LifeLabs®

INSIDE Diagnostics ONTARIO

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THE DIAGNOSTIC NEWSLETTER
FOR **HEALTHCARE PROVIDERS**

ONTARIO MEDICAL DIRECTOR UPDATE – COVID-19 AND IMPACT ON COMMUNITY LAB SECTOR

J. Timothy (Tim) Feltis
MD FRCPC
Ontario Medical Director, LifeLabs

The COVID-19 pandemic has had a significant impact on the practice of Laboratory Medicine in the Community Lab sector. While there have been multiple negative effects such as reduced testing volumes and temporarily closed locations because of staffing challenges, there are also many positive outcomes that have and continue to be realized, as the pandemic evolves. In this update, I would like to focus on some of the positive effects of the pandemic as they relate to the future practice of laboratory medicine.

Thank you to LifeLabs Employees

First of all, I would like to thank all of our employees for their dedication and for truly living out LifeLabs values of being Customer Driven, Agile, Caring, and One Team. There are countless examples of how we as an organization pulled together to continue to safely provide service to our Health Care Providers (HCPs) and to our patients despite rapidly changing environment. This was especially evident in the earlier stages of the pandemic when public health rules and regulations changed frequently, almost on a daily basis. The spirit of co-operation between the various divisions of our organization has never been better, and I am certain that we can continue to build on this to the benefit all our customers.

I would also like to specifically recognize exceptional efforts of our Employee Health and Safety Department, who has been spearheading LifeLabs response to the pandemic with the strong support from our Medical/Scientific and the Quality and Regulatory teams.

As we establish the "new normal", LifeLabs continues to look for and find ways to improve the level of service for each of you and your patients.

Accelerated Progress Towards E-Ordering Implementation

With the various lockdowns and reductions in service, most HCPs started to offer some form of 'Virtual Care' to their patients. One of the many challenges of virtual care was getting a signed OHIP laboratory requisition to the patient. For a number of years, Ontario community laboratories have been in discussions with the Ministry of Health to develop a system for electronic ordering (E-ordering) of laboratory tests. The pandemic has brought the importance and the need for E-ordering to the forefront.

Since March 2020, LifeLabs has worked quickly to put in place various strategies to enable electronic receipt of OHIP lab requisitions. This includes Fax and Email receipt of requisitions, as well as deployment of some E-Order pilots. The initial option to receive requisitions by Fax was enhanced by a capability to send requisitions by Email. This allows patients to present at any one of our patient service centers (PSCs), email their requisition to a dedicated, secure LifeLabs Email, and our staff are able to pull it up in the system. Many HCPs have taken advantage of this service. The ultimate goal would be for a HCP to order tests on an OHIP requisition right from their Electronic Medical Record (EMR), and then forward it to the laboratory (or a central repository), so that when the patient presents at a PSC, the requisition in already in the patient's file.

ONTARIO MEDICAL DIRECTOR UPDATE – COVID-19 AND IMPACT ON COMMUNITY LAB SECTOR (CON'T)

Full E-ordering of tests will take time to roll out, as it requires changes to our IT infrastructure and the interfaces to the various EMRs. We have already run a successful pilot on E-ordering with a large group of physicians in the GTA using OSCAR and CHS EMRs. We will endeavor to keep you informed of the progress of this important change.

There are many potential positive implications of E-ordering implementation, including reduction in transcription errors, ensuring correct physician address are recorded, reduction in potential fraudulent ordering of tests, and limiting the impact on the environment. Based on the internal audit of 2019 reports, we found that we had incorrect physician or incorrect physician address 34 times in 4944 audited reports. The other categories that we looked at were incorrect tests ordered and missing tests which accounted for 1.92% of all errors. E-ordering would substantially reduce all of these types of errors.

Rapid Expansion of COVID-19 Diagnostic Testing Capacity

As the demand for COVID-19 laboratory testing grew, LifeLabs responded quickly to assist the province in providing rapid and accurate results for COVID-19 molecular diagnostic testing (e.g. PCR testing). We quickly expanded our molecular testing capabilities. Between our Microbiology department and Genetics Laboratory, we are now able to perform close to 5000 tests per day. This required a tremendous amount of teamwork on the part of our Operations, Quality and Regulatory Affairs and Medical/Scientific teams, and I am extremely proud of their efforts.

