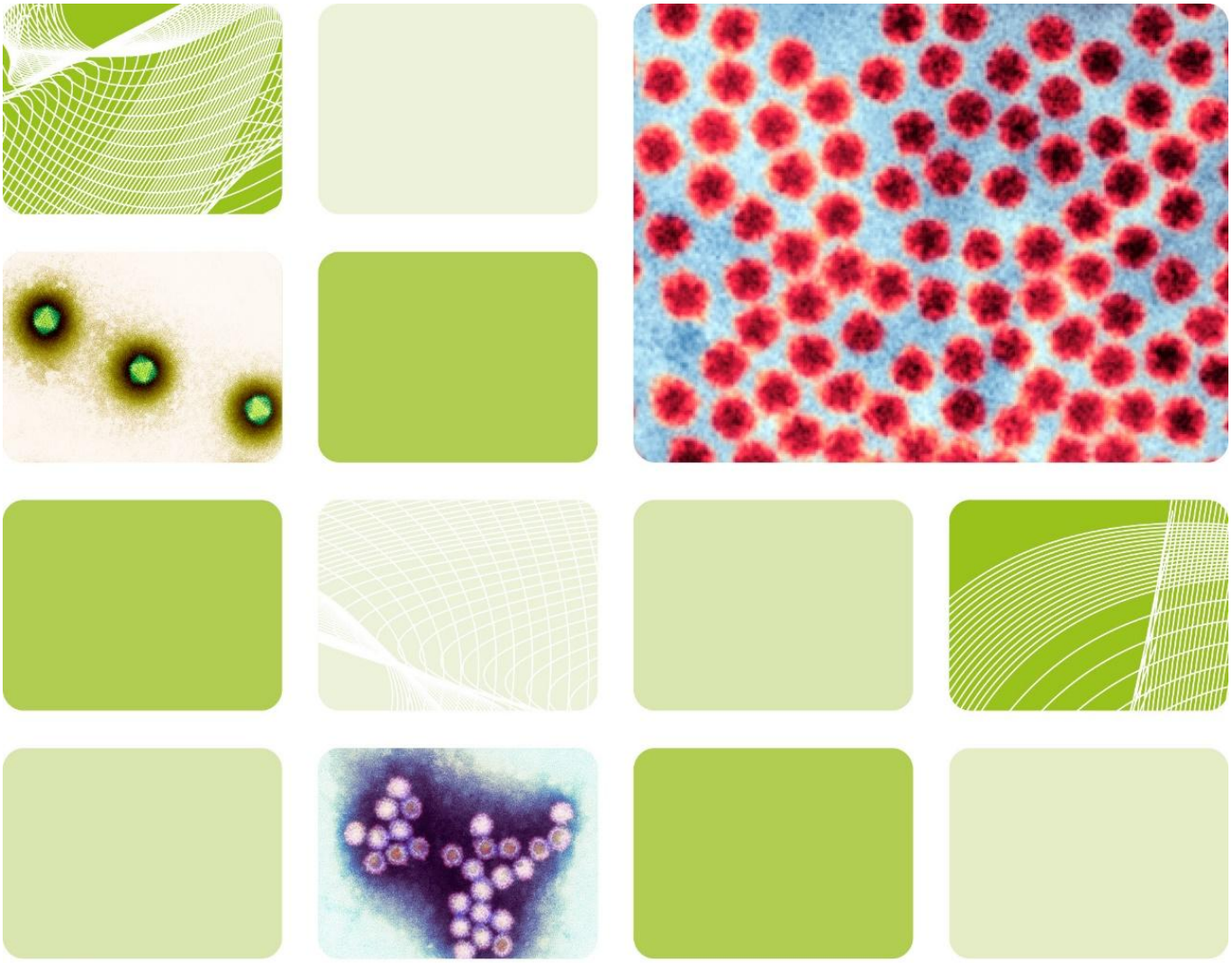
UK Health Security Agency

UK Standards for Microbiology Investigations

Laboratory diagnosis of hepatitis C virus



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Acknowledgments

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UK SMIs are produced in association with:

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Amendment table

The amendments since the previous version of this UK SMI document are listed in the amendments table below.

Any alterations to this document should be controlled in accordance with the local document control process.

