicates the limit of detection for the TaqPath combo kit (37 Ct), and the dotted line indicates the limit of detection for SalivaDirect (40 Ct). (Source: SalivaDirect: A simplified and flexible platform to enhance SARS-CoV-2 testing capacity https://doi.org/10.1016/j.medj.2020.12.010)

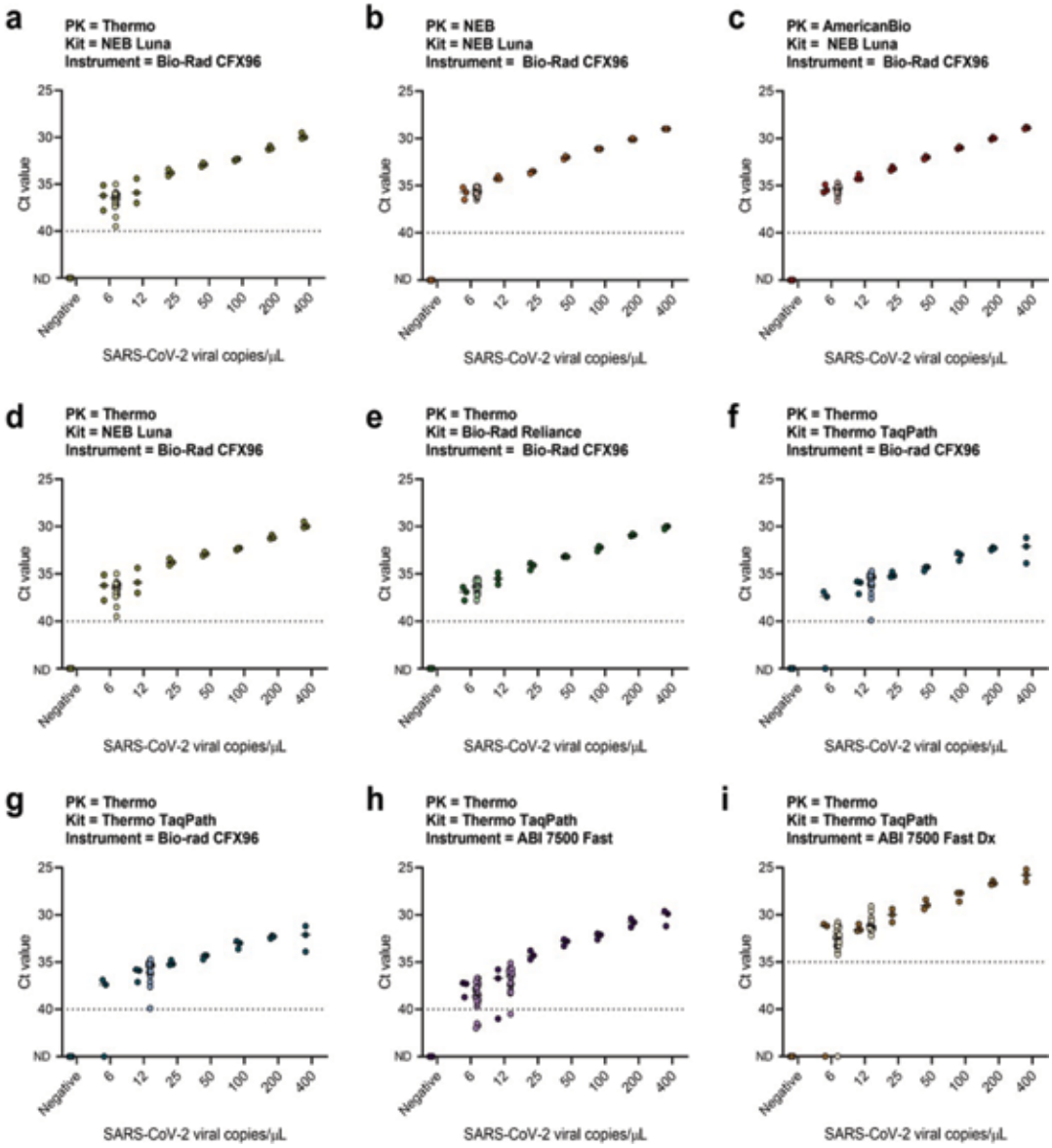

Figure 6: Validation of SalivaDirect from Multiple Venders. We determined the lower limit of detection of SalivaDirect with a two-fold dilution series (400, 200, 100, 50, 25, 12, and 6 copies/µL) of positive saliva spiked-in negative saliva. Initially, each concentration and the negative saliva was tested in triplicate to determine the preliminary limit of detection (dark-colored dots). The limit of detection was confirmed with 20 additional replicates (light-colored dots) for which 19 out of 20 needed to be detected. Limit of detection when tested with (a-c) proteinase K, (d-f) RT-qPCR kits, and (g-i) RT-qPCR instruments from different vendors, while keeping the other conditions constant. Panels a and d, as well as f and g are duplicates to enable comparisons between the different combinations of reagents or instruments within a single row. Shown are the Ct values for the N1 primer-probe set. (Source: Yale School of Public Health: SalivaDirectTM Publichealth.yale.edu/salivadirect)

Section III: A Response to COVID-19 through qPCR, Robotics, and Safety Measures

Author: Kajol Majhail

Introduction

Beginning in early January, Severe Acute Respiratory Syndrome Coronavirus 2, also known as SARS-CoV-2, was identified in the United States. The virus began to spread across the country very quickly and many people were ordered into isolation due to the unknown complications of the disease. The full genetic sequence of SARS-CoV-2 from early human cases and the sequences of many other viruses show that SARS-CoV-2 has an ecological origin in bat populations (Lofti et al., 2020). CoVs are a large family of single-stranded RNA viruses (+ssRNA) that can be isolated in different animal species. CoVs are positive-stranded RNA viruses (V'kovski et al., 2020). This is significant because they are a group of related viruses that have positive-sense, single-stranded genomes made of ribonucleic acid. The positive-sense genome can act as messenger RNA (mRNA) and can be directly translated into viral proteins by the host cell's ribosomes. Positive-strand RNA viruses encode an RNA-dependent RNA polymerase (RdRp) which is used during replication of the genome to synthesize a negative-sense antigenome that is then used as a template to create a new positive-sense viral genome. This means that RNA viruses mutate and replicate faster than DNA viruses (Positive Strand, 2020). For reasons yet to be explained, these viruses can cross species barriers and can cause, in humans, illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome Coronavirus (MERS) and Severe Acute Respiratory Syndrome (SARS). Thus, SARS-CoV-2 belongs to the beta CoVs category. Like other CoVs, it is sensitive to ultraviolet rays and heat (Hasoksuz et al., 2020).

In Mid-March of 2020, The ABCTL created its technology to detect coronavirus infection in samples of saliva from potentially infected individuals (Dr. Carolyn Compton, Dr. Joshua L. LaBaer, and Dr. Vel Murugan, ABCTL, 2020). The ABCTL is a CLIA-registered COVID-19 testing center and the first location in Arizona to offer a saliva-based diagnostic test (ABCTL, 2020). In order to achieve a fully working lab, certifications, contracts and partnerships were required. For every activity in the lab, an SOP had to be made to state what was being done in the lab. In the ABCTL, they use a TaqPath COVID 19 Combo Kit to execute the detection of SARS-COV-2 (TaqPath, 2020). The combo kit uses real-time RT-PCR, to detect viral nucleic acid from the specimens collected.

The ABCTL continued to grow daily to meet the new demands of the university and community for saliva- based testing, however as more people get vaccinated and get tested less, the demands of the lab are decreasing. This multi-level project is being conducted to record all aspects and endeavors of the ABCTL. In particular, I will be focusing on the laboratory aspects including: qPCR, robotics, and biosafety measures. At the end of this project, different groups will compile manuscripts, which will eventually be made into a documentary that highlights the work of the ABCTL.

After students began coming back to ASU in August of 2020, there was a significant spike in cases due to the lack of responsibility and social distancing among students at the Tempe campus. Through internal tracking done by the Arizona Department of Health Services ZIP code data, it can be seen that when students came back to campus there was an increase in cases in the ZIP codes that are associated with ASU (Myskow, 2020). With that said, some students did take on the responsibility of keeping themselves and those around them safe However, other students did not and carried on with a lifestyle of partying, breaking mask mandates, and failing to get tested for COVID-19. Those people then unknowingly spread the virus, either because they do not know they have it, due to a lack of testing or simply do not care. COVID-19 has permanently affected everyone around the world, as many people were physically and mentally challenged. Many people were not ready for this pandemic and its severity hurt many families.

It created a division among friends and families, with some people not caring for the pandemic, while others were fighting for their lives in hospitals. The severity of this virus and unknown side effects scared people into isolation for almost a year now. The ABCTL has been a tremendous resource for ASU and the surrounding community, as it has provided easy and fast testing for COVID-19 when many places did not have this.

This is a situation I became all too familiar with because after three weeks of being in Tempe, I caught COVID-19. This was all due to the carelessness of other students around me and the lack of education on the disease. This day ended up being one of the most stressful days because the disease affects people differently. Not only was I stressed about how this disease affected me, but I had to worry about people who I have seen and could have infected. With no responsibility taken from other students, they do not realize how large of an impact they can have by spreading COVID-19 or by not isolating when awaiting results. In the end, if students or others do not take COVID-19 testing seriously, then it can lead to many people becoming infected.

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Background SARS COV-2

On January 30, 2020, the World Health Organization (WHO) declared the outbreak of SARS-CoV 2 a public health emergency of international concern. The outbreak began in Wuhan, Hubei Province, China and afterwards spread to almost every country in the world. From January to March more cases began to appear and the virus began to spread rapidly throughout many countries. On March 11, the WHO declared the outbreak of SARS-CoV 2 a pandemic. The virus leads to a disease now named, Coronavirus Disease-19 (abbreviated COVID-19). On January 26th, Arizona State University had its first case confirmed from a student and it was the 5th case in the United States. The student was infected with the virus from human-to-human interaction while traveling internationally: interactions through traveling became a common cause of the international spread. Between traveling and human contact, the virus spreads at a very fast pace if no precautions are taken.

SARS-CoV-2 comes from a family of coronaviruses, with six other human coronaviruses identified. Coronaviruses are a family of viruses that cause respiratory illness in people and can circulate between animals and humans. SARS-CoV-2 likely evolved from a virus previously found in animals (Human Coronavirus Types, 2020). Symptoms from this disease can vary from person to person but typically include a loss of taste/smell, fever, fatigue, muscle aches, etc. The list of symptoms is vast, and every patient is not guaranteed to exhibit all of them. Those with previous medical conditions and weakened immune systems tend to exhibit more severe symptoms from COVID-19, which highlights the importance of taking precautions. However, some people show no symptoms, meaning they are asymptomatic even though they have contracted the SARS-CoV 2 virus. Being asymptomatic makes it difficult to know if a person is infected unless they get tested regularly or know they came in contact with someone who was positive for COVID-19. Potential symptoms ranging from no illness to hospitalization showcases the severity of the disease and the importance of regular testing or isolation.

Coronaviruses (CoVs) are a group of enveloped viruses, having a positive single-stranded RNA genome. COVID-19 is caused by the SARS-CoV-2, which is a more pathogenic form in comparison to previously identified SARS-CoV (2002) and Middle East respiratory syndrome coronavirus (MERS-CoV, 2013).

SARS-CoV-2 is more pathogenic because it has an adaptation of the S glycoprotein and its affinity for ACE2 determines the severity of SARS-CoV-2 infection (Fani et al., 2020). CoVs have the largest RNA viral genome, ranging from 26 to 32 kb in length. Structurally, SARS-CoV-2 contains four structural proteins, which include spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins.

CoVs rely on their spike (S) proteins for binding to the host cell-surface receptor during host cell entry. The S protein binds to the host receptor through the receptor-binding domain (RBD) in the S1 subunit, followed by the fusion of the S2 subunit to the cell membrane. The host receptor is a cell-surface receptor known as angiotensin-converting enzyme 2 (ACE2); this receptor normally helps regulate blood pressure in the body, but the virus uses it as a method of entering the cell (Huang et al., 2020). Additionally, each protein has a different function, the E protein is an integral membrane protein expressed during infection of a cell. The M protein is the structural protein and helps determine the shape of the viral envelope. Finally, the N protein enters the host cell while bound to the virus RNA genome to facilitate its replication and assist in viral assembly. Out of the seven pathogenic CoVs, many of them including, HCoV-NL63, HCoV-229E, HCoV- OC43, and HCoV-HKU1 cause mild clinical symptoms. SARS-CoV, MERS-CoV, and the newly identified SARS-CoV-2 infection cause severe respiratory illness and can result in death. Potential adaptive mutations in the SARS-CoV-2 genome possibly made it highly pathogenic and difficult for drug and vaccine development. See Figure 1, Appendix 1, to see the schematic representation of novel coronavirus showing target proteins and its mechanism of host entry (Naqvi et al., 2020).

New Strains of SARS-CoV-2

COVID-19 is an RNA virus, which generally have very high mutation rates compared to DNA viruses because viral RNA polymerases lack the proofreading capability of DNA polymerases. The genetic diversity of RNA viruses is one reason why it is difficult to make effective vaccines against them (Steinhauer et Holland, 1987). With any virus, there is constant change through mutation and new variants of a virus are expected to occur over time. Sometimes new variants emerge and disappear. Other times, new variants emerge and persist. Multiple variants of the virus that causes COVID-19 have been documented in the United States and globally during this pandemic. The virus that causes COVID-19 is a type of coronavirus and is named for the crown- like spikes on their surfaces. Changes to the virus are being monitored and these changes can happen to the spikes on the surface of the virus. Multiple variants of the virus that causes COVID- 19 are circulating globally; The United Kingdom (UK) identified a variant called B.1.1.7, South Africa identified B.1.351, and Brazil discovered a variant called P.1 (About Variants of the Virus, 2020). These variants seem to spread easier and quicker than other variants, which may lead to more cases of COVID-19.

In the ABCTL, The ThermoFisher TaqPath assay is a PCR assay that is used in the lab that detects three distinct SARS-CoV-2 targets: orf1-ab, N gene, and S gene. Due to a deletion (at position 69-70) in the Spike protein of the UK variant (lineage B.1.1.7) the TaqPath assay S gene component yields a Not Detected result when testing the UK variant (but the two other targets are Detected). This is referred to as S gene target failure (SGTF) or S dropout (Laboratory Detection, 2021). If all three targets are detected in the TaqPath assay, then the specimen does not contain the UK variant. The UK variant has been detected in the ABCTL and more research is going into finding these variations as well as other variants of the virus.

Transmission and Shedding of COVID-19

As the disease rapidly spreads worldwide, one of the most important factors to reducing the number of cases is looking at transmission rates. The disease can be transmitted either by COVID-19-positive individuals or from a contaminated environment. COVID-19 is primarily transmitted human-to-human via oral and respiratory aerosols and droplets with the virus-contaminated environment playing a lesser role in the propagation of disease. The highest viral load in COVID-19 patients is in the sputum, saliva, and

upper airway secretions, although the virus may also be found in blood, pharynx, and anus. Viral loads of SARS-CoV-2 in the respiratory tract decrease rapidly after symptom onset, with higher loads shifting from the upper to the lower respiratory tract. Patients with severe disease have higher respiratory viral loads than those with mild disease, although all loads decline with time (Meyerowitz, 2021). See Figure 2 to see the period of infectiousness for immunocompetent, symptomatic adults. Researchers estimated the duration of RNA shedding from various sites based on a detailed sample analysis of 49 patients with COVID-19 and reported a median duration of shedding from the nasopharynx of 22 days for mild and 33 days for severe cases, with some persons shedding for longer than 2 months. The figure above shows the period of infectiousness and respiratory tract viral load in the cycle threshold with time (Meyerowitz, 2021).

The dominant route of transmission of SARS-CoV-2 is respiratory. Growing evidence indicates that infectious viruses can be found in aerosols and exhaled breath samples. The virus can be transmitted at a distance through aerosols under certain circumstances, including aerosol- generating activities like singing or indoor environments with poor ventilation. When a non- affected individual inhales one of these droplets infected with the SARS-CoV-2 virus, it will begin attaching itself to the inner lining of the throat. The binding of the viral spike (S) protein to the host angiotensin-converting enzyme 2 (ACE2) receptor is a critical step for cell entry, and as a result, host ACE2 distribution determines viral tropism. ACE2 normally helps regulate blood pressure in the body but the virus uses it as a method of entering the cell. Viral load is highest in the upper respiratory tract (nasopharynx and oropharynx) early in the disease and then increases in the lower respiratory tract (sputum), suggesting that the upper respiratory tract is the usual initial site of viral replication, with subsequent descending infection.

The WHO has stated that education, isolation, prevention, controlling the transmission, and treatment of infected persons are the critical steps in controlling contagious diseases like COVID- 19 (Advice for the Public). It is possible to minimize the spread of infection through the following recommendations: staying at home (home quarantine) and avoiding any direct contact with any healthy (possible asymptomatic patients) or infected person, which has been called shielding; avoiding nonessential travel; observing social distancing rules like avoiding crowded public places and maintaining at least two meters of distance between each person; frequently washing hands for at least 20 seconds with soap and water or hand sanitizer with at least 60% alcohol, and disinfecting surfaces using household sprays or wipes. It should be mentioned that due to the long incubation period and presence of asymptomatic patients, using a medical mask (especially N95) or a respirator (especially FFP3) is recommended. These masks should primarily be worn by medical staff and those actively working with patients who are positive with COVID-19. This is due to the environment in which they work, where it is difficult to maintain a six-foot distance or stay in quarantine, as they are working on the front lines. Although this agenda is somewhat practiced by hospitals with confirmed COVID-19 patients, the general population is not completely compliant, thus, putting them at extremely high risk of exposure to infections from colleagues, household members, and the community.

Persons who have SARS-CoV-2 infection can transmit virus whether or not they have symptoms Those without symptoms may be presymptomatic, developing symptoms later (after testing) or may remain asymptomatic throughout their infection. Transmission can occur from persistently asymptomatic persons, although they seem to be less likely to transmit, and when they are most infectious is currently unknown. Researchers determined that transmissibility peaks around 1 day before symptom onset. Assuming an incubation period of 5.2 days, they estimated that infectiousness started 2.3 days before symptom onset, peaked around a day before symptom onset, and declined rapidly within 7 days (Meyerowitz et al., 2021). Viral loads of SARS-CoV-2 in the respiratory tract decrease rapidly after symptom onset, with higher loads shifting from the upper to the lower respiratory tract. Patients with severe disease have higher respiratory viral loads than those with mild disease, although all loads decline with time.

Clusters of local transmission must be identified to improve control of spread through preparedness, readiness, and response actions. Control of the spread of COVID-19 also requires precise information on human mobility, epidemiological, and genetic data at local, regional, and global levels. This information will ensure success in the deployment of resources in the mitigation of COVID-19 transmission.

QPCR Testing of Saliva Samples

There are several tests available for COVID-19 diagnosis, mostly based on viral genetic or antigen testing or on serological tests for COVID-specific antibodies. The molecular methods for detection of the viral genome are quantitative Real-time Polymerase Chain Reaction (qPCR) and E gene PCR. These tests have been effective in the detection of COVID-19 infections from respiratory secretion samples. Testing COVID-19 through saliva spit samples uses Reverse Transcriptase-qPCR. RT-qPCR tests use a sample from an individual and match the components of the sample to a portion of the SARS-CoV-2 genome. Small sequences of the viral genome, also known as primers, are the blueprints that code for certain proteins. RT-qPCR encompasses a two- step method, typically comprising two enzymes; the first step uses an RNA-dependent DNA polymerase, also known as reverse transcriptase, to copy RNA into DNA (cDNA). The saliva sample is mixed with primers, reagents, dNTPs, reverse transcriptase, and DNA polymerase, which are used to make cDNA and amplify it. The second step then switches to the use of *Taq* polymerase, which amplifies the cDNA as in a standard PCR test (Bustin et al., 2020).

The saliva sample is mixed with primers, reagents, dNTPs, reverse transcriptase, and DNA polymerase, which are used to make cDNA and amplify it. The second step then switches to the use of Taq polymerase, which amplifies the cDNA as in a standard PCR test. Then during PCR, the cDNA will be doubled after each cycle depending on if the virus has replicated inside of the individual who provided the sample. If there are viral nucleic acids present in the patient saliva sample, then the primers will bind to the cDNA generated from the viral RNA and replicate it during the PCR process. If there are no viral nucleic acids, then the primers have nothing to bind to, so they do not show amplification. RT-qPCRs are reported as cycle thresholds or Ct values. The Ct values provide a measurement of viral load. This Ct value is already determined from the amplification baseline to ensure that the sample can be deemed positive or negative. When looking at the final results, the amplification of 2 or more primers above their Ct value indicates that the patient sample is positive (ThermoFisher). Additionally, an internal control known as MS2 is added as an additional gene in RT-qPCR, to help the validity of the results. If there ends up being the wrong amount of amplification of MS2 above the Ct value, then the sample results are invalid because of a quality issue and get re-run until the final results match the normal MS2 values.

This method of RT-qPCR is used by the ABCTL to determine COVID-19 results. The process begins with extracting RNA from a patient sample using the MagMAX Viral/Pathogen Nucleic Acid Isolation Kit using the KingFisher Flex system. Then MS2 Phage is used to monitor RNA extraction and act as an internal control. Next Purified nucleic acid is reverse transcribed into cDNA and PCR amplified using the TaqPath RT-PCR COVID-19 Kit and the Applied Biosystems QuantStudio Fast Dx Real-Time PCR instrument. Then probes anneal to three specific SARS-CoV-2 target sequences located between three unique forward and reverse primers for ORF1ab, N Protein ,and S Protein Genes. Finally, results are interpreted and shown in Figure 3, Appendix 1 (ABCTL, 2020). The oligonucleotide primers and probes for detection of SARS-CoV- 2 were selected from regions of the virus Gene Orf-1ab, N protein, and S protein genes. The panel is defined for specific detection of the SARS-CoV-2. Finally, an additional primer/probe set to detect the MS2 phase internal RNA extraction control is also included in the panel. The presence of all four nucleic acid regions was detected using a multiplex Taqman assay (TaqPath COVID- 19, 2020).

However, on January 8, 2021, the US Food and Drug Administration issued a Letter to Clinical laboratory staff and health care providers to clarify that genetic variants of SARS-CoV-2 may lead to false-negative

results when using molecular tests to detect SARS-CoV-2. In order to combat this, the FDA gave many recommendations to make sure false negatives do not take place. For the TaqPath COVID-19 Combo Kit, it was shown that the test had significantly reduced sensitivity due to certain mutations, including one of the mutations in the recently identified B.1.1.7 variant (Laboratory Detection, 2021). To combat these false negatives, the FDA recommended that labs be aware of the pattern of detection associated with certain mutations, including the B.1.1.7 variant, specifically a pattern of 2/3 positive targets showing the S-gene drop out (reduced sensitivity with the S-gene target), when using the TaqPath COVID-19 Combo Kit (Center for Devices).

Development of the ABCTL

Prior to COVID-19, the ABCTL did not exist at ASU. It was developed in response to the coronavirus pandemic. In mid-March of 2020, ASU transformed one of its existing labs into the ABCTL. This lab re-purposed existing equipment and personnel to SARS-CoV-2 testing. The ABCTL has used a federally authorized diagnostic testing system from ThermoFisher that is based on qPCR amplification of 3 viral genes, to quickly identify coronavirus for individuals who may be infected and experiencing symptoms. The ABCTL itself is CLIA-certified and is the first location in Arizona to offer a saliva-based diagnostic test. To operate as a clinical lab, the ABCTL must perform its tests under the guidance of HIPPA (Health Information Portability and Accountability Act) to keep patient data confidential and securely return the results to patients.

Beginning in March the ABCTL used nasopharyngeal (NP) swabs to determine if a patient was infected with COVID-19. Now the lab has fully transitioned to using saliva-based samples, due to the many benefits of it compared to the NP swabs. In order to determine the accuracy of the saliva-based testing, both saliva and NP samples were collected from a patient and sent to clinical laboratories to reference the results. In the end, the saliva test matched the NP results, and the saliva-based test became the main test used for the ABCTL. COVID-19 saliva testing is accurate, less invasive, less labor-intensive, and requires fewer medical personnel. The laboratory is run 7 days a week to keep up with the changing demands of the pandemic and continue to support the ASU community and have expanded to support the Arizona Public and other states. Through this project, the ABCTL team has demonstrated its capability to process 2,400 samples in 24 hours.

ABCTL Automated WorkFlow

When a patient gets tested for COVID-19 through ASU, they begin the process by registering themselves in the HIPAA-compliant Point n Click system, inputting all their personal data and contact information. The Point n Click system is a portal, where patients can register their covid test and receive their results. This information does not get released when getting tested for COVID-19. After register,ing the patient provides a saliva sample in a Micronics tube, which will be traced back to the patient based on a barcode that is entered into Point n Click, linking the specific tube to the patient. These samples are collected at many sites and transferred to the ABCTL where they are processed. Before being processed, the samples undergo heat inactivation. Up to 400 samples will be put into a large incubator for 75 minutes at 65 degrees Celsius to kill any active virus particles (Interim Guidelines for COVID-19). The samples will then be transferred to Biomek i7 Automated Workstation (Biomek i7). This machine will then aliquot the samples into a 96 deep well block, containing proteinase K. However, there will be only 94 patient samples and there will be one negative control and one positive control, located in the bottom left corner in wells G 12 and H 12. This can be seen in Figure 4, Appendix 1 of this section.

Connected to the i7 are smaller machines known as IntelliXcap™, Sample Tube Capping & Decapping Systems (IntelliXcap, 2020). These machines will uncap the patient samples, then place them back onto the i7, allowing the machine to aliquot 200 microliters of sample to be placed into the 96 deep well blocks. Then the Capper and Decapper will cap the Micronic tubes to keep them sterile. In total the i7 can aliquot 376 samples per one run. The 376 samples are placed into 4 different 96 deep-well blocks.

Each 96 deep well block is then placed onto a Biomek FX Automated Workstation, which will aliquot MS2 phage into each well of the 96 deep well block, as an internal control. Then the 96 deep well blocks will be placed into the Kingfisher Flex machines (KingFisher Flex, 2020). High-throughput processing for the 96 samples will take place and the final samples will be placed onto the i7 once again, to be mixed with the assay mix and then aliquoted into a 384 well plate. Once the assay and patient samples are placed into the 384 well plate, this plate will go into the QuantStudio™ Dx Real-Time PCR Instrument, where qPCR will take place within the machine to analyze the patient samples and send the final results to be sent out to individuals (QuantStudio, 2020).

Safety Measures

While working with patient specimens, many precautions have to be put in place to protect the samples as well as those handling the samples. Since COVID-19 is a virus that can easily be transmitted, many precautions are put into place to keep the lab personnel safe. Since the saliva samples contain possible transmissible infectious agents, including COVID-19 and other infectious agents, employees wear PPE. This includes eyewear, separate clothes for only the lab, N-95 masks to prevent aerosol particles from entering the mouth or nose, and lab coats in case of any spills (Interim Guidelines for COVID-19). Surfaces within the lab are constantly disinfected with Microkill and ethanol; Microkill is a bleach germicide effective against many microorganisms with three minutes of contact time on hard - nonporous surfaces (Micro-Kill). All secondary containers and Micronic tubes are disinfected when the patient gives their sample to the testing site, then these containers are decontaminated before they get sent out to the testing sites again. Once a patient gives their sample to the testing site, the sample gets placed into a Micronic rack, to prevent any spilling. These Micronic racks are placed into secondary containers, which are then placed into coolers that are packed with ice packs and additional paper towels. These paper towels can show if any samples have spilled as they will be wet, so when arriving at the testing site, staff members can verify if anything has spilled. Before being shipped to the testing facility, the samples are counted and verified by staff members, then the transport cooler is locked with a zip tie.

When the samples enter the testing facility, they are heat-inactivated at 75 degrees Celsius, as this prevents the virus from being transmissible (Interim Guidelines for COVID-19). However, precautions still need to be in place because the samples can contain other harmful transmissible agents. All personnel at the testing site have to undergo specific training programs that include HIPAA and ASU COVID-19 training courses. Additional training is required depending on the position of the staff member and what they become trained on. When in the lab, all samples must be handled in biosafety cabinets, while the employees are in full PPE. In addition to the lab staff's safety, each patient's sample has to be handled with care. Each sample has a specific barcode and the barcode is recorded throughout the process to ensure the accuracy and safety of the sample.

Personal Experience With COVID-19

When COVID-19 started to spread rapidly throughout the US, many were ordered into isolation and all were in constant fear of what they were seeing on the news. My family and I found ourselves in the same situation; we stayed home, rarely went to the grocery store, and wiped down everything we brought into the house. We were all very careful and had a continuous fear of contracting the virus. Especially because some of my family members were immuno-compromised, including myself. When the summer ended, I decided to go back to university and live in my apartment. My family was concerned for my well-being, but I promised them that it would be just as safe. Unfortunately, after just 3 weeks of being back at university, I contracted COVID-19. I remember getting a call from the ASU's contact tracing team. Although my test results had not come back yet, I was known to be potentially exposed. In the middle of the call, my results came back positive. Immediately, a huge wave of stress washed over me. I had never felt worse. I was scared to tell my family members as I had promised them I would be safe, and I was scared to tell my roommates because I put them in danger. I was scared for the few people with whom I had come in

contact. Immediately, I called and told everyone I had seen to get tested and made sure they knew the circumstances. I then proceeded to call my family and tell them that I had tested positive for Covid-19. I remember crying on the phone and having a huge headache. My family assured me that everything was going to be fine. I began to obsess about how sick I could become. I have asthma and knew that people with underlying health conditions are prone to severe illness when they contract this virus.

Thankfully, I had a good support system. I was able to move away from my roommates to keep them safe and stay in isolation. My family members took care of me. In the end, I ended up being okay, as I developed no symptoms. Not only was that a relief for me, but the biggest relief was that it appeared I had not spread the virus to anyone else. All those around me tested negative. The possibility of spreading the virus was the biggest stress, wondering whom I could have contaminated unknowingly and fearing the potential of getting others seriously ill. The outcome of my infection was a huge relief, and I was glad to know the precautions I took paid off for those around me. However, I knew that many people in my community fail to take these same precautions, and unfortunately, that is how I contracted the virus in the first place. Many people did not take the virus seriously. Thus, more than 750,000 people in the U.S. have died from COVID, and the death toll is still on the rise (November 2021).

Conclusion

COVID-19 has existed for a year, and the virus will continue to be around indefinitely. The pandemic has been a learning experience on may levels for everyone around the world, revealing the weaknesses that exist in healthcare systems, government, and many other societal institutions. People have been challenged physically and mentally throughout the pandemic. After more than a year, people can only hope that the situation will improve. The importance of the work of the ABCTL has contributed to the control of the virus, helping to keep people safe and assisting communities in Arizona as well as other states. The lab is constantly changing the process of COVID-19 testing to make it more efficient and accurate. The ABCTL is making testing easily accessible with “Devils Drop Off,” which is a new system that allows students to use testing kits at home, instead of having to go to a COVID-19 testing site. All these new and improved ways of testing and helping the community will only be more beneficial in the future, as we have learned that pandemics can take place at any moment in time, no matter how prepared we are. Although this specific project is coming to an end, the COVID-19 pandemic will continue to be around and present challenges on a daily basis. However, this allows institutions like the ABCTL to continue to adapt and grow, while doing all that it can to help its community as the needs of the pandemic change. As a pre-med student and researcher, I am proud of ASU’s efforts to fight the pandemic and am hopeful for what the future brings.

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Appendix: Section III

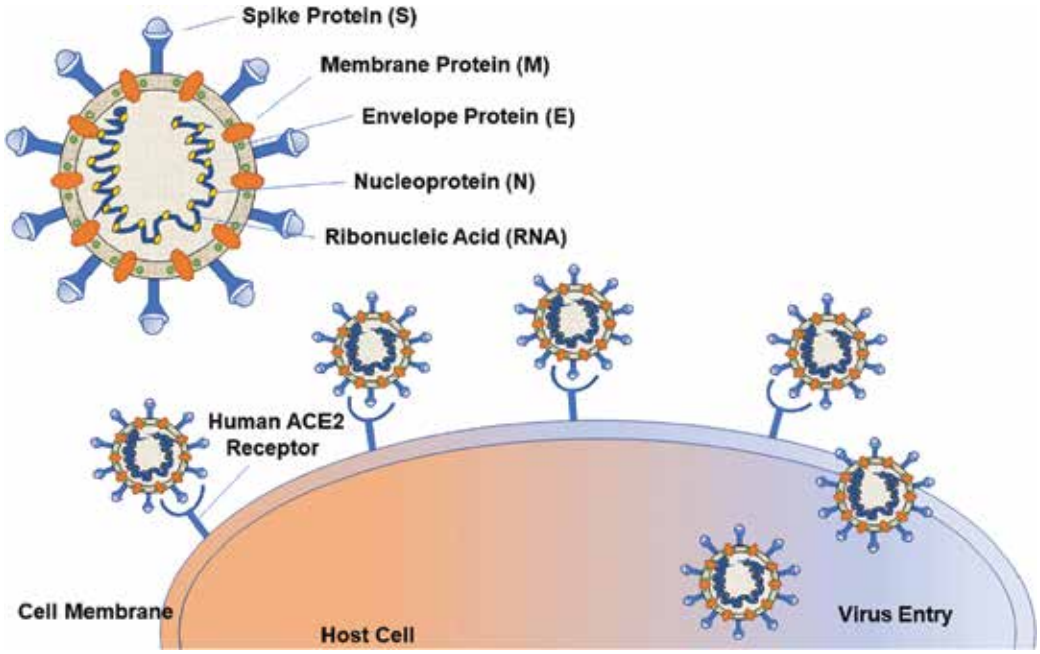

Figure 1. The schematic representation of novel coronavirus showing target proteins and its mechanism of host entry. Source: Naqvi et al., Insights into sars-cov-2 genome, structure, evolution, pathogenesis and therapies: Structural genomics approach (2020).

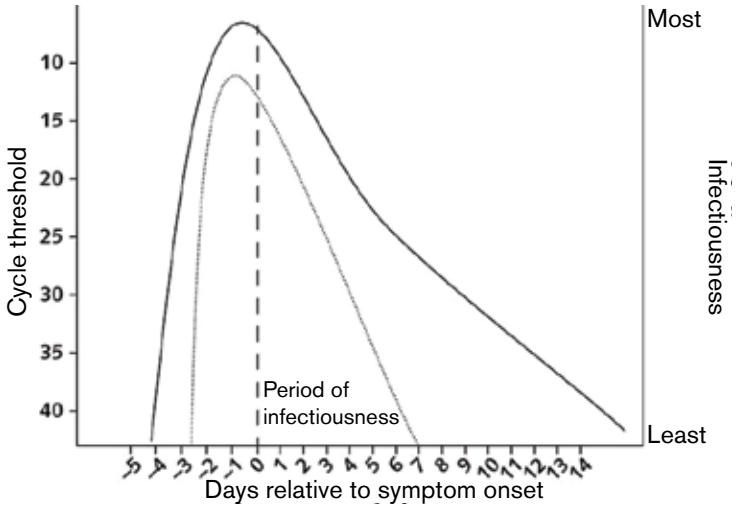

Figure 2. The period of infectiousness for immunocompetent, symptomatic adults (dotted line), and respiratory tract viral load with time (solid line). The vertical dashed line represents symptoms onset. Source Meyerowitz, E. A., Richterman, A., Gandhi, R. T., & Sax, P. E. (2021). Transmission of sars-cov-2: A review of viral, host, and environmental factors. Annals of Internal Medicine, 174(1), 69-79. doi:10.7326/m20-5008

OFR1ab	N gene	S gene	MS2	Status	Result	Action
NEG	NEG	NEG	NEG	Invalid	NA	Repeat test. If the repeat result remains invalid, consider collecting a new specimen
NEG	NEG	NEG	POS	Valid	SARS-CoV-2 Not Detected	Report results to healthcare provider. Consider testing for other viruses.
Only one SARS-CoV-2 target = POS			POS or NEG	Valid	SARS-CoV-2 Inconclusive*	Repeat test. If the repeat result remains inconclusive, additional confirmation testing should be conducted if clinically indicated.
Two or more SARS-CoV-2 target = POS			POS or NEG	Valid	Positive SARS-CoV-2	Report results to healthcare provider and appropriate public health authorities.

*Samples with a result of SARS-CoV-2 Inconclusive shall be retested one time.

Figure 3. Final results for a saliva based COVID-19 test are analyzed from this table. Source: ThermoFisher Scientific. TaqPath™ COVID-19 Combo Kit and TaqPath™ COVID-19 Combo Kit Advanced Instructions for Use. (2020).

Fig.1 384-well qPCR stamp layout

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
A	A1		A2		A3		A4		A5		A6		A7		A8		A9		A10		A11		A12	
B																								
C	B1		B2		B3		B4		B5		B6		B7		B8		B9		B10		B11		B12	
D																								
E	C1		C2		C3		C4		C5		C6		C7		C8		C9		C10		C11		C12	
F																								
G	D1		D2		D3		D4		D5		D6		D7		D8		D9		D10		D11		D12	
H																								
I	E1		E2		E3		E4		E5		E6		E7		E8		E9		E10		E11		E12	
J																								
K	F1		F2		F3		F4		F5		F6		F7		F8		F9		F10		F11		F12	
L																								
M	G1		G2		G3		G4		G5		G6		G7		G8		G9		G10		G11		Neg	
N																								
O	H1		H2		H3		H4		H5		H6		H7		H8		H9		H10		H11		Pos	
P																								

Figure 4. The layout for the 384 Well plate, where both the controls are in the bottom right corner. Source ASU Biodesign Clinical Testing Laboratory. ASU-SARS-CoV-2 Saliva Test. (2020).

Section IV: Exploring SARS-CoV-2 Antibody Testing

Author: Ellen Ruan

Background

Introduction to the Disease

In December 2019, patients reported with an unknown source of pneumonia. It was first identified in Wuhan, China. The causal agent was identified to be a novel coronavirus designated as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). On February 11, 2020, in a press briefing, the World Health Organization (WHO) reported the disease as coronavirus disease 2019 (COVID-19)(Inc, n.d.).

It was then declared a public health emergency of international concern in March 2020. On March 13, 2020 it was declared a national emergency in the United States("Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak," n.d.). As of March 20, 2021, there have been 29.6 million cases of COVID-19 in the United States.

In Arizona, the Arizona Department of Health and Safety announced the first confirmed case of COVID-19 on January 26, 2020. On March 12, 2020 Arizona Governor Doug Ducey declared a public health emergency to limit the spread("Gov. Ducey Declares Health State of Emergency for Arizona to Fight Coronavirus Outbreak | Arizona and Regional News | Tucson.Com," n.d.). A statewide stay at home order was issued on March 30, 2020 to stop the spread of SARS-CoV-2 and was lifted May 15, 2020 ("Coronavirus: Stay-at-Home Order Issued by Arizona Gov. Doug Ducey," n.d.). After the lockdown was lifted, the moving average of COVID-19 cases in Arizona increased from 377 cases per day to 3,249 cases on July 15. Almost a year from then, as of March 20, 2021, there has been 835,765 COVID-19 cases in Arizona. At the beginning of the pandemic, there was a shortage of testing nationwide and in Arizona due to shortages in the supply chain for testing kits. The Arizona Department of Health Services had only performed 183 tests by March 15, 2020. During this time, Arizonans were unable to get tested for COVID-19 and experienced long wait times for their results("Lack of Testing for COVID-19 in Arizona, Here's What We Know," 2020),("COVID-19 Test Results Are Taking Weeks, Affecting Arizona's Outbreak," n.d.). Recognizing the need for rampant testing in the community, a laboratory at Arizona State University (ASU) decided to shift its capabilities to become a certified clinical testing laboratory.

ASU transformed one of its purely research laboratories into a clinical testing laboratory by repurposing some of its existing laboratory equipment to expedite processing and testing. Led by Dr. Carolyn Compton, Dr. Joshua LaBaer, and Dr. Vel Murugan, The ASU Biodesign Clinical Testing Laboratory (ABCTL) created systems that met federal approval to begin COVID-19 testing on March 16, 2020("Overview | Biodesign Institute | ASU," n.d.). This included following the standards set by the Health Insurance Portability and Accountability Act (HIPAA) and Clinical Laboratory Improvement Amendments. HIPAA ensures that the ABCTL protects patient privacy and confidentiality which is important for providing test results. This includes making sure that the right results were sent to the correct individuals and that their data was stored appropriately. The Clinical Laboratory Improvement Amendments certification ensures the accuracy and quality of the work done in the ABCTL. These certifications make the ABCTL a clinical laboratory.

At the beginning of the pandemic, the nasopharyngeal swab was the standard sample collection method that was used for the quantitative polymerase chain reaction (qPCR) test which measured the amount of viral RNA in a participant's body. However, it began facing supply chain issues due to the high demand. Sample collection using nasopharyngeal swabs also required more highly trained staff and personal protective equipment (PPE) for the staff as the swabs caused participants to cough or sneeze on the testing staff. Recognizing these challenges and understanding the need for increased testing, the ABCTL

developed the first saliva-based test in Arizona and was the first to make this type of test available to the public("State Recognizes ASU Biodesign Institute's Response to COVID-19 with Innovator of the Year Award," n.d.). The saliva test from the ABCTL eliminated some of these supply chain issues as it required fewer highly trained testing personnel and PPE due to the decreased discomfort by using saliva collection. The ABCTL was able to automate sample processing thereby increasing COVID-19 testing in the community. By using robots and machines, 2,400 samples can be processed within the span of 24 hours using the qPCR test. The results of these tests are returned in the span of 24-48 hours. From March 15 to September 15, 2020, the ABCTL was able to process 16,000 tests weekly ("Overview | Biodesign Institute | ASU," n.d.). This rapid testing helped identify infected individuals in the community and allowed them to be informed in a timely manner.

The ABCTL also made testing widely available to the public by partnering with local organizations and underserved populations to provide testing for essential workers. They also partnered with the Arizona Department of Health Services to provide free COVID-19 testing to communities throughout Arizona and the Four Corners with 100 available sites per week("Overview | Biodesign Institute | ASU," n.d.). Following the mission of the university, the ABCTL was able to transform COVID-19 testing in Arizona.

Severe Acute Respiratory Syndrome Coronavirus-2

SARS-CoV-2 is a positive sense RNA virus. It was sequenced and found to encode 29 proteins total with the main proteins being the structural proteins that provide its unique shape and allow it to enter human cells. The main proteins are the membrane (M) protein, the spike (S) protein, the envelope (E) protein, and the nucleocapsid (N) protein with its RNA. The S protein allows the virus to enter human cells by binding its receptor-binding domain (RBD) to the angiotensin-converting enzyme 2 (ACE2) receptor found in human cells. In order to deliver the virus's genetic information into the human cell, the virus needs to also fuse with the plasma membrane of the cell. Thus, it needs to be cleaved in order to be activated. The S protein is cleaved by proteases on the human cell: transmembrane serine protease (TMPRSS2) and furan; these cleave the tip of the spike protein and allows fusion with the cell membrane (Hoffmann, Kleine- Weber, Schroeder, et al., 2020; Hoffmann, Kleine-Weber, & Pöhlmann, 2020). Once the virus is fused with the plasma membrane, it can insert its viral genome into the cell and begin using the host cells organelles to make copies of its genome and begin replicating, ultimately infecting human cells.

Clinical Presentation of COVID-19

Patients with COVID-19 have diverse clinical presentations and experience differing severity. The most common symptoms are fever, cough, and difficulty breathing (Guan et al., 2020). The severity of this disease is classified based on the clinical presentation. According to the WHO-China Joint Mission on Coronavirus Disease, it was determined that around 80% of laboratory confirmed COVID-19 patients present with mild to moderate symptoms and approximately 20% have severe disease ("Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)," n.d.). Patients can also be considered asymptomatic, meaning that they did not present with any symptoms throughout the course of their disease. The proportion of the population with asymptomatic COVID-19 cases is contested and has been estimated to be between 40% to 45% (Oran & Topol, 2020). Patients with mild to moderate cases are recommended to stay at home and monitor their symptoms. Severe COVID-19 cases are defined as having one of the following features: acute respiratory distress syndrome (ARDS), low oxygen saturation, or severe disease complications including respiratory failure, septic shock, or non- respiratory organ failure (Liu et al., 2020). These patients require hospitalization. Patients with severe COVID-19 also present with pneumonia, lymphopenia, exhausted lymphocytes and cytokine storm (Cao, 2020). Lymphopenia and exhausted lymphocytes indicate that the immune system is functioning poorly. Cytokine storm in COVID-19 involves the release of pro- inflammatory cytokines that harm the body's cells. The massive, uncontrolled inflammatory response is the reason for severe cases of COVID-19.

Immune Response and COVID-19

The Immune System

The immune system is the body's protection against pathogens. It can be divided into two different lines of defense: innate and adaptive immunity. Innate immunity is not specific to a certain pathogen and is the first to respond to infection. Components of the innate immune system include mast cells, natural killer cells, eosinophils, and basophils. The phagocytic cells of the immune system are macrophages, neutrophils, and dendritic cells. Phagocytes digest infected cells and destroy the pathogen. Innate immune cells can activate adaptive immunity by processing antigens through phagocytosis and presenting these to the adaptive cells (Chaplin, 2010). Innate immunity uses cell signaling pathways to alert other cells of the infection. These pathways depend on chemical messengers including cytokines. A particular type of cytokine, interferons, help launch the initial antiviral response (Schoggins et al., 2011). Interferons are produced by the infected host cell and activate antiviral responses in uninfected cells, informing them of the virus (Payne, 2017). They also send signals to infected cells, telling them to die before the virus can finish replicating and continue to spread. Interferons also recruit other lymphocytes which can generate long-lasting immunity.

Adaptive immunity is known as the memory immune response and is specific to the pathogen. It works to clear the virus from the immune system. It begins contributing to the immune response a few days after initial infection. B lymphocytes, T lymphocytes, and antigen-presenting cells are the major components of adaptive immunity. Their receptors recognize specific antigens and can carry out specific cell-mediated responses. Within the adaptive immune response, there are two types of adaptive immune responses: the humoral response and the cell-mediated response. The difference between them is the location where they occur relative to the infected cells.

Humoral immunity works extracellularly (outside of infected cells) and cell-mediated immunity occurs within infected cells. Humoral immunity involves primarily B lymphocytes. In the humoral response, B lymphocytes get activated by the virus and produce antibodies, also known as immunoglobulins. Antibodies are proteins that identify and bind to pathogens in the body, preventing them from infecting other cells or marking them for destruction. They can either be bound to B lymphocytes or they can be on their own. There are five different types of antibodies—IgA, IgD, IgE, IgG, and IgM. IgA, IgM, and IgG play a pivotal role in viral infection. IgA antibodies can be found in the lung and other organs with mucosal membranes. IgM is the first antibody produced in response to a pathogen and provides short- term protection. IgG is the most common antibody; they are produced after IgM antibodies and are used for long-term immunity. IgM antibody levels decline after IgG antibodies are produced. Antibody-mediated immunity is known as humoral immunity. Antibodies can be neutralizing or non-neutralizing. Neutralizing antibodies bind to the pathogen and prevent it from interacting with human cells. This binding prevents the pathogen from binding to the receptor of the human cells. Neutralizing antibodies can also interfere with the virus so that it does not release its genetic information successfully in the human host cell.

Non-neutralizing antibodies, also known as binding antibodies, also bind to pathogens, but they do not inactive them. They can be used to alert other immune cells in the body of an infection, but they do not prevent infection. IgG and IgA antibodies are neutralizing, and IgM can be neutralized (Long, Liu, et al., 2020),(Charles A Janeway, Travers, Walport, & Shlomchik, 2001). A special type of B lymphocyte is the memory B cell which is specific for a pathogen and can survive for many years. They generate a faster, stronger immune response should reinfection of a particular virus occur(Seifert & Küppers, 2016).

Cell-mediated immunity kills the virally infected cells and involves primarily T lymphocytes. In order to trigger a T cell immune response, antigens are presented on macrophage surfaces and other cells. T lymphocytes are activated through cell-to-cell interaction between the antigen on antigen-presenting cells and their own antigen receptors; they aid in the regulation of the immune response. Specific types of T lymphocytes include T helper cells (TH). When activated, these cells secrete signals known as cytokines

which regulate immune response. There are regulatory T cells (Treg) that contribute to immune response regulation by ending the T-cell mediated immunity and suppressing immune response after the virus has been reduced to low enough levels; this prevents autoimmune diseases (Vignali, Collison, & Workman, 2008). Cytotoxic T cells (TC) kill infected cells which are marked with a specific antigen. Memory T cells, like memory B cells, when activated will also lead to a stronger immune response. The immune system has built up strong and efficient defenses against foreign pathogens including viruses by separating into these different types of responses.

Immune Response to SARS-CoV-2

The disease progression of COVID-19 involves the entry of the virus into the human host cell, recognition of this foreign pathogen, and the activation of signaling pathways that direct the immune response. SARS-CoV-2 enters human cells by binding its S protein to cells expressing the ACE2 receptor; this leads to TMPRSS2 cleaving the ACE2 receptor, allowing the virus to enter into the cell (Hoffmann, Kleine-Weber, Schroeder, et al., 2020; Zhang, Penninger, Li, Zhong, & Slutsky, 2020). Once the virus is in the human cell, it can begin replicating. In response to this pathogen, the host cell becomes inflamed and dies. This alerts cells and macrophages next to it to produce pro-inflammatory cytokines and chemokines including interleukin 6 (IL-6), interferon gamma (IFN), monocyte chemoattractant protein 1 (MCP1), and interferon gamma-induced protein 10 (IP-10) (Guan et al., 2020; Tay, Poh, Rénia, MacAry, & Ng, 2020). These signals attract other immune cells like macrophages and T cells to the site. This initial response of the innate immune system influences the severity of COVID-19. The severity of COVID-19 is associated with inflammation during disease progression as patients with more severe cases have more pro-inflammatory cytokines (Gong et al., 2020). Patients with asymptomatic or mild cases of COVID-19 have a robust and early innate response which effectively fights the virus. The initial inflammation attracts T cells to the site that dispose of the infected host cells before the virus is able to spread, effectively defeating it and launching a proper adaptive immune response. In contrast, patients with severe cases have an inefficient or delayed innate response. The late response leads to an increased accumulation of immune cells in the lungs causing an excessive production of pro-inflammatory cytokines which destroy the cells in the lung; patients with severe disease have been found to have higher levels of IL-2, IL-6, IL-7, IL-10, macrophage inflammatory protein 1, and tumor necrosis factor (TNF) (Tay et al., 2020; Grifoni et al., 2020; Huang et al., 2020). This overproduction of cytokines is known as cytokine storm and causes immunopathology leading to multi-organ failure and death (Cao, 2020, p. 19). For patients with asymptomatic or mild cases, the adaptive immune system can also produce neutralizing antibodies which can bind to SARS-CoV-2 and prevent them from further infecting other cells (Tay et al., 2020). This also marks them for digestion by macrophages, removing them from the body. In patients with severe COVID-19, the B cells of the adaptive immune response produce non-neutralizing antibodies which increase the viral infection through antibody-dependent enhancement (Tay et al., 2020). SARS-CoV-2 induces B and T cell responses around seven days after the onset of symptoms. CD4+ T helper cells prime the CD8+ T cytotoxic cells and B cells. The T helper cells also control the production of cytokines, bringing other immune cells toward the site. There is evidence supporting the correlation between adaptive immune response and severity of COVID-19. Asymptomatic individuals have lower levels of antibody response than those with mild or severe cases (Long, Tang, et al., 2020). Patients with severe COVID-19 had stronger and broader T cell responses than patients with mild disease (Peng et al., 2020). These are important findings that can be used for the creation of therapeutics and for understanding immunity.

Humoral immunity plays an important role in the COVID-19 immune response. The virus induces the response of IgA, IgM and IgG antibodies against the S protein and N protein within the first two weeks of symptom onset (Seow et al., 2020). IgA antibodies are prominent in the initial immune response and contribute to the neutralizing effect (Sterlin et al., 2021). IgM antibodies respond first like other immune responses due to its ability to be expressed without the need for isotype switching. The amount of time that these neutralizing antibodies last is still being determined, but IgM antibodies have been found to last for around 2.5 months (Iyer et al., 2020). IgG antibodies are produced shortly after IgM and can last

for around 4 months with neutralizing antibodies (Iyer et al., 2020). These antibodies have a neutralizing effect, binding to the virus and preventing it from infecting other cells. These neutralizing antibodies target the S protein, preventing SARS-CoV-2 from entering other human cells (Jiang, Hillyer, & Du, 2020). It is important to measure the neutralizing strength of antibodies in order to determine immunity and how long it lasts. The humoral response of immunity against SARS-CoV-2 has been greatly studied due to the ability of neutralizing antibodies to block infection. It is also easy to measure the level of antibodies for diagnostic purposes. This information is important in determining long- term immunity and possible reinfection. However, the cell-mediated response from T lymphocytes also needs to be considered as the memory B and T cells play a role in long-term immunity. In Figure 1 (see Appendix), both of these immune responses work to provide immunity against SARS-CoV-2 as they are different defense mechanisms. Thus, it is important to consider both aspects of immunity when creating vaccines or determining long-term immunity.

Antibody Testing

General Antibody Testing

Antibody testing is not used for diagnostic purposes and instead provides information about a previous infection. They are usually taken after an infection as the body takes a few weeks to develop antibodies. The basic mechanism underlying the test involves the binding of the antibody to the target antigen. There are many different types of antibody tests as they can vary in the target antigen, the type of antibody being tested, and the technology platform being used. The target antigen is specific to the disease and can include different proteins of the virus which induce the production of antibodies in the human body. The testing platforms provide different forms of technology that depict the antibody-antigen binding. There are many different types of antibody tests including enzyme-linked immunosorbent assays (ELISA), chemiluminescence immunoassays (CLIA), lateral flow immunoassays (LFIA), and neutralization assays.

