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METHODOLOGY

Implementation of the Louisville COVID-19 Surveillance Protocol: Experiences from the University of Louisville Center of Excellence for Research in Infectious Diseases (CERID)

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Abstract

The lack of available testing for SARS-CoV-2 has been one of the primary challenges in the development and implementation of a comprehensive approach to infection prevention and transmission in the United States (US). In response to the need for increased testing capacities and capabilities, the University of Louisville (UofL) Division of Infectious Diseases, Center of Excellence for Research in Infectious Diseases (CERID) initiated the Louisville Coronavirus Surveillance Program, a comprehensive approach to surveillance and testing of patients and healthcare workers. The first specimens were accepted on March 12, 2020 and parallel testing was done using a high-capacity testing process and the Division of Infectious Diseases CLIA-certified laboratory to ensure concordant results. Steps in the testing process began with validation of the testing methods and included database development, acceptance of specimens, tracking and cataloging the specimens, testing, and reporting of results. Quality metrics were developed and used to prevent error and facilitate rapid reporting. Between March 12, 2020 and April 30, 2020, more than 5500 tests were performed identifying more than 850 patients and healthcare workers infected with COVID-19 in the Louisville, Kentucky area. Although the process used high-capacity robotics for testing procedures, the methods described here are applicable to settings employing a variety of laboratory testing methods.

Background

The lack of available testing for SARS-CoV-2 has been one of the primary challenges in the development and implementation of a comprehensive approach to infection and infection transmission in the United States (US). State health departments and the US Centers for Disease Control and Prevention (CDC) were the first, and the only, sites for testing in the US before mid-February. Their capacities were far less than the need and the demand for laboratory testing. In response to the need for increased testing capacities and capabilities, the University of Louisville (UofL) Division of Infectious Diseases, Center of Excellence for Research in Infectious Diseases (CERID) initiated a planning group aimed at development of a comprehensive approach to surveillance and testing of patients and healthcare workers. This approach would use the existing CERID research enterprise as the platform and engage new partnerships within and outside UofL to build and rapidly implement a high capacity testing process for the Louisville and surrounding areas in Kentucky. For more than thirty years, researchers in the Division of Infectious Diseases at the University of Louisville have been involved in clinical research, primarily in the Louisville area's nine adult and one pediatric acute care hospitals. The research program has steadily grown and matured and in 2018, elements of the program were aligned into a comprehensive clinical research enterprise. **Figure 1** provides a graphic description of CERID and its components. Success of this novel approach to testing would require reliance upon existing relationships and partnerships with the area hospital personnel and leadership coupled with the expertise of CERID personnel and the organizational capacity of that research enterprise.

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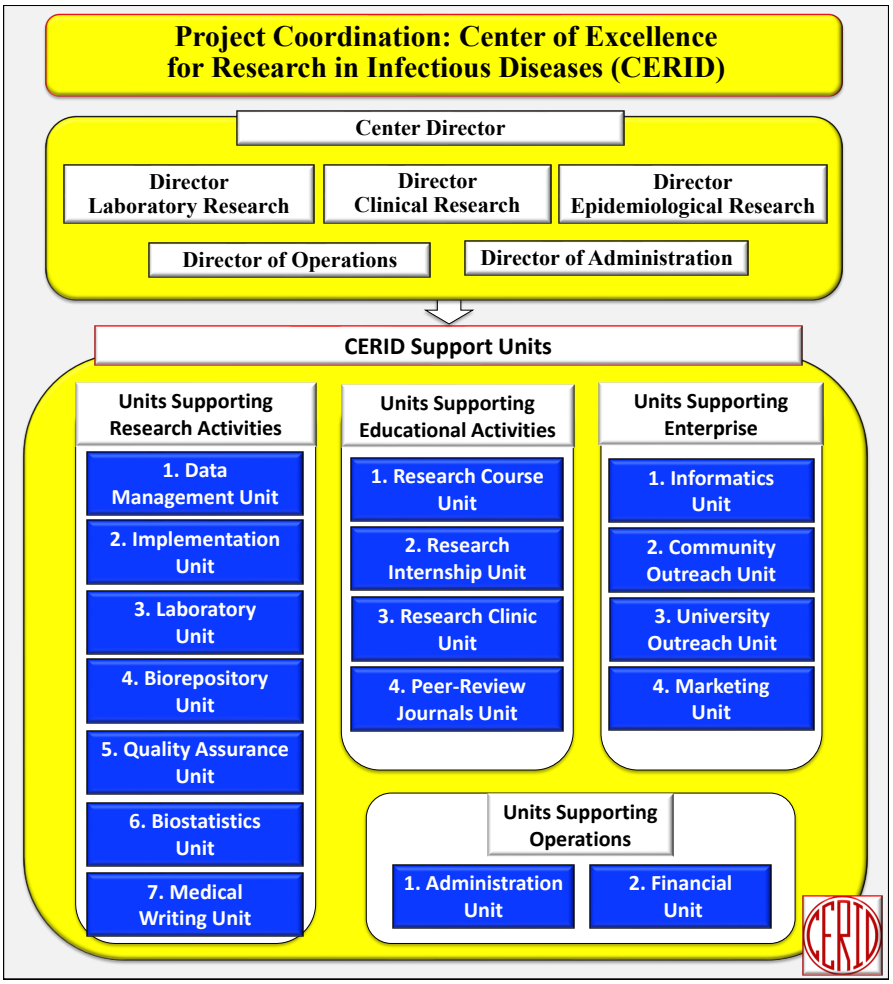

Figure 1. University of Louisville Center of Excellence for Research in Infectious Diseases (CERID) Research Enterprise.

In early January 2020, Luminex Corporation reached out to the UofL Division of Infectious Diseases (ID) Laboratory asking to partner in development of a multiplex test for SARS-CoV-2. This partnership involved assisting with the testing and validation of the real-time PCR assay on the ARIES® instrument for submission to the FDA for Emergency Use Authorization (EUA). This work was completed by March 11, 2020 and a white paper published describing these efforts. [1] Happening at the same time, in mid-February 2020, the University of Louisville's Center for Predictive Medicine (UofL-CPM) received a reference strain of the SARS-CoV-2 virus from BEI resources to initiate basic research geared toward understanding the characteristics of the virus and develop a model system for identification. The National Biocontainment Laboratory at the University of Texas Medical Branch in Galveston proposed that the network of eleven regional biocontainment laboratories in the United States focus on development of new testing methods in response to the outbreak and limited testing capacities. As one of the regional biocontainment laboratories in that network, the UofL-CPM responded to the initiative. Once the virus was successfully grown and the real-time PCR assay developed by CDC was implemented in the UofL-CPM, discussions began regarding how the research process might facilitate laboratory testing for the virus using the UofL-CPM high-capacity instrumentation. The potential for expanded access to testing was quickly recognized as a valuable addition to the limited testing capabilities present throughout the Commonwealth of Kentucky and the US. This expanded testing capability formed the basis for a strategic surveillance approach that was developed and published for broad access through the University of Louisville *Journal of Respiratory Infections* on March 10, 2020. [2] The following information outlines the implementation approach of the Louisville COVID-19 Surveillance Program (LCSP) process that began with the first specimen received on March 10, 2020.