Amendment number/date	10/30.10.26
Issue number discarded	7
Insert issue number	8
Anticipated next review date*	30.12.29
Section(s) involved	**Amendment**
Title	Title changed from ‘Screening for hepatitis C infection’ to ‘Laboratory diagnosis of hepatitis C virus’ to reflect the expanded scope of the document.
Whole document	• Reformatted to align with the current UK SMI template and formatting conventions. • Updated to reflect UKHSA governance arrangements. • Updated web links including direction to UK SMI webpages on the RCPath website. • Content from *UK SMI V8 Vertical and perinatal transmission of hepatitis C* reviewed and incorporated • References updated throughout
Section 1: General information	Generic UK SMI background information removed and replaced with references to the UK SMI webpages on the RCPath website
Section 2: Scientific information	Generic UK SMI scientific information removed and replaced with references to the UK SMI webpages on the RCPath website
Section 3: Scope of document	Scope revised and expanded to incorporate content from *UK SMI V8 Vertical and perinatal transmission of hepatitis C,* including additional specimen types,

	patient-group-specific testing recommendations, result interpretation and reporting guidance, and assay validation requirements. Exclusions have been clarified for donor screening, most POCT/self-testing strategies, saliva testing, and treatment monitoring and sustained virological response.
Section 4: Introduction	Introduction revised and updated to incorporate relevant content from *UK SMI V8 Vertical and perinatal transmission of hepatitis C*. Updated epidemiology, transmission routes, HCV classification and diagnostic approaches have been included, together with new subsections on stages of infection and markers of infection. Laboratory diagnosis guidance has been updated to reflect current practice.
Section 5: Safety considerations	Standard references have been replaced with a link to the relevant page on the website. Information revised and expanded, including guidance on specimen collection, transport, storage, processing and handling. Hazard classification information and references to current safety and containment guidance have been updated.
Section 6: Pre-laboratory processes	Expanded to include patient-group-specific testing recommendations, incorporating content from *UK SMI V 8 Vertical and perinatal transmission of hepatitis C*. This includes section 6.5.3 with recommendations for: • HCV testing during pregnancy. • Repeat testing in women with ongoing risk factors. • Follow-up and testing of infants born to HCV-infected mothers. • Paediatric specialist referral pathways. • Management considerations for women who acquire infection during pregnancy and babies born to women who inject drugs.

	Technical limitations revised to reflect current molecular and serological testing strategies, specimen types and special population testing requirements
Section 7: Laboratory processes	Algorithm has been revised, incorporating relevant principles from *UK SMI V8 Vertical and perinatal transmission of hepatitis C.* Standalone infant testing algorithms have been removed. The HCV core antigen confirmation algorithm has been removed and the HCV antibody testing pathway updated to reflect HCV RNA NAAT confirmation, reflex RNA testing, testing of immunocompromised and high-risk individuals, DBS and capillary blood testing, and quantitative HCV RNA reporting.
Section 8: Post-laboratory processes	Reporting guidance revised and simplified. Reporting terminology, interpretation of HCV antibody and HCV RNA results, reporting of diluted HCV RNA specimens, and public health management information have been updated. The reporting table has been revised to reflect current practice based on HCV antibody testing with HCV RNA confirmation. HCV core antigen reporting pathways have been removed.
Section 9: Referral to reference or specialist testing laboratories	Added guidance covering referral of specimens to specialist and reference laboratories.
Section 10: Public health responsibilities of diagnostic laboratories	New section added outlining the role of diagnostic laboratories in public health surveillance, specimen referral, enhanced characterisation testing and national surveillance programmes.
References	Reference list completely reviewed and updated.

∗Reviews can be extended up to 5 years where appropriate.

1 General information

View general information related to UK SMIs.

2 Scientific information

View scientific information related to UK SMIs.

3 Scope of document

This UK Standards for Microbiology Investigation (UK SMI) document provides a detailed review of initial and supplemental laboratory-based serological and Nucleic Acid Amplification Tests (NAAT) for the detection and exclusion of hepatitis C virus (HCV). Refer to UK SMI S 1: Acute infective hepatitis for further information regarding clinical presentations of acute infective hepatitis and associated tests.

This document covers a range of specimen types, including whole blood, plasma and serum and the various methods of collection including venous and capillary blood sampling and dried blood spot (DBS) collection. It also addresses testing in specific patient groups. In addition, the algorithm aims to assist clinicians and laboratories in their decision making, by providing a framework for testing. Reporting and interpretation of the test results are provided in section 8.1, Table 1.

All assays should be verified prior to use. If assays are to be used outside the scope for which the manufacturer has designated for them, these should be validated and shown to be fit for purpose by the laboratory for their intended use. For more information, refer to UK SMI Quality-related guidance

This UK SMI is intended for use in the laboratory diagnosis of HCV infection within healthcare settings. It is not intended to cover:

- testing of blood prior to organ or blood donation (refer to the SaBTO Guidance on the microbiological safety of human organs, tissues and cells used in transplantation).
- testing methods or strategies commonly used in community testing such as POCT, self-sampling, or self-testing excluding DBS and finger-prick capillary testing.
- testing of specimens other than blood, plasma and serum, such as oral fluid and saliva.
- monitoring of HCV RNA viral load and sustained virological response (SVR) for those undergoing treatment.

For the investigation and management of occupational exposure, refer to UKHSA (formerly PHE) and HSE guidelines (1-4).

For blood-borne virus (BBV) testing in the dialysis setting, including pre-entry, readmission, and following dialysis away from base (DAFB), refer to DHSC guidelines (5,6).

