
L7INFORMATICS
Contamination
Source
Identification®
CSI-Dx™
Taking on the Pandemic:
Transforming Your Clinical Lab into a
COVID-19 Ready Lab
Using NGS + RT-qPCR

COVID-19 Data Challenges

COVID-19 response has demonstrated great advancements in
- Scientific knowledge at a molecular level
- Benefits of real-time epidemiology
- Positive use of mass communications

Reflecting on initial response:
- Initial testing response was built around government labs
- Subsequent responses were disjointed across suppliers and labs
- Assay platforms and reagent supplies were limiting testing

Challenges going forward:
- Testing capacity is still limiting
- Data is varied and imperfect
- Data is buried in siloed local systems

Next Generation Digital Platforms

Next generation digital platforms should be able to **provide better integration of the science, laboratories, health systems and data management**

- exchange for standardizing, adapting, and distributing testing methods
- interchangeable data model that make it possible to correlate different testing results with the epidemiological mapping
- modeling of virus movement and drift while integrating patient data vs outcomes would give us the opportunity to move into proactive response

Through our partnership with CSI, L7 has developed and qualified an integrated workflow for performing COVID-19 diagnostic testing

Contamination Source Identification® CSI-Dx™

L7INFORMATICS

Contamination Source Identification®

CSI-Dx™

BACTERIA

There are approximately 39 trillion bacterial cells living amongst our 30 trillion human cells.

DIAGNOSE

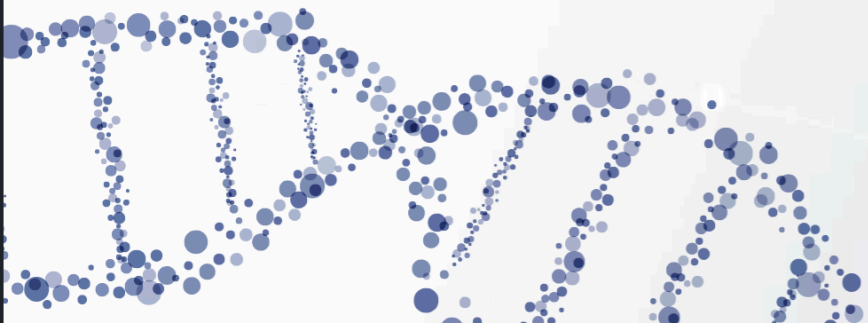
verb: to identify the nature of an illness by examination of the symptoms.

a : unique in kind or quality
b : unprecedented

DETECT

verb: to identify or perceive that which is hidden.

a : new and original
b : revolutionary



Diagnosis has always been at the heart of medicine.

At CSI, we are no longer diagnosing disease, we are detecting it.

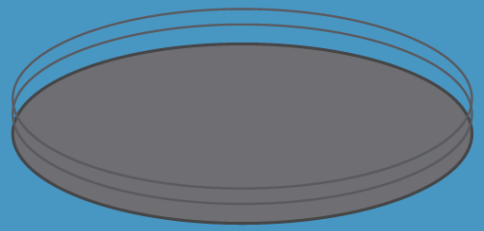
THE ~~GOLD~~ *brass* STANDARD:

exposed

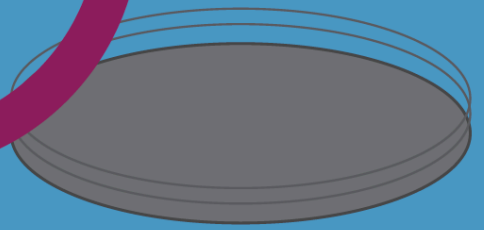
verb: to reveal the true nature of.

a : to make visible or uncover
b : to publically reveal

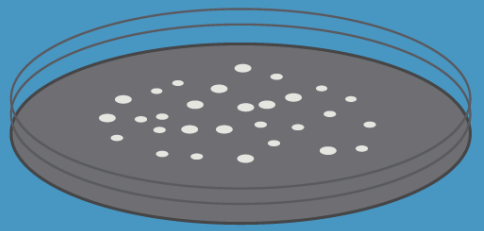
Up to 49% of sepsis cases are culture negative.



No Growth



Positive Growth



Patient

Whole Blood

Bacterial Culture

Culture Results

OUR SOLUTION

bleeding edge

noun: the very forefront of technological development.

a : innovative or pioneering
b : featuring new methods; advanced and original

Sample tracking throughout the process for fast, accurate results.

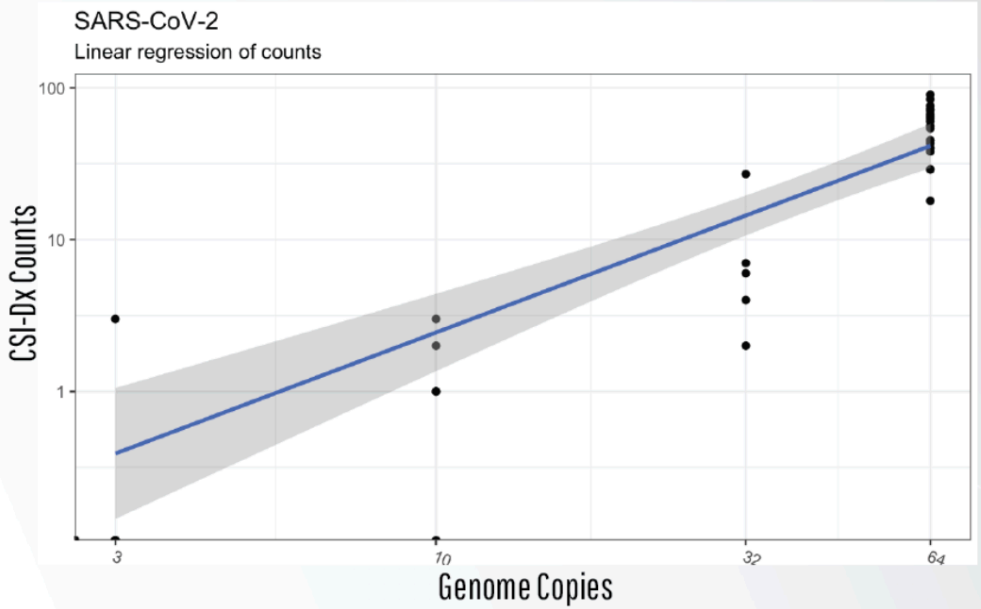
Patient → Urine Collection → Sample Processing → Sequencing → Analysis → Results