The expansion of molecular testing platforms also greatly enhances our capacity for other types of molecular testing, which have the potential to revolutionize the way in which microbiology testing is performed. Molecular testing has the potential to greatly improve turnaround times as well as both sensitivity and specificity of clinical microbiology tests.

COVID-19 Serological (Antibody) Testing

Many of you have been asking about serological testing for SARS-CoV-2. Effective since August 6. 2020, OHIP-insured COVID-19 antibody test has been available through Public Health Ontario Laboratory for a very limited number of clinical indications, including Multisystem Inflammatory Syndrome in Children (MIS-C).

LifeLabs Ontario plans to offer an uninsured COVID-19 serological test (SARS-CoV-2 Total Antibody) in October 2020, which can be used to assess recent or prior infection with SARS-CoV-2 virus.

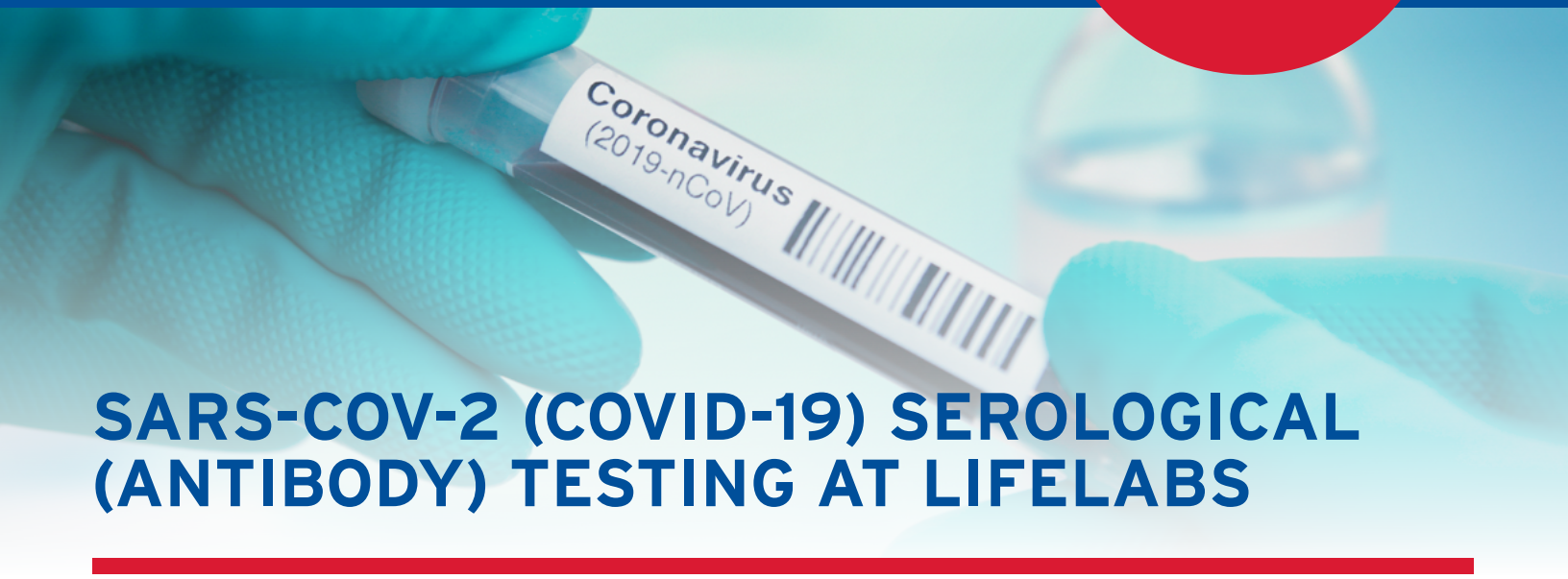
For detailed information about both OHIP-insured and uninsured COVID-19 antibody testing, please see the article below.

I am pleased to report that members of our Medical/Scientific Team, through their professional organizations, have co-authored a Narrative Review in the CMAJ titled Van Caeseele, P., *et al.* SARS-CoV-2 (COVID-19) serology: implications for clinical practice, laboratory medicine and public health. *CMAJ* **192**, 34, E973-979 (2020). https://doi.org/10.1503/cmaj.201588

The review was a result of a collaborative effort between five Canadian clinical and public health organizations.

It has been a challenging year for Canada and the rest of the world. Despite many obstacles, our team continues to ensure LifeLabs provides timely and high quality test results to Canadians during this crisis. We would like to thank you and your patients for your ongoing support!