ELISA can be used for antibody testing by using the high binding affinity of the antibody. The antibody is linked with an enzyme that when conjugated, can produce an effect that is measurable and detectable. There are many forms of ELISA tests such as the direct, indirect and sandwich types. These differ in terms of both antigen and antibody placement as well as the binding and number of antibodies used. The typical ELISA antibody test done is the sandwich method which uses two antibodies that bind to the antigen making it very sensitive and specific. The antibody binds to the antigens in the plate, and once bound the second antibody detects this complex and produces a signal that can be measured. ELISAs are laboratory tests and take a few hours to process. Another popular ELISA is the direct ELISA (Figure 2, see Appendix). In the direct ELISA, two antibodies are used as well. The primary antibody is the patient antibody, and the detection antibody is a class-specific secondary antibody that is enzyme-labeled. The antigen is directly attached to the plate. When the labeled antibodies and antigens bind, a reaction occurs causing a color change that can be measured to quantify the number of antibodies a patient sample contains. These steps of a direct ELISA testing for COVID-19 antibodies are highlighted in Figure 2. Chemiluminescence immunoassays are similar to ELISA, using the binding affinity of antibodies and antigens, but they involve using a chemical reaction that emits light. This is also a laboratory-based technique. Both of these processes can be automated, and the results can be quantifiable. Thus, they can be expensive and require more technology.

Lateral flow tests, also known as rapid tests, are quantitative tests that rely on reading a result produced. They are cassette-based tests and use a few drops of blood. The test strip uses capillary flow to move the antibodies to bind with the antigens. There are anti-human antibodies that bind to the antigen-antibody complex and allow them to be colored and read in the indicator region. Lateral flow assays are able to test for multiple antibodies. They contain a control line as well to ensure that the test works correctly. The benefits of lateral flow immunoassays include taking only 15-20 minutes to receive a result and not requiring extensive lab equipment. Because they operate like a pregnancy test, it is quick and easy to

perform for large populations. It also does not require highly trained professionals. Neutralization assays are used to determine the presence and levels of neutralizing antibodies. These are important for the creation of new therapeutics as neutralizing antibodies prevent the pathogen from infecting other cells by binding to antigens. They do not measure all antigen-antibody bindings and instead focus on the binding of neutralizing antibodies and antigens. Not all antigens will generate a neutralizing antibody response so these tests are important for identifying which antigens produce a neutralizing response. These tests use live virus and thus require a biosafety level 3 laboratory. There are many tests that can be used to determine the presence of antibodies with varying degrees of technology and trained personnel needed.

In order to determine the best type of test, there are different factors that should be considered. These include sensitivity and specificity. Sensitivity is known as the true positive rate. It is the test's ability to identify individuals with antibodies to the disease. Specificity is the true negative rate meaning it is the test's ability to identify individuals without antibodies to the disease. These are measured by comparing the results from the tests to the true number of individuals who are confirmed to have the infection or not. These factors are important in determining the positive predictive value and the negative predictive value. These are calculations that are also based on the prevalence rate of the disease. The prevalence rate is the percentage of individuals who have antibodies to the disease. The positive predictive value is the quotient of the true positive of the disease and the predicted positive rate of the condition. The negative predictive value is the quotient of the true negative and the predicted negative rate of the condition. These values are important when determining the accuracy of antibody testing. Every laboratory test has false positives—where an individual tests positive but does not have the disease—and false negatives— where an individual tests negative but does have the disease. False positives and false negatives can be limited by having both a highly sensitive and specific test. If there is low prevalence of a disease, this would mean a low positive prevalence rate which can lead to more false positives. All of these values can be calculated and are used in the determination of which antibody tests should be given to the public.

COVID-19 Antibody Testing

There are many forms of tests that are associated with COVID-19 and SARS-CoV-2. These include the polymerase chain reaction (PCR) test, the antigen (rapid) test, and antibody (serology) tests. The PCR test and antigen tests are used for diagnostic purposes whereas the antibody tests provide information of a past infection of COVID-19. There are many forms of COVID-19 antibody tests. They differ based on the type of antibodies being tested, the technology, and the target antigen. The main antibody types that are used in serologic testing include IgG, IgM, IgA, or a combination of antibodies called a total antibody test. IgM antibodies are produced first and signal a recent infection. IgG antibodies are produced after IgM antibodies. Because this is an infection in the respiratory tract, the mucosal immune system produces IgA antibodies. IgA antibodies play an important role in neutralizing the virus during an infection and are produced at measurable concentrations in the immune response for COVID-19 (Sterlin et al., 2021). SARS- CoV-2 antibodies can be detected around two to three weeks after symptom onset but have been discovered to occur earlier (Long, Liu, et al., 2020; Xiang et al., 2020). The most popular antibodies tested for COVID-19 are IgM and IgG. These are able to be measured and detected one to three weeks after infection and can remain in the body for weeks and months due to the memory immune response as seen in Figure 3 (see Appendix).

There are a variety of antibody tests that were produced that use the typical antibody testing technologies like ELISA, CLIA, or LFIA assays. For SARS-CoV-2, typical target antigens include the S protein, the RBD of the S protein, and the N protein. Many manufacturers create different types as they each have their benefits and detriments. The FDA has given emergency use authorization for multiple serology tests based on their specificity and sensitivity from validation studies and their assumptions of 5% for both positive and negative predictive values (Health, 2021). The first antibody test for SARS-CoV-2 was approved by the FDA in April 2020. This test was made by Cellex and was a LFIA testing for detecting the presence of IgG and IgM antibodies (Mandavilli, 2020). In May 2020, the FDA began reviewing safety and

efficacy data of commercial antibody tests for their use. Laboratories who developed their own antibody tests did not have to undergo FDA review. This led to the development and creation of numerous antibody tests. Thus, in order to determine the best type of antibody test, there are many logistical factors that need to be considered.

In order to determine which serology test is best to use, a comparison of their specificities and sensitivities must be done. There has been increased focus on creating LFIA due to their ease of use and fast return of results. The workflow is fairly simple as seen in Figure 4. LFIA tests can be completed anywhere as it only requires a few drops of blood and does not require highly specialized staff to read because it produces

an easily understandable result (Figure 4, see Appendix). However, the specificity and sensitivity of these tests must be considered especially in relation to other antibody assay types when considering which COVID-19 antibody tests should be used and determining if there is a major difference between the technologies. Sensitivity and specificity are important in determining the strengths and weaknesses of the tests as they measure who is confirmed or excluded in disease screening.

Antibody tests can differ in many ways—type of target antigen, type of human antibody being tested, and technology type. All of these factors can impact the sensitivity and specificity of a test. Many antibody tests are being produced, but the question remains as to which one should be implemented and used as a standard for antibody testing for COVID-19. Thus, a comparison between sensitivities and specificities must be made between the different tests in order to determine if there is a best antibody test that should be used.

A meta-analysis of multiple antibody tests was completed and published in Diagnostics. Kontou et al., conducted a systematic review of literature for COVID-19 serological tests to determine the pooled sensitivities and specificities of these tests following the bivariate method for meta-analysis of diagnostic tests using information from 38 papers published in PubMed, medRxiv, and bioRxiv. They considered multiple factors that could impact sensitivity and specificity in addition to the type of test technology, including the type of target antigen and type of antibody. Along with analyzing ELISA, CLIA, and LFIA technologies, they also analyzed fluorescence immunoassays (FIA). FIA—like CLIA—use the same basis as ELISA tests, but instead emit light instead of creating a color change. The light emitted can be measured to determine the level of patient antibodies. They also included papers for antibody tests that used N antigen, S antigen, or both and tests that measured IgG, IgM, or both.

The bivariate meta-analytic method uses transformations of the true positive rate and false positive rate to model specificity and sensitivity. Meta-regression was performed in order to determine the possible effect of other variables on sensitivity and specificity of these antibody tests. They also use Begg's and Egger's tests to detect publication bias and other small study effects. Both of these were performed on antibody tests with five or more studies. It was determined that only CLIA IgG tests had some evidence for publication bias (Table 1). The meta- regression analysis revealed the influence from the factor of mean number of days from disease onset influencing ELISA IgG, LFIA IgG, LFIA IgG/IgM, and CLIA IgG tests (Table 1). The ELISA IgG was also influenced by the proportion of individuals with severe COVID-19 (Table 1). These covariates affect the determined sensitivity and specificity of the tests and must be taken into consideration when viewing the results of this study.

When comparing the results between the different antibody testing technologies, Kontou et al. determined that ELISA and LFIA tests detecting both IgG and IgM antibodies had the best pooled sensitivity

when compared to tests that detected only one type of antibody (Figure 5, see Appendix). In Table 1 (see Appendix), this is seen as for ELISA and LFIA testing for both IgM and IgG have higher pooled sensitivities than their counterparts that test for only IgM or IgG. They also confirmed that IgG antibody tests show higher sensitivity when the patient samples were collected a few weeks after symptom onset. In addition, ELISA and CLIA showed the greater pooled sensitivity than LFIA and FIA (Figure 5). The pooled specificity of all of these methods is high, with ELISA and LFIA reaching 99% (Figure 6 and Table

1) (Kontou, Braliou, Dimou, Nikolopoulos, & Bagos, 2020). Based on these results, they suggest that ELISA is the safer choice for antibodies during the current stage of the pandemic. Although LFIA might be better-suited for seroprevalence studies, its lower sensitivity should be considered when creating these studies in the population as they may not be as accurate and may underestimate the true number of individuals infected with COVID-19.

They also looked at the tests individually to determine the effect of the different factors on specificity and sensitivity like target antigen and type of antibody tested. When looking at ELISA tests only, they determined that ELISAs made using the S antigen are more sensitive than ones with the N antigen (Kontou et al., 2020). This is seen in Table 1 with the pooled sensitivities of ELISAs with S antigen ranging from 0.817 to 0.935 and the pooled sensitivities of the ones with N antigen ranging from 0.722 to 0.808. The combined IgG/IgM ELISA has higher pooled sensitivity (0.935) than the ones for IgG (0.814) and IgM only (0.817) (Table 1). A majority of the LFIA tests used both N and S as target antigens, so these cases were not stratified for target antigen. For LFIA, the combined IgG/IgM tests had higher pooled sensitivity (0.777-0.828) than IgG or IgM alone (Table 1). However, LFIA pooled sensitivity was still lower than CLIA and ELISA test sensitivities (Figure 5). CLIA methodology showed higher pooled sensitivity of IgG (0.944) than IgM (0.810) with the combined IgG/IgM having a lower pooled sensitivity of (0.907) which does not follow the same trend as the LFIA tests (Table 1 and Figure 6). However, the CLIA test for IgG may be biased as seen in the results from the meta-regression which showed the influence from the mean number of days from disease onset. The FIA tests had smaller sample sizes and there was not much difference between FIA tests for IgG and for IgM in terms of pooled sensitivity and specificity (Figure 5 and 6). The pooled specificities of all tests were similar and high meaning they were able to identify individuals who do not have the disease as negative and have a low false positive rate (Figure 6). Thus, the type of antigen and antibody being tested for should be taken into consideration when determining the exact antibody test that should be the standard.

Based on these results, if public health officials wanted to determine the best antibody test based on the calculated sensitivities, they should choose the tests with the highest sensitivities. Higher sensitivity means that there is a lower false negative rate and can identify a greater number of true positives. If they wanted to use an ELISA to detect the seroprevalence of COVID-19, they should use one that uses S protein as the target antigen because it is more sensitive. If they wanted to use a LFIA for a seroprevalence study, the best choice would be one that measures both IgG and IgM antibodies due to the higher sensitivity (Figure 5). The LFIA technology also makes it practical for large-scale applications. For CLIA, it is difficult to make a decision due to the bias so more research should be studied before choosing a test. However, based on the results from this paper alone, a test measuring IgM would be reasonable as it still has a high sensitivity that is not affected by bias. As for FIA, the best choice would be the one testing for IgG antibodies due to the higher sensitivity. The results from this study provide a good base for determining a standard for antibody testing, but more research needs to be conducted and examined in order to reach a decision.

There is increased focus on LFIA due to their rapid results and ease of use as in addition to the previously mentioned reasons, they can also test for multiple antibodies including IgM and IgG. Thus, these tests can be interpreted to inform on the general timeline of a COVID-19 infection. There are combinations of testing positive and negative for IgM and IgG that could determine the status of infection and the stage of immunity. Individuals who test positive for IgM but negative for IgG could be having a recent infection where their body is just beginning to produce antibodies (Jacofsky, Jacofsky, & Jacofsky, 2020). Similarly, individuals who test negative for IgM and positive for IgG could have had a previous infection to where their body is no longer producing those early antibodies. Information from these results provide more information about humoral immunity that is needed in vaccine creation or the disease process itself. These are especially useful in large populations.

There is no gold standard for serological testing like there is for diagnostic testing. There are tradeoffs that occur between the different tests. These are important to consider and should be acknowledged when determining which antibody tests are appropriate. The tradeoffs can differ between varying populations as well. Thus, it is important to continue testing available tests and comparing them to each other to determine which tests are best to use. There are still many questions left unanswered like the concentration of neutralizing antibodies and how long this immunity lasts. Antibody testing plays an important role in answering both of these questions.

Antibody Testing at the ABCTL

The ABCTL is in its early stages of collecting serology samples of its students and staff to get a better look at the effect of COVID-19 in the community. However, large-scale publicly available antibody testing is coming to the ABCTL. Since its creation, the main focus of the laboratory has been on developing a certified RT-PCR test for COVID-19 as it is a true diagnostic test. This was the best option for the community at the beginning of the pandemic as diagnostic testing is more effective at preventing the spread than antibody testing. As its RT-PCR saliva test is refined, the ABCTL has begun exploring other crucial tests that can help the community including antibody testing. Current commercial antibody tests are commonly the ELISA tests. However, these tests can be expensive, and they require the use of purified proteins which can be difficult to make. They are also not as efficient because they can only test one protein at a time. LFIA are good for large populations like the one that ASU serves, but the technique can be improved upon and when done in large batches, can also be expensive. Therefore, there is still a market for creating an innovative and efficient antibody test.

Using previous technology from ASU, the ABCTL is able to create a new type of antibody testing that is able to meet the demands of the community for a more informative form of serology testing. This new antibody test follows a Nucleic Acid-Programmable Protein Array. It provides each protein a unique DNA barcode that can be used for the expression of multiple proteins on a single array. This can be used to test for multiple antibodies, not just ones to SARS-CoV-2 but to other strains of coronaviruses and influenza viruses as well which will be beneficial in the future. This simplifies the process of antibody testing as it doesn't require the purification of proteins and is highly specific and sensitive (Díez et al., 2015). It is able to perform both the validation and discovery in a single step and is not biased against different protein arrays. The ABCTL undergoes continuous refinement expanding its ability to provide the community with Zinnovative solutions to help end the pandemic.

Importance of Antibody Testing

Antibody testing informs the public about the status of the pandemic and can be used to create policies and for vaccine development. Many public health measures have been put in place in response to the pandemic including mask mandates and lockdown strategies. A way to determine an exit lockdown strategy would be looking at the immunity of the community. This can be done by doing antibody tests. Serology tests can also inform about the mortality and morbidity rates of the disease. Scientists and public health officials can also determine the spread of the pandemic through antibody testing. Testing blood or antibodies can be used to determine a more accurate number of people who have been infected with coronavirus (Vogel, 2020). Herd immunity, which has been widely debated, can also be determined from the results of antibody testing.

In Arizona, officials and volunteers from Mayo Clinic, the Maricopa County Department of Public Health and ASU conducted a large scale serosurvey from September 12, 2020 to September 23. They sampled individuals from neighborhoods that were chosen by the CDC as a statistically representative sample of Maricopa county. It found that 10.7% (470,000) of Maricopa residents have antibodies for COVID-19. At the time, only 177,000 COVID-19 cases had been reported to the county. This discrepancy led them to believe that there were more individuals in Arizona that were infected with COVID-19 than the amount

getting tested (Innes, n.d.). This type of data is valuable because it informs the officials about the status of the disease in the area and is vital when making policy changes to help stop the spread. It also highlights the areas that need to be improved in order to understand the spread of the disease. In order to truly understand how SARS-CoV-2 is spreading in the community, there must be antibody testing.

The vaccine developments depended on the results of these serology tests to determine how an immune response is launched and how long neutralizing antibodies last. Serology tests can continue to be used to determine immunity against COVID-19 as they can be used to also detect the type of neutralizing antibodies.

Conclusion

As SARS-CoV-2 continues to spread and mutate around the world, there is still much to be learned. When this paper is reviewed, the COVID-19 pandemic would have only been present for a little more than a year. While there are foundations of knowledge that have been discovered since the beginning of the pandemic, it is important to continue looking into the immune response of COVID-19 especially in consideration to long-term immunity and vaccine development. The implementation of antibody testing at the ABCTL is on the way. Improvements will continue to be made to the ABCTL as effects of COVID-19 will continue to be present in society. New diseases are being discovered and it is important to continue outlining the research in order to prepare for the future. SARS-CoV-2 will not be the last pathogen that the ABCTL encounters.

Section IV: References

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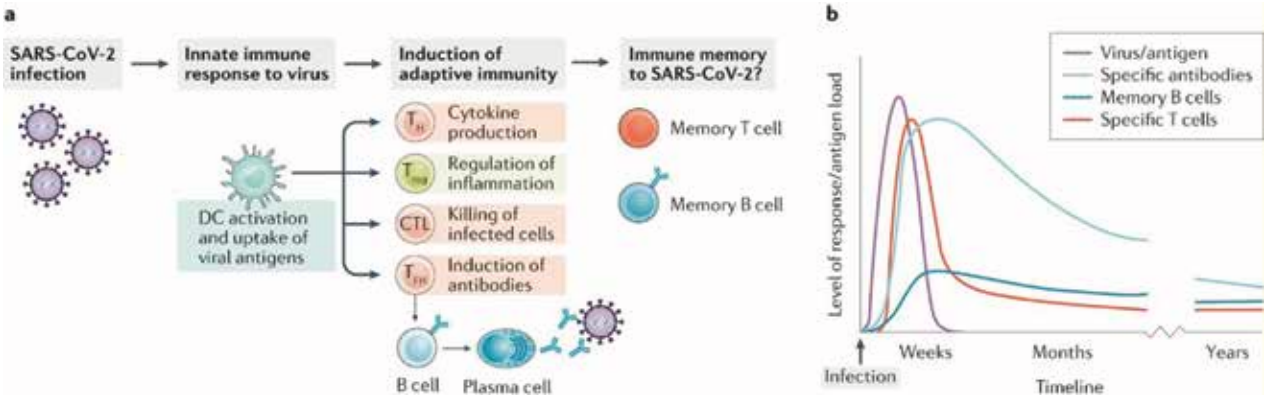
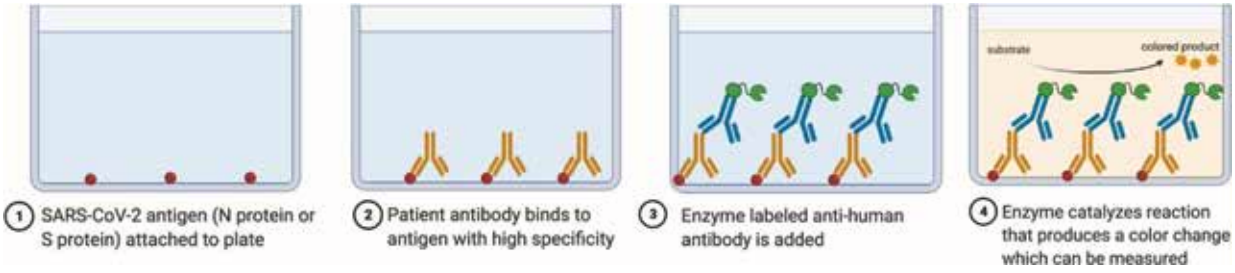
Section IV: Appendix

Figure 1 Immune Response to SARS-CoV-2 and the time course of immunity.



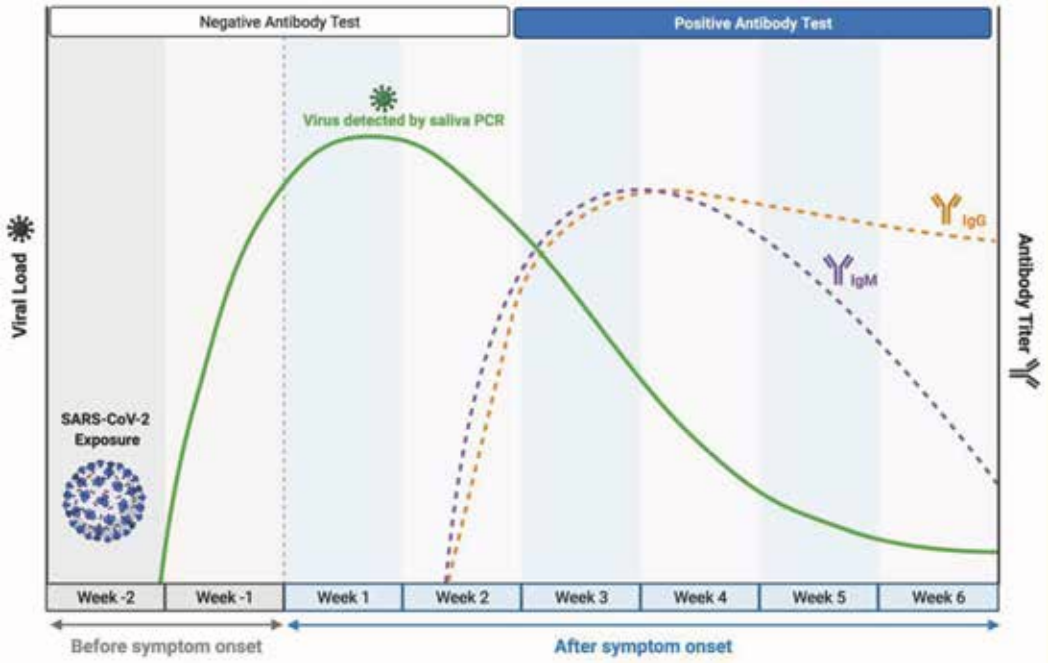
The immune response involves both the innate and adaptive immune responses. Long-term immunity lasting for years is achieved through both memory B and T cells signifying that both humoral and cell-mediated immunity play important roles in immune response. Figure retrieved from Not just antibodies: B cells and T cells mediate immunity to COVID-19 by Cox, R. J., et. al (2020) https://doi.org/10.1038/s41577-020-00436-4

Figure 2 Direct ELISA test steps for SARS-CoV-2.



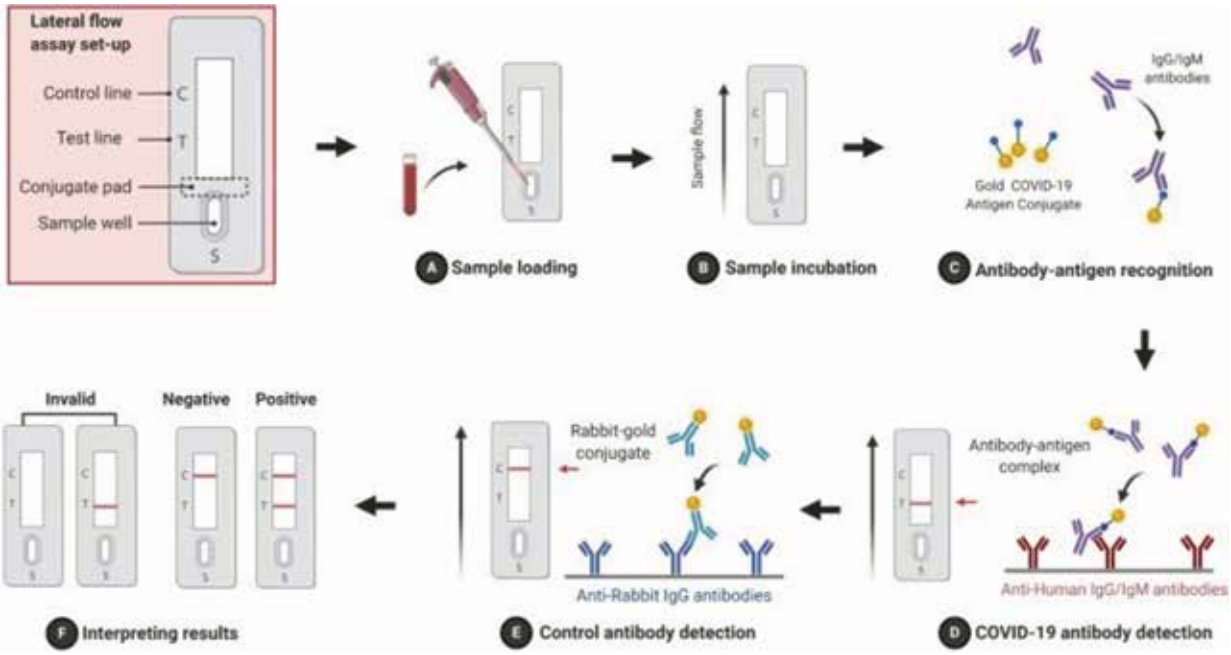
1) The antigen is located on the well. For SARS-CoV-2 this could be the N protein, S protein, or RBD of the S protein. 2) The patient antibody is added to the well and it binds with the antigen. 3) The secondary antibody is added. This is an anti-human antibody enzyme labeled so it binds to the patient antibodies. 4) The enzyme catalyzes a reaction to produce a measurable color change that can determine the quantity of patient antibodies. Created with BioRender.com

Figure 3 Infection of COVID-19, Antibody Response and Test Positivity.



IgM antibodies are produced first, and IgG antibodies are produced later on in the disease course. An individual only tests positive for antibodies a few weeks after infection. Created with BioRender.com

Figure 4 Lateral Flow Immunoassay (LFIA) Steps for detecting COVID-19 antibodies.

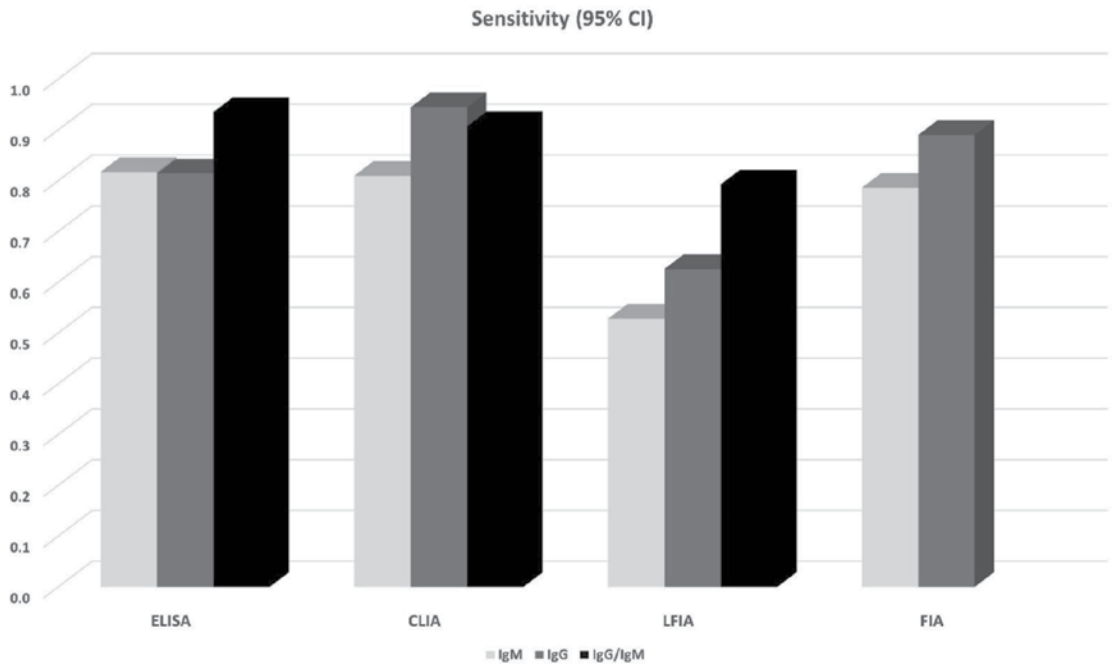


A) Patient sample is added to mechanism, only requires a few drops of blood. B) The sample moves across the test through capillary action. C) Antibodies specific for COVID-19 bind to the gold COVID-19 antigens in the conjugated pad. D) Sample enters testing well and binds to the anti-human antibodies forming a readable line. E) The control line to determine if the test is valid. It is seen from the binding of rabbit antigen and anti-rabbit IgG antibodies. F) Results are read and determined. Positive COVID-19 LFIA is where both T and C strips are present, and negative is when T strip is missing. C strip is needed to determine the validity of the test. Figure retried from COVID-19: Molecular and Serological Detection Methods by Dhamad, A.E. and Rhida, M.A.A., 2020, https://doi.org/10.7717/peerj.10180

Method	Ab	Ag	Students/ Patients	Sensitivity (95% CI)	Specificity (95% CI)	Covariates	Begg's/ Eggtr's
ELISA	lgG	N	8/1472	0.747 (0.509, 0.984)	0,994 (0,988, 0.999)	mdfo, severe	-/-
ELISA	lgG	S	7/1072	0.814 {0.688, 0.940)	0.961 (0.910, 1.000)	-	-/-
ELISA	lgM	N	8/1717	0.722 {0.449, 0.996}	0.995 {0.989, 1.000)	-	-/-
ELISA	lgM	S	6/1328	0.817 (0.704, 0.931}	0.991 (0.976, 1.000)	-	-/-
ELISA	lgG/lgM	N	2/423	0.808 (0.764, 0.853}	0.967 (0.915, 0.987)	NA	NA
ELISA	lgG/lgM	S	5/1244	0.935 (0.900, 0.971}	0.987 (0.973, 1.000)	-	-/-
LFIA	lgG	S	2/535	D.537 (0.123, 0.951}	0.914 (0.853, 0.951)	NA	NA
LFIA	lgG	NS	8/944	0.650 (0.404, 0.895)	0.988 {0.973, 1.000)	mdfo	-/-
LFIA	lgG	S/NS	10/1479	0.626 (0.439, 0.814)	0.964 (D.922, 1.000)	-	-/-
LFIA	lgM	S	2/535	0.663 (0.236, 1.000)	0.914 (0.852, 0.951)	NA	NA
LFIA	lgM	NS	9/1059	0.528 (0.329, 0.726)	0.986 (0 974, 0.998)	-	-/-
LFIA	lgM	S/NS	11/1594	0.555 (0.352, 0.758)	0.979 {0.958, 0.999)	-	-/-
LFIA	lgG/lgM	S	2/824	0.828 (0.770. 0.886}	0.994 (0.984, 0.998)	NA	NA
LFIA	lgG/lgM	NS	8/1373	0.777 (0.592. 0.962)	0.986 {0.973, 1.000)	mdfo	-/-
LFIA	lgG/lgM	S/NS	10/2197	0.793 (0.643; 0,942)	0.989 (0.976, 0.999)	mdfo	-/-
LFIA	lgG/lgM	S/N/NS	11/2376	0.800 (0.663, 0.935}	0.984 {0.969, 0.999)	mdfo	-/-
CLIA	lgG	NS	12/2320	0.944 (0.906, 0.983)	0.971 (0.931, 1.000)	mdfo	-/+
CLIA	lgG	N/NS	13/2479	0.935 {0.896, 0.975}	0.974 {0.953, 0.994)	mdfo	-/+
CLIA	lgM	NS	12/2411	0.810 {0.722, 0,897}	0.984 {0.970, 0.999)	-	-/-
CLIA	lgM	N/NS	13/2570	0.799 (0.737, 0.860}	0.967 (0.927, 1.000)	-	-/-
CLIA	lgG/lgM	NS	2/790	0.907 (0.753, 1.000)	0.981 (0.944, 1.000)	NA	NA
CLIA	lgG/lgM	N/NS	3/949	0.902 (0.811, 0.993)	0.954 (0.875, 1.000)	NA	NA
FIA	lgG	NS	2/318	0.859 (0.339, 1.000)	0.950 (0.923, 0.977)	NA	NA
FIA	lgG	S/NS	3/327	0.890 (0.591, 1.000)	0.950 (0.923, 0.977)	NA	NA
FIA	lgM	NS	2/318	0.860 {0.500, 1.000)	0.950 {0.923, 0.977)	NA	NA
FIA	lgM	S/NS	3/327	0.786 (0.531, 1.000)	0.950 (0.923, 0.977)	NA	NA

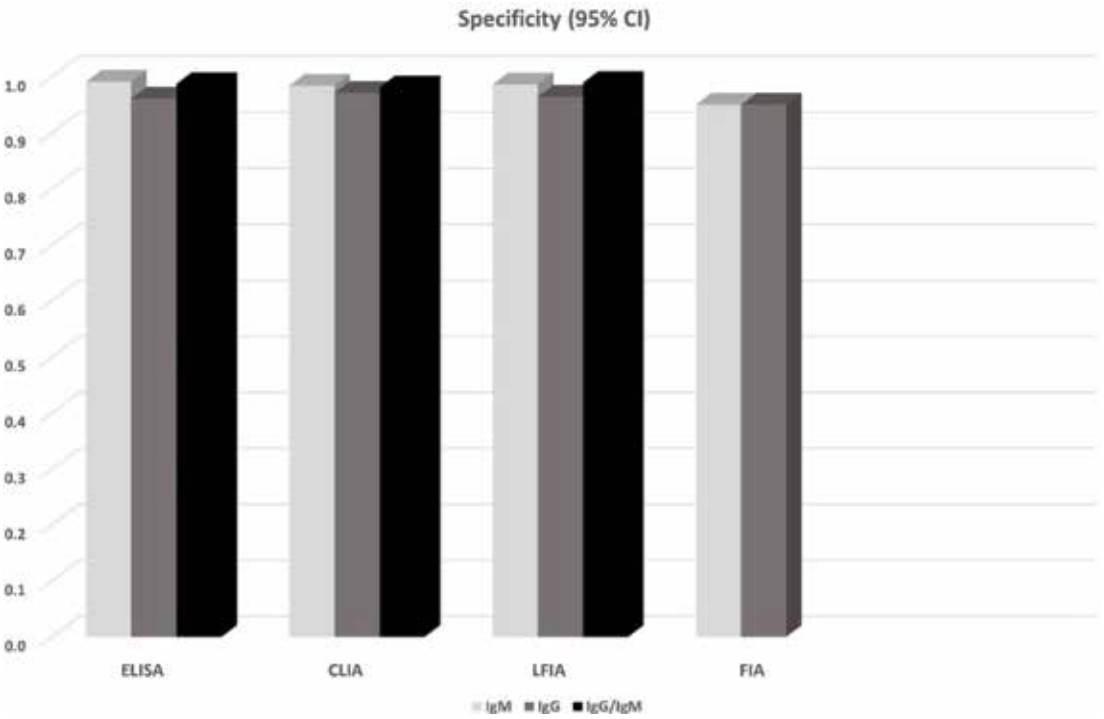
Figure 5: Results of the meta-analysis of 38 papers organized by technology of test. Each test includes information about its method, antibody being tested for (Ab), target antigen (Ag; N: nucleocapsid; S: Spike; NS: nucleocapsid and Spike), number of studies and patients whom they retrieved the information from, pooled sensitivity, pooled specificity, covariates (mdfo: mean days from onset; severe: patients characterized with severe COVID-19; NA: not applicable) and results of Begg's/Egger's tests (-: no effect; +: some effect). Retrieved from Antibody Tests in Detecting SARS-CoV-2 Infection: A Meta-Analysis by Kontou et al, 2020 https://doi.org/10.3390/diagnostics10050319

Pooled Sensitivity



Confidence intervals for pooled sensitivity of the different tests based on type of antibody measured: IgG, IgM, or both. Retrieved from Antibody Tests in Detecting SARS-CoV-2 Infection: A Meta-Analysis by Kontou et al, 2020 https://doi.org/10.3390/diagnostics10050319

Pooled Specificity



Confidence intervals for the pooled specificity of the different tests based on type of antibody measured: IgG, IgM, or both. ELISA, CLIA, and LFIA had higher specificities than FIA. All specificities are greater than 90% in the confidence interval calculated. Retrieved from Antibody Tests in Detecting SARS-CoV-2 Infection: A Meta-Analysis by Kontou et al, 2020 https://doi.org/10.3390/diagnostics10050319

Section V: Deconstructing the Saliva Sample Collection Process and Preanalytical Standardization

Author: Jennifer Smetanick

Introduction

COVID-19 is a highly transmissible respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This coronavirus gains entry into human cells by first interacting and binding its spike glycoprotein with the human cell membrane receptor ACE2, an essential step for cell membrane fusion (Lan et al., 2020). ACE2, which stands for angiotensin-converting enzyme 2, is a component of the renin-angiotensin-aldosterone system and plays a major role in regulating blood pressure, vasoconstriction, and inflammation (Bhalla et al., 2020). ACE2 is present in most organs, including the lungs, heart, kidney, and intestines, and counters the activity of ACE by catalyzing the hydrolysis of angiotensin-II, a vasoconstrictor, into Ang(1-7), a vasodilator (Keidar et al., 2007). Therefore, inhibiting ACE2 would manifest into a host of negative symptoms characteristic of COVID-19 such as cough, difficulty breathing, fever, and nausea. See Figure 1, Appendix, for a more detailed outline of the ACE2 pathway.

On March 11th, the World Health Organization (WHO) declared COVID-19 to be a global pandemic. New customs had to be put into place immediately to lessen transmission among people. This included social distancing six feet away from others, wearing face coverings to reduce droplet transmission, and keeping a close eye on common COVID-19 symptoms such as fever, cough, and shortness of breath. COVID-19 originated in Wuhan, China but it had quickly spread throughout the world. Businesses, travel, and every-day life how we knew it was forced to extremely modify or shut down. Other than the effects that COVID-19 has directly on a person's health, including being an asymptomatic spreader, developing fever, loss of taste or even death, this pandemic has even broader effects for how we live our daily lives going forward (Haleem et al., 2020). Many Americans saw the challenges and lack of financial support within the healthcare field, large economic slowdown especially for small businesses, as well as major restructuring of social activities. Large sporting events, international traveling, cultural or festive events, and other areas of recreation (like theatres, clubs, and gyms) were all required to shut down. Though this is a necessary precaution for the health of the citizens, there are definitely disadvantages to the mental health of many Americans during this period of isolation.

Background on SARS-CoV-2 (The Virus) and COVID-19 (The Illness)

Coronaviruses

Coronaviruses are a large family of viruses named for the crown-like spikes on their surface (Centers for Disease Control and Prevention, 2020). Though there are hundreds of coronaviruses that circulate mostly in non-human animal reservoirs, three have caused serious and even fatal disease within humans. These include: SARS-CoV that caused Severe Acute Respiratory Syndrome (SARS) from 2002-2004, Middle East Respiratory Syndrome (MERS) in 2012, and the current SARS-CoV- 2 that causes COVID-19 (National Institute of Health, 2020). Coronaviruses are large, enveloped viruses recognized for their ability to rapidly evolve due to high rates of nucleotide substitution and recombination (Artika et al., 2020). These viruses are notably large in size and are approximately four times the size of picornavirus genomes (viruses that cause a range of diseases including the common cold, poliomyelitis, meningitis, and hepatitis).

Another important characteristic of the coronavirus is its genetic material: positive single- stranded RNA. Not only for coronaviruses, but approximately 85% of emerging viruses have single stranded RNA genomes as well (Rosenberg et al., 2013). These types of genomes are more prone to uncorrected errors during replication compared to DNA. RNA polymerase does not have the proofreading capabilities or

repair mechanisms that DNA polymerase possesses. For these reasons, coronaviruses have been known to rapidly evolve because of these high nucleotide substitution rates (Lim et al., 2016).

There are 29 proteins in the SARS-CoV-2 genome, four of which are key structural proteins: the spike (S), nucleocapsid (N), membrane (M), and envelope (E) proteins (Katsnelson, 2020). The spike protein plays a critical role in cell receptor recognition and the membrane fusion process (Huang et al., 2020). This protein has also been a focus in vaccine design because it is the main antigen present of coronavirus surfaces (Li, 2016; Tortorici et al., 2019). Of the nonstructural proteins are two large polyproteins that are cleaved into sixteen smaller proteins which include 3- chymotrypsin-like protease, papain-like protease, and RNA-dependent RNA polymerase within the ORF region (Huang et al., 2020). Many of the other nonstructural proteins are still poorly understood at the time. See Figure 2, Appendix, for a schematic representation of SARS-CoV-2.

COVID Epidemiology and Relevance to Arizona

As of January 5th 2020, 59 people in Wuhan, China have been infected with what we now call SARS-CoV-2 and 7 were in critical condition (Cyranoski, 2020). Other highly infectious respiratory diseases such as SARS and MERS were immediately ruled out by authorities, leaving many uncertain of the global threat this novel virus could carry. In the early reports of the disease, little was known regarding the virus' transmissibility, but it was evident that people aged over 60 were at substantially higher risk for infection that would be fatal. After more data became available, epidemiologists reported that COVID-19 had high pandemic potential as the virus could be transmitted by asymptomatic COVID-19 positive individuals (J. T. Wu et al., 2020). By the end of January, the WHO declared this virus as a Public Health Emergency of International Concern, but many countries at the time including the United States, did not begin preparing for the medical demands of the disease (Maxmen, 2021).

By March, the number of cases began to soar across the world (approximately 50,000 new cases worldwide) and COVID-19 was officially deemed a pandemic. It was difficult to determine treatment plans or drugs to combat this novel disease. Social distancing and mask mandates were put into place for public areas to help reduce the spread of coronavirus. Current unknowns and epidemiological challenges are the emergence of new variants in different countries such as the B.1.1.7 variant first identified in the United Kingdom which is potentially more severe than other earlier lineages of the virus (Nature, 2021). These new findings pose great concern for the diagnostic testing and vaccine production for COVID-19.

Soon a whole year had passed, but because of extremely weak methods of disease response in many countries, cases were at an all-time high of approximately 750,000 new cases worldwide with the United States possessing around 250,000 of them in January 2020 (The New York Times, 2020). During this month, Arizona had the highest rate of new COVID-19 cases and deaths in the nation (Steinbach, 2021). These statistics highlight just how vital the ABCTL was for the COVID-19 response in our community. By March 2021, cases were steadily decreasing and more and more individuals are being vaccinated with the Moderna, Pfizer, or Johnson & Johnson COVID-19 vaccines. See Figure 3 in the Appendix of this section for the published COVID-19 case numbers in Arizona from March 8th, 2020 to March 7th, 2021.

Transmission and Pathogenesis

The primary means of transmission of SARS-CoV-2 is through direct person-to-person respiratory transmission (Meyerowitz et al., 2021). It typically occurs through close-range contact via respiratory droplets that can be released when an infected individual coughs, sneezes, or talks to another individual. The basic reproduction number (R0), which indicates how many cases will be generated, on average, from a single person who is infected and correlates with the risk of epidemic spread, is estimated to be within a range of 2.0 and 3.0 for COVID-19 (Dhar Chowdhury & Oommen, 2020). Therefore, social distancing at least 6 feet apart and always wearing medical- grade masks or face coverings in public settings is vital to

lower rates of transmission. Another form of transmission is fomite transmission such as hand contact with contaminated surfaces and transferring the virus when touching the eyes, nose, or mouth. This however is not a major route of transmission.

Once SARS-CoV-2 has entered the host cell, many studies have revealed that the virus exerts cytopathic effects (apoptosis and cell lysis) within kidney cells and the formation of syncytia (cellular fusion) in lung tissue (Naqvi et al., 2020). These processes can be observed in the cell through the mobilization of vesicles to form replication complexes and the disruption of Golgi complexes during viral replication (Naqvi et al., 2020). SARS-CoV-2 pathogenesis involves both the innate and adaptive immune system. The infection can be divided into three stages: (1) the asymptomatic state, (2) upper/conducting airway response, and (3) progression to acute respiratory distress syndrome (ARDS). Stage 1 marks the initial 1-2 days of infection and typically there is a limited innate immune response as the viral load is low. However, these individuals are still infectious. In Stage 2, the virus propagates down the respiratory tract and the innate immune response is triggered followed by the adaptive immune response (Mason, 2020). T cells and secondary messengers like cytokines will play an important role to reduce the effects of the disease and restrict the virus to mostly the upper and conducting airways. At this stage, 80% of infected patients will have a mild disease and be able to recover, however, 20% will progress to Stage 3 during which the virus infects alveolar type II cells and triggers those cells to undergo apoptosis. The pathological results of COVID-19 infection include alveolar damage and severe scarring. Elderly populations are especially at risk because of their lower immune response and reduced ability to repair and regenerate damaged epithelium.

Clinical Manifestations of COVID-19

The effects of COVID-19 disease ranges from asymptomatic to critical including mortality. A summary report of 72,314 cases from the Chinese Center for Disease Control and Prevention showed that 81% of cases exhibited mild symptoms (no/mild pneumonia), 14% were severe, and 5% were critical, including conditions such as respiratory failure and septic shock (Dhar Chowdhury & Oommen, 2020). Fever, dry cough, and loss of taste are very common symptoms of the disease. Other clinical manifestations include gastrointestinal symptoms such as abdominal pain, nausea, and diarrhea. Risk factors for the disease are the elderly and patients with comorbidities such as cardiovascular disease, diabetes, chronic respiratory disease, cancer, and hypertension (Z. Wu & McGoogan, 2020).

Testing for SARS-CoV-2

Molecular Testing for the Viral Genome

The molecular test for the viral genomic RNA is known as RT-PCR (real time polymerase chain reaction), qPCR (quantitative PCR), or just PCR and is considered the gold standard for COVID-19 diagnostic testing. This is the test that the ABCTL utilizes to return rapid and accurate results. PCR involves three major steps: denaturation, annealing, and extension. Since SARS-CoV-2 possesses an RNA genome, the first step is to reverse transcribe the RNA sample into complementary DNA (cDNA) using reverse transcriptase (Neidler, 2017). DNA dependent DNA polymerase is used to make the single-stranded cDNA into double-stranded DNA. Denaturation occurs when the double-stranded DNA template is heated to high temperatures (94-95 °C) to separate the strands. Annealing occurs when the temperature is lowered (50-56 °C) so the DNA primers can attach to the template strand. Extension occurs when the temperature is raised (72 °C), and a new strand of DNA can be made from the provided Taq polymerase (an enzyme that polymerizes DNA). See Figure 4, Appendix, for a schematic representation of PCR.

These three steps are typically repeated 20-40 times. In each cycle, the number of DNA copies double, which is characterized by exponential growth (2n). RT-qPCR utilizes fluorescent probes to indicate if the viral DNA had amplified to clinically relevant levels (Oswald, 2020). In this method, oligonucleotide probes are placed on both the 5' (a fluorescent reporter) and 3' (a fluorescent quencher) end of the DNA strand.

Therefore, fluorescence is only detected when the probes separate (which is a RT-qPCR by-product). Clinically relevant levels can be determined by comparing with a predetermined threshold cycle (Ct value) that indicates whether a sample is positive (contains DNA at or above the Ct value) or negative (DNA does not reach threshold). To calculate the Ct value, researchers must view the fluorescence curve in its entirety and agree upon a horizontal threshold line at a point where the reaction is in the exponential phase (to not be confused as a background signal). For COVID-19 detection, a common Ct value was 32 ± 2 (Pasomsub et al., 2021). See Figure 5, Appendix, for an example of how to determine the Ct value from a fluorescence curve.

Saliva as a Test Specimen

Saliva is produced by the salivary glands and is composed of 99.5% water (Maddu, 2019). However, within that remaining 0.5%, there are many other important substances such as electrolytes, enzymes, immune cells, and epithelial cells (that carry DNA). Saliva plays a role in swallowing, initial digestion of starches and fats, and protecting the oral mucosa from drying out. The use of saliva as a diagnostic tool is not a new concept and has successfully been used to identify the viruses that cause Ebola, Zika, Yellow Fever, as well as SARS and MERS (Niedrig et al., 2018). The greatest benefit of a saliva test is the non-invasive nature of the test and the easy collection of considerable quantities of viral RNA (necessary for a PCR diagnostic test).

In the early stages of COVID-19 diagnostic testing, using nasopharyngeal (NP) swabs was the golden standard as the samples returned very high accuracy rates when analyzed with PCR. However, as months passed and diagnostic testing needs only continued to grow, new forms of collection needed to be utilized. There were shortages of personal protective equipment, NP swabs, and highly trained medical staff to administer the test (Greenwood, 2020). Additionally, the nasopharyngeal test can be uncomfortable or even painful for some patients. There is also room for error if the swab causes the patient to sneeze excessively around their surroundings and potentially infect many others.

Saliva testing became a top candidate for COVID-19 testing as it alleviated many of the issues associated with the NP swabs. Unlike the swab testing, saliva tests are easily collected without highly trained medical personnel. This means that the test can be cheaper, has potential to be collected at home, and is much less invasive for patients. Many consumers may have familiarity with this type of test if they ever completed DNA testing kits like 23andMe. Since saliva testing was becoming the most promising method, it was vital to study and compare the accuracy of this test with the NP golden standard.

Preanalytical Vulnerabilities

Before PCR can be performed, there are many factors that need to be standardized beforehand. This section will detail major sources of pre-analytical vulnerabilities of the saliva test before it enters the lab. Saliva can easily be contaminated. Most common causes include presence of interfering substances in the sample (such as food or beverage), not enough or too much sample being provided, or incorrect patient identification when tracking the saliva sample. To mitigate some of these risks, patients are instructed to produce a 2 mL sample of clear sample by spitting in the provided test tube. For a clean sample, participants cannot eat, drink, smoke, vape, chew gum or tobacco, or take medication for at least 30 minutes before the test (ABCTL, 2020). Certain strong food/beverages such as coffee could even affect the sample beyond 30 minutes and should be cautioned against. The sample collection process itself takes approximately 20-25 minutes. During this time, the sample should be protected from airborne sources of contamination by making sure to tightly secure the test tube cap when not actively producing the sample.

Accuracy Results

After rigorous testing trials, the saliva test was shown to be comparable to the NP swab test. In February 2021, Pasomsub et. al., published a cross sectional study regarding saliva and its candidacy for COVID-19 diagnostic testing. Two hundred sample pairs of nasopharyngeal/throat swabs (NP/T) and saliva samples were collected in this study. The participants' median age was 36 years, median onset of symptoms was 3 days, and 69 (34.5%) individuals were men. They concluded that the sensitivity of the saliva test was 84% with a 95% confidence interval (CI) of 60.4% - 96.6% and the specificity of the test was 98.9% with a 95% CI of 96.1% - 99.9% (Pasomsub et al., 2021). Discrepancies in the sensitivity of the saliva sample may be due to demographic differences, chance occurrence, or procedural variations in sample collection. See Figure 6, Appendix, to access the table used in the study.

In medical diagnosis, test sensitivity and specificity are important metrics to determine how reliable a test is. Sensitivity describes how well the test can correctly identify true cases of the disease (true positive rate), whereas specificity describes the ability to correctly identify those without the disease (true negative rate). Currently, saliva is a widely used sample for COVID-19 diagnostic testing as it has been shown in many comparative studies to have strong agreement in diagnosis with the standard NP swab sample.

Another important factor to address is false positive (when the test gives a positive result but the person does not have the infection) and false negative (when the test gives a negative result but the person is infected) results. In the preliminary comparison studies, the saliva test had a higher rate of false negative results. This is because, in many early published trials, the saliva samples were much more diluted than the NP sample. For this reason, some infections could not be identified. Fortunately, with more studies and methods of preparing the saliva sample, these issues can be circumvented. The implications of a false positive test mean that a participant may have to take days off of work, quarantine, and notify those close around them, for a result that was not correct. This can cost a person a lot of money, time, and worry. The implications of a false negative test however can be far more dangerous. This means that a COVID-19 positive individual is incorrectly being told they are negative for the virus and therefore aren't following the necessary quarantine and medical guidance they should be doing. Now, that individual can unknowingly spread the disease to even more people in their community. Therefore, optimizing sample collection to reduce these risks is a top priority at the ABCTL.

Conclusion

The COVID-19 global pandemic has changed much of our lives within the past year and will have a lasting impact for years to come. During this time, we were able to see the disease's devastating health effects on people across the globe, its rapid transmission through international travel, and the rise of anti-Asian racism and xenophobia fueled by COVID-19 (Vang & Nguyen, 2020). For many individuals across the United States, the pandemic highlighted the holes in our governmental agencies to prepare for and respond to COVID-19. Though through the uncertainty, researchers across the globe were working quickly to develop tools, tests, studies, and vaccines to help address the disease. The creation of the ABCTL reflects these efforts and stands out as one of the first COVID-19 diagnostic laboratories in Arizona. Many of the milestones of the ABCTL marked great successes such as utilizing saliva testing early, having the capacity to test all ASU students and many Arizona community partners, drop-off sample collection sites, and swift result turnaround time (24-48 hours). SARS-CoV-2, the virus that causes the COVID-19 disease, belongs to a large family of viruses named for their crown-like spikes on the virus surface. The ABCTL utilizes RT- qPCR testing to be able to accurately diagnose COVID-19 from a self-collected saliva test. Saliva as a testing medium has several considerations as well. To produce a viable test to be analyzed, the sample must not be contaminated with other foreign objects (like food, drink, gum, or medications) at least 30 minutes before collection. After much testing and comparative analyses with the standard NP swab samples, saliva has been confirmed to have high sensitivity and specificity to make

a quality diagnostic sample for COVID-19 detection. The extremely high standards of the ABCTL will be of service not only to the current diagnostic needs of the lab, but also for future endeavors in the years to come.

At the time of this writing, the U.S. will have endured the pandemic for over a year. As a country, we have learned a lot of the impact of COVID-19 on our mental and physical wellbeing. It is so important to not lose hope and to continue to trust reputable figures in the scientific field regarding the virus. The ABCTL and this project seeks to provide swift testing results and insight into this world of diagnostics to any individual. By the end of this project, the pandemic will not be over. However, this means that the ABCTL and its story will still grow and evolve to meet the ever-changing needs of our community. As Dr. Compton put it, we must strive "onward and upward!"

