Hepatitis C | *Hepatitis C Virus*

Laboratory case definition

The Public Health Laboratory Network (PHLN) has developed standard case definitions to inform the diagnosis of key diseases in Australia. This document contains the laboratory case definition (LCD) for hepatitis C virus.

Version	Status	Authorisation	Consensus Date
1.1	Updated case definition criteria Updated background information	PHLN	14 November 2024
1.0	Initial PHLN Laboratory Case Definition	PHLN	15 December 2011

1 PHLN summary laboratory definition

1.1. Condition

Hepatitis C due to infection with hepatitis C virus.

1.1.1. Recent hepatitis C

- Detection of confirmed anti-HCV antibody in a patient shown to be anti-HCV antibody negative within the last 6 months

  OR

- Detection of HCV RNA in a patient shown to be anti-HCV antibody negative in the last 6 months

  OR

- Detection of HCV RNA from a child 2 to 6 months of age

1.1.2. Chronic hepatitis C

- Detection of HCV RNA in a patient shown to be confirmed anti-HCV antibody or HCV RNA positive at least 6 months previously.

1.1.3. Unspecified hepatitis C

- Detection of confirmed anti-HCV antibody from a patient >18 months of age

  OR

- Detection of HCV RNA from a patient > 6 months of age

  AND

- Does not meet the criteria for recent or chronic hepatitis C.

1.2. Confirmed anti-HCV antibody

A repeatedly reactive anti-HCV antibody enzyme immunoassay and:

- a reactive supplemental enzyme immunoassay that is different to the screening assay

  OR

- detection of HCV RNA

1.3. Links to related documents

- CDNA (clinical) case definitions: Hepatitis C (newly acquired) case definition (http://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-nndss-casedefs-cd_hepcnew.htm) and Hepatitis C (unspecified) case

definition (http://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-nndss-casedefs-cd_hepcun.htm)

- Fact Sheet: (http://www1.health.gov.au/internet/main/publishing.nsf/Content/hepatitis+C-2)
- NPAAC ; Requirements for laboratory testing for human immunodeficiency virus (HIV) and hepatitis C virus (HCV) Fourth Edition 2023

  https://www.safetyandquality.gov.au/sites/default/files/2023-04/requirements_for_laboratory_testing_for_human_immunodeficiency_virus_and_hepatitis_c_virus_fourth_edition.pdf

  National HCV Testing Policy

https://testingportal.ashm.org.au/national-hcv-testing-policy/what-is-new/

2 Introduction

Hepatitis C virus (HCV), a notifiable disease in Australia, is responsible for 58 million chronic infections worldwide causing 400,000 deaths each year, due to decompensated cirrhosis or hepatocellular carcinoma. The virus is a small enveloped single stranded positive-sense RNA virus, a member of the family *Flaviviridae*, genus *Hepacivirus* (Greek *hepatos*). The *Hepacivirus* genus is distantly related to the arthropod-borne *Orthoflavivirus* genus but, unlike Orthoflavivirus, has limited ability to grow in cell culture. Within the *Hepacivirus* genus, HCV infects humans whereas GB virus-B and several other hepaciviruses infect monkeys and other mammals, respectively (1).

The HCV genome is approximately 9.6kb and has a single open reading frame encoding a polyprotein flanked by 5'- and 3'- non-coding regions. The structural proteins (core, two envelope, possibly p7) are located in the N-proximal portion and the non-structural proteins (cysteine protease, serine protease/RNA helicase, cofactors involved in replication, RdRP) are toward the C terminus. Six genotypes (1 to 6) and a series of subtypes of HCV have been identified, with a possible genotype 7. Genotypes 1 to 3 are distributed worldwide while genotypes 4 and 5 appear mostly in Africa and genotype 6 in Asia (2). HCV is transmitted predominantly by blood exposure, making people who use intravenous drugs the highest risk group in Australia. Aboriginal and Torres Strait Islander people of Australia have higher notification rates of HCV than non-Aboriginal and Torres Strait Islander people (3). Organ and blood transfusion transmission is extremely unlikely with the current standard of risk factor, serological and molecular HCV donor screening in Australia. Vertical transmission is uncommon (approximately 5.8% from HCV-infected mothers) but is higher (10.8%) in

HCV/HIV co-infected pregnant women (4). Vaginal intercourse is considered of low risk, compared to anal intercourse.

