Health Canada Santé Canada

Canada

COVID-19 Diagnostic Testing

Diagnostic technologies and sampling alternatives

Conference of Deputy Ministers of Health

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YOUR HEALTH AND SAFETY... OUR PRIORITY.

Scaling Testing Capacity

Testing Objectives

Long-term Perspective
Most diagnostic testing will be done by PCR though other technologies may increasingly be available to complement it. Options beyond point-of-care testing should be explored to increase access to diagnostic tests (e.g. mobile labs).

Strategy
Diagnostic capacity is of primary importance. Sero-epidemiological research will support public health decisions regarding vaccination.

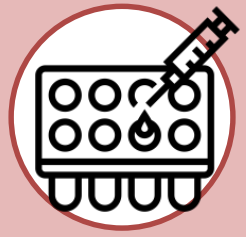
International Examples
Emerging technologies seek authorization in the US first, as is standard for medical devices.

Manufacturing Capacity
NRC, ISED, PHAC challenges focus on domestic suppliers, but are unlikely to contribute to diagnostic capacity in the short term

Effectiveness
The shortcomings of any test must be well-understood to enable appropriate deployment and decision making

Molecular-based testing

- Detects the presence of viral genes and therefore detect active infection
- RT-PCR
- LAMP



Serological Testing

- Measures the level of antibodies present in blood / serum / plasma and assesses the overall immune response to the virus

Other Technologies

- Antigen Testing
- Next-Generation Sequencing
- Gene-editing
- Saliva samples
- Swish and spit
- Dry nasal samples

Authorized for use

Potential

Types

Current Environment

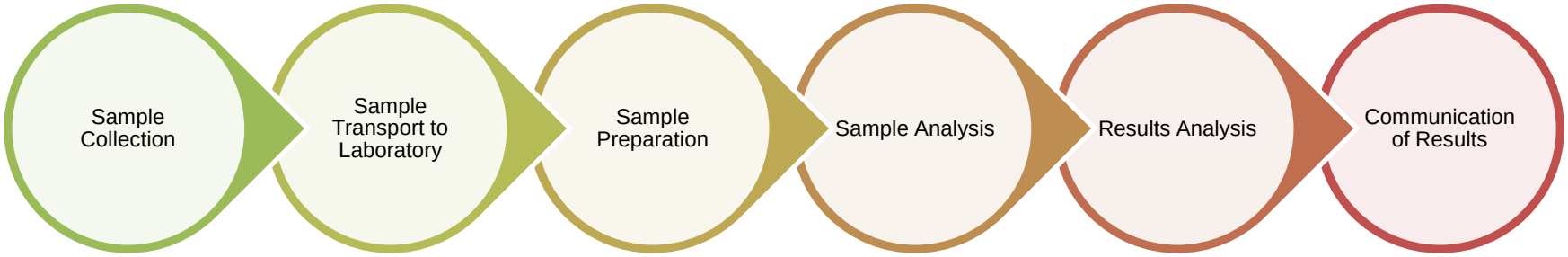
- 29 authorized tests in Canada, based on 2 technologies
  - **24* molecular-based tests** detect the presence of viral genes and therefore detect active infection
  - **5 serological tests** measure the level of antibodies present in blood / serum / plasma and assess the overall immune response to the virus
- All but two are authorized only for use in a laboratory (lab-based testing)

* Includes two which are authorized for research use only.

Testing Strategy Approach

Key Questions	Current Environment
1. How can accuracy of results be integrated with the need for broader testing options in different use settings?	Alternative technologies exist or are in development, but majority of testing is through PCR.
2. How market ready are some of the emerging options?	Further research is required into testing options, including sample types such as saliva, before they can be considered as market ready.
3. What is the impact of emerging options on Canada's testing capabilities?	Various options with antigen technology presenting the most potential, despite the potential reduced sensitivity. Throughput remains a consideration.

Testing Process and Throughput



- Impacts to any of these steps can reduce the time to receive results and increase capacity
- Testing capacity can be increased by choosing authorized tests **with higher capacities and shorter run times**, where appropriate

Example of **Testing Throughput** of **Lab-Based Platforms**

Testing Machine	Capacity (samples)	Time per run	Number of Compatible Authorized Tests
Applied Biosystems 7500 Fast DX	96	30 min	6
Roche cobas 8800 System	960	8 hours	1
Biomeme Franklin Real-time aPCR Thermocycler	9	60 min	1

These estimates ignore the time required to prepare samples and send results back to patients. Some tests require more manual intervention than others.