For HCV testing and management in infants, refer to national or local paediatric HCV guidelines.

For the management and treatment of HCV infection, refer to the EASL recommendations on treatment of HCV and BHIVA guidelines for the management of hepatitis viruses in people living with HIV (7,8).

UK SMIs should be used in conjunction with other relevant UK SMIs.

3.1 Abbreviations

Abbreviation	Definition
HCV	hepatitis C virus
BBV	Blood-borne virus
DBS	Dried blood spot
POCT	Point of care testing
PWID	People who inject drugs
NAAT	Nucleic acid amplification test
DAAs	Direct-acting antivirals

3.2 Definitions

For all antibody and NAAT testing, the following definitions apply:

Reporting stage for serology:

These terms are used for final or preliminary reports.

Positive – Report-stage for reactive result.

Negative – Report-stage for a non-reactive result.

Indeterminate – Manufacturer's or locally validated, evidence-based equivocal range.

Reporting stage for molecular assays:

These terms are used for final or preliminary reports.

Scenarios	Qualitative result	Quantitative actual value	Quantitative Log_{10} of actual value
1	Detected	Actual value	Calculated log from actual value of the assay
2	Detected	Below the lower limit of quantitation of the assay	Calculated to the lower limit of the assay value
3	Detected	Above the upper limit of quantitation of the assay	Calculated to the upper limit of the assay value
4	Not detected	Not applicable	Not applicable
5	Inhibitory	Not applicable	Not applicable
6	Insufficient	Not applicable	Not applicable
7	Invalid	Not applicable	Not applicable

For reporting terminologies please refer to section 8: Post-laboratory processes.

4 Introduction

In the UK, hepatitis C virus (HCV) infection remains an important public health concern. The UK government has aligned its national efforts with the World Health Organisation's (WHO) global goal of eliminating HCV (and hepatitis B virus) as a public health threat by 2030. In 2016, the UK government committed to the WHO's Global Health Sector Strategy on Viral Hepatitis (GHSS) and, in 2022, adopted the updated 2022-2030 strategy (9).

Significant progress has been made towards the elimination of HCV across the UK, supported by national strategies and surveillance programmes in England, Scotland, Wales and Northern Ireland (10-13). Recent reports demonstrate continued reductions in chronic HCV prevalence and improvements in testing, including the use of point-of-care testing (POCT) in settings serving people at increased risk of HCV infection who may face barriers to accessing conventional healthcare, alongside opt-out testing programmes in emergency departments. Together with widespread access to highly effective direct-acting antiviral (DAA) therapies, these approaches have improved case finding and treatment uptake and remain central to achieving the WHO elimination targets by 2030 (14-18).

4.1 Hepatitis C Virus (HCV)

HCV is a blood-borne virus currently classified within the family *Hepaciviridae*, genus *Orthohepacivirus* (formerly *Hepacivirus* within the family *Flaviviridae*) (19,20). It is a single-stranded, positive-sense enveloped RNA virus with a genome of approximately 9600 bases (21). There are eight known genotypes of HCV (1 to 8) to date, each with multiple subtypes that are distributed worldwide (22-25). The most common genotypes in the UK are HCV genotypes 1 and 3 (26,27).

4.2 Stages of HCV infection

New acute HCV infections are usually asymptomatic (85% - 90% cases) and therefore acute infection is rarely diagnosed. Around 30% (15% - 45%) of infected people spontaneously clear the virus within 6 months of infection without any treatment (19,28-30). Spontaneous viral clearance is rare beyond 4 to 6 months of infection, therefore the detection of HCV RNA for longer than 6 months is defined as chronic HCV infection (19,28-30). Levels of HCV RNA remain relatively stable over time in chronically infected patients.

Sustained viral clearance, also referred to as a sustained virological response (SVR), is defined as the absence of detectable HCV RNA in blood at least 12 weeks after completion of antiviral therapy, confirmed using a sensitive nucleic acid amplification test (NAAT). Achievement of SVR is considered equivalent to virological cure (7,31,32).

HCV reinfection is defined as the reappearance of HCV RNA at least 6 months after an SVR with a different HCV genotype or strain (7).

4.3 HCV diagnostic approaches

WHO recommends that all adults have access to and be offered HCV testing with linkage to prevention, care and treatment services (19). WHO also recommends general population testing of adolescents and adults in settings with intermediate and high HCV antibody seroprevalence defined as ≥ 2% (19).

In addition, it recommends blood donor screening, as well as focused or targeted testing of specific high-risk groups, including migrants from endemic regions, health-care workers, people who inject drugs (PWID), people in prisons and custody, men who have sex with men (MSM), sex workers and people living with HIV (19).

Targeted and more frequent HCV screening in people who are at increased risk of infection is also strongly recommended by UK bodies such as UKHSA, British HIV Association, British Association of Sexual Health and HIV, and National Institute for Health and Care Excellence to address the need to improve rates of earlier diagnosis (8,19,33,34).