J. Timothy (Tim) Feltis
MD FRCPC
Ontario Medical Director, LifeLabs



SARS-COV-2 (COVID-19) SEROLOGICAL (ANTIBODY) TESTING AT LIFELABS

Serological testing for COVID-19 involves the detection of antibodies, in blood, serum or plasma, specific to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Although nucleic acid testing is currently considered the gold standard for the diagnosis of COVID-19, serological assays can help identify those individuals with prior exposure to SARS-CoV-2 and also assess COVID-19 exposure at a population level.

Humoral Response to SARS-CoV-2

The SARS-CoV-2 genome encodes four major structural proteins including the surface or spike protein (S), nucleocapsid (N), envelope and membrane proteins. Virus entry into the cell is mediated by the S protein which binds to angiotensin-converting enzyme-2 receptors and mediates fusion between the virus and cell membrane of the host. Current serological assays are directed toward the S or N proteins.

Although the humoral response is not fully elucidated, most studies indicate both immunoglobulin G (IgG) and immunoglobulin M (IgM) COVID-19 antibodies appear at detectable levels approximately two to three weeks after symptom onset or exposure to the virus.[1] Serology testing is not recommended to diagnose SARS-CoV-2 infection during the first two weeks (14 days) following symptom onset primarily due to the lag time between exposure and the development of detectable antibodies.[2, 3]

Reports suggest the antibody response to SARS-CoV-2 is associated with disease severity where patients with severe disease show the highest antibody production.[4] In immunosuppressed patients, or those with mild disease or asymptomatic, antibodies may remain undetected or may not develop.[5] Furthermore, lower antibody levels have been reported in smokers and users of anti-inflammatory medication.[6] There may also exist age, gender, and ethnicity – specific differences in the antibody levels, but they are not well understood and are the subject of ongoing research studies.

Serological (Antibody) Testing for SARS-CoV-2

Commercially available serological assays target one or more of three antibody isotypes (i.e IgA, IgG, IgM) or total immunoglobulin. As of 20. September 2020, nine laboratory assays have obtained Health Canada approval for the detection of antibodies to SARS-CoV-2. To date, there is insufficient evidence to support the use of point-of-care COVID-19 serology tests and no assay has received Health Canada approval for this purpose.

Serological testing currently has limited utility and is only recommended for the following indications:

1. A patient suspects exposure or COVID-19 infection at least 3 weeks previously.
2. Pediatric patients presenting with symptoms compatible with Multisystem Inflammatory Syndrome in Children (MIS-C) who do not have laboratory confirmation of COVID-19 by PCR
3. Epidemiological purposes (e.g. estimate prevalence in a given population/region)

SARS-COV-2 (COVID-19) SEROLOGICAL (ANTIBODY) TESTING AT LIFELABS (CON'T)

Serological Testing for SARS-CoV-2 at LifeLabs – OHIP-Insured and - Uninsured Testing

A. OHIP-Insured Serological Testing for SARS-CoV-2

Effective August 6, 2020, Public Health Ontario's (PHO) Laboratory started testing for COVID-19 IgG antibodies (serology). COVID-19 serology testing is used to determine recent or prior exposure to SARS- CoV-2 virus.

Clinical Indications for OHIP-Insured COVID-19 Serology Testing:

- COVID-19 serology may be considered for clinical use as an adjunct to COVID-19 PCR testing **only** in:
  - Pediatric patients suspected to have Multisystem Inflammatory Syndrome in Children (MIS-C) with a negative, indeterminate, or inconclusive PCR test result or who were not tested.
  - Other clinical scenarios of severe illness with negative PCR tests where serology results **may be helpful for clinical action and decision making may be considered and require consultation and approval by a PHO microbiologist prior to collection.** The microbiologist can be contacted through the PHO Laboratory Customer Service Centre at **416-235-6556 / 1-877-604-4567.**
  - **Specimens submitted for testing for indications other than MIS-C or without prior approval will be rejected**

How to order:

- Please use the **PHO lab COVID-19 Serology Requisition** to order the test: https://www.publichealthontario.ca/-/media/documents/lab/covid-19-serology-test-requisition.pdf?la=en
- Please ensure section 6 of the requisition is filled in. Healthcare providers (HCPs) must get approval from PHO to order the test for reasons other than MIS-C.

LifeLabs does not obtain the requisition or the approval for the patient.