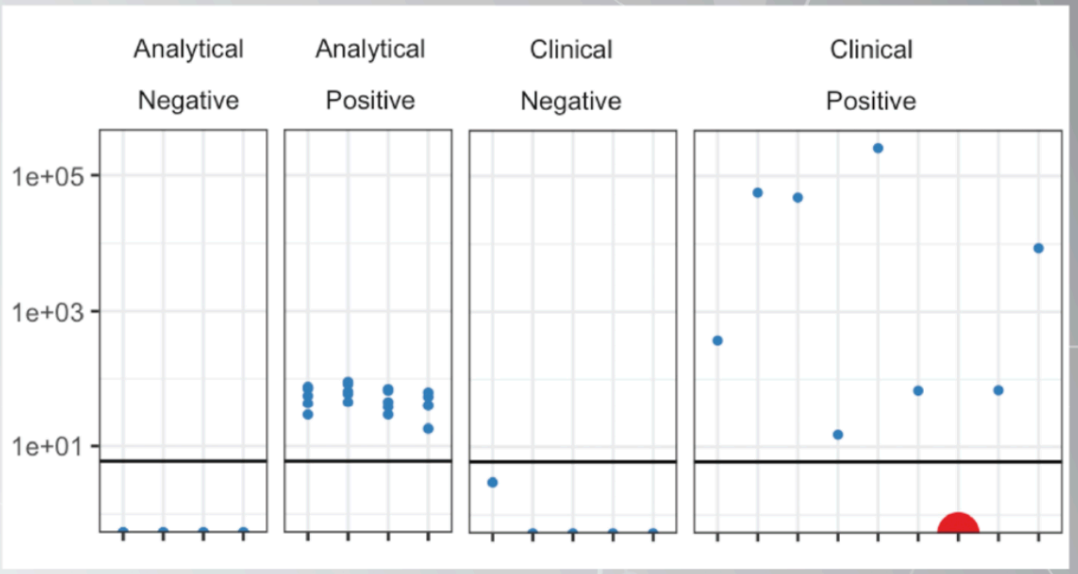
Proprietary bacterial amplification technique

Proprietary RAPID-Dx™ bioinformatic pipeline

CSI-Dx™ Solution

VALIDATION of SARS-CoV-2 Detection





LIMIT OF DETECTION

"Spike-ins" of known counts of SARS-CoV-2 genome copies were spiked into pooled VTM of confirmed negative COVID-19 samples at increasing concentrations:

LOD of SARS-CoV-2: 10-32 Genome Copies per µL

ANALYTICAL & CLINICAL ACCURACY

Analytical validation compares 20 confirmed negative samples against 20 negative samples "spiked" with SARS-CoV-2 at 2x LOD:

Analytical Sensitivity: 100% Analytical Specificity: 100%

Clinical validation assess the CSI-Dx result against qPCR results of clinical specimines:

Clinical Sensitivity: 89% Clinical Specificity: 100%

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CSI-DX Implementation Case Study

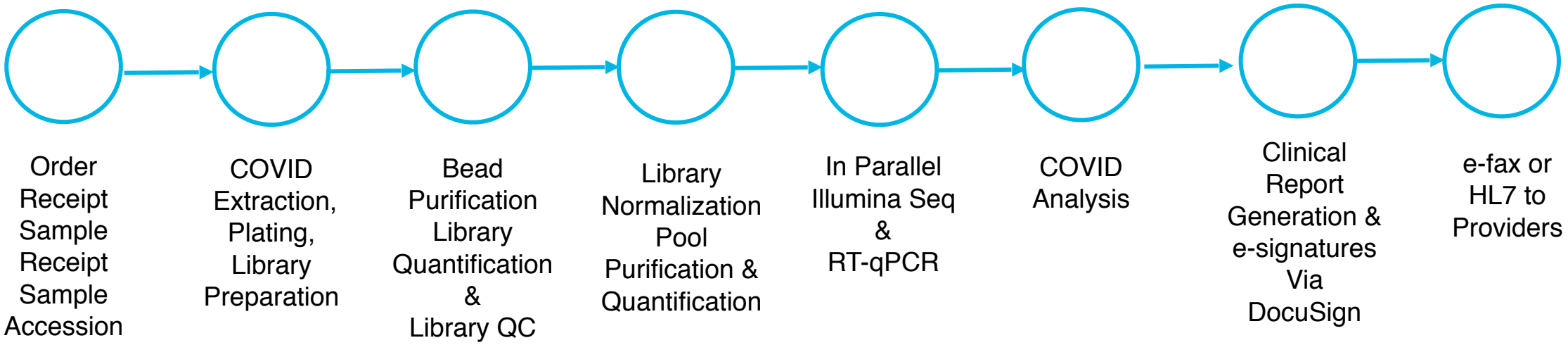
Using L7 ESP Platform

Contamination Source Identification®

CSI-Dx™

CSI-DX process for COVID-19 detection using NGS and RT-qPCR

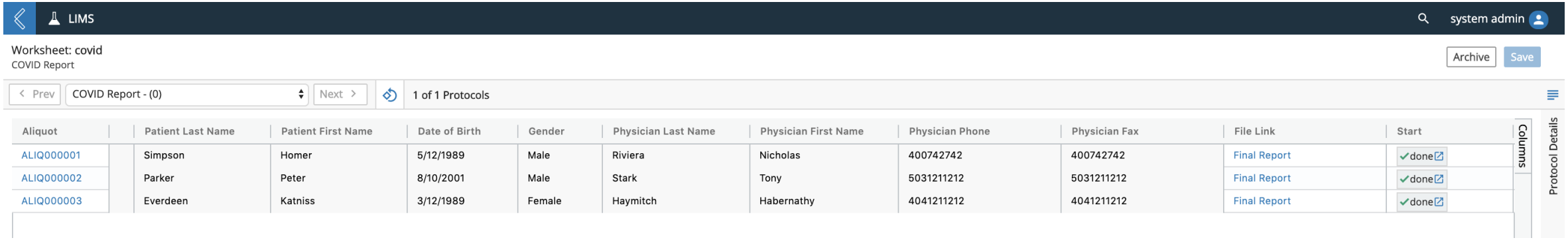
single platform to manage wet lab process, bio-informatics and lab operations



ESP CSI- Ordering and Accessioning Applet

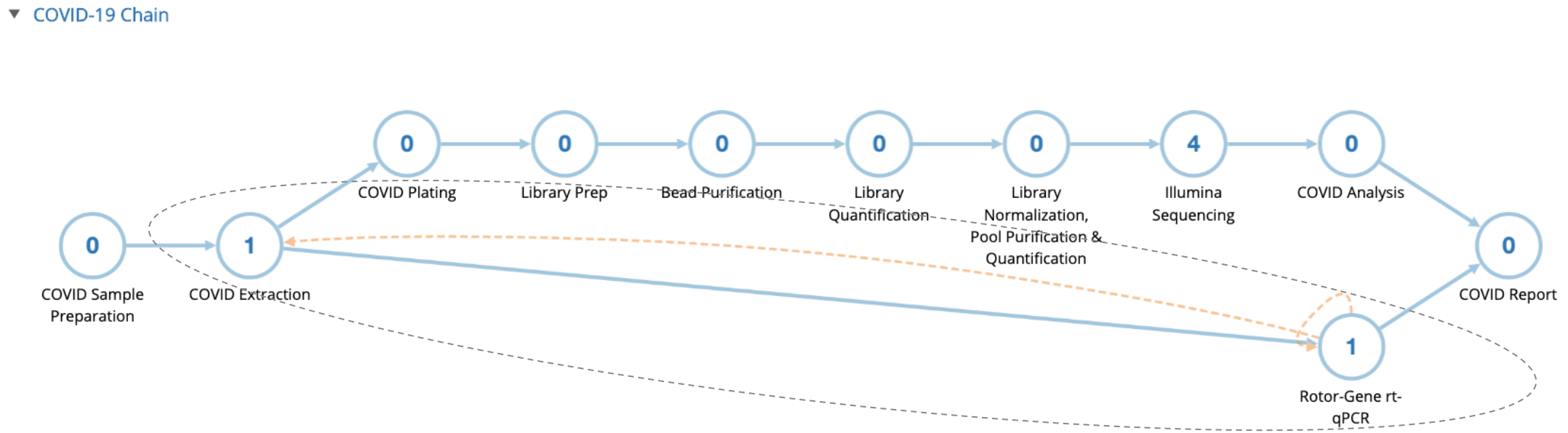
Description: bulk ingest of accessions (done by clinics/hospital). Hospitals log into ESP and upload a CSV file with patients/sample info.