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Section V: Appendix

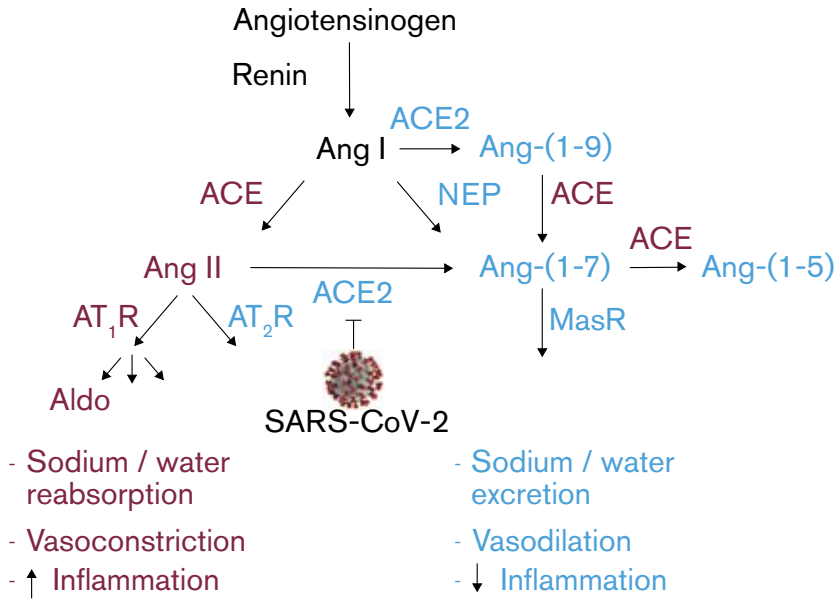

Figure 1. Visualization of the renin-angiotensin-aldosterone system (RAAS). ACE2 is a SARS- CoV-2 binding site and therefore inhibits typical ACE2 functioning within the RAAS. This leads to many of the respiratory symptoms experienced with COVID-19 infection (Bhalla et al., 2020).

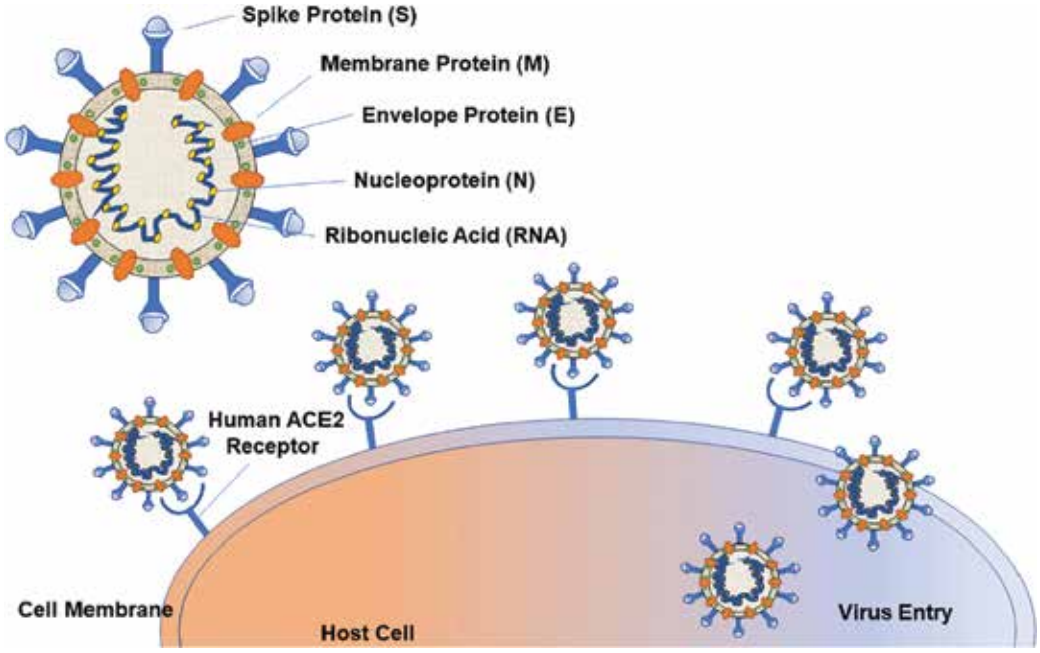

Figure 2. Visualization of the SARS-CoV-2 virus features and pathway of entry into the host cell. Key features of the virus include the spike glycoprotein (S), envelope membrane protein (E), membrane protein (M), nucleoprotein (N), and genomic RNA (Naqvi et al., 2020).

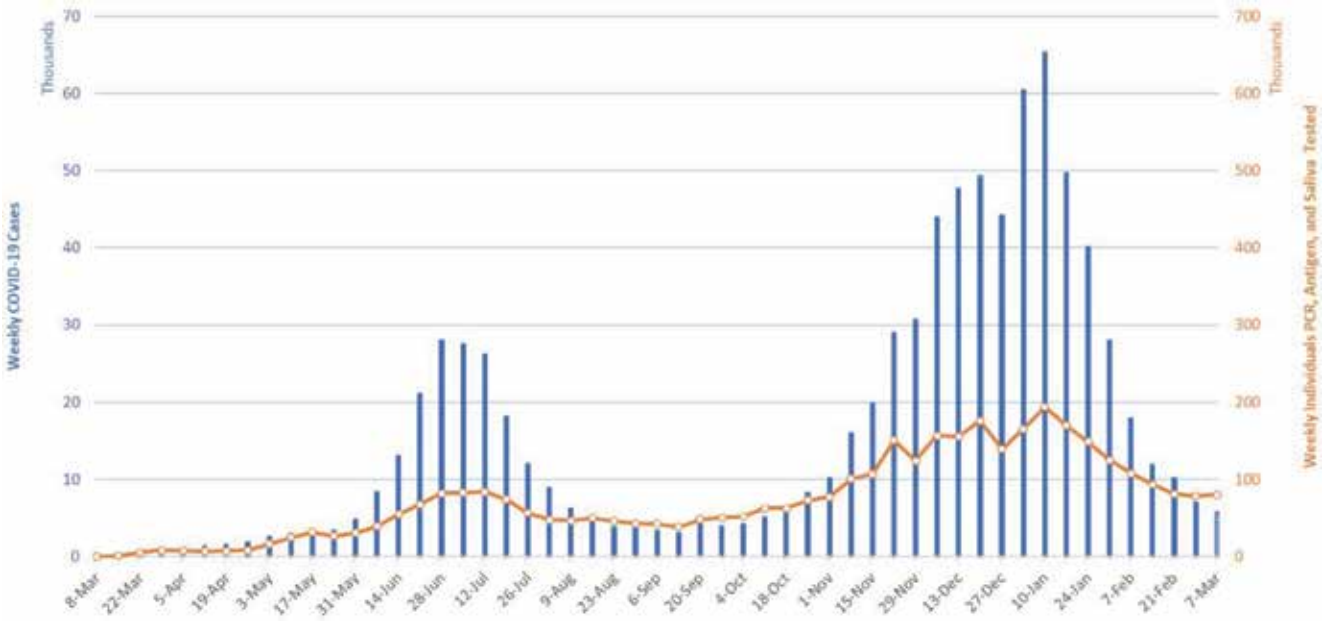

Figure 3. Newly diagnosed COVID-19 cases in Arizona and number of individuals undergoing diagnostic testing from March 8th, 2020 to March 7th, 2021 (Gerald, 2021).

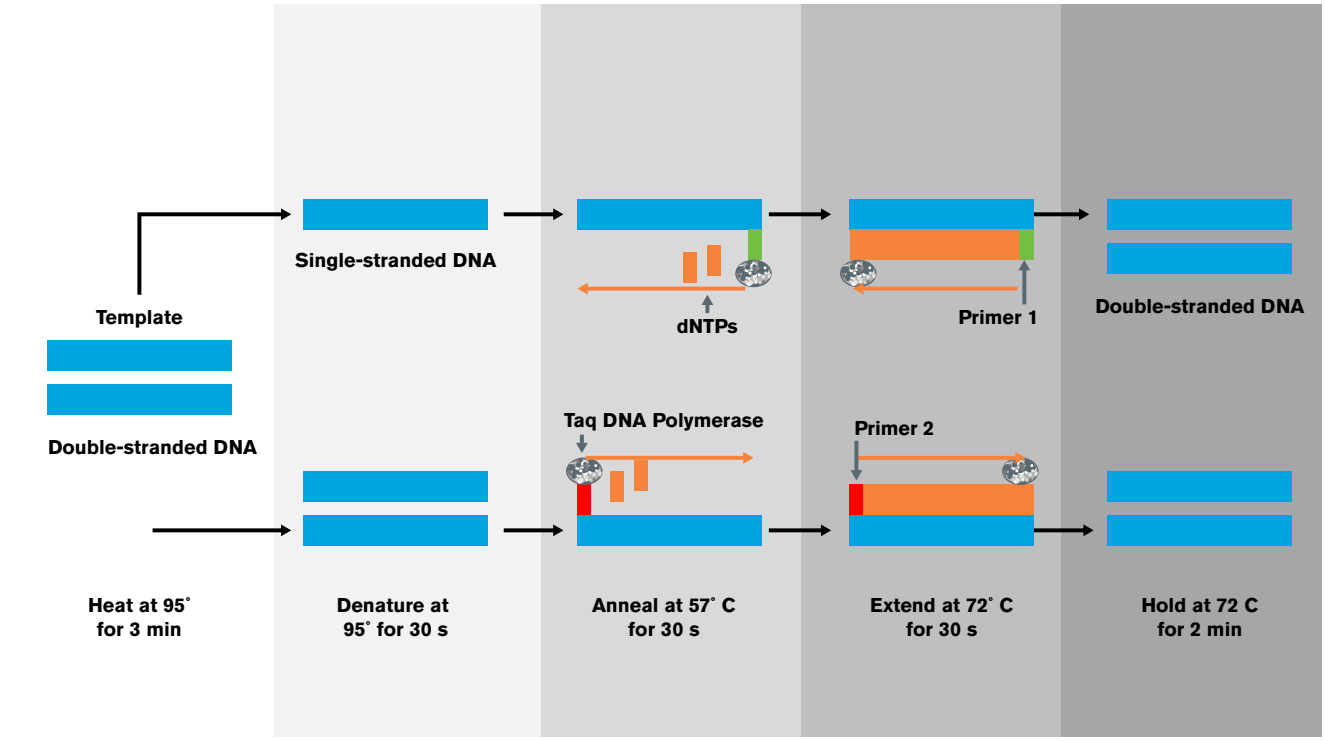

Figure 4. Summary of a basic PCR cycle. The template can be DNA or RNA (needs to be reverse transcribed into cDNA) depending on the sample. For SARS-CoV-2 detection, the ABCTL uses the viral RNA as a template. Required materials for PCR include: the template strand, primer (to isolate the S protein), nucleotides, DNA polymerase, and buffer mix. RT-PCR requires reverse transcriptase and DNA dependent DNA polymerase in addition.

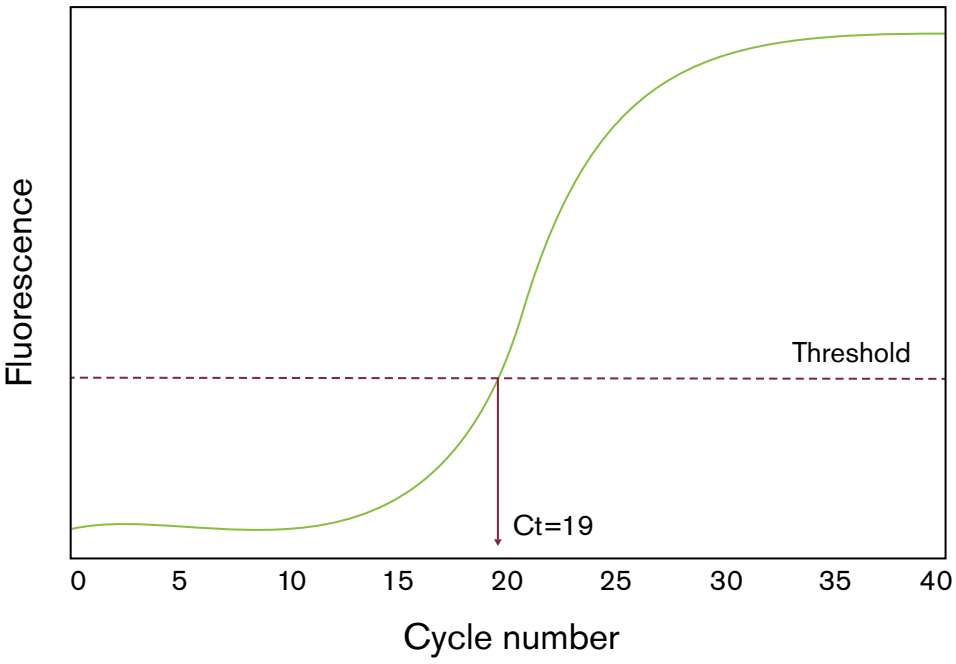

Figure 5. Example how to determine Ct value for a qPCR fluorescence curve (Bradburn, 2018).

The comparison of the detection of SARS-CoV-2 by RT-PCR between nasopharyngeal (NP) and throat swab and saliva samples.			
Nasopharyngeal and throat swab			
Saliva sample	**Positive**	**Negative**	**Total**
Negative	179	3	182
Positive	2	16	18
Total	181	19	200

Figure 6. SARS-CoV-2 detection sensitivity based on RT-qPCR analysis of saliva and NP/T swab specimens. Among the 181 total negative tests, the saliva test returned 2 false positive results. Among the 19 total positive tests, the saliva test returned 3 false negative results (Pasomsub et al., 2021).

Chapter 5

The Making of a COVID Lab

A Focus on Legal Standards and Considerations

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Submitted in fulfillment of requirements for the honors baccalaureate program of Barrett, The Honors College at Arizona State University

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Faculty Leaders, Law Group: Professor Adam Rigoni and Professor Michael Stanford, Barrett, The Honors College

August 2020 – May 2021

Introduction to Chapter 5

There are many legal standards that apply to the ASU Biodesign Clinical Testing Laboratory (ABCTL) during its operation. Due to its nature as a clinical testing facility, the ABCTL must adhere to the Clinical Laboratory Improvement Act, or CLIA, which governs the lab's standards through the issuance and enforcement of a CLIA Certificate of Compliance.

Next, in order for the ABCTL to legally test patients, the laboratory has to ensure that its test is authorized by the FDA. Specific to public health emergencies, diagnostic tests are authorized under FDA Emergency Use Authorizations. The lab must also follow the Privacy Rule and Security Rule, which are components of the Health Insurance Portability and Accountability Act of 1996. These rules have to do with protecting the personally identifiable health information of patients. These specific laws and regulations are described, reviewed within the context of the ABCTL, and future forecasts for the lab are outlined. Finally, aside from following the guidelines explicitly set out for it in the law, the lab must be vigilant about meeting the standard of care for the field in order to avoid being held liable for breaches of responsibility. Fortunately, the lab can benefit from state and federal liability protections that mean it is well-insulated against lawsuits.

The Clinical Laboratory Improvement Amendments (CLIA) are governed by the Centers for Medicare & Medicaid Services, or CMS. Under this law, the lab undergoes inspections and proficiency testing - any failure to comply with CLIA, gaps, or oversights mean potential liability for the ABCTL. The ABCTL holds a CLIA Certificate of Compliance and will soon be seeking CLIA accreditation.

The FDA has the power to authorize diagnostic tests and medical devices for use during a public health emergency through Emergency Use Authorizations. This is an extremely valuable tool as it allows the FDA to quickly verify the validity of diagnostic tests and authorize their use, bypassing the lengthy FDA approval process. The ABCTL's diagnostic tests were covered under certain Emergency Use Authorizations throughout the course of the pandemic.

In 1996, Congress passed the Health Insurance Portability and Accountability Act of 1996 (HIPAA), which requires covered entities to follow certain guidelines for maintaining the security of personally identifiable health information. The ABCTL is a covered entity, and therefore is subject to HIPAA. The U.S. Department of Health and Human Services' Privacy and Security Rules explain the guidelines that the lab must follow to protect patients' privacy.

Were it not for liability protections, any plaintiff harmed by the lab who could show the lab had a duty and breached it and that the breach of duty caused harm would be able to bring a lawsuit against the lab. The Public Readiness and Emergency Preparedness (PREP) Act, and potentially additional local legislative efforts, afford the lab legal protections in return for the contributions it has made to public health efforts during the COVID-19 pandemic.

Section I: Examining Legal Liability Issues and Standards of Care for the Arizona State University Biodesign Institute Clinical Testing Laboratory

Author: Anna Espinoza

Introduction

The COVID-19 pandemic brought life as we knew it to a crashing halt. It quickly became clear, in the early days of the onset of the pandemic at ASU, that one of the most difficult challenges our community had to overcome was the lack of a swift, reliable, and well- developed testing system that could diagnose members of the community with the virus in order to facilitate their isolation and treatment and stop the spread of sickness (Kass, 2020). Testing was particularly important for the University, as residents on and around the Tempe campus are of a younger median age and thus far more likely to be asymptomatic carriers of COVID-19. When a carrier is asymptomatic, testing is the only way to identify and subsequently isolate a carrier to stop the spread.

The legal aspects of the lab merit close scrutiny, particularly because this is the first instance in which an ASU entity has actually practiced medicine, administering and running tests patients use to make decisions about their health. The law dictates how almost all aspects of the lab can and must function. When it comes to testing, the law requires accuracy, safety, privacy, security, licensure, and public access to some information about positive tests. It regulates the quality of the products used in the lab. And, most importantly for this paper, the law, at least in theory, guarantees a remedy for those harmed by mistakes made by the lab, and as a result, continually holds the lab's employees to a certain standard of care.

In order to explore the legal aspects of the lab in more detail for Dr. Compton's project, "The Making of a COVID Lab" Law Group, which was made up of undergraduate students at Barrett, the Honors College, was established. During Spring 2021, the team met frequently with Dr. Compton, as well as our advisors, Dr. Adam Rigoni and Dr. Michael Stanford, to present on a variety of topics related to law and the lab.

While the ASU Office of General Counsel had obviously ensured the lab was compliant with the law prior to our embarking on this project, we treated the lab as a mock "client" during a series of sessions in which we talked about the legal frameworks relevant to the lab, gave our opinions on best practices, and addressed hypotheticals. The Law Group was composed of myself(Anna Espinoza), Marina Filipek, Nathaniel Ross, Madeline Salvatierra, and Landon Jenkins. We each dealt with a separate legal issue for the lab-- General Liability and Standard of Care, the Clinical Laboratory Improvement Act (CLIA), the Health Insurance Portability and Accountability Act(HIPAA) Privacy, HIPAA Security, and the Food and Drug Administration In Vitro Diagnostic Emergency Use Authorization(FDA IVD EUA), respectively.

General Liability and Standard of Care

In the simplest terms, liability means legal responsibility for one's acts and omissions (Encyclopedia Britannica, 2020). If the lab were to be held liable for doing x or for not doing x, the lab would be held legally responsible for doing x or not doing it. Early on in the research process, the Law Group needed to understand how to distinguish general liability from the other types of liability that were being studied in the course of the larger project, namely, contractual liability and statutory liability.

Contractual liability was studied by the Business group. Contractual liability is responsibility that one party assumes on behalf of another under a contract, and it arises from breaking that contract (Bonner, 2020). For example, if a medical supplier is under contract to provide the lab with 1000 test tube caps, they are responsible for providing the test tube caps and must make good on that promise. If they do not make good on it, they may have to suffer the consequences outlined in the contract, or even additional consequences.

Statutory liability was being studied by most of the Law Group. Statutory liability is responsibility for an act contrary to a well-established law, or a law not open to interpretation (Kagan, 2021). CLIA, HIPAA, and the FDA requirements are such laws. Take CLIA as an example-- CLIA says the lab must do x. If x is not done, it doesn't matter if no bad things happen or no damages arise because the lab did not do x. They still must do x, otherwise, statutory liability will arise from violating CLIA requirements.

General liability means responsibility for all other acts or failures to act (Hill, 2020). If a plaintiff were to seek to hold the lab liable for an action or inaction in a court of law, the evidence brought would go to prove four different aspects of the lawsuit-- duty, breach of duty, causation, and damages. The plaintiff has to show that the lab had a duty to them. They have to show that the lab breached that duty. They then have to prove causation, which is divided into two parts, direct cause and proximate cause. For direct cause, the plaintiff has to show that but for the lab's breach of duty, there would have been no harm or damage done to the plaintiff. For proximate cause, the plaintiff has to show that it was reasonably foreseeable to the lab that their actions or inaction would cause harm to the plaintiff. Finally, the plaintiff has to prove damages. This means they have to show proof of some harm that was done to them, as well as quantify that harm, usually by putting a monetary value on it.

As an example, the route that a sample travels through the Biodesign Institute. The ABCTL has carefully implemented numerous precautions to allow employees to move saliva samples safely throughout the building. For example, the samples take a specially designed route through the building in order to avoid contamination or breakage. They don't travel through hallways with windows, and they don't go over bumps. Should the employees at Biodesign fail to take care with the samples,and instead take them around the side of the building in order to deliver them from point A to point B, a plaintiff riding their bike could crash into the cart of samples, breaking specimen vials, and becoming contaminated with virus. They might sue the lab if they develop a severe case of COVID.

The plaintiff would be able to show that the lab had a duty to maintain the safety of their employees and people on ASU campus by designing a safe route for the samples to travel. They breached their duty when they sent the samples outside and around the building instead of through a safer internal route. But for the lab's decision to send the samples outside, the plaintiff wouldn't have contracted COVID-19 (for our purposes let's say the plaintiff is very safe and COVID-conscious). They might have crashed their bicycle, but they wouldn't have gotten sick. The plaintiff can also show that it was reasonably foreseeable to the lab that if they sent the sample outside, an accident might occur, since ASU is a pretty heavily trafficked campus. Finally, the plaintiff can show that because of what happened, they suffered damages, since they missed work and school, not to mention they experienced the symptoms of COVID-19.

The standard of care factors heavily into almost all lawsuits involving the practice of medicine or the highly technical business of clinical testing. The standard of care is the amount of care that the reasonably

prudent person would act with under similar circumstances in order to protect others from harm. In the lab's case, "standard of care" generally refers to the degree of care and skill of the average clinical testing laboratory employee (Goguen, 2020). Would a reasonable person working at a different COVID-19 clinical testing lab do more or less to keep people and property safe? If the reasonable COVID lab employee would do more, the plaintiff might have a case that the lab did not meet their duty. Ensuring that the lab maintains the standard of care is one of a great many reasons why the lab should maintain a dialogue with similarly situated labs testing the population for COVID-19. The fact that ASU is on the cutting edge of COVID-19 testing development is advantageous for the lab, because when ASU is the first institution to perfect and use a testing method, ASU is the first to contribute to the idea of the standard of care. In fact, I would not be very surprised if ABCTL employees have expert witness engagements in the future and go to testify about the standard of care that a COVID-19 testing labs should have met during the pandemic. However, ASU's legacy of innovation alone obviously does not insulate against liability. In fact, there is no way to 100% avoid liability for the lab's actions and lack of actions.

Federal and State Liability Protections

That being said, because of its mission and purpose, the lab is remarkably well-insulated from civil lawsuits of all kinds. At the federal level, the Public Readiness and Emergency Preparedness Act (PREP Act) authorizes the United States Secretary of Health and Human Services to issue a Declaration which provides liability immunity to certain individuals and entities against any claim of loss caused by the manufacture, distribution, administration, or use of medical countermeasures, unless that claim involves willful misconduct (Kadlec, 2020). The Secretary may subsequently amend the Declaration to expand or contract the range of liability protections granted by it. The Secretary made a Declaration under the PREP Act for medical countermeasures against COVID-19 on March 17th, 2020 and has so far amended the Declaration 7 times since then. The Declaration and the liability immunity granted by it extend through October 1st, 2024.

The lab falls squarely within the scope of the PREP Act and the Secretary's Declaration. For example, some of the people who work within the lab count as "program planners", or people "who supervise or administer a program with respect to the administration, dispensing, distribution, provision, or use of a Covered Countermeasure". A "covered countermeasure" is a "qualified pandemic or epidemic product" meaning "a drug or device...or a biological product that is (i) manufactured, used, designed, developed, modified, licensed or procured to diagnose, mitigate, prevent, treat, or cure a pandemic or epidemic or limit the harm such a pandemic or epidemic might otherwise cause". A saliva test would be a covered countermeasure. A "qualified person" means a "licensed health professional or other individual authorized to prescribe, administer, or dispense Covered Countermeasures under the law of the state in which the Covered Countermeasure was prescribed, administered, or dispensed". These are lab employees and the people who administer tests at ASU's different testing sites. "Administration of a Covered Countermeasure" means "physical provision of the countermeasures to recipients, or activities and decisions directly relating to public and private delivery, distribution, and dispensing of the countermeasures to recipients; management and operation of countermeasure programs; or management and operation of locations for purpose of distributing and dispensing countermeasures". This covers most everyone involved in any way with the ABCTL's testing efforts.

The Secretary's subsequent amendments to the original March 2020 don't do much to change the liability protections initially granted to the lab, and instead grant additional protections to telehealth providers and persons involved in vaccine distribution.

At the State Level, the construction of liability protections began for the lab with the issuance of Executive Orders 2020-26 and 2020-27 soon after the beginning of the pandemic. Governor Doug Ducey issued these orders, which, although they did not have all the force of law, expressed his view that healthcare

workers fighting the pandemic should be immune from liability for lawsuits related to their heroic actions. These orders are often referred to as “Good Samaritan” orders. It’s only recently, with the rollout of Senate Bill 1377, that the Governor’s policy wishes have begun to approach becoming law.

While SB 1377 has not yet become law, if it does, it will mean a person or provider (this includes healthcare providers) “that acts in good faith to protect a customer, student, tenant, volunteer, guest or neighbor or the public from injury from the public health pandemic is not liable for damages in any civil action for injury, death or loss to person or property that is based on a claim that the person or provider failed to protect them unless it is proven by clear or convincing evidence that the person or provider failed to act or acted with willful misconduct or gross negligence” (Shivers, 2021). The situation involving SB 1377 has changed significantly as of late. ASU itself has lobbied for this particular policy, which is evidently in their self-interest as it would protect the University from lawsuits. However, other organizations have legitimate concerns about how difficult this law would make it for plaintiffs to bring cases against employers and businesses that don’t take the threat of COVID-19 seriously and who are not motivated as healthcare providers are to keep people safe and healthy but are motivated by a desire for profit. Amendments that narrow the scope of protections to solely healthcare providers are being considered. If the bill does become law, it will bar lawsuits brought over incidents that happened between March 11th, 2020 and December 30, 2022.

An “Advisory Opinion” on SB 1377

One question that arose during our discussion of SB 1377 was the question of how SB 1377 is consistent with the Arizona Constitution. Article 2, Section 31 of the State Constitution reads, “no law shall be enacted in this state limiting the amount of damages to be recovered for causing the death or injury of any person, except that a crime victim is not subject to a claim for damages by a person who is harmed while the person is attempting to engage in, engaging in or fleeing after having engaged in or attempted to engage in conduct that is classified as a felony offense”.

First, we questioned why and how Arizona decided to prohibit capping damages for personal injury lawsuits, and second, we questioned how it was that liability immunity could be afforded to healthcare workers in a state where the amount of damages to be recovered for causing injury cannot be limited.

In answer to the historical question, I found that while Article 2 Section 31 was recently amended by Referendum with the Crime Victims Protection Act of 2012 (State of Arizona Constitution Timeline, 2021), the prohibition of liability limitations is as old as the Constitution itself. In fact, when Arizona was looking towards statehood, President William Howard Taft encouraged the state not to incorporate such a progressive idea into their Constitution. His impulses “put him squarely in conflict with the progressive Arizonans, who like their counterparts nationally, saw the judiciary as one of their principal opponents” (Leshy, 1988). In 1909, Taft, in a speech to Arizona residents, encouraged them “not to model their new constitution after that of Oklahoma”. This was a reference to the progressive features of the Oklahoma Constitution, such as the prohibition of legislative limitations on liability.

However, since legislative history is only as good as the judge who decides that it matters, we have to look to past cases to see whether or not the Arizona Supreme Court has interpreted “no law shall be enacted in this state limiting the amount of damages to be recovered for causing the death or injury of any person” as “no law shall be enacted in this state limiting liability”. The short answer is that they haven’t interpreted it that way. Past rulings indicate that the Arizona Supreme Court has allowed the effective reduction of the amount of damages and accepted the idea of liability immunity in civil suits. There are three reasons to believe this.

First, the Court allows the “pure comparative fault theory” to effectively limit the number of damages that can be recovered. Pure comparative fault means that “the amount of damages a plaintiff can recover in a personal injury suit is reduced by a percentage that reflects the plaintiff’s degree of fault” (Enjuris, 2020).

For example, if a driver runs a red light and crashes into you, but you were driving with your headlights off, the jury can find at trial that you are 20% at fault and the defendant is 80% at fault and you would only be able to recover 80% of your damages (Wicker, 2013). Pure comparative fault theory is a potential

limitation to the amount of damages you can recover in a lawsuit, but the Court has ruled that this is not an unconstitutional damages cap(Jimenez v. Sears, Roebuck & Co, 1995). They've also allowed other laws to mandate liability regardless of fault (Inspiration Consolidated Copper Co. v. Mendez, 1918). For example, "making an employer liable for all injuries to employees without the fault of employees and regardless of the employer's fault" is valid because it doesn't limit the amount which may be recovered". Statutes "which provide a limited amount in satisfaction of damages and leave to the parties interested the right to elect

to abide by its provisions are controlled by other principles of law and justice and should not be confused with statutes imperative in their terms". In other words, the relevant statute here is not mandatory. The parties can elect to abide by its provisions. This means the situation differs from a categorical mandate that limits damages, which would be unconstitutional. Finally, the court has accepted barring liability for certain entities. In short, immunity is distinct from a cap on the amount of damages to be recovered. Immunity bars an action's being brought against a party, but immunity doesn't bar the amount of damages to be recovered (Dietz v. General Elec. Co, 1991), making SB 1377, at least at face, consistent with the State Constitution.

Breaking the Chain of Custody: Devils' Drop-off

Devil's drop-off is a recently developed testing method that involves the patient picking up a saliva test tube, registering their tube online, then giving their saliva sample and dropping it off at a box stationed on campus that is regularly emptied so that samples can be brought to be tested. We considered two different hypotheticals involving fraudulent samples.

Scenario 1: Party X files suit against the lab for providing inaccurate results. Party X was unaware that they had COVID-19 until they reached a late stage of sickness. Party X provided a fraudulent sample to the lab.

There are multiple ways plaintiff X can be barred from recovering damages in Scenario 1. First, the plaintiff can be barred from recovery at the stage where plaintiff X would be required to show that the lab had a duty to prevent the sample from being a fraudulent one. It's unlikely that a judge or jury would find that the lab had a duty to observe sample collection. When it comes to taking steps to prevent the acceptance of fraudulent samples from at-home specimen collection, it's arguable that the lab doesn't need to do much besides ask for an oath from the patient that the sample is their own. Few at-home tests on the market include specific fraud prevention measures. Vault's at-home specimen collection is witnessed and guided by a health care professional in an online meeting with the patient. American Airlines also requires that prospective passengers who choose the at-home testing option with LetsGetChecked prior to their flight schedule an online meeting with a health professional who will witness sample collection. But given the number of other at-home tests on the market that allow independent, private sample collection, witnessing specimen collection is not standard practice. Therefore, for purposes of general liability, observing sample collections goes beyond the standard of care. Only a couple of tests require sample collection observation by a healthcare professional.

The plaintiff can also be barred from recovery at the stage where they would be required to show that the lab breached its duty to prevent the sample from being a fraudulent one. If the judge or jury does not find that the lab had a duty to prevent the fraudulent sample, there can be no breach of duty. You can't breach a duty that doesn't exist.

They can also be barred from recovery at the stage where plaintiff X would be required to show that the lab caused damage by failing to prevent the fraudulent sample from being collected. Let's break down

causation a bit more. The plaintiff has to show that but for the lab's failure to prevent the fraudulent sample from being collected, the damage would not have happened, and that it was reasonably foreseeable to the lab that they would provide a fraudulent sample.

Early lawsuits related to COVID-19 demonstrate these are tough standards to meet. For example, it's hard to prove that but for their visit to a certain restaurant/store, a plaintiff would not have gotten COVID-19. It would be equally hard for plaintiff X to prove that but for the lab testing a fraudulent sample, they wouldn't have gotten as sick as they did in Scenario 1. Causation is also where the doctrine of illegality/ex turpi causa non oritur comes into play. The Latin translates to "from a dishonorable cause an action shall not arise" (*Rogers Solicitors, 2016*), meaning plaintiff x cannot recover damages if the underlying action in the case is their own illegal or immoral one. It's clear that the lab's actions aren't the only actions that could have caused the damage in this scenario. There is also a policy argument for the doctrine-- we shouldn't have to walk around assuming that other people are going to do the wrong thing. We should be able to assume that they will do the right thing. Scenario 2: Party Y brings suit against the lab for providing inaccurate results. Party Y suffered damages due to the sickness of Party X. Party X provided a fraudulent sample to the lab.

There are multiple ways plaintiff Y — a third party — can be barred from recovering damages in Scenario 2 as well. First, at the stage where plaintiff Y would be required to show that the lab had a duty to prevent party x's sample from being a fraudulent one, and at the stage where plaintiff Y would be required to show that the lab breached its duty to prevent the sample from being a fraudulent one, for the same reasons as given in Scenario 1.

Plaintiff Y could also be blocked from recovery when trying to prove causation. The plaintiff Y has to show that but for the lab's failure to prevent the fraudulent sample from party x from being collected, the damage to them not have happened, and Plaintiff Y has to show that it was reasonably foreseeable to the lab that party x would provide a fraudulent sample. Again, early lawsuits related to COVID-19 demonstrate these are tough standards to meet. It would be hard to prove that but for their contact with Party X and the fraudulent test, Party Y would not have gotten COVID-19. Party x's conduct is also what's called third party conduct as a superseding cause(Carson, 2019). Because party x provided the fraudulent sample, it's clear it isn't just the lab's conduct that caused the damage. It's also x's conduct.

While fraudulent samples are not a liability concern because of both the fraudulent plaintiff's tendency to break the chain of causation and the liability protections afforded at the federal and state level, there are still additional issue and best practices to consider, such as the questions of what's happening with the samples as they are waiting to be picked up by the lab staff and what steps have been we taken to make sure they are under supervision/secured/at the right temperature/are picked up on time, and what happens if pickup doesn't go smoothly. Additionally, even if the fraudulent plaintiff's attempt to show causation will tend to fail, it never hurts to take extra precaution such as writing an indemnity clause into the online test tube registration form.

Conclusion

During our project, Dr. Compton expressed her wish that The Making of a COVID Lab students would recognize the project for what it was — a once in a lifetime opportunity to be involved with and really understand the response to the pandemic. Engaging with hypothetical questions about what duties the lab has and what standard of care the lab should meet truly was a once in a lifetime kind of experience. We have now passed laws and we now understand realities about the COVID-19 pandemic that we did not have or understand when I began researching this topic in July 2020. A combination of factors-- ASU's position at the cutting edge of testing efforts and the changing nature of pandemic law and pandemic science-- made the project a dynamic and intellectually challenging one and one that I am grateful to have had the opportunity to participate in.

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Section II: A Deconstruction of the Clinical Laboratory Improvement Amendment Applied to the Arizona State University Biodesign Clinical Testing Laboratory

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Background

Following the outbreak of the Coronavirus Disease 2019, or COVID-19, and the subsequent COVID-19 pandemic declared in March 2020 (World Health Organization) with a significant and sudden worldwide impact, the Arizona State University, or ASU, community – supporting almost 75,000 students along with a large faculty and staff (ASU Enrollment Campus Reporting) – acted quickly to promote wellness. A SARS- CoV-2 clinical testing laboratory was set up to serve ASU and the greater Phoenix metropolitan area. The ABCTL represents ASU's first venture practicing clinical medicine.

The quick pivot of the Biodesign Lab from academic research to clinical testing was, naturally, no small endeavor during an unprecedented and tumultuous time, during which COVID-19 safety restrictions needed to be prioritized along every step of the way. According to an ASU Now news article, "Compton's main duty was making sure the lab met the strict standards of the Clinical Laboratory Improvement Act that governs how labs that produce medical data must monitor and verify the people and instruments doing the tests. [According to Compton,] 'CLIA inspections are a very serious thing,'" [ASU Now].

A Deconstruction of the Clinical Laboratory Improvement Amendment Applied to the ABCTL

The ABCTL tests for active cases of COVID-19 through molecular testing of saliva to amplify sections of the genome of the SARS-CoV-2 virus. Previously, the ABCTL conducted nasopharyngeal (NP) secretion testing with the use of NP swabs. This method, however, was uncomfortable for the patient; caused the patient to sneeze and cough, which can spread COVID; required a numerous force of personnel fully outfitted in personal protective equipment (PPE); and was a difficult test to administer. Not only are the current saliva samples easier to collect, but they are a more accurate way to test – saliva is more sensitive for SARS- CoV-2 detection than NP swab specimens, detection is less variable between repeat sample collections with saliva, and the virus is stable at four degrees Celsius and room temperature for four days (Dr. Compton). The ABCTL's big switch to the saliva test was highly visible in the Arizona community and beyond, drawing positive attention to the lab and its revolutionary work.

Of course, the type of test is not the only aspect of the ABCTL subject to change and adaptation – the patient flow also underwent several adjustments throughout the ABCTL's continuing life. In order to understand the patient flow, it is first vital to understand the lab workflow. Generally, a participant registers and receives results within 24 to 48 hours; samples are both processed and analyzed at the ABCTL through automated systems with minimal human intervention; informatics analysts provide database and data quality control (QC); Technical Directors review the raw data; and results are reviewed and approved by the ABCTL's Medical Director, Dr. Compton, before the secure release of the result to the patient (Dr. Compton). Although this general workflow of the ABCTL's internal operations continues to apply, the patient has varied. Currently, there are two options for a patient to test with the ABCTL: in- person testing and drop-off testing. The latter is discussed in depth later in this paper. For an in- person test at an ABCTL testing site, the patient registers beforehand, answers some screening and identifying questions to label the test vial, receives instructions and the test kit, safely collects a usable saliva sample, and submits the sample for processing to ABCTL personnel with identity confirmation.

A one-test lab may seem simple, but the legal workings behind it are the same as those of any medical testing facility, large or small. By its very nature, the ABCTL is required to adhere to federal and state regulations, such as those imposed by the Food & Drug Administration (FDA), as well as the Clinical Laboratory Improvement Act (CLIA). Any failures, gaps, or oversights mean potential liability. This Section focuses on the importance of CLIA and the ABCTL's adherence to this law.

Analytical Framework and Findings

The Clinical Laboratory Improvement Amendment, or CLIA, covers approximately 260,000 laboratory entities overall. It governs the standards of the ABCTL. There are four certification types, all of which are valid for a two-year period:

- Certificate of Waiver
- Certificate of PPM (provider-performed microscopy)
- Certificate of Compliance
- Certificate of Accreditation (CDC)

Arizona labs apply for CLIA certification through the Office of Laboratory Licensure and Certification (OLLC) CLIA Program (Arizona Department of Health Services). The ABCTL received CLIA certification on March 23, 2020. This certification is valid through March 23, 2022. The certification type is "Certificate of Compliance," and the certification number is 03D2180875 (Arizona DHS).

Under CLIA, "laboratory" or "clinical laboratory" means "a facility for the biological, microbiological, serological, chemical, immune-hematological, hematological, biophysical, cytological, pathological, or other examination of materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings" (42 U.S. Code § 263a)

CLIA was the brainchild of collaboration between the Centers for Disease Control and Prevention, or CDC, and the Centers for Medicare and Medicaid Services, or CMS, both of which fall under the U.S. Department of Health and Human Services, or HHS (CDC). As shown in Figure 1 (refer to the Appendices), the CMS is responsible for governing CLIA.

The CMS uses CLIA to regulate all lab testing, aside from research, performed on humans in the U.S. The Quality, Safety, and Oversight Group within the Center for Clinical Standards and Quality under the Division of Clinical Laboratory Improvement and Quality implements and enforces CLIA (CMS). Despite its stature under the CMS, CLIA can face effects from other departments, including the FDA. Figure 2 (refer to the Appendices) details the separation. Nevertheless, these centers exist for exclusive purposes – there is no such thing as a CLIA-approved test; tests themselves require FDA approval.

Different laws may apply to multiple areas of a laboratory, so it is inevitable that there is some overlap. It is important to understand wherein the distinctions lie. For example, the FDA makes sure the equipment a lab uses for testing meets their regulatory standards. By contrast, during a CLIA inspection, it is not the equipment itself that falls under scrutiny – instead, it is the procedures and behavior of lab personnel, the qualifications of lab directors, and the test results themselves that are subject to monitoring.

CLIA and the ABCTL

CLIA certification is required "for facilities that test specimens for the purpose of diagnosis, treatment, and prevention of disease" (Arizona DHS). This applies to the ABCTL one- test facility, which seeks to diagnose COVID-19 through a saliva test. Table 1 (refer to the Appendices) displays select CLIA certification exceptions followed by the determined application to the ABCTL.

Thus, it is evident that a startup like the ABCTL indeed requires CLIA certification. The process to receive certification begins with an application by the lab. The application must include a great deal of detailed information: the number and type of lab examination and other tests; methodologies for lab examinations and other procedures; qualifications and education of the directing, supervising, and performing personnel; and other information to determine compliance, including changes in information. Moreover, the lab must agree to permit inspections and make records available (42 U.S. Code § 263a).

Following CLIA certification, labs are required to adhere to high standards, and they are subject to quarterly tests to ensure these standards are upheld satisfactorily. Inspections occur at the collection/testing site, and they can be either announced or unannounced; the ABCTL has already undergone a surprise inspection. Moreover, these inspections must occur during the lab's regular hours of operations, with the inspectors provided access to everything (facilities, equipment, materials, records, and information) that will help them make an informed decision regarding the lab's adherence – or deviation – from CLIA (American College of Physicians).

This means that the lab must maintain records of standard operating procedures as well as any non-conforming events. At the ABCTL, Morgan Nelson is the Quality Manager and files all such documents.

Aside from inspections, another aspect of CLIA certification is ensuring that the lab is competent in conducting tests. Checking the accuracy and reliability of a lab's tests is known as CLIA's "proficiency testing program" (APS). During proficiency testing, or PT, unknown samples are sent to a lab. The lab must then test these samples the same way they test any patient specimen and report back the results. The PT program that sent the samples measures the lab's performance (CMS). The ABCTL has not had any issues (to date) with their PT performance.

If a laboratory fails an inspection or does not perform acceptably, there are a variety of next steps or consequences. Depending on the nature and severity of the violation, the lab may be required to undertake additional technical training or enroll in an enhancement program; CLIA may impose sanctions, such as correction plans or monetary penalties; the lab may suffer a revocation of its CLIA certificate; or the lab directors will face imprisonment (42 U.S. Code § 263a).

Due to the COVID-19 emergency, regulatory agencies adapted their usually inflexible guidelines to make it easier for labs to implement SARS-CoV-2 tests. On September 25, 2020, the CMS reduced paperwork and authorization delays, specifically surrounding CLIA certification fees, which are based on the certificate type and can also be affected by the annual volume and type of testing (CMS). Later, on December 7, 2020, the CMS stated that they would not cite facilities with a CLIA Certificate of Waiver when conducting point of care testing for SARS-CoV-2 on asymptomatic individuals (CMS). Point-of-care (POC) tests are rapid tests that can provide results within minutes of the test administration. With reference to COVID-19 testing, molecular or antigen tests may qualify as POC, whereas saliva tests like the ones the ABCTL administers do not.

As is expected when pioneering uncharted territory, such as a large-scale rapid lab startup during a global pandemic, there are some gray areas when it comes to legal matters. For many of the legal challenges the ABCTL analyzed during its journey, there exists no past precedent from which to model the ABCTL's practices. One example of this is Devil's Drop Off.

Devil's Drop Off describes a later phase implementation of testing procedure. Detailed in Figure 3 Section I Appendix, rather than collecting the specimen at the testing site under supervision, participants can utilize a pick-up and drop-off system to collect the sample at home and submit it for ABCTL processing.

This method raised concern as a potential opening of liability for the lab. During the pandemic, certain situations like travel require proof of a negative COVID test. If the lab is unable to confirm that the saliva sample belongs to the individual who submitted it, and the negative result is attributed to an individual who is actually COVID positive, is the ABCTL liable under CLIA?

The ABCTL's Devil's Drop Off is not necessarily a novel concept; there are comparable at-home kits available. For example, the FDA displays LabCorp (FDA) and Everlywell (FDA) kits on their website. These are both nasopharyngeal secretion tests, and instead of physical pick- up and drop-off locations, they are shipped to the patient and then back to the lab. Neither kit requires the patient to record themselves taking the sample to prove the specimen originated from the patient. However, the LabCorp test does require a specimen confirmation form, which serves the same purpose as the Devil's Drop Off double barcode registration. Based on this comparison, it seems unlikely that the Devil's Drop Off process will be a source of liability for the ABCTL. Additionally, CDC COVID-related guidelines state, "A saliva specimen collected by the person being tested, either at home or at a testing site under supervision" is deemed an acceptable specimen, including saliva collection by the patient without supervision (CDC).

Furthermore, the CMS has been more flexible regarding labs testing for COVID, since the issue of the pandemic has been so time-sensitive. The focus has generally been primarily on proficiency and safety, and the ABCTL seems to be following all the recommended steps by labeling their specimen with barcodes for tracking and verification. Therefore, the ABCTL's Devil's Drop Off procedure appears to be fully CLIA compliant, although measures such as an ensured indemnity clause or sample confirmation could serve to strengthen this position.

Conclusion and Future Forecast

CLIA's intensive criteria lose intimidation when applied to the specificity of the ABCTL. Up through and including its current state and initiatives, the ABCTL has acted exactly as it is meant to under CLIA. The ABCTL, already a CLIA certified lab, is looking forward to receiving CLIA accreditation in the near future. Overall, the ABCTL is clear evidence of an entrepreneurial mindset pioneering a successful, legal operation to promote wellness in the community and help people better understand public medicine during the COVID-19 pandemic.

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Section II: Appendix

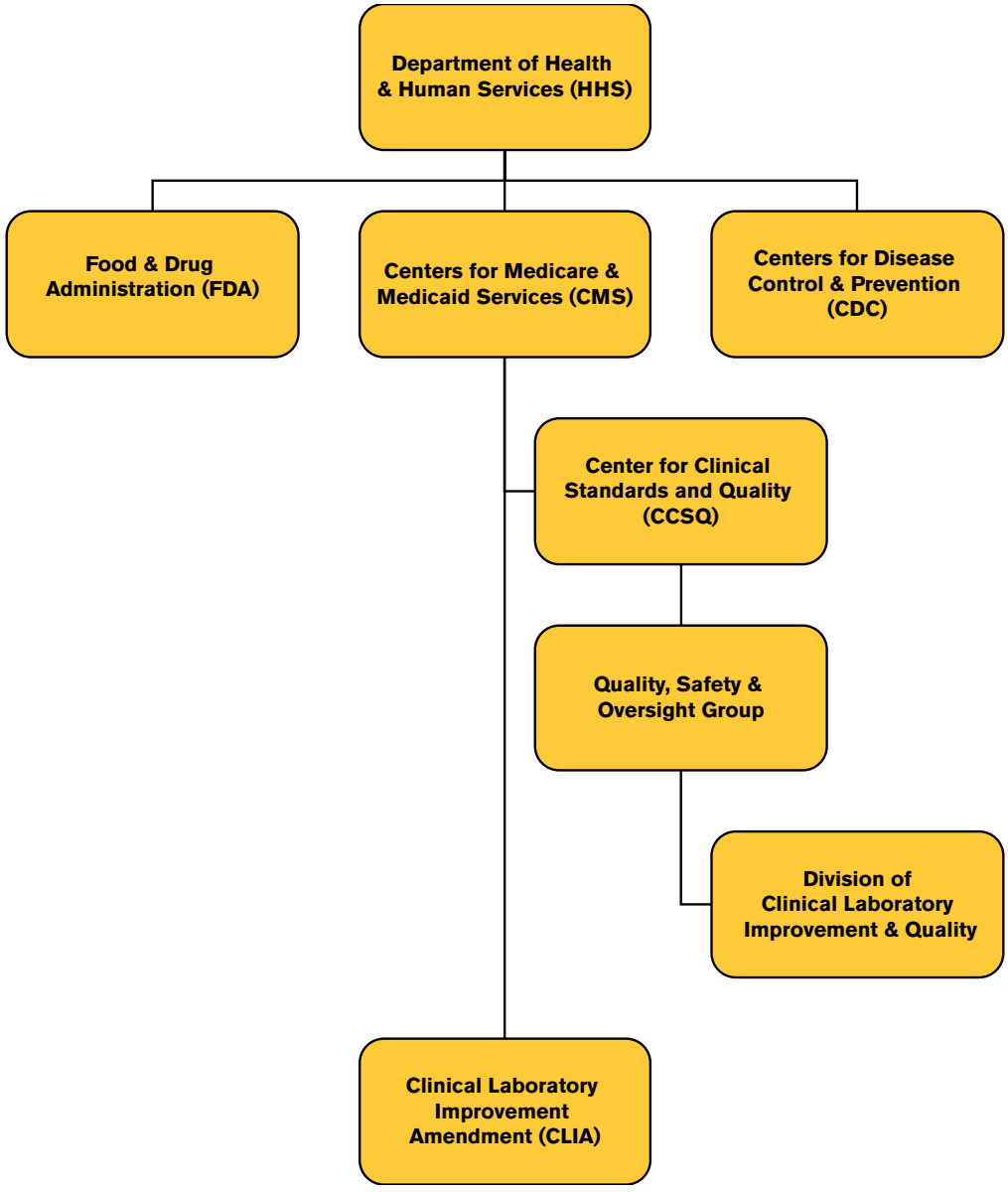


Figure 1: CLIA Governance & Organization

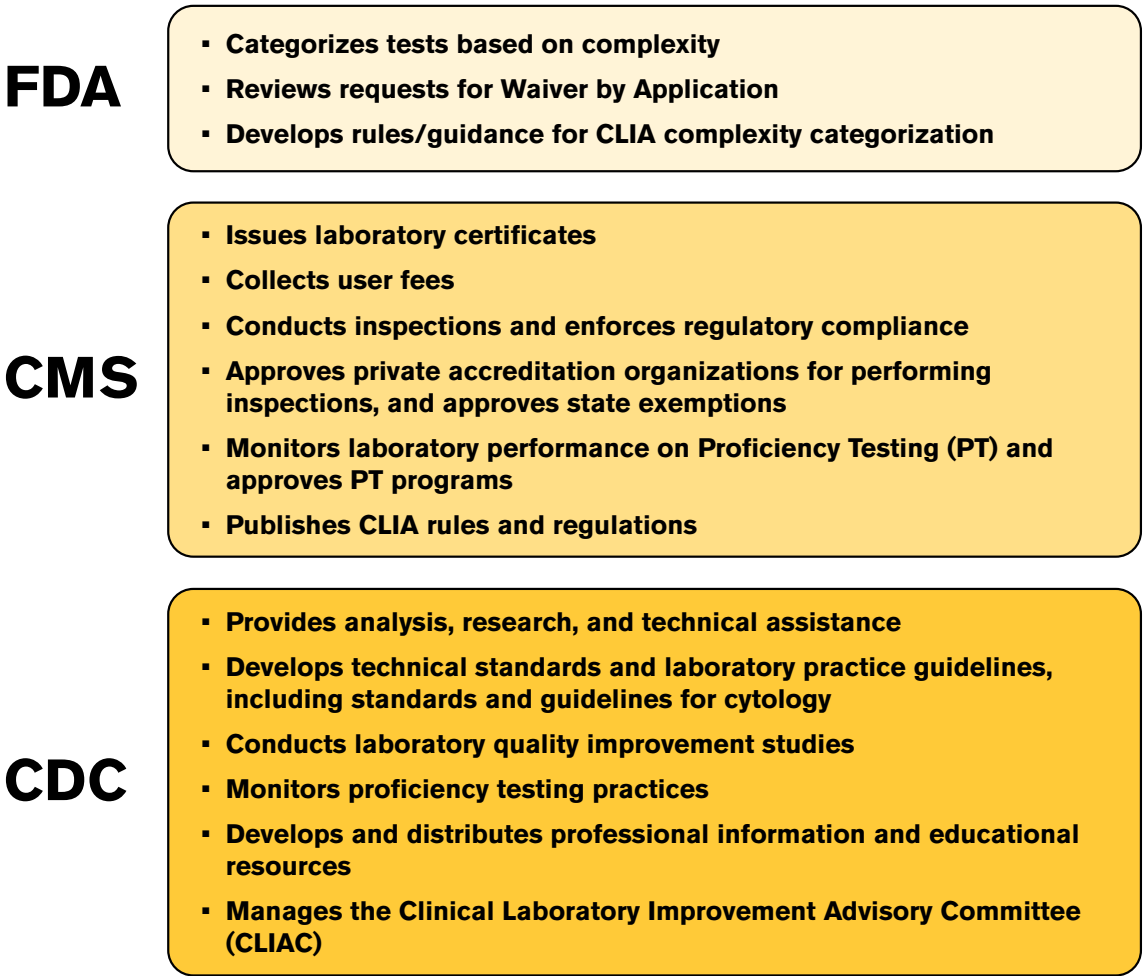


Figure 2: Departmental Influences on CLIA (FDA)

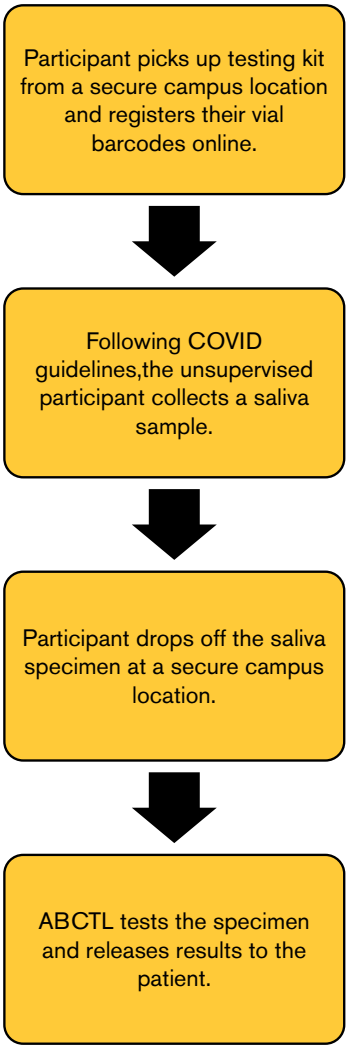


Figure 3: Procedure Diagram

Table 1: CLIA Certification Exceptions Applied to the ABCTL (Arizona DHS)

CLIA Certification Exception	ABCTL Application
If only collecting specimens to be sent out for testing at another facility, then CLIA certification is NOT required.	The ABCTL collects AND tests saliva specimens. This exception DOES NOT apply to the ABCTL.
Labs are CLIA-exempt if they are performing research-only testing, operated directly by the federal government, or testing for the hiring or termination of employees.	The ABCTL operates under ASU, a public research university, for the purpose of determining whether or not a participant is infected with the COVID-19 virus at the time of the test. Despite a great deal of research stemming from the ABCTL, the testing cannot classify as 'research-only. This exception DOES NOT apply to the ABCTL.