Specific groups are usually screened for HCV by specialist service providers. These include blood, organ or tissue donors, end-stage kidney disease patients, new healthcare workers who will perform exposure-prone procedures (EPPs) and healthcare workers following occupational exposure.

Pregnant patients should be assessed for HCV infection in accordance with current national guidance and local policy. Those at increased risk of infection should be offered testing (35,36). National recommendations regarding routine antenatal HCV screening continue to evolve as new evidence emerges. Testing strategies should be implemented in accordance with relevant national policies and local care pathways.

Routine laboratory diagnosis of established infection is commonly based upon the detection of antibodies to HCV using serological methods, followed by the detection of the virus using HCV RNA NAAT on the same specimen to confirm viraemia (33,37-40).

The approach to HCV infection diagnosis and monitoring is tailored to individual patient circumstances, considering factors such as immune status and risk behaviours. According to the UKHSA, since the introduction of screening of blood and blood-derived products, PWID remain the group at greatest risk of acquiring HCV in England, with a particularly high burden of infection among those in prison settings and those experiencing homelessness (12).

Antibodies to HCV are detected using Enzyme-Linked Immunosorbent Assays (ELISA), Enzyme Immunoassays (EIA), and Chemiluminescent Immunoassays (CLIA) (41). Confirmatory serology tests, including Recombinant Immunoblot Assay (RIBA) and other second-line antibody tests are no longer commonly used. However, laboratory protocols may differ based on local practice and resource availability. Assays have evolved over time: second generation assays incorporate core proteins and non-structural proteins 3 and 4; third generation assays additionally incorporate

non-structural protein 5; and fourth generation assays combine antibody detection with direct detection of HCV capsid antigen (39)

The diagnosis of recently acquired or chronic HCV infection is based on the detection of HCV RNA by qualitative or quantitative molecular methods (7). An HCV RNA assay with target sensitivity level of 15 IU/mL or lower is recommended (7). Reflex NAAT testing on existing HCV antibody positive or indeterminate specimens is recommended to streamline the HCV care pathway (42-44).

Molecular methods are preferred for confirmation due to their higher sensitivity. Hepatitis C virus core antigen testing may be used as an alternative in some settings; however, it has lower sensitivity compared to RNA detection and may miss low-level viraemia. Therefore, RNA testing remains the recommended approach for confirmation of active infection (45-47).

4.4 Types of HCV diagnostic tests and markers of infection

- **HCV RNA** in peripheral blood is a marker of replicating virus. HCV RNA may be detected as early as 1 to 3 weeks after initial infection, approximately 1 month before the appearance of total HCV antibodies.
- **HCV immunoglobulin G (IgG) antibodies** emerge after IgM antibodies and persist lifelong beyond the clearance of HCV RNA. Most assays are designed to detect IgG, which becomes detectable at approximately 8 to 12 weeks following exposure (48). Testing for IgM antibodies is not routinely available.

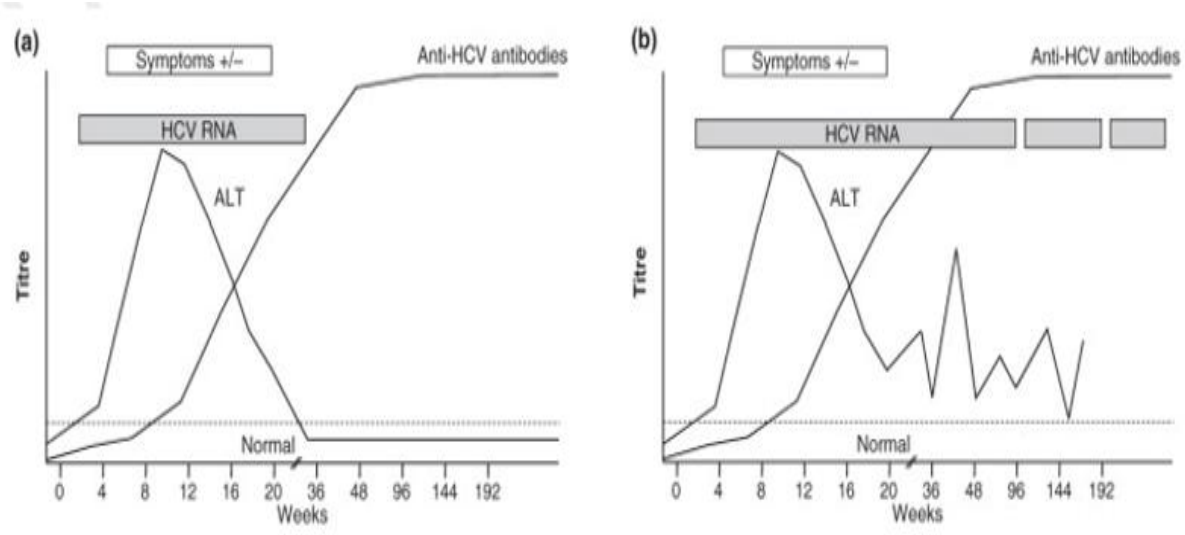


Figure 1. Kinetics of virological markers during acute (a) and chronic (b) hepatitis C virus (HCV) infection. Reproduced from S. Chevaliez, 2010 (49).