Advantage: Moved accessioning responsibility outside of the lab. Lab users just have to confirm that the information entered matches the received physical/faxed copy and that the sample is in good condition.



Aliquot	Patient Last Name	Patient First Name	Date of Birth	Gender	Physician Last Name	Physician First Name	Physician Phone	Physician Fax	File Link	Start
ALIQ000001	Simpson	Homer	5/12/1989	Male	Riviera	Nicholas	400742742	400742742	Final Report	done
ALIQ000002	Parker	Peter	8/10/2001	Male	Stark	Tony	5031211212	5031211212	Final Report	done
ALIQ000003	Everdeen	Katniss	3/12/1989	Female	Haymitch	Habernathy	4041211212	4041211212	Final Report	done

COVID RT-qPCR branch

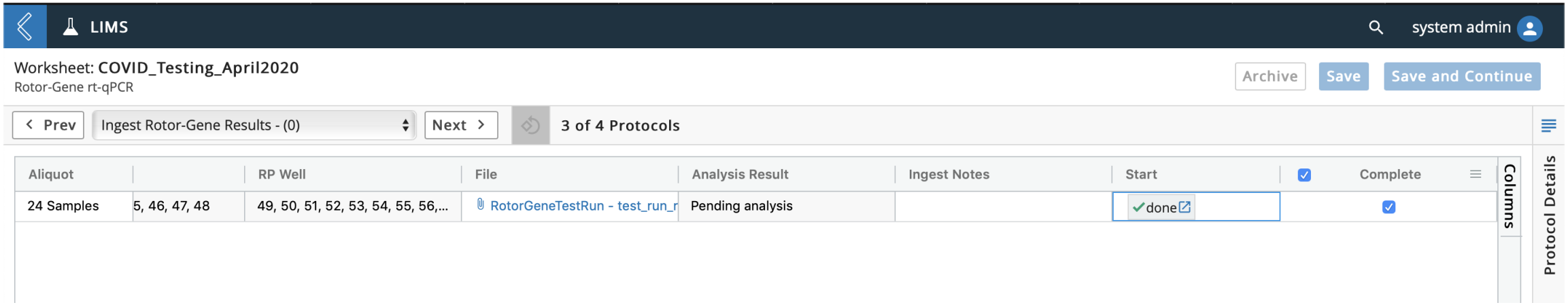


COVID RT-qPCR

COVID-19 RT-qPCR Bulk Results Ingest

Description: ingest results from RT-qPCR. Results for the 3 probes are mapped back to samples in ESP.

Advantage: No need to manually input data (i.e. reduced human error). Generated report can be printed and the heatmap can highlight contamination issues.



COVID RT-qPCR

Rotor-Gene Standard Report, 2020-04-03T16:23:40.573906

Expected Controls Results

Control Type	Name	2019 COV N1	2019 COV N2	RP	Expected CT Values
Extraction	HSC	-	-	+	<40 CT
Negative	NTC	-	-	-	None
Positive	nCoVPC	+	+	+	<40 CT

Controls Results

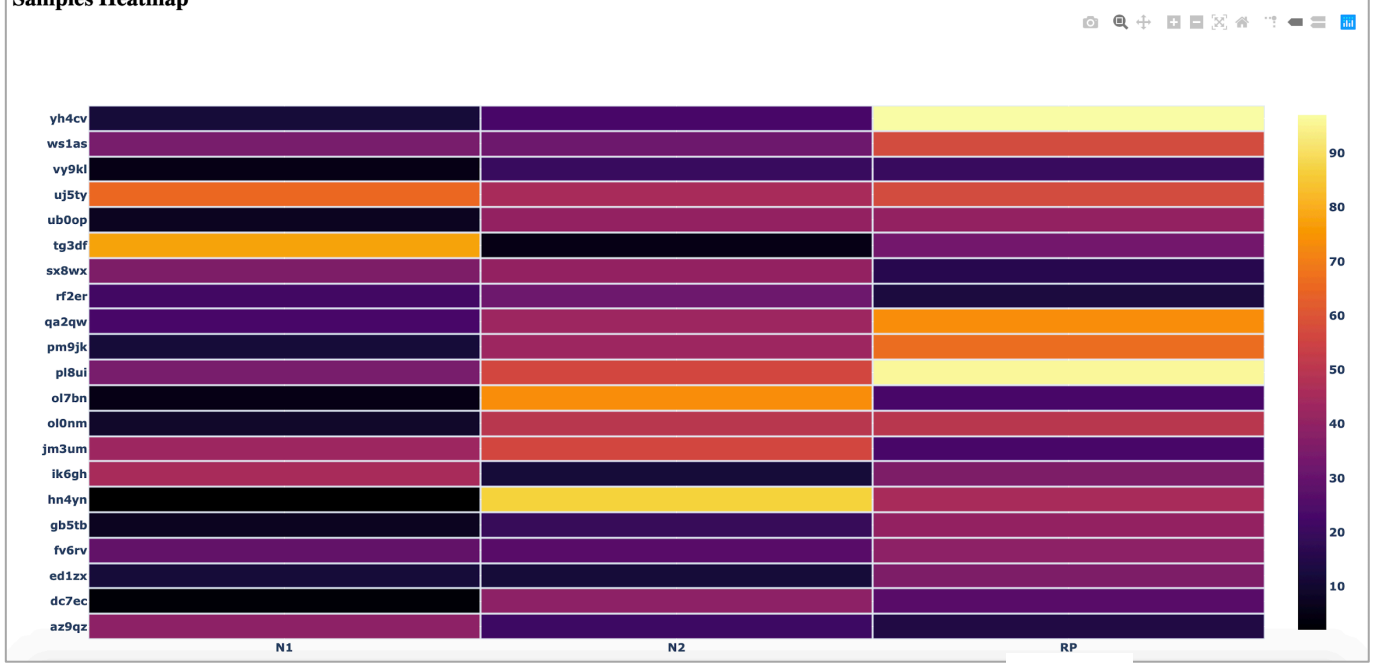
Control	Replicate 1	Replicate 2	Replicate 3
HSC	19	35	23
NTC	51	21	33
nCoVPC	236	532	162