Approximately 30% of infected individuals spontaneously clear the infection, usually within 6 months, with the remainder developing chronic HCV infection. Prevention of chronic HCV complications can be achieved by pan-genotypic direct-acting antiviral treatment that yields a sustained eradication of HCV infection in almost all cases. Since the introduction of diagnostic testing in 1990, the use of serological and nucleic acid tests has become essential in the management of HCV infection in order to diagnose infection, guide treatment decisions and assess the virological response to antiviral therapy.

The World Health Organisation (WHO) developed the global health sector strategy on viral hepatitis 2016–2021, with the goal to eliminate viral hepatitis as a public health threat by 2030. However, in 2019, only 21% of the 58 million persons with chronic HCV infection had been diagnosed, and 13%, treated (5). To address the major gap in testing and treatment the WHO has recommended simplifying the diagnostic approach to HCV infection, with the introduction of reflex HCV RNA testing of anti-HCV antibody positive people and point of care HCV tests to speed commencement of treatment for hard to reach or marginalised populations.

3 Laboratory diagnosis

3.1. Detection of HCV RNA

3.1.1. HCV qualitative RNA detection

Qualitative HCV RNA assays are based on the principle of target amplification using either conventional PCR, real-time PCR or transcription-mediated amplification (TMA). In PCR-based assays HCV RNA is extracted and reverse transcribed into single-stranded DNA, which is subsequently amplified to generate a large number of detectable double-stranded DNA copies. In TMA single-stranded RNA copies are generated. Detection of amplified products is achieved by hybridizing the amplicons with specific probes in conventional PCR or TMA techniques.

In real-time PCR, each round of amplification leads to the emission of a fluorescent signal which is proportional to the amount of HCV RNA in the starting sample. Automated platforms which perform both extraction and target amplification are available. Qualitative HCV RNA assays are very sensitive, with lower limits of detection of 12-15 international units (IU)/mL. This is well below the level of viraemia expected in chronic HCV infection where the 99th percentile for the lower limit of HCV RNA is 214 IU/mL (6). Qualitative assays are used for

the detection of active HCV infection, acute or chronic, and are used for the monitoring of therapy to decide on sustained virological responses (SVR). For interferon-based HCV therapies SVR is defined as HCV RNA negative at 12 weeks after cessation of treatment, whereas for direct-acting antiviral treatment testing a negative HCV RNA four weeks after treatment cessation appears reliable.

HCV RNA will become detectable one to two weeks after infection, during the prolonged serological window period and before clinical symptoms or biochemical liver abnormalities occur. HCV RNA may be the only detectable marker of HCV infection in the immunosuppressed who may mount a delayed or absent serological response. As HCV RNA detection indicates active viral replication a negative HCV RNA test does not exclude a past infection following either spontaneous clearance of HCV or successful antiviral treatment.

Rarely, in acute HCV infection there may be negative HCV RNA results, presumably due to transient reduction in HCV RNA levels below the limit of detection of the HCV RNA test. Transient HCV RNA detection may occur in the neonatal period from an HCV-infected mother, which does not necessarily indicate chronic infection of the neonate. It is recommended testing with an HCV-RNA assay be delayed until 2 months of age. Detection of HCV RNA in the infant beyond 2 months does not necessarily indicate life-long chronic infection, with some infants spontaneously clearing the infection up to 3-4 years of age (7).

3.1.2. HCV quantitative RNA detection

The mean HCV viral load in chronic HCV is between 5 and 6 log IU/mL with lower level viraemia more likely in the 18–30-year age group, women, genotypes 2 and 3 infection, and those with cirrhosis (6). HCV RNA can be quantified by means of target amplification techniques (competitive PCR or real-time PCR) or signal amplification techniques (branched DNA assay) which can be coupled in automated platforms with nucleic acid extraction.