HCV antibodies appear following the acute phase of infection (Fig 1a and 1b). HCV RNA persists beyond 6 months in chronic HCV infection (Fig 1b).

5 Safety considerations

This section covers specific safety considerations related to this UK SMI and should be read in conjunction with the general safety considerations.

HCV is classified as a Hazard Group 3 agent; however full containment level 3 measures may be derogated based on local risk assessment.

All guidance should be supplemented with local COSHH and risk assessments.

6 Pre-laboratory processes

6.1 Specimen type

Whole blood, serum or plasma, dried blood spot (DBS), or finger-prick capillary blood sample.

Note: Venous blood is the preferred specimen for HCV testing providing serum or plasma specimens for routine serological and molecular assays (50,51). However, alternative specimen types can also be used. DBS or capillary blood specimens are increasingly employed in underserved and hard-to-access populations such as in prisons, those experiencing homelessness and in people who inject drugs (PWID) and can be used for HCV serology and qualitative NAAT testing for HCV diagnosis (15,52).

Use of specific specimen types in individual assays is subject to local verification and validation requirements, alongside the manufacturer's instructions.

6.2 Specimen collection and handling

Collect specimens as soon as possible after onset of symptoms.

Use aseptic technique to collect blood.

Collect adequate and appropriate specimens in appropriate CE/UKCA marked leak-proof containers that meet the required regulatory standards for safety and quality, and transport in sealed plastic bags.

Specimens collected in Ethylenediaminetetraacetic acid (EDTA), or serum separator tubes are generally acceptable for testing. Refer to the manufacturer's instructions for specimen acceptability.

Providing adequate specimen volume is essential for maintaining test sensitivity and accuracy. If dilution of a specimen is performed by the laboratory, it is recommended that the dilution factor is reported with the results.

Refer to local laboratory protocols or the manufacturer's instructions for specific requirements on serum or plasma separation for NAAT.

Laboratory procedures that give rise to infectious aerosols must be conducted in a microbiological safety cabinet.

Refer to current guidance on the safe handling of all organisms covered in this UK SMI.

6.3 Specimen transport and storage

This section covers specimen transport and storage considerations related to this UK SMI, and should be read in conjunction with the scientific information on the UK SMI webpages.

Specimens should be transported and processed as soon as possible (53). If processing is delayed, refrigeration is preferable to storage at ambient temperature (53).

Note: Specimens for NAAT can be stored long-term at - 20°C or lower (e.g., - 70°C) to minimise RNA loss/degradation (54).

Specimens should be retained in accordance with The Royal College of Pathologists guidelines 'The retention and storage of pathological records and specimens' (55).

Compliance with postal, transport and storage regulations is essential.

6.4 Technical limitations

6.4.1 Specimen types and collection methods

The standard specimen types are whole blood, serum and plasma. DBS and capillary blood specimens have been adapted for use in HCV serology and qualitative NAAT for HCV diagnosis (56-59). These specimens are useful in identifying individuals with HCV but may be limited by lower sensitivity for HCV RNA quantification, particularly for monitoring purposes and by potential inhibition due to the nature of the specimens (60-62). Therefore, appropriate local validation and/or verification is required prior to their use to ensure accuracy and effectiveness in both diagnostic and monitoring context.

For more information on managing inhibition and contamination in molecular methods, refer to UK SMI Q 4: Good practices when performing molecular amplification assays.

6.4.2 Immunoassays

HCV antibody tests

The limitations of HCV antibody tests are most evident when they are used in isolation, particularly in low-risk populations and in immunocompromised individuals (e.g., transplant recipients, people living with HIV, or those receiving immunosuppressive therapy). In these groups, results may be unreliable, and individuals with recent exposure, suspected acute hepatitis C, or who are immunocompromised should undergo HCV RNA testing using NAAT. In low-prevalence settings, weakly positive antibody results are more likely to represent false positive results (63).

Antibody production is delayed following infection, typically becoming detectable after 8-12 weeks in immunocompetent individuals and potentially much later, or not at all, in immunocompromised patients (63,64). This delay reduces the clinical utility of antibody testing during the window period and in patients with impaired immune responses.

Additionally, antibody tests cannot differentiate between:

- past resolved infection
- chronic infection
- reinfection with a different HCV genotype

For these reasons, individuals who are immunocompromised or have risk factors for recent acquisition for HCV infection should be assessed using HCV RNA detection by NAAT (63-65).