Public Health Ontario | Santé publique Ontario

COVID-19 Serology Test Requisition

4. Test(s) Requested ☑ SARS-CoV-2 IgG

5. Specimen Type

Specimen Collection Date (yyyy/mm/dd): _____ (required)

☐ Serum / Clotted Blood ☐ Other (specify): _____

6. Reason for test

☐ Suspected Multisystem Inflammatory Syndrome in Children (MIS-C)

Other reason requires PHO approval. Contact PHO at +1-877-604-4567.

- Patients must present with the PHO lab COVID-19 Serology Test Requisition for the sample to be collected at LifeLabs patient service center.
- OHIP, PHO general test requisitions, and other non-PHO requisitions will not be accepted or collected.

For additional information please contact:

- Public Health's Website: https://www.publichealthontario.ca/en/laboratory-services/test-information-index/covid-19-serology or
- Public Health Ontario – Laboratory Customer Service Centre at **416-235-6556 / 1-877-604-4567.**

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SARS-COV-2 (COVID-19) SEROLOGICAL (ANTIBODY) TESTING AT LIFELABS (CON'T)

B. Uninsured Serological Testing for SARS-CoV-2

Effective October 19. 2020 LifeLabs will start offering uninsured serological testing for SARS-CoV-2.

SARS-CoV-2 Total Antibody Assay:

LifeLabs validated multiple test platforms, and the Roche Elecsys Anti-SARS-CoV-2 assay was selected. This assay detects total antibodies (IgG and IgM) against the nucleocapsid protein of the SARS-CoV-2 virus, favoring high affinity antibodies such as IgG.[7] This assay is Health Canada approved.

Internal validations performed at LifeLabs ON, and a review of the scientific literature provided a clinical sensitivity of 96% when samples were tested >3 weeks post-symptom onset, and a clinical specificity >99%.

The sensitivity indicates the percentage of patients who have been diagnosed with COVID-19 that actually developed a detectable level of antibodies against SARS-CoV-2. Antibody levels may be undetectable for COVID-19 patients if they had developed a mild infection, if they are immunocompromised, or if the test was performed early in the disease course.[3]

The specificity studies indicated <1 % chance of a false positive result. While highly specific, the low prevalence of the disease in the general population increases the likelihood of a false positive result. Based on a prevalence of 1 %, this test is expected to have a **positive predictive value (PPV)** of 76 %. The PPV indicates the probability of a patient with a positive test that actually had the disease. Thus, it is often recommended to use this test under the right clinical indications to reduce the likelihood of a false positive result.

Based on current scientific knowledge, a positive serology test does not provide information on protective immunity. It should also not be used for the diagnosis of an acute COVID-19 infection or to determine infectious status. The molecular COVID-19 test is recommended for the latter purposes.

How to Order:

Under 'Other' category, the test can be ordered by writing: "SARS-CoV-2 Antibody" OR "COVID19 Antibody" OR "COVID-19 Serology" on OHIP requisition.

For additional information please contact: LifeLabs Customer Care Centre 1-877-849-3637.

C. Interpretation of the COVID-19 Antibody Test

IF A PATIENT HAS A REACTIVE (POSITIVE) RESULT...

They most likely had COVID-19 at some point in the past, but it is not known if they are currently infectious or have protective immunity against re-infection. A positive test result cannot be used to inform decisions regarding physical distancing or to lessen the use of personal protective equipment.

IF A PATIENT HAS A NON-REACTIVE (NEGATIVE) RESULT...

Correlation with clinical and travel information is strongly indicated, and if very low probability of infection or exposure, a negative result indicates that they have not been infected with SARS-CoV-2. The above mentioned considerations for a false negative result should also be considered.

SARS-COV-2 (COVID-19) SEROLOGICAL (ANTIBODY) TESTING AT LIFELABS (CON'T)

POINTS TO REMEMBER:

- PCR-based testing, and not serological testing, is most reliable test for the acute diagnosis of COVID-19.
- Serological testing can be used to assess recent or previous SARS-CoV-2 infection
- Serological testing cannot be used to infer immunity, make decisions regarding physical distancing, or the use of protective personal equipment.
- For OHIP-insured serological testing, unless MIS-C is indicated, approval by PHO microbiologist is required. Please use PHO lab COVID-19 Serology Requisition to order the test.
- For uninsured serological testing, effective October 19. 2020, LifeLabs ON will start offering the Roche Elecsys SARS-CoV-2 Total Antibody assay which is Health Canada approved (internal validation shows clinical sensitivity of 96% for samples tested > 3 weeks post-symptom onset, and clinical specificity of >99%).