Originally, the HCV RNA quantitative units used in the various assays, such as copies/mL, did not represent the same amount of HCV RNA in a given clinical sample until the WHO established an international standard of HCV RNA quantification allowing reporting in international units (IU), which is used in all commercial HCV RNA quantitative assays. This allows recommendations and guidelines from clinical trials to be derived and applied in clinical practice with any of the HCV RNA quantitative assays. The quantitative assays are reliable for all the HCV genotypes and subtypes and show good precision with CV%<5%. The linear range is wide, from approximately log 1.2 IU/mL to log 8 IU/mL. The HCV viral

load does not predict the natural history of HCV infection and testing is not indicated for management outside of HCV treatment.

Quantitative HCV RNA testing can be used to monitor the response and predict the probability of sustained virologic response early during a course of antiviral therapy, as measured by changes of HCV RNA levels. There may be slight differences between the results given for the same samples by different assays, so it is recommended that monitoring of a patient over time be performed with the same assay.

3.1.3. HCV molecular genotype detection

The six HCV genotypes are geographically distributed around the world, with genotypes 1 and 3 the most prevalent in Australia. The genotype has some impact on the natural history of chronic HCV, with genotype 1b and 3 having a possible increased risk of progression to cirrhosis and liver cancer. Genotype 3 is also associated with an increased rate of metabolic dysfunction-associated fatty liver disease. The genotype is also predictive of response to treatment with genotype 1 being less responsive to interferon-based HCV therapies when compared to genotypes 2 and 3. With the advent of highly effective pan-genotypic direct-acting antiviral treatments the genotype is still important, as genotype 3 HCV infection responds less well when compared to genotype 1, if cirrhosis is present. Genotyping may also be used to define re-infection after a previous infection with a different HCV genotype. This may be helpful if an SVR has not been documented following antiviral treatment, but cannot distinguish re-infection with the same genotype.

The reference method for HCV genotype determination is direct sequencing of highly conserved regions such as NS5, core, E1 and 5’ noncoding region of the HCV genome, followed by sequence alignment with prototype sequences and phylogenetic analysis. In clinical practice, the HCV genotype can be determined by various commercial assays, some fully automated, using direct sequence analysis of the 5’ noncoding region or PCR to identify genotypes and subtypes.

Mistyping is rare, but mis-subtyping may occur in 10% to 25% of cases when the 5’ noncoding region alone is used. Reverse hybridization analysis using genotype-specific oligonucleotide probes targeting the 5’ noncoding region, core and NS5B regions have been developed to improve this accuracy. Mixed infections are not usually detectable by genotyping methods as one genotype tends to be dominant in an individual. Genotyping may also be performed by other methods such as real time PCR-based melting curve analysis with probes against the core region, microarray systems, and matrix-assisted laser desorption ionization time of flight (MALDI-TOF) technology.

3.1.4. Suitable specimen types

Laboratory-based automated HCV RNA assays require 5-10 mL of serum or plasma (EDTA or citrate). Smaller capacity HCV RNA assays can use whole blood finger-prick samples or dried blood spots.

3.1.5. Specimen collection and handling

Plasma or serum can usually be stored up to a week at 4^0C or up to 12 weeks frozen at -20^0C prior to testing, dependent on the assay manufacturer.

3.1.6. Test sensitivity

Test sensitivities are 99% or higher for most manufacturers. The usual lower limit of detection for manufacturers of < 50 IU/mL is well below the lower limit 99th percentile for chronic HCV of approximately 200 IU/mL.

3.1.7 Test specificity

Test specificities are 99% or higher for most manufacturers.

3.1.8 Suitable test acceptance criteria

Appropriate indications for qualitative HCV RNA testing include assessment for active HCV infection in those anti-HCV antibody positive, assessment of acute HCV in the seroconversion window period, and assessment of HCV infection in seronegative immunosuppressed persons. Quantitative HCV RNA testing is indicated for monitoring of treatment response. HCV genotype assessment is indicated for clinical evaluation or treatment decisions.

