Health Canada
Health Products and Food Branch
Medical Devices Directorate

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Testing 101
Frequently Asked Questions

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1. Roles

1.1. Testing across Canada – who does what?

Health Canada (HC) is the regulator for medical devices that are sold in Canada. It authorizes manufacturers to sell COVID-19 testing devices following a successful scientific evaluation of evidence to support the device's safety, effectiveness and quality.

Following authorization, Health Canada monitors the safety and effectiveness of tests. If a concern is found, it takes action, to protect the health and safety of Canadians. This is called surveillance and it is how we gather information that tells us whether we need to adjust the intended use of the test, or remove it from the market if it is not working as it should.

Health Canada also watches for the sale or distribution of devices and tests that have not been authorized for sale. If any are found, HC takes action to protect Canadians, using a number of tools, including recalls, public communications, or by removing the products from the market. This is called compliance and enforcement and it is how we manage the risks to Canadians, using the most appropriate tool.
Health Canada is taking all steps available to give Canadians and our health system access to as many testing options as possible, as quickly as possible, without compromising safety.

Health Canada is closely monitoring new technology. When we become aware of promising new tests that are not yet available in Canada, we proactively reach out to manufacturers to seek their interest in entering the Canadian market.

We engage the health products sector to find COVID-19 solutions by:

- meeting with industry leaders to identify and track potential health products
- ensuring that the regulatory review of promising health products is done in a timely manner
- hosting information sessions on our regulatory response
- maintaining a centralized COVID-19 website with relevant information for industry and health professionals

We are working with our international partners, including US, Australia, UK, Japan, or South Korea, on a well-aligned approach to this global pandemic. This ensures that health products are effective and quickly available to Canadians.

Specifically, our international engagement involves discussing, collaborating and leveraging resources on issues related to:

- clinical trials and investigational testing
- drug and medical device market authorizations
- health product risk assessments
- potential drug and medical device shortages

The **Public Health Agency of Canada** (PHAC) leads Canada's public health response to COVID-19. For testing, PHAC's National Microbiology Laboratory (NML) works with public health laboratories across Canada to test specimens received from provinces and territories and also to develop accurate tests. PHAC also publishes the number of people tested in Canada every day. The NML also performs in lab assessment of test devices to inform on their performance. NML shares its assessment results with Health Canada for consideration in the context of the scientific evaluation.

Provinces and territories are responsible for the delivery and administration of health care services, including tests that have been developed in public and private laboratories. Laboratories can develop their own sample collection and testing methods for COVID-19. They are responsible for ensuring that these tests provide accurate and reliable results and ensuring that laboratory-developed tests and test collection methods are safe and effective. Public and private laboratories that develop their own tests and offer testing services are not regulated by Health Canada. They are regulated by Provincial and Territorial Health Authorities.

2. Types of Tests

2.1. What are the different testing technologies? What can they be used for?

There are two main categories of COVID-19 tests: those that diagnose an active infection, and those that detect a previous infection.

For tests to diagnose COVID-19, the standard type of testing Canada has been using is called molecular polymerase chain reaction (PCR) tests.

There are several ways that healthcare professionals can collect a sample from a patient to do a PCR test for COVID-19, including nasopharyngeal (nose and throat) swabs. These samples are then evaluated in a laboratory. It usually takes one to three days for Canadians to get their results back. Since March, we have authorized 27 PCR testing devices.

In addition to PCR tests, Health Canada expects to soon authorize antigen tests. These tests detect proteins on the surface of the virus. Swabs are still required to collect the samples, but these tests are expected to have a few advantages. They are easier to perform with limited training and can be evaluated where the sample is collected which is called "point of care". The results are ready quickly, often in 15 minutes. The main disadvantage is that antigen tests for COVID-19 are usually less sensitive than PCR tests, so they are less accurate.

The second category of tests is those that detect a previous COVID-19 infection. We call these serology or antibody tests. Since May, we have authorized 10 of these. Serology tests help us understand how people develop immunity after they have been infected by the virus. These results will also help us understand how many Canadians have been exposed.

2.2. How many testing devices have been authorized by Health Canada to date?

As of October 7, Health Canada has authorized 39 COVID-19 testing devices. This has been done through an expedited regulatory review process, called Interim Order, issued on March 18, 2020. The list of authorized testing devices is available on Health Canada's website and is updated as on a daily basis.