6.4.3 Molecular methods

HCV RNA is a marker of active viral replication, but low-level results in EDTA blood and serum should be interpreted with caution, particularly near the assay's limit of detection. Such results may reflect assay variability or occur during antiviral therapy; a single low-level result cannot reliably determine virological status. Laboratories should therefore provide detailed quantification for more informed clinical interpretation. Careful evaluation, including repeat testing or clinical correlation, may be required. In addition, if dilution is performed, it is recommended to report the dilution factor with the HCV RNA results to ensure accurate interpretation of viral load and support clinical decision-making.

Follow manufacturer's instructions for assay thresholds and recommended dilutions.

Some assays may require non-standard dilutions (e.g., 1:2.5 or 1:5.0), and local laboratory practice may also determine when dilution is performed. When reporting diluted specimens, the adjusted threshold or corrected result should be clearly stated. All results must be interpreted in conjunction with clinical information.

For examples of how to report the dilution factor, please see below, including a result comment and a dilution factor comment. An example calculation is also provided for information and is not intended for inclusion in the final report.

- For a "not detected" result after dilution, a suitable combined comment is:

  "HCV RNA was not detected following a 1:x dilution. After applying the dilution factor, the adjusted threshold is [value] IU/mL. Results should be interpreted within the clinical context."

- For a "detected" result after dilution, a suitable combined comment is:

  "HCV RNA detected. After applying the 1:x dilution factor, the final viral load is [value] IU/mL. Results should be interpreted within the clinical context."

- Example calculation (if needed): an analyser readout of 200,000 IU/mL with a 1:2 dilution produces a final reported value of 400,000 IU/mL.

6.5 Test selection

The choice of test can be influenced by risk factors.

Please note that HCV RNA NAAT may be recommended as the initial test, in certain patient populations or situations to avoid missing cases of HCV infection. This ensures early detection and appropriate management.

6.5.1 Immunocompetent individuals

The initial HCV screening assay should be a 3rd or 4th generation antibody assay, which if positive should be followed by an HCV RNA NAAT to determine whether the patient is currently infected with HCV. Individuals at risk of acute HCV infection or HCV reinfection should also be screened using HCV RNA NAAT. Confirmation of HCV antibody with a second antibody assay is usually not required, however, local protocols should be followed.

6.5.2 Immunocompromised individuals

Screen using HCV RNA NAAT.

For guidance on immunisation in people who are immunocompromised or receiving immunosuppressive therapy, refer to UKHSA Immunisation against infectious disease.

6.5.3 Pregnancy and infected babies

During pregnancy, those at increased risk for HCV infection should be tested at their prenatal visits by testing for HCV antibodies. If the initial result is negative despite on-going risk factors for HCV infection, testing should be repeated later in pregnancy, ideally during the third trimester (35,66). It should be noted that routine testing for HCV infection during pregnancy is not currently recommended (67).

Routine testing of babies born following a pregnancy with evidence of HCV antibodies but negative HCV RNA is not required, although it may be considered where there is clinical or historical evidence of recent maternal infection (68).