3.1.9 Suitable test validation criteria

The HCV RNA assay must be listed on the Australian Register of Therapeutic Goods (ARTG). For donor testing the assay must be TGA registered as a class 4 IVD. The test should be validated for all six HCV genotypes for sensitivity. Reproducibility and repeatability should be assessed. Specificity should be validated against known negative plasma or serum and a panel of microorganisms including blood borne viruses, bacteria and fungi more commonly found in blood cultures. Interfering substances should be assessed including bilirubin, haemoglobin, triglycerides, antiviral medications and blood from patients with autoimmune diseases. Quantitative HCV RNA assays should be validated using the HCV WHO Standard across the linear range of the assay.

3.1.10 Suitable internal controls

HCV RNA assays should include a low and high positive control to assess for successful extraction and amplification and exclude inhibition, and a human plasma negative control to control for contamination.

3.1.11 Suitable external quality assurance program (proficiency testing)

All laboratories performing HCV RNA testing must be enrolled in an external quality assurance program (EQAP), as stipulated in the National Hepatitis C Testing Policy 2020. An HCV RNA EQAP program is available from the National (Serology) Reference Laboratory (NRL) for qualitative HCV RNA and genotyping and from the Royal College of pathologists of Australasia (RCPA) for qualitative and quantitative HCV RNA.

3.1.12 Point-of-care HCV RNA testing

Point-of-care (POC) HCV RNA assays have been developed for use on both fresh blood (venesection and finger-prick) and dried blood spots. A POC HCV RNA assay with a limit of detection of 1,000 IU/ml would have greater than 97% clinical sensitivity for confirming HCV viraemia. The HCV POC viral load RNA assays performed on blood show very high diagnostic performance across all assays, with pooled sensitivity and specificity of 99% and 99%, respectively (8), with the finger-prick assay having a reported limit of detection of 40 IU/ml. Dried blood spot assays also show good performance with a sensitivity of 97.8% and a specificity of 99.2% (9). Despite these high specificities, the positive predictive value falls when the HCV prevalence is below 10%, suggesting these tests are best performed in high-risk settings. At the time of writing dried blood spot HCV RNA testing has not been approved in Australia. The performance of POC HCV RNA assays should comply with the management framework as documented in the NPAAC Requirements for point of care testing (Second Edition 2021) (https://www.safetyandquality.gov.au/publications-and-resources/resource-library/requirements-point-care-testing-second-edition-2021).

3.2. Detection of anti-HCV antibody

3.2.1. Enzyme Immunoassay

The laboratory diagnosis of HCV infection is usually first made by the detection of circulating antibodies. Qualitative determination of anti-HCV antibody in blood is measured using enzyme immunoassays employing recombinant or synthetic HCV antigens. With the discovery of HCV and the sequencing of its genome in 1989, the first generation of anti-HCV enzyme immunoassays was produced using recombinant NS4 antigen. However, sensitivity and specificity was limited. Second generation tests, which added HCV antigens from the

core and non-structural regions, NS3 and NS4, resulted in a marked improvement in sensitivity and specificity. Third generation tests initially included antigens from the NS5 region and had further improved sensitivity, though this was more likely due to the improvements to the core and NS3 antigens rather than the inclusion of the NS5 antigen. Current third generation tests all include recombinant and/or synthetic antigens from the core and NS3 regions, with some assays also including antigens from the NS4 or NS5 regions. Third generation anti-HCV antibody enzyme immunoassays can be fully automated, have the convenience of random access, and are well adapted to large volume testing.