Samples Results

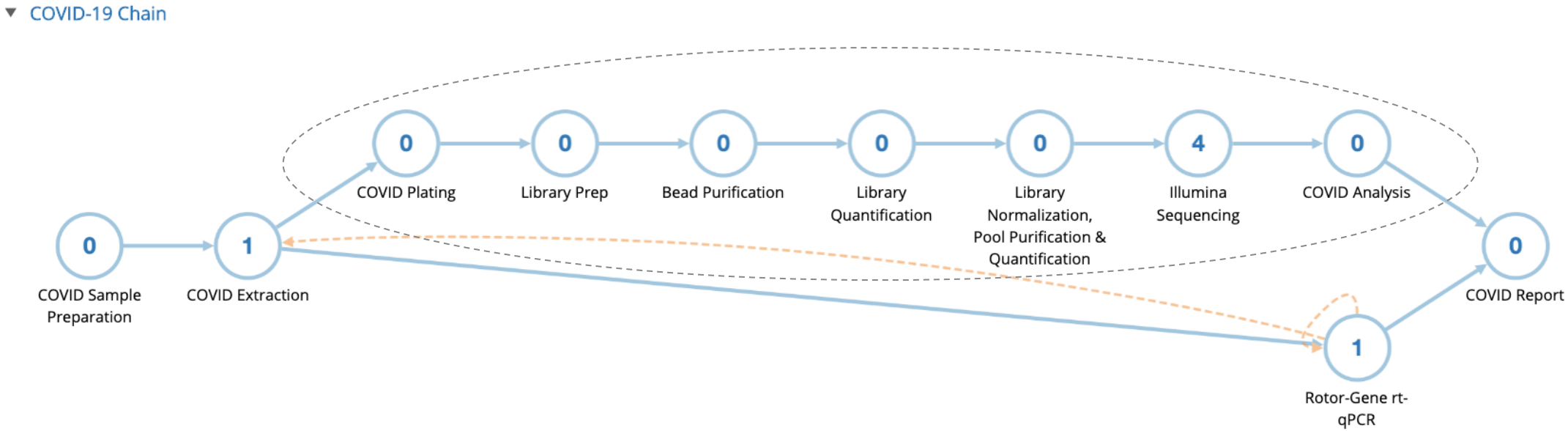
Type	Name	N1	N2	RP
	az9qz	39	21	14
	dc7ec	3	39	27
	ed1zx	12	12	35
	fv6rv	29	27	39
	gb5tb	7	19	40
	hn4yn	2	87	45
	ik6gh	45	12	35
	jm3um	43	56	23
	ol0nm	9	50	50
	ol7bn	5	74	23
	pl8ui	34	56	96
	pm9jk	12	43	67
	qa2qw	23	43	74
	rf2er	22	32	13
	sx8wx	35	40	16
	tg3df	78	5	33
	ub0op	7	40	40
	uj5ty	65	46	57
	vy9kl	5	20	20
	ws1as	34	32	57
	yh4cv	12	23	97

Explore RT-qPCR results directly in ESP with a table of Control and Sample measurements, as well as an interactive heatmap to highlight contamination Issues

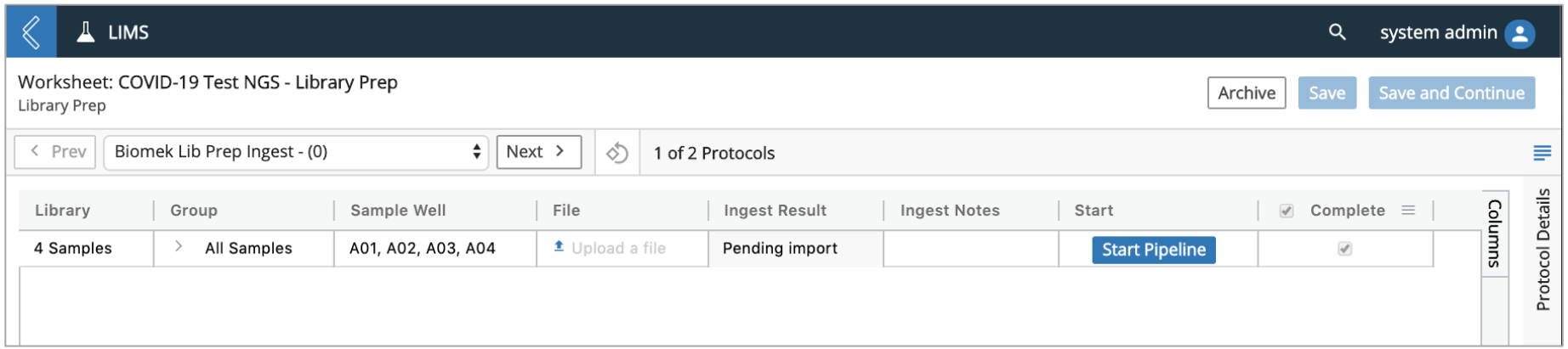
Samples Heatmap



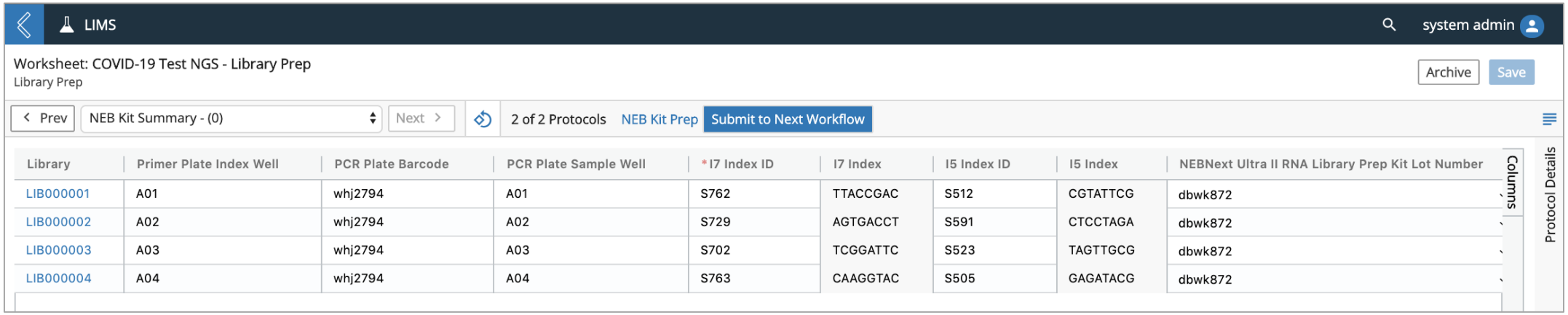
COVID NGS branch



COVID Library Prep



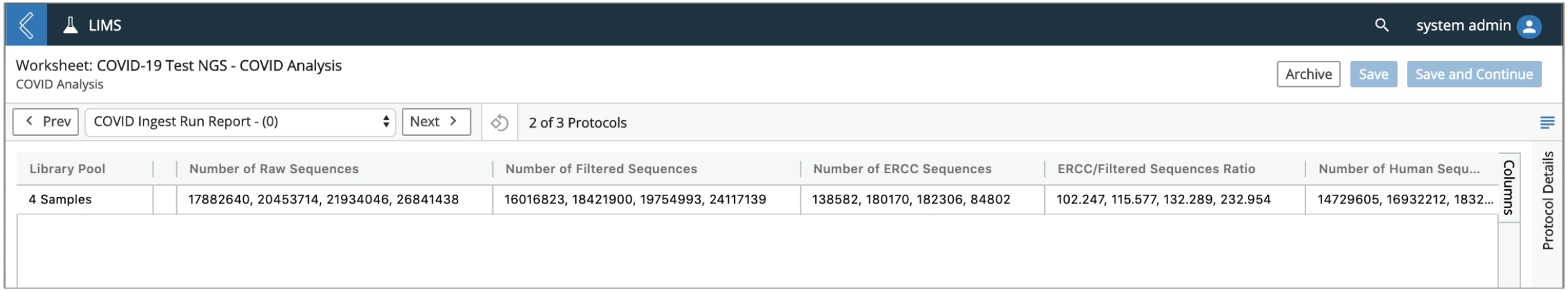
Bulk ingest library prep details



Select lot numbers

COVID Analysis

Submit bioinformatics scripts to be run remotely and ingest results from pipeline