2.3. Are there tests authorized for home-testing or to be used with saliva?

Health Canada has not yet received any submissions for test kits that can be done at home without the need for a healthcare professional to collect a sample. If Health Canada does receive an application, it will be reviewed as a priority. For all types of tests, Health Canada's focus is to ensure that tests authorized for sale in Canada, provide accurate results, and that they are safe.

Health Canada is currently reviewing submissions for saliva tests, and will prioritize new and innovative testing options such as rapid tests and home tests, as they are submitted by companies.

3. Rapid Testing

3.1. What are rapid tests?

The term "rapid test" usually means tests that can be carried out at the point of care (POC) and that will produce results within less than an hour. It is not a term that is

defined by regulations, but rather is used for marketing. Although tests that are carried out in labs can also be rapid, generally, the term "rapid test" does not refer to a test that would be done in a laboratory.

There are a variety of types of tests that could be done as rapid tests at the point of care. Molecular, antigen and antibody technologies can all be delivered as rapid tests.

3.2. Is Health Canada speeding up the review of the rapid test kits?

The review of testing devices is prioritized and Health Canada is working as quickly as possible toward the approval of rapid, point-of-care diagnostic and monitoring tests based on nucleic acid and antigen technologies in order to meet Canadian testing needs.

Under the regular application process, companies submit and application to Health Canada showing how their device meets our requirements for safety, effectiveness and quality. The length of time it takes for Health Canada's review varies, but it generally takes months. This is comparable to the performance of other reputable regulators, including the US.

With the COVID-19 outbreak, we needed a streamlined process to enable the review of applications for COVID-19 devices. That's why the Minister of Health signed an Interim Order in March that gives Health Canada more flexibility to accept different information, or information that comes in over time, to meet Canada's strict safety, effectiveness and quality standards. Health Canada also assigned more evaluators, so that reviews can be done faster.

For all medical device applications, including the COVID applications, Health Canada has a commitment to respond to companies within 15 days after it receives their submission.

We then conduct the scientific evaluation. For COVID devices we issue either a request for information, an authorization or a refusal within 40 days once the application is considered to be complete – compared to 75 days for non-COVID devices under the regular process. These service standards are guidelines and Health Canada strives to finalize the review of critical testing devices as quicky as possible without compromise patient safety. To our knowledge, we are the first regulator to publish service standards

Health Canada publishes guidance for industry to help make the submission and review process as smooth as possible.

3.3. What are the different technologies that could be used for rapid testing?

PCR
First, the gold standard for COVID-19 diagnosis in Canada is molecular testing which detects the genetic material of the virus. HC has authorized a few point of care molecular tests: the Cepheid Gene XpertXpress, Hyris bCube and Abbott ID Now. The Spartan Cube is also a point of care molecular test for research use only, at this time.

Some of these tests take longer to produce results than others but they can process more than one sample at a time. Of this group, the Abbott ID Now is the fastest, with results on a single sample in 13 minutes or less. The Hyris bCube is the slowest, requiring 1hr45min, but it can process 6 samples at a time.

Rapid antigen testing
A new technology that may be used to monitor and diagnose infection is antigen testing, which detects proteins on the surface of the virus. Antigen test technology can come in a disposable format much like a pregnancy test (called a lateral flow format), and these tests can often return results in less than 30 minutes.

Health Canada has authorized a first antigen test on October 5 (Panbio from Abbott), and is working hard completing the review of other applications to issue further authorizations. Applications for other antigen testing devices such asthe BD Veritor and Quidel Sofia (which have been approved in the US) are currently under review in Canada. While the Abbott BinaxNow has been approved in the US, it has not been submitted for approval in Canada. Instead, Abbott has made a business decision to offer their Panbio antigen test to the rest of the world, including Canada.

Antigen technology is less sensitive than molecular testing because the test sample or 'target' is not amplified (or multiplied) before the test tries to detect it. This means that antigen tests may miss detecting infections in people who may have low numbers of the virus in their bodies. For this reason, the Public Health Agency of Canada is developing guidance on how antigen testing should be used by public health authorities across Canada. This guidance will probably advise that antigen tests should be confirmed by molecular tests in some circumstances.

Rapid antibody testing
Third, there are tests to detect antibodies which develop after an individual has been infected. These tests are not currently a priority because they do not help meet the urgent need for additional tests to diagnose COVID-19 in Canada. It is also unclear how

the results of these tests would be used because we still know so little about how Canadians are developing immunity to COVID-19.

