

PUBLIC HEALTH LABORATORY

The North Dakota Department of Health's (NDDoH) Laboratory Services section provides laboratory test services for various diseases related to public health. These services range from human tests for Chlamydia, Gonorrhea, Tuberculosis, Syphilis, to various respiratory and enteric (intestinal) pathogens. As a Tier 2 institution, the laboratory may retain more volatile substances, is part of the National Laboratory Response Network that tests for biothreat agents such as anthrax, plague, and brucella, and is regulated by the [Federal Select Agent Program](#).

In addition, animal and environmental tests are performed and include rabies tests, and screens dead birds, mosquitos, and ticks for human pathogens. The environmental laboratory provides microbiological water analysis, dairy sample analysis, and surface/lagoon water analysis.

This document provides an overview of the laboratory and responds to frequently asked questions.

NDDoH LABORATORY OVERVIEW

The laboratory is located in Bismarck, ND and was staffed by 18 FTEs and one temporary employee prior to the SARS-CoV-2 pandemic. The state's laboratory has played a significant role in the pandemic response.

- Scaled to meet COVID-19 testing demand from 197 COVID samples per day in March 2020 to 7,500 COVID-19 samples per day in December 2020
- Implemented whole-genome sequencing of SARS-CoV-2. Whole-genome sequencing can map the entire genetic sequencing of a virus which allows for the detection of drift and shift in the genetic code. For example, it can identify and confirm variants that may match variants circulating in other areas of the country and world
- Validated and confirmed 61 new tests, equipment and procedures in nine months
- Added 37 new instruments for SARS-CoV-2 related tests:
 - Extractors for isolating RNA from human samples:
 - Qiagen Ez1 extractor
 - Roche 96 extractor
 - ThermoFisher KingFisher extractors (5)
 - ABI 7500 Fast DX (9), a PCR analyzer for the amplification and detection
 - Whole genome sequencing instrumentation for detection of viral sequences:
 - Illumina MiSeq
 - Minlon Gridiron

- Agilent tape station
 - BioRad Thermocyclers (2)
 - Perkin Elmer Cyclone
- Automated systems to reduce manual labor and increase efficiency for SARS-CoV-2 molecular methods (how viral RNA can be processed and detected).
 - ThermoFisher Amplitude System
 - Abbott M2000 system (4)
 - Hologic Panther system (3)
 - Cepheid GeneXpert row of drawers
 - Biofire Microfilm Array platform
 - Qiagen QiAgility
- Qiagen Sofia 2 systems (3), an antigen test system
- Diasorin Liaison, a serology platform for the detection of antibodies
- Grew from 18 FTEs and one temporary employee to over 180 team members at the peak of the pandemic response
- Resulted over 930,000 COVID samples
- Of the last 400,000 COVID samples received, 97% were resulted in less than 36 hours and 65% were resulted in less than 24 hours
- Scaled a distribution program from 150 COVID-19 sample collection orders a day, to over 9,000 a day supplied to more than 300 laboratories and/or facilities
- Collaborated with research universities to increase laboratory capacity. Worked with the NDSU vet diagnostic laboratory to establish CLIA accreditation to perform COVID-19 tests and transferred equipment to the UND Medical Laboratory Science program
- Supported an increase in COVID-19 testing capacity at two hospital laboratories in North Dakota by providing equipment and reagents – Altru in Grand Forks, ND and Essentia in Fargo, ND
- Maintained pre-pandemic routine human test menu for other diseases
- Completed several building upgrades and improvements to become more energy efficient and reduce costs. These upgrades were part of the UNESCO project to make the laboratory more energy efficient and included improving lighting, air handling, occupancy sensors, and fume hoods (ventilated enclosures where harmful chemicals can be utilized safely). In addition, the laboratory completed a major roof repair, three mobile laboratories were added in the parking lot and a generator was installed and tested to provide emergency power



NDDoH LABORATORY FREQUENTLY ASKED QUESTIONS



WHAT IS THE ROLE OF THE CLIA DIRECTOR AND DID THE LABORATORY, AT ANYTIME, OPERATE WITHOUT A CLIA DIRECTOR?

- [Dr. Linz](#) has been the CLIA laboratory director for the NDDoH since 2005. She was previously engaged as a contractor through another organization and was hired on October 1, 2020 as a temporary employee with the NDDoH. This was a seamless transition and there were no gaps in CLIA directorship.
- A CLIA director is [responsible for](#) the overall operation and administration of a laboratory. The responsibility includes assuring compliance with all applicable regulations. Directors may direct up to five laboratories. Dr. Linz is currently the CLIA Laboratory Director at two laboratories – NDDoH and NDSU Vet Diagnostic Laboratory.

WHAT IS DR CHRISTIE MASSEN'S ROLE?