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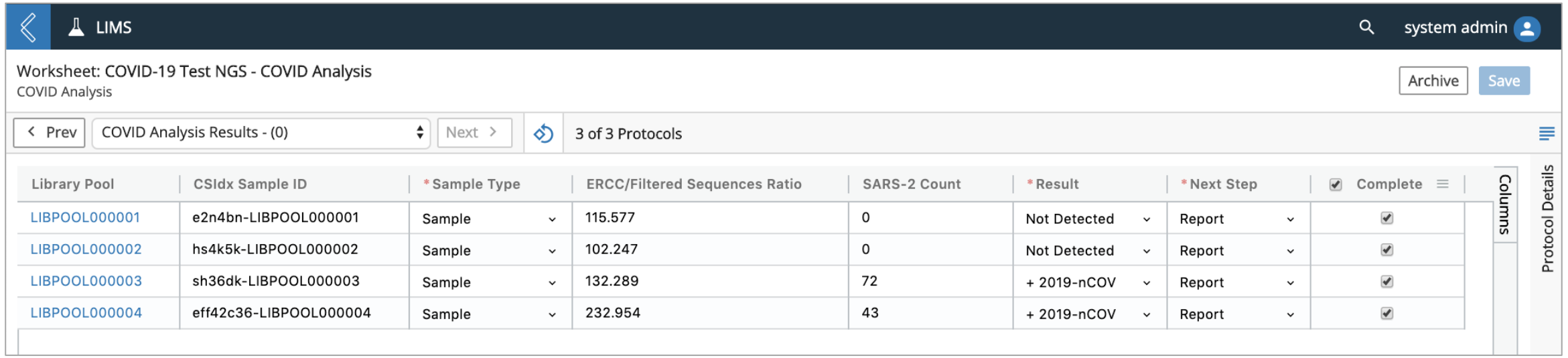
Contamination Source Identification CSI-Dx