As of October 7, Health Canada has authorized 10 antibody tests, but these all have to be carried out in a lab. We have received a number of applications for point of care antibody tests as well. Like antigen tests, these can be delivered in a disposable format like a pregnancy test and can often return results in less than 30 minutes. Health Canada has a number of these under review, but for now we are prioritizing diagnostic point of care technologies in order to respond to Canada's testing needs.

3.4. How are tests deployed?

Scientists at Canada's National Microbiology Laboratory (NML) are determining a national strategy to distribute point of care tests in the best way possible to meet the needs of those most at risk.

The Public Health Agency of Canada (PHAC) distributes the testing devices based on a needs analysis—in coordination with provinces and territories and Indigenous Services Canada—to get devices to communities that are at greatest risk if there were to be an outbreak of COVID-19. As of October 7, 109 point-of-care testing devices and over 35,000 tests have been deployed across Canada to support in-community diagnostics.

3.5. Would it be possible to test for COVID at home?

Antigen tests could be suitable for home testing since they can be produced in disposable formats. Molecular tests cannot be delivered in a home-test format – they have to be performed using specialized equipment.

Health Canada has not yet received any applications for home-testing, but we will prioritize their review if we receive any.

One key difference for manufacturers of home testing devices is that, in addition to having to demonstrate that their tests will work on people with symptoms, they will also have to demonstrate that it works for people without symptoms. We expect that people with no symptoms will want to be able to test themselves at home.

3.6. Why are Canadians tested with swabs and not just using saliva samples?

A variety of different methods are approved for collecting samples. The gold-standard sample for molecular diagnosis is the nasopharyngeal (nose and throat) swab. Other

sample types have been authorized for use with some tests, including oropharyngeal (ear and throat) swab, nasal (nose) swab and (spit) sputum. All the technologies for rapid tests that have been received by Health Canada to date use one of these sample types.

Saliva is a sample of interest because it is so much easier to collect. Health Canada has received a small number of applications for tests that use saliva samples. These are all lab-based tests. However, we have spoken to some companies that are developing antigen technologies for point of care use with saliva samples. HC looks forward to receiving those applications and will prioritize them once received.

3.7. Has the swish and spit method developed in British Columbia been authorized by Health Canada?

Health Canada has not received any applications for commercial tests that use the swish and spit method. However, the British Columbia Centre for Disease Control (BC CDC) has tested the swish and spit sample with a number of tests authorized by Health Canada.

The swish and spit method that has been developed by the BC CDC shows real promise. Health Canada is working with the BC CDC and could consider allowing the use of swish and spit samples with authorized tests if sufficient supportive information is available.

3.8. Why aren't all the tests available in other jurisdictions also available in Canada?

Each jurisdiction has different rules and approval processes. Each regulator requires different criteria to meet the needs of their unique health care systems.

Health Canada's consistent approach throughout the pandemic has ensured that the testing devices available for sale in Canada have been accurate and reliable. As a result, we have avoided some of the problems other countries have experienced with lower-quality tests.

Health Canada welcomes new technologies. We are actively reaching out to companies around the world to encourage them to apply for authorization in Canada. However, we cannot dictate if or when a company decides to apply for authorization in Canada. That's one of the reasons why we may not always have the same tests or types of tests as other countries.

4. Approval of rapid tests in other countries

4.1. Have other jurisdictions authorized rapid tests? Are these authorized in Canada?

Not all the tests approved in other jurisdictions are available in Canada. Health Canada actively contacts manufacturers that have obtained authorizations in other countries to suggest they come to Canada as well. If they want to sell in Canada, manufacturers have to submit an application for review and get an authorization.

Health Canada monitors authorizations of tests in other jurisdictions.

For example, the US has approved five (5) point of care tests kits using PCR technology under their Emergency Use Authorization. Of those, two have been authorized for sale by Health Canada: the Xpert Xpress SARS-CoV-2 test from Cepheid and the ID Now COVID 19, Abbott. The Roche Molecular Systems "cobas SARS-CoV-2 & Influenza A/B Nucleic Acid Test for use on the cobas Liat System" is under review. Health Canada has contacted the manufacturers of the other two tests but they are not interested in submitting an application to sell their products in Canada.

The US has also approved four (4) antigen rapid test kits under their Emergency Use Authorization. Two of the four test kits have been submitted to Health Canada for review: the Sofia 2 SARS Antigen FIA, Quidel; and the BD Veritor System for Rapid Detection of SARS-CoV-2.