Various detection formats such as enzyme-linked immunosorbent assay (ELISA), chemiluminescent immunoassay (CLIA), electrochemiluminescent immunoassay (ECLIA), chemiluminescent microparticle immunoassay (CMIA) and microparticle enzyme immunoassay (MEIA) are available. Assessment of the performance of the enzyme immunoassays is hampered by the lack of a gold standard serological method, but using modified gold standard strategies such as multiple enzyme immunoassay consensus with HCV RNA the sensitivity and specificity of third-generation enzyme immunoassays is 99% or greater in immunocompetent persons. The major problem of anti-HCV antibody screening in low-prevalence populations is the low positive predictive value despite the high analytical specificity. This mandates that a reactive HCV antibody immunoassay must be confirmed by supplemental testing. Anti-HCV antibody is usually detected a median of seven to eight weeks after infection, compared to one to two weeks for HCV RNA, but delayed seroconversion, up to 12 months, is described. HCV infection in the immunosuppressed may result in a delayed or absent serological response. Also, seroreversion may occur following the onset of immunosuppression or after a sustained virological response to treatment, especially if treated during acute HCV infection (10).

Maternal transfer of anti-HCV may be detectable in the child's blood until up to 18 months of age, although most infants lose detectable anti-HCV antibody by 10 to 12 months. Anti-HCV antibody testing of children born to HCV-infected mothers is recommended at 12-18 months of age. Children who are anti-HCV positive after 18 months of age should be tested with an HCV RNA assay to confirm chronic HCV infection (11). Antigen-antibody (fourth-generation) tests detecting both antibodies to HCV, as for third generation tests, and HCV antigen are available.

3.2.2. HCV immunoblot and line immunoassay

The immunoblot and line immunoassays assays are enzyme immunoassays for the confirmation of anti-HCV antibody. Detection of anti-HCV antibody is based upon fixing specific antigenic HCV polyproteins onto a nylon membrane support. With each individual recombinant or synthetic antigen applied as separate line to the membrane, the antibody reaction to the different antigens can be distinguished. The line immunoassay antigens are derived from the core, E2 hypervariable, NS3 helicase, NS4A, NS4B and NS5A regions. The immunoblot antigens are derived from the core, NS3, NS4, and NS5 regions. Visualization of anti-HCV antibody reactivity in specimens to the individual HCV-encoded proteins is accomplished using standard enzyme immunoassay techniques.

The application of established criteria to interpret the patterns of reactivity observed permits greater specificity. However, not all those infected with HCV produce a positive immunoblot or line immunoassay and many equivocal screening enzyme immunoassay results also produce indeterminate immunoblot or line immunoassay results, requiring a recommendation for repeat testing. These tests are also labour-intensive, require extended incubation periods, and present a workflow issue for laboratories due to the relatively large number of screening anti-HCV antibody reactive results requiring confirmation. The HCV immunoblot and line immunoassay is therefore no longer used for anti-HCV antibody confirmation in Australia.

3.2.3. Confirmatory serology testing

The low positive predictive value of a repeatedly reactive anti-HCV antibody test from a low prevalence population mandates supplemental testing to confirm the result. Supplemental tests such as line immunoassay and HCV immunoblot have been used for this purpose and are commercially available, however, their performances are insufficient to resolve equivocal results. This resulted in a two-step enzyme immunoassay strategy, originally advocated by the Public Health Laboratory Service Virus Reference laboratory, UK in 1992 (12) soon after introduction of the commercial enzyme immunoassays, which continues in many countries, including Australia. Specificity of this two-step approach was achieved without the use of an immunoblot by requiring the two assays, with different antigenic specificity, to be reactive while allowing a cheaper and simpler algorithm which could be automated for larger scale testing. Once anti-HCV antibody is confirmed HCV RNA testing is recommended to diagnose active HCV infection. Unfortunately, this often does not occur as it requires a specific order for HCV RNA testing from the requesting practitioner for the laboratory to perform the test. A major impediment to the WHO's goal of HCV eradication by 2030 is the low rate of active HCV diagnosis and treatment. To hasten and increase the timely

diagnosis of active HCV infection the WHO and many other national authorities have recommended reflex HCV RNA testing of confirmed anti-HCV antibody positives. To further facilitate this, the use of an HCV RNA test to both confirm the screening enzyme immunoassay result and assess for active infection is now recommended by the US Centers for Disease Control and Prevention, Public Health England (PHE), and the WHO.