The objectives of this manuscript are to 1) describe the steps in the Louisville COVID-19 Surveillance Program (LCSP) process and 2) demonstrate the organizational capacity needed to support the efforts.

Date	CERID Activity	CPM Activity
2/6/2020-2/14/2020		Permission from CDC to receive SARS-CoV-2 virus by CPM and initiation of a surveillance concept within the US Regional Biosafety Laboratory Network using CDC PCR assay
2/14/2020	Concept development for surveillance testing for patients and healthcare workers.	Proposed that the CPM can make RNA prep/real time PCR automation for SARS-CoV2 virus with 96 samples/run.
2/24/2020	First drafts of surveillance process protocol for IRB.	Development of real time PCR with control plasmid, harvesting and amplification of the CoV strain.
2/28/2020	ID lab contacted by Luminex Corporation to be a site evaluating ARIES platform for COVID-19 testing.	
3/3/2020	ARIES test kit validation completed and FDA white paper submitted	By 3/5/20, RT PCR available for use.
3/7/2020	Presentation of surveillance process to IRB	
3/8/2020	Submission of Louisville COVID-19 Surveillance Program to IRB	
3/9/2020	IRB approval #20.0225	
3/10/2020	Testing of patient samples for COVID-19 in ID lab and CPM lab in parallel Daily review of ID lab and CPM results, then results discussed with Chief Medical Officers of each submitting hospital	Testing of patient samples for COVID-19 in ID lab and CPM lab in parallel. Submission of results to ID reviewers at evenining meetings held each day.
3/11/2020	Daily oral report and daily written reports provided to Chief Medical Officers of each submitting hospital	
3/13/2020	Submission of first 5 positive and first 5 negative test samples to the KDPH State Laboratory for verification of results	
3/14/2020	Receipt of notification of results verification from the KDPH State Laboratory	
3/15/2020	Samples being received from 10 Louisville hospitals and 2 southern Indiana hospitals	By close of the day on 3/15/2020 had tested 205 samples and identified 7 positives. 100% congruence between ID lab and CPM lab results.

Figure 2. Timeline of Events Relevant to Planning and Implementation of the Louisville Coronavirus Surveillance Program.

Approach

The process used to implement the COVID-19 surveillance included developing and testing a proof of concept for the process, then implementing the process continuous quality assessment and improvement at its core.

Concept of the Testing Process

Planning for testing for patients hospitalized in the ten Louisville area acute care hospitals began on February 22, 2020. A timeline of events relevant to the planning and implementation of the LCSP is shown in **Figure 2**.

Before receipt of the first sample for testing, a process was conceptualized that would begin with the collection of a sample from one of the ten Louisville area hospitals, travel through the delivery, processing and testing steps, and end with interpretation and sharing of results. Steps in the process were simulated to identify testing capabilities; validity, reliability, and capacity; process and capability gaps, opportunities for error that exist at any step, and opportunities for improvements and efficiencies. A member of the LCSP team transported a representative sample from one of the Louisville area hospitals to the COVID-19 testing center. The sample was moved from receipt, through the testing process, and finally to storage in a biorepository. A first-generation database able to capture patient information, specimen movement, results, and biorepository storage was developed using REDCap™. Specimen handling and testing procedures were simulated to ensure safe and optimal laboratory practices. Interpretation of results and processes for communicating results and related information were tested through simulation and role-play. At each phase in the process, team members cataloged the steps, identified opportunities for error and efficiencies, documented proposed changes in the process and the impact the changes, as well as quality indicators necessary to ensure a standardized, safe and error-free process. On March 10, 2020, the first specimens were received for testing, signaling implementation of the LCSP process.

Implementation of the testing process

The process for developing and implementing a surveillance testing approach using high-capacity, high-throughput instrumentation included the following steps: 1) test instrument validation and result verification; 2) specimen database development; 3) specimen movement from hospitals to the testing site; 4) data entry; 5) cataloging the specimen for movement to the laboratory for processing; 6) assignment of the specimen barcode; 7) specimen testing; 8) integration of results from the testing instrument to the specimen database; 9) analysis of test results; 10) communicating test results; and 11) development and implementation of quality measures.

1. Test Instrument validation and result verification

One of the first steps in the process involved determination of existing capabilities and capacities for testing. For more than twenty years, the University of Louisville Division of Infectious Diseases has operated a CLIA-certified laboratory focused on clinical research and diagnostic testing, serving as a reference laboratory. Luminex Corporation selected the laboratory as one of the five US laboratory sites to validate their ARIES® instrument and primers for submission to the US Food and Drug Administration (FDA) as Emergency Use Authorization (EUA) test for COVID-19. [1] The Luminex ARIES® test evaluated the sample for SARS-CoV-2 detection using two viral genes and an internal control (N1, N3 and human RNaseP). Per the FDA, the ID laboratory was then required to submit the first five positive and first five negative specimens to the Kentucky Department for Public Health Division of Laboratory Services for confirmation. This validation process was completed on March 13, 2020. Validation enabled the UofL ID laboratory to test up to thirty samples in every three-hour run using the Luminex Aires® test. At the same time, the UofL-CPM had begun testing the high-capacity high- throughput robotic testing machine capable of testing 176 samples in each four-hour run. This process used the CDC primers N1, N2, and N3 in addition to the internal control human RNaseP. Use of the UofL-CPM testing capability brought immediate capacity, but there was a need to evaluate results to ensure validity. Validation was done by running parallel samples using both the Luminex ARIES® test and the UofL-CPM CDC primers in the first 200 samples received. The result of this parallel testing demonstrated 100% concordance with positive and negative results. With this concordance, we had confidence in reliance upon the high-capacity test instrument for all surveillance testing moving forward.

2. Specimen database development

A REDCap database was developed to capture all information necessary to track the specimen from receipt to result. **Figures 3, 4, 5, 6, and 7** show the most current five database sections developed for this project including: 1) test request form, 2) barcode, 3) laboratory/biorepository, 4) results, and 5) Louisville Coronavirus Surveillance Report. The initial database was improved repeatedly during the first three weeks of operation to ensure information of importance to the hospitals, public health, and other stakeholders was included. Individual reports were developed and made available on day one of the project, as were access portals to facility results via individual facility REDCap links. These links were made available to these partners after the first three weeks of operation. This approach facilitated the goal of real-time access to the data for hospitals and public health.