Section III: The FDA Emergency Use Authorization Pathway's Impact on the ABCTL

Author: Landon Jenkins

Background

In the United States, clinical testing is monitored by the federal and state governments, held to standards to ensure the safety and efficacy of these tests, as well as maintaining privacy for patients receiving a test. In order for the ABCTL to lawfully operate in the state of Arizona, it had to meet various legal criteria. These major legal considerations, in no particular order, are: Clinical Laboratory Improvement Amendments compliance; FDA Emergency Use Authorization (EUA); Health Insurance Portability and Accountability Act compliance; state licensure; patient, state, and federal result reporting; and liability.

In this Section, the EUA pathway will be examined and contextualized in relation to the ABCTL. This will include an examination of the FDA regulations and policies that affect the laboratory during its operations, as well as a look at the different authorization pathways for diagnostic tests present during the COVID-19 pandemic.

Analysis

IVD Classifications

The Code of Federal Regulations Title 21, Volume 8 defines in vitro diagnostics (IVD) as follows:

> *Those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. These products are devices as defined in section 210(h) of the Federal Food, Drug, and Cosmetic Act (the act), and may also be biological products subject to section 351 of the Public Health Service Act.1*

These types of tests are primarily used to detect and diagnose diseases and underlying medical conditions and can play a major role in determining a patient's treatment going forward.2 These tests are powerful tools in limiting the spread of infectious diseases and ensuring the accurate diagnosis of these conditions. The widespread and regulated use of diagnostic tests during public health emergencies is not a recent development. For example, the FDA has authorized tests for detecting the Zika virus, leukemias, a variety of cancers, and many other human pathogens.

With the spread of the novel coronavirus to the US in early 2020, the scientific community recognized the necessity of widespread COVID-19 testing to better understand and better contain the virus. A myriad of companies and laboratories across the country began to develop safe and effective in vitro diagnostic tests that could detect the SARS-CoV-2 virus in saliva and nasopharyngeal swab samples. There are two major types tests that have been developed: diagnostic tests and antibody tests (also referred to as serology tests). Diagnostic tests, as mentioned before, are used to determine whether or not a patient is infected with SARS- CoV-2. Antibody tests, on the other hand, are used to determine whether or not a patient was infected with SARS-CoV-2 in the past, by detecting any antibodies produced in response to a prior infection. This Section focuses on diagnostic testing, as performed in the ABCTL.

Molecular Tests

The FDA further splits the diagnostic category into two different types of tests: molecular tests and antigen tests. Molecular tests typically rely on a common laboratory technique called PCR, or polymerase

chain reaction. In cases where a patient is infected with SARS-CoV-2 this technique can amplify the amount of viral genetic material from the sample, allowing for detection by the test providers. Molecular testing is the most common testing method at the moment and is also the testing offered by the ABCTL. Antigen testing, by contrast, is typically less common. These tests are commonly used in point of care testing sites, in which the test is performed and yields a result at the same location. These tests detect antigens rather than nucleic acids. Note that typically, a test consists of the specific reagents, required controls, workflow/instructions, and necessary testing technology/equipment. All of this information is required when Emergency Use Authorization requests are sent to the FDA for review.

As mentioned before, the ABCTL uses molecular testing to detect SARS-CoV-2 infections in the patient population. Specifically, the ABCTL uses a modified version of the ThermoFisher Scientific TaqPath RT-PCR COVID-19 Combo Kit. This product includes the workflow, reagents, and controls necessary to efficiently test saliva samples using PCR. On top of this, the ABCTL uses the Applied Biosystems QuantStudio Fast Dx Real-Time PCR instrument to perform the PCR.

First, saliva samples are heat-inactivated for safety. The samples are then digested, the internal control is added, and the mixture is heated at 95°C for 5 minutes. The samples are then inputted into the RT-PCR COVID-19 Combo Kit and the QuantStudio Fast Dx Real-Time PCR. Here, the included probes and primers bind to sequences corresponding to the ORF1ab, S, and N genes of SARS-Cov-2. Then, these sequences are amplified through PCR and fluorescence is measured to determine test results.

There are multiple intersecting regulatory pathways that determine if an IVD can be used in the public. There is the FDA emergency use authorization (EUA), which is of particular importance to the current COVID-19 pandemic and the specific diagnostic test used in the ABCTL. Next, there are the Clinical Laboratory Improvement Amendments of 1988, which apply to all laboratories and facilities working with human samples "for health assessment or to diagnose, prevent, or treat disease." 5 Finally, there is the traditional FDA IVD approval pathway, which applies to all unreviewed or not CLIA-waived IVDs. This pathway will be the primary approval pathway for COVID-19 IVDs after the FDA's EUAs are eventually rescinded. In this paper, the focus will be the FDA EUA.

The FDA EUA Pathway

Since COVID-19 emerged suddenly, the normal FDA IVD regulation process was inadequate to meet the immediate testing demand. Instead, the FDA used emergency use authorizations, which allow the FDA to provisionally approve the use of unapproved medical products in response to a public health emergency. This authority also can be used to approve the alternate, unapproved use of FDA approved devices. The FDA's authority to release EUAs comes from the Federal Food, Drug, and Cosmetic Act. Section 360bbb-3 outlines this power:

> The Secretary may authorize the introduction into interstate commerce, during the effective period of a declaration under subsection (b), of a drug, device, or biological product intended for use in an actual or potential emergency (referred to in this section as an "emergency use").

However, there are certain criteria a drug, device, or biological product must meet in order to be considered for an EUA:

1. that an agent referred to in a declaration under subsection (b) can cause a serious or life-threatening disease or condition; and
2. that, based on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that—
    A. the product may be effective in diagnosing, treating, or preventing—
        (i) such disease or condition; or
        (ii) a serious or life-threatening disease or condition caused by a product authorized

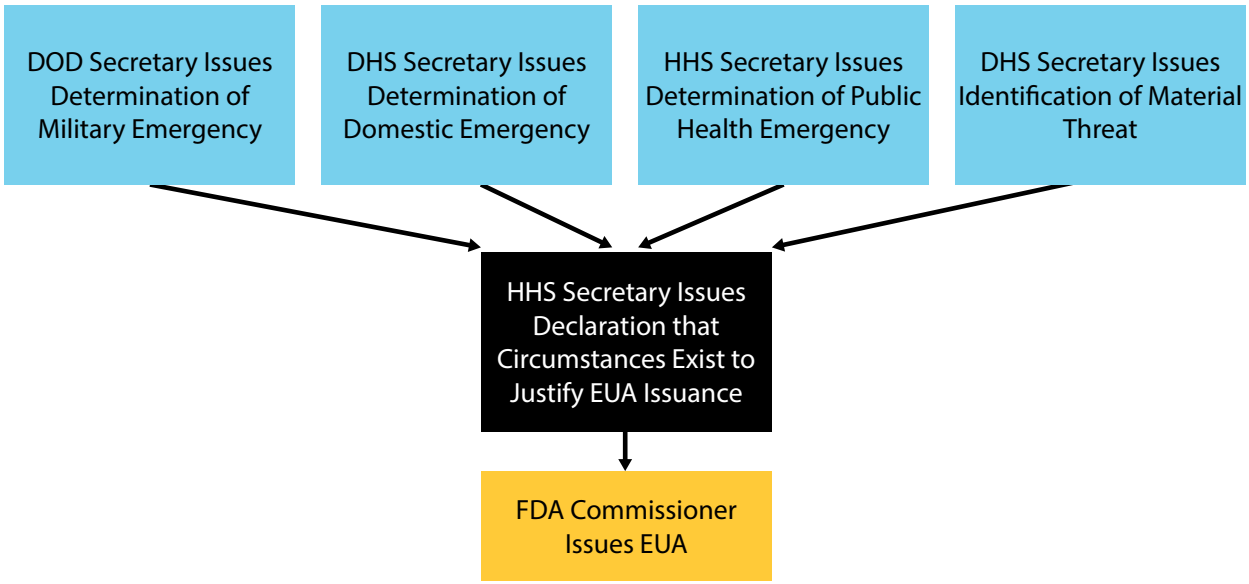
under this section, approved or cleared under this chapter, or licensed under section 351 of the Public Health Service Act [42 U.S.C. 262], for diagnosing, treating, or preventing such a disease or condition caused by such an agent; and

B. the known and potential benefits of the product, when used to diagnose, prevent, or treat such disease or condition, outweigh the known and potential risks of the product, taking into consideration the material threat posed by the agent or agents identified in a declaration under subsection (b)(1)(D), if applicable;

3. that there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such disease or condition;
4. in the case of a determination described in subsection (b)(1)(B)(ii), that the request for emergency use is made by the Secretary of Defense; and
5. that such other criteria as the Secretary may by regulation prescribe are satisfied.6

In summary, the device must target a life-threatening condition, present minimal risks compared to its benefits, must not be already approved by the FDA or is approved for a different use, and there must not be any adequate alternatives. This is the bulk of the criteria that must be met in order to warrant an EUA. The FDA, however, is not allowed to release EUAs until another department declares a public health emergency. In fact, they need to wait for an emergency determination from either the Department of Defense Secretary, the Department of Homeland Security Secretary, or the Department of Health and Human Services Secretary (HHS) first. Then, the HHS Secretary must release a declaration that justifies an FDA EUA. Finally, the FDA Commissioner can issue an EUA.

In the case of the COVID-19 pandemic, the pathway started with the HHS Secretary, Alex Azar. On February 4, 2020, the HHS Secretary determined that there was a public health emergency in the form of the first outbreak of COVID-19 in the US. This declaration acts as the first necessary determination for EUA issuance. On March 24th, 2020, the HHS Secretary also determined that the circumstances of the public health emergency justify the issuance of EUAs for diagnostic devices by the FDA.7 This aligns with the second necessary determination for EUA issuance. Since these two requirements were fulfilled, the FDA was now authorized by the Federal Food, Drug, and Cosmetic Act to issue EUAs.



This graphic illustrates the EUA issuance process

The FDA typically issues EUAs, at least in the case of the COVID-19 pandemic, in two ways. The first and most common way is through individual EUA's. In these cases, individual laboratories or manufacturers

have developed an in vitro diagnostic test and send a request to the FDA for an EUA. The FDA provides an EUA template for test designers to fill out and submit to the FDA for review. The second way is through "umbrella" EUAs, in which the FDA grants a nonspecific EUA to a group of authorized test manufacturers/distributors. For molecular tests, the FDA has granted one "umbrella" EUA for Laboratory Developed Tests from CLIA-approved laboratories. These types of tests and this EUA will be covered in a later section.

As mentioned before, the FDA provides an EUA template for manufacturers and laboratories to submit individual EUA requests for COVID-19 molecular diagnostic tests. These requests are reviewed by the Center for Devices and Radiological Health, one of the many centers of the FDA. These templates provide a broad overview of the basic requirements of an EUA, although in actuality specific requests are also guided by communications between the test-maker and the FDA. To submit an EUA request using these templates, that laboratory must be a CLIA certified high-complexity laboratory.

In the EUA submission, the laboratory is required to notify the FDA of the diagnostic test's intended use, the genetic sequences/detectable molecules targeted by the test, and the equipment used in the test's workflow. On top of this, there is a lengthy section for a detailed description of the diagnostic test. This includes the entire workflow of the test (the steps performed in sequential order), the positive control, the negative control, the extraction control, the internal control, and the results of the test.

Validation and EUA Requests

While drafting an EUA request, laboratories must perform a validation study to ensure that the test meets the FDA's standards of accuracy and specificity before use with patients. In other words, the FDA needs to ensure that the test yields a positive result for patients with a confirmed COVID-19 infection, and that the test yields a negative result for patients confirmed to not have a COVID-19 infection. There are four major components of the FDA's validation requirement: the limit of detection, inclusivity, cross-reactivity, and a clinical evaluation.

The limit of detection is a term used to describe the lowest concentration of viral particles a diagnostic test can detect. The FDA requires a laboratory to perform a study to assess its test's limit of detection. To do this, a laboratory must determine its preliminary limit of detection by first finding the lowest concentration of viral particles in a single sample its test can detect. Then, the laboratory must confirm this value by testing it across a total of 20 samples, where the final limit of detection is the lowest concentration of viral particles in which the test yields positive results in 19 or 20 samples. The experimental design and details of this study should be included in the EUA request.

Inclusivity refers to the test's ability to detect all of the currently known strains of SARS- CoV-2. The FDA requires that a laboratory's primers (small, engineered strands of genetic material that can bind to viral genetic material used to direct RNA/DNA synthesis) and probes (small, engineered strands of genetic material that are complementary to a specific sequence of viral genetic material) can bind to all strains of SARS-CoV-2. The details of the laboratory's study are included in an EUA request.

Cross-reactivity testing is the next component of a complete validation study. Here, the FDA wants to ensure that the primers/probes used in the test adequately match the targeted viral genetic sequence, and do not match sequences found in other pathogens. For example, a test should not yield a positive result for COVID-19 in a sample only infected with Influenza. The FDA's benchmark for homology (the percentage of matching nucleotides in two sequences) is 80%. Thus, the laboratory must provide a study indicating that the test yields negative results in samples infected with pathogens other than SARS-CoV-2, and that the test's probes and primers do not match sequences in other microorganisms to the degree the FDA has indicated.

Lastly, the laboratory must evaluate their test using samples from actual patients in a step called clinical evaluation. The FDA provides different guidance based on the sample used for each test. Since the ABCTL tests saliva samples, classified as alternative specimens, this paper will only discuss the FDA's

requirements for these types of tests. In these cases, the FDA requires that the laboratory uses paired samples to evaluate the test, meaning that the laboratory must obtain one nasopharyngeal sample and one saliva sample from each individual patient. The FDA requires that the laboratory obtains at least 30 positive paired samples and 30 negative paired samples. These samples should be tested using an FDA authorized test to confirm the status of the samples (confirmed positive/negative). The test that is under review should yield the correct result in these samples. Again, the details of this study should be included in the EUA request. This covers the majority of the information included in an EUA request for a COVID-19 molecular test. The laboratory is also required to draft fact sheets for patients, infographics that explain the test in understandable language to patients.4

Once a test has been validated, the FDA allows laboratories to use their test with patients and report positive cases to local, state, and federal authorities. The FDA recommends that they notify the FDA of the laboratory's independent validation immediately. After validation, the laboratory has roughly 15 days to submit an EUA request to the FDA.9

EUAs and the ABCTL

IIn early 2020, the ABCTL developed a modified version of the Thermo Fisher Scientific TaqPath COVID-19 Combo Kit (which already had an EUA), called the ASU-SARS-CoV-2 Test. The difference between these tests was that the ASU test utilized a thermocycler, devices used to amplify genetic material in PCR reactions, in its workflow. The Thermo Fisher test, on the other hand, did not. The reagents, primers, probes, controls, and other basic components of the tests were the same. It is also worth noting that this early version of the ABCTL's test was used primarily with nasopharyngeal swab samples, and not saliva samples (these became the primary sample in summer 2020). In March 2020, the ABCTL validated their test and drafted an EUA submission for this test. However, due to its similarity to the Thermo Fisher test, the FDA communicated to the ABCTL that an EUA request was unnecessary, and that the FDA would not object to the use of this test. This authority comes from the FDA's guidance document, Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency. The FDA states that the "FDA does not intend to object to the use of a test, without notification to FDA or a new or amended EUA, where the test is a modification of an EUA-authorized test and the modified test is validated using a bridging study to the EUA-authorized test."9 Since there was not a change to the Thermo-Fisher EUA either, the FDA only requires validation data sent informally by email. Thus, the ABCTL was using a validated and modified form of the Thermo-Fisher test, which meant the laboratory fell under the scope of the Thermo-Fisher EUA as an "Authorized Laboratory."

In the summer of 2020, the ABCTL decided to primarily test saliva samples, moving away from the nasopharyngeal samples they were using before. Saliva samples are particularly advantageous because they are much more approachable for the everyday person, who may find the swabbing technique uncomfortable. With the switch to saliva sampling, the ABCTL faced a similar situation as to what happened during their first EUA request, as the FDA communicated that the ABCTL also did not need to submit an EUA request for this modification. The Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency again provides guidance on these types of specimen modifications:

> When a laboratory makes a modification to an EUA authorized test for use of a new specimen type, FDA does not intend to object to the use of such a modified test without notification to FDA or a new or amended EUA where the new specimen type has been previously authorized for another test of the same technology and where the EUA authorized test is validated for the new specimen type.

Saliva testing was already authorized under an EUA issued for a Yale School of Public Health test, called SalivaDirect. Thus, to switch to saliva sampling, all that was required of the ABCTL was a validation study testing their modified Thermo Fisher test with saliva samples. The EUA templates for molecular testing provide guidance for validating studies with an alternative sample type. The most important component is paired samples testing for the clinical evaluation section, which basically requires that the

test yields similar results for a saliva and nasopharyngeal sample from the same patient. The ABCTL, in their validation study, found 20 patients that tested positive with nasopharyngeal testing and 128 patients that tested negative with nasopharyngeal testing. Testing saliva samples from the same patients, they yielded 19 positive results from the 20 patients who tested positive with nasopharyngeal testing, and 127 negative results from the 128 patients who tested negative with nasopharyngeal testing. This corresponded to 95% positive agreement (proportion of results that match between sample types in positive patients) and 99% negative agreement (proportion of results that match between sample types in negative patients).10 The ABCTL conducted another one of these studies, finding 96.1% positive agreement and 96.3% negative agreement in the second study. For reference, the FDA considers 95% or greater positive agreement adequate.

Recently, the ABCTL modified its test again to make its workflow more efficient. Using new technology, the laboratory eliminated an early step in the process that required the extraction of mRNA from the saliva samples. Now, the laboratory uses a method called direct saliva which allows them to directly test saliva samples faster. Since this change was a significant modification of their authorized test under the Thermo Fisher EUA, the ABCTL validated this new method and submitted a new EUA request.

Included with this EUA request was another EUA request for a home specimen diagnostic test. The ABCTL has recently implemented a new sample collection method called Devil's Drop-off, a program that allows patients to collect their own saliva samples at home and submit them for testing at marked sample drop-off locations. A Devil's Drop-off kit includes a screw cap tube and label, a straw, a biohazard bag, an alcohol prep wipe, and instructions. An EUA request for home specimen is similar to the molecular diagnostic EUA requests, requiring a validation study. Exclusive to the home specimen testing EUA requests, the stability study requirement ensures that the workflow and sampling process do not degrade the samples, which could lead to erroneous results.11 The ABCTL tested their method by simulating the testing in different temperature conditions with variable sample "shipping" times (the sample are not actually shipped as they are quickly transferred in a cooler from the campus drop-off location to the campus testing facility via golf cart or car).

It is also worth covering the labelling requirements of the home collection kit. The labelling must state, "For Emergency Use Authorization (EUA) only, For prescription use only, For in vitro diagnostic use only, For professional use only, For use by people 18 years of age or older, The collection device is only authorized for use in conjunction with an in vitro diagnostic (IVD) test for the detection of SARS-CoV-2 that has been issued an EUA and is authorized for use with this collection device."

While the direct saliva method was validated, the ABCTL has had trouble yielding proper results with this new strategy after more testing. Specifically, many test results are considered invalid. Since the FDA does not require validation studies to use large sample sizes, these errors may go unnoticed until the test is used more. Nonetheless, the ABCTL is working with the FDA to correct these issues and is planning to submit a second EUA request.

EUA Requirements for Laboratories

When an EUA request is reviewed and authorized by the FDA, they will publicly release a letter of authorization on their website, containing their reasoning behind authorizing the test and the requirements for the authorized test and laboratories. First, the letter discusses the details of the specific institution's EUA request, and any modifications to the EUA request that may have occurred. Then, the letter will note the FDA's authority to issue EUAs, specifically Section 564(c) of the Food, Drug and Cosmetic Act. This is followed by a description of the authorized test and its components, like its controls and the associated patient and provider fact sheets.

Lastly, there are multiple sections outlined the FDA's requirements for the test designer and the laboratories authorized to use this test. The requirements of the test designer are shown below (some specifics excluded):

A. Your product must comply with the following labeling requirements under FDA regulations: the intended use; adequate directions for use; appropriate limitations on the use of the device; and any available information regarding performance of the device.

B. You will make your product available with the authorized labeling to authorized laboratories.

C. You will make available on your website(s) the Fact Sheet for Healthcare Providers and the Fact Sheet for Patients.

D. You will inform authorized laboratories and relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to your product and authorized labeling.

E. You will ensure that the authorized laboratories using your product have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

F. You will maintain records of the laboratories you designate as authorized laboratories, and you will also maintain records of test usage by all such authorized laboratories.

G. You will collect information on the performance of your product. You will report to FDA any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the product of you become aware.

H. You are authorized to make available additional information relating to the emergency use of your product that is consistent with, and does not exceed, the terms of this letter of authorization.

I You may request changes to this EUA for your product, including to the Scope of Authorization (Section II in this letter) or to the authorized labeling. Such requests should be submitted to the Division of Microbiology (DMD)/Office of Health Technology 7 (OHT7)-Office of In Vitro Diagnostics and Radiological Health (OIR)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH) and require appropriate authorization from FDA prior to implementation.

J. You will evaluate the analytical limit of detection and assess traceability of your product with any FDA-recommended reference material(s). You will update labeling to reflect the additional testing.

K. Upon request, you will conduct post-authorization studies and/or data analysis concerning the performance of saliva specimens with your authorized test.

L. You will track adverse events, including any occurrence of false results, from testing at your institution and report to FDA.

M. You will develop a laboratory procedure whereby authorized laboratories can verify that the RUO instruments authorized with your product are capable of performing the test with sufficient accuracy, as stated in the authorized labeling. You should submit the procedure to FDA within 21 calendar days of authorization.12

There are fewer requirements for authorized laboratories. The FDA requires that the laboratories provide the fact sheets alongside test result reports. The laboratories are required to use the test as authorized by the FDA. Laboratories are required to report results to the relevant authorities, as well as track the performance of the test and any false positive/negative results. Finally, laboratory staff must be trained to perform RT-PCR and all necessary lab skills associated with the test. These are the requirements that apply to the ABCTL under the Thermo Fisher EUA.

Laboratory Developed Tests and PREP Act Coverage

Mentioned earlier, there is a separate classification for diagnostic tests called laboratory developed tests (LDT). According to the FDA, an LDT is "a type of in vitro diagnostic test that is designed, manufactured

and used within a single laboratory."13 These tests are not typically regulated by the FDA, meaning that they are not legally subject to premarket review and the normal FDA IVD regulatory process. Unfortunately, the LDT regulatory framework is not very concrete and is surrounded in controversy, making it difficult to gauge the FDA's current stance on LDT regulations.

In response to the COVID-19 pandemic, the FDA did release an "umbrella" EUA for LDTs from laboratories with a CLIA certification for high-complexity molecular testing. This EUA covered tests that are used solely in the laboratory they were developed in. On top of this, the test components must be considered research-use-only and bought from 3rd party manufacturers or must be developed at the laboratory. To be eligible for this EUA, laboratories still must submit either an accelerated EUA request or other forms of data and details to the FDA for review and authorization. The reasons for this separate LDT EUA's issuance are unclear, as it seems to have the same requirements as a typical individual EUA.

However, in August, the DHHS, announced that the FDA "will not require premarket review of laboratory developed tests ("LDT") absent notice-and-comment rulemaking" and that "those seeking approval or clearance of, or an emergency use authorization ('EUA') for an LDT may nonetheless voluntarily submit a premarket approval application, premarket notification or an EUA request, respectively, but are not required to do so."14 While there is somewhat conflicting guidance from the FDA and the DHHS, it appears as if any test developed and used within a single laboratory is exempt from the EUA requirement. The details on how LDTs are regulated are somewhat unclear, although it appears as if the majority of the important requirements relate to CLIA and the operation of the testing.

Laboratories still are incentivized to pursue an EUA for their test, specifically because of the Public Readiness and Emergency Preparedness Act (PREP Act). The PREP Act "immunizes a covered person from legal liability for all claims for loss relating to the administration or use of a covered countermeasure." In order to qualify for this legal immunity, the covered person, in this case the medical director of a laboratory, must be distributing a covered countermeasure. A covered countermeasure, specifically in relation to in vitro diagnostics, refers to "a drug, biological product, or device that the U.S. Food and Drug Administration (FDA) has authorized for emergency use."15 Thus, if a laboratory seeks coverage under the PREP Act for their own test, requesting an EUA for their test is necessary. It is worth noting that any laboratory (like the ABCTL) using a test that already has an EUA or is using a validated and authorized modified version of a test that already has an EUA, should qualify for protection under the PREP Act.

Conclusion

It is important to recognize the complex situations that affect these FDA regulations. First, as suggested by its name, Emergency Use Authorizations truly act as the last resort for device authorization/approval. It is not a perfect process, with the majority of official FDA guidance serving as suggestions rather than the official stance of the FDA, like the EUA templates for example. It may be difficult for laboratories who have developed their own test to know exactly how to go about getting authorization. After researching the EUA process, it is clear that frequent correspondence and communication with the FDA and the CDRH is the best way to stay compliant with federal regulations and to navigate the authorizations. Since the guidance documents and suggestions of the FDA have changed over the course of the pandemic, laboratories seeking the current stance of the FDA should contact them directly and discuss their questions. Second, although the EUA process has had its flaws, especially the unclear distinction between LDTs and IVDs, it has been relatively successful in authorizing the many different tests that are critical in the fight against the pandemic. The EUA process shows promise and should be refined in preparation for future epidemics and pandemics.

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Section IV: The Clinical Laboratory Improvement Amendments and Its Implementation in the ASU Biodesign Clinical Testing Laboratory

Author: Nathaniel Ross

Background

Research Question

What were the processes by which the ABCTL rapidly obtained Clinical Laboratory Improvement Amendments (CLIA) certification to conduct clinical human specimen testing and how can this process best be conveyed to a general audience in the form of a documentary?

Methods

The scope of this project is to contribute to a group thesis that presents the transformation of the ASU Biodesign Clinical Testing Laboratory (ABCTL) from a pure research laboratory to a clinical laboratory. This thesis cohort divided the subject areas into legal, biomedical, business, communications, information technology, and documentary subspecialties. The information gathered and documented by the cohort will be presented in a documentary film titled "The Making of a COVID Lab," which will be presented to a general audience.

This particular study focused on one aspect of the legal cohort's subject matter, the Clinical Laboratory Improvement Amendments (CLIA). The beginning of this research consisted of identifying the history and role of CLIA and investigating the state and federal agencies involved in its enforcement. This was followed by the exploration of national practices in regard to CLIA certification, particularly during the era of COVID-19 as well as other examples of non- medical facilities transitioning to patient care. Dr. Michael Standford, and Dr. Adam Rigoni, legal experts, helped clarify the complex legal issues surrounding this investigation through interviews and conversations via Zoom virtual meeting software. Particular questions involved how various cases or legal statutes play a role in the ABCTL and its approval process for human specimen clinical testing.

In order to have a better understanding of the ABCTL's experience with CLIA, Zoom interviews with the Medical Director of the ABCTL, Dr. Carolyn Compton, were conducted. Dr. Compton is listed as the diagnosing physician for every COVID-19 test performed by the laboratory. Since Dr. Compton is highly involved in the lab's inner workings, she provides the cohort with a wealth of first-hand knowledge that we could access. Additionally, Compton was able to provide ABCTL specific and CLIA-relevant documentation for examination.

The final component of this project was to translate the technical and legal jargon into digestible information for a non-lawyer general audience. Since a non-lawyer is performing this study, research was performed regarding lay-people working in legal contexts. This is a common practice in common law systems of justice which use lay-judges (Johansen, 2018). These lay- judges are thrust into the legal field and must rely on non-technical phrasing (Johansen, 2018). This process will be similar in that the final outcomes for this study will be articulated for a general audience and non-lawyers. Additionally, when writing for non-lawyers, a key concept is to avoid standard legal terms by substituting more commonly-used synonyms (Fordyce-Ruff, 2015). These previous cases of lay-people conveying legal information will provide a blueprint which the final product can follow.

Background

During a public health crisis, it often becomes imperative to increase the availability and accessibility of essential services, including emergency medical services, treatments, and diagnostic testing. In the case of the COVID-19 pandemic, institutions that did not typically facilitate healthcare quickly adapted to manage growing demands for care (Vanuytsel et al., 2020). The ABCTL is one such facility. Soon after COVID-19 was introduced into the United States, ASU formed the ABCTL. In addition to other standards, the transformation from a purely scientific laboratory to a clinical diagnostic laboratory requires adherence to significant legal regulations to ensure the information transmitted to patients is accurate and safely maintained. One such regulatory requirement is the Clinical Laboratory Improvement Amendments (CLIA).

CLIA

In 1967, CLIA began as regulatory requirements for any laboratories involved in interstate commerce (Berger, 1999). Over the following two decades, federal authority in medical regulation increased. Following a series of incorrect laboratory reports from Pap smears testing for cervical cancer, the CLIA of 1988 expanded the regulatory requirements (CMS, 2006). As a result, any laboratory that handles human specimens intending to diagnose or treat a health concern must adhere to the CLIA guidelines (Berger, 1999). Three agencies, the Centers for Medicare & Medicaid Services (CMS), the Food and Drug Administration (FDA), and the Centers for Disease Control and Prevention (CDC), are in charge of monitoring CLIA laboratories (CMS, 2006). Today, more than 250,000 laboratories require biennial CLIA certification (CMS, 2006). The key regulatory shift provided by CLIA is the change in focus to what test is being done rather than who was performing the test (CMS, 2006). This ensures that tests maintain the same quality level regardless of whether they were performed at a hospital or a local doctor's office.

Test Categories

Under CLIA, there are three types of tests: waived tests, moderate complexity tests, and high complexity tests (Berger, 1999). Waived tests are basic tests with little room for error and do not have to adhere to most CLIA guidelines such as glucose and cholesterol tests, whereas the latter two testing categories are far more heavily regulated (Berger, 1999). The way CLIA- certified laboratories are examined is through proficiency testing (CMS, 2006). This testing externally evaluates lab result accuracy to ensure consistent quality (CMS, 2006). Moderate and high complexity testing facilities must have means of monitoring equipment functionality in order to pass CLIA inspection (CMS, 2006). Every two years, moderate and high complexity laboratories must undergo onsite inspections conducted by the Federal CLIA program to ensure quality control within the lab examining protocols outlined in the lab's standard operating procedures (CMS, 2006).

Analytical Framework and Findings

To better illustrate the context of rapid CLIA certification and the scalability of healthcare services given at non-healthcare facilities, two case studies will be presented. Both are central to the work completed by the ABCTL as well as giving further real-world examples of the processes undergone by the ABCTL.

- The first study will discuss Boston Medical Center's response to the COVID-19 pandemic, with the development of a novel COVID-19 diagnostic test, and the subsequent CLIA approval process.
- The second examines the expansion of vaccine distributions to decentralized non- healthcare facilities, in this case pharmacies.

Case Study #1: Rapid CLIA Approval

When the COVID-19 pandemic began to rapidly spread through the United States, the growing demand for healthcare was quickly overwhelming the American healthcare system (Vanuytsel et al., 2020). Particularly challenging was getting the SARS-CoV-2 diagnostic testing off the ground (Vanuytsel et al.,

2020). This unprecedented need exposed severely underprepared public health officials and organizations (Sharfstein, Becker & Mello, 2020).

Without testing, there was not enough information about where the virus was or where personal protective equipment should be prioritized (Vanuytsel et al., 2020). Particularly vulnerable populations in normal health circumstances also faced disproportionate impacts of COVID-19 due to "higher prevalence of pre-existing conditions and substance use disorders, lower health maintenance, unstable housing, and a propensity for rapid community spread" (Vanuytsel et al., 2020). This information indicates the importance of a rapid diagnostic testing avenue for hospitals and physicians to implement (Vanuytsel et al., 2020).

Vanuytsel et al., examined the current need within the COVID-19 pandemic and considered the social impact that the virus was having on their local community (2020). Seeing the need for a rapid test that can be widely available, Vanuytsel et al., designed a qRT-PCR assay with a very quick turnaround time (2020). This test passed Clinical Laboratory Improvement Amendments (CLIA) certification and uses Nasopharyngeal swab samples (Vanuytsel et al., 2020). The lab conversion from a "research laboratory to a CLIA-certified SARS-CoV-2 diagnostic facility" took only seven days (Vanuytsel et al., 2020).

Case Study #2 - Health Service Scalability Through Non-Health Care Facilities

In times of health crisis, it may become essential to decentralize the healthcare framework to expand the points of contact that a patient may interact with. Previous research indicates success with this decentralization with vaccinations (Herbin et al. 2020). Most local pharmacies can currently provide vaccinations, a situation seen as impossible twenty years ago (Herbin et al., 2020). Herbin et al. utilized data regarding vaccination's 20-year progression, identifying legal and legislative barriers for program implementation. They regarded these issues as significant hurdles to address so that there is not unnecessary halting of expansion based on legal issues (Herbin et al., 2020). Herbin et al.'s research found that "roughly 9,000 pharmacies in the United States possess a CLIA certificate of waiver" (2020). This indicates the potential viability of a pharmacy-based disease management program (Herbin et al., 2020). Additionally, Herbin et al. identified components of the pharmacy-based model of care that allow for effective implementation (2020).

The purpose of this study was to identify a framework from vaccination decentralization to assist with the implementation of "point of care" testing decentralization. Point of care testing is a diagnostic test that gives rapid and actionable information to health providers in typically under 15 minutes (Herbin et al. 2020). Such rapid results are of great service to health care providers, as in many cases, time and early detection play a key role in improving patient outcomes (Kozel and Burhham-Marusich, 2017). There is growing interest in adapting this point of care technology to supplement efforts to diagnose infectious diseases with a readily available tool (Kozel & Burnham-Marusich, 2017) (Gubbins et al., 2003). This study and its application demonstrate the ability for clinical services to be implemented in a non-hospital setting as well as provide a precedent for the construction of implementation guidelines to increase the rate of adoption of these services.

The ABCTL

Response to a Public Health Emergency

In less than one year since its May 2020 formation, the ABCTL has cemented itself as a national leader and trailblazing institution with its response to the COVID-19 pandemic (ASU, 2020). In a matter of two weeks, the Institute converted from a purely research enterprise to one that handles patient samples (ASU, 2020). A vital consideration for rapid diagnostic testing is the ease of collection; saliva outputs are much easier to access than urine, blood, or the previous COVID-19 standard of nasopharyngeal swab tests (Kozel & Burhham-Marusich, 2017). The ABCTL designed Arizona's first saliva-based test, which has made the testing far more accessible to the broader community (ASU, 2020). Additionally, the facility

was able to streamline the regulatory approval processes mandated by federal and state agencies. This included identifying HIPAA compliant servers, using FDA emergency use authorizations, and obtaining CLIA certification all over just two weeks (ASU, 2020).

Potential for Societal Benefit
Identifying similarities within the two case studies, the ABCTL can serve as a testing ground for widespread implementation within other college laboratories in cases of future pandemics. In the first case study, the experiences of Vanuytsel et al. underlie the possibility of healthcare facilities receiving rapid approval under CLIA for their SARS-CoV-2 diagnostic test and facility. Such circumstances mirror the ABCTL in their creation of their own saliva-based test as well as their swift CLIA approval. This indicates the ABCTL is not anomalous in its ability to receive CLIA certification quickly. In Case Study #2, examining the gradual implementation of point-of-care testing demonstrated how slow the adoption process can be outside of hospital settings. The sluggish pace of pharmacy clinical health services expansion is highlighted when juxtaposed to the conversion and approval time for the ABCTL. Understanding how ASU rapidly obtained CLIA certification as a university rather than a hospital will identify ways of reducing regulatory barriers that other universities have to overcome to also become clinical testing laboratories. This will facilitate rapid adoption and aid in alleviating the COVID- 19 diagnostic testing burden from healthcare facilities.

Perspectives on the ABCTL

The following information was provided during an interview with Dr. Carolyn Compton: C.-C. Compton, personal communication, February 23, 2021

What made the ABCTL so effective at succeeding where commercial laboratories failed?
According to Dr. Compton, speed of diagnostic turnaround was the most significant factor that allowed the ABCTL to compete with and even outcompete major commercial laboratories. Other laboratories were so backed up that they could not turn the cases around (Compton, 2021). Additionally, even other institutions were sending covid tests to the ABCTL despite having the facilities to perform the tests themselves. One such institution was Phoenix Children's Hospital, where they had the personnel and equipment to perform tests, but they were only certified to perform tests of patients, not the staff (Compton, 2021). As a result, the ABCTL was responsible for that testing.

In this case, Phoenix Children's Hospital was collecting the samples; however, the ABCTL was responsible for maintaining documentation that the specimen collectors offsite were operating under the standards of CLIA, which also holds true as well for the ABCTL's own collection sites (Compton, 2021). This documentation is vital to guarantee that they are maintaining the sample's integrity such that it is biologically fit for purpose. The ABCTL, through its standards and procedures, is responsible for the molecular quality from the moment it comes out of the patient throughout its time at the laboratory (Compton, 2021). Additionally, there is a requirement to maintain the fidelity of the sample throughout the process: "All of this was new for ASU. We had never done medical testing before.." (Compton, 2021). There was the equipment and personnel; however, the CLIA process was not required for the previous lab work which focused on biomarkers. In order to generate diagnostic tests, this frame of mind had to completely shift for the lab.

How do you ensure that this speed is coupled with high quality results?
"In my mind, it is a legal issue," says Dr. Compton. "We had people volunteering to work under CLIA in this highly regulated environment. People who were not trained or paid to perform in that setting who were just stepping up to the plate, so liability has always been on my mind" (Compton, 2021). However, the quality of the lab is not in question for Dr. Compton. Total quality management is the primary focus of the lab. Within the ABCTL, they have constructed a team and set of procedures that allow them to analyze failure

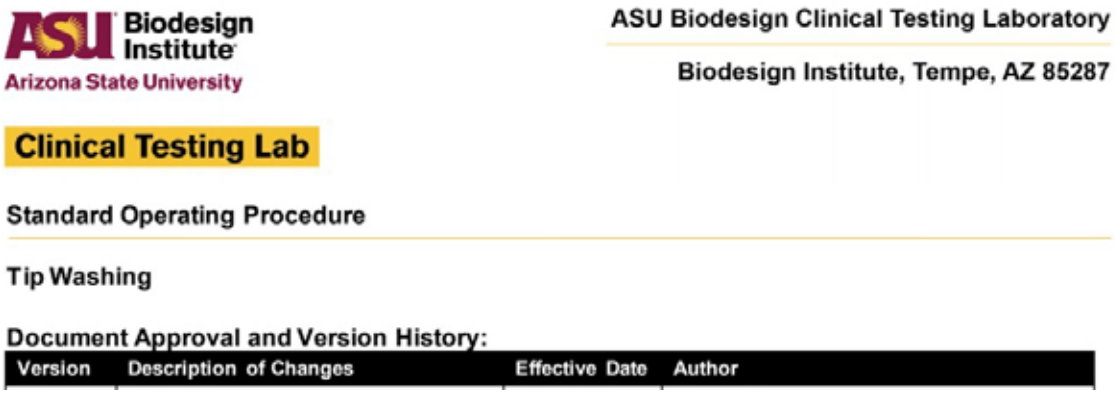
within the systems (Compton, 2021). Some system failures would put the ABCTL out of business, and they have to be able to analyze that and rank situations and problem areas in terms of their effect and put proactive and prospective corrective actions in place: "The certainty of how we can deliver the message of a positive or negative test result depends on the quality of everything underneath" (Compton, 2021).

What practices are important for CLIA certification?
As part of inspection for the ABCTL, standard operating procedures (SOPs) have to be clearly documented. In fact, even the procedure for drafting and creating an SOP requires the existence of an SOP (Compton, 2021). Everything that the lab does has to be described in writing and signed by the laboratory director, Dr. Carolyn Compton, as well as the technical director, the author of the SOP, and others involved in the process, so that it can be traced back to its origin (Compton, 2021). All of this is within a collection called the CLIA manual at the ABCTL (Compton, 2021). CLIA mandates documenting both policies and true-to-reality procedures. An example Dr. Compton gave was that the inspectors will immediately examine the SOP and identify individuals who claim to have passed certain competency requirements. They can then ask for the records of that competency. All of this is to ensure that a lab is doing what they claim. Deficiencies can close the lab depending on how serious they are (Compton, 2021). Using an actual SOP document from the ABCTL, I will explain the anatomy of the SOP and how the documentation allows for increased ease in quality management.

Anatomy of an SOP

For documentation purposes, the ABCTL maintains standard operating procedures in the same seven section format. An example SOP from the ABCTL will be used to illustrate the systematic nature by which these procedures are documented. This documentation was provided by Dr. Carolyn Compton:

Document approval and Version History:
At the beginning of each SOP there is documentation of when the original SOP was made effective. This allows for a paper trail should any improvements be made to conform to CLIA standards following


ASU Biodesign Institute
Arizona State University

ASU Biodesign Clinical Testing Laboratory

Biodesign Institute, Tempe, AZ 85287

Clinical Testing Lab

Standard Operating Procedure

Tip Washing

Document Approval and Version History:

Version	Description of Changes	Effective Date	Author

Image 1: Version History of ABCTL Tip Washing SOP

Procedural Components of ABCTL SOP:
The following are the various sections of the lab SOPs:

1. **Purpose** — Defines the relevance of the SOP within the Lab.
2. **Scope** — Explains what role this procedure plays within the ABCTL's purpose.
3. **Safety Precautions** — Identifies the personal protective equipment necessary to safely perform the procedure.

4. **Specimen Collection, Handling, and Storage** — Allows for easy identification of any sample-related requirements.
5. **Materials** — Image 2 is an example of the information provided in the materials section. This specificity allows for the proper identification of quality standards within the equipment used.

Materials Required

Instruments			
SKU	**Supplier**	**Description**	**Needed**
NA	Grenova LLC	TipNovus System	1+
NA	Grenova LLC	TipLumis System	1+
Equipment			
NA	Grenova LLC	TipNovus tip adapter (custom per each tip type)	1+
NA	Grenova LLC	TipLumis rack	1+
NA	Grenova LLC	TipLumis rack center	1+
NA	MLS	Shaker or stir plate assembly	1
NA	MLS	Flask, beaker, or other mixing receptacle	1

Image 2: Materials Table from ABCTL Tip Washing SOP

6. **Procedure** — This section will specifically outline the procedure that must be followed to ensure the quality of the test. This section may also refer to other SOPs in the ABCTL CLIA manual that must be referred to prior to beginning the test.
7. **References** — This section is used to cite the sources for why the SOP was written with the procedures it contains.

7.0 References
7.1 Grenova TipNovus User Manual v1.7
7.2 Grenova TipLumis User Manual v2.0Image 3: References from ABCTL Tip Washing SOP

Image 3: References from ABCTL Tip Washing SOP

Approvals:
The final component of the SOP includes the signatures of approval, along with the date of approval. As described in the SOP introduction, these signatures provide proof of receipt for CLIA inspectors to trace the origins of a SOP to ensure quality control.

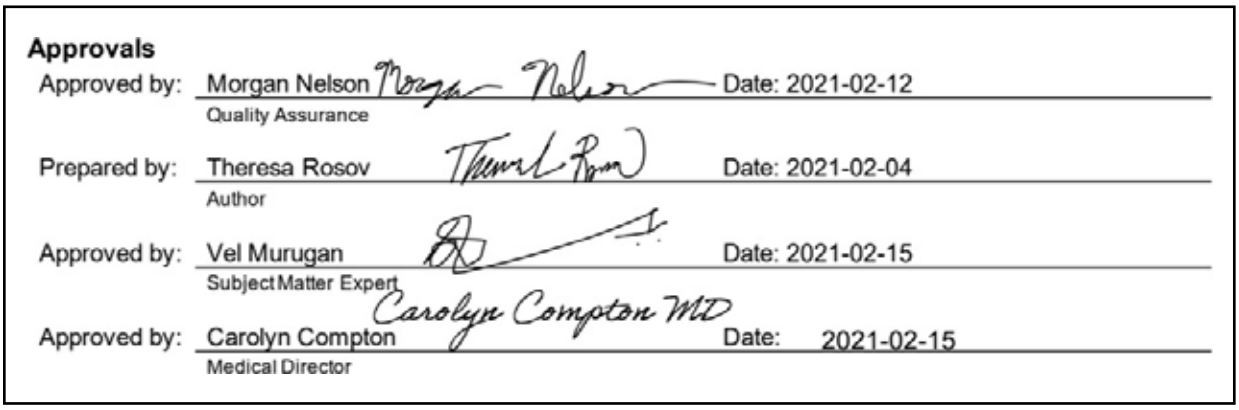


Image 4: Signatures from ABCTL Tip Washing SOP

Conclusion and Future Forecast

With vaccines rapidly being administered into the American population, there comes a decreased demand for COVID-19 diagnostic testing. During an interview with Dr. Compton, she explained the uncertain future of the ABCTL, particularly with regards to CLIA.

Are there plans for the ABCTL to become involved in sequencing for new variants?
At the moment, there are no immediate plans to set up sequencing in the Current CLIA environment (C.-C. Compton, personal communication, February 23, 2021). At the time of this interview, all forms of sequencing of SARS-CoV-2 are being done in a research capacity, which curtails CLIA's enforcement capabilities since patient care is not being impacted (Compton, 2021). There are financial barriers that present itself with this route, as well as possible lack of public health justification due to rapidly increasing numbers of vaccinated individuals (Compton, 2021). "If the virus has no place to go, then our job will be easier," says Compton. She believes they will be most useful in terms of campus-level testing, pending funding (Compton, 2021).

Will the ABCTL be able to perform antibody testing on patients?
Antibody testing is currently being performed; however, it is not being used to give diagnostic or medical recommendations. This research focuses on the pace of antibody production after an infection, as well as the trail off and compares the immune response caused by the variants of SARS-CoV-2 (Compton, 2021). Additionally, this research is investigating whether or not the immunity created through natural infection is more or less durable than immunity created through inoculation (Compton, 2021). There are many research questions that require monitoring, however since this is research-focused rather than patient-focused, CLIA does not govern these experiments.

What will happen to the ABCTL after the pandemic?
According to Dr. Compton, there is not a clear plan that the ABCTL will follow after COVID-19 is no longer considered a health emergency. Further, there are doubts that the lab will even remain at the ASU Biodesign Institute (Compton, 2021). A possible relocation would be to the new Health Futures Center in Phoenix, Arizona (Compton, 2021). This facility is designed for clinical training, which would benefit from proximity to the Mayo Clinic as well as to any clinical trials being performed in this space.

Conclusion

Perhaps the most apt way to conclude this exploration into the ASU Biodesign Clinical Testing Laboratory is by considering a metaphor used by Dr. Carolyn Compton herself. Compton compares the journey of the ABCTL to that of a decathlete, where each challenge the lab faced was like an event in this decathlon. "We don't have to be the best in any one of these events, but if we are not able to throw the shot put at all, we are never going to win the decathlon" (Compton, 2021). The making of a COVID lab requires that you be competent in all things. This idea is what encapsulates the concept of total quality management. Any "event" in the decathlon the ABCTL fails could bring down the whole operation. Filing and gaining CLIA certification is one massive hurdle in the "Law" focused component of the decathlon; however, failure to clear this hurdle can result in disqualification from the event entirely. As a result of the critical and difficult nature of CLIA certification, completing this process in rapid fashion stands as a testament to the dedication to quality and community health of the ABCTL and Arizona State University at large.

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Section V: Health Insurance Portability and Accountability Act (HIPAA)

Author: Madeline R. Salvatierra

Introduction

In 2020, the COVID-19 virus spread across the globe, infecting millions of people. Organizations, like the ABCTL raced to develop quick, effective, and affordable COVID-19 tests to determine who was actively infected with COVID-19. The early tests involved a painful swab inside the patient's nose (Compton, ABCTL full team meeting, 2020). The ABCTL developed a faster, less painful test that was sufficiently effective in testing for active COVID-19 infections (Compton, ABCTL full Law Group meeting, 2020). This test required participants to provide a saliva sample for the lab to test. In addition to being less painful for participants, it was also safer to administer, since participants could collect their samples on their own (Compton, ABCTL full Law Group meeting, 2020).

ASU has never had a diagnostic lab before, so creating the ABCTL and administering COVID-19 tests was a new practice for the university (Compton, ABCTL full Law Group, 2020). Practicing medicine requires adherence to various laws and regulations, which had not previously been an issue for ASU. What happens if someone sues the lab for a false test result? Can the lab report positive results to public health agencies? Can ASU require COVID-19 testing? For my thesis, I worked with a team of students to research the legal implications of the lab to address these questions, among others. I focused on the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and its related laws and regulations. This paper provides an overview of HIPAA and discusses the answers to timely questions regarding COVID-19 testing and HIPAA compliance.

HIPAA Overview

In 1966, a federal law know as HIPAA that regulates how private medical information can be shared, used, transmitted, and stored was enacted (Centers for Disease Control, 2018). As federal law, it applies to every US jurisdiction, including the State of Arizona. After Congress passed the act, it turned to US Department of Health and Human Services (HHS) to create the rules and regulations that would turn the act into action (Centers for Disease Control, 2018). In the US, agencies such as the Central Intelligence Agency, the US Department of Agriculture, the Department of Homeland Security, and the HHS, have the power to enact and enforce rules and regulations (Markos, 2021). These agencies convert lengthy congressional legislation into rules that people and organizations must follow. HHS created two main rules for HIPAA: the Privacy Rule and the Security Rule (Centers for Disease Control, 2018). There are also other rules, such as the Breach Notification Rule and the Enforcement Rule, that govern other aspects of HIPAA (Centers for Disease Control, 2018). In 2009, Congress passed the Health Information Technology for Economic and Clinical Health (HITECH) Act, which served as a follow-up to HIPAA that updated parts of the act and discussed electronically stored health information (Office for Civil Rights, 2017). HHS's rules, regulations, and updated guidelines also apply to the HITECH Act, in addition to the original HIPAA law.

HIPAA and the ABCTL

It is essential to determine whether HIPAA applies to the ABCTL. If HIPAA does not apply to the lab, then the lab need not worry about the regulations associated with HIPAA. If HIPAA does apply to the lab, the lab must ensure it is compliant with all applicable rules and regulations.

HIPAA applies to any organization or individual that is considered a "covered entity" under the HHS Administrative Simplification regulations (Centers for Medicare and Medicaid Services). The lab is a "covered entity" if it bills or receives payment for healthcare and if it transmits "covered transactions" electronically (Centers for Medicare and Medicaid Services). First, we must ask, does the lab bill or receive payment for healthcare? Yes, it does, according to Dr. Carolyn Compton, medical director of the lab (Compton, ABCTL Law Team Meeting, 2021). Dr. Compton stated that the lab's billing process is different from other labs because it does not have a billing department, and it does not bill each patient. Instead, it gets paid directly from the Arizona Department of Health Services, or from companies such as Arizona Public who want employees tested for the virus (Compton, ABCTL Law Team Meeting, 2021). Additionally. Dr. Compton explained that the lab tests certain populations such as inmates in the Arizona correctional system or people experiencing homelessness. The Arizona government pays the lab to test these populations, and the lab does not bill these patients' insurance (Compton, ABCTL Law Group meeting, 2021). Because the lab receives payment for healthcare and transmits covered transactions electronically, it is a "covered entity". As a "covered entity", the lab is subject to HIPAA.

What is Protected Health Information under HIPAA?

The term "protected health information" is central to HIPAA law. "Protected health information" (PHI) is "individually identifiable health information" that the covered entity holds and/or transmits (Office for Civil Rights, 2003). "Individually identifiable health information" is information that could reasonably be used to identify the individual, including Social Security number; name; birth date; payment for the individual's healthcare in the past, present, or future; health history; and other information (Office for Civil Rights, 2003). The Privacy Rule regulates the sharing of PHI (Office for Civil Rights, 2003). Electronic protected health information (e-PHI) is PHI that is created, stored, or transmitted electronically (Centers for Disease Control, 2018). e-PHI is used in conjunction with the Security Rule, which regulates how e-PHI is stored and shared (Centers for Disease Control, 2018).

The Privacy Rule

Understanding the Privacy Rule is essential for understanding HIPAA regulations. The Privacy Rule regulates how a covered entity can use PHI (Office for Civil Rights, 2003). There are three instances in which a covered entity can use PHI (Office for Civil Rights, 2003). It can use PHI if the individual gives written authorization, if the individual or HHS requires the covered entity to disclose the PHI, or if the Privacy Rule allows it to (Office for Civil Rights, 2003).

