MAYO CLINIC LABORATORIES

Test Definition: HCVG

Hepatitis C Virus Genotype, Serum

Overview

Useful For

Determining hepatitis C virus (HCV) genotype (1 to 5) to guide antiviral therapy in patients with chronic hepatitis C

Differentiating between HCV subtypes 1a and 1b

This assay should **not be used** as a screening test for HCV infection. It should be performed only on specimens obtained from patients confirmed to have HCV RNA levels in serum of 500 IU/mL or higher.

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
HCVGR	HCV Genotype Resolution, S	No	No

Testing Algorithm

Specimens generating indeterminate, genotype 1 without subtype, or mixed genotypes containing genotype 1 without subtype results will be automatically evaluated by genotype resolution at an additional charge.

The following algorithms are available:
-Chronic Hepatitis C Treatment and Monitoring Algorithm: Direct Antiviral Antigen (DAA) Combination
-Hepatitis C