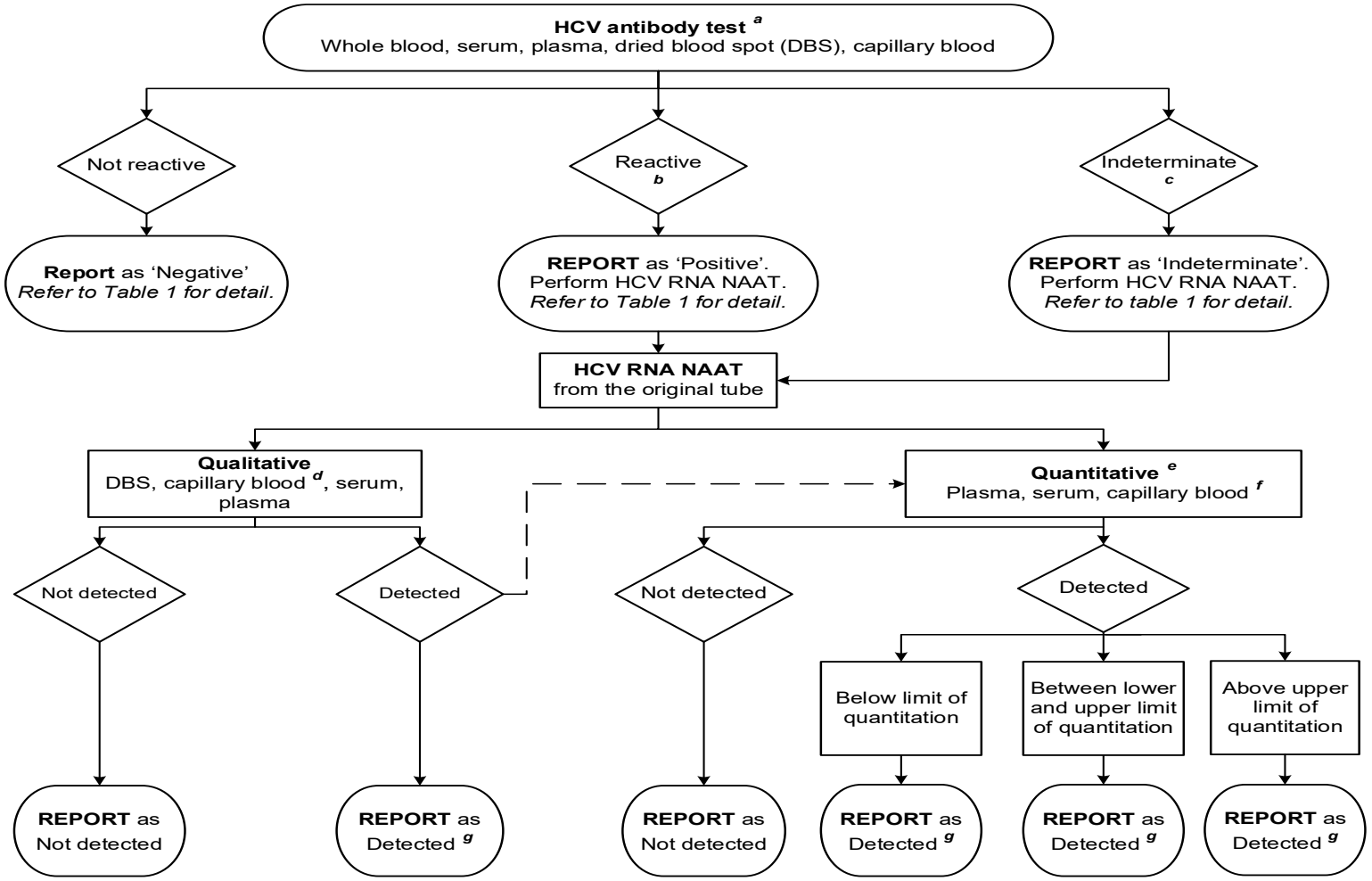
Where HCV infection is acquired during pregnancy but viraemia subsequently clears, the baby should be followed up appropriately.

Consider testing children from previous pregnancies or partners where maternal HCV RNA is currently positive.

Please refer to local or national guidelines for paediatric HCV testing and management.

7 Laboratory processes

7.1 Investigation of hepatitis C infection by HCV antibody testing confirmed by HCV RNA NAAT (7,37,40,69)



Footnotes:

a Screening directly with HCV RNA NAAT is required for certain patient groups, particularly those who are immunocompromised or for whom the risk of recent or ongoing infection is high, as NAAT is more reliable in these cases than HCV antibody testing.

b Report at this stage as an interim report if additional testing will be delayed and the result may have immediate significance for patient management; suggested wording “Initial HCV antibody reactive. Hepatitis C RNA result to follow”.

c Some HCV antibody kits do not provide an indeterminate range. Indeterminate ranges may be established using local data.

d Follow up with quantitative HCV RNA NAAT is recommended for both DBS and capillary blood specimens, where qualitative HCV RNA is positive, to assess viral load and guide treatment decisions.

e For detected results, quantitative HCV RNA NAAT reports include three fields: ‘Detected’, Actual value in IU/mL and Log of actual value. Report according to manufacturer’s instructions for assay limits. For non-detected results, only ‘Not detected’ is reported.

f Capillary blood may be used for quantitative reporting if validated according to local protocols and manufacturer guidance.

g For specimens with very low-level detection near the assay’s sensitivity threshold, consider an interpretive comment indicating that the result is close to the assay limit and may require clinical correlation or repeat testing.

8 Post-laboratory processes

8.1 Interpretation and reporting of results

Reporting terminology should be determined through local laboratory clinical governance, ensuring results are communicated in a way that optimises patient safety and supports accurate clinical interpretation. Laboratories should use clear, consistent terminology appropriate to their users, reflecting local clinical pathways and risk management processes. While UK Standards for Microbiology Investigations (UK SMIs) provide guiding principles, the final choice of wording remains a matter of local clinical judgement, informed by local disease epidemiology and accountability.

The final result should be able to distinguish active HCV infection from resolved infection using a combination of antibody and NAAT tests.

It is recommended that when HCV test results are obtained from diluted specimens, the dilution factor is included in the report to aid interpretation of low-positive results and support clinical decision-making.

Following an initial (first specimen) positive result, it is best practice to request a repeat specimen for confirmation of HCV status and patient identity.

Table 1. Investigation of HCV infection by HCV antibody testing confirmed by NAAT.