If the individual gives written authorization that their PHI may be used, stored, or transmitted by the covered entity, the covered entity is permitted to use the PHI in the specified way (Office for Civil Rights, 2003). If students, faculty, staff, community members, or anyone else utilizing the services of the ABCTL authorize the lab in writing to utilize certain pieces of PHI, the lab is authorized to do so (Office for Civil Rights, 2003).

Additionally, there are instances in which a covered entity may be required to disclose PHI. These instances include if the individual asks for the information about themselves (i.e., a patient asking for their own medical records), or if the HHS asks for information for the purposes of an investigation or enforcement (Office for Civil Rights, 2003).

Finally, covered entities are authorized to use PHI if it is for a use allowed by the Privacy Rule. There are six instances in which covered entities can disclose PHI without an individual's written consent (Office for Civil Rights, 2003). In the Office for Civil Rights of HHS's "Summary of the HIPAA Privacy Rule", it writes that these are the six instances when the lab could disclose PHI without an individual's written consent:

> (1) to the Individual; (2) Treatment, Payment, and Health Care Operations; (3) Opportunity to Agree or Object; (4) Incident to an otherwise permitted use and disclosure; (5) Public Interest and

> Benefit Activities; and (6) Limited Data Set for the purposes of research, public health or health care operations" (Office for Civil Rights, 2003).

Out of six the instances, Public interest and Benefit Activities is the most interesting and timely for the coronavirus pandemic.

Public Interest and Benefit Activities

"Public Interest and Benefit Activities" are one of the reasons for which covered entities can disclose PHI without written authorization from the individual to whom the PHI pertains (Office for Civil Rights, 2003). To define "Public Interest and Benefit Activities", HHS provides twelve national priority purposes that are considered "Public Interest and Benefit Activities" (Office for Civil Rights, 2003). Out of the twelve national priority purposes, the most relevant for the ABCTL are "Public Health Activities", "Research", "Serious Threat to Health or Safety" or "Required by Law".

National Priority Purpose for Public Interest and Benefit Activities: Public Health Activities
"Public Health Activities" are a national priority purpose for which covered entities can disclose PHI under the "Public Interest and Benefit Activities" prong of the Privacy Rule (Office for Civil Rights, 2003). In other words, the lab could disclose a patient's PHI without their consent if it is for a "Public Interest and Benefit Activity". There are twelve purposes that HHS considers "Public Interest and Benefit Activities", and one of those is "Public Health Activities" (Office for Civil Rights, 2003). "Public Health Activities" is further divided into four situations (Office for Civil Rights, 2003). Two of the four situations are more relevant for the ABCTL.

The first definition of "Public Health Activities" is as follows:

> [Covered entities may disclose PHI to] (1) public health authorities authorized by law to collect or receive such information for preventing or controlling disease, injury, or disability and to public health or other government authorities authorized to receive reports of child abuse and neglect, (Office for Civil Rights, 2003).

The part of this definition that is most relevant is the part about "preventing or controlling disease". The COVID-19 tests that the lab administers are important for tracking the spread of the virus and reporting the results to public health authorities could help public officials control disease. Are there public health authorities that are "authorized by law" to "collect or receive" COVID-19 test results for "preventing and controlling disease"?

Yes, according to HHS, the lab is authorized to report test results and other relevant and necessary PHI to public health authorities for the purpose of limiting the spread of COVID-19. HHS states in a March 2020 bulletin that "a covered entity may disclose to the CDC protected health information on an ongoing basis as needed to report all prior and prospective cases of patients exposed to or suspected or confirmed to have COVID-19" (Health and Human Services, 2020). Here, HHS clearly indicates that the lab can disclose results to the CDC. What about local public health authorities, such as the Arizona Department of Health Services? Based on HHS's definition of a "public health agency", any state or local agency "responsible for public health matters as part of its official mandate" is authorized to receive test results, case information, etc. (Office for Civil Rights, 2003). Arizona Department of Health Services is responsible for public health matters in its official mandate, so the lab can share PHI with the department for controlling the spread of the virus (Arizona Department of Health Services, n.d.).

Moreover, another definition of "Public Health Activities" refers to tracing people who may have been exposed to a communicable disease. HHS states that covered entities can disclose PHI to "(3) individuals who may have contracted or been exposed to a communicable disease when notification is authorized by law" (Office for Civil Rights, 2003). The amount and type of PHI that the lab can disclose is limited and

will be discussed later in this paper. The ABCTL Thesis Project focuses exclusively on the lab's testing processes, rather than contact tracing initiatives, so further analysis of this is beyond the scope of the project. However, a topic for further research would be analyzing what data can be shared for contact tracing, with whom the data can be shared, and how the data must be stored.

National Priority Purpose for Public Interest and Benefit Activities: Research

Another relevant national priority purpose for "Public Interest and Benefit Activities" is "Research" (Office for Civil Rights, 2003). HHS defines "research" as "any systematic investigation designed to develop or contribute to generalizable knowledge" (Office for Civil Rights, 2003). The lab can use PHI for research without an individual's permission if it meets one of these requirements:

- If the lab obtains approval from the IRB or a Privacy Board that the lab does not need an individual's authorization;
- If the information is necessary for the research, if the information will stay within the covered entity, and if the PHI will only be used to prepare a research protocol;
- Or if the information is necessary for the research, the information will be used to research decedents only, and if death certificates will be sought for the individuals whose information is being used (Office for Civil Rights, 2003).

If the lab meets any of those criteria, it can use PHI for research without an individual's permission. The lab should still take care to avoid using any PHI beyond what is necessary (Office for Civil Rights, 2003).

Alternatively, the lab can use a Limited Data Set of PHI for research purposes without needing to meet these conditions (Office for Civil Rights, 2003). Recall that there are six instances in which covered entities can use PHI without an individual's authorization, per the Privacy Rule. "Public Interest and Benefit Activities" is one of those situations, and "Limited Data Set" is another (Office for Civil Rights, 2003). "Limited Data Sets" are conglomerations of data with specific PHI redacted so that individuals cannot be identified from the data (Office for Civil Rights, 2003). Limited data sets can be used for research or other purposes, but the entity receiving the data must protect the data (Office for Civil Rights, 2003). Although certain PHI is redacted in the limited data set, possessors of the data must still secure it, since some PHI will remain (Office for Civil Rights, 2003).

National Priority Purpose for Public Interest and Benefit Activities: Serious Threat to Health or Safety

Additionally, the lab may disclose PHI if there is a "Serious Threat to Health or Safety". "Serious Threat to Health or Safety" is one of the twelve national priority purposes for "Public Interest and BenefitActivities" (Office for Civil Rights, 2003). HHS states the following in its "Summary of the HIPAA Privacy Rule":

> Covered entities may disclose protected health information that they believe is necessary to prevent or lessen a serious and imminent threat to a person or the public, when such disclosure is made to someone they believe can prevent or lessen the threat (including the target of the threat)… (Office for Civil Rights, 2003).

In order for the lab to use the "Serious Threat to Health or Safety" justification for disclosing PHI, COVID-19 must be considered a "serious and imminent threat to a person or the public". Is COVID-19 considered a "serious and imminent threat to a person or the public"?

As far as I could find, HHS did not explicitly say that COVID-19 is a "serious an imminent threat", but the HHS's February 2020 bulletin suggests that it is (Office for Civil Rights, 2020). The language in the February 2020 bulletin refers to "the serious and imminent threat" (Office for Civil Rights, 2003). Because the entire bulletin is specific to the pandemic, it can be inferred that the use of "the" when referring to the

threat means that COVID-19 is the "serious and imminent threat"; therefore, the justification for disclosing PHI under the "Serious Threat to Health or Safety" national priority purpose is valid.

Also, the bulletin indicates that disclosures must abide by state/local/case law and the provider's "standards of ethical conduct" (Office for Civil Rights, 2020). This means that any disclosures the lab makes under this justification must comply with the State of Arizona, Maricopa County, the City of Tempe, and Dr. Compton's credo.

National Priority Purpose for Public Interest and Benefit Activities: Required by Law

The final national priority purpose that is most relevant to the lab is the purpose titled "Required by Law". If a law requires the lab to use or disclose PHI without an individual's written permission, it is allowed to do so (Office for Civil Rights, 2003). The "law" can include statutes, court orders, and regulations (Office for Civil Rights, 2003). This national priority purpose is flexible, and can be based on federal, state, or local statutes; agency regulations; or court orders from a federal, state, or local court (Office for Civil Rights, 2013). The lab is permitted to use PHI if required by any law.

The Sharing of PHI

When a covered entity is authorized to share a patient's PHI, they must only share the minimum amount necessary (Office for Civil Rights, 2003). There are a few instances in which covered entities are not limited to the minimum necessary. These include when the lab is required by law to disclose the information, when the individual to whom the information pertains requests the information, when required for HHS investigations or enforcements, or when communicating with a health care provider regarding the patient's treatment (Office for Civil Rights, 2003). In these situations, the lab need not limit sharing of PHI to the minimum necessary.

Summary of Privacy Rule

To summarize, complying with the Privacy Rule is a primary requirement of HIPAA. As a covered entity, the ABCTL must comply with the Privacy Rule. Under the privacy rule, the lab can use or disclose Protected Health Information if it has an individual's written authorization or if it meets one of six approved conditions. PHI is considered "individually identifiable health information" such as health history, social security number, birth date, payment information, etc. One of those conditions for which the lab can disclose PHI is "Public Interest and Benefit Activities", which means that the lab can use or disclose PHI if it is for Public Health Activities, Research, preventing a Serious Threat to Health or Safety, or if Required by Law. Even if the lab is permitted to use PHI, it must still limit such use/disclosure to the minimum amount necessary.

The Security Rule

In addition to the Privacy Rule, the Security Rule is an HHS rule to implement the requirements of the HIPAA and HITECH Act legislation. The Security Rule focuses on electronically stored protected health information, or e-PHI (Centers for Disease Control, 2018). According to HHS's "Summary of the HIPAA Security Rule" webpage, "The Security Rule requires appropriate administrative, physical and technical safeguards to ensure the confidentiality, integrity, and security of electronic protected health information" (Office for Civil Rights, 2013). The Security Rule applies to all covered entities that transmit PHI electronically (Centers for Disease Control, 2018). The lab transmits PHI electronically, according to my conversation with Dr. Compton, so the lab is subject to the Security Rule (Compton, ABCTL Law Team Meeting, 2021). The Security Rule is designed to be flexible so that it can apply to entities of all sizes, and it lets covered entities determine what security measures will best help them meet the requirements of the rule (Office for Civil Rights, 2013).

There are four general principles with which covered entities that are subject to the Security Rule must comply (Office for Civil Rights, 2013). These principles are as follows:

- "Ensure the confidentiality, integrity, and availability of all e-PHI they create, receive, maintain or transmit;
- Identify and protect against reasonably anticipated threats to the security or integrity of the information;
- Protect against reasonably anticipated, impermissible uses or disclosures; and
- Ensure compliance by their workforce" (Office for Civil Rights, 2013).

These principles demonstrate that the central purpose of the Security Rule is to maintain data security and ensure no unauthorized individuals access data they are not supposed to access. HHS recommends various administrative, physical, and technical safeguards that covered entities can utilize to meet these general principles (Office for Civil Rights, 2013). For many of the safeguards, the details of how the safeguards are implemented and which specific safeguards are implemented is up to the discretion of the covered entity (Office for Civil Rights, 2013).

The administrative safeguards have to do with the processes in place at the organization to ensure only those who are supposed to access data may access it. Some of these safeguards include conducting regular risk analysis of e-PHI security and taking measures to reduce those risks; having a designated "security official" in charge of security policies; having a system of role-based access for accessing e-PHI; training, supervising, and disciplining (if needed) employees, and periodically evaluating security measures to ensure they are compliant (Office for Civil Rights, 2013).

Next, the physical safeguards pertain to the physical security of the data. These may include preventing unauthorized individuals from entering the lab; specifying the appropriate uses of technology in the workspace; and having policies for the movement, use, and/or disposal of electronically stored content (Office for Civil Rights, 2013).

Finally, the technical safeguards relate to technical barriers to the data, rather than physical barriers. Some of the recommended technical safeguards include preventing unauthorized people from accessing e-PHI both in the lab's systems and as the data is being transmitted electronically; tracking the movement and usage of e-PHI; and having electronic measures in place to ensure e-PHI is not being changed or deleted inappropriately (Office for Civil Rights, 2013).

Additionally, HHS has various documentation requirements for the Security Rule. HHS states that covered entities must have "reasonable and appropriate policies and procedures to comply with the provisions of the Security Rule" (Office for Civil Rights, 2013). The documentation requirements relate to the documentation of these policies and procedures. For instance, the lab must maintain records for six years after they were created or last effective, according to HHS (Office for Civil Rights, 2013). The records that must be kept include "written security policies and procedures and written records of required actions, activities or assessments" (Office for Civil Rights, 2013). Documentation must also be available to the people who need to implement the policies listed in the documentation, and documentation must be reviewed and updated periodically (Office for Civil Rights, 2013).

Enforcement Rule

The Enforcement Rule relates to enforcement of Privacy and Security Rules, investigations, penalties, and hearings (Office for Civil Rights, 2020). It is the way that the HHS enforces its HIPAA regulations. The Office for Civil Rights (OCR) of HHS is responsible for enforcement (Office for Civil Rights, 2020). There are three main ways that HIPAA violations are enforced: investigations of complaints, compliance reviews, and efforts to educate covered entities on the requirements (Office for Civil Rights, 2017). If OCR finds any criminal violations, it will report them to the Department of Justice (DOJ) (Office for Civil Rights, 2017). Below are further explanations of complaints and compliance reviews, along with the penalties that OCR may impose for violations.

Complaints

OCR receives thousands of complaints each year, but not all complaints result in an investigation (Office for Civil Rights, 2017) (Office for Civil Rights, 2020). In order for OCR to take action on a complaint, the complaint must meet multiple conditions. (Office for Civil Rights, 2017). First, the complaint must be against a covered entity (Office for Civil Rights, 2017). You cannot file a HIPAA complaint against an organization or provider that is not subject to HIPAA. Additionally, the incident that the complaint references must have occurred after the Privacy Rule and/or Security Rule went into effect, in 2003 and 2005, respectively (Office for Civil Rights, 2017). Next, the complaint must refer to a violation of the Privacy or Security Rule (Office for Civil Rights, 2017). In other words, you cannot file a HIPAA complaint about something that is not a violation of HIPAA. Lastly, the complaint must be filed within 180 days of knowledge of the incident, for most situations (Office for Civil Rights, 2017). All of these requirements must be satisfied for OCR to investigate the complaint.

If the above conditions are met and the OCR investigates, covered entities are legally required to cooperate with the investigation (Office for Civil Rights, 2017). The investigation involves both the complainant and covered entity providing information about the incident (Office for Civil Rights, 2017). If OCR finds a violation, it will follow one of the methods described in the “Penalties” section below.

Compliance Reviews

Compliance reviews are extremely rare (Office for Civil Rights, 2020). The overwhelming majority of HIPAA investigations are done because of a complaint, rather than a compliance review (Office for Civil Rights, 2020). For example, in 2019, OCR received nearly 30,000 complaints but only conducted 338 compliance reviews (Office for Civil Rights, 2020). The data is similar for 2017 and 2018 too, suggesting that OCR typically performs only a few hundred compliance reviews per year, compared to the tens of thousands of complaints they receive (Office for Civil Rights, 2020). Therefore, complaints are the primary way OCR enforces the HIPAA rules.

Penalties

OCR has various strategies for disciplining covered entities who violate the rules (Office for Civil Rights, 2017). First, note that criminal offenses will be reported to the DOJ (Office for Civil Rights, 2017). OCR may use its own strategies to penalize covered entities for non-criminal violations. If the covered entity is found not to be compliant, OCR will attempt "voluntary compliance; corrective action; and/or resolution agreement" (Office for Civil Rights, 2017). These strategies are OCR's first-choice, but if those strategies fail, OCR can impose "Civil Money Penalties (CMPs) on the covered entity" (Office for Civil Rights, 2017). Like compliance reviews, CMPs are extremely rare. In 2019, only 0.0255% of HIPAA violation cases resulted in a CMP, demonstrating how rare they are (Office for Civil Rights, 2020). In the case of a CMP, the covered entity has the right to a hearing with an "HHS administrative law judge" (Office for Civil Rights, 2017). Additionally, the money gained from a CMP goes to the U.S. Treasury, not to the complainants (Office for Civil Rights, 2017). Although OCR and HHS have the right to impose financial penalties on covered entities who violate HIPAA regulations, they rarely do so.

Enforcement Discretion for Community-Based Testing Sites During the Pandemic

In a memo released on April 9, 2020, HHS's Office for Civil Rights (OCR) declared that it will not enforce HIPAA violations for community-based testing sites (Severino, 2020). The memo stated the following:

> OCR will exercise its enforcement discretion and will not impose penalties for violations of the HIPAA Rules against covered entities or business associates in connection with the good faith participation in the operation of COVID-19 testing sites during the COVID-19 nationwide public health emergency, (Severino, 2020).

The memo is retroactive and affects March 13, 2020 onward (Severino, 2020). This enforcement discretion update is specifically for Community Based Testing Sites (CBTS), which are testing sites that only do testing and/or specimen collection (Severino, 2020). For instance, a hospital that performs a variety of functions and sees patients for a variety of conditions is not a CBTS. The ABCTL exclusively performs COVID-testing, and does not perform any other health care functions (Compton, ABCTL Law Team Meeting, 2021). Therefore, it seems that the lab is covered, as long as it acts in "good faith".

The April 2020 memo states that reasonable safeguards to protect PHI are encouraged, but violations will not be penalized if acting in good faith (Severino, 2020). Some safeguards to protect PHI could include making sure samples are able to be collected in a private setting. The ABCTL now allows patients to drop-off their saliva sample in a secure drop-box, which enables patients to collect their sample in the privacy of their home (Salvatierra, 2021). Prior to the change to a drop-off model, patients could collect their sample by themselves in the privacy of their cars or in a partitioned section of the gym (Salvatierra, 2021). The privacy afforded by all of the lab's specimen collection methods demonstrate the lab's efforts to protect patients' PHI.

This memo is critical because it suggests that the lab will not be penalized for any violations of HIPAA, so long as it is acting in good faith. Although the lab should still do its best to protect PHI and adhere to HIPAA guidelines as much as possible, it need not spend all of its energy on ensuring HIPAA compliance.

Conclusion

HIPAA is an area of regulatory law that is critical for protecting people's private health information. The ABCTL must take care to keep PHI secure. Luckily, as a community-based testing site, it is less likely to be penalized for any HIPAA violations. Nonetheless, the lab has a duty to keep PHI safe. The ABCTL has provided simple, easy, and accurate COVID-19 tests to many people in Maricopa County, and it has played a critical role in tracking the spread of COVID-19.

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Chapter 6

The Making of a COVID Lab

A Focus on Quality Management Systems

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Introduction to Chapter 6

The Arizona State University Biodesign Clinical Testing Lab (ABCTL) currently faces significant pressure to maintain the quality and improve the speed of producing results from testing salvia samples for COVID-19. It is well established that collecting data supports modeling, value stream mapping, and supports finding the identification of root causes in the lab that might be hindering its efficiency. This research aims to provide ideas for the lab to implement in the future to improve the way in which data is collected throughout the process of testing a salvia sample for COVID-19 and improve the overall efficiency and productivity of the lab. A lot traveler was originally distributed to the lab to determine a baseline rate at which samples traveled through the lab. It was quickly determined there were major roadblocks to the data collection process, thus obscuring discoveries from being made about the efficiency of the lab and obstructing the process for identification of root causes of slow speeds and poor quality within the lab. It was concluded that a better data tracking system is needed in the lab to meet their capacity goal of producing results for 16,000 samples per day.

The ABCTL provides "saliva testing to identify the presence of COVID-19" ("Overview." Accessed January 13, 2021. https://Biodesign.asu.edu/research/clinical-testing.). These tests protect our communities by allowing swift responses to the identification of positive cases, which is incredibly important. The Medical Director of ABCTL, Dr. Carolyn Compton, initiated a large multidisciplinary Barrett honors thesis project. The purpose of this project was to assist ABCTL in its goals of the reduction of turnaround time (TAT) and the increasing of capacity. The specific objectives were to reduce TAT to be under 24 hours and to increase capacity to at least 16,000 samples per day.

To work towards these objectives, a group of Barrett students interested in various aspects of engineering and process improvement was formed. The group was composed of students from Industrial Engineering, Engineering Management, Computer Science, and Business Data Analytics. This team acted under the advice and lead of Dr. Daniel McCarville, a Professor of Practice at the Fulton Schools of Engineering, who teaches Industrial Engineering. The team was also advised by Dr. Esma Gel, Morgan Nelson, and Clayton Taylor.

The team members started this project by training in Lean Six Sigma and becoming certified as Lean Six Sigma yellow belts. The team then focused on data collection and process mapping to better understand the circumstances of the laboratory. Upon gaining some understanding of the laboratory, each member of the team initiated individual research to consider different focus areas regarding the laboratory. The members also continued to work on data collection and followed up on the data with further analysis and simulation. The team presented a defense of this thesis project on April 16, 2021.

Keywords: COVID-19, medical testing lab, efficiency, modeling, value stream mapping, root causes, data collection, tracking system

Section I: Lab Material Tracking Systems

Author: Ishna Barwey

Background and Focus

Materials tracking is an essential addition to the medical laboratory environment, as it drives further improvements in workflow and turnaround rates. Tracking systems can range in complexity from a paper form to a remote scanning system. They involve physical tracking of assets and recording of data regarding the assets as they move through the workflow. The use of tracking systems allows for greater ease of detection of workflow bottlenecks as well as status of specimens. While the addition of such systems will inevitably lead to interruptions in the personnel's work in the laboratory, higher level tracking systems minimize staff effort in the recording process to maximize efficiency. Aside from bottlenecks, the tracking expose errors in the lab's process that can then be removed through application of Lean and Six Sigma methodologies on the systems. There is a sharp decline in human errors and non-value-added lulls in the process when these observations are acted upon. The below figure displays the drastic decrease in errors after implementation of a barcode scanning system for specimen in a Yale laboratory (Pantanowitz & Balis, 2012).

Figure 1. "Graph showing the steep decline in errors following the implementation of a bar code tracking solution in the anatomic pathology laboratory at Yale in New Haven, Connecticut."

In the case of the ASU's COVID-19 testing labs, it is necessary to investigate materials tracking systems to track each test tube containing a sample as it goes through each step in the lab's testing process. An understanding of the timing and locations of these test tubes in the current system provides key insight into shortening the test result turnaround time and increasing the lab's efficiency towards its 24-hour goal.

Lot Travelers

The Quality Management Systems group began an initiative to implement lot travelers in the lab to gauge the time increments between and during each step of the COVID-19 testing process. The travelers were paper forms which we printed and attached to select batches. The staff who worked at each step were then asked to manually record the times and plate numbers for the samples with a pen. Through the

lot travelers, our group was able to follow the lifetime of each test tube through the system and track its location in relation to each step. These serve as an initial, bare-bones materials tracking which we have been using to gather data since November. The form was certainly not used for every batch of tubes, but we tracked a variety of batches on multiple days and different months in order to attain worthwhile data and conclude generalized trends. The physical format of the forms lead to issues in the data. Not at the fault of any individual, many of the staffed volunteers in the lab worked long hours and were not properly

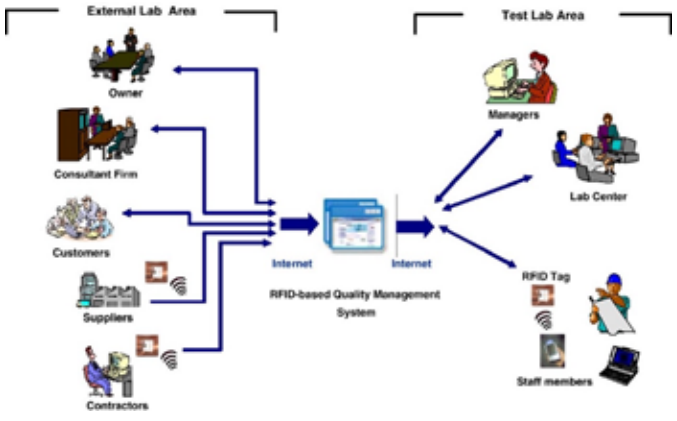
communicated on the importance of the data collection. Asking them to now enter the exact times of the start and end of each process with details such as plate numbers and machine IDs led to inaccurately reported or absent data. The QMS team manually typed data from the scanned travelers into excel sheets for digital analysis, where the illegibility of some numbers and the lack of consistency in the timestamps led to extreme outliers and inaccuracies. Furthermore, the process of manually entering the times and plate numbers costed hours of time on the QMS team's side and certainly impacted the flow of the testing lab where this could be avoided with a more sophisticated materials tracking system. A majority of our efforts as a team went towards attempting to gather meaningful data from the travelers, but the potential analysis and conclusions from the data were obstructed by human error on both ends. Our team was able to salvage some insightful information; however, if the ABCTL is expected to stay open for a significant amount of time in the future, it demands a more reliable and robust method of materials tracking.

Radio Frequency Identification (RFID)

An efficient and tried form of materials tracking which could remove the obstacles of the lot traveler is web-based tracking such as barcode scanning or Radio-Frequency Identification (RFID). After having experienced the cons of labor-intensive information collecting methods through our implementation of the lot travelers, methods were sought that put less burden on the already taxed staff, lead to an improvement in data collection, and improve the time efficiency of the lab.

RFID tag tracking involves two components: a tag to be placed on tracked item(s) and a reader to activate and access data from the chip. This system is primarily used for tracking inventory in warehouses but has versatile application and can be used for any materials tracking scenario based on the type of tags and readers used. RFID tags can be active, using battery power, or passive, allowing for a smaller size and using the reader for power (Center for Devices and Radiological Health, 2018). The passive tag "draw[s] power from a reader that sends out electromagnetic waves which activate the tag. The activated tag in turn transmits (''chirps'') back at a particular frequency, allowing the reader to capture unique data" (Pantanowitz & Balis, 2012). This variant of RFID tracking is more compact than the active tag due to the lack of a battery and therefore is generally cheaper and easier to attach to smaller assets. Active tags, however, "have their own power source in addition to a transmitter, which broadcasts a unique signal to a reader" (Pantanowitz & Balis, 2012). They are more robust and durable, an ideal option for heavy inventory or warehouse tracking. Both of these tag types stay attached to the sample itself, while readers can be attached to the cart or personnel and can operated by staff or, in some cases, automated. RFID systems can be incorporated with three types of reader-tag combinations: Passive Reader Active Tag (PRAT), Active Reader Passive Tag (ARPT), and Active Reader Active Tag (ARAT) (Dua, 2016). The PRAT system offers a wider physical range, but this benefit is not necessary in the close quarters between the ABCTL's samples and the operators. The ABCTL would benefit most from incorporating the ARPT method, as the less intrusive passive tag can be easily placed onto samples while the active reader can be operated by staff to selectively retrieve and input information from the tags at the beginnings and ends of steps.

Figure 2. RFID System Information Flow



The previous diagram depicts information flow through RFID in a laboratory environment (Wang, 2008). With this system, our current efforts to manually enter data for analysis can be removed altogether, as data is readily available to whoever has access to the tracking software. This would allow for quicker transmission of data in the final steps of the testing lab where previously, delays in receiving necessary files or granting access to these files led to delays in meaningful change in the systems. Tags can hold multiple pages of data as opposed to the limited data of barcodes and lot travelers, which implies the potential to utilize the materials tracking for more detailed descriptions of the samples (Center for Devices and Radiological Health, 2018). While the QMS team struggled to gather all relevant data for a single sample from multiple sources including emails, inventory sheets, and lot travelers, the RFID tracking system can centralize all data to a single source where it can be directly updated through corresponding software. For instance, the samples chain of custody, time stamps of steps, heat inactivation data, and perhaps the result of the COVID-19 test itself can be stored in the tag and easily accessed virtually.

RFID technology provides a more rigorous version of barcode scanning for materials tracking, and "unlike barcodes, RFID tags do not require line-of- sight to be read; they only need to be within the reader's radio range" (Wang, 2008). Furthermore, RFID scanning can read multiple specimens at a time, meaning access to more data with significantly less effort. This is particularly useful for ABCTL, where the samples are put into batches. GAO RFID Inc. reports that the time to read an RFID tag is roughly 100 milliseconds (RFID vs. Barcoding for Specimen Tracking, 2020). RFID scanning does not require the tag to be physically in front of the reader, only for it to be in the reader's vicinity. This saves a significant amount of time as opposed to the action of physically scanning a barcode or writing times down on paper. Currently, completing the lot traveler itself has become a non-value-added activity in the process. While the lab was prepared to sacrifice this time in order to gain insight into the system, the RFIDs would effectively eliminate this delay; the operation of the reader on the tag is a simple process without any effort necessary from the operator. Sacrificing time for data is not necessary with the use of RFID.

Software

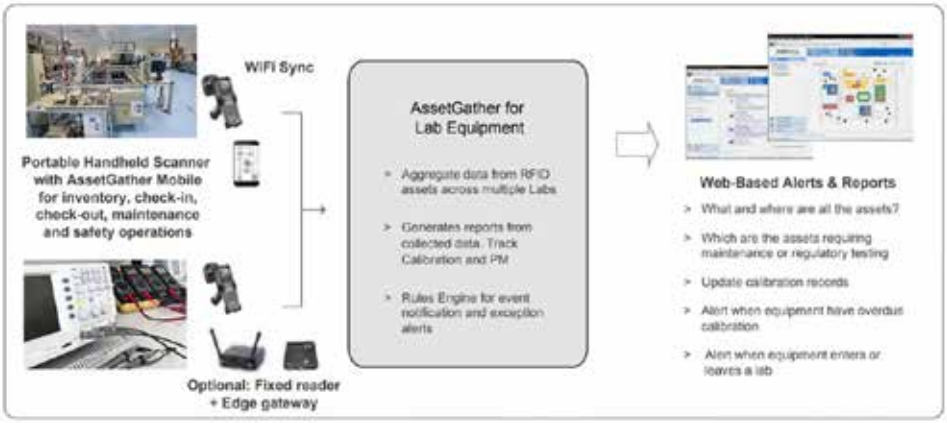
In order to implement and properly utilize the RFID tagging, the lab should consider investing in a software which will help oversee the scanning processes. An RFID intensive study identified three levels of complexity which should be maintained in an ideal tracking software (Pantanowitz & Balis, 2012). The first level is Auditing, by which the software should analyze workflow, store tracking history of specimens, and maintain records of actions with specimen. Another level, Constrained Workflow, requires that the software only allow access to data based on permission levels to prevent leaking of confidential information and sacrificing patient confidentiality. This can be accomplished with encryption levels and permissions based on accounts or devices. The final level is Drive Workflow, which ensures the software is constantly updating to reflect the current state of the laboratory and its needs. Any delays or data updates should be acted upon immediately. These standards allow for a software to serve the needs of a materials tracking system with efficiency and safety.

Perhaps the most suited application for this case is the GAO RFID Specimen Tracking System. GAO RFID Inc. hosts a collection of RFID systems as well as tags and readers and antenna solutions; the most applicable system of theirs to the ABCTL interests is the Specimen Tracking System. This system incorporates RFIDs and allows for tracking on small objects such as transport vials, containers, and biohazard bags (Specimen Tracking System: Sample Tracking System, 2020). The system involved applying the tag to the sample as soon as it enters the lab from its site, and at this point the identifying information for the sample should be entered. The system utilizes GPS paired with the RFID scanning to identify where the sample is at the time of scanning in the reader with a generated map of the laboratory. ABCTL can use this GPS feature to compare the physical location of the sample with the timing and details of the scans per step. As the sample passes through set checkpoints which will correspond with the lab testing steps, individuals with access to the software have the ability to trace the specimen in real time or to look at its recorded history. The samples can also be paired with temperature tracking,

a possible benefit for this lab with its cooling and heating steps (Specimen Tracking System: Sample Tracking System, 2020). This software offers multiple options for the range of the scanner, out of which ABCTL would benefit from the Medium Reading Distance (MRD) RFID, which has a 3-to-15-foot range and scans multiple specimens in a box or tray.

An alternative option to GAO is the AssetPulse's AssetGather software which utilized RFID tracking along with a mobile app so that staff can report immediately on maintenance needs and update data as necessary (AssetGather for Tracking Equipment in Labs, 2021). The web reports allow for secure remote access of data, which would greatly ease the accessibility of certain data to the Quality Management Systems team as well as any authorized personnel. While the software is primarily for lab equipment, AssetPulse provides a variety of sizes for the durable, heat-resistant tags, meaning this can be applied to the COVID-19 testing samples. The diagram below details the process of scanning data into the AssetGather software (Lab Equipment Tracking System: Laboratory RFID SYSTEM: AssetGather, 2021).

Figure 3. Asset Gather Software Information Flow



Conclusion

Close inspection of the two methods reveals that RFID serves is a more suitable tracking system for ABCTL's purposes than barcode scanning. Table 1 summarizes the ways in which RFID proves as the better option in the context of materials tracking theory. Regarding the LIMS software options which would facilitate the use of the RFID, the GAO RFID systems would best carry out this purpose for the ABCTL lab as opposed to others discussed. The implementation of this technology with DMAIC analysis is essential to keeping the ABCTL systems consistent and efficient.

	RFID	**Barcode**
Efficiency	Can scan and track multiple samples at once	Tracks one sample at a time; speed dependent on personnel efficiency
Price	Price varies based on type of hardware, but does not greatly exceed barcode prices	Cheaper hardware
Ease of Use	Simpler and quicker scanning based on location	Each sample must be physically scanned; simple but time consuming
ABTCL Applications	Better overall application; will allow for greater data pool	A good option for ABCTL tracking with less complexity

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Section I: Appendix

Figure 1. "Graph showing the steep decline in errors following the implementation of a bar code tracking solution in the anatomic pathology laboratory at Yale in New Haven, Connecticut."

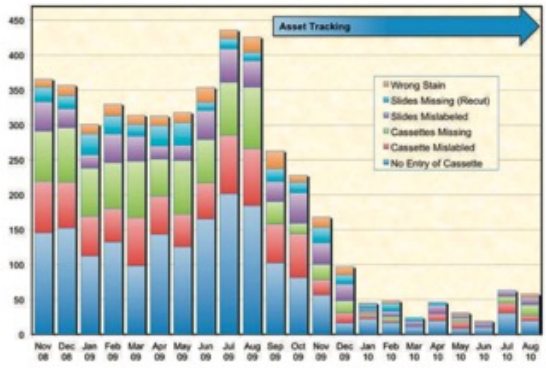

Figure 2. RFID System Information Flow

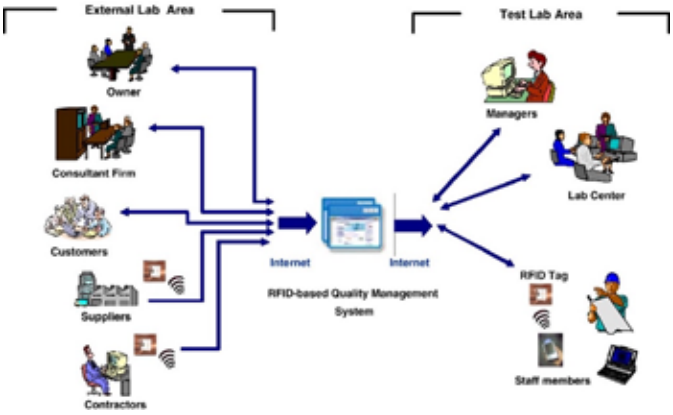

Figure 3. Asset Gather Software Information Flow

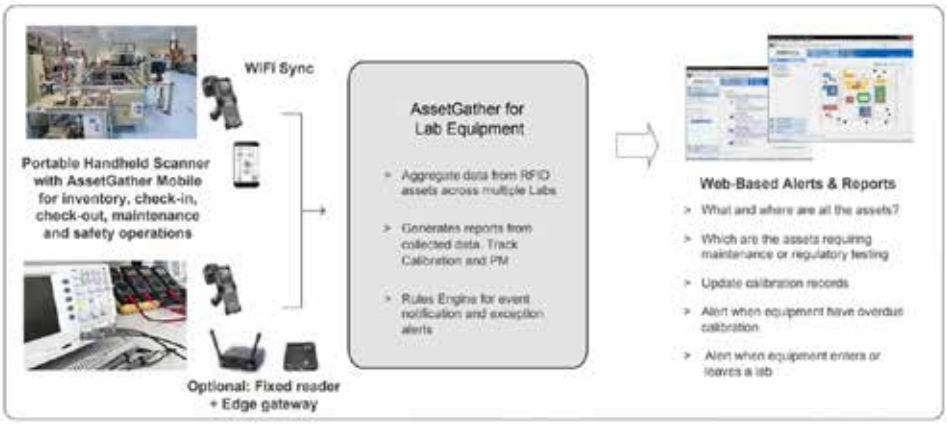

Table 1. Comparison of RFID and Barcode Implementation

	RFID	**Barcode**
Efficiency	Can scan and track multiple samples at once	Tracks one sample at a time; speed dependent on personnel efficiency
Price	Price varies based on type of hardware, but does not greatly exceed barcode prices	Cheaper hardware
Ease of Use	Simpler and quicker scanning based on location	Each sample must be physically scanned; simple but time consuming
ABTCL Applications	Better overall application; will allow for greater data pool	A good option for ABCTL tracking with less complexity

Section II: Employee Feedback Improvement Systems in a Clinical Testing Lab

Author: Ashley Bruner

Background and Focus

Employee feedback improvement systems are critical to maintaining a constructive and positive workplace for both employers and employees. These workplaces are not just limited to office buildings, but other work environments as well such as restaurants, factory plants, and even clinical testing labs. Employee feedback improvement systems are programs or systems that are designed to give both individual employees and employees as a group both positive, yet constructive criticism to implement and incorporate into their everyday routines in which their jobs are completed. The focus of employee improvement should be about changing the work environment rather than trying to change employees' attitudes towards their jobs, something that should occur naturally. However, in some instances, changing employees' attitudes can contribute in significant ways as well. The success criteria of employee feedback improvement systems include simply providing employees with feedback that they can implement into their daily routines to increase productivity and efficiency.

Environmental Management System

One way in which an employee feedback system can be implemented is through an environment management system (Govindarajulu & Daily, 2004). Companies have seen in recent years a need to focus on environmental management, and the research that has been done by Nalini Govindarajulu and Bonnie F. Daily on how employees have benefited from implementing an environmental management system can be applied to other industries as well as other management systems to produce the same results. One important takeaway from the research was that the implementation of an employee feedback system was critical for success; in this case, improving environmental performance was the goal.

As seen in Figure 1, an environment management system has four main elements: management commitment, employee empowerment, rewards, and feedback and review that "[stand] out as key elements in encouraging employees for enhanced environmental performance" (Govindarajulu & Daily, 2004). These elements are all important to creating environmental performance improvement with the main results being a greener company, but improved quality and improved customer satisfaction are also goals that can be applied elsewhere. In this research, it is critical to understand the basics of every factor to understand why one factor, feedback and review, is not only vital to improving environmental performance, but also how it can be vital to a successful workplace in general.

Four Factors Influencing Environmental Performance

Management Commitment

In order for any improvement to be made, management needs to begin by having a clear and measurable work standard. This may sound obvious, but employees first need to know and have some direction on what it is they are supposed to be doing and what standards they are supposed to be meeting. According to Govindarajulu and Daily (2004):

> Commitment from top management is like a framework for environmental improvement. Top management decides the environmental policies to establish, the level of training and communication required. Sans a solid framework, it is almost impossible to motivate employees to take effective steps for environmental improvement (p. 364).

Environmental improvement is made is by management first through specifically committing to adopting a formal environmental management system, because that system will allow for management to showcase specific standards the employees can work toward, as well as formally documenting the commitment to improvement (Govindarajulu & Daily, 2004). It is unrealistic for any change or improvement to occur if employees are not aware of the standards their company wants them to achieve. This idea is reiterated by Feeney (1982), as he states one of three things needed for good employee performance is that "employees must know specifically what is expected of them – this is accomplished by establishing measurable job standards and communicating them to employees". Feeney concludes that without a baseline measurement, management cannot judge whether or not the performance improvement program they implemented was successful (Feeney, 1982).

In lieu of management commitment, senior managers need to tackle the problems within organizational culture (Govindarajulu & Daily, 2004). "Organizational culture is composed of a set of assumptions and values that guide individuals' daily work behaviors" (Govindarajulu & Daily, 2004). It is extremely important to address organizational culture because companies that have strict, bureaucratic structures typically have problems enforcing changes that result in substantial environmental performance improvement. Improvement is more likely to occur when structures are less rigid, and where innovative ideas and risk-taking decisions are supported, not opposed, from management (Govindarajulu & Daily, 2004).

Employee Empowerment

Employee empowerment is the second key factor to consider when evaluating environmental performance. "Empowered employees are motivated and committed to participate and engage in good environmental practices" (Govindarajulu & Daily, 2004). Employees can be empowered by organizational change, which is another reason why addressing organizational culture is so significant. Companies should try to partake in participative managements with a flatter, more horizontal organizational structure in which employees will feel empowered and feel free to make suggestions and decisions, and thus perform their duties better (Govindarajulu & Daily, 2004).

Rewards

Govindarajulu and Daily (2004) state that "rewards can be a reinforcement to continuously motivate and increase commitment from workers" (p. 368). Feeney (1982) again reinforces this idea as the third of three things needed for good employee performance by stating that "good performance must have rewarding consequences that may be financial but may also take the form of praise, official recognition, or promotion" (p. 2). Feeney (1982) also states that rewards must be contingent upon measurable performance improvement, they must be administered after occurrence of the desired action, and they should be provided frequently (p. 5). Rewards, however, can be difficult to implement in the workplace. Govindarajulu and Daily (2004) discuss the following:

> Managers cannot follow a "one program fits all" approach to employee incentives. They must keep in mind the different motivating factors of the various employees in the organization and develop a reward system that satisfies everybody. In addition, it is up to managers to observe what factors motivate employees and customize compensation packages to suit each employee (p. 369)

It is because rewards must be designed with such delicate craftmanship, that introducing rewards can be challenging. However, regardless of what type of reward mangers deem is best to fit the results of the employees' actions, the rewards need to be benefits that fit the needs of the employees (Govindarajulu & Daily, 2004, p. 369). Mangers need to appropriately reward employees when both small, daily goals are completed, as well as when large, company-wide goals are met that may have taken many long weeks or months to reach.

Feedback and Review

The final factor that Govindarajulu and Daily (2004) deemed as an influencing factor to environmental performance improvement was feedback and review. "In order to achieve long-term success, most managerial programs need some form of review and feedback for continued improvement" (Govindarajulu & Daily, 2004). Again, Feeney's (2004) thoughts confirm this as he states the second thing out of three to occur for good performance from employees is that "employees must get some sort of feedback on performance" (p. 1). Both supervisors and employees need to know exactly how well their performance matches the standards, which can be done effectively through feedback. To do this, outputs must first be defined, and standards must be set for things like the number of items produced over a certain time period, the accuracy, and the timeliness of employees in a process. Next the baseline of the current level of production needs to be measured. After these steps are taken, it is time to give the employees feedback based on their performance (Feeney, 2004). According to Govindarajulu and Daily (2004), providing feedback improves employee relations, satisfaction and productivity and a positive feedback system needs to be based on trust between employees and supervisors.

The four factors discussed by Govindarajulu and Daily about improving a company's environmental performance, and reinforced by Feeney's comments about improving employee performance, can be applied to medical testing labs such as Arizona State University's Biodesign Clinical Testing Lab; specifically, implementing an employee feedback improvement system, to help produce better efficiencies and desired results.

Relation to the ABCTL

In response to the unprecedented COVID-19 pandemic, Arizona State University's Biodesign Clinical Testing Lab, also known as the ABCTL, works daily to produce COVID-19 test results in a timely and efficient manner. This medical testing lab could be improved through the implementation of an employee feedback improvement system, as well as the other factors that contribute to environmental performance improvement. As Feeney (1982) states, it is necessary to analyze the causes of performance deficiency in order to improve employee performance. These six questions must be asked to determine what is causing the deficiencies:

1. Are the standards for performance (performance expectations) complete and have they been communicated to the employees?
2. Are feedback systems provided to the worker, supervisor, and manager adequate?
3. Are the consequences of both good and bad performance to the worker, manager and supervisor strong enough to encourage high levels of performance?
4. Do the employees have the necessary tools for work performance?
5. Do the employees know how to utilize the available tools and do the job?
6. Are procedures easy to follow and cost effective?

Feeney's final three questions must all be answered about the basics of the jobs employees perform before any improvement can be seen in the ABCTL's COVID-19 testing process solely through a feedback and rewards system implementation.

The first question relates directly to Govindarajulu & Daily's first factor influencing environmental performance, management commitment (2004, p. 364) and can be applied to the management at the Arizona State University Biodesign Clinical Testing Lab. They must communicate clearly to its workers both the small and large goals that they want to see happen in the testing lab. However, the goal here is not to improve the environment, but rather improve efficiencies. Whether it is communicating that management wants to improve times and eliminate waste at one step of the process, for example specifically cutting down time at the heat inactivation stage, or communicating that management wants

to process 16,000 COVID-19 tests in one day with a 24-hour process lead time with exceptional quality, those goals need to be made known to every worker.

The second and third questions that need to be asked and answered to develop an effective employee feedback improvement system relate to Govindarajulu & Daily's third and fourth factors for environmental performance improvement (2004). Feeney (1982) states that "feedback is central to all human activity, and increasing the amount and quality of feedback can improve performance in almost any area". It is essential that all areas of the workplace receive daily feedback. In the ABCTL's case, to improve performance, each worker from each designated workstation must receive daily feedback on not only the completeness of their tasks, but also their timeliness and efficiencies. In order to do this data must be collected and analyzed that reports employee specific times. The feedback needs to be presented to employees individually, so they know specifically how they are doing in regard to meeting standards, not just how they are doing as part of a group (Feeney, 1982).

In terms of beneficial feedback, organizational culture is important because employees cannot be afraid to give their own feedback to management. When inquiring about computer systems in transnational firms, Giskeødegård (2012) focused on the possibility to give feedback on how those systems were working and found that:

> [An] employee therefore seemed to think that coming forward with problems with the tools they were given served nothing but to weaken his own position as he was met with responses referring to a lack of training, which ultimately brought the issue back on him (p. 713)

In this instance employees were reluctant to give their own feedback about tools they needed to use and in turn their company was not benefiting from problems that could have been solved. In effective employee feedback systems, the supervisors and the employees need to be comfortable giving feedback to each other. This means that in the ABCTL, the employees need to be able to communicate when they think their tools are ineffective or not working properly.

Conclusion and Future Forecast

The ABCTL could greatly benefit from introducing an employee feedback system that gives employees daily, individual feedback on their performances, and by creating an organizational culture that allows employees to give their own feedback when necessary to management. This will be an extremely important addition to the lab that will prepare the ABCTL managers and employees for any new tests or procedures it plans to implement in the future.

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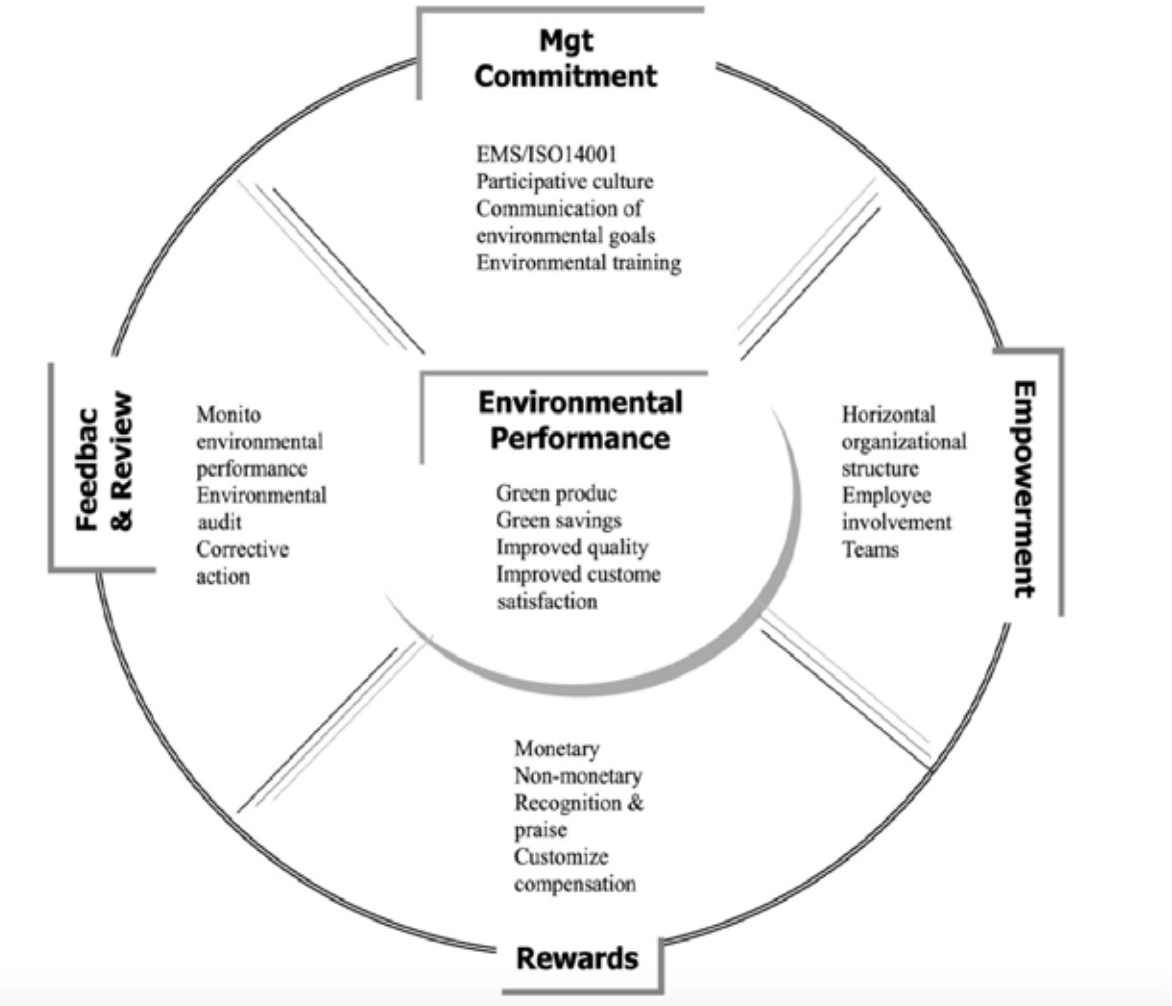
Section II: Appendix

Figure 1: Four Contributing Factors for Environmental Performance



(Govindarajulu & Daily, 2004, p. 365)

Section III: Clinical Laboratory Supply Chain Optimization

Author: William Hymer

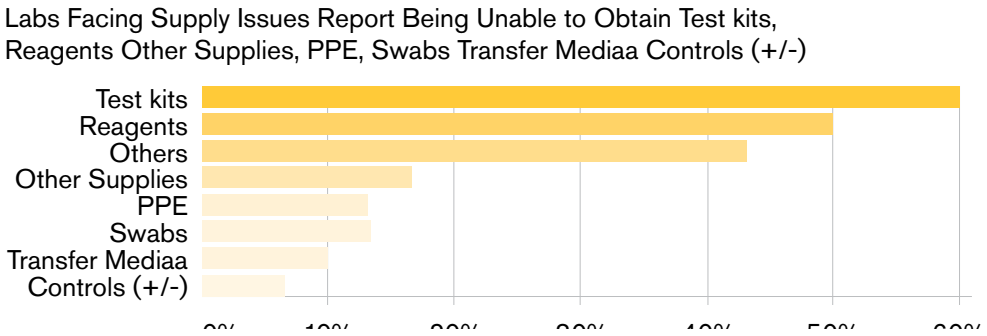
Background

Clinical testing laboratories have been an integral part of the global response to the COVID-19 pandemic, identifying those infected and mitigating further spread of the virus. This Section highlights methods of optimizing clinical laboratory supply chains, specifically in the case of the ABCTL. The COVID-19 pandemic has had a tremendous impact on demand for supplies and has created unique circumstances for clinical laboratories to operate in. To account for the current environment, this paper will detail supply chain optimization methods that are applicable in uncertain supply environments, as well as established optimization methods that are best applied when supply is stable and predictable. Methods include implementing Laboratory Information Management Systems (LIMS), improvising to maintain an effective supply chain, and utilizing various inventory management techniques. The ABCTL may find value in applying one or more of these methods to their COVID-19 testing supply chain in the future.

The supply chain of a clinical testing laboratory—particularly during a global pandemic—differs greatly from typical supply chains due to the uncertain nature of the surrounding environment. Medical supply chains were massively disrupted in Spring 2020, with a global shortage of personal protective equipment and reagents, among other laboratory essentials. A globalized supply chain was put on hold due to a mixture of travel restrictions, factory closures, and labor shortages. Manufacturers in China, for example, account for an estimated 40% of all active pharmaceutical ingredients used worldwide. (Xu, et al., 2020) When COVID-19 began spreading rapidly around the world, the lockdowns of large exporters like China caused global shortages in necessary medical supplies and personal protective equipment.

Even a year later, many clinical laboratories are still struggling to acquire or keep up with the demand for test kits, swabs, or reagents necessary to conduct testing. A study conducted by the American Association for Clinical Chemistry (ACAA) in January 2021 showed that 58% of laboatories were unable to obtain supplies necessary to run COVID-19 tests. (ACAA, 2021) Among the supplies in demand are test kits, reagents, and other supplies such as pipette tips. To combat these shortages, many laboratories are relying on donations, reusing supplies, and other creative options such as 3D-printing. Seeing as that COVID-19 testing is not going away anytime soon, clinical laboratories will have to continue improvising until the supply chain catches up to the volatile demand of testing.