4.2. How does our regulatory regime for medical devices compare to other international jurisdiction?

The US Food and Drug Administration (FDA) has a similar regulatory regime as Health Canada with regards to the premarket and quality requirements for medical devices.

Like Canada, the US has an expedited process for the review and authorization of medical devices. The issuance of Emergency Use Authorization (EUA) by the US Food and Drug Administration (FDA) enables the expedited authorization of devices or the alternative use of devices that are already authorized. Under the EUA, medical devices do not need to meet the same requirements as under a regular FDA review, and manufacturers are able to provide minimal evidence and validation. Medical products that may be considered for an EUA are those that "may be effective" to prevent, diagnose, or treat serious or life-threatening diseases or conditions.

4.3. How are other international jurisdictions approving testing devices?

The European Union (EU) approach for medical device approval is different than Health Canada's approach. Currently under the EU Directives, test kits for COVID-19 are self certified by the manufacturer – this is the regular pathway, there is no emergency use pathway. Manufacturers of testing devices do not require an authorization from EU regulators but they have to obtain a CE marking certification, from a private third-party firm (notified bodies) prior to being able to sell on the EU market. CE marking indicates that a product has been assessed by the manufacturer and deemed to meet EU's quality management requirements, where applicable, as well as the EU essential principles of safety and performance.. It is required for products manufactured anywhere in the world that are then marketed in the EU.

The UK MHRA follows the EU's approach since they themselves do not conduct a premarket review of the testing devices. There is not an emergency use authorization pathway in the UK either. They however only procure tests they have assessed at their National Laboratory.

Australia's Therapeutic Goods Administration does not have an emergency use pathway. All manufacturers must register their product for sale in Australia under their regular pathway. Manufacturers of COVID-19 testing devices must submit an application that contains analytical and clinical studies as well as certification to the quality management system standard ISO 13485.

In the US, manufacturers are required to submit similar data than in Canada. Canada often leverages the work of the US FDA, and in the context of the pandemic Health Canada recently formally adopted the US guidance for antigen tests. The US FDA also accepts evidence for effectiveness not necessarily based on clinical settings. In Canada, effectiveness has to be demonstrated through clinical data.

4.4. Why doesn't health Canada authorize tests on the basis that they are approved in other countries?

Each jurisdiction has different rules and approval processes. Each regulator requires different criteria to meet the needs of their unique health care systems.

Health Canada's consistent approach throughout the pandemic has ensured that the testing devices available for sale in Canada have been accurate and reliable. As a result, we have avoided some of the problems other countries have experienced, including recalling lower-quality tests. Health Canada accepts submissions made to another

jurisdiction and assesses that data independently. This speeds up the application and review process while allowing companies to reuse as much information as possible.

4.5. Does Health Canada ask for additional information from manufacturers for devices that have already been approved in the US?

Yes, Health Canada sometimes requests additional information from manufacturers for devices that have already been approved in the U.S. The most common modifications or additional information requests relate to the labelling of devices or to the instructions for use that is provided with the device.

One change we request on a regular basis relates to statements on the label that the product can only be used under US authorities. For example, the US labelling for the Diasorin Liaison SARS-CoV-2 IgG test included the following statements :

- *Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C 263a, that meet requirements to perform moderate or high complexity test.*
- *The LIAISON® SARS-CoV-2 S1/S2 IgG is only for use under the Food and Drug Administration's Emergency Use Authorization.*

Health Canada always requests that this type of exclusive language be removed from labels as it is not appropriate in the Canadian context. This type of language appears in most of the applications we receive.

Another more specific example would be the two changes we requested be made to the Abbott ID NOW labelling to ensure that its label reflected the evidence upon which the authorization was granted.

1. Abbott had submitted labelling that expressed the performance of their device (sensitivity and specificity) according to their study of contrived (lab-developed) samples. They were reporting 100% sensitivity and specificity. When they provided us their interim clinical data upon our request, we learned that the clinical performance of their device was actually 92.9% sensitivity and 98.2% specificity. We therefore required that this information be included on the label so as to accurately communicate the performance of the device to users.

2. Abbott's labelling included statements that swabs other than the proprietary swab part of their kit could be used to collect samples for use with their kit. However,

they had no data validating the use of any of those swabs. For this reason, we required them to insert a limitation statement indicating that the use of those swabs was not validated (akin to a 'use at your own risk' type of statement).