	1st Assay	2nd Assay	Interpretative comments	Notes
	HCV Ab	**HCV NAAT**		
1	Negative	Not tested	HCV antibody negative.	In the case of suspected acute hepatitis C or in immunocompromised patients, HCV RNA testing should be part of the initial evaluation.
2	Negative	RNA detected [quantitative value as appropriate]	Evidence of active HCV infection. Advise referral to an appropriate specialist for further assessment/treatment. Hepatitis A and B vaccines recommended if appropriate.	For a first detected HCV RNA specimen: This indicates either acute HCV infection or possibly a chronic infection in an immunocompromised patient. Please ensure hepatitis A and B vaccination status is known and vaccination given if needed. Reflex genotyping may be considered for HCV RNA detected specimens to support surveillance, treatment decisions, or local policy requirements. BBV testing should also be considered unless already performed. For a second and subsequent HCV RNA detected specimen: Known active HCV infection
3	Positive	RNA detected [quantitative value as appropriate]	Evidence of active HCV infection. Advise referral to an appropriate specialist for further assessment/treatment. Hepatitis A and B vaccines recommended if appropriate.	For a first detected HCV RNA specimen: HCV antibody positive in the presence of HCV RNA allows one to infer with confidence that the HCV antibody reaction is a true positive. Please ensure hepatitis A and B vaccination status is known and vaccination given if needed. Reflex genotyping may be considered for HCV RNA detected specimens to support surveillance, treatment decisions, or local policy requirements. BBV testing should also be considered unless already performed. For a second and subsequent HCV RNA detected specimen: Known active HCV infection

	1st Assay	2nd Assay	Interpretative comments	Notes
	HCV Ab	**HCV NAAT**		
4	Indeterminate	RNA detected [quantitative value as appropriate]	Evidence of active HCV infection. Advise referral to an appropriate specialist for further assessment/treatment. Hepatitis A and B vaccines recommended if appropriate.	For a first detected HCV RNA specimen: If HCV antibody assay is indeterminate and RNA detected, this may indicate recent infection. Consider review of the clinical history and previous results to determine whether HCV antibody seroconversion has occurred. Please ensure hepatitis A and B vaccination status is known and vaccination given if needed. Consider requesting HCV genotyping and other BBV testing unless already performed. For a second and subsequent HCV RNA detected specimen: Known active HCV infection
5	Positive	RNA not detected	No evidence of active HCV infection.	HCV antibody positive result may indicate past HCV infection. EASL 2020 recommends that “Anti-HCV antibody-positive, HCV RNA-negative or HCV core antigen-negative patients with suspected *de novo* recently acquired HCV infection should be retested for HCV RNA 12 and 24 weeks later to confirm definitive clearance” (7).
6	Indeterminate	RNA not detected	No evidence of active HCV infection.	If HCV antibody assay is indeterminate and HCV RNA is not detected this may represent false reactivity or waning of antibody (70-72).

8.2 Public health management

All confirmed cases of HCV infection should be reported to local public health authorities.

For information regarding notification refer to:

https://www.gov.uk/government/collections/notifications-of-infectious-diseases-noids

For further information on public health management refer to: https://www.gov.uk/government/collections/hepatitis-c-guidance-data-and-analysis

In addition to reporting new positive diagnosis to UKHSA Health Protection Teams, participating laboratories should also report into sentinel surveillance programmes for HCV.

In the UK, guidance for HCV infected health care workers (HCW) is available. See link: https://www.gov.uk/guidance/bloodborne-viruses-in-healthcare-workers-report-exposures-and-reduce-risks

For the final report published on the Infected Blood Inquiry in May 2024 refer to the following link: Reports | Infected Blood Inquiry

9 Referral to reference or specialist testing laboratories

When sending away isolates to reference or specialist testing laboratories for processing, ensure that the specimen is placed in the appropriate package and transported accordingly. Follow local regulations and instructions provided by the reference or specialist testing laboratories for sending isolates.

Contact the appropriate reference laboratory (refer to the links provided below) for information on the tests available, turnaround times, transport procedure and any other requirements for specimen submission.

England

Wales

Scotland

Northern Ireland

10 Public Health Responsibilities of diagnostic laboratories

Diagnostic laboratories have public health responsibility as part of their duties. Amongst these are additional local testing, or referral to further characterise the organism as required and notify causative agents, primarily for public health purposes e.g. routine *Cryptosporidium* detection; serotyping or microbial subtyping; and a duty to refer appropriate specimens and isolates of public health importance to a reference laboratory.

Diagnostic laboratory outputs inform public health intervention, and surveillance data is required to develop policy and guidance forming an essential component of healthcare. It is recognised that additional testing and referral of specimens may entail some costs that has to be borne by the laboratory but in certain jurisdictions these costs are covered centrally.

Diagnostic laboratories should be mindful of the impact of laboratory investigations on public health and consider requests from the reference laboratories for specimen referral or enhanced information.

References

An explanation of the reference assessment used is available in the scientific information section on the UK SMI website.

For suggested citation of UK SMIs, refer to UK SMI Development.

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