Fig 1. COVID-19 Testing Challenges Survey (ACAA, 2021)

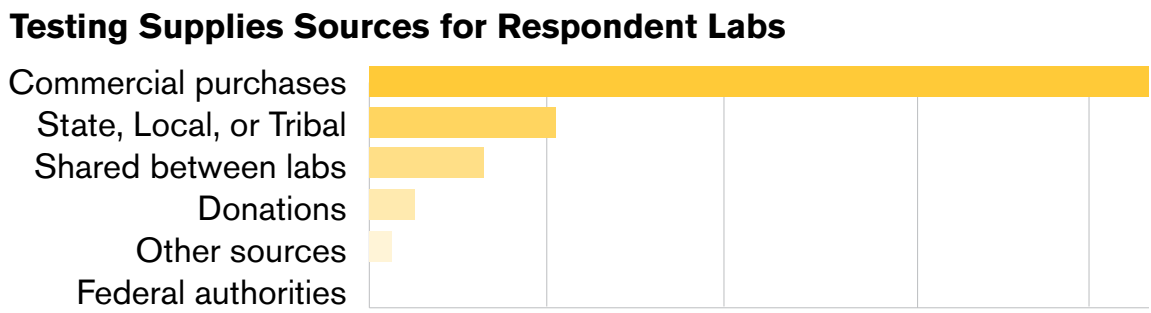


Analytical Framework and Findings

Efficiency is defined as an internal standard of performance and effectiveness as an external standard of fit to various demands. (Pfeffer and Salancik, 1978) Supply chain optimization—at its core—is the practice of operating a supply chain at peak efficiency. Unfortunately, this oftentimes comes at the cost of effectiveness. And in the context of clinical laboratory supply chains, effectiveness is an indisputable priority. The quality of the testing being conducted has a direct impact on the client, and there may be significant ramifications if test results are late or inaccurate. Whereas some organizations can afford to sacrifice measures of effectiveness such as customer satisfaction in favor of reducing costs, decisions made by clinical laboratories to improve efficiency must not reduce the value they are providing to the client.

A critical component of retaining supply chain efficiency in times of uncertainty is simple improvisation. In the context of supply chain management, researchers from Oakland University state that "as a complementary activity to planning, improvisation has been proposed as an effective way to deal with emergent problems and opportunities that can't be predicted beforehand." (Deng, et al., 2003) The massive influx in demand for plastics, reagents, and test kits during the COVID-19 has forced clinical laboratory supply chains across the globe to improvise in order to provide testing to their communities.

Fig 2. COVID-19 Testing Challenges Survey (ACAA, 2021)



As suppliers run out of stock, many laboratories have turned to any retailer they can find, including Amazon. Donations, state/local stockpiles, and shared supplies between laboratories have also been relied on to keep critical supplies in stock this year. (ACAA, 2021) Improvisation will continue to be a key factor in keeping clinical laboratories in stock until global supply chains finally catch up to the unprecedented demand for the laboratory supplies critical to COVID-19 testing.

While effectiveness is critical, the improvement of effectiveness and efficiency is not mutually exclusive. One method of boosting both the efficiency and effectiveness of a clinical laboratory is to implement a Laboratory Information Management System (LIMS). Laboratory Information Management Systems are multi-functional, allowing for efficient sample tracking, inventory management, and reporting. Reducing the need for manual data entry is one of the largest benefits of LIMS, reducing human error and facilitating quick tracking of inventory. A study conducted at Brigham and Women's Hospital demonstrated a 92% decrease in preanalytic errors per month following the implementation of a LIMS. (Petrides, et al., 2017) This is alongside significant decreases in turnaround time and stat orders.

Another study conducted by a healthcare facility in Saudi Arabia showed that after implementation of a LIMS, "81.6% [of staff] agreed that the LIMS improves the workflow and management of the laboratory." In addition, "83.9% accepted that the accuracy and speed of laboratory test is enhanced after LIMS implementation." (Aldosari, et al., 2017) While every lab certainly has different needs, budgets, and goals, this data illustrates that the implementation of a LIMS can quickly show positive results.

Typically applied to business contexts, the ABC Inventory Management Support System can be useful in reducing costs associated with the inventories of clinical laboratories as well. This system separates inventory items into three inventory classifications, placing emphasis on “A” items, which are the highest annual dollar demand items. The Pareto Principle is usually applied, which assumes that 20% of items in inventory establish 80% of the annual dollar value of demand. (Beheshti, et al., 2012) After classifying the inventory, an economic order quantity (EOQ) model is developed using holding costs, order costs, and total annual costs to find an optimal order quantity. While this model gives an optimal output assuming no parameters, a “what-if” analysis can be performed to evaluate variation and ensure that there will be sufficient safety stock for important testing supplies.

Fig 3. ABC Classification (Beheshti, et al., 2012)

TABLE 1 ABC Classification

		Percent of Total in Category	
Item Category	Level of Management	Line Items	Annual Dollar Amount
A	High	15-20	70-80
B	Medium	25-30	15-25
C	Low	50-60	5-10

This is the primary advantage of the ABC Inventory Management System: it is a spreadsheet-based decision support system with enough flexibility for managers to find a practical balance between the optimal order quantity and the safest order quantity. Other inventory management systems like the “just-in-time” system are impractical for use in a clinical laboratory, as they emphasize minimizing inventory on hand at any given time. While efficient, models like this discourage the safety stock necessary for a clinical laboratory to test with confidence in their capacity.

Fig 4. Economic Order Quantity (Beheshti, et al., 2012)

Relation to the ABCTL

In response to the COVID-19 pandemic, Arizona State University’s Biodesign Institute transformed a laboratory from a purely academic facility into a certified clinical testing laboratory. The spring and early summer were largely defined by improvisation measures, searching every avenue possible for the necessary supplies and personal protective equipment to operate the lab. One year later, the laboratory has conducted over 750,000 tests for the state of Arizona. (ASU, 2021) There are still challenges in the supply chain due to shortages, however. Much like other clinical laboratories, the ABCTL has struggled to attain critical supplies such as personal protective equipment and sample tubes. This was remedied

through a quick and coordinated response, sourcing materials from donors and various retailers. Volunteers helped manually label sample tubes for months in order to meet the increasing testing demands.

Fast-forward to present day, the ABCTL has made major strides in terms of both process improvement and supply chain stability. Robotics have been a key factor in facilitating testing, as well as liaisons in the scientific community that have allowed access to much needed supplies. As the testing process continues to evolve, the main concern of supply chain managers in the ABCTL is the supply of plastic pipette tips, used by the KingFisher Purification System to purify saliva samples. While the current supply is enough for the laboratory to remain effective, there is not enough safety stock to be completely comfortable yet.

To further optimize the ABCTL supply chain at the moment, the implementation of a Laboratory Information Management System could be exceptionally beneficial. A system like this would make it easy to track inventory, create reports, and eventually run analytics to determine usage rates for reorder points. Using a system with a multi-user license could provide broader visibility as well, allowing for more open communication between materials management and the laboratory itself. While the initial cost incurred is high, a LIMS system could prove to be a good long-term investment if the lab is aiming to operate more efficiently.

Once the supply of all materials—including pipette tips—has stabilized, usage of the ABC Inventory Management System should be investigated to optimize the cost of inventory ordering. Research conducted by Hooshang M. Beheshti in ABC Inventory Management Support System with a Clinical Laboratory Application shows promising results with a flexible, cheap to implement system. The most attractive feature of this system is the ability to perform "what-if" analyses to adjust for the unique needs of the lab, such as levels of safety stock desired.

Conclusion and Future Forecast

Overall, it appears that the ABCTL has done an exceptional job developing their supply chain alongside innovations in the testing process itself. While there is no way to predict the demand for COVID-19 testing as vaccination numbers continue to rise, it is imperative to continue refining the laboratory's supply chain. Optimizing performance throughout the ABCTL provides the flexibility to effectively pivot to other types of testing with ease if needed. Placing effectiveness over efficiency, continuing to improvise, and exploring the implementation of new systems will help the laboratory meet the demands of a wide variety of clinical testing as time goes on.

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Section III: Appendix

Fig 1. COVID-19 Testing Challenges Survey (ACAA, 2021)

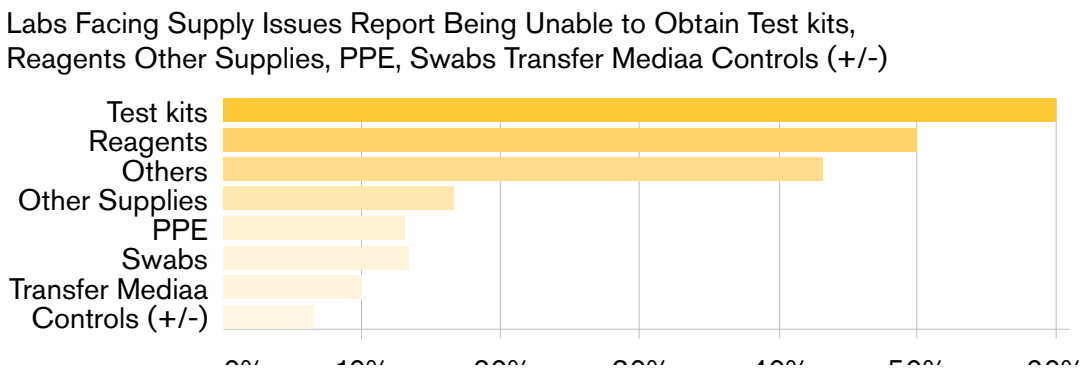

Fig 2. COVID-19 Testing Challenges Survey (ACAA, 2021)

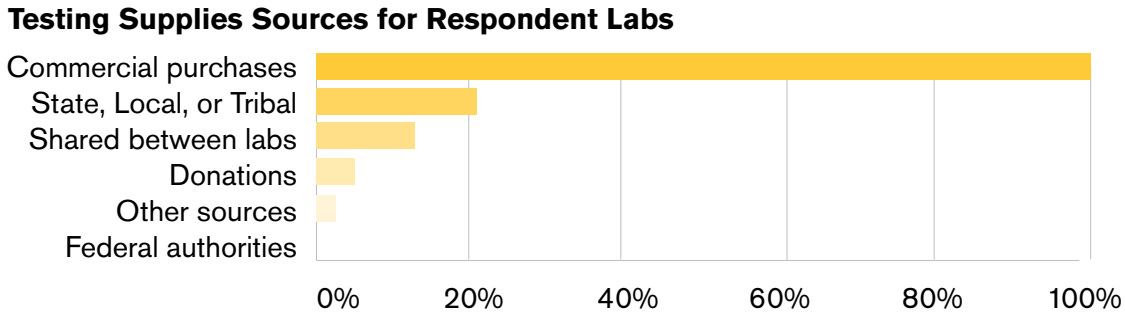

Fig 3. ABC Classification (Beheshti, et al., 2012)

TABLE 1 ABC Classification

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Fig 4. Economic Order Quantity (Beheshti, et al., 2012)

Section IV: Process Improvement: An Application of Medical Testing Laboratory Improvement Techniques on the ABCTL Testing Process

Author: Abby Krell

Background

The ABCTL testing lab process was developed to operate as the primary testing site for all ASU staff, students, and specified external individuals. Tests are collected at various collection sites, including a walk-in site at the Sun Devil Fitness Complex and various drive-up sites on campus; analysis is conducted on ASU campus and results are distributed virtually to all patients via the Student Health Services patient portal and the Employee Wellness Patient Portal. this Section describes how the implementations of various process improvement techniques in the ABCTL helped the lab achieve its operational goals.

Analytical Framework and Findings

Identifying Bottlenecks

It is proven highly effective to identify process bottlenecks via a process map, where further analysis can be done on bottlenecks through pareto chart analysis. This technique was previously demonstrated in the effort to reduce immunosuppressant drug turnaround time (Barakauskas et al., 2016). In this study, the process map exposed several steps with potential to delay testing result reporting, including the analytical run schedule, late sample collections, analytical or instrument delays, and difficulty drawing from a patient (p. 186). Through pareto analysis, the team determined the bottlenecks with the highest leverage and implemented improvements accordingly.

Additionally, it is beneficial to consider, from past research, the process steps in medical testing in which the majority of errors occur. Though errors can occur at any point in a medical testing process, Hallock et al. (2006) determined that, from emerging research on diagnostic testing processes, the majority of errors occur in the pre-analytic phase. This consideration may be helpful in the effort to identify bottlenecks, where it is more likely they will be observed upstream. Lippi et al. (2006) further emphasize this concept, stating the significance of implementing proactive measures further upstream upon arrival of laboratory specimens. In the case of the ABCTL laboratory, pre-analytic process steps include sample transportation, cooling, heat inactivation, plate transfer, accessioning, and sample aliquot. Even with this consideration, however, Hallock et al. (2006) still observed many types of testing errors throughout the entire diagnostic testing process in their study – test orders, sample collection and delivery, processing, and result dissemination errors were observed and evaluated for potential improvement initiatives. Table 1A in the appendix displays all observed variances in this study.

Patient Misidentification

Another significant consideration when identifying bottlenecks is the detriment of patient misidentification and collection of unsuitable samples for testing – these were observed at the most prominent sources of error in a study on phlebotomy testing processes (Lippi et al., 2006). These errors will reduce total patient throughput, which is often a priority in medical testing process improvement. To combat the possibility of misidentification errors, and therefore reduce a potential detriment to patient safety, barcode identifiers should be placed on samples or specimens in the pre-analytic phase – verifying a sample barcode with the patient during sample collection is the most effective way to ensure proper identification throughout the entire sample analytic phase (Lippi et al., 2006).

Priority Alignment

Fernald et al. (2015) developed a general process improvement toolkit for medical laboratory testing with the understanding that testing errors may occur at any point in these processes. A significant portion of the toolkit provides guidance on aligning laboratory priorities with various possible improvement methods. This is an integral step in determining which techniques have the most leverage for a specific process and should therefore be implemented. Priority alignment should be used in coordination with pareto analysis of all observed bottlenecks to determine improvement initiatives most beneficial to the laboratory.

Pareto Analysis

The pareto principle posits that 80% of benefits can be obtained from 20% of the work. Pareto analysis was developed and often used to determine the bottlenecks of a process that have the most leverage on reaching specific laboratory goals. Barakauskas et al. (2016) conducted a pareto analysis to determine the "vital few" bottlenecks with the most potential for improvement in their process. A pareto chart is shown in Figure 2A in the Appendix of this section. The analytical run schedule and samples collected after 8:45 PM were determined to be the most critical bottlenecks to focus on eliminating for process optimization.

Improvement Initiatives

When implementing any improvement initiative, it is important to focus on the system itself rather than placing blame on individuals who perform the process activities. Previous studies determined that the majority of medical issues resulted from systematic problems rather than from individual provider performance (Lippi et al., 2016). Additionally, it is a common understanding – from a system engineering perspective – that analysis teams should avoid conducting a "root blame analysis" in an effort to determine bottlenecks and corresponding improvement initiatives.

Turnaround Time

Prior research has demonstrated that a transition to a point-of-care (POC) testing system has reduced overall testing turnaround time (Boelstler et al., 2015), though this is often unfeasible for a medical testing laboratory due to financial constraints. In this case, other methods must be implemented to reduce turnaround time. In a study on emergency department troponin testing turnaround time, "multidisciplinary collaboration and teamwork between the ED and laboratory" were integral factors to improvement success (p. 310). Additionally, the process was reconstructed to batch various activities into single process steps and reordering process steps to achieve a higher level of efficiency. This is a common approach to reducing turnaround time (testing process cycle time).

Human Factor Methods

While medical testing process improvements are often implemented with traditional quality improvement techniques, Hallock et al. (2006) suggested that other methodologies, including variance analysis and macro-ergonomic analysis, serve as alternatives that may be more beneficial. Human factor methods are significantly related to open system improvement – open systems exist within an external environment from which they obtain inputs and deliver outputs. It is important to identify and consider the boundaries in an open system so as to obtain all relevant environmental factors and inputs (Hallock et al., 2006). Both open systems and macro-ergonomic theories focus on the living organisms that function within a system. Though human factor methods focus on personnel, it is still important to avoid placing blame on clinical staff for poor system performance.

Testing Accuracy

Testing accuracy improvements are often implicitly realized as a result of turnaround time improvements – when turnaround time is significantly reduced and throughput objectives become feasible, the pressure

to perform is alleviated and clinical staff may produce more accurate results. However, there are improvement initiatives that can be implemented to directly increase testing accuracy. Medical testing errors can significantly compromise patient safety, especially with false negative results or failure to notify a patient of abnormal results (Hallock et al., 2006).

Process Monitoring

Teams should implement some form of process control and monitoring to ensure the preservation of process improvements after implementation. This should be executed following the analysis of quantifiable improvement metrics – without these, there is no apparent value proposition for teams to continue investing in process improvement initiatives (Fernald et al., 2015). When implementing a control process, analysis teams should remain aware of the Hawthorne effect – "behavior modification that occurs because the process is being monitored" (Barakauskas et al., 2016, p. 188). This is a significant consideration regarding the true value of the improvement initiative and its potential to be maintained in the absence of active process monitoring. Process control charts should be utilized to monitor system performance – in the ABCTL, process control charts for turnaround time and sample throughput should be implemented following process improvement efforts.

ABCTL Applications

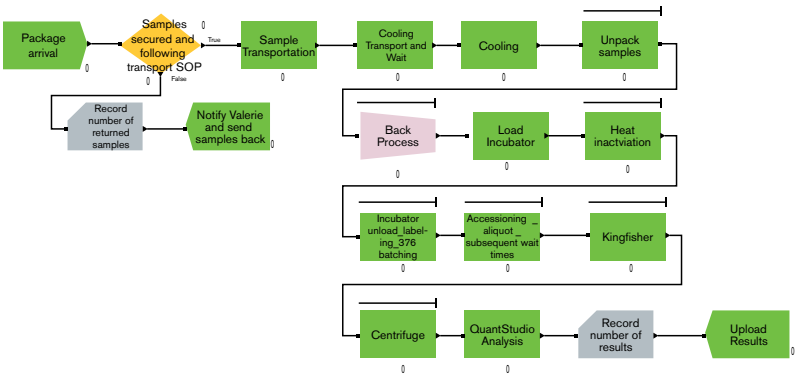
Laboratory Goals

The ABCTL laboratory has a current focus of reducing testing turnaround time to twenty-four hours and achieving a daily 16,000 sample throughput. To initiate the improvement effort, bottlenecks should be determined through process mapping and pareto analysis – only those that align with the laboratory priorities should move to implementation. Additionally, special consideration should be placed on proactive measures in the upstream pre-analysis portion of the process. Though process-specific bottlenecks may be identified, multidisciplinary collaboration and effective communication will remain initiatives with high potential to improve the process. In addition to process-specific bottlenecks, the boundaries of the process should be identified and considered to obtain all relevant environmental factors and inputs that influence system performance. Finally, when monitoring process improvement initiatives following implementation, the analysis team should remain consistently aware of the Hawthorne effect and take this into account when evaluating improvement initiate effectiveness.

Stochastic Simulation

The figure below displays the Arena model implementation of the process flow in the laboratory – this was developed by the team. This differs from an ordinary process flow in that all individual process steps are configured according to their respective underlying probability distributions; the implementation of probability distributions adds a stochastic nature to the model. Simulation is an effective tool for understanding and predicting system behavior; no model is perfect, but a model can provide further visibility and a chance to experiment with certain inputs and experimental scenarios.

Figure 1: Stochastic Simulation Arena Model Implementation



Data analysis is shown in Figures 2A-10A and Tables 2A-10A in the appendix. Each figure shows all fitted distributions; each table shows the data of the distribution of best fit for each individual process step. The team configured each individual process step in the Arena model according to the specified underlying probability distribution – as mentioned below in future work, this is a significant opportunity for further visibility and understanding of system behavior and further experimentation. The inputs of the model can be manipulated in ways that increase system understanding and potential improvement techniques.

Conclusion

Project Findings in the Laboratory

The team determined the underlying distributions for every individual process step, including sample arrival times – sample packages arrive according to an underlying bimodal distribution, indicating two separate arrival intervals which may cause inefficiencies. The initial process revealed high levels of package arrival in the morning and a separate interval of high arrival levels in the afternoon. It is critical to obtain a uniform underlying distribution so as to guarantee consistent, predictable package arrivals throughout the daily working hours. Additionally, the initial shifts in the laboratory process map significantly hindered potential for implementing improvements, so the initial suggestions by the team should continually be considered during future laboratory work as the process reaches its current steady-state behavior.

Future Work

The team completed the model implementation in Arena software in preparation for conducting a "what-if" analysis. This is a significant opportunity for future work, as simulation can provide additional visibility of laboratory behavior, and experimenting with various scenarios can help the team understand what inputs have significant leverage on the efficiency of the lab. Other simulation software packages may increase ease of the simulation process, including AnyLogic and MATLAB. Experimental scenarios should manipulate the underlying arrival time distributions, batching within the process, and utilizing advanced machinery (Kingfisher, QuantStudio, the ASU Health Portal system, etc.). Additionally, teams should consider the macro ergonomic framework for understanding open and social-technical systems, in addition to the concepts of open systems theory.

Section IV: References

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Section IV: Appendix

Table 1A: Observed Variances in a Diagnostic Testing Process

Step	Variances
Test order	Wrong patient identified Special requirements not listed Patient improperly prepared Poor test ordering practices No testing guidelines Test usage not monitored
Sample collection	Wrong collection tube Mislabeled specimen Wrong time scheduled Wrong patient drawn
Sample delivery	Specimen delivery delayed Unsuitable conditions for delivery (specimen exposed to bright sunlight, excessive temperature changes) Specimen not iced properly for transport (blood gases)
Processing	Specimen rejection by Pathology Department (PD) Request form rejection by PD Excessive time delay Transcription error Specimen out of sequence Specimen missed
Result dissemination	Unnecessary inquiries made when results not available Dispatch of unnecessary duplicated reports Delay in obtaining results

Figure 1A: Pareto Analysis for an ISP Diagnostic Testing Process

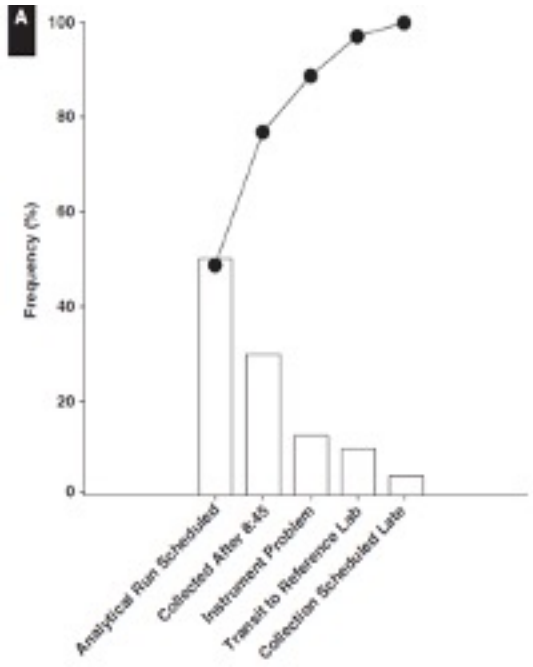

Figure 2A: Underlying Distribution for Sample Transportation

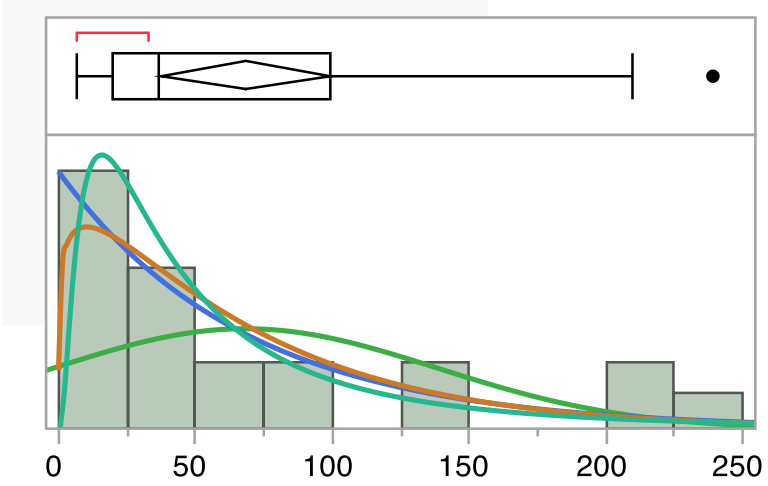

Table 2A: Fitted Lognormal Distribution for Sample Transportation

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	μ	3.7424558	0.2113822	3.3093934	4.1755182
Shape	σ	0.9914703	0.1494698	0.7576076	1.375903

Figure 3A: Underlying Distribution for Cooling, Transport, and Wait

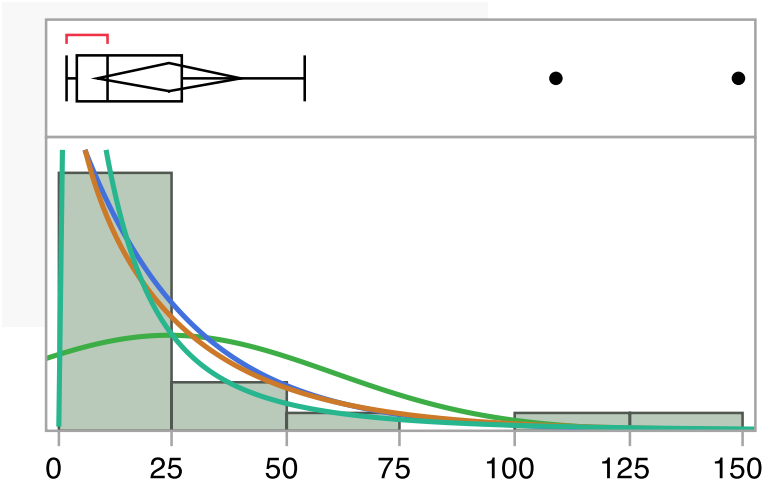

Table 3A: Fitted Lognormal Distribution for Cooling, Transport, and Wait

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	μ	2.4605576	0.244062	1.9615185	2.9595967
Shape	σ	1.1704803	0.1725779	0.8992329	1.6114362

Figure 4A: Underlying Distribution for Cooling

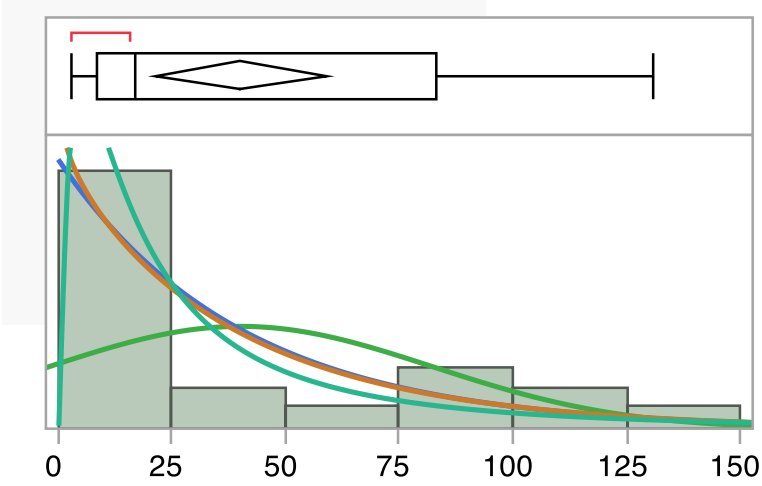

Table 4A: Fitted Exponential Distribution for Cooling

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	σ	40.136164	8.5571015	27.156106	62.890349

Figure 5A: Underlying Distribution for Unpacking Samples

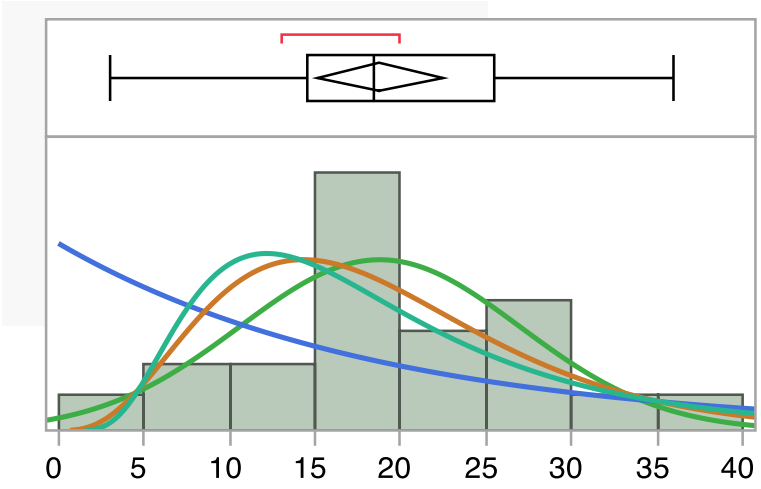

Table 5A: Fitted Normal Distribution for Unpacking Samples

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Location	μ	18.772727	1.7493744	15.344016	22.201438
Dispersion	σ	8.2052934	0.4473579	7.37371	8.9538657

Figure 6A: Underlying Distribution for Load Incubator

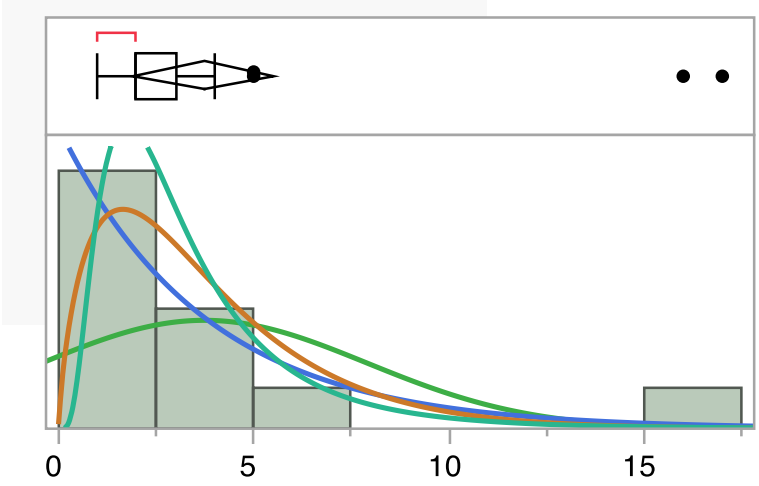

Table 6A: Fitted Lognormal Distribution for Load Incubator

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	μ	1.0142892	0.1407343	0.7265676	1.3020109
Shape	σ	0.6748419	0.0995	0.5184538	0.9290756

Figure 7A: Underlying Distribution for Heat Inactivation

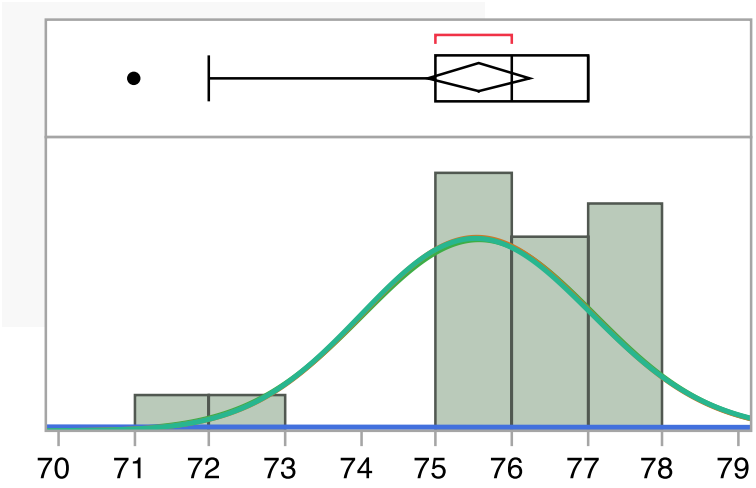

Table 7A: Fitted Normal Distribution for Heat Inactivation

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Location	μ	75.565217	0.3194987	74.939012	76.191423
Dispersion	σ	1.5322618	0.1887697	1.2035598	1.6657157

Figure 8A: Underlying Distribution for Incubator Unloading, Labeling, and Batching

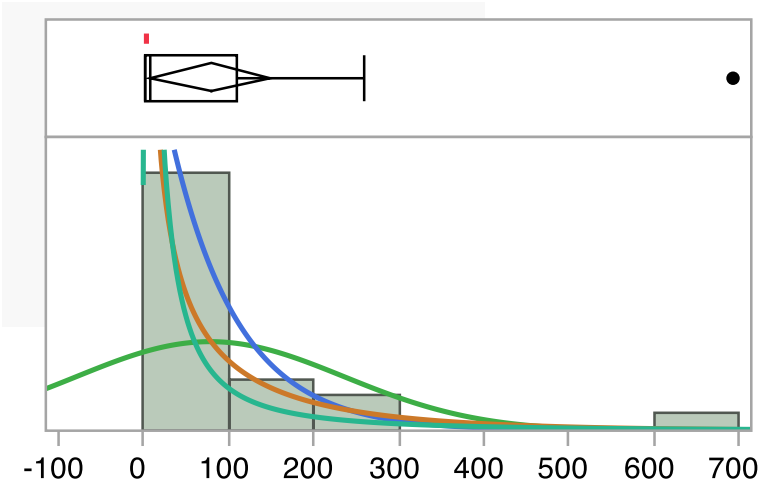

Table 8A: Fitted Lognormal Distribution for Incubator Unloading, Labeling, and Batching

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	μ	2.6170415	0.416944	1.7630458	3.4710372
Shape	σ	1.9551718	0.2947532	1.4939962	2.7132701

Figure 9A: Underlying Distribution for Transport to Biodesign B and Accessioning Wait

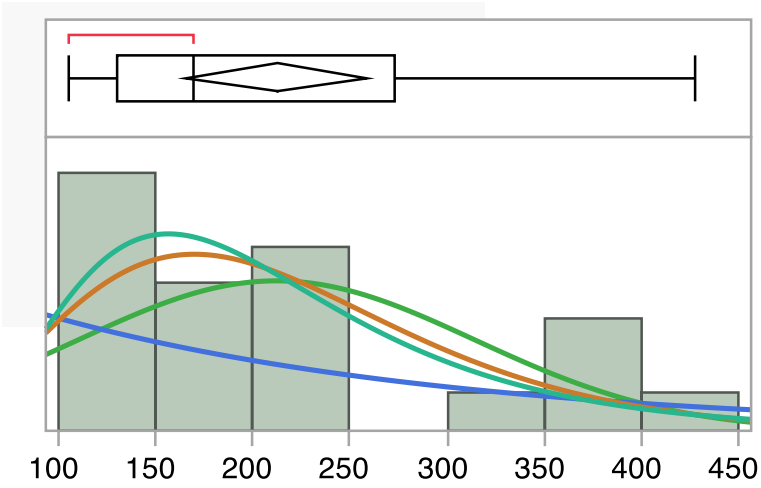

Table 9A: Fitted Lognormal Distribution for Transport to Biodesign B and Accessioning Wait

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	μ	5.2550143	0.0977635	5.0542953	5.4557333
Shape	σ	0.4480086	0.0091292	0.3403706	0.6270699

Figure 10A: Underlying Distribution for Accessioning, Aliquot, and Wait Times

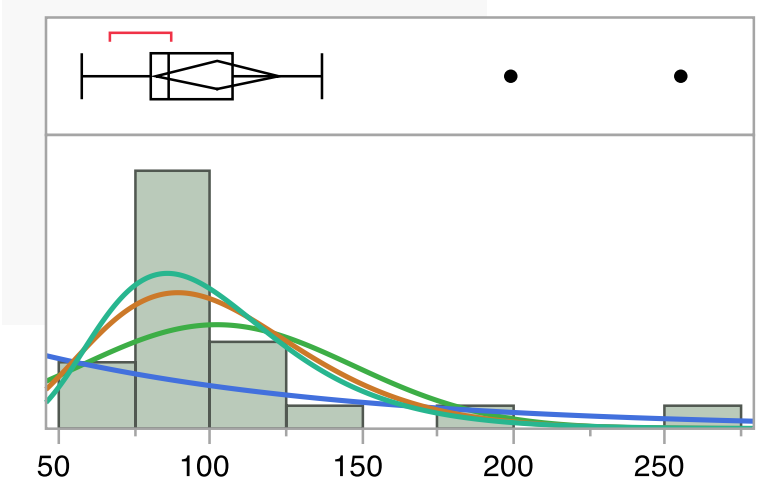

Table 10A: Fitted Lognormal Distribution for Accessioning, Aliquot, and Wait Times

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	μ	4.5628523	0.0706505	4.4181093	4.7075953
Shape	σ	0.3313803	0.0499575	0.2532161	0.4598698

Section V: Lean Six Sigma in a Clinical Lab Space

Author: Gabriel Lewis

Introduction

"Laboratory data must be available on time, every time to have maximum clinical value.1" The ASU Biodesign Clinical Testing laboratory (ABCTL) provides "saliva testing to identify the presence of COVID-19" ("Overview." Accessed January 13, 2021. https://Biodesign.asu.edu/research/clinical-testing.). These tests protect our communities by allowing swift responses to the identification of positive cases, which is incredibly important. To this end, the ABCTL sought to reduce turnaround time (TAT) to be within 24 hours from reaching the lab until results are sent out. Lean Six Sigma (LSS) can provide effective means to reduce TAT.

Measuring a Process

A Serbian health care institution instituted a LSS project they called "Improvement of a sample analysis process in a microbiological laboratory3". The first step taken was to develop "an As-Is process flowchart3". An As-Is flowchart displays the steps in a process as they are currently, not as the steps would be after the project. This allows the project team to better understand the process they are working to improve. A different study described the benefits of process mapping as such: "It is critical to have a good understanding of the entire process of sample collection, transportation to laboratory, sample preparation, analytical procedures, post-analytical sample handling, and validation of results, to devise appropriate solutions for the laboratory.2" The Serbian laboratory labeled the steps in the flowchart into three categories: "activities which produce an added value and which are optimally realized…; activities which could be improved… by using an automated system…; and activities which do not add value3". This provided guidelines for project improvements, by highlighting areas that need significant improvement and highlighting the waste.

After obtaining relevant training, the first steps that our team took for ABCTL QMS was to map out the process and obtain As-Is data. Figure 1 in the Appendix shows a Value Stream Map (VSM) developed by our team. A VSM is a specialized process map, focusing on identifying the time spent during the process during which value is actually added, and it is used to determine which steps may limit the capacity of the entire system. We obtained the data used in the VSM through lot travelers, pieces of paper that would follow samples through the lab. For each step, the operator would write down the time the process started and the time it ended. This data describes the duration of each process step and how much time is spent between steps. We are treating process duration as value added and the time between processes as non-value added. Please see figures 2 and 3 in the appendix for the templates of the lot travelers we used to collect the data.

Our process mapping led to critical insights. Of the total time that a sample spends in the laboratory, which we have calculated to be 9.4 hours on average, only 56% of it actually adds value. We also found that the step taking up the most time on average is heat inactivation, at 3 hours on average, which is when samples are put in an oven to ensure safety prior to any other processing. Since we produced our VSM, there have been changes and improvements made in the laboratory. More recently, we have obtained a more detailed process map from the Clinical Quality and Compliance Specialist at ABCTL, shown in figure 4 in the Appendix of this Section.

Our group used this new process map to better reflect current conditions in the laboratory. We also obtained more data, from other sources, which are discussed by other members of this group. Using this more recent data, we have also updated our VSM to more clearly display the current conditions in the laboratory. This new VSM, shown as figure 21 in the appendix, displays the states of the lab in February

and November. The data used in this VSM has shown that the time a sample spent in the lab may have been closer to 10 or 11 hours, rather than the 9 described by the earlier data. This discrepancy may have been caused by issues with the data itself or caused by light or heavy periods in the lab during data collection.

Analyzing the System

Another important step is to determine the metrics which are to be used to evaluate progress. One example of a metric is the mean time that the sample spends in the laboratory, which was discussed above; another example is the Process Value Efficiency (PVE), the percentage of time spent that actually adds value, also mentioned above. There are countless metrics that could be used to evaluate the performance of a system. It is, therefore, paramount to determine which metric best fits the intent of the project. A study focused on reducing the length of stay in the emergency department at the Oklahoma University Medical Center by means of LSS in their testing laboratory makes use of an incredibly valuable metric. They note that "while there is a correlation between [emergency department (ED)] length of stay and turnaround time means, a much stronger relationship was observed between ED length of stay and [turnaround time outlier percentage (TAT-OP)].1" That is to say, the average time it took to analyze a sample was not as beneficial to consider compared with the percentage of samples that took too long to be analyzed. This makes sense, since any sample that takes too long could lead to impatience from both the patients and the physicians, potentially leading to "stat test requests1", which would then throw off the analysis of other samples, leading to more outliers. The laboratory in this study had experienced this destructive loop, to the extent that nearly half of their tests had stat requests to avoid delays prior to the implementation of LSS.

Optimally, the ABCTL was seeking to reduce TAT to be within 24 hours. The two metrics that stand out the most to work towards this goal are the mean TAT and TAT-OP. Although a 24-hour TAT is the goal of the laboratory, the current standard for the laboratory is a 48-hour TAT. Thus the 24-hour and 48-hour TAT-OPs are considered. Using data from the lab, for the months of June through December, we could calculate the TAT as the time the sample was initially collected subtracted from the time the results were released to the patient. Figures 5-20 in the appendix are histograms representing this data. The TATs for each month have been calculated, as well as the TATs for the total. The histograms show how many samples during each period were returned in certain lengths of time. Due to some samples being extreme outliers, in part due to erroneous data, such as the result returned 8 hours prior to the sample being collected, each histogram is provided with both raw data and with fixed data, such that any TAT less than 0 hours is set equal to 0 and, since we are looking at TAT-OP, any TAT greater than 48 hours is set equal to 48. These histograms make the incredibly large TAT-OP visible, as well as provide some insight into the statistical properties of the data, such as the mean TAT.

For all of the data combined, the mean TAT was about 31 hours, the 24-hour TAT-OP was 80%, and the 48- hour TAT-OP was 12%. In June, the earliest accessible data, the mean TAT was about 38 hours, the 24-hour TAT-OP was 82%, and the 48-hour TAT-OP was 9%. In December, the most recent accessible data, the mean TAT was about 31 hours, the 24-hour TAT-OP was 89%, and the 48-hour TAT-OP was 4%. Considering this data, the laboratory is operating at around a 3σ level, if the goal is a 48-hour TAT. Considering a 24-hour TAT, however, the laboratory is operating below a 1σ level.

Improvements Caused by Lean Six Sigma

Due to the application of LSS, the laboratory at the Oklahoma University Medical Center, despite a workload increase of "78% from 2004 through 20111", TAT-OP had achieved a 6σ level. They were also able to reduce expenses such that they had a return on investment of 35%. The Serbian laboratory was able to free up multiple hours of daily staff work through their application of LSS and claim that "modification made in the sample analysis process in a microbiological laboratory by the introduction of

Lean and Six Sigma concepts led to significant savings3", though specifics are not given. A laboratory in Turkey was able to eliminate "3 h and 22.5 min of non-value-adding work2", reduce TATs for stat samples by 9 minutes, and reduce "steps prone to medical errors and posing potential biological hazards to receptionists… from 30% to 3%.2".

Control of the Laboratory

Lean Six Sigma is able to provide significant benefits to a clinical testing laboratory. It can be used to reduce turnaround times, costs, and safety hazards. Beyond what has been described in this paper, there are many more tools provided by the LSS framework, such as 5S, spaghetti diagrams, and root cause analysis. The greatest benefit of LSS, however, is not in the specific tools, though they are incredibly useful, but in the analytical and critical mindset it requires. Any attempt to implement Lean Six Sigma at the ASU Biodesign Clinical Testing Laboratory would likely provide great benefits.

Section V: References

- Blick, K. (2013). Providing critical laboratory results on time, every time to help reduce emergency department length of stay: How our laboratory achieved a Six Sigma level of performance. *American Journal of Clinical Pathology, 140*(2), 193–202. https://doi.org/10.1309/AJCPNUTIPQTRRG0D
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Section V: Appendix

Figure 1

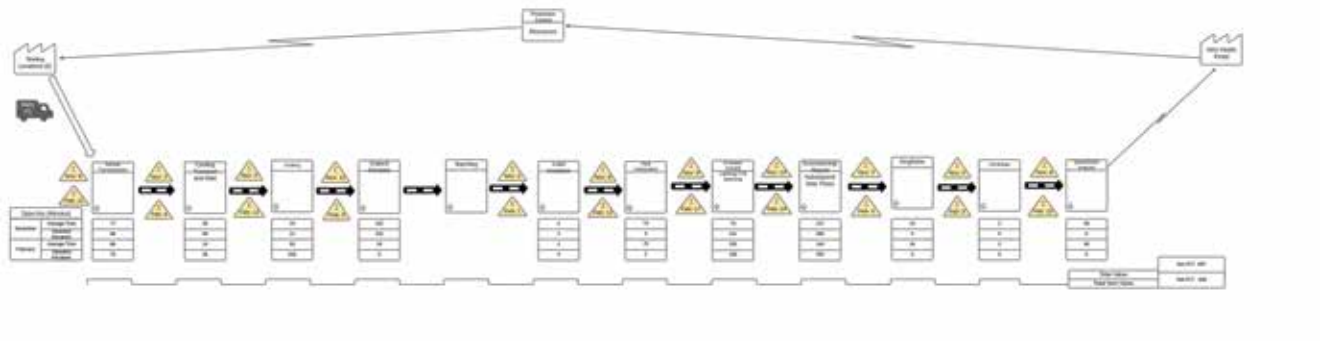


Figure 21

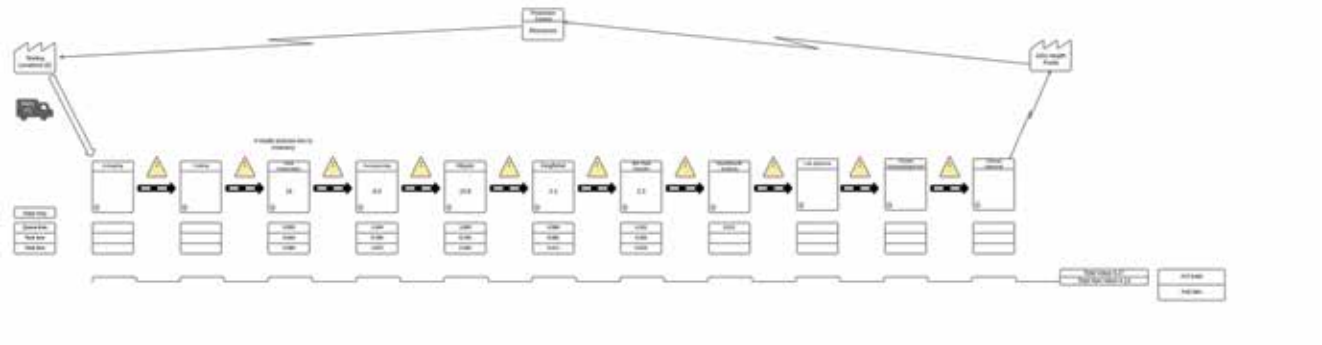


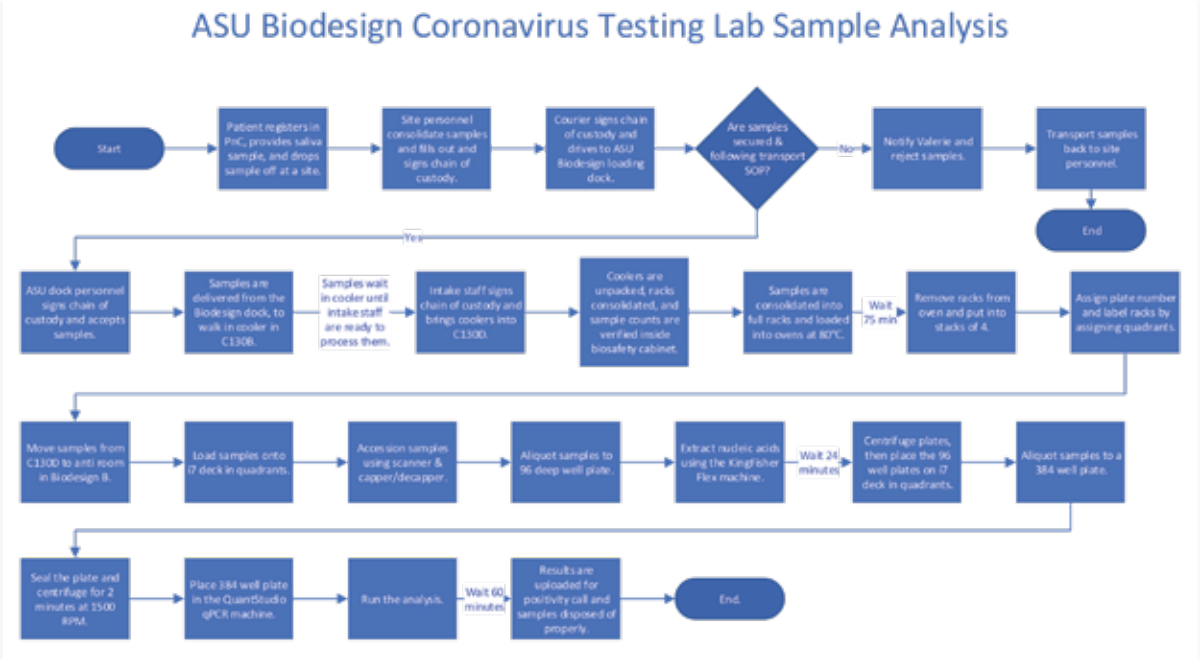
Figure 2

Process	**Initials**	**Equip ID#**	**Start Date (MM/DD)**	**Start Time (HH:MM)**	**Finish Date (MM/DD)**	**Finish Time (HH:MM)**
Refrigerator					/	: AM PM
Heat Inactivation		1 2 3 4 5 6 7	/	: AM PM	/	: AM PM
Accessioning			/	: AM PM	/	: AM PM
Plate #						
Observations:						
Prior to starting each process step, please enter your initials, Equipment ID# if applicable, starting date and time.						
Upon completing each process step, and prior to sending the next step, please enter the finishing date and time.						
After completing Accessioning, please enter the Plate #; this must be included to enable traceability.						
Please leave this lot traveler in the collection box.						

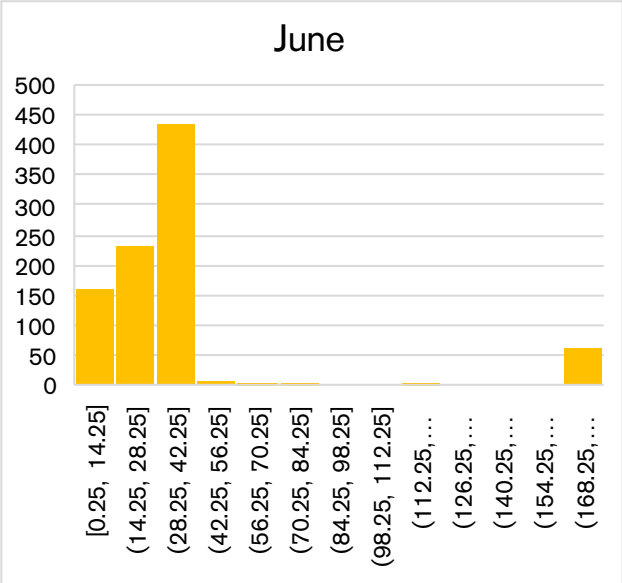
Figure 3

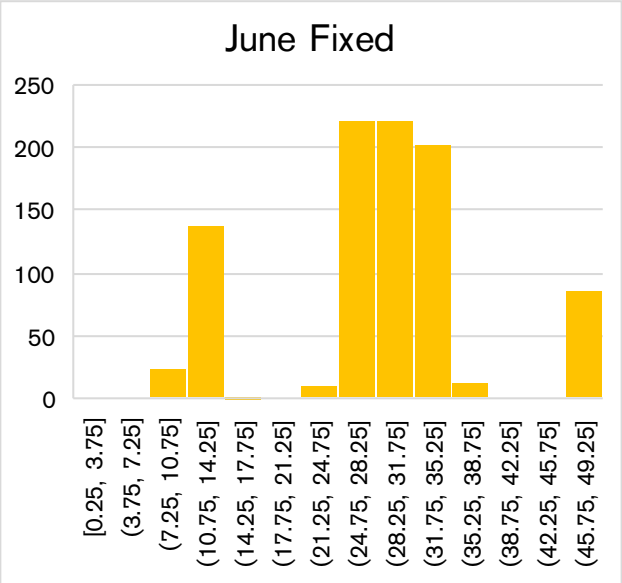
Plate #						
Process	**Initials**	**Equip ID#**	**Start Date (MM/DD)**	**Start Time (HH:MM)**	**Finish Date (MM/DD)**	**Finish Time (HH:MM)**
Aliquot			/	: AM PM	/	: AM PM
Kingfisher		1 2 3 4	/	: AM PM	/	: AM PM
384 Plate Transfer			/	: AM PM	/	: AM PM
QuantStudio Analysis		1 2 3 4	/	: AM PM		
Observations:						
Please enter the Plate #; this must be included to enable traceability.						
Prior to starting each process step, please enter your initials, Equipment ID# if applicable, starting date and time.						
Upon completing each process step, and prior to sending to the next step, please enter the finishing date and time.						
After completing the QuantStudio Analysis, please leave this lot traveler in the collection box.						