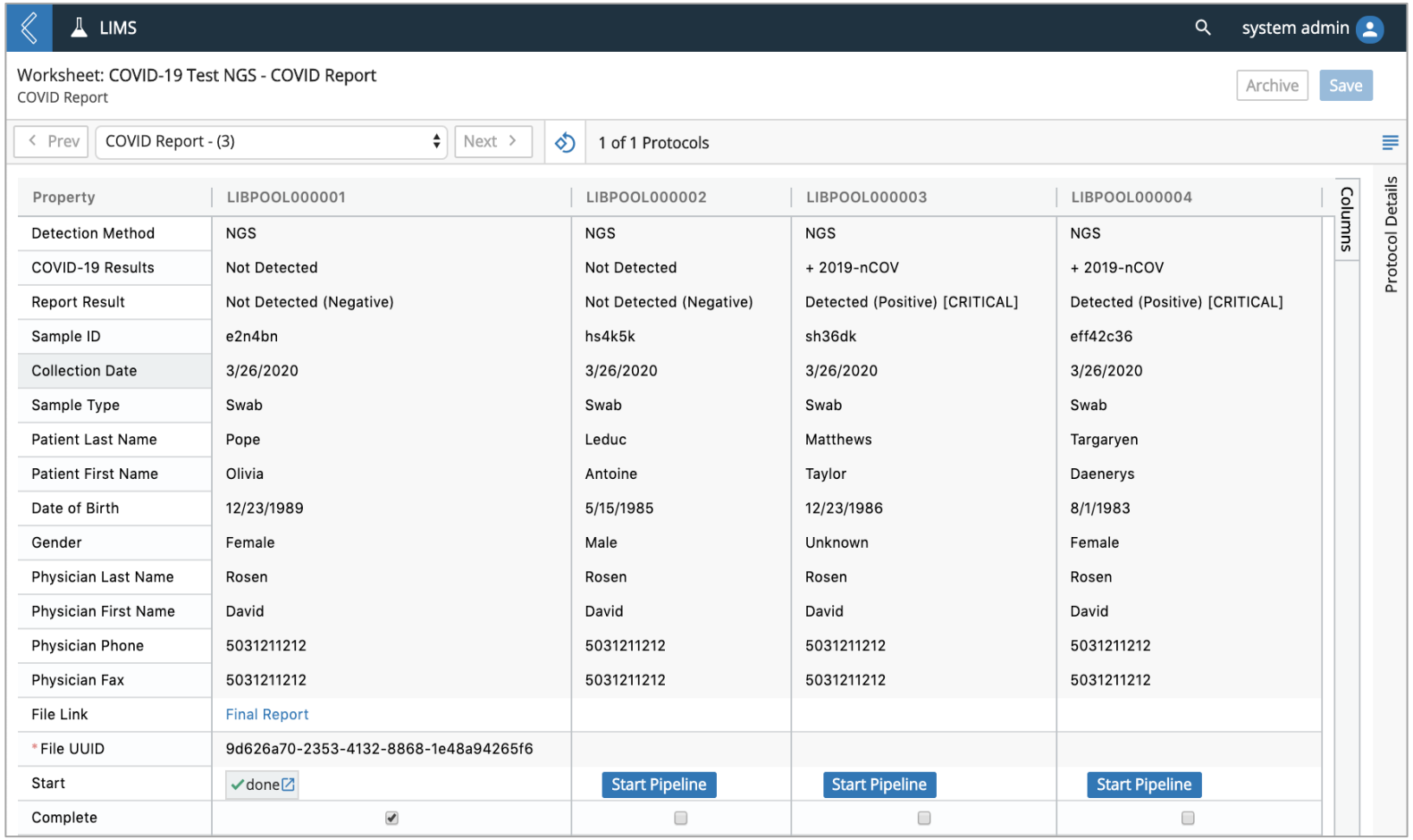
CSI-DX Interpretation process



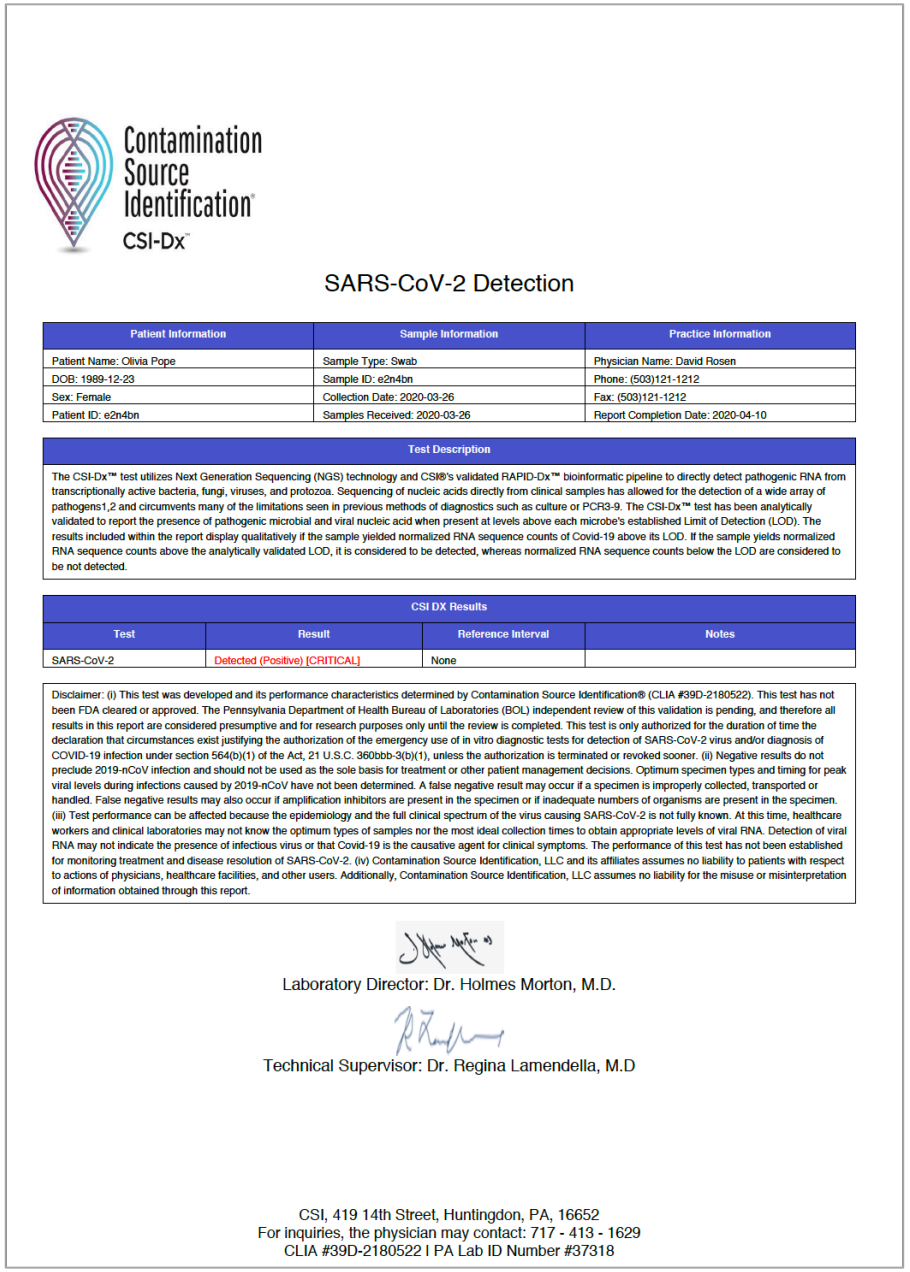
Library Pool	CSIdx Sample ID	*Sample Type	ERCC/Filtered Sequences Ratio	SARS-2 Count	*Result	*Next Step	Complete
LIBPOOL000001	e2n4bn-LIBPOOL000001	Sample	115.577	0	Not Detected	Report	☑
LIBPOOL000002	hs4k5k-LIBPOOL000002	Sample	102.247	0	Not Detected	Report	☑
LIBPOOL000003	sh36dk-LIBPOOL000003	Sample	132.289	72	+ 2019-nCOV	Report	☑
LIBPOOL000004	eff42c36-LIBPOOL000004	Sample	232.954	43	+ 2019-nCOV	Report	☑

COVID Report Generation

Generate physician ready reports with one click



Property	LIBPOOL000001	LIBPOOL000002	LIBPOOL000003	LIBPOOL000004
Detection Method	NGS	NGS	NGS	NGS
COVID-19 Results	Not Detected	Not Detected	+ 2019-nCOV	+ 2019-nCOV
Report Result	Not Detected (Negative)	Not Detected (Negative)	Detected (Positive) [CRITICAL]	Detected (Positive) [CRITICAL]
Sample ID	e2n4bn	hs4k5k	sh36dk	eff42c36
Collection Date	3/26/2020	3/26/2020	3/26/2020	3/26/2020
Sample Type	Swab	Swab	Swab	Swab
Patient Last Name	Pope	Leduc	Matthews	Targaryen
Patient First Name	Olivia	Antoine	Taylor	Daenerys
Date of Birth	12/23/1989	5/15/1985	12/23/1986	8/1/1983
Gender	Female	Male	Unknown	Female
Physician Last Name	Rosen	Rosen	Rosen	Rosen
Physician First Name	David	David	David	David
Physician Phone	5031211212	5031211212	5031211212	5031211212
Physician Fax	5031211212	5031211212	5031211212	5031211212
File Link	Final Report			
* File UUID	9d626a70-2353-4132-8868-1e48a94265f6			
Start	✓done	Start Pipeline	Start Pipeline	Start Pipeline
Complete	☑	☐	☐	☐



Contamination Source Identification CSI-Dx

SARS-CoV-2 Detection

Patient Information	Sample Information	Practice Information
Patient Name: Olivia Pope	Sample Type: Swab	Physician Name: David Rosen
DOB: 1989-12-23	Sample ID: e2n4bn	Phone: (503)121-1212
Sex: Female	Collection Date: 2020-03-26	Fax: (503)121-1212
Patient ID: e2n4bn	Samples Received: 2020-03-26	Report Completion Date: 2020-04-10

Test Description

The CSI-Dx™ test utilizes Next Generation Sequencing (NGS) technology and CSI®'s validated RAPID-Dx™ bioinformatic pipeline to directly detect pathogenic RNA from transcriptionally active bacteria, fungi, viruses, and protozoa. Sequencing of nucleic acids directly from clinical samples has allowed for the detection of a wide array of pathogens1,2 and circumvents many of the limitations seen in previous methods of diagnostics such as culture or PCR3-9. The CSI-Dx™ test has been analytically validated to report the presence of pathogenic microbial and viral nucleic acid when present at levels above each microbe's established Limit of Detection (LOD). The results included within the report display qualitatively if the sample yielded normalized RNA sequence counts of Covid-19 above its LOD. If the sample yields normalized RNA sequence counts above the analytically validated LOD, it is considered to be detected, whereas normalized RNA sequence counts below the LOD are considered to be not detected.

CSI DX Results

Test	Result	Reference Interval	Notes
SARS-CoV-2	Detected (Positive) [CRITICAL]	None	

Disclaimer: (i) This test was developed and its performance characteristics determined by Contamination Source Identification® (CLIA #39D-2180522). This test has not been FDA cleared or approved. The Pennsylvania Department of Health Bureau of Laboratories (BOL) independent review of this validation is pending, and therefore all results in this report are considered presumptive and for research purposes only until the review is completed. This test is only authorized for the duration of time the declaration that circumstances exist justifying the authorization of the emergency use of in vitro diagnostic tests for detection of SARS-CoV-2 virus and/or diagnosis of COVID-19 infection under section 564(b)(1) of the Act, 21 U.S.C. 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner. (ii) Negative results do not preclude 2019-nCoV infection and should not be used as the sole basis for treatment or other patient management decisions. Optimum specimen types and timing for peak viral levels during infections caused by 2019-nCoV have not been determined. A false negative result may occur if a specimen is improperly collected, transported or handled. False negative results may also occur if amplification inhibitors are present in the specimen or if inadequate numbers of organisms are present in the specimen. (iii) Test performance can be affected because the epidemiology and the full clinical spectrum of the virus causing SARS-CoV-2 is not fully known. At this time, healthcare workers and clinical laboratories may not know the optimum types of samples nor the most ideal collection times to obtain appropriate levels of viral RNA. Detection of viral RNA may not indicate the presence of infectious virus or that Covid-19 is the causative agent for clinical symptoms. The performance of this test has not been established for monitoring treatment and disease resolution of SARS-CoV-2. (iv) Contamination Source Identification, LLC and its affiliates assumes no liability to patients with respect to actions of physicians, healthcare facilities, and other users. Additionally, Contamination Source Identification, LLC assumes no liability for the misuse or misinterpretation of information obtained through this report.