- [Dr. Christie Massen](#) is a nationally certified, North Dakota Board of Clinical Laboratory Practice (NDBCLP) licensed Medical Laboratory Scientist (MLS) who serves as the NDDoH's Chief Laboratory Officer. Dr. Massen oversees the laboratory's General Microbiology, Special Microbiology, Biothreat, and Quality Assurance divisions. She is responsible for the daily operation and administration of the laboratory. Her duties include the supervision of division directors and other staff, personnel management, applying for and securing funding, budget management and preparations, and working with NDDoH leadership to identify goals and plans for the laboratory that align with the department's mission.

DOES THE LAB USE MEDICAL LABORATORY ASSISTANTS TO RUN THE EXTRACTION PHASE OF PCR TESTING?

- Extraction is the purification of RNA genetic material from a human sample that will be analyzed for the presence of RNA that is specific for the targets related to the SARS-CoV-2 virus.
- The laboratory works closely with the CLIA director and the NDBCLP to ensure compliance with all federal and state regulations.

The regulations did not specifically address whether the process of sample extraction is considered part of the pre-analytical or analytical phase of the test (the factor that dictates what level of credentials are needed to perform the test). The level of credential topic was discussed [on March 25, 2020 at a special meeting](#) with the NDBCLP. While there was no official statement from the NDBCLP, there was agreement that sample extraction was part of the pre-analytical phase of the test. Therefore, the need for a licensed individual to conduct sample extraction was not required by the NDBCLP and CLIA's requirement related to state licensure was not applicable.

Non-licensed laboratory assistants, who were trained and competent, performed extractions on the ThermoFisher platform. All extraction plates/maps were reviewed by a NDBCLP licensed medical laboratory technician or medical laboratory scientist prior to the approval of results. No issues or negative patient outcomes resulted from non-licensed laboratory assistants performing extractions.

On December 10, 2020 the state CLIA director received an email from Bridget Weidner with the NDDoH Division of Health Facilities reporting that CLIA viewed extraction as part of the analytical phase. The laboratory took immediate action and stopped using non-licensed laboratory assistants for the extraction process. In an email response from CLIA on January 12, they now consider the situation resolved.

HOW DOES THE LABORATORY DECIDE WHAT CYCLE THRESHOLDS (CT) ARE USED FOR PCR TESTS?

- A polymerase chain reaction (PCR) test detects RNA (or genetic material) specific to the virus and can detect the virus within days of infection, even those who have no symptoms. PCR tests are extremely accurate for infectious disease testing with high sensitivity and specificity.
- To improve the test's ability to detect virus, a PCR test creates many copies of the same genetic material from the virus in a process called amplification. The cycle threshold, or CT value, is the point at which a reaction reaches a fluorescent intensity above background levels. The CT value indicates when the nucleic acid target sequence is detectable in the amplification process. If the correct sequences are present in the specimen, the test will be positive.
- In accordance with the Food & Drug Administration (FDA), the NDDoH follows manufacturer guidelines for all PCR tests. Laboratories across the country performing PCR tests for COVID-19 (including Altru, Sanford, Trinity, etc.) follow manufacturers' guidelines. Laboratory tests are validated to perform the FDA's emergency use authorization version of each test.

- Testing for COVID is a screening test that requires high sensitivity. Cycle thresholds are set by the manufacturers. For more information, view the package inserts: [Abbott M2000 System](#), [BioFire Multiplex](#), [Hologic Panther System](#), [ThermoFisher Amplitude System](#), [ThermoFisher TaqPath](#), [Cepheid GeneXpert Xpress](#)

CAN A CT VALUE DETERMINE HOW MUCH VIRAL GENETIC MATERIAL IS PRESENT IN AN INDIVIDUAL'S SAMPLE?

- A CT value from a PCR test does not indicate how much virus is present, but only whether viral genetic material was detected at a defined threshold. PCR tests can be qualitative or quantitative. Qualitative PCR tests determine whether the virus is present or absent, whereas quantitative PCR tests read the amount of virus present in the sample. Since there are no FDA Emergency Use Authorized quantitative COVID-19 PCR tests, the state laboratory only performs qualitative PCR tests and only positive or negative results are reported as instructed by the manufacturer.

CAN A CT VALUE PREDICT HOW INFECTIOUS AN INDIVIDUAL WITH COVID-19 IS?

- According to the [Centers for Disease Control and Prevention](#), the answer is no. CT values should not be used to determine a patient's viral load, how infectious a person may be, or when a person can be released from isolation or quarantine.

HOW DOES THE LABORATORY ENSURE QUALITY?