3. Specimen movement from hospitals to the testing site

Patient samples were collected by hospital personnel and sent to their respective laboratories for pickup by LCSP personnel. For facilities preferring to courier their samples to the testing site, LCSP was able to accept those specimens and move them into the process. Hospitals were asked to package each specimen in a biohazard bag with identifying information on the specimen container (e.g., patient label) and complete a COVID-19 specimen test request form placing it in a pocket on the outside of the biohazard bag. This form contained patient information such as name, date of birth, medical record number; the type of specimen (e.g., nasopharyngeal); date and time of specimen collection; and any other hospital-specific information important to that facility (e.g., laboratory accession number). LCSP personnel reported to a designated pick-up area at each hospital laboratory three to four times throughout the day (0700, 1100, 1200, and 1700) seven days a week, to retrieve samples and transport in temperature-controlled containers back to the testing site. Team members wore gloves during handling of the specimen bags. Clear plastic transport containers with closable lids and biohazard labels were disinfected with a healthcare-grade registered (e.g., quaternary ammonium) germicide following each transport event.

4. Data entry

Upon receipt of the specimen bags, LCSP personnel entered data into REDCap by completing the test request and biorepository/laboratory sections. (**Figures 3 and 5**) The data entry process consisted of teams of two researchers and two quality reviewers. One researcher entered data into REDCap and the second researcher was responsible for handling the specimen bag. (**Image 1**) The researcher handling the specimen bag provided the information from the specimen test requisition form—or specimen tube label if no requisition form was available—to the researcher entering the data. If no test requisition form accompanied the specimen, a generic form was completed at that time. This facilitated data entry and quality processes. Specimen biohazard bags remained closed and the specimen tube information was

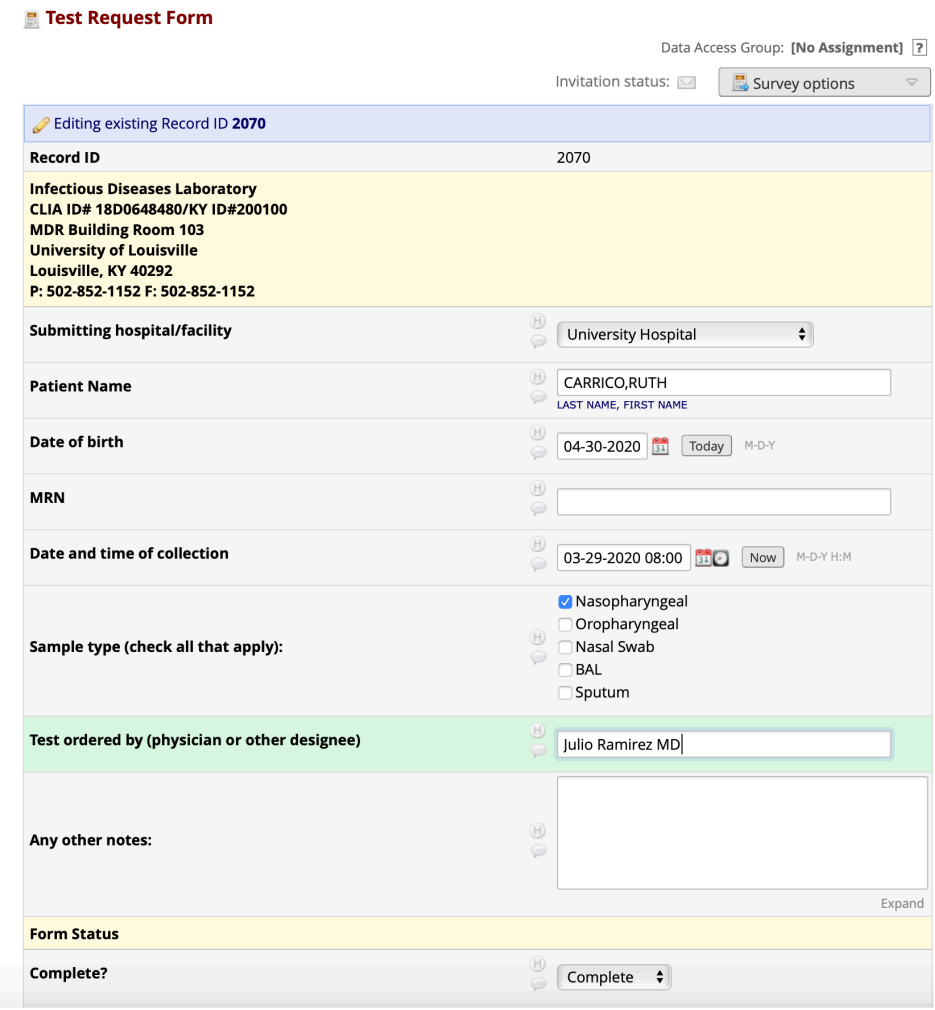

Figure 3. REDCap Database Test Request Form Page.

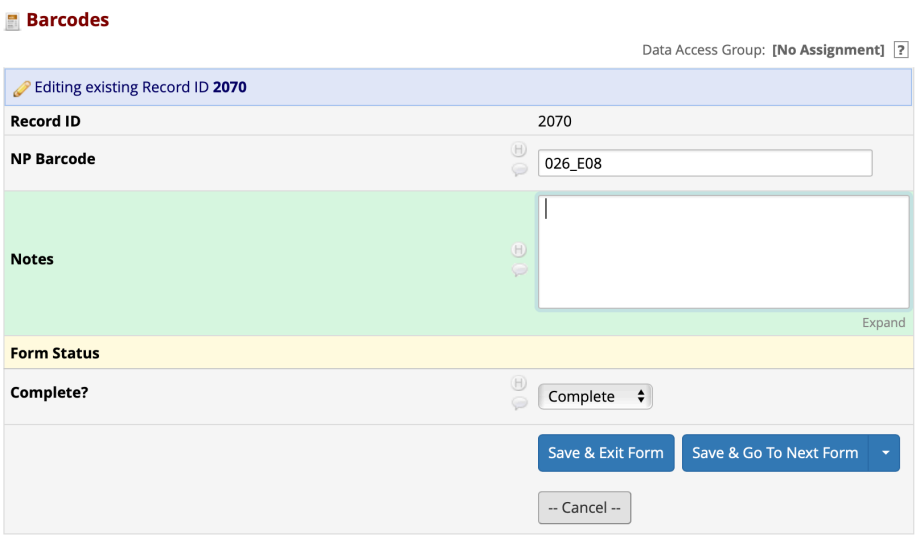

Figure 4. REDCap Barcode Page.