Laboratory Director: Dr. Holmes Morton, M.D.

Technical Supervisor: Dr. Regina Lamendella, M.D

CSI, 419 14th Street, Huntingdon, PA, 16652
For inquiries, the physician may contact: 717 - 413 - 1629
CLIA #39D-2180522 I PA Lab ID Number #37318

Final clinical report generation and electronic signatures

Physician Clinical Report Generation

Description: one-click final report generation.

Advantages: No need to look for different pieces of information across spreadsheets, LIMS, Analysis and Order forms nor input them into a PDF.

ESP generates Ready to fax PDF with e-signatures

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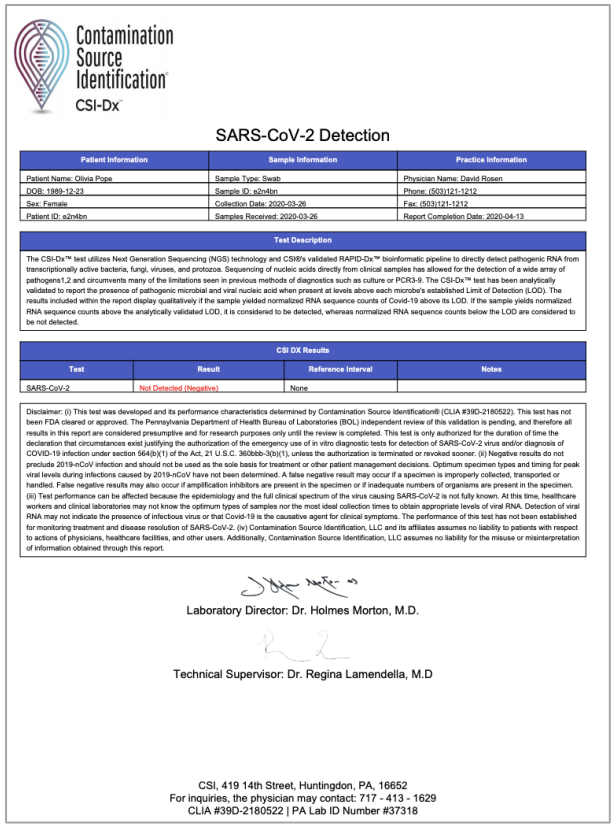
Contamination Source Identification CSI-Dx

COVID Report

Report elements are dynamic and depend on detection method (i.e. NGS or rt-qPCR), as well as test result.



Contamination Source Identification
CSI-Dx

SARS-CoV-2 Detection

Patient Information	Sample Information	Practice Information
Patient Name: Olivia Pope	Sample Type: Swab	Physician Name: David Rosen
DOB: 1989-12-23	Sample ID: e2n4bn	Phone: (503)121-1212
Sex: Female	Collection Date: 2020-03-26	Fax: (503)121-1212
Patient ID: e2n4bn	Samples Received: 2020-03-26	Report Completion Date: 2020-04-13

Test Description

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CSI DX Results

Test	Result	Reference Interval	Notes
SARS-CoV-2	Not Detected (Negative)	None	

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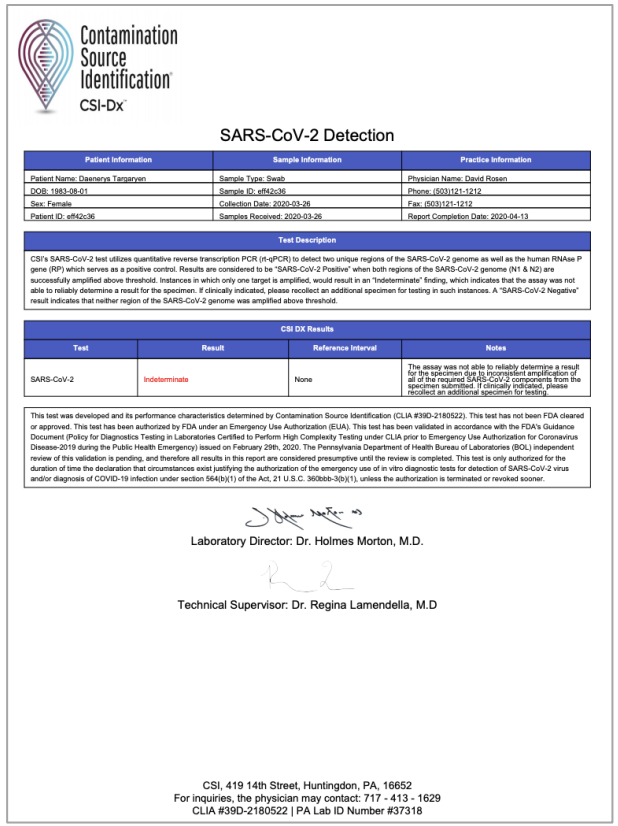
CLIA #39D-2180522 | PA Lab ID Number #37318

NGS Negative/Positive



Contamination Source Identification
CSI-Dx

SARS-CoV-2 Detection

Patient Information	Sample Information	Practice Information
Patient Name: Daenerys Targaryen	Sample Type: Swab	Physician Name: David Rosen
DOB: 1983-08-01	Sample ID: eff42c36	Phone: (503)121-1212
Sex: Female	Collection Date: 2020-03-26	Fax: (503)121-1212
Patient ID: eff42c36	Samples Received: 2020-03-26	Report Completion Date: 2020-04-13

Test Description

CSI's SARS-CoV-2 test utilizes quantitative reverse transcription PCR (rt-qPCR) to detect two unique regions of the SARS-CoV-2 genome as well as the human RNAse P gene (RP) which serves as a positive control. Results are considered to be "SARS-CoV-2 Positive" when both regions of the SARS-CoV-2 genome (N1 & N2) are successfully amplified above threshold. Instances in which only one target is amplified, would result in an "Indeterminate" finding, which indicates that the assay was not able to reliably determine a result for the specimen. If clinically indicated, please recollect an additional specimen for testing in such instances. A "SARS-CoV-2 Negative" result indicates that neither region of the SARS-CoV-2 genome was amplified above threshold.

CSI DX Results

Test	Result	Reference Interval	Notes
SARS-CoV-2	Indeterminate	None	The assay was not able to reliably determine a result for the specimen due to inconsistent amplification of all of the required SARS-CoV-2 components from the specimen submitted. If clinically indicated, please recollect an additional specimen for testing.

