

HIV testing technologies

HIV testing technologies are used to determine if a person has HIV. Several types of HIV testing technologies are used in Canada. These tests differ in several ways, including where the test is conducted, how the test detects HIV infection, the length of its window period, and how long it takes to receive results.

How are testing technologies used to diagnose HIV infection?

To test for HIV, a sample of a person's blood is taken (either a vial of blood from a vein or a couple of drops of blood from a finger prick). This blood is either tested immediately for HIV at the location it was taken – also known as rapid or point-of-care (POC) testing – or it is sent to a laboratory to be tested for HIV (standard testing).

While the removal of blood for HIV testing can be conducted in a variety of different settings in Canada – including hospitals, health clinics and in the community – it must always be performed by a trained individual.

Laboratory testing

Most HIV testing of blood samples is conducted in a laboratory. This type of testing requires a vial of blood to be taken by a trained individual and sent to a laboratory for analysis.

The first test used at a laboratory to analyze a blood sample is referred to as a screening test. All laboratories in Canada use fourth-generation HIV testing technologies for screening blood samples.

If a fourth-generation screening test indicates that the person who gave the blood sample does not have HIV (also known as a non-reactive test or testing negative or HIV negative), no further testing is normally performed and the negative result is sent back to the healthcare provider or clinic that ordered the test.

If the screening test indicates that the person is infected with HIV (also known as a reactive test or testing positive or HIV positive), then a confirmatory test is performed to ensure the screening test was correct. If the confirmatory test indicates that the person is HIV positive, the positive result is sent back to the

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healthcare provider or clinic that ordered the test. If the *confirmatory* test is indeterminate (that is, unable to determine whether the result is positive or negative) or provides a different result from the screening test, then a supplementary test may be used at the laboratory or it may be sent to another laboratory for further testing to confirm if the result is negative or positive. The supplementary test may be a p24 antigen test or NAAT.

It can take up to one or two weeks for a person to receive their test result if laboratory testing is conducted.

Dried blood spot testing

Dried blood spot (DBS) testing uses a sample of blood from a finger prick that is collected as a blot on a card. The blood spot is dried at room temperature and mailed to a public health laboratory for screening and confirmatory testing (as described above). Currently, this collection technique is in limited use in Canada because very few public health laboratories can process the DBS cards.

DBS testing has the advantage of being able to be used in rural and remote areas because the samples are very stable once collected and do not need to be refrigerated. Samples can also be collected by non-medical staff. Dried blood spots can also be used to test for other blood-borne infections, including hepatitis B and hepatitis C.

Rapid testing

Some HIV testing in Canada occurs at the location where the blood was taken. This is known as rapid or point-of-care (POC) testing. Rapid tests are a type of screening test that can provide results within minutes. These tests only require a few drops of blood from a finger prick to test for HIV.

If a rapid test indicates no HIV infection is present (a non-reactive test result), then no further testing is normally performed and the person who was tested can be immediately informed of their HIV-negative result. However, if a rapid test indicates that a person is infected with HIV (a reactive test result), this is *not* a final diagnosis. Instead, a vial of blood must be taken and sent to a public health

laboratory for confirmatory testing. It can take up to one or two weeks to receive the results from confirmatory testing.

In some cases, if the rapid test is non-reactive and there is reason to believe the person being tested has recently become infected with HIV (and is in the window period – see below for more details), a vial of blood can be taken and sent to a laboratory to be tested with a test that has a shorter window period.

Home-based testing and self-testing

HIV home-based tests, also known as self-tests, allow people to test themselves for HIV in their home (or other locations) without a healthcare provider present. In the United States, a rapid HIV test can be bought over-the-counter at stores or online and used at home (or other locations) by the person who purchased the test. No self-tests have been approved for sale in Canada. However, there are reports of some people in Canada purchasing self-test kits online or buying test kits in other countries and bringing them to Canada.

Some HIV test kits bought online may be of poor quality and provide incorrect results.

How do different testing technologies detect HIV infection and how long are their window periods?