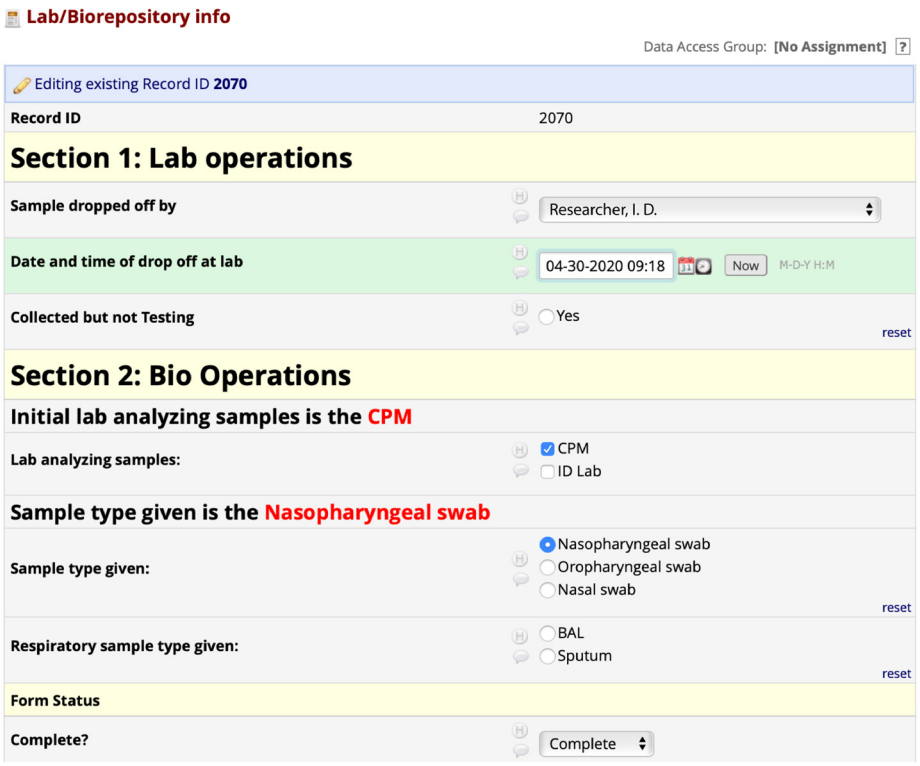

Figure 5. REDCap Laboratory/Biorepository Page.

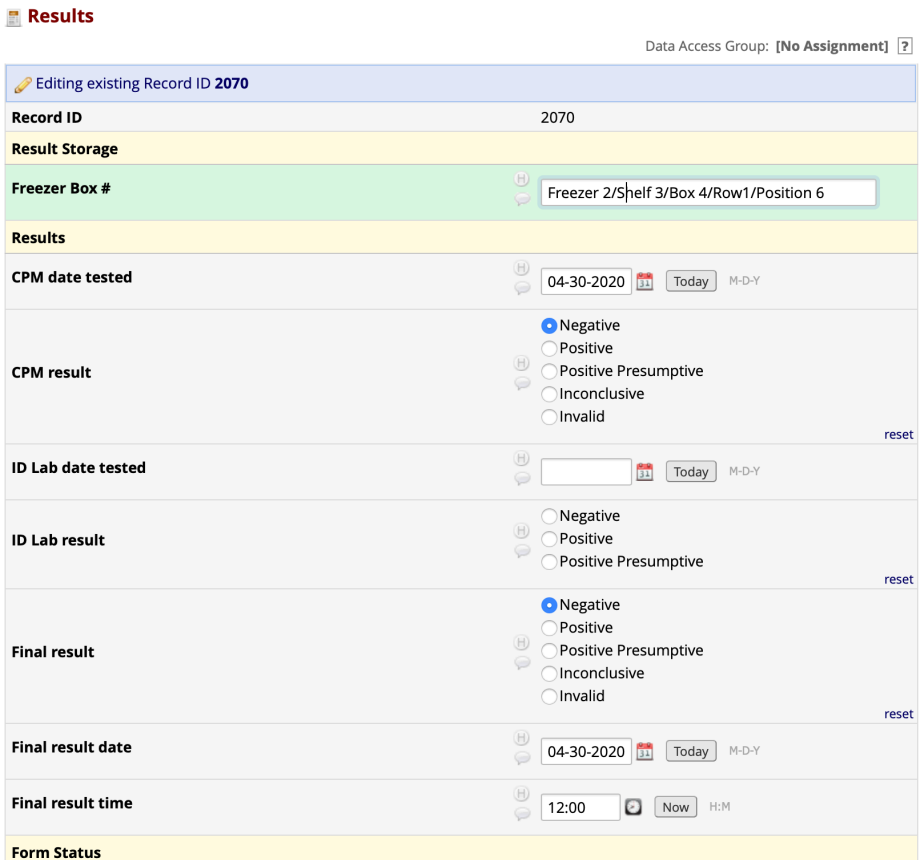

Figure 6. REDCap Results Page.

Louisville SARS-CoV-2 Surveillance Report

Data Access Group: **[No Assignment]**

Editing existing Record ID **2070**

Record ID	2070
Name:	CARRICO,RUTH
Hospital:	University Hospital
Date of birth:	04-30-2020
MRN:	———
Date of sample collection:	04-30-2020 09:21
Date of surveillance test:	04-30-2020 12:00
Surveillance test result:	Negative
Form Status	
Complete?	Incomplete

Save & Exit Form | Save & Go To Next Form

Figure 7. REDCap Louisville Coronavirus Surveillance Program Report Page.

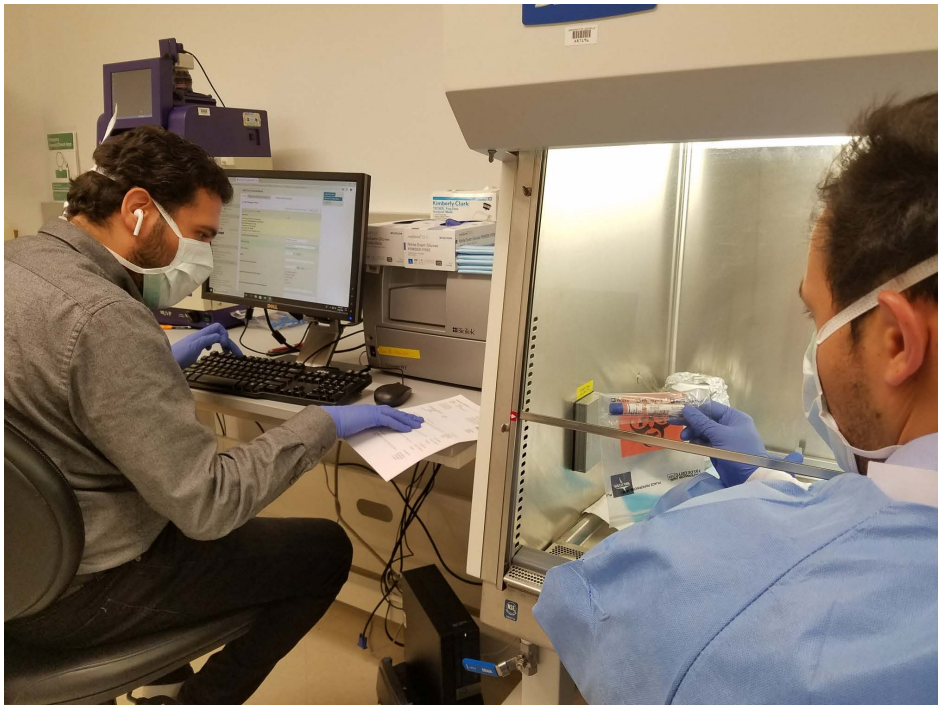

Image 1. Researchers Entering Data into REDCap From Patient Specimen.

visualized through the biohazard bag. The team member handling the closed bag wore gloves and hands were washed after glove removal. After completing the data entry process, the specimen tubes still inside the closed biohazard bags were placed back into the clear plastic lockable container and taken to the biosafety cabinet area to begin the racking and cataloging process.