The NPAAC Requirements for Laboratory Testing for HIV and HCV (4th Ed) stipulates an initially reactive HCV antibody enzyme immunoassay may be reported as anti-HCV antibody positive by either reactivity in a second enzyme immunoassay with a different antigen combination, HCV RNA detection or HCV antigen detection. The difficulty with the second enzyme immunoassay approach is that the antigenic composition of the HCV enzyme immunoassays, and thus their antigenic specificity, is not released by the manufacturers and thus not readily available to laboratories. Also, for compliance to the NPAAC standards dedicated samples for HCV RNA testing or use of aliquots taken prior to immunoassay screening is required. In contrast, PHE permit HCV RNA testing from the original tube for HCV antibody confirmation but recommend repeat HCV RNA testing on a subsequent sample. This pragmatic approach enables both reflex HCV RNA testing and confirmation of screening anti-HCV antibody reactive results to be performed on all samples. If the reflex HCV RNA assay is negative a second enzyme immunoassay is required to confirm the reactive screening result.

3.2.4. Serological detection of genotype

The previously available assay determined the HCV genotype by targeting antibodies directed to genotype-specific HCV epitopes with a competitive enzyme immunoassay. The assay identified the genotype, but did not discriminate between the subtypes, in approximately 90% of chronically infected patients. Mixed serological reactivities were sometimes found that could be related to either mixed infection, cross-reactivity or recovery from one genotype infection and persistence of viremia with another genotype. This assay is no longer used in Australia.

3.2.5 Point-of-care serology testing

Point-of-care anti-HCV antibody tests use the lateral flow immunoassay method on venous blood, serum, plasma, finger-stick blood and oral fluid. Antigen targets are derived from the core, NS3 and NS4 regions of the genome. The pooled sensitivity and specificity of these tests performed on blood is 98% and 98%, respectively. Oral anti-HCV antibody assays also have a pooled sensitivity compared to blood reference tests of 94% but this ranges from 72% to 100%, with specificity ranging from 91% to 100% (8). In high-risk settings with anti-

HCV antibody prevalence less than 74%, combined POC anti-HCV antibody and POC RNA testing is a more cost-effective strategy than POC RNA testing alone (13). At the time of writing one POC test for anti-HCV antibody has been approved in Australia.

3.2.5. Suitable specimen types

HCV immunoassay testing can be performed on individual patient serum and plasma, both living and cadaveric.

3.2.6. Specimen collection and handling

Samples for immunoassay from the living may usually be stored on or off the clot or RBCs for up to a week at room temperature, or up to 2 weeks at 4^0C. Samples can usually be stored frozen after removal from the clot or RBC's for months at -20^0C. Cadaveric samples may have different storage requirements, such as shorter acceptable times at room temperature.

3.2.7. Test sensitivity

Sensitivity for the automated platform immunoassays is usually greater than 99%, which is maintained for cadaveric blood.

3.2.8. Test specificity

Specificity for the automated platform immunoassays is usually greater than 99%, which is maintained for cadaveric blood.

3.2.9. Predictive values

Despite the high specificity of the enzyme immunoassays the positive predictive value in low prevalence populations, such as the general population in many Western countries, can be much lower, around 73% (14).

3.2.10. Suitable test acceptance criteria

Appropriate requests for anti-HCV antibody testing include screening of living and cadaveric (usually up to 24 hr after death) blood, including donors, as part of an algorithm for the diagnosis of past or current HCV infection. The tests are not intended for cord blood samples. For donor testing the assay must be TGA registered as a class 4 IVD. Suitable test validation criteria

The anti-HCV antibody enzyme immunoassays must be listed on the Australian Register of Therapeutic Goods (ARTG). The test should be validated against all 6 HCV genotypes for

sensitivity. Reproducibility and repeatability should be assessed. Specificity should be validated against known negative plasma or serum. Interfering substances should be assessed including bilirubin, haemoglobin, and triglycerides along with patients with common medial conditions, including autoimmunity. Tests with a claim for cadaveric testing should be validated independently against this matrix.