Testing technologies detect HIV infection in different ways. Some tests (such as rapid HIV tests) detect anti-HIV antibodies, which are proteins produced by the body's immune system in response to HIV infection. Other tests are able to detect the virus itself.

Tests that detect the virus itself include antigen tests and nucleic acid amplification tests (NAATs). Antigen tests diagnose infection by detecting an HIV protein called the p24 antigen. This protein is found on the surface of the virus and inside HIV-infected cells. NAATs detect HIV's genetic material (also known as RNA). RNA is found within HIV itself and inside HIV-infected cells.

The window period refers to the time from when a person becomes infected with HIV to when a

testing technology can detect their HIV infection. During the window period, a test may incorrectly find a person who is infected with HIV to be *not* infected with HIV. The window period varies for each type of test and for each individual. In general, tests that only detect anti-HIV antibodies have a longer window period than tests that detect the virus itself.

The window period for screening tests used in Canada (rapid tests and fourth-generation tests) can exceed one to three months in some individuals. However, in the majority of people, these tests can detect HIV within one month of infection.

Below is a description of different types of HIV testing technologies used in Canada and their window periods.

Screening tests

Fourth-generation tests

All laboratories in Canada use fourth-generation HIV tests as screening tests. These tests can detect both the p24 antigen and anti-HIV antibodies. These HIV tests are sometimes referred to as antigen-antibody combination tests.

Tests that detect the p24 antigen generally have shorter window periods than tests that only detect antibodies. This is because most people have detectable levels of p24 antigen by 20 days after infection, which is generally earlier than antibodies can be detected. However, levels of p24 antigen in the blood begin to decrease three to four weeks after infection and are *no longer* detectable five to six weeks after infection. This is why fourth-generation HIV tests were designed to also detect anti-HIV antibodies, as antibodies generally remain detectable for the entire course of HIV infection.

Fourth-generation HIV tests can detect HIV infection in 50% of people by 18 days after infection; 95% of people by 34 days after infection; and 99% of people by one and a half months after infection.

Rapid tests

Currently, only one rapid HIV screening test has been approved in Canada. This test only detects

anti-HIV antibodies and is known as the INSTI test. Rapid tests that detect the virus itself are not available in Canada.

The window period of the INSTI test is estimated to be the same as, or up to one week longer than, the window period for third-generation HIV tests. Third-generation HIV tests are antibody-only laboratory screening tests, which are no longer used in Canada. Third-generation tests can detect HIV infection in 50% of people by 22 days after infection; 95% of people by 40 days after infection; and 99% of people by three months after infection.

The rapid self-test approved in the United States (Oraquick) detects anti-HIV antibodies in saliva. The average window period of this test is estimated to be six to 12 weeks (42 to 84 days).

Table 1. Summary of screening tests available in Canada

| Name of test | Availability in Canada | What the test is looking for | Average window period |
|------------------------|------------------------|---|-----------------------------------|
| Rapid test (INSTI) | Yes (some provinces) | Anti-HIV antibodies | 22 days (can be up to 3 months) |
| Fourth-generation test | Yes (all provinces) | Anti-HIV antibodies and HIV P24 antigen | 18 days (can be up to 1.5 months) |

Confirmatory tests

Geenius™ HIV-1/2 Confirmatory Assay

The Geenius™ assay detects antibodies to HIV. It has replaced the Western blot as the confirmatory diagnostic test following a reactive HIV screening test. The Geenius™ assay is used by all public health laboratories in Canada that conduct HIV confirmatory tests. The Geenius™ assay is able to detect both HIV-1 (the most common type of HIV) and HIV-2, whereas the Western blot could only detect HIV-1.

Nucleic acid amplification tests (NAATs)

NAATs are used as confirmatory tests in some laboratories in Canada. They may also be used when the confirmatory test for HIV is indeterminate or has a different result from the screening test.

NAATs have the shortest window period of all types of HIV tests and can detect HIV infection as early as seven to 14 days after infection.

Some provinces/territories are considering using NAATs as screening tests because of their very short window period. However, the high cost of NAATs is a potential drawback. Since NAATs are expensive, a “pooled” strategy can be used to minimize the number of tests performed. With pooled NAAT, blood samples from several different clients are combined and tested as a single sample. If the pooled sample tests positive, the original samples are then tested individually to determine which one(s) contain HIV.