REFERENCES:

1. Van Caeseele, P., et al. SARS-CoV-2 (COVID-19) serology: implications for clinical practice, laboratory medicine and public health. CMAJ 192, 34, E973-979 (2020). https://doi.org/10.1503/cmaj.201588
2. Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19: Serologic Testing https://www.idsociety.org/practice-guideline/covid-19-guideline-serology/
3. Bailey, D., et al. Canadian Society of Clinical Chemists (CSCC) interim consensus guidance for testing and reporting of SARS-CoV-2 serology. Clin Biochem, In Press.
4. Pan, Z. et al. Disease severity dictates SARS-CoV-2-specific neutralizing antibody responses in COVID-19. Sig Transduct Target Ther 5, 180 (2020). https://doi.org/10.1038/s41392-020-00301-9
5. Long, Q. et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. Nat Med 26, 1200–1204 (2020). https://doi.org/10.1038/s41591-020-0965-6
6. Gudbjartsson, D., et al. Humoral Immune Response to SARS-CoV-2 in Iceland. N Engl J Med 2020 Published online 2020 Sep 1. https://doi.org/10.1056/NEJMoa2026116
7. Roche Elecsys Anti-SARS-CoV-2 product insert.

Additional Resources

8. CDC – Serology Testing: https://www.cdc.gov/coronavirus/2019-ncov/lab/serology-testing.html
9. FDA https://www.fda.gov/media/137470/download
10. Health Canada requirements for serological antibody tests submitted under the COVID-19 Interim Order: guidance can be found in: https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/application-information/guidance-documents/covid19-requirements-serological-antibody-tests.html#a64
11. Lab Tests Online COVID-19 Page: https://labtestsonline.org/tests/coronavirus-covid-19-testing

Nicole White-Al Habeeb *PhD FCACB*
Clinical Biochemist, LifeLabs ON

Uvaraj Uddayasankar *PhD FCACB*
Clinical Biochemist, LifeLabs ON

Cherise Ens
Quality and Regulatory Affairs, LIfeLabs ON

Michelle Collins
Quality and Regulatory Affairs, LIfeLabs ON

URINALYSIS TESTING
THE IMPORTANCE OF CORRECT SPECIMEN COLLECTION AND STORAGE

Chemical and Microscopic Urinalysis test results may be adversely affected by inadequate storage conditions, and by a delay between specimen collection and testing.

At room temperature, urine specimen stability is limited to 2 – 6 hours, depending on the urine constituents tested.[1,2] **Refrigerated** urine specimens are stable for 24 hours without chemical preservative added, or three days when preserved (LifeLabs in-house specimen stability study, 2018).

When specimens with compromised stability are tested, falsely elevated (e.g. proteins) or falsely decreased (e.g. red blood cells, white blood cells) results may be obtained.

Based on the urine stability limitations, we recommend health care providers follow these steps when collecting specimens and interpreting results for urinalysis testing:

1. Please avoid sending urine specimens kept at room temperature for longer than 2 hours. These specimens should be recollected.

2. Always provide date and time of collection on the specimen container and/or on the OHIP requisition (see Figure 1). In case we receive specimen without the date and/or time of collection, LifeLabs will alert the health care provider of potentially affected result, using the following interpretive comment:

   "Interpret results with caution as date and/or time of collection was not provided to the lab. Urine is stable for 24h when refrigerated."

3. Please pay attention to the interpretive comments provided with the urinalysis results. In addition to the above comment when date and/or time of collection is not provided, LifeLabs will also inform the health care provider in case the specimen arrived in the laboratory more than 24 hours after the collection, and will reject the sample that arrived in the laboratory more than 48 hours after the collection.

For further information on specimen handling please visit LifeLabs Test Information Directory: http://tests.lifelabs.com/Laboratory_Test_Information/Homepage.aspx

Please also refer to the LifeLabs Inside Diagnostics Newsletter from December 2018 for the information on how other specimens at LifeLabs are handled when received without collection date and/or time: https://www.lifelabs.com/hcps-newsletter/inside-diagnostics-december-2018-copy/

Ensuring urine specimens are properly collected and stored prior to being sent to the laboratory will ensure that the health care providers receive accurate test results.

LifeLabs is dedicated to providing timely quality results to our patients and with your help we can continue to do so.