5. Cataloging the specimen for movement to the laboratory for processing

The racking of tubes and spreadsheet production process (cataloging) consisted of teams of two researchers (#1 and #2) and one quality reviewer. The laboratory cataloging process involved the use of a biosafety cabinet (BSC, Level 2) with controlled airflow and a protective sash that could be lowered providing a safe work environment commonly referred to as “under the hood”. Once under the BSC, the specimen bags were opened, and the specimen tubes were prepared for placement in the specimen tube racks. Researcher #1 handling the specimen tubes wore personal protective equipment including gown, gloves, and facemask. Researcher #1 would remove the test requisition form from the sample bag and verify that the patient demographic information on the form matched information listed on the specimen

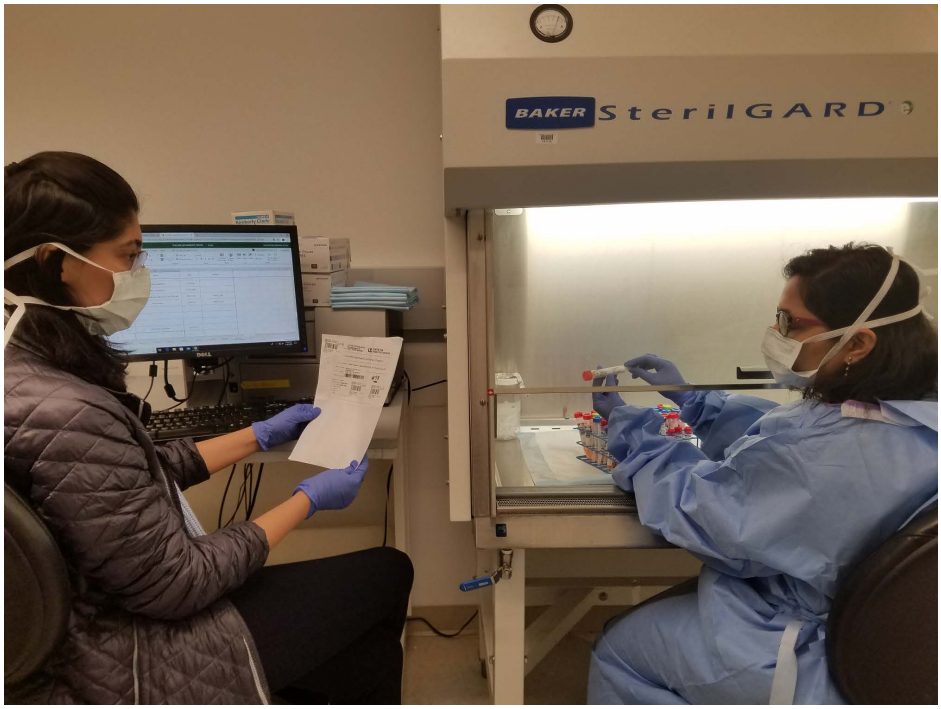

Image 2. Researchers Racking Tubes and Cataloging Specimen for Processing.

tube. Upon completion of this verification, researcher #1 would write a unique serial tube number (1-88) in three locations: cap of the sample, on the sample tube itself, and the test requisition form. Researcher#1 would then place that numbered tube into the test tube rack in sequence. Tubes were racked in groups of 88 as the testing instrument used by the UofL-CPM analyzed 88 samples in each testing batch, in addition to the spaces reserved for controls. (**Image 2**)

At the same time researcher #1 is working in the BSC, researcher #2 would construct the specimen catalog. An electronically shared Excel spreadsheet process was used to develop that specimen catalog enabling real-time visual access for specimen location and quality monitoring. Data in the spreadsheet included: current date, time of the testing run, collection date of the specimen, tube number, REDCap identification number, name, date of birth, and a location for the barcode that would be provided. Researcher #1 would read aloud the patient's name, date of birth, and write a tube number (1-88) on the cap of the specimen sample as well as the body of the sample. Researcher #2 entered those data elements into the specimen catalog spreadsheet. The tube number provided a way to identify any given tube if the tube was needed for additional testing. Following completion of the process, the researcher #2 would work with the quality reviewer to perform a quality crosscheck with the REDCap database and add the patient's unique identifying number (assigned in REDCap) to the catalog. This would ensure that the patient specimen had been entered into REDCap and the specimen used for testing was correct (e.g., nasopharyngeal swab versus sputum). At this point, the specimen cataloging process was complete. The specimens were placed in a locked biohazard transport container and transported to a designated area for the UofL-CPM personnel to take possession of the samples for laboratory processing.

6. Assignment of the specimen barcode

The specimen barcoding process included application of a unique barcode identifier to each specimen tube. This unique barcode with human readable characters identified the location of the sample on the test plate and linked the result to the individual patient. The specimen barcoding process required two laboratory technicians. The barcoding process began after the LCPS team provided the completed specimen catalog spreadsheet to the UofL-CPM lab personnel. This important communication process confirmed that the sample tubes were prepared, a quality review of the REDCap data entry had been completed and the catalog spreadsheet had been completed. Once verified, the barcoding process could begin. Laboratory technician #1 would work under the BSC in the laboratory area where they would pick up the first tube from the rack and call out the name on the tube. This would enable technician #2 to crosscheck the specimen catalog and apply the barcode to the specimen tube and the catalog sheet. (**Image 3**) This would ensure that the same bar code was assigned to the patient specimen tube, the catalogue sheet, and to the aliquot from that specimen tube that was placed into the test well. This process continued until all 88 specimen tubes had been barcoded, the barcodes entered on the cataloging sheet, and the aliquot placed into the test well. The specimen catalog sheet

