Interpretation of hepatitis C test results

Anti-HCV screening test results (EIA)	HCV RNA (PCR)	RIBA	Interpretation	Comments
Nonreactive	N/A	N/A	Negative	Not infected with HCV.
Nonreactive	Positive	Negative	Confirmed HCV case	Active HCV infection; test subject is likely immune compromised.
Reactive	Positive	Positive	Confirmed HCV case	Active HCV infection.
Reactive	Positive	(Not done)	Confirmed HCV case	Active HCV infection.
Reactive	Negative	Positive	Confirmed HCV case	Possible resolved infection. However, a single negative HCV RNA result does not rule out active infection. Follow-up HCV RNA test needed in ≥ 6 mos.
Reactive	Negative	Indeterminate	Negative	Not infected with HCV. False positive EIA test result.
Reactive	Negative	Negative	Negative	Not infected with HCV. False positive EIA test result.
Reactive	Negative	(Not done)	Possible HCV case	Possible false positive EIA test result or resolved infection. However, a single negative HCV RNA result does not rule out active infection. Follow-up HCV RNA test needed in ≥ 6 mos.
Reactive	(Not done)	Positive	Confirmed HCV case	Active or resolved infection. HCV RNA test needed
Reactive	(Not done)	Indeterminate	Unknown	HCV antibody infection status not determined. HCV RNA test needed.
Reactive	(Not done)	Negative	Negative	Not infected with HCV.
Reactive with high s/co*	(Not done)	(Not done)	Confirmed HCV case	Active or resolved infection. HCV RNA test needed.
Reactive with low s/co*	(Not done)	(Not done)	Possible HCV case	HCV RNA or RIBA test needed.

Adapted from: Centers for Disease Control and Prevention. Guidelines for laboratory testing and result reporting of antibody to hepatitis C virus. MMWR 2003;52(No. RR-3):11.

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* The signal to cut-off ratio is based upon the EIA test result.

Hepatitis C Laboratory Assays

Enzyme Immunoassay (EIA)

EIA detects the presence of antibody to hepatitis C virus (anti-HCV) in the serum. This test is commonly used for initial screening for hepatitis C. The EIA does not differentiate between acute, active, or resolved infection. The EIA is highly sensitive but may yield false negative results in the window period between exposure and seroconversion (the window period varies, but averages 8 weeks) or in patients with immunologic disorders that impair production of antibody. The EIA may be falsely positive due to cross-reactivity with other antigens. The false positivity rate of the EIA increases as the prevalence of hepatitis C antibody positivity decreases in a population.

While the specificity of the most widely used EIAs is ≥99%, this does not provide the desired predictive value for a positive test among a population with a low prevalence of HCV infection. Among immune competent populations with anti-HCV prevalences <10%, the proportion of false-positive results averages approximately 35%. Among immunocompromised populations, the proportion of false-positive results averages 15%.

EIA signal to cutoff ratio

EIA results are reported as "reactive" or "nonreactive" and the EIA signal to cutoff (s/co) ratio may also be reported as "high" or "low." The EIA s/co ratio is a comparison of the optical density of the patient's positive EIA result to the optical density of the laboratory's positive EIA control. If the ratio is high, the positive predictive value (that the patient truly has HCV antibody in the blood) of the patient's result is high and therefore does not require confirmatory testing using the RIBA. The threshold for a s/co ratio predictive of a true positive is unique to each manufacturer's assay (see the CDC review of s/co ratios for commercially available assays at http://www.cdc.gov/hepatitis/hcv/LabTesting.htm).

Recombinant Immunoblot Assay (RIBA)

RIBA is a very specific test that detects the presence of anti-HCV in the serum. Like the EIA, the RIBA does not differentiate between acute, active, or resolved infection. The RIBA can be used to confirm a positive EIA in certain clinical situations, such as the patient with a reactive EIA with a high s/co ratio or a patient with a reactive EIA and negative HCV RNA test. RIBA results are reported as positive, negative, or indeterminate.

Indeterminate test results are reported when partial reactivity occurs between the test antigens and proteins in the patient's serum. Indeterminate supplemental test results have been observed in recently infected persons who are in the process of seroconversion as well as in persons infected with HCV. Indeterminate anti-HCV results also might indicate a false-positive result, particularly in those persons at low risk for HCV infection. Indeterminate results are best resolved by performing an HCV RNA test.

HCV Ribonucleic Acid (RNA)

HCV RNA tests detect the presence of HCV in the patient's blood, indicating an active infection.

Qualitative HCV RNA Tests

Qualitative HCV RNA tests (e.g., reverse transcriptase polymerase chain reaction [RT-PCR] amplification of HCV RNA) detect the presence or absence of HCV and are reported as "positive" or "negative."

Quantitative HCV RNA Tests

Quantitative HCV RNA tests (e.g., RT-PCR amplification of HCV RNA, branched chain DNA [b-DNA]) measure the amount of virus in blood plasma. Results are expressed as viral RNA copies per milliliter (ml) of plasma or as International Units per ml (IU/ml) of plasma.

Because detection of HCV RNA during the course of infection may be intermittent, a single negative test result for HCV RNA is not conclusive. Therefore, a negative HCV RNA should be followed by a repeat HCV RNA no earlier than six months after a negative HCV RNA test result is obtained.

Important: HCV Case Reporting to Local Health Departments

Hepatitis C is a reportable communicable disease (Wisconsin Administrative Code DHS 145). All positive HCV assays should be reported to the local health department within 72 hours of identification.