Figure 4

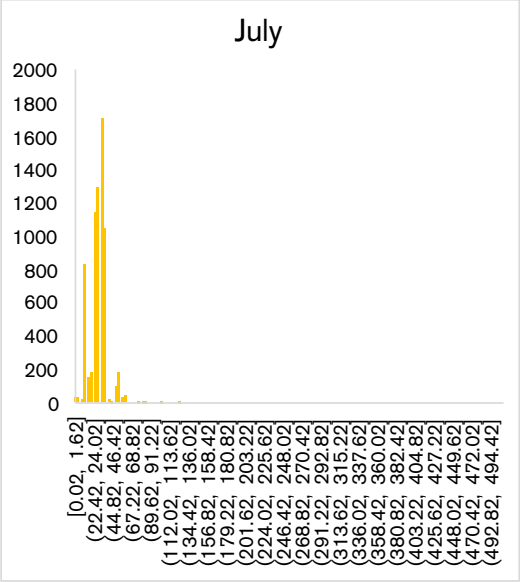


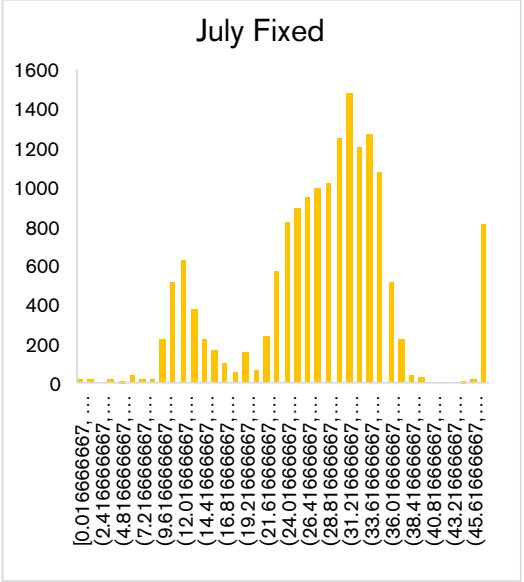
Figures 5 and 6



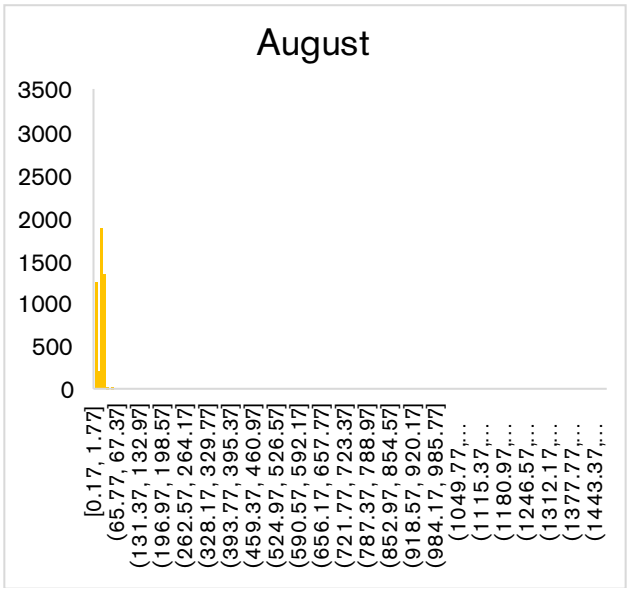


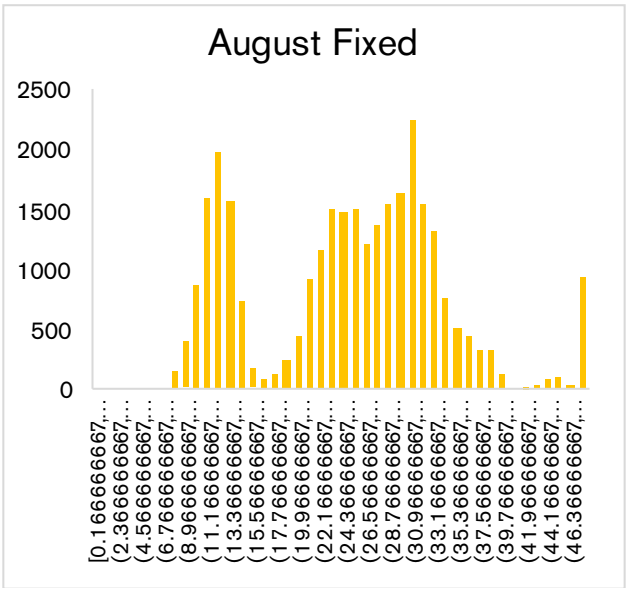
Figures 7 and 8





Figures 9 and 10





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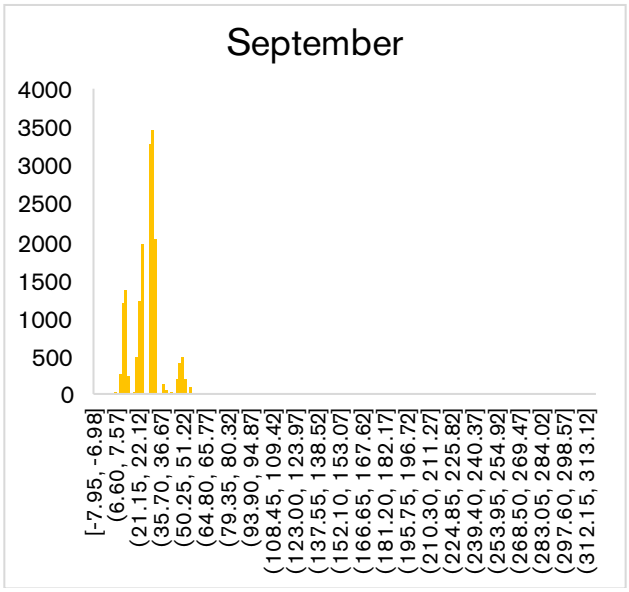
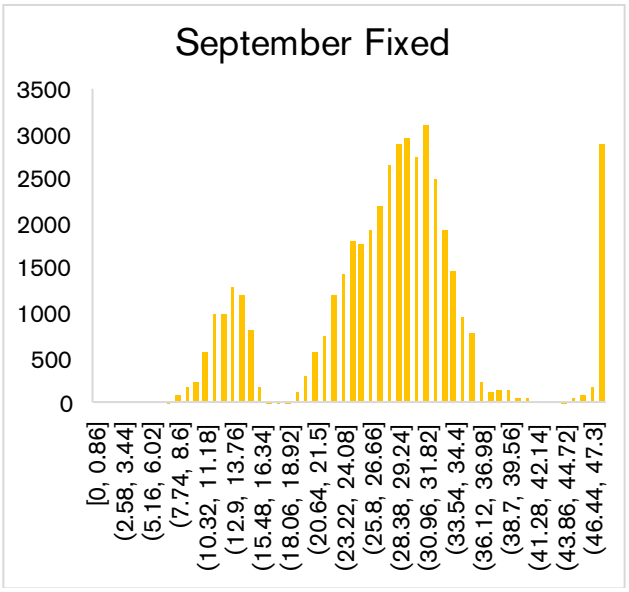
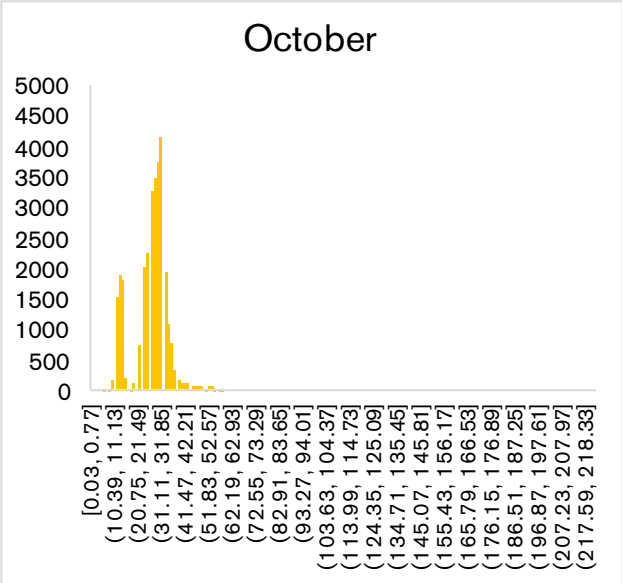
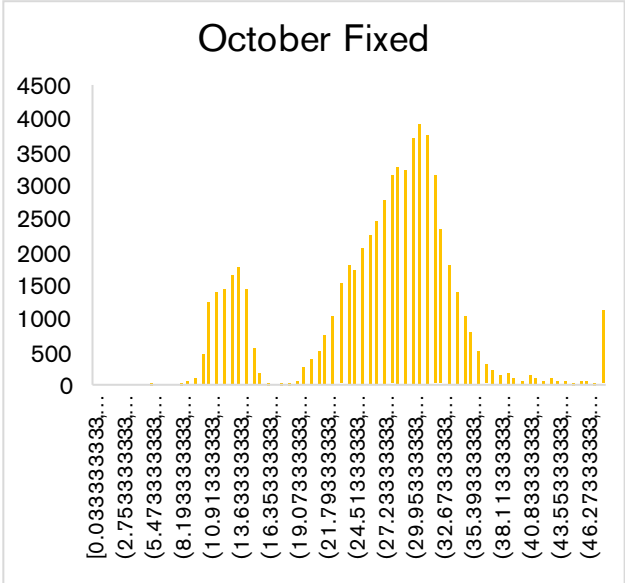




Figures 13 and 14





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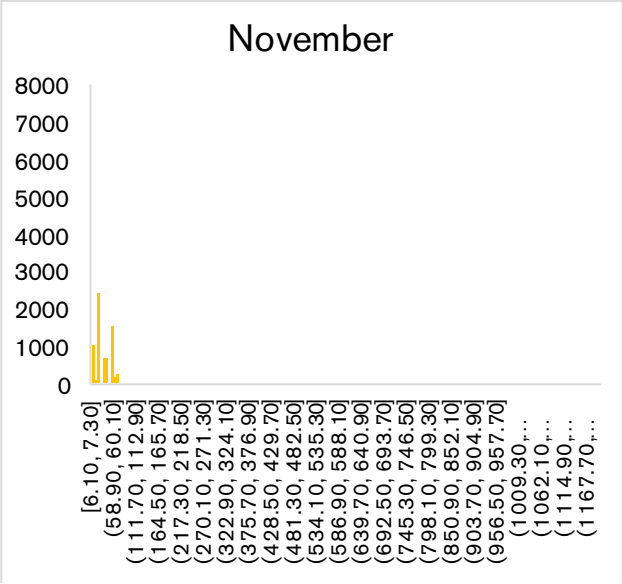

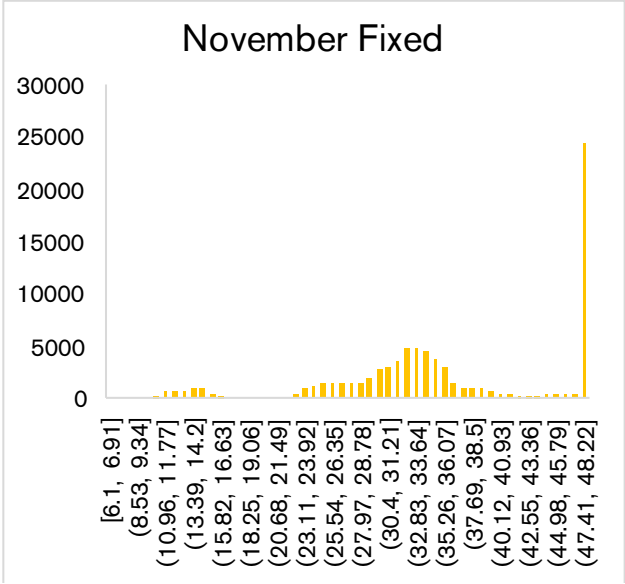

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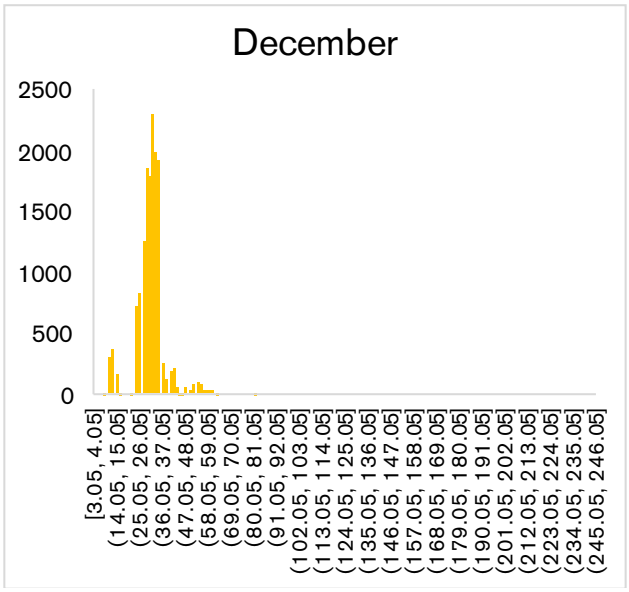

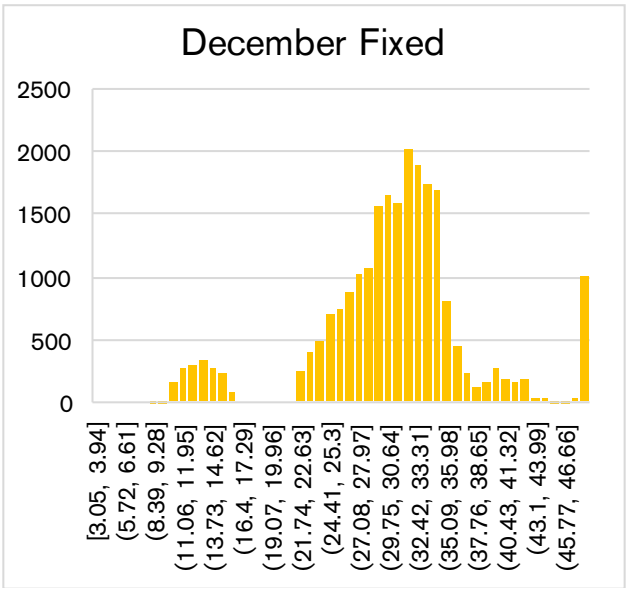

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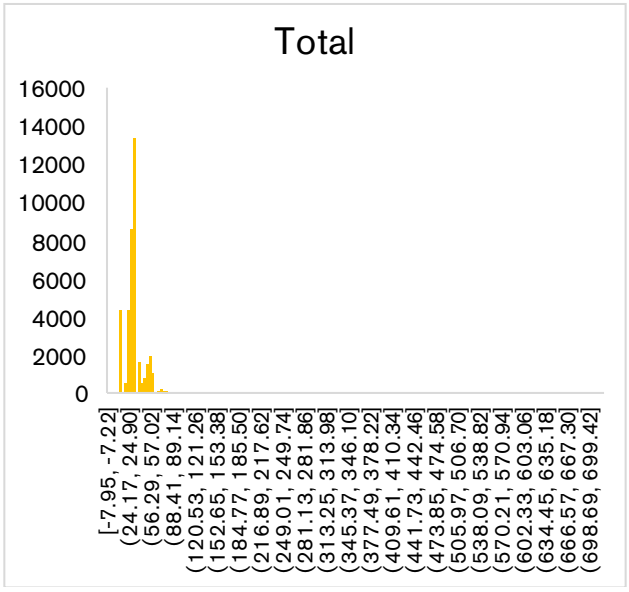

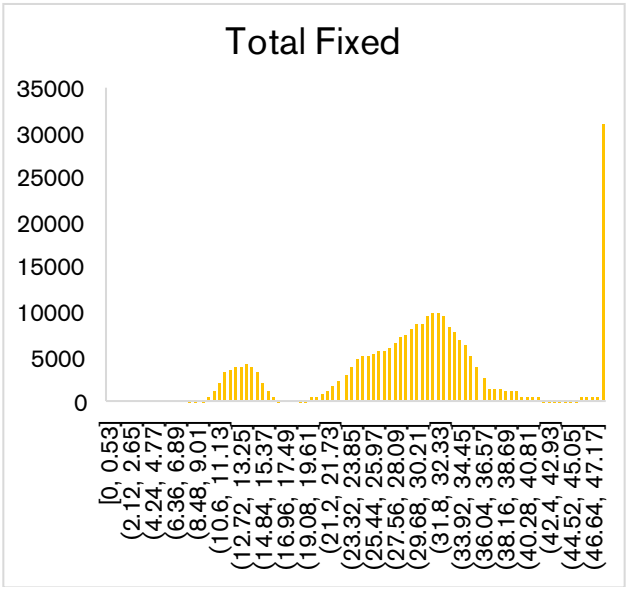

Section VI: Training Certification Database and Tracking System

Author: Jack Myers

Background

When selecting which database solution provides the optimal results, it depends very heavily on the particular problem and what factors are most important in the final solution. This Section first provides background information about two kinds of databases, relational and non-relational, and discusses a study comparing the efficiency of each in the clinical space. This is followed by an analysis of several different database solutions and the strengths and weaknesses of each before concluding with recommendations for the lab to consider when deciding which to ultimately use.

Analytical Framework and Findings

For decades, Structured Query Language (SQL) databases, also known as relational databases, have dominated database management systems. Relational databases have predefined schema (Sánchez-de- Madariaga et al., 2017). Schema consists of tables, which have a definite number of columns. Tables have relationships between each other, and a pivot table connects different tables together. SQL databases utilize structure query language to define and manipulate data, so they typically are a good fit for a complex query intensive environment (Digital Media Technology News 2016). SQL databases are vertically scalable, but they are not horizontally scalable. This means that if something were to change in the future and you wanted to start tracking a new attribute, you would not be able to add that attribute to an existing table. You would need to create a new table to keep track of that attribute, and then use a pivot table to be able to join the tables together (Sánchez-de-Madariaga et al. 2017).

Alternatively, NoSQL databases, also known as non-relational databases, do not have any schema. There are a couple different categories of NoSQL databases. The first category is Key-Value, in which arbitrary data is stored under a key (Corbellini et al. 2016). The second is Wide Column, which saves data by column rather than by row. The third is Document-oriented, which saves data as a series of fields with attributes. Typically these documents are in semi-structured formats such as XML(eXtensible Markup Language) or JSON (JavaScript Object Notation). These are similar to Key-Value databases, but the key will always be the document's ID and the value is the document. The document's type (e.g. JSON, XML) is known, but the schema can vary (Corbellini et al. 2016). Because non-relational databases have no schema, they do not support joins of data. This potentially means that a non-relational database may be very inefficient if a subpart of a document references parts of other documents, since the database must process the entire document. However, if the task can be performed within the one document, then non-relational databases typically perform better than relational databases (Digital Media Technology News 2016). Generally, NoSQL implementations can be faster and more scalable when data sizes are extremely large and do not have any internal document references (Sánchez-de-Madariaga et al. 2017).

A study conducted by Sánchez-de-Madariaga et al. examines the performance of SQL and NoSQL databases for querying standardized electronic health records. The study investigates the performance of three examples of different database system methodologies: relational (MySQL), document-based NoSQL (MongoDB), and native XML NoSQL (eXist) (Sánchez-de-Madariaga et al. 2017). MongoDB stores and produces files in JSON form, and eXist does the same but in XML form. The study tests a small, medium, and large sized database of each of the three types. Each of the nine databases then perform six different queries of increasing complexity.

The results of the study show that MySQL and MongoDB yield very similar results in smaller sized databases, but in the largest size databases MongoDB performs much faster than the relational database

does. eXist is a distant third for all queries on most sizes, with the exception that it performs better on the large database size than the relational databases for all but the most intense query. Part of the reason the relation database takes longer is that it returns its results in a table-like form, so it must take time to reconstruct the documents. The non-relational databases simply return the entire JSON/XML document as a result. The results from the study are displayed below (Sánchez-de-Madariaga et al. 2017).

Table 2 Response times in seconds of the six queries performed on MySQL relational ORM database

ORM	5000	10,000	20,000	slope (*10^{-6})
Q1	0.0429	209.0284	1082.7872	72,182.95
Q2	101.6196	>10,000	>10,000	>>
Q3	0.1256	4.1982	12.6110	832.36
Q4	0.1843	400.6388	1598.7410	106,570.45
Q5	200.8954	>10,000	>10,000	>>
Q6	0.7362	65.1898	185.2420	12,300.39
Database size	4.8GB	9.7GB	19.8GB	
Total extracts	5000	10,000	20,000	

*stands for the multiplication sign

Table 3 Response times in seconds of the six queries performed on MongoDB NoSQL database

MongoDB	5000	10,000	20,000	slope (*10^{-6})
Q1	0.0460	0.0570	0.1221	5.07
Q2	34.5181	68.6945	136.2329	6780.99
Q3	0.0480	0.0580	0.1201	4.81
Q4	0.0520	0.0610	0.1241	4.81
Q5	38.0202	75.4376	149.9330	7460.85
Q6	9.5153	18.5566	36.7805	1817.68
Database size	1.85GB	3.95GB	7.95GB	
Total extracts	5000	10,000	20,000	

*stands for the multiplication sign

Table 4 Response times in seconds of the six queries performed on eXist NoSQL database

eXist	5000	10,000	20,000	slope (*10^{-6})
Q1	0.6608	3.7834	7.3022	442.76
Q2	60.7761	129.3645	287.362	15,105.73
Q3	0.6976	1.7710	4.1172	227.96
Q4	0.6445	3.7604	7.3216	445.17
Q5	145.3373	291.2502	597.7216	30,158.93
Q6	68.3798	138.9987	475.2663	27,125.82
Database size	1.25GB	2.54GB	5.12GB	
Total extracts	5000	10,000	20,000	

*stands for the multiplication sign

The study concludes by stating that relational databases perform well if databases are not very large in size. Document-based NoSQL solutions such as MongoDB perform considerably better than the relational databases for larger sizes, and are faster than native XML databases such as eXist for all sizes. Document-based NoSQL systems surpass relational systems in throughput and in query execution time (Sánchez-de-Madariaga et al. 2017).

Relation to ABCTL

MongoDB

The first solution is the aforementioned NoSQL document-based MongoDB. MongoDB is available either as an on-premises server or on the cloud via MongoDB Atlas ("MongoDB"). Atlas takes the responsibility of hosting, patching, managing and securing the MongoDB cluster (Gray 2018). Having Atlas handle these tasks makes this solution more secure and reliable than the on-premises solution. Unless the training certification data has any compliance or privacy statements preventing it from being stored on the cloud, I would recommend using Atlas rather than an on-premises MongoDB server.

SQL Server

Additionally, another potential solution is the relational SQL Server. My understanding is that the lab has implemented SQL Server on a SharePoint Server previously. However, this implementation does have some limitations. According to Microsoft's officially documentation, Microsoft does not support directly querying or modifying databases that support SharePoint Servers 2016 or 2019, and SharePoint Server databases have sizing and configuration limitations that are not standard for SQL server (Overview of SQL Server in SharePoint Server 2016 and 2019 environment, 2020). Due to these limitations, I do not recommend using SQL Server in SharePoint as a permanent solution.

However, SQL Server can also be run on an Azure Virtual Machine instance. Implementing SQL Server this way does not have any of the limitations that the SharePoint implementation does. It has similar benefits to MongoDB Atlas, as the scaling and security are handled by the cloud provider (SQL Server on Azure, n.d.). There is also Azure SQL Database, which is the Platform as a Service alternative. The main difference is that this service does not require the user setting up a virtual machine, but it can be more expensive than running SQL server on a virtual machine would be.

MySQL

Comparatively, another relational solution is MySQL, which was studied previously in this paper. MySQL did not perform as well as the NoSQL solutions in that study. However, MySQL also offers MySQL Document Store, which is a hybrid of SQL and NoSQL. Document Store allows users to mix and match relational data and JSON documents in the same database. Both data models can be queried and results can be in table, tabular or JSON formats (MySQL Document Store, n.d.). This option could be attractive because it provides the benefits of both the relational and non-relational approaches. However, according to a study which directly compares MySQL Document Store with MongoDB, the latter performed better than the former in every single test that was done (Andersson & Berggren, 2017). It appears that the hybrid architecture of MySQL Document Store affects performance significantly. If the hybrid approach is not essential to the lab, then I would not recommend MySQL Document Store due to its slow performance.

Amazon Web Services

Lastly, Amazon provides relational and non-relational solutions in the form of Amazon Relational Database Service (RDS) and Amazon DynamoDB on Amazon Web Services (AWS). RDS allows the user to choose from a pool of different database engines, such as Amazon Aurora, MySQL or SQL Server. The benefits of using RDS is that it allows the database to be set up in minutes and provides scaling with no

downtime (Amazon Relational Database Service, n.d.). It is very similar to the Azure SQL Database, but Azure does claim to be cheaper to use (SQL Server on Azure, n.d.). Amazon DynamoDB is the NoSQL alternative. It is serverless, and automatically scales up and down to adjust for capacity and performance. It is capable of either provisioned or on-demand capacity, so the lab can choose to pay for specific capacity or to only pay for the resources consumed. This provides many of the same benefits of being on the cloud as MongoDB Atlas does. However, one big difference is that DynamoDB integrates with other AWS services, which could be useful if the lab ever decides to use them in future or is currently using them.

Conclusion and Future Forecast

After considering and evaluating all of the options above, it does not seem that there is one clear superior solution, as the best solution depends largely on what factors the lab determines to be the most important. Firstly, if there are any compliance or security issues with using the cloud, that would rule out using Atlas, Azure, or AWS. Among the on-premises choices, if the lab prefers to use a relational database to store and query the data in table form, then I would recommend using MySQL. If the lab wants the data to be in a document-based format, such as JSON or XML, then MongoDB would be a better option. If the lab is indifferent, MongoDB did perform better than MySQL when tested (Sánchez-de-Madariaga et al., 2017).

If the lab is able to use the cloud, I would recommend choosing one of the cloud solutions rather than an on-premises solution because they can be created more quickly and allow the lab to pay only as resources are used, as it will scale itself. If the lab has any current solutions that use AWS or Azure, then it might make sense to stay within the product family. Otherwise, Azure is cheaper than AWS and I don't see any significant differences between the two. If the lab chooses to use a NoSQL solution, DynamoDB would be recommended if the lab wants to commit to AWS long term. DynamoDB offers zero portability (DynamoDB Vs. Mongo Atlas, n.d.), so it would be very difficult to ever leave it in the future. If the lab chooses to not integrate this database with anything, MongoDB could also be used.

All in all, relational and non-relational databases both have their advantages and disadvantages. The lab must decide if it makes more sense to store their data as tables or as documents. Then, the lab must decide if they want to store the data on the cloud or on-premises. I personally would recommend using a NoSQL solution on the cloud, because it will provide optimum performance and require minimum time from the lab maintaining the database. However, if the lab has constraints not allowing it to use this solution, they may decide to go with one of the other possible solutions discussed as well.

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Section VII: Reagent Tracking Systems for ABCTL

Author: Frankincense Ramesh

Background and Focus

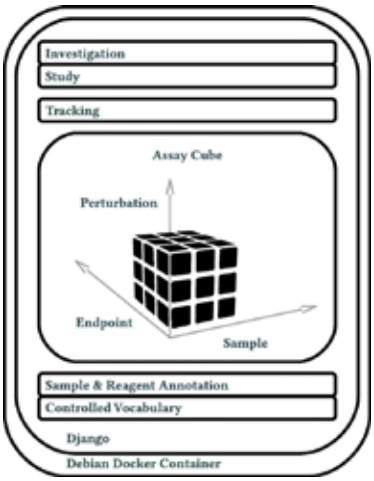
In the laboratory, there are many processes that are involved in carrying out an operation. This is especially true for the ABCTL, the first lab in the Western United States to offer public saliva testing to identify the presence of COVID-19. With many materials and tools being purchased to keep this operation running, it is important to keep track of what is used in the lab. Reagents, specifically are a critical part of COVID-19 testing because they are used in patient samples to determine a positive or negative COVID-19 result. ABCTL currently tracks reagents in the lab by manually filling out reagent accountability forms. A form is used for each stage the reagent goes through from being received, lot to lot tests and analysis, reagent usage, and when it is discarded if it has expired. The kinds of details included in these forms are: name, reference no., lot number, expiration date, volume used, SOP No., SOP version, and Operator. They are organized in reagent tracking binders. While this way of tracking reagents is working for the lab, it can be significantly improved by using software specialized in reagent tracking.

Utilizing a digital reagent tracking system is essential for the COVID Lab to operate at an optimal speed and helps the overall process of testing samples to be more efficient. If laboratory management is improved in this area, the time that is saved can be used to focus on critical parts of the lab. In addition, by optimizing resource management this will enable the lab to optimize the space in inventory, prevent wastage of expired reagents or situations where the reagent stock has run out. A reagent tracking system will reduce costs, remove the period of waiting time for supplies, improve productivity in the lab and ultimately create value for the lab. This paper will discuss explore some of the current digital reagent tracking systems that could be potentially used in the lab.

Analytical Framework and Findings

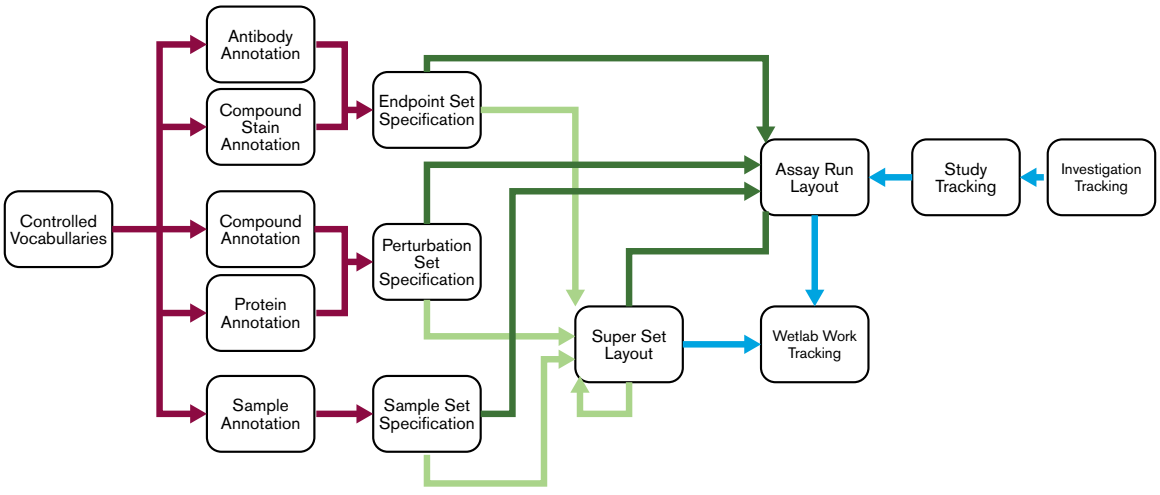
The first reagent tracking system I looked at is Annot: a Django-based sample, reagent and experiment metadata tracking system. Annot is described to be a novel web application that provides a flexible solution for complex laboratories where multiple things are happening at the same time. For this lab, the purpose of our team is to collect data from the lab to analyze and convert into models which can be used to predict patterns in the lab and identify when certain procedures are slowing down the whole process. With such experimental procedures being done in the lab, it is important to collect accurate metadata to interpret the results. Annot is described to “track highly structured sample, reagent, and assay metadata”. It achieves this by using controlled vocabulary in its software and structured formats for downstream analyses. This software is adaptable to different experiments and is broad enough to be applied to many labs. This database was created to satisfy the needs of both computational and experimental scientists and it was developed as a web framework so that the database would be accessible to all staff throughout the laboratory. Its implementations include loading standard ontologies, exporting metadata files, and system backup. Annot’s web framework was implemented with Django to utilize its libraries. The libraries of Django give the database a robust GUI and give the function of searchable drop-down menus. This platform has basic security measures employed to protect sensitive information from SQL injections, cross-site scripting, cross-site request forgery, and click-jacking. Furthermore, data quality is monitored by including a field which indicates the user who entered the information into the database. A cool feature of this tracking system is the use of controlled vocabularies which “cover diverse aspects of biological experiments.”

Figure 1. Schematic representation of the Annot Django code base stack.



The figure above shows how the controlled vocabulary layer establishes the basis for sample and reagent annotation in the brick layer. In the assay cube layer, sample and reagent bricks can be assembled into any experimental layout using Python3 scripting (Bucher 2019). Annot automatically stores the most recent ontology version so that it can easily be retrieved through the user interface. The ultimate goal of this software platform is to track essential metadata from procedures in the lab so that the data collected across different experiments can be jointly analyzed. There are some more details provided about the implementation of this software which is that the high cost to populate Annot with detailed sample and reagent annotation makes this platform more appropriate for large-scale and high-throughput experiments which give large data sets . The cost of this tracking system might be higher compared to systems free of charge, but it depends on the needs of the lab and how much metadata needs to be sorted and analyzed. The figure shown below shows the process by which reagents and samples move through from first being annotated via the Annot web interface to being combined into endpoint, perturbation, and sample sets. The red arrows show when details like the reagent concentrations, cell seeding density, or cell passage number can be specified. The light green arrows show when super sets can be generated for assays involved with robot pipetting, array spotting, or cyclic staining. The dark green arrows show that for each assay: run, endpoint, perturbation, sample, and super sets are merged to a run specific assay layout. Annot directly tracks assays and supersets that are regularly being processed by the lab, along with specification of the date, protocol and laboratory personnel. The blue arrows indicate how assays can be grouped into studies and studies into investigations (Bucher 2019).

Figure 2. Annot Workflow Representation



Another software tracking software system I looked at is Quartzy, which is noted to be a leading life science product distributor and provides 10 million plus products which includes reagents, chemicals, and supplies from 1,800 leading brands. It is said to simplify the lab workflow and it works in three simple steps. The first step is browse their catalog and create custom requests. Approval is the second step, to manage incoming supply requests for approval or immediate purchase in one place. Quartzy also provides product comparisons to show if the user could be getting a more competitive quote. Real time updates and proactive support is also provided by this service. The third step is to mark supplies as received while automatically updating the inventory data and alerting the lan when supplies are back in stock and where to find them. They have a customizable lab inventory manager which allows users to track important details for lab supplies or lab-made material to ensure regulatory compliance and improve communication i the lab. Order requests can be submitted directly from the inventory to prevent any second guessing on whether the right product was purchased. Quartzy provides information on quantities, location, expiration alerts, and MSDS forms. It is easy to transition from what the lab is currently using to track reagents as any existing lab inventory in Excel, CSV, or a FileMaker can be uploaded in to the user's account using their import tool. Quartzy is described to be completely customizable as not only does it track commercial products like chemicals and supplies, but also lab made items such as plasmids, cell-lines, and oligos. Specific fields can be easily created to track all item types. With Quartzy, the lab can track item locations and freezer boxes. It allows the user to create locations and sub-locations for all items. The location of items in freezer boxes can be tracked through their interactive graphical interface. The interface also supports an advanced search and a filtering function to quickly find the item needed. Everyone in the lab would know where things are kept, so time would not be wasted looking through the lab for things. Sometimes managing relationships with multiple vendors is complex or time consuming when purchasing a diverse selection of lab supplies. It can also be difficult to share inventory information with various groups in the lab, which can leave teams unsure of how to plan for certain processes. Quartzy aims to solve these problems by centralizing inventory data and making it accessible to all science teams using Quartzy's inventory manager. Preparation time for processes can be reduced and lab communication across science and purchasing teams can be improved. I think that the highlight for using Quartzy is enhancing awareness of all teams in the lab when it comes to keeping track of the reagents being used in the lab.

The next reagent tracking system I looked into is eLabInventory. This system is unique in the sense that it utilizes 2D barcode labeling. With eLabInventory, barcode labels with 2D barcodes can be generated and printed by connecting a DYMO labelwriter. Barcodes can be scanned, information can be retrieved, and sample actions can be performed by using the Mobile App for smartphones or tablets. A generic 2D barcode scanner can be used to identify and handle samples efficiently in the lab. The barcodes can label sample tubes, boxes, and devices. ELabInventory is marketed to be flexible and adjustable for any lab. With this system any sample, specimen, consumable, chemical, or instrument can be tracked in the lab. Templates can be set up to track any information about any item in the lab inventory, such as cell lines, tissue specimens, bacterial strains, DNA, RNA, proteins or any biobank. It is also described to be intuitive and easy-to-use. The entire lab and visualized and storage locations can be set up according to lab specifications. Storage locations can easily be browsed through to store or locate samples. Similar to the other tracking systems mentioned, the entire lab inventory can be centralized with eLabInventory.

Moreover, with this system stocks can be kept up-to-date. Orders can be centralized by keeping track of quantities and notifications will be sent when chemicals, samples, and consumables run out of stock. This system was designed by scientists for scientists and its intuitive user interface allows the user to navigate the system. There would be no need to be familiarized with complex software because it is simply set up to be set up and initiate tracking the lab's inventory more easily. In terms of security, data is protected by hosting products in three data centers in different geographic locations that replicate and load-balance data in real time. eLabInventory also runs daily encrypted, off-site back-ups which enables to recover x`any lost data at all times. It also supports SSO single sign on logins for department or institute-wide implementations of eLabInventory. Two-step verification is also made available for all members of the lab.

For this the eLabInventory Mobile App can be used to generate the security code to sign into the account. There are also user roles and permissions that can be set up for every role in the lab for group leaders, senior scientists, PhD students, lab managers, technicians and guests. This will enable the lab to control the user's system abilities to perform, view, add, update, and delete actions. I think this feature would be helpful for collaborations in the lab.

Relation to ABCTL

As a member of the data quality and management systems team, I have seen how the data from multiple runs of the lab is merged to paint a bigger picture of the lab's processes. Spread-sheets were commonly used for various processes in the lab to record and analyze data. Using spreadsheets makes it difficult to easily contain and interpret data from complex experimental paradigms and the work needed to maintain them can be tedious. Spreadsheets are also vulnerable to many simple and commonly made errors which was observed in our work. Due to human errors made both by technicians in the lab and by our team, there are some flaws with the recorded data which affects the accuracy of the results significantly. While it might be difficult to achieve perfection when recording data, the lab can progressively make efforts to come close to it. The first step to achieving this is to convert physical forms used in certain parts of the lab to digital versions. Doing this will make it easier for technicians to input data, will reduce human errors, and allow for data to be jointly analyzed in a more efficient manner. As our student team collaborated with the lab throughout the past year, a major concern that emerged was protecting the privacy of individuals and their test results which are protected under HIPAA. There were certain data sets that our student team was not allowed to look at when examining the data. This made it difficult for us to assess the capacity of the lab each month, as we were not able to get certain recorded data quickly enough from the manager to construct our own models. I think for future collaborations, making use of certain features like roles and permissions in reagent tracking system software would make it helpful for other students to obtain data they can use in a more practical way. When implementing a reagent tracking system some recommendations are to ensure that materials are labelled properly, fields of storage and inventory items are defined correctly, inventory is organized according to the RTS, and responsibility is taken to continuously update the system.

Conclusion

It is important to employ a system in the lab that will track the reagents that are being used for each test. By automating this function, it will make it easier for the lab to track the stock of reagents and reorder as necessary so supplies in the lab can be managed properly. Without such a system in place the lab's stockroom will not be well organized and reagents needed at crucial times may not be on hand readily or easily obtained. With emerging technologies that are made available for such purposes, the lab should make use of digital solutions to ease this part of the process in testing samples for COVID-19. When the fields of medicine and technology are allowed to merge and overlap, it brings forth many interesting opportunities, a digital reagent tracking system being one of them.

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Section VII: Appendix

Figure 1. Schematic representation of the Annot Django code base stack.

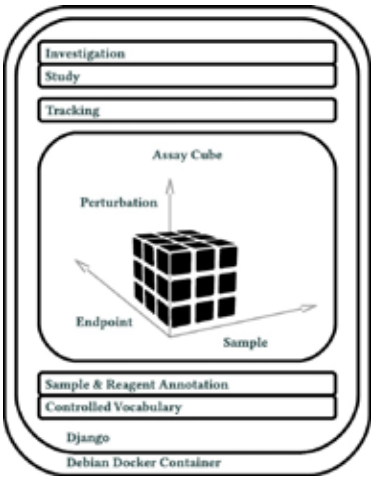
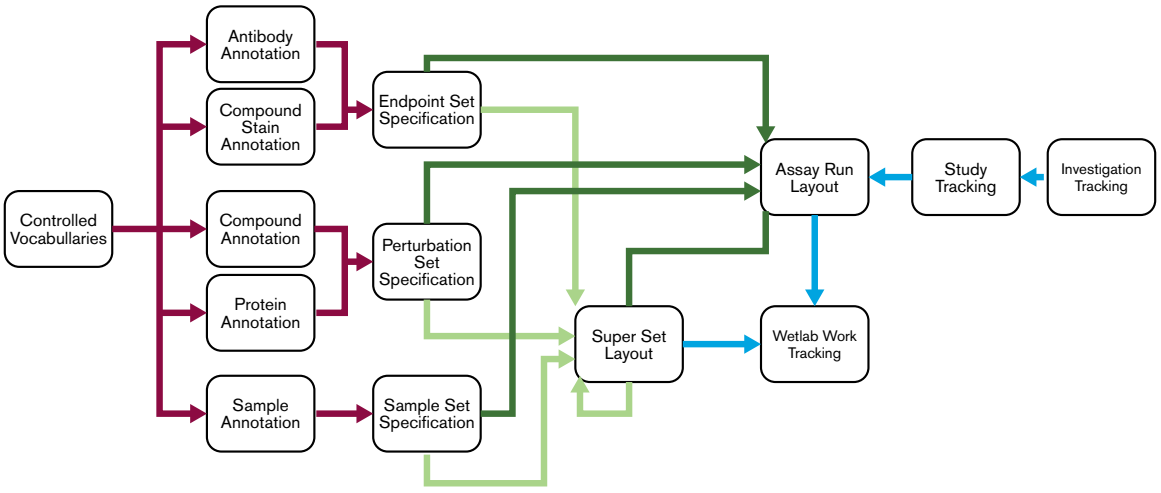


Figure 2. Annot Workflow Representation



Section VIII: Prevention and Correction of Non- Conforming Events

Author: Sage Reagan

Background and Focus

Corrective and preventative actions, or CAPA, is a system to investigate nonconforming events and determine a proper solution to ensure this event will not reoccur (Cagle, 2000). CAPA is required by the FDA, who states the purpose is to "collect information, analyze information, identify and investigate product and quality problems, and take appropriate and effective corrective and/or preventive action to prevent their recurrence" ("Corrective and Preventative Actions'', Narrative Section). The FDA inspects labs, checking the effectiveness of the lab's CAPA system (''Corrective and Preventative Actions'', Inspectional Objectives Section). Unfortunately, because there is not a standardized procedure for CAPA within laboratories, the FDA has reported that many manufacturers do not fully understand CAPA (Nour, 2018, Abstract). Currently, the Biodesign Clinical Testing Lab's CAPA system is to report nonconforming events to the Clinical Quality and Compliance Specialist. These events can either be reported through emails sent by employees, through customer complaints via hotline, or with CLIA or CAP. After the events have been reported, they are inputted into an excel spreadsheet. These events are then handled through emails between members of the lab that are often inaccessible.

Analytical Framework and Findings

Six Sigma Reporting

To ensure effective corrective and preventative actions have been implemented, labs should integrate Six Sigma methodologies into their CAPA systems. Six Sigma focuses on the reduction of variation to improve quality and uses DMAIC to execute this goal. DMAIC stands for Define, Measure, Analyze, Improve, and Control (Kumar, 2009, Six Sigma Framework Section). Ideally, the lab would have a standard operating procedure (SOP) describing when and how to initiate a CAPA procedure. If they did not have an effective SOP, DMAIC would help to improve their SOP (Nour, 2018, p.45). Defining the problem is central to finding the solution of a nonconforming event. The first step when approaching a nonconforming event, is to write a detailed problem statement (Rodrigues, 2016, p. 39). A correct problem statement should include "where the event happened, what happened, when it happened, who was involved, how many pieces of whatever were involved, and how the event occurred" (Rodriguez, 2016, p. 39). Rodriguez (2016) also suggests that nonconformance events can be identified using statistical tools (p.40). One essential tool is the pareto chart (Kumar, 2009, Six Sigma Framework Section). In a pareto analysis, issues are input into a chart, and then prioritized based on frequency. (Kumar, 2009, Six Sigma Framework Section).

Non-Punitive Reporting

Problems within a lab are often captured through employee or customer reports (St. Helene-Kraft, 2013, pp. 6-7). St. Helene-Kraft (2013) suggests multiple feedback systems that enable the customer's voice, including "direct contact, surveys, observations, and the analysis of event data that captures complaints and compliments" (p.5). Employee feedback is also essential, as they can directly "report errors, violations, accreditation, or regulatory requirements" (St. Helene-Kraft, 2013, p.7). However, St. Helene- Kraft (2013) also emphasizes the importance of a non-punitive environment to encourage employee reporting (p.7). Employees protected from the negative impacts of reporting an error are more likely to report said error (St. Helene-Kraft, 2013, p.7). That said, employees still must understand that their work is their responsibility (St. Helene-Kraft, 2013, p.7). To create this type of environment, non-conforming events should be viewed as "lessons learned", and celebrated (St. Helene-Kraft, 2013, p.62). Non-conforming

events should be categorized as “unintended human error, an at risk behavior, or a reckless behavior” and have consistent and specific expectations as to how these events are dealt with, based on the categorization (St. Helene-Kraft, 2013, p.65-67).

Six Sigma - Measure

The next step in the DMAIC process is Measure. During this step, the lab must determine a baseline (based on industry standard or historical record) for the process, and then compare the current process to the baseline. To obtain proper measurements, more data needs to be collected concerning the nonconforming event. This can be accomplished by interviewing employees related to the nonconforming event (St. Helene-Kraft, 2013, p.39). During these interviews, it is critical to determine the usual performance of the process and decide “the magnitude of noncompliance” (St. Helene-Kraft, 2013, p.39). This is an important step because the FDA “requires that nonconforming product discovered before or after distribution be investigated to the degree commensurate with the significance and risk of the nonconformity”, therefore, the extent of the investigation is determined by risk analysis (Rodriguez, 2016, p. 47).

Six Sigma - Analyze

The Analyze phase of DMAIC focuses on breaking down the problem to find the root cause (Nour, 2018, p.41). This root cause analysis should be assigned to a team with an assigned leader, who must collaborate to find a solution (Rodriguez, 2016, p.102). The DMAIC process often uses a Fishbone diagram, which can help find the root cause of a problem. The fishbone diagram breaks down the problem into key components, and then further breaks these components down to find the leading cause. Components usually consist of the materials used, measurements, machines involved, method or procedures, environment or condition of the workplace, and people such as management or training (Rodriguez, 2016, p. 111-112). After the factors surrounding the event are identified, the team can use the ‘5 whys’ technique to find the root cause (Rodriguez, 2016, p.42). The 5 whys are simply a continuous cycle of questioning why a symptom of the problem occurred, until the problem’s root is found (Nour, 2018, p.41). The FDA also requires that the nonconforming event has been controlled and will not affect any other areas of the production, during root cause analysis (“Corrective and Preventative Actions”, Inspectional Objectives Section). Controlling the nonconforming event while investigating the problem is critical, but it’s important to remember that this containment is just a “band aid action” and should only be used for as long as it takes to find the root cause and solve the problem (Rodriguez, 2016, p. 108).

Six Sigma - Improvement

Next is the Improve stage, which involves “identification, evaluation, and selection of the right improvement solutions and development of change in management approach to assist the company in adapting to the changes introduced through solution implementation” (Nour, 2018, p.25). In this stage, focus on creating a corrective or preventative action plan for the nonconforming event. The FDA, when inspecting labs, specifically looks for evidence that the plan of action was determined to be effective before it was implemented (“Corrective and Preventative Actions’’, Inspectional Objectives Section). Therefore, when the root cause analysis team is creating a solution, it is critical that this plan addresses the root cause in a detailed, timely manner (Rodriguez, 2016, p.144). The plan of action should include “items to be completed, document changes, any process, procedure, or system changes required, employee training, and any monitors or controls necessary to prevent the problem or recurrence of the problem” (Rodriguez, 2016, p.153).

Six Sigma - Control

The final step in the DMAIC process is Control. During this step, the main focus is to implement the plan of action and integrate the solution into an updated SOP (Nour, 2018, p.26). To verify that the updated procedure is effective, Nour (2018) suggests “Creating a CAPA checklist to ensure that all CAPA

regulatory requirements are covered during CAPA detection and execution" and "Using tracking and monitor tools to record and monitor all CAPA activities" (p. 44). This should ensure that the changes were completed, and the actions taken have truly solved the problem (Rodriguez, 2016, p. 154). During this step, there should also be through documentation of the investigation and subsequent actions (Rodriguez, 2016, p. 159).

Work Engine for Organization

The DMAIC process can provide value, but it is essential that the system is organized. One way the lab can organize is by using a work engine, or even components of a work engine, to improve their CAPA process. An example of a work engine is TrackWise. TrackWise is a "quality management tracking software for FDA-regulated manufacturers" (Cagle, 2000, paras. 1). This system can be used to identify and investigate non-conforming events, as well as creating, validating, and implementing a plan of action, and then following up on the effectiveness of this plan (Cagle, 2000, paras. 3). Some of the benefits that TrackWise advertises are an adaptable graphical user interface, and contains the ability of "Assigning responsibilities, applying corrective actions and responding to customers" (Cagle, 2000, paras. 5-6). Some other notable features are the ability to generate statistical analysis that can be formatted into reports, "automatically issue notifications and alerts'' as well as perform escalations and check for the need of follow ups (Cagle, 2000, paras. 8-10). Finally, Trackwise can assign access to certain people and things based on their security settings (Cagle, 2000, 6). Although Trackwise allows customization, because of this flexibility, some users complain that it has a large learning curve (K, David, 2021) (B, Andrea, 2018).

Relation to ABCTL and Conclusion

Based on the previous information, there are several improvements the ABCTLcould make to their CAPA system. First, it seems that a single individual, the Clinical Quality and Compliance Specialist, has the primary, and perhaps sole responsibility to address the nonconforming event. I would suggest developing a team trained in Six Sigma who would be able to collaborate on solving non-conforming events; this would alleviate the single point of failure. Tools such as the fishbone diagram and '5 whys' provide value but are most useful when multiple people can collaborate to investigate and address the root cause. Also, a detailed SOP, guiding the approach to address a nonconforming event, would be helpful for multiple reasons. Firsts, it would provide management with a clear definition of a non-conforming event and provide recommendations to handle these human errors. The instructions should include guidelines to create a non-punitive environment (assuming the employee wasn't displaying risky or reckless behavior). This would help employees feel less intimidated to report nonconforming events. Furthermore, the lab would benefit from more precise documentation of investigation results and corrective actions. Currently, the lab uses a spreadsheet to track non-conforming events. While it is unclear exactly what goes into this spreadsheet, I would ensure the tracking system has a thorough and structured report of the situation This way should the FDA ever do an investigation, the documentation will be clear and reportable, and if follow-up is required, the team assigned to the follow-up would know exactly what occurred. Finally, a user-friendly database would improve the reporting and organization of a non-conforming event. A database exists, but lab employees have reported issues with accessing it. It would be beneficial for all lab employees to have access to the database, but a database would provide improved value even if just for the use of a CAPA team. In the database, all the previously mentioned documentation could be stored, and it could potentially help the team to track and analyze the data over time. This could assist the team in creating pareto charts, which could help identify problem frequency and create a baseline. While not necessarily suggesting buying TrackWise, it may be useful to improve on the current tracking system with similar attributes that worked specifically for this lab.

Section VIII: References

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Group Commentary: Data Analysis

One of the greatest challenges our group had to overcome was being able to gain access to data that we could use. For safety reasons, our team was only physically able to see the lab one time. This made it difficult to understand the full end-to-end process of the lab. Additionally, we first attempted to try to gather data by using a lot traveler. This lot traveler is a piece of paper that would follow one sample through each stage of the lab, and the technician performing each stage would record the start and stop time of the stage. Unfortunately, in its current state, collecting this data is a very painful and tedious process for the lab technicians. Very few of the lot travelers we asked the lab to fill out were returned to us with complete data, and we decided to pivot to other methods of data collection.

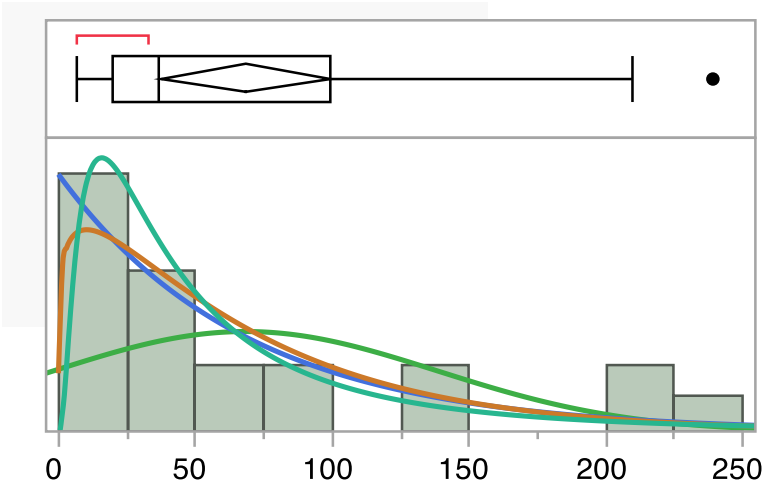
Due to much help from Mr. Nelson, we were later able to gain access to data in the form of four different types of forms: intake sheets, summary reports, chain of custody forms, and heat inactivation forms. The forms were not connected in anyway, and in some cases, forms would be missing or incomplete for a given sample. Out team manually entered the data from the forms them into a central spreadsheet, which also lead to some human errors from mistyping or misreading the forms. After double checking the data and correcting any strange values, we were finally able to analyze the data.

The manual data entry combined with a limited number of samples that were complete from start to finish meant that our final sample size was rather small. In total, the group was able to follow 60 racks of samples end-to-end from initial transportation to the final results reporting. Below are the distributions from the month of February (n=30) which provide a better understanding of what is causing the variation in total processing time. Many of these distributions look nearly identical, with a significant right-skew. These are best approximated by lognormal or exponential distributions, as labelled below.

Except for “Heat Inactivation” and “Unpack Samples” which are close to being normally distributed with relatively small standard deviations, every distribution has at least one massive outlier. These are believed to be a result of the samples sitting overnight. In many cases, the samples that arrived at the laboratory later than 6pm did not make it through every stage of the process and were put in the cooler overnight, until they were processed in the morning. In this case, the outliers are worth looking into as they are responsible for a significant amount of the variation at each stage.