POINT TO REMEMBER:

To ensure accurate results, all specimens collected by a third party, including urines for Chemical and Microscopic Urinalysis, require adequate handling and date and time of collection provided.

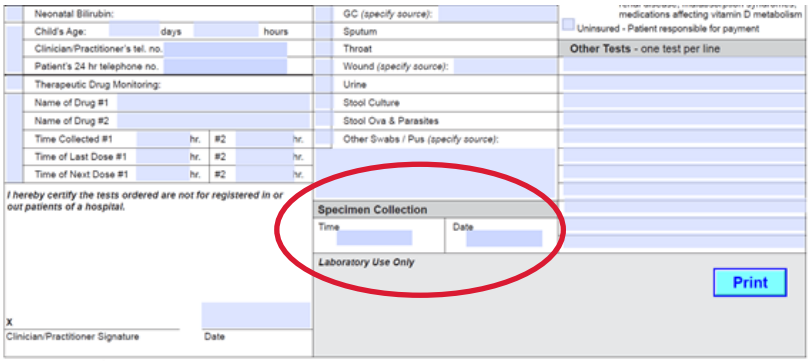
URINALYSIS TESTING
THE IMPORTANCE OF CORRECT SPECIMEN COLLECTION AND STORAGE (CON'T)

Please contact the LifeLabs Customer Care Centre 1-877-849-3637 for all enquiries. We welcome your feedback!

REFERENCES:

1. Veljkovic K, Rodriguez-Capote K, Bhayana V, et al. Assessment of a four-hour delay for urine samples stored without preservatives at room temperature for urinalysis. Clin Biochem 2012; 45: 856-858.
2. Delanghe JR and Speeckaert MM. Preanalytics in urinalysis. Clin Biochem 2016;49: 1346-1350.

Figure 1. OHIP requisition with specimen collection time and date field indicated.



Kika Veljkovic *PhD FCACB*
Clinical Biochemist and Discipline Head,
High Volume Chemistry, LifeLabs ON

LifeLabs®

For more information, please visit our site at **www.LifeLabs.com**

Dr. Huda Almohri
Deputy Ontario Medical Director, Discipline Head, Microbiology
416-675-4530 ext.42105
huda.almohri@lifelabs.com

Dr. Abdel Belhaj
Medical Microbiologist
416-675-4530 ext.42344
abdel.belhaj@lifelabs.com

Dr. Uvaraj Uddayasankar
Clinical Biochemist
416-675-4530 ext.4221 1
Uvaraj.Uddayasankar@lifelabs.com

Dr. Mohamed Abouelhassan
Clinical Biochemist
416-675-4530 ext.42216
Mohamed.Abouelhassan@lifelabs.com

Dr. Afaf Erfaei
Hematopathologist
416-675-4530 ext.42944
afaf.erfaei@lifelabs.com

Dr. Timothy Feltis
Ontario Medical Director
416-675-4530 ext.42801
tim.feltis@lifelabs.com

Dr. Theano Karakosta
Mass Spectrometry Specialist
416-675-4530 ext.42029
theano.karakosta@lifelabs.com

Dr. Danijela Konforte
Discipline Head, Special Chemistry
416-675-4530 ext.42207
danijela.konforte@lifelabs.com

Dr. Daniela Leto
Medical Microbiologist
416-675-4510 ext.32310
daniela.leto@lifelabs.com

Dr. Patrick St.Louis
Clinical Biochemist
416-675-4530 ext.42253
patrick.st.louis@lifelabs.com

Dr. Tracy Morrison
Clinical Biochemist
416-675-4530 ext.42975
tracy.morrison@lifelabs.com

Dr. Dorothy Truong
Clinical Biochemist
416-675-4530 ext.42208
dorothy.truong@lifelabs.com

Dr. Nicole White-Al Habeeb
Clinical Biochemist
416-675-4530 ext.42099
Nicole.White-AlHabeeb@lifelabs.com

Dr. Krystyna Ostrowska
Medical Microbiologist
416-675-4530 ext.42892
krystyna.ostrowska@lifelabs.com

Dr. Difei Sun
Mass Spectrometry Specialist
416-675-4530 ext.42296
difei.sun@lifelabs.com

Dr. Kika Veljkovic
Discipline Head, High Volume Chemistry
416-675-4530 ext.42832
kika.veljkovic@lifelabs.com

Dr. Miranda Wozniak
Deputy Ontario Medical Director, Discipline Head, Hematology
416-675-4530 ext.42040
miranda.wozniak@lifelabs.com