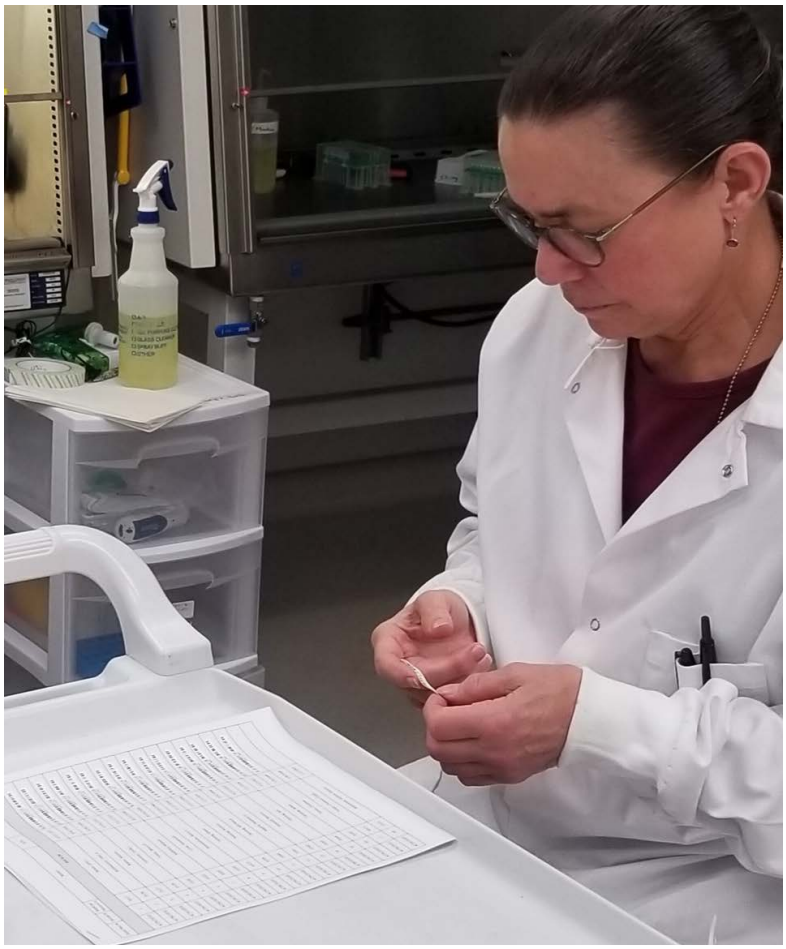

Image 3. Assignment of Barcode.

was then given to LCSP personnel who then scanned the barcode from the specimen catalogue into REDCap (**Images 4 and 5**). The alphanumeric barcode would then be visible in REDCap as shown in **Figure 4**. Following completion of this process, two quality team members performed a review of the barcode scans for each specimen in the run to ensure accuracy of the tube assignment and visibility of the barcode in REDCap.

7. Specimen testing

After barcoding, the UofL-CPM staff assumed responsibility for the specimen and testing began in a biosafety level 2 laboratory with an enhanced biosafety practice. This area was chosen as biosafety cabinets and space were readily available. The two UofL-CPM personnel responsible for the specimen processing wore gowns, gloves, and facemasks. UofL-CPM virology personnel opened specimen samples under a BSC, obtained an aliquot from the specimen tube, and pipetted it into the testing block. Samples were tested for SARS-CoV-2 with a real-time-PCR assay detecting viral RNA. Samples (up to 100 ×L) were treated with Trizol reagent, which inactivated the virus and released RNA from the sample. Then, the total RNA in the sample was extracted and purified using a magnetic beads-based method.

RNA extraction was performed using laboratory automation (Tecan Evo100 with MCA96) with a script developed in-house. Eighty-eight total samples were processed as a batch in a 96-well plate along with four negative controls (healthy volunteers) and four positive controls (viral RNA extracted from *in vitro* culture). Detection of viral RNA in the extracted RNA was performed with the real-time PCR technology with the primer/probes (2019-nCoV CDC EUA Kit), developed by CDC and manufactured by IDT using a one-step master mix (TaqPath CG, Thermofisher). Real-time RT-PCR was conducted with QuantStudio7Pro in a 384-well plate format. The human RNAse P gene was used for an internal control to ensure human cells were present and to detect any sample inhibition that might be present. A Ct value less than 39 was considered as positive for the target. While one technician worked with the specimen, the second technician monitored placement of the aliquot in the test well and assured the assigned bar code was linked to the corresponding patient in the test instrument. Once completed, the original sample tubes were returned to the refrigerated

Image 4. Scanning Barcode into REDCap.

A	B	C	D	E	F
DATE REC #	SERIAL #	REDCAP RECORD#	PATIENT NAME	DOB	BARCODE
4/29/2020 12:00 Run					
4/28/20	1	5472	PATIENT NAME	12/3/49	dw070_a01
4/28/20	2	5475	PATIENT NAME	12/3/49	dw070_a02
4/28/20	3	5473	PATIENT NAME	1/8/25	dw070_a03
4/28/20	4	5474	PATIENT NAME	1/8/25	dw070_a04
4/28/20	5	5476	PATIENT NAME	2/13/39	dw070_a05
4/28/20	6	5477	PATIENT NAME	2/13/39	dw070_a06
4/28/20	7	5479	PATIENT NAME	1/11/32	dw070_a07
4/28/20	8	5480	PATIENT NAME	7/25/48	dw070_a08
4/28/20	9	5478	PATIENT NAME	10/15/51	dw070_a09
4/28/20	10	5481	PATIENT NAME	11/30/85	dw070_a10
4/28/20	11	5482	PATIENT NAME	8/19/94	dw070_a11
4/28/20	12	5483	PATIENT NAME	1/2/53	dw070_b01
4/28/20	13	5484	PATIENT NAME	8/10/78	dw070_b02

Image 5. Specimen Catalog with Barcode.

area for pickup by LCSP personnel.

8. Integration of results from the testing instrument to the specimen database

After each testing cycle, the instrument recorded results that were analyzed by the principal virologist. Once satisfied with the quality of the results and test process, the results were sent in an Excel spreadsheet via internal secured email to the LCSP biostatistics and informatics personnel for uploading into REDCap. This upload linked individual results to their unique barcode and populated the Results section in REDCap for each patient.

9. Analysis of test results

LCSP personnel reviewed the test result information provided by the virologist using the specimen catalog spreadsheet to verify that each result had linked to the correct patient barcode. REDCap was programmed to assign a completion status for all results identified as "negative" or "invalid". Results identified as "inconclusive" would await another run using the original specimen (not the aliquot). A second "inconclusive" result would be finalized. All results finalized as "inconclusive" or "invalid" were communicated to the submitting facility so they could make the clinical determination as to whether a new specimen should be collected and resubmitted for testing. All "positive" results required manual entry into REDCap and completion of result verification as a final check to ensure there were no positive results entered in error. The completion work was done by one of the Infectious Diseases faculty members with a quality partner to prevent patient/barcode identification errors. (**Figure 6**)

10. Communicating test results

The primary purpose of the surveillance program was to identify patients with and without disease so healthcare personnel could evaluate the necessity for isolation, use of personal protective equipment, and healthcare worker occupational exposure assessment. Therefore, it was critical to ensure results were shared promptly with individuals empowered to make local decisions. Results were reviewed as the principal virologist released them. This process occurred at least once each day and sometimes twice if multiple testing runs occurred. Results were shared via telephone with the Chief Medical Officer of each hospital facility the day results were received. A written report with a cumulative list of all patients tested from that facility was emailed the following day using a secured and encrypted process. Included in that report was a cover page with an explanation of the test interpretation. This helped recipients understand what action was indicated in the event the result was noted as "invalid" or "inconclusive". A summary report was also sent to the Kentucky Department for Public Health and the local health departments (e.g., Louisville Metro Public Health and Wellness, Floyd and Clark counties in neighboring southern Indiana). Excel files of patient results were also sent to the laboratory contact at each facility so they could integrate results into their separate electronic health record systems. Individual patient reports were not provided. By week five of the project, a REDCap data portal was developed with access provided to each facility submitting patient samples for testing. This portal access was made available to a point person at each facility enabling them to have real-time access to finalized test results. (**Figure 8**)