This test was developed and its performance characteristics determined by Contamination Source Identification (CLIA #39D-2180522). This test has not been FDA cleared or approved. This test has been authorized by FDA under an Emergency Use Authorization (EUA). This test has been validated in accordance with the FDA's Guidance Document (Policy for Diagnostics Testing in Laboratories Certified to Perform High Complexity Testing under CLIA prior to Emergency Use Authorization for Coronavirus Disease-2019 during the Public Health Emergency) issued on February 29th, 2020. The Pennsylvania Department of Health Bureau of Laboratories (BOL) independent review of this validation is pending, and therefore all results in this report are considered presumptive until the review is completed. This test is only authorized for the duration of time the declaration that circumstances exist justifying the authorization of the emergency use of in vitro diagnostic tests for detection of SARS-CoV-2 virus and/or diagnosis of COVID-19 infection under section 564(b)(1) of the Act, 21 U.S.C. 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

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rt-qPCR Indeterminate

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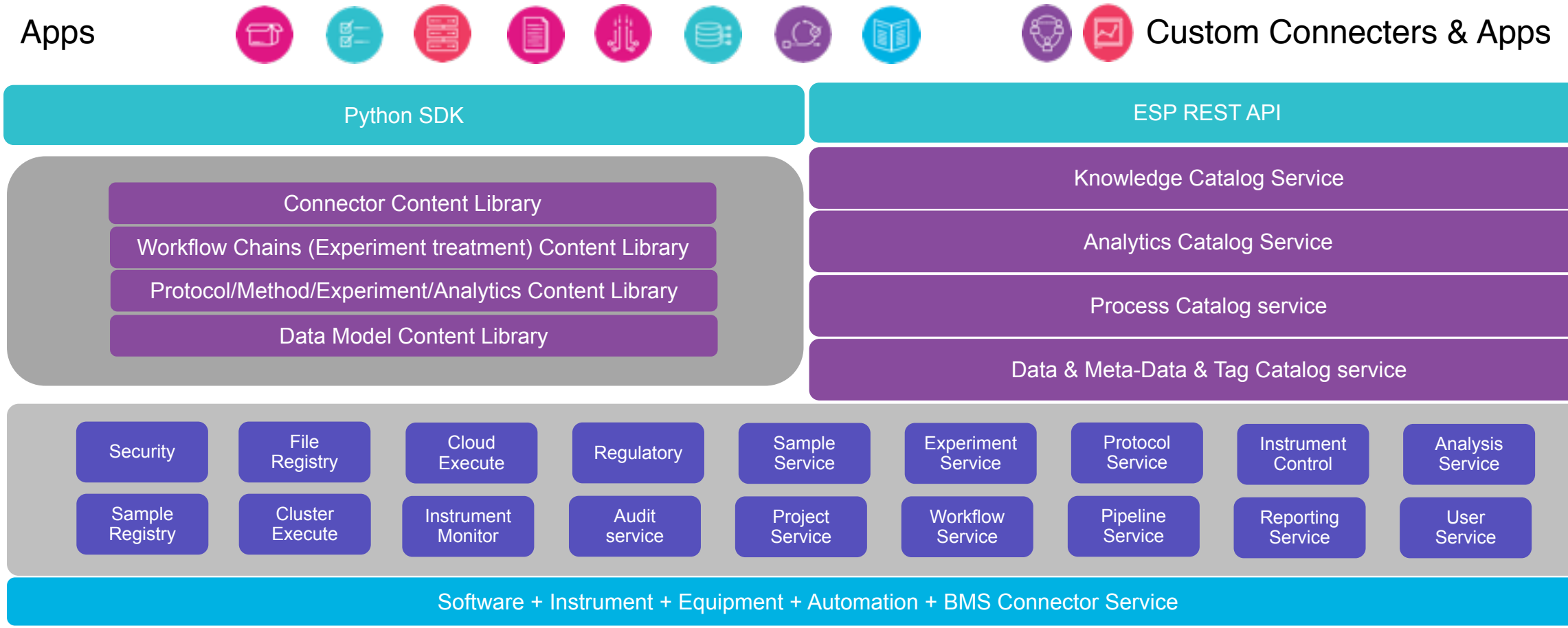
Contamination Source Identification
CSI-Dx

ESP Enterprise Science Platform™

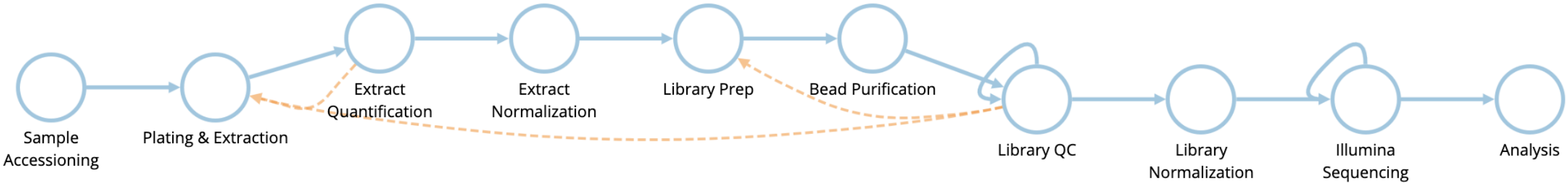
L7 ESP Platform Overview

ESP architecture allows users to define content



CSI had previously implemented ESP Content for pathogen detection – Lyme Disease using urine samples

Contamination Source Identification®
CSI-Dx™



The process begins when ESP ingests a Sample Accessioning form is received from a clinical institution. As the samples move through the Sequencing workflow, ESP is gathering data from Illumina Sequencers, fluorimeters, a Biomek Liquid Handling Robot, and various bioinformatic pipelines. ESP enables the scientists to determine presence of a given pathogen in the patient's blood, and smoothly inform any physicians of the findings.

All of this data is kept inside ESP in a secure and query-able fashion.

CSI responded to Covid-19 market demand in < 2 weeks

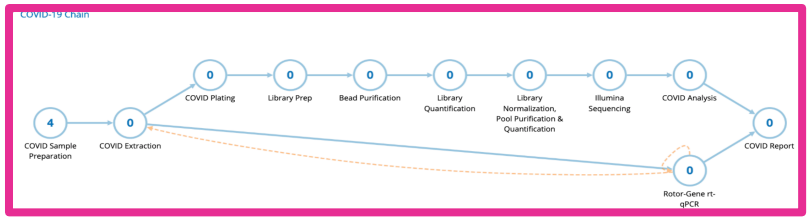
Apps

Custom Connecters & Apps

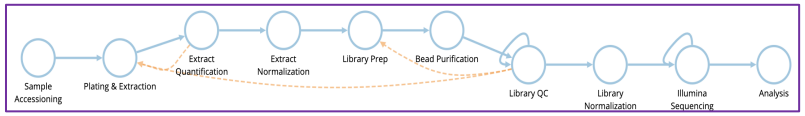
Python SDK

ESP REST API

Covid-19 Dx



Lyme Dx



Knowledge Catalog Service

Analytics Catalog Service

Process Catalog service

Data & Meta-Data & Tag Catalog service

Security | File Registry | Cloud Execute | Regulatory | Sample Service | Experiment Service | Protocol Service | Instrument Control | Analysis Service

Sample Registry | Cluster Execute | Instrument Monitor | Audit service | Project Service | Workflow Service | Pipeline Service | Reporting Service | User Service

Software + Instrument + Equipment + Automation + BMS Connector Service

CMS DB

Informatics

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