- The laboratory has an extensive [quality assurance plan](#) and quality control procedures in place to ensure results are accurate and consistent. This plan was established before the COVID-19 pandemic and is frequently reviewed and updated as needed. The quality assurance plan ensures that [CMS guidelines](#) are followed for each test platform and testing personnel.
- As part of the [CMS guidelines](#), each laboratory must establish and maintain written policies and procedures that monitor quality. These quality assessments are done with every sample run and have been part of standard protocol long before the COVID-19 pandemic.
- The laboratory is constantly reviewing and improving processes. For example, on November 28, 2020, additional guidance on how to do a quality assessment of each run was sent in an email after a concern was raised when two facilities reported a substantial number of new positives. The issue was fully addressed, the errors were corrected before the results were reported, and the process was improved.
- Heather Sease serves as the lab's Director of Quality Management and is a nationally certified, North Dakota Board of Clinical Laboratory Practice (NDBCLP) licensed Medical Laboratory Scientist (MLS). Heather oversees the examination of records, forms, and

results of all tests within the Division of Laboratory Services as well as ensure that all policies and procedures meet the CMS guidelines. She meets with the CLIA Laboratory Director monthly or more often, as needed.

HOW DOES THE LABORATORY KNOW IF A PLATFORM IS NOT WORKING OR IF TEST RESULTS ARE NOT ACCURATE?

- Laboratorians are trained to review and assess every batch looking for abnormalities in results. They immediately bring any issues forward to a supervisor or manager and document the abnormality. If an issue is identified, it is thoroughly [investigated](#).
- In addition to regular training that includes how to report issues, laboratory leadership promotes creative and bold thinking, encouraging team members to complete process improvement forms to suggest ways to improve laboratory operations. Currently, leadership at the laboratory is not aware of any reported issues from staff related to abnormally high numbers of positive cases.
- It may appear that certain platforms have a higher likelihood of positives but it can be easily explained. It is common for samples from certain facilities to regularly run on the same platform. It is not unusual to see higher positivity rates on runs that primarily include samples from hospital and clinic facilities who test more symptomatic individuals.

IS THE LABORATORY TRANSPARENT ABOUT ISSUES?

- Any issues identified or brought to the attention of the NDDoH have been thoroughly investigated and addressed quickly and transparently. Examples are noted below. The NDDoH has been praised on social media for their transparency and quick response to issues.
- On September 4, 2020, 349 COVID-19 samples from a Fargo testing event could not be analyzed because of a handling error; the samples were placed in the wrong refrigerator. When the samples were found, they had timed out and it was too late to process. All individuals whose samples had been misplaced, were contacted and offered another test. The public was informed through social media, the issue was fully addressed, the errors were corrected and steps were taken to ensure the refrigerator is no longer used for COVID-19 samples.
- May 19-21, 2020, two Abbott M2000 instruments malfunctioned on several runs over the course of the three days. An investigation commenced and led to the discovery of plate seals that did not adhere correctly and caused minimal contamination. All Abbott M2000 instruments were shut down and an in-depth decontamination protocol was performed. The laboratory worked closely with the manufacturer on the issue and it was found that a



specific lot number of the plate seals were defective. All defective plate seals in this lot number were returned to the manufacturer. Out of an abundance of caution, 82 positive results were determined to be inconclusive. All 82 individuals were quickly contacted, offered another test, and a social media announcement was posted.

- Most recently on January 8, 2021, the laboratory began investigating a software malfunction on the ThermoFisher Amplitude System. This piece of equipment was added to the laboratory on November 7, 2020 and has resulted over 80,000 tests. A manufacturer's software issue was identified when additional testing was done on another platform for further data analysis and there was a discrepancy in the results. This prompted a look back which identified the same issue on previous runs. To date, 181 positive results between December 25, 2020 to January 8, 2021 were changed to inconclusive and although the issue has been resolved, laboratorians have continued to manually review all raw data from the ThermoFisher Amplitude System prior to the results being released. In addition, the laboratory has increased the frequency of routine maintenance and software verification. The issue has been reported to ThermoFisher, the individuals have been contacted and a news release and social media were distributed.
- These three issues account for a total of 612 errors and the vast majority of the laboratory issues/errors since March 2020. While the team strives for zero errors, this level of issues/errors is very low given over 932,000 samples have been analyzed at the state laboratory since March 2020.

IS THE STATE LABORATORY SUBJECT TO INSPECTION?

- The NDDoH Public Health Laboratory is in good standing with Clinical Laboratory Improvement Amendments (CLIA) and is [inspected every two years](#). The laboratory is also [inspected every three years](#) by the Federal Select Agent Program.

Throughout the pandemic and always, the NDDoH's Laboratory Services section delivers on its mission to provide legally defensible quality analytical laboratory services within a reasonable time for the department and the state of North Dakota.

For more information, please contact Dr. Christie Massen, Chief Laboratory Officer, at 701-328-6272 or clmassen@nd.gov.