11. Quality measures

Ensuring quality at every step in the process involved identifying activities prone to error (e.g., manual data entry) as well as activities that were subject to errors of high consequence (e.g., misidentification of specimen, barcoding error). Each step in the process was evaluated to determine possible errors and a corresponding approach for quality monitoring. **Figure 9** provides a summary of the quality indicators for each process step. Specific personnel were assigned to the quality measurement function, each serving as an independent evaluator of the process. These personnel were trained in each step of the process and helped craft the indicators. Quality reports were developed and shared with the LCSP teams as a way of tracking process errors as well as identifying opportunities for quality improvement and efficiencies.

Organizational Capacity

The CERID research enterprise provides the framework and support necessary for a robust program focused on population-based clinical research capable of studying health conditions present in patients receiving care in hospitals, long-term care facilities, and outpatient settings. The CERID enterprise structure enabled quick access to trained personnel and organizational capacity. Having this structure in place enabled the rapid implementation of a surveillance team and process to address the COVID-19 pandemic.

Operationalizing the surveillance process incorporated use of each component of the CERID enterprise. A brief description of those units and their responsibilities shown in **Figure 1** are described below:

The *Data Management, Biostatistics,* and *Informatics Units* were responsible for working together to develop the initial REDCap database and respond to improvements that resulted over the first five weeks of its use. These three groups worked together to develop reports and reporting processes as well as respond to technologic requests from hospitals,

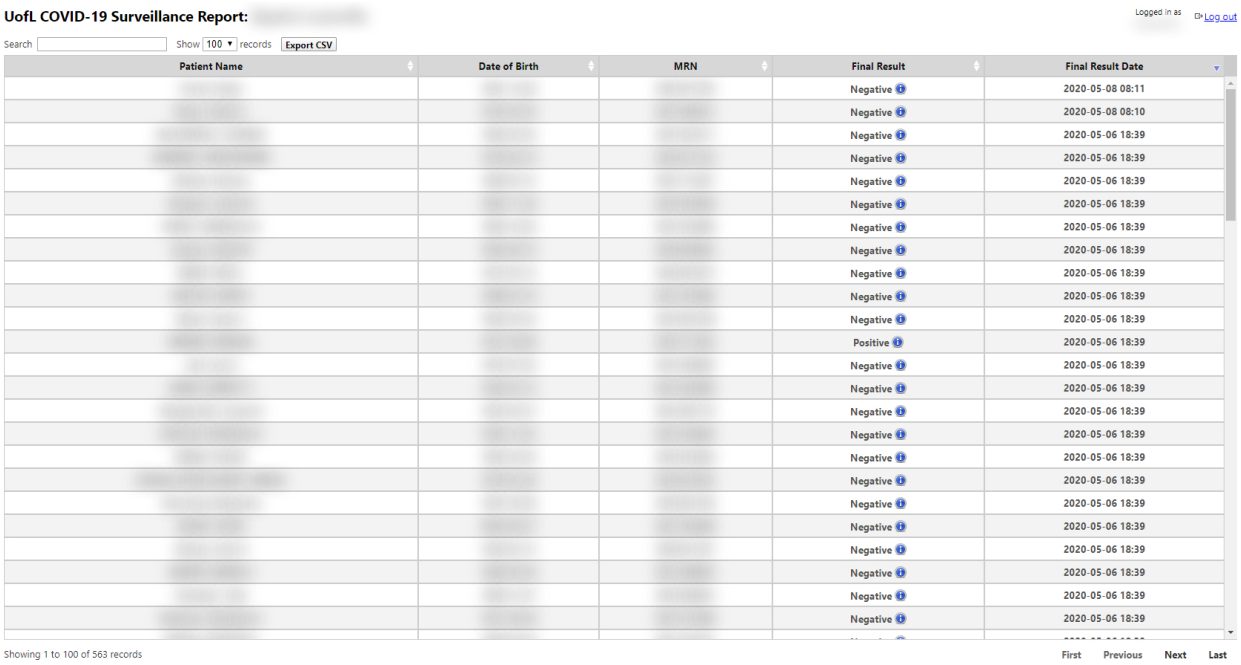

Figure 8. REDCap Database Portal View.

long term care facilities and public health concerning real-time, read-only data access. This real time access required that individual portals be developed so facilities could see only their data while public health officials were able to access all data.

The *Implementation Unit* was responsible for surveillance activities including specimen retrieval, data entry, cataloging, and barcoding. This group consisted of personnel with specific training in clinical research and all aspects of a standardized operational approach.

Laboratory Unit personnel possessed expertise in the handling and management of clinical and research specimens, so they were quickly able to transition their work from clinical research studies to assisting with specimen management and handoff to the UofL-CPM testing team. These personnel were also critical in developing an understanding of good laboratory practices as are present in the ID Division Reference Laboratory. In addition, these personnel provided the necessary expertise in understanding test results, their limitations, and approaches for providing useful information back to the participating facilities and healthcare personnel.

The *Biorepository Unit* was responsible for developing the process to track and maintain all specimen in the event it was necessary to retest. This unit also managed the process for freezing all positive specimens for validation or subsequent re-testing. The REDCap database provided the opportunity to document and catalogue precise specimen location for easy retrieval. (**Figure 5**)

Members of the *Quality Assurance Unit* were responsible for identifying steps in the process where error could occur. This included identification of steps that were prone to error and situations where error occurred or where there was a 'near miss'. This team provided reports of those occurrences back to the team leader and each were addressed immediately. This work involved process change (e.g., a numbering system added to tubes), error prevention (e.g., implementing a 3-day save the tube procedure), and identifying near miss situations (e.g., individual specimen identification instead of multiple samples under a single REDCap identification number). With any change, staff were re-trained.

The *Community and University Outreach Units* worked with researchers across the University of Louisville campuses and the community to identify their areas of expertise and interest in surveillance program participation as well as designing research questions. Researchers in the Speed School of Engineering worked to develop products that could use the 3D printing capability to address care-related capacity such as production of face shields for nurses and printing of an alternative swab in light of the shortages in that critical supply.