Potential Testing Technologies

A number of potential testing technologies exist that could potentially improve throughput and add to an overall testing strategy

Antigen Tests

State of readiness

Technology

- Detects coronavirus proteins on the surface of the virus

Advantages

- Inexpensive to produce and simple to conduct
- Easily adapted to point-of-care application

Disadvantages

- May be less sensitive than molecular tests due to no amplification step
- Challenge in scaling up tests for mass production

Regulatory Landscape

- Submissions: 4

Potential Testing Technologies

State of readiness

Loop-Mediated Isothermal Amplification (LAMP)

- Technology
  - Identifies viral material through amplification at a constant temperature
- Advantages
  - Inexpensive ($1/test) and fast (many tests in less than 1 hour)
  - Because it works at constant temp, the technology is potentially adaptable for use outside the lab
- Disadvantages
  - May be less accurate than PCR
- Regulatory Landscape
  - Submissions: 5

Potential Testing Technologies

Next Generation Sequencing (NGS)

State of readiness

- Technology
  - Catch-all term to describe a number of different modern sequencing technologies that allow for sequencing of DNA and RNA much more quickly and cheaply
  - Also known as high-throughput sequencing
- Advantages
  - 100,000 samples in 1 run of 12 hours
  - Can be combined with **sample pooling technologies** that add identifying 'molecular barcodes' to samples before pooling and decoding all at once while still able to identify which samples were positive
- Disadvantages
  - Requires specialized equipment in centralized facilities; very few available in Canada
  - Designed for research, not medical diagnosis. Further assessment re. quality control would be needed
- Regulatory Landscape
  - Submissions: 1

Potential Testing Technologies

Gene-editing technology (e.g. CRISPR)

State of readiness

- Technology
  - CRISPR technology is able to specifically identify and target genetic sequences and “find a needle in a haystack” in a high background of non-target sequences
- Advantages
  - Extremely specific, excellent for precise research needs
- Disadvantages
  - Exceeds the level of precision required for medical diagnosis of COVID-19
  - Not ready to form a substantial pillar of the testing strategy
- Regulatory Landscape
  - Submissions: none

Alternate Sampling Modalities: Saliva

- Technology
  - Detects virus in saliva samples
- Advantages
  - Allows non-invasive collection by the patient without the need for a swab
  - Yale University studies have shown that results from swabs and saliva samples of hospitalized patients were virtually the same
- Disadvantages
  - Saliva may not be as sensitive as other samples
    - Japanese research shows only 85% of results from saliva are the same as the results from swab tests (reduced sensitivity)
    - PHAC-NML preliminary evaluation found a decrease in sensitivity of 30-40% for saliva compared to swabs; similar results were obtained using a commercial assay
- Regulatory Landscape
  - Submissions: 2

Alternate Sampling Modalities: Emerging options

- Swish and Spit
  - Novel approach where saline is gargled and spit into a cup
  - Early results demonstrate higher concordance with the results obtained via the gold standard NP flocked swabs than just saliva

- Home-based nasal self-swabs
  - From the Bill & Melinda Gates Foundation
  - Allow for the collection of a mid-nares sample in the home
  - The dry nature of the sample simplifies shipping and there is evidence that the samples remain stable for 56 hours under elevated temperatures

- PHAC-NML Challenge for home-based or near-home detection
  - 4 companies have made proposals where either saliva or self-swabs are used

Incenting Innovation

- ISED, PHAC and NRC have all launched challenges to identify Canadian companies that can meet specific testing needs.
  - PHAC and NRC have sponsored a challenge to create point-of-care and home diagnostic test kits
    - https://www.ic.gc.ca/eic/site/101.nsf/eng/00100.html
    - 2 companies are expected to move into clinical evaluation starting end of September
  - IRAP supported test kits - *However,* 6 of these are serological tests and cannot be used for diagnosis
    - 8 point-of-care kits
    - 4 lab-based kits
- These companies are provided funding and access to regulatory guidance and support, as well as expert lab assessment from NRC, Health Canada and PHAC
- Submission for authorization of these devices would follow completion of all required trials, which could take several months

Alternative Options to Increase Testing Capacity

Options can be explored that use existing PCR technology in more efficient and flexible ways:

PHAC-NML is leading a project to use **existing federal lab infrastructure** across Canada to increase testing capacity nation-wide

Mobile lab-based testing could be set up in areas of high-traffic, like airports, to eliminate sample shipping time

Testing services by independent providers could expand capacity.

A multi-pronged approach, founded on prioritization of Canada's specific testing needs will continue to identify additional testing options for Canada

Connect

- Proactive reach out to international manufacturers of interest
- Identification and support of potential Canadian test manufacturers (IRAP and ISED Challenge)

Research

- Research by PHAC and provincial and territorial partners on saliva and other sample types to increase probability of success
- Assessment of emerging technologies and Canadian tests in development

Procure

- Setting up appropriate procurement agreements at federal level to facilitate access nationwide

Review

- Reviewing a wide range of technologies for quality and effectiveness
- Prioritizing based on Canada's needs to increase capacity and enable access in rural and remote locations

Annex 1 Glossary of Terms

- ISED: Innovation, Science and Economic Development Canada
- IRAP: Industrial Research Assistance Program
- LAMP: Loop-Mediated Isothermal Amplification
- NML: National Microbiology Laboratory
- NRC: National Research Council
- PCR: polymerase chain reaction
- PHAC: Public Health Agency of Canada
- RT PCR: real-time PCR
- Run time: time required to complete analysis of a single set of samples
- Throughput: number of samples that can be tested at once in any given time frame