In some parts of British Columbia, blood samples from men who have sex with men (MSM) that are HIV negative when screened using fourth-generation HIV tests are also tested using pooled NAAT. For MSM who test HIV negative with a rapid HIV test, a vial of blood can also be taken and sent to a laboratory to be tested again using pooled NAAT. This has been shown to improve the detection of people who were recently infected with HIV.

p24 antigen-only tests

Tests that only detect the p24 antigen are used as confirmatory tests in some laboratories in Canada. They may also be used when the confirmatory test for HIV is indeterminate or has a different result from the screening test. In some parts of Canada, if a rapid test is non-reactive and there is reason to believe the person being tested has recently become infected with HIV (and is in the window period for the rapid test), a vial of blood can be taken and sent to a laboratory for p24 testing.

Table 2. Summary of confirmatory tests available in Canada

| Name of test | Availability in Canada | What the test is looking for |
|---|------------------------|------------------------------|
| Geenius™ | Yes (all provinces) | Anti-HIV antibodies |
| Nucleic acid amplification test (NAAT) ¹ | Yes (some provinces) | HIV RNA |
| p24 antigen ² | Yes (some provinces) | HIV p24 antigen |

1 For gay men and other MSM in some parts of British Columbia, pooled NAAT is used to test blood samples that are non-reactive when screened with fourth-generation HIV tests. For MSM who test negative using a rapid HIV test, a vial of blood can also be taken and sent to a laboratory for pooled NAAT testing.

2 In some parts of Canada, those who test HIV negative with a rapid HIV test, and who may have recently become infected with HIV, can have a vial of blood taken and sent to a laboratory for p24 testing.

How accurate are HIV tests?

HIV tests are very accurate. Once confirmatory testing has been performed, the chance of a positive result being false is essentially zero. When outside of the window period, the chance of a negative result being false is very low. However, the chance of false positives is a greater concern for rapid tests, particularly when testing lower-risk individuals.

Sensitivity and specificity

Sensitivity and specificity are measures of the accuracy of an HIV test. *Sensitivity* refers to the probability that a test will correctly indicate that an HIV-positive person is infected with HIV. Lower sensitivity increases the chance of false negatives (testing negative when actually HIV positive). *Specificity* refers to the probability that a test will correctly indicate that an HIV-negative person is not infected with HIV. Lower specificity increases the chance of false positives (testing positive when actually HIV negative).

Fourth-generation HIV tests and the INSTI rapid test have a *sensitivity* of about 99.9%. In other words,

if 1000 HIV-positive people were tested for HIV, 999 would test positive and one would incorrectly test negative. Since the vast majority of people who get tested for HIV are actually HIV negative, the chance of a negative result being false is extremely low.

The *specificity* of these tests is slightly lower, about 99.5%. In other words, if 1000 HIV-negative people were tested, 995 would test negative and five would incorrectly test positive. Therefore, the chance of false positives is extremely low, but slightly higher than the chance of false negatives. This is why all positive test results are sent for confirmatory testing with the Geenius™ assay, which has a specificity of 100%. This means that the chance of a false-positive result after confirmatory testing is essentially zero.

False positives are a particular concern with rapid testing. This is because an HIV-negative person could be given a false-positive test result and then must wait for confirmatory testing to be completed, causing significant anxiety and stress. Theoretically, the risk of false positives is expected to be higher when used in populations with a low HIV prevalence. However, experience from using the rapid INSTI test in Canada suggests false positives are rare. For example, over an 18-month period in British Columbia, 17,029 rapid tests were performed, of which 1% (168) were positive and only 5.4% (nine) of these were false positives.

The Oraquick test approved in the United States has a lower sensitivity than other tests, about 98%. In other words, if 1000 HIV-positive people were tested, 980 would test positive and 20 would incorrectly test negative. This means that the chance of false-negative results for this test can be higher than for other tests. However, since the vast majority of people testing for HIV are actually HIV negative, the chance of a negative result being false is still very low.

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