Process Step	Quality Indicators
1. Test instrument validation and result verification	1A. Concordant results using two different test methods; one in CLIA-certified lab and one in research lab
2. Database development	2A. Manual entry restricted to demographic section 2B. Dropdown options available for all data items 2C. Portal access can be developed 2D. Individual facility reports 2E. Barcode capability 2F. Result import acceptable 2G. Phone friendly iOS and Android
3. Specimen movement from hospitals to the testing site	3A. Packaged appropriately for transport 3B. Test request form accompanying each specimen 3C. Test request form and specimen match 3D. Specimen labelled 3E. Specimen label legible
4. Data entry	4A. Correct spelling of patient name 4B. Correct date of birth 4C. Specimen assigned to correct facility 4D. Correct specimen type 4E. Identity of data entry personnel
5. Cataloging the specimen for movement to the laboratory for processing	5A. Appropriate PPE worn by personnel 5B. All work performed in biosafety cabinet 5C. Specimen tubes numbered 5D. Specimen tubes in rack 5E. Catalog completed with all data elements entered 5F. Catalog data elements accurate 5G. Tubes transported to CMP refrigerator in closed container to await testing 5H. PPE removed, placed in biohazard bag, hand hygiene by personnel 5I. Specimen catalog placed with tubes in CPM refrigerator to await barcode placement
6. Assignment of the specimen barcode	6A. Barcode placed on specimen catalog sheet by CPM personnel 6B. Barcode sheet retrieved by LCSP personnel 6C. Barcode scanned into REDCap 6D. Barcode verified to ensure capture in REDCap and on correct patient 6E. Multiple barcode acceptance
7. Specimen testing	7A. Process supports standard test run times 7B. Result concordance with parallel testing 7C. Definitive results 7D. Process demonstrates accepted good laboratory practices
8. Integration of results from the testing instrument to the specimen database	8A. Imports accepted by Excel 8B. Data imports allowing finalization of select results
9. Analysis of test results	9A. Definitive results 9B. Reliable barcode links
10. Communicating test results	10A. Direct communication with hospital chief medical officers 10B. Direct communication with public health officials 10C. Direct communication with facility point person 10D. Portal available with file download options 10E. Printed report option

Figure 9. Quality Indicators for Each Process Step.

The *Medical Writing Unit* and the *Peer-Review Journals Unit* continued their responsibility for disseminating knowledge gained as part of the COVID-19 response. As new information was learned regarding the process, a mentored writing and publication process began with articles submitted for peer-review in both the *Journal of Respiratory Infections* and the *Journal of Refugee and Global Health*.

Members of the *Marketing Unit* served as the communication link with local media, community partners, and public health so there was ongoing awareness of activities and findings. For example, this Unit was responsible for working with radio, television, and other social media connections interested in the surveillance operation and findings.

Coordination of all personnel activities occurred within the *Administration Unit* of CERID. This group managed personnel decisions, addressing University quarantine and activity 'pauses', and communication with all University divisions and leadership. Reassignment of job responsibilities, additional training and competence documentation constituted the majority of the responsibilities handled by this unit.

The *Financial Unit* was critical in ensuring that costs associated with the surveillance program were captured and managed. An initial investment of $500,000 by the University of Louisville President and the Executive Vice President for Research and Innovation enabled the operation to begin while community and grant support was explored and

captured. This Unit was also responsible for providing ongoing reports concerning the financial impact on the entire CERID enterprise, including current research outside of COVID-19 response.

Discussion

The UofL CERID leadership team set specific goals for the LCSP that included: 1) increasing the COVID-19 testing capacity for Kentucky and southern Indiana (Kentuckiana); 2) providing an ability to study the burden of the COVID-19 pandemic on the local population; and 3) supporting healthcare facilities as they developed local policies guiding their responses to COVID-19 in patients and healthcare workers.

Between late February and early March, there was considerable concern regarding a lack of COVID-19 testing capacity in Louisville and across Kentucky. Without access to testing, the healthcare infrastructure and healthcare workers remained at tremendous risk. In Louisville, healthcare is a primary industry with 10 area hospitals, more than 45 long-term care facilities, headquarters for health insurers and pharmaceutical companies, and specialty centers for cancer, HIV, and trauma care. This level of healthcare industry present in the community led to recognition of the importance of protecting this element of the workforce and economy by early testing and disease recognition. As the LCSP program was conceptualized then implemented, with the financial support of UofL President Bendapudi, all aspects of the program were clearly focused on healthcare facilities and healthcare workers. The University provided space and CERID assumed responsibility for identifying and training the necessary personnel for activities within the scope of practice and competence. For testing capacity, specialists in the area of virology with expertise in high-capacity testing platforms helped define the new process. Research meetings began with outreach across the University along with development of white papers and grant submissions. As an example, the focus on healthcare personnel surveillance and testing was submitted to the Centers for Disease Control and Prevention on March 25, just 12 days after LCSP implementation. Broad and transparent collaboration and sharing occurred to encourage engagement across the University campus communities. With the breadth of activities, there have been challenges at every step. During this time of healthcare, economic, and social disruption, it has been challenging to infuse a sense of normalcy. Reliance upon existing systems has been challenging, but using existing relationships and professional connections have enabled progress and quality outcomes. The real consequences of using a new process for COVID-19 testing, along with shortages in the supply chain, and using just-in-time training for new personnel to obtain specimens, were challenges to understanding all the results and conveying them in the context of clinical relevance.

After six weeks of operation, more than 5000 samples were tested with more than 730 positive patients and healthcare workers being identified. Samples were received from fifteen hospitals and seventeen long-term care facilities in the Kentuckiana area. The operation involved faculty time from Infectious Diseases, Laboratory Medicine, Microbiology, Virology, and Research & Innovation. More than 30 CERID personnel played a role in the processes, in addition to staff representing other areas of the University such as building security, maintenance and Environmental Health and Safety. The operational costs, not including laboratory supplies and laboratory personnel, have been approximately $50,000 per week.

There are several lessons learned from this process that can be of help to others as they address the challenges posed by the COVID-19 pandemic. First, the process is applicable to other testing methods beyond high-capacity testing. Most of the same steps outlined here can help with traditional laboratory processes when test request capacity exceeds historic capabilities. Second, success with a new approach during a time of chaos and upheaval can be achieved when there is an ability to rely upon existing systems and staff knowledge. Experiences with research processes, database development, just-in-time training, attention to detail, and innovation were critical elements. Third, developing a vital public health response requires an ability to seek and nurture new partners with shared interests. For the LCSP team, methods to best address the ongoing challenges of the COVID-19 pandemic required that existing relationships and capacities be maximized and there be a continuous focus on supporting the healthcare infrastructure and safety of the healthcare workforce.

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Author contributions

RC, DB, AA, MS, WJ, MA: responsible for primary writing of the manuscript.
AL, DC: responsible for primary writing and editing of the manuscript sections involving the UofL-CPM testing processes.

SF: responsible for sections involving the REDCap database and report development.
JR, RC: responsible for critical review of the manuscript.
All authors have reviewed and approved the final version of this manuscript.

Appendices

Appendices are available upon request. Due to formatting constraints, the *Journal of Respiratory Infections* is unable to publish appendices.

Appendix 1: CERID Coronavirus Study Group

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