It is worth noting that the lab’s ability to track the start and stop times of each stage is limited at the moment, and manual data entry is not by any means a long-term solution. For future sample tracking, it may be useful to utilize QR or RFID technology to measure the end-to-end testing process more efficiently. Time distributions at each individual stage can be used to provide insight into the root-cause of variation or to create stochastic simulation models in the future.

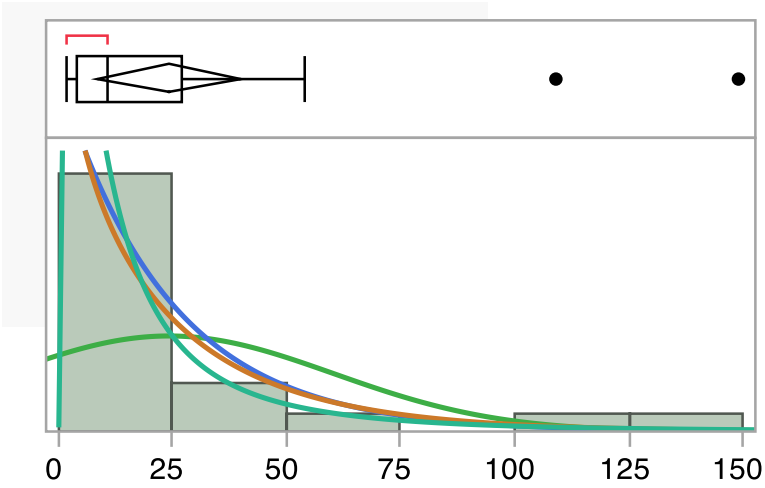
Underlying Distribution for Sample Transportation



Fitted Lognormal Distribution for Sample Transportation

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	μ	3.7424558	0.2113822	3.3093934	4.1755182
Shape	σ	0.9914703	0.1494698	0.7576076	1.375903

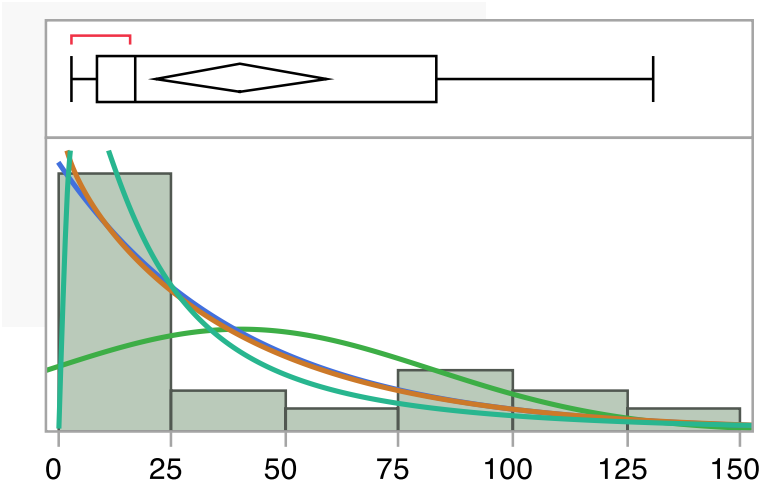
Underlying Distribution for Cooling, Transport, and Wait



Fitted Lognormal Distribution for Cooling, Transport, and Wait

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	μ	2.4605576	0.244062	1.9615185	2.9595967
Shape	σ	1.1704803	0.1725779	0.8992329	1.6114362

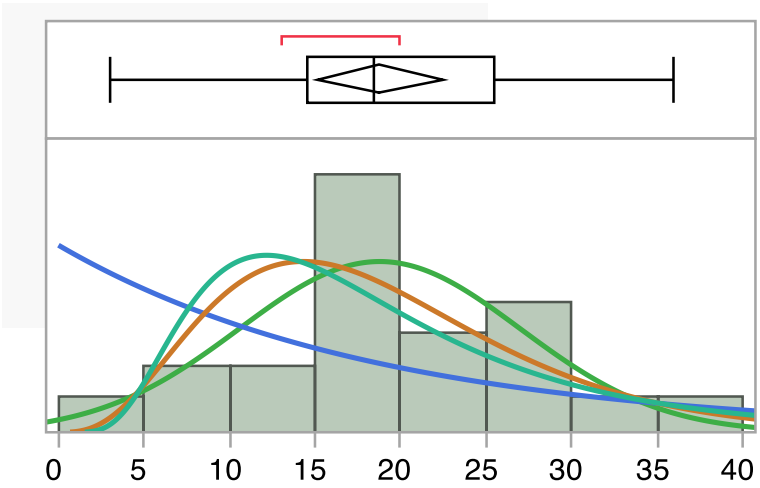
Underlying Distribution for Cooling



Fitted Exponential Distribution for Cooling

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	μ	40.136364	8.5571015	27.156106	62.890349

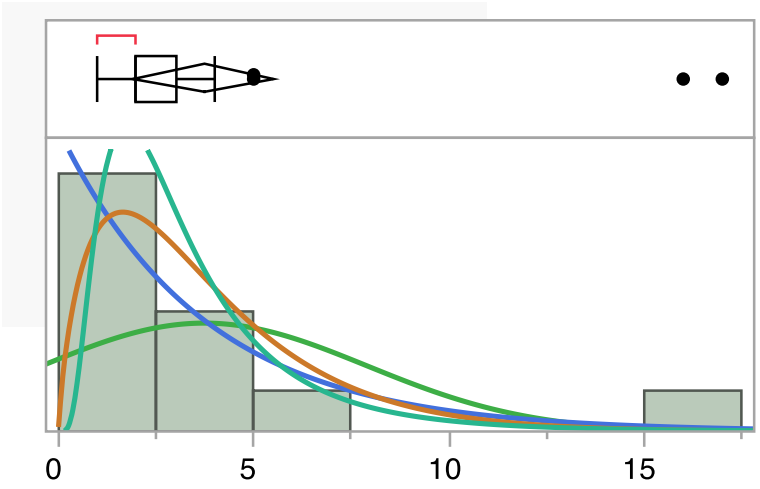
Underlying Distribution for Unpacking Samples



Fitted Normal Distribution for Unpacking Samples

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Location	μ	18.772727	1.7493744	15.344016	22.201438
Dispersion	σ	8.2052934	0.4473579	7.37371	8.9538657

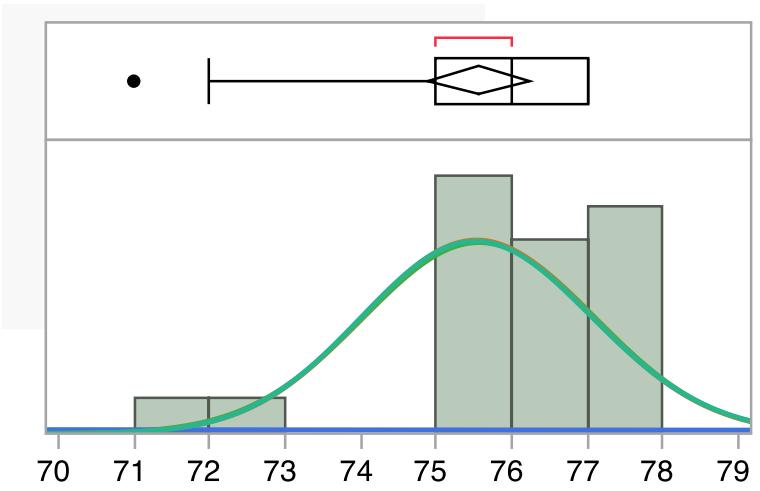
Underlying Distribution for Load Incubator



Fitted Lognormal Distribution for Load Incubator

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	μ	1.0142892	0.1407143	0.7265676	1.3020109
Shape	σ	0.6748719	0.0995	0.5184538	0.9290756

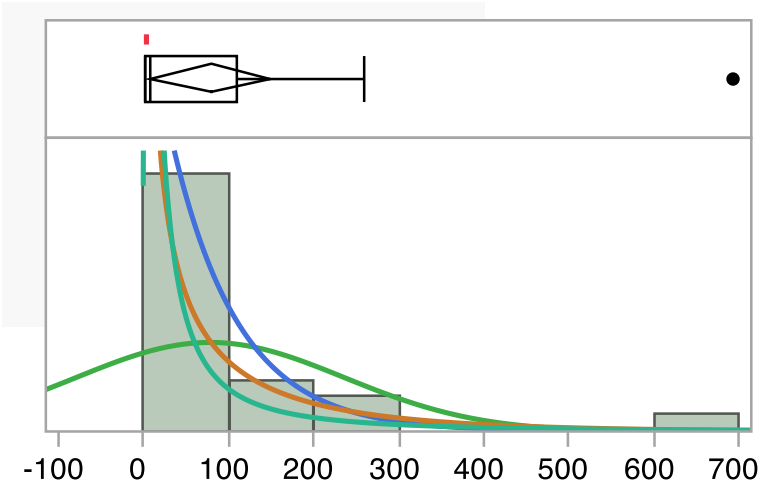
Underlying Distribution for Heat Inactivation



Fitted Normal Distribution for Heat Inactivation

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Location	μ	75.565217	0.3194987	74.939012	76.191423
Dispersion	σ	1.5322618	0.1887697	1.2035598	1.6657157

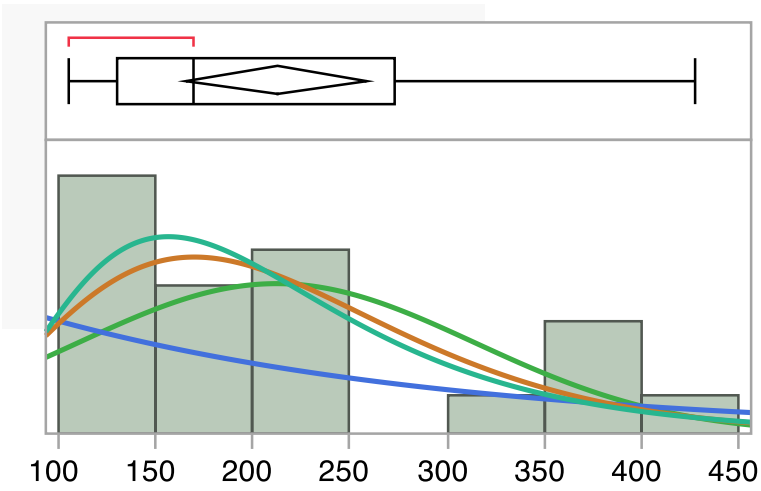
Underlying Distribution for Incubator Unloading, Labeling, and Batching



Fitted Lognormal Distribution for Incubator Unloading, Labeling, and Batching

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	μ	2.6170415	0.416844	1.7630458	3.4710372
Shape	σ	1.9551718	0.2947532	1.4939962	2.7132701

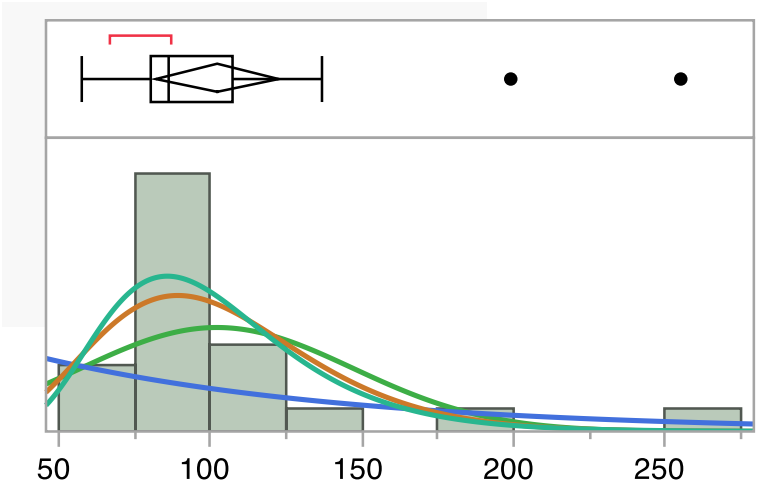
Underlying Distribution for Transport to Biodesign B and Accessioning Wait



Fitted Lognormal Distribution for Transport to Biodesign B and Accessioning Wait

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	μ	5.2550143	0.0977635	5.0542953	5.4557333
Shape	σ	0.4480086	0.0691292	0.3403706	0.6270699

Underlying Distribution for Accessioning, Aliquot, and Wait Times



Fitted Lognormal Distribution for Accessioning, Aliquot, and Wait Times

Parameter		Estimate	Std Error	Lower 95%	Upper 955
Scale	μ	4.5628523	0.0706506	4.4181093	4.7075053
Shape	σ	0.3313803	0.0499575	0.2532161	0.4598698

Chapter 7

The Making of a COVID Lab

Creating a Documentary Film Entitled “Let’s Go Save Some Lives”

Authors/Creators: Sierra Bardfeld, Joriel Cura, Nikhil Dholaria, Hannah Foote, Tara Liu, Julia Raymond and Mahima Varghese

Submitted in fulfillment of requirements for the honors baccalaureate program of Barrett, The Honors College at Arizona State University

Thesis Director: Professor Carolyn Compton, School of Life Sciences

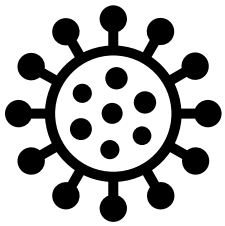
Faculty Leader: Documentary Film Group: Professor Nita Blum, Sidney Poitier New American Film School

Subject Matter Experts: Stephen Filmer, ASU Media Relations and Strategic Communications; Sandra Leander, Media Relations at ASU Knowledge Enterprise; Amy Pate, Teaching Innovation Center for the School of Life Sciences

August 2020 – May 2021

The documentary film made by this group can be viewed here:
youtu.be/QKoko2QZIMM

The AZ PBS news segment devoted to this documentary can be viewed here:
azpbs.org/horizon/2021/06/asu-lab-stepped-up-to-help-az-through-the-pandemic/



Section I: Through the Lens of the Documentary's Editor

Author: Sierra Bardfeld

Ever since my freshman year at Barrett, The Honors College at Arizona State University,my ultimate goal for my thesis project was to produce a documentary where I could shine light on important topics and share my findings with diverse audiences through visual storytelling. Out of all the aspects of filmmaking, post-production editing is my favorite, and I feel fortunate to be able to utilize my expertise to be the editor of the Barrett thesis documentary titled, "ABCTL: Let's Go Save Some Lives." The film tells the story of the ASU Biodesign Clinical Testing Laboratory, the first lab in the western United States to offer public saliva testing to identify the presence of COVID-19.

Throughout the Fall2020 and Spring 2021semesters, I have had the chance to collaborate with other honors students and my thesis director Dr. Carolyn Compton, a professor in School of Life Sciences at Arizona State University and medical director of the Biodesign Institute, to create a captivating film that illustrates the development of the groundbreaking ASU-SARS-CoV-2 Saliva Test. When I discovered this unique opportunity, it immediately captured my interest as it is not only an opportunity for journalism and film students, but it is a way to apply my creative storytelling methods to produce a stimulating documentary with individuals of all diverse backgrounds and skills about a time that will resonate with us for decades to come.

As the documentary's editor, it is my responsibility to ensure the film's storyline flows. Since the purpose of documentaries is to educate audience members about a particular subject, it is also essential I incorporate truthful information. The research for this creative thesis project was conducted with assistance from the ABCTL, its contacts and through the documentary's interviews. I attended all interview sessions during the production process, which is very beneficial for the editing process as I was fully able to learn about the lab and each of the subject's specific experiences on a more personal level. These interviews allow audience members to be introduced to the individuals who have played an imperative role in the lab's progression. The interviewees include:

1. Dr. Carolyn Compton: Medical Director of the Biodesign Institute at ASU
2. Dr. Joshua LaBaer: Executiv Director of the Biodesign Institute at ASU
3. Joseph Miceli: Project Manager of the Biodesign Institute at ASU
4. Morgan Nelson: Quality Analyst of the Biodesign Institute at ASU
5. Valerie Harris: Assistant Director of the Biodesign Institute at ASU
6. Brianna Ungaro: ASU Nursing Student/Volunteer for the Biodesign Institute at ASU

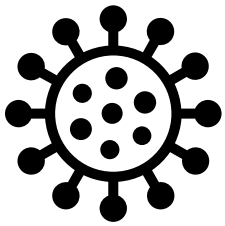
From the interviews, I was able to obtain valuable information, especially from the medical professionals in the field such as Dr. Carolyn Compton and Dr. Joshua LaBear. Acquiring authentic information regarding the ABCTL, its development of the saliva test and its current state through these interviews provided me

with the necessary skills and knowledge to effectively incorporate the research into the film. The interviews were captured by Joriel Cura, my partner and director of the documentary, on his personal camera. Joriel and I worked together throughout the interview process in order to ensure we were getting all the content we needed, especially for when it came down to editing and putting everything together on an extensive timeline. The specific interview questions include:

1. What is your name, title and role at the ABCTL?
2. Can you please describe the successes and challenges in creating a clinical testing laboratory in response to theCOVID-19 pandemic?
3. What did it take to create such a laboratory?
4. Why is testing so important?
5. How has the ABCTL helped with the testing process?
6. What are the next steps?
7. After this pandemic, what do you envision the ABCTL doing?
8. If you had to describe the reason for the success of the ABCTL in one word, what would it be and why?

After the production process, the team and I went through an immense amount of content, including interviews, transcriptions, data-driven research, B-roll, sound bites, music and graphics. I organized the footage, timestamped specific points and located certain segments of the videos that the team would want to include in the final version. Throughout the past two semesters, I have accumulated video footage, interviews, data and other necessary materials to ensure I am on track and staying up to date with the research before the thesis defense on Thursday, April 22, 2021, from 6 to 8 p.m. The documentary's film premiere will serve as my team's overall thesis defense.

Besides being the film's editor, my role for this project has largely been defined by teamwork. My teammates and I have consistently worked together—whether that's on Zoom or in person—to utilize the information from the other ABCTL teams and incorporate that research into a compelling documentary. The other teams include honors students who examine the lab from the business, communications, quality management and training, information technology, law and laboratory analysis perspectives. It has been an honor to collaborate with motivated and well-rounded individuals who have allowed me to branch out and further my interest in using digital media as a medium to educate. The connections my team and I have met along the way have made this film to be as powerful as it is. As a Barrett senior concluding my academic and personal journey at Arizona State University, working on this thesis has made my final semester rewarding and worthwhile. It has been an invaluable experience participating in a documentary project based around the COVID-19 pandemic and the steps ASU and the Biodesign Clinical Testing Laboratory are continuing to take to combat the virus. I am fortunate to not only be a part of history, but to document history and share the story of the ABCTL with diverse audiences across the world. ■



Section II: Documentary Learning Experience

Author: Joriel Cura

Creating the documentary "ABCTL: Let's Go Save Some Lives'" was a massive effort that could not have been done without focused and compassion-fueled collaboration. It truly was a team effort and it was personally inspiring to witness my team members, who hail from so many different fields of study like journalism and life sciences, bring their unique talents and experiences to the table. Their skills helped drive this project forward and I am super appreciative of that. With all that said, it was an incredible honor and experience to lead this team as the director of the documentary. Overall, my duties as the director revolved around guiding the team through the three principal stages of production (pre-production, production, and post-production) and helping craft the encapsulating themes and aesthetic of the film. Again, this documentary could not have been done without meticulous collaboration and laying out our process of production shows evidence of that.

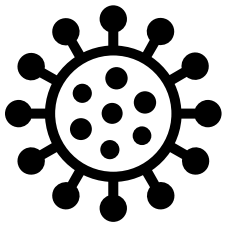
In terms of pre-production, I directed most of the storyline in terms of deciding how we wanted to structure the documentary. In the end, we decided to go for a three act structure which ordered out as follows: 1). The conception and early beginnings of the lab. 2). The current state of the lab. 3). The future ambitions of the lab. In this way, we hoped to express the story of the ABCTL lab through a "past, present, and future" lens. In each of these acts, I worked with the team to determine the exact content and topics that were to be covered. For example, in Act 1, or "the conception and early beginnings of the lab", we found it best to include topics such as why testing is so crucial especially in terms of stopping the spread of the COVID virus, the need for testing in Arizona and specifically ASU, and the various federal-law-related and ethical hurdles that the ABCTL faced in building its lab and distributing testing. Once we had crafted this storyline, I worked with our writers and producers to determine potential interviewees for the different subject matters in each act. After that had been accomplished, I again worked with our writers on creating interview questions to ask the interviewees. These questions served as a steady baseline and script for how we would order and structure the content of our documentary moving forward. With our interviewees locked and our script/questions ready, we were ready to move forward with production.

During our production phase, the majority of our filming consisted of gathering interviews. As the director, I made decisions such as filtering which questions we would ask during interviews as well as being present for each interview to communicate with the interviewees our goals and vision for the documentary. In addition to being the director, I also picked up director of photography duties. With that, I brought along our camera equipment for each interview shoot and handled the camera during shooting. I worked alongside our producer, Hannah who was also our audio technician, to procure visuals and audio for each interview. At times, when there were extra bodies to handle the camera equipment, I would also take leads in conducting the interview and asking our interviewees questions. Overall, the production stage of the documentary was extremely enlightening in terms of learning more about the efforts of the ABCTL. Being able to hear about the inner workings of the lab from the organizers themselves such as Dr. Compton, Joshua LaBaer, and Valerie Harris were immensely helpful in sharpening our story in a more concise,

but substantial way. Other notable interviewee subjects included Brianna Ungaro, a student from ASU’s Edson College who gave us insight into the efforts of student volunteers in SeoSurvey Testing. With production a success, we moved towards completing the documentary in post-production.

Post-production was probably our most strenuous, but rewarding effort. In post-production, my role as the director consisted mainly of guiding my editor Sierra in stringing together the interviews in a cohesive, sensible, and powerful way. Furthermore, throughout the many editing sessions Sierra and I went through, we also managed to secure B-Roll footage through various news and media sources such as Statepress and ASU’s media relations department. With our interviews ordered according to the three-act structure previously mentioned, Sierra and I planted B-roll throughout each act to give visual support and emphasis to the interviewee’s words. This combination of B-Roll and interview clips, paired alongside carefully-curated music that matched the different waves of feelings in each act, helped to cultivate our documentary’s overall narrative and aesthetic. The last few bits in the post-production stage consisted largely of creating graphics. With that, our producer Hannah, who is also a graphic designer, created various graphics including our intro title card. As for me, I also created graphics such as the various titles introducing each act as well as the end credit graphics. We decided to create simple, but colorful graphics to match the softer feel of the documentary.

In summary, my role as the director of “ABCTL: Let’s Go Save Some Lives” consisted of guiding the creative goals and visions of the film as well as building the larger framework of our narrative. As I mentioned earlier, this project could not have been done without the collaboration of my teammates and I, and to them I owe all my gratitude and awe. ■



Section III: My Transition from Student to Scriptwriter

Author: Nikhil Dholaria

As part of the ASU Biodesign Clinical Testing Laboratory film team, my specific role stands as a scriptwriter. Though I would describe myself as inexperienced in the creation of film, I have had experiences requiring interviewing and creating stories which makes me suitable to take on such a role. Nevertheless, I do have some experience in using and manipulating cinematography "on field" while utilizing editing software "off field." These are specific skills that I have gained in the past and am currently (and will continue to) incorporating them into the creation of this documentary film. While we were "off track" last semester, I still think my time with Professor Filmer brought these skills back to life. Originally, I had planned to delve into the role psychology plays in creating a diverse, interdisciplinary team ready to address the COVID-19 pandemic locally, and by means of the film, nationally. What I wanted to capture was the group collectivity and the requirement of professionals of all fields to band together and create a saliva test that is more comfortable than the nasopharyngeal swab test and has a much quicker turnaround time to deliver test results. I wanted to capture that the creation of such a test and the response to such a health crisis does not solely rely on the work of medicine and science, though still quite helpful. Instead, I wanted to show how this work is interdisciplinary, requiring the knowledge and wit of multiple professions at ASU.

Even though this was my original Thesis Prospectus, I still do believe that these are important concepts to address in our current process of film creation. I have recommended my ideas to the team and everyone does seem on board. From here, I, along with the other 2 scriptwriters, drafted interview questions. While the other 2 did create notable interview questions that were specific to the role of the interviewee in the creation of the ABCTL, I tried to create more general questions. These general questions indirectly frame the interviewee's response to capture the "bigger picture" (as I call it) of this story. It captures the "why" of everyone in being committed to create the ABCTL to "go save some lives." It captures the highs and the lows and essentially, what it takes to respond to a health crisis like COVID-19.

We are still in the beginning of the production period and are making advances in obtaining interview footage. Soon after, I believe that we will (individually and collectively) go through already accessible footage and decide if and how we can implement it into the final documentary film. I did go to an interview and was able to ask questions to the interviewee and we have a few more to videotape. Following this and the assortment of pre-existing footage, we may determine if there is anything else to capture on film to tell the story.

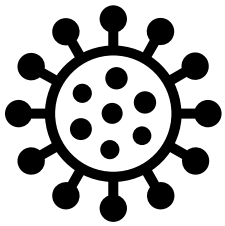
So far, it may seem that my role in the film team is very all over. While my official title is "scriptwriter" and my formal role includes generating interview questions and storylines, each member of the film team acknowledges that the work is much more collaborative than being strictly confined to our roles. For that reason, we all decided to work together to create a tentative division of the film into parts for better organization and flow – this was made to accommodate to a lay audience. Additionally, brainstorming

ideas to incorporate into the film is largely based on collaboration, as opposed to assigning one person the work. I can admit that we have not been too busy yet, but I anticipate us getting much busier as we finish interviewing and transition into the editing stage, which I also think that I may be able to aid in.

While I have little experience in post-filming work (mainly just personal projects), I do believe that I will have some sort of role in helping the editor. There are a lot of videos to peruse through; it would be in our best interest to divide up the videos and timestamp certain points or to collectively find certain segments of the videos that we would want to include in the final project. Regardless, this too becomes a collaborative style of work. Our roles may have us commit to certain tasks, but the major tasks in film-making require all of us.

While I have listed many of the roles and responsibilities that I have (many of which contribute over to other positions in the film team), I think it is also important to address this project as a consistent learning experience, which feeds into the quality of work that we do. From my experience insofar, I believe that the first semester (though not much filming went on besides for Professor Filmer's work) was dedicated to being introduced to the topics of storytelling, narratives, journalism, and film. Professor Filmer underscored the importance of capturing the human experience of stories, as it enables a diversified audience to connect more easily and understand the "bigger picture" – which in this case is the sense of collaboration and community in addressing the COVID-19 pandemic in Arizona. Our weekly meetings with Professor Filmer invigorating my passion to listen to the stories of others, and this has directly translated into my role as a scriptwriter. Writing the storyboards and creating interview questions are embedded with my propensity to include the humanity aspect of the ABCTL. A student in the first semester, I have now transitioned to a scriptwriter and filmmaker to the second.

With the "data dump" documents that the team has collectively created, I think that we are making progress to finally take the preproduction material and create a documentary film. My role is still strictly scriptwriter, but I know that my responsibilities are much. The number one responsibility being towards the team, since this is largely collaborative. Besides my technical roles of the scriptwriter, my role in this team has been largely defined by the team. We are continually working together, whether via zoom or occasionally in person, to utilize the information from the other teams in the project and organize it into a documentary film portraying the successes and challenges, and most importantly, the unique humanity and interdisciplinary action required to responding to a national health crisis like COVID-19. ■



Section IV: Producing a Documentary Film

Author: Hannah Foote

As the producer of our documentary, I focused on making preparations and plans for our team to be able to successfully carry out our artistic vision. I set up and organized all of the logistics to make it possible to shoot outside the Biodesign Institute and interview prominent members of the laboratory and ASU community. With a background in journalism, I focused on determining who our team should reach out to interview and worked alongside everyone to create a strong, clear artistic vision. We created multiple documents to collaborate that allowed us to be prepared for every interview ahead of time. I also took care of the audio production of the film, a new skill I learned on the spot, and created illustrations and graphics to aid the visual elements of the film.

I think, as a whole, everyone on the team had an exciting opportunity to learn new skills and work alongside people with different levels of experience and coming from different professional and academic backgrounds. I truly believe that this was a great example of the interdisciplinary work that the Biodesign Institute is known for. Our team consisted of people with medical, journalism, film and other experience. Working with this team of diverse skill sets was essential in our success. We learned a lot from each other along the way and took every chance to demonstrate the community focus of the laboratory and the impact it had.

Our vision changed a lot over time depending on what was accessible and realistic for us to carry out with such a short deadline. We wanted to focus on the fact that the Biodesign Institute reinvented itself to develop COVID-19 testing efforts from researchers, medical personnel, organizers, volunteers, lab workers, and countless other professionals to ensure quick turnaround times in a time of desperate need for high speed testing with accurate results.

The lab was able to turn around results within two days and adhered to Clinical Laboratory Improvement Amendments (CLIA) and Food and Drug Administration (FDA) regulations and approvals. With this in mind, our team went in hoping to display that one of the only consistencies the laboratory could truly rely on has been facing obstacles. The hurdles the lab has jumped to continue being successful in an already stressful time continue to demonstrate the medical leaders' ability to move forward despite consistent challenges. The lab's impact stretches farther than our ASU community. With local and national outreach, ASU Biodesign Institute has done nothing short of reducing COVID-19 cases and deaths, with their ultimate goal to "save lives."

Our initial goal was to section the film out by how the lab started, what barriers there were, and how they overcame those barriers. What we did not understand right off the bat is just how many different challenges they faced and overcame. We ended up sectioning it off with more attention to detail in order to include specifics for each subgroup that the non-film teams focused their research and planning on. This came to include legal, medical, technical, supply chain, and other challenges. With this goal in mind,

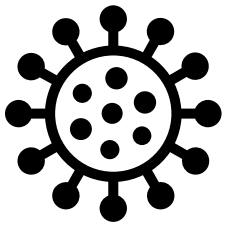
we were able to put together some of the larger accomplishments made by the lab and the amazing team that has supported them, despite consistent obstacles.

As the producer, I helped see these visions through and worked with the entire team to ensure our creative goal was accomplished. We were truly successful because it was a large effort from a multidisciplinary background. Without all of the expertise and knowledge from different fields, our takeaway would have been far more narrow and less developed. By putting together all of these pieces, we were successful in being able to illustrate for our audience just how big of an effort these testing efforts were and are. They took a lot of people to do it and they saved a lot of people in the process.

I personally started with the communications team and was transferred over to the film department rather quickly. Having been in both of those meetings at some point, I recognized how vastly different but crucial all of our roles were. We had to use contacts and knowledge pulled from every team to be able to put this all together. The hardest part, from my perspective, was overcoming a lot of the challenges that COVID-19 placed not only on the lab, but also on our film team.

There were a lot of limitations that were unique to our filming experience because we were filming a documentary about COVID-19 in the middle of the pandemic. This meant that many indoor areas were off limits for gathering original footage, most of our communication with sources happened virtually until the final interviews, and we had to make sure we were holding ourselves accountable as a team in conducting our storytelling in safe, permissible ways. Since our interviews were conducted on ASU campuses, our permits were outdoor only and some of our creative decisions were made for us, like the requirement of our interviewees wearing a mask at all times and the limitations for where and when we could shoot.

Under normal circumstances, we would have been able to make more artistic decisions with these processes, but we focused that creativity onto what we did have control over. This became crucial in the way we conducted interviews, incorporated footage from the Biodesign Institutes’ PR team, allocated news media resources to aid the storytelling, developed original narration, and edited the entire documentary together. Because of this, we were successful in creating a compelling and honest narrative showcasing the Biodesign Institute’s contributions to saving lives during the pandemic. ■



Section V: Learning the Art of Storytelling

Author: Tara Liu

Film is a perfect way to encapsulate a compelling story of how the ABCTL was created, and how it impacted the community and beyond. I have always found the process of filmmaking remarkable because of the intersection between visual arts, storytelling, and audio which creates an experience that reaches the audience, whoever it may be. Storytelling is an art on its own, and the overlay of visuals and audio makes documentaries a one-of-a-kind art form that I was compelled to be a part of. As part of the ASU Biodesign Clinical Testing Laboratory film group, I am tasked as one of the scriptwriters of the documentary. I have previous experience in the visuals department where I had designed a website for a nonprofit organization. This experience cultivated my interest in art, especially visuals. At the start of this film process, I considered myself a beginner in the realm of filmmaking. However, through the experiences of planning, filming, and my past positions, I have gained a substantial set of skills that I can apply now to current projects and works in the future.

Originally with Professor Filmer, each team member was responsible for a specific part of the film. I worked individually on the business part of the film. For example, I created a prospectus focusing on the supply chain of the ABCTL Lab and the need for resources to run a successful clinical testing lab. Through multiple meetings on zoom, I learned about the extensive history of the lab to get a better understanding of the role of the ABCTL in Arizona State University and the community. I reviewed the work of the business team to learn about the background of the supply chain and the repository of resources that funded the lab with the intent of taking on the business section of the film. Also, I attended the meetings where the process of filmmaking was taught. Additionally, the large group meetings were beneficial because they updated everyone on the current progress of different teams. The team was set to reconvene after everyone finished their portion of their research. For example, another team member focused on psychology during the pandemic. This direction was drastically different from mine. Having different study areas was intentional because we wanted a film that covered a diverse set of topics. Once everyone was done, we would then combine our research to gain factual information to create the film. Importantly, the first half of the project was dedicated towards preparing for the film. Filmmaking requires many skills to create a cohesive film. It was important for me to fully understand the approach to filmmaking. The first semester was spent learning about the techniques to filmmaking, and the next semester was dedicated to executing the film.

The second semester was spearheaded by another team of talented leaders. I have pitched my ideas to the team from my prospectus, and we discussed the compelling parts of everyone's research from the first semester. The next step consisted of drafting the top ten areas from each sub-group to include in the film. I attended meetings with Dr. Compton and fellow members to whittle down our top ten list and to receive a comprehensive review on the history of the ABCTL.

Moreover, I helped the team come up with a list of interviewees we wanted to talk to. To kick start the interviewing process, two other scriptwriters and I created questions to ask for our film. I was in charge of coming up with questions that were more specific in topics and were unique to each individual who had a major role in the success of the lab. I researched the biographies of two of the interviewees to align my questions to their experiences. These questions highlighted everyone's diligence and dedication in running the ABCTL. I also asked questions along the lines of the challenges they have faced while running a saliva Covid-19 testing lab. For example, I asked about the importance of their role and the testing at ASU and at a larger scale and the hurdles they had to clear when they were presented with a problem. After finishing the list of final questions, we were "on field" interviewing the guests. We met at ASU Biodesign near the C building to interview our guests. I attended 4 out of the 6 interviews due to conflicts in my class and work schedule. I was tasked with asking the questions to the interviewee, setting up the mic, and cleaning up.

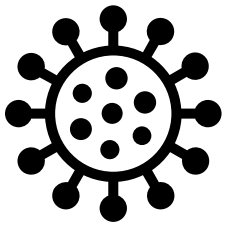
Although we each have a role, our responsibilities vary, and we are not confined to strict limitations. On top of screen writing duties, I have scheduled multiple zoom meetings in the brainstorming phase of the project. The team meets every week, usually on Saturdays. During these weekly meetings, I would share documentaries that I have enjoyed, and specific techniques that were used to convey a message. I watched more documentaries for the sake of this project to understand the format of this kind of film. For instance, reenactments were used in the film "Social Dilemma" on Netflix which helped portray the effects of social media on the polarization of America. I hope to implement reenactments to show the inner workings of the lab. Additionally, I am currently working on reviewing the b-roll footage and categorizing them into the themes we have brainstormed together. Some of these clips do not have audio, so we must overlay music and quotes to create a cohesive documentary. Dr. Filmer has given us a head start by capturing multiple processes varying from receiving a test to pictures that depict the inside of the lab which are extremely useful for the film. On multiple weekends, I met up with the team to review the b-roll footage to gain a better understanding of what visuals we currently have and what videos we need to shoot in the next few weeks to fill in the gaps. We realized that the only interviewing clips we had were over zoom. This prompted us to figure out interviewing schedules to get high quality footage for our film. Over time, I worked more with my team members to plan for the filming process. At first, we researched by ourselves, and progressively, we began to collaborate more and share ideas with each other to proceed in the project. We switched from individual work to a more collaborative environment from the first semester to the second semester.

Afterwards, I have developed an outline with the team that clearly breaks down the portions of the film into different themes: the past, the present, and the future implications of the Covid-19 testing lab. I used the top ten list that we have dwindled down earlier to create a clear outline. These topics organize the film to portray how the lab transformed into a saliva testing lab with the accommodation of more equipment, supplies, and volunteers. The storyline also streamlines the plot of the film and organizes our thoughts into a clear and concise manner that makes it easier to understand when formatting the documentary. I helped brainstorm conclusions and introduced ideas to the film and collaborated with team members to determine the best way to present the information we have gathered over the course of the semester.

Notably, I enjoy having a variety of duties that are not limited to one set of roles because it allows me to explore the world of filmmaking more. I have shadowed and assisted the producer and the director as they set up their cameras at different angles to obtain professional shots. Having a flexible role has been helpful when I want to explore different positions within filmmaking. Once we have finished filming, post production events such as editing will finalize the entire documentary. I plan to work with the editing team to learn more about the techniques as well as the process of editing for a big documentary. Although I was named one of the scriptwriters, my role encompasses more duties than a general scriptwriter has on average. I helped write the voiceover and credit scene and assisted the editors when needed. This allows me to explore different avenues of filmmaking which gives me a more comprehensive look into the overall picture of the art form. As a biological sciences major, creative projects are rare, and this Barrett thesis

opportunity allows me to explore a different academic pursuit. It combines art, medicine, and storytelling into one where the final product can help thousands understand the importance of testing. With more people receiving tests, ASU can alert the people who have tested positive. Then, people are aware of their positive status and will be cautious about going out. This will prevent the spread of the Covid-19 virus.

This documentary is more than just a thesis project for me. It opened so many avenues into art that I have never thought of before. I have learned over the two semesters that storytelling is a humbling experience because people are vulnerable enough to share their experiences during a stressful, uncertain time. From the insight of lab leaders to students, the film highlights the experiences of the community and the people that surround us. I find many similarities between medicine and filmmaking. First, both need practice. Over many years. Improvement is possible in both areas. Second, they are both based on science and factual evidence that serves the community in different ways. For example, medicine is founded on scientific discoveries where filmmaking is built from the research of past events. Lastly, they depend on an agreed collaboration between many parties. For medicine, an agreement between the physician and patient is necessary. For storytelling, a conversation between an interviewer and the interviewee is needed. Teamwork is the key for medicine and filmmaking and I am humbled to get to experience both. There is no better way to serve the community through a film. ■



Section VI: Journey of the ABCTL Documentary

Author Julia Raymond

Working with the ABCTL was an experience that I never thought I would have the opportunity to be a part of. As a junior studying biomedical sciences, I was under the pressure of figuring out my thesis in order to graduate with honors. I was lucky enough to receive an email to interview for a role to work with Dr. Carolyn Compton. There was little to no information provided as we were caught in a pandemic that was under constant change. I interviewed assuming I would get a role to work on the science side of the project but when I got the news that I was accepted onto the documentary team I was so excited for this new learning experience. Our team was assembled of other biology majors, along with journalism and film. We had so many different minds working together and I think that is what made us so strong.

Going into this project, I had amateur experience in film. I was able to apply my work in producing videos for biomedical companies that demonstrated and promoted diagnostic products to medical practitioners and investors. I had worked with companies such as i-calQ, where I gained knowledge in the development and use of their mobile bio-diagnostic product for antibody COVID-19 testing and Iron Horse Dx on their ALS diagnostic test. Even though I had these previous skills, I knew I had so much more to learn.

Throughout the two semesters working on this project, we were provided a handful of professors who contributed their professional experience and advice to guide us through this process. We originally started with Professor Filmer who taught us about the importance of storytelling and connecting with an audience. He tasked us with picking individual stories that this pandemic has had an impact on. I chose to look at how minority groups have been disproportionately affected by Covid-19, their access to testing, and how the ABCTL would have a positive impact on their health. By doing this I was able to learn how to take a topic, turn it into a story, and find ways to impact the audience and produce emotions.

At the start of the second semester, we were introduced to Nita Blum. She was able to organize our group into roles that matched our unique abilities, from director to editors, scriptwriters, and more. She assembled our team and provided abundant advice on how to make this project as professional as possible.

I was given the role of assistant producer and knew this was going to be challenging but rewarding. As the assistant producer, I worked alongside the director and producer, Joriel and Hannah, to make sure all their needs were met to create this documentary. I set up our schedule and organized meetings for us to ensure we were always on track and aware of deadlines.

I acted as the liaison to the other groups and was their point of contact to compile all the information and documents we needed to contribute to our film. Each of the sub-groups compiled a "top ten list" of all of the most important topics covered by their subject area. We used this information and condensed it down

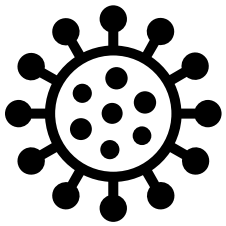
to give us the perfect path to follow for our documentary. Not only was I there for administrative support, but I was also able to be a part of the creative side and post-production. We all had individual roles but never missed an opportunity to work as a group. We had weekly creative meetings to set up our ideas for the documentary and outline our goals of what we wanted to accomplish from this project.

In order to have an idea of what we wanted our documentary to look like, we did extensive research by watching all different kinds of documentaries and getting a feel for the unique genres. We decided to focus on an educational film but still wanted to ensure the audience was entertained. After coming to this conclusion, we created our outline and decided to separate the documentary into three parts: the creation of the lab, the present face and impact of the lab, and the future of the ABCTL. Now that we had our rough ideas completed, we were able to start the hands-on creative work.

As a group, we made sure to all be a part of the filming and interviewing process. For me, this was such a valuable experience to learn about the camera setup and audio work. By the end of the semester, I was able to work with Sierra and Joriel to help with editing. We were lucky enough to gain access to large amounts of b-roll which came in handy to emphasize the points made by the interviewees. I was so lucky to learn new skills and techniques from them that I would have never done as a biomed major.

Although this was an incredibly enjoyable experience, there were challenges that we needed to overcome throughout the year. Due to the ever-changing status of the pandemic, guidelines were loose, and the future was unknown. As this was a creative project, we did not have a strict rubric to follow which created its own difficulties. Not being able to meet in person for the first semester caused a lack of connection and possible miscommunications about what was expected of us. Thankfully, with the amazing advisors and professors we were given and the bond between our group members, we were able to overcome all the obstacles we faced.

Being able to film the process of the Arizona State University Biodesign Lab and how it affected our community was a once in a lifetime opportunity. Working with Dr. Compton and the other 37 Barrett students on this unique thesis experience has been one of my favorite accomplishments. The skills I have gained throughout the last two semesters will forever hold value in my future work. From storytelling to filming and editing, this documentary is the perfect way to capture the incredible work of ASU and all the individuals involved in the ABCTL. ■



Section VII: My Role as a Scriptwriter

Author: Mahima Varghese

By March of 2020, Arizona began its fight against the highly transmissible organism known as SARS-CoV-2. As the state began to be engulfed by this lethal organism, leading to a geometric progression of cases, the ASU Biodesign Institute reinvented itself to build the only tool for controlling the virus at the time. The ASU Biodesign Clinical Testing Laboratory (ABCTL) developed a federally approved diagnostic saliva-based test (ASU-SARS-CoV-2), the first of its kind in the western US to test using saliva samples to rapidly detect the coronavirus in individuals who might have contracted it. The story of the creation of the ABCTL is more than extraordinary. It took the toil and tears of many including medical professionals, researchers, organizers, volunteers and many more unsung heroes. In today's world, educating ourselves about important issues and finding reliable information is critical. Documentaries, being a powerful tool in bringing such important topics to the table not only address the facts and important information but also bring a human face on topics that might seem unrelatable. Hearing the stories and experiences of real people who are involved helps the audience find an emotional connection with the topic addressed. The idea of creating a documentary to tell the story of the ABCTL was nothing but appropriate; helping bring together the factual and human aspect of the story.

The documentary team had initially geared towards focusing on various storylines, with each student researching on one particular topic. This initial path with Dr. Filmer as our mentor, was focused on creating separate videos by each student, focusing on the different aspects of the creation story, which would then be put together to create a "big picture" documentary. My initial prospectus with my topic of research was to pursue a line of inquiry about the mechanicals of creating and using the ASU COVID-19 Spit Test and to also delve into the backstory of some of the early adopters of the Saliva Test, specifically utility workers. More specifically, I was to investigate the challenges, logistics, and resources employed for the older Naso-Pharyngeal Swab test and how those problems were met with the development and adoption of the less invasive Saliva Test. I was also tasked with investigating the problems faced by utility workers early on during the pandemic such as working in tight spaces and in groups, and the challenges that led them to approach ASU for COVID-19 testing will be inquired into. Both the silos would investigate how it achieved the overall effort to create and deliver the saliva test. While both these silos are important topics involved in the story of the ABCTL and should be addressed in our current process of film making, this pathway taken however did not address the overall goal of the documentary team. Focusing in-depth about one particular topic within the lab could deviate the audience in understanding the main purpose of the documentary, which was to explain the story of the creation of the lab itself and what it took to create it. This unfortunately put us "off track" for one semester. However, while it did put us behind in terms of achieving our main goal, we as a team learned some valuable lessons. We were able to learn about some of the important people who are part of the project, attend some interviews of the people involved, and most importantly, gain a basic understanding of the story of the creation of the ABCTL Lab. Our weekly meetings with Dr. Filmer taught me to understand the emotions involved in every individual, and the

importance of collaboration in such huge projects. I learned that every media project is more than the facts presented, it is also about the human experience and emotions that they went through as they took on their roles.

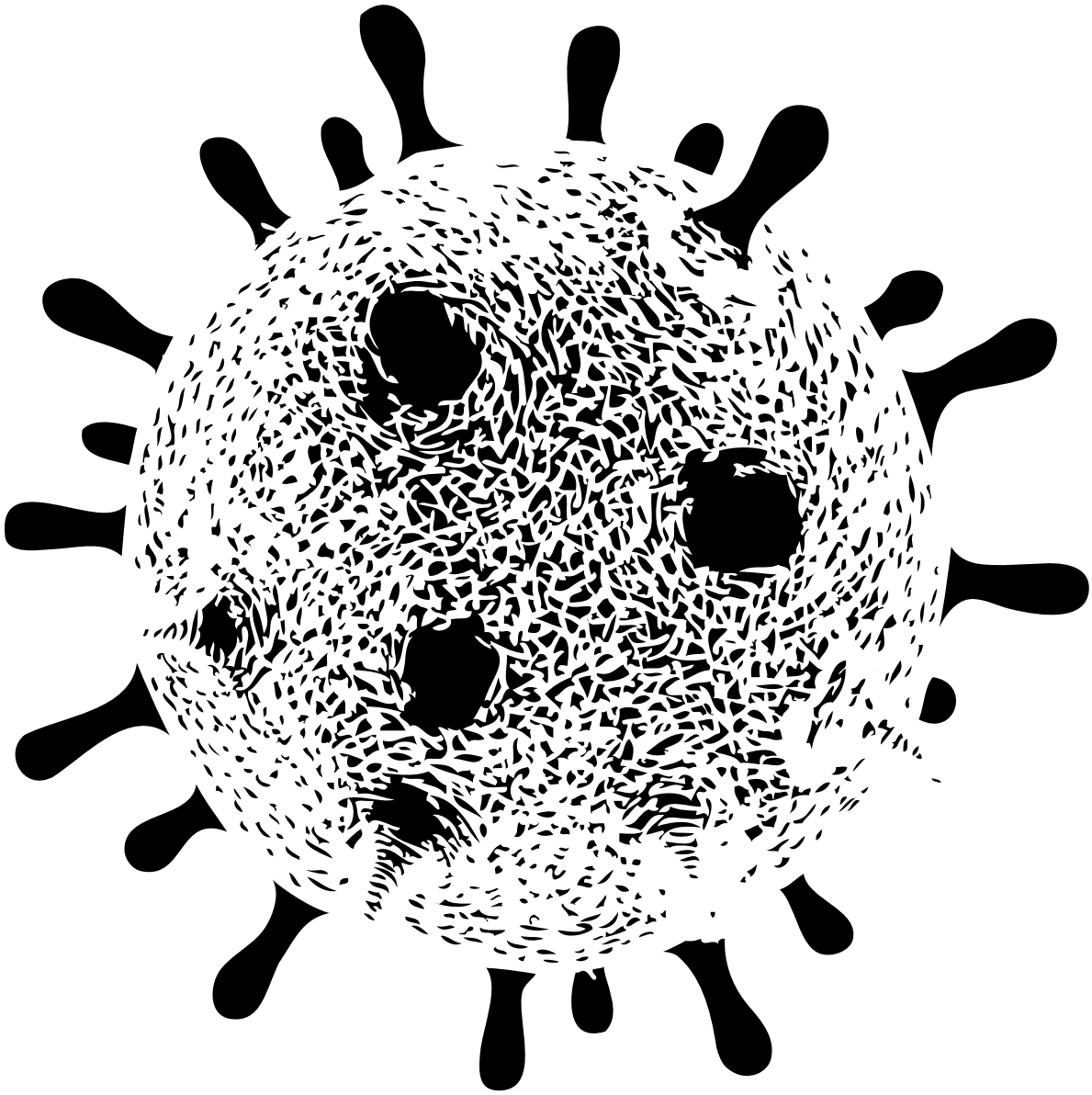
In January of 2021, the ABCTL documentary team had their first semester meeting to reconvene the group and set the main task of the team. We decided to once again touch upon the purpose of the documentary team and what our goals were. It was decided that our final project would be to create a documentary that inculcates the story of the creation of the ABCTL COVID-19 Testing Lab. To capture the story of an entire team that brought together and saved the lives of millions across the state is more than just extraordinary. Within the first 3 weeks of the month, we got new mentors to help us out, and we decided to delegate the tasks depending on our skills and areas of expertise. We labeled the positions as producer, associate producer, director, editor, and scriptwriters- with my specific role being a scriptwriter.

The art of storytelling is valuable regardless of what form of media is used. The words and tone captured can change the mood of the audience and the way in which they perceive it. It can ignite fire, create sorrow, and cause the audience to feel empathy, pride and so many more emotions that we want them to feel. A well drafted storyline can create an unfathomable power in sharing information. With such important aspects involved in storytelling, the role of a scriptwriter is nothing but crucial.

My role as a scriptwriter was completely new to me. While I do have experience in writing articles for school newspapers and yearbooks, scriptwriting for the purpose of creating a documentary was something I had never had experience in. The story of the creation of ABCTL is not simple, the intricacies of multiple people and the collaboration of multiple departments formed what it is today. As a scriptwriter, my role is to create a story line describing the creation process of the ABCTL. In essence, my task is to create a blueprint for the entire documentary, putting into words the visual masterpiece that will be seen by the audience. As a screenwriter, it is important that we know every detail and fact of the creation process. It is important that we know every person involved in the project, their role, who they are and what they did. In addition, we need to know the timeline of when things happened and create a timeline that we think would work for this documentary. It is not necessary that everything is presented in film in the order that it happened. At times, creating a unique timeline, one that is not sequential adds more drama and tells a better story. As a scriptwriter, along with 2 others, I have addressed some of the topics that I would like to cover in the documentary. One of the most important aspects of any media production, that I have learned from watching numerous documentaries and movies, is the angle in which it is told and the mood and tone in which it is presented. It was clear from the beginning that showcasing the drama and chaos of creating the lab was something our mentors wanted us to do. Our first task as script writers was to create a storyline that was specific to the details of the lab we wanted to focus on and inculcated the tone and mood of the documentary. While creating the storyline was a group effort, each of the scriptwriters had an important role to play in it. I addressed the importance of bringing in drama into the storyline by incorporating the chaos that was going on around the world and in Arizona with cases increasing, hospitals reaching full capacity, universities closing down etc. and how the world reached a standstill by March of 2020. We divided the storyline into 3 main parts: what we did, what we are doing, and what will be done; each part encapsulating the important aspects of the lab, while having an in-built timeline. As a scriptwriter, I am also in charge of researching all the important individuals we will be spotlighting in the documentary and preparing questions for interviewing based on their background. The script writers have created 4-5 specific interview questions, along with 2 general questions that capture the “why” of them being involved in the ABCTL project. I was mainly in charge of researching the background of the individual and creating the specific questions that helped understand the role of the individuals, what they achieved from their role, and how their role had changed as the lab continues to evolve.

We are currently in the stage of beginning production and finishing up interviews of people we want to highlight. My next task as a scriptwriter involves going through all the interview footage, transcribing the audio into text for easy access during editing, and putting together a final story line based on the footage and B-roll we have. I must address that all of this is a collaborative effort. While the scriptwriters do take lead in creating interview questions and the storyline, everyone else involved in the project also plays an important role in bringing out the story of the ABCTL. Apart from the scriptwriting role, I also undertake minor roles in assisting during interview set up and clean up, creating documents and files for specific tasks, emailing professors and mentors about specific questions that the group might have and other trivial but essential tasks that are involved in creating the documentary. I also took the initiative to develop a treatment plan i.e. a short description, that encapsulates the main theme we want to portray to our audience.

The duty I have undertaken in telling the story of the ASU Biodesign COVID-19 testing lab is nothing less than fundamental. It is an honor and a momentous task to showcase the impacts of the ABCTL in reducing the number of COVID cases in the state of Arizona. The hard work and sacrifice of numerous individuals to transform and build a certified clinical testing lab is beyond what can be expressed in a documentary. Yet, for the world to know about the story and the hard work of those individuals, creating a documentary is the least we can do to celebrate these individuals and their timely effort to save a state that was drowning with COVID cases. The emotions they went through, the challenges they faced, the highs and lows they went through, are all instrumental for me as a scriptwriter to reveal to the audience. I hope that the collaborative effort of my team along with other teams in the project will help in telling this unique story of the creation of the ASU Biodesign COVID-19 testing lab and celebrate the efforts of all that helped in saving lives across the state. ■



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