3.2.11. Suitable internal controls

Automated platforms must undergo calibration as per the manufacturer's recommendation. The negative and positive control values must be within the acceptable range specified by the manufacturer. In addition to the kit assay and release controls, an external positive control is recommended.

3.2.12. Suitable external quality assurance program and proficiency testing

All laboratories performing anti-HCV antibody testing must be enrolled in an EQAP, as stipulated in the National Hepatitis C Testing Policy 2020. An HCV antibody EQAP program is available from the RCPA.

3.3. Detection of HCV antigen

3.3.1. Immunoassay

The HCV core antigen (HCV Ag) is present in the blood of infected individuals, probably in both complete virions and RNA-free core protein structures. Various HCV Ag assays indicate that the kinetics of HCV Ag are similar to those of HCV RNA in all phases of infection, as such the concentrations of HCV Ag and HCV RNA roughly correlate. It has been estimated that 1 pg of HCV core Ag is equivalent to approximately 40,000 IU of HCV RNA (15). All HCV genotypes and subtypes can be detected with a lower detection limit of approximately 3 fmol/L, corresponding to a viral load of 3,000 IU/mL (6). With a blood HCV viral load of at least 3,000 IU/mL, the sensitivity and specificity of HCV Ag in plasma is 97.7% and 100%, respectively and in dried blood spots is 88.6% and 97%, respectively (16).

HCV antigen testing is not suitable for assessing sustained virological response to treatment due to its reduced sensitivity when compared to HCV RNA assays. In acute HCV the HCV Ag assay may become positive within a day of HCV RNA positivity. Antigen-antibody (fourth-generation) tests detect antibodies to HCV, as for third generation tests, and HCV core antigen. During seroconversion they usually become positive 2-10 days after HCV RNA positivity. These combination antigen-antibody HCV assays are more user-friendly and cost-efficient than HCV RNA tests, thus have potential in low-income countries as an affordable tool for active HCV screening and potentially as a supplemental assay for anti-

HCV antibody tests where NAT is unavailable and HCV screening is often conducted by rapid tests. HCV Ag and HCV antigen-antibody tests are available in Australia.

4 Typing

The international nomenclature for the organism is Family *Flaviviridae*, Genus *Hepacivirus*, species hepatitis C virus.

5 Laboratory nomenclature for national data dictionary

SNOMED CT code	Concept name	Description
62944002	Organism	*Hepatitis C virus*
72165005	Substance	*Antibody to hepatitis C*
313612007	Procedure	*Hepatitis C antibody test*
314706002	Finding	*Hepatitis C antibody test positive*
314707006	Finding	*Hepatitis C antibody test negative*
406104003	Finding	*Hepatitis C enzyme immunoassay test positive*
406105002	Finding	*Hepatitis C enzyme immunoassay test negative*
104375008	Procedure	*Hepatitis C antibody, confirmatory test*
121204002	Substance	*Hepatitis C RNA*
122366001	Procedure	*Hepatitis C RNA assay*
398513000	Procedure	*Hepatitis C nucleic acid assay*
399117003	Procedure	*PCR test for hepatitis C virus*
397662006	Procedure	*Hepatitis C genotype determination*

6 References

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7 Glossary

ARTG – Australian Register of Therapeutic Goods

CIA – Chemiluminescent immunoassay

DNA – Deoxyribonucleic acid

EIA – Enzyme immunoassay

ELISA – Enzyme linked immunosorbent assay

IVD (device) – In vitro diagnostic medical device

MALDI-TOF – Matrix-assisted laser desorption ionization-time of flight

NAAT – Nucleic acid amplification test/ing

NPAAC – National Pathology Accreditation Advisory Council

NRL – National Serology Reference Laboratory

PCR – Polymerase chain reaction

POC – Point-of-care

EQAP – External quality assurance program

RCPA – Royal College of Pathologists of Australasia

Test sensitivity – Ability of a test to correctly identify patients with a disease

Test specificity – Ability of a test to correctly identify people without the disease

TGA – Therapeutic Goods Administration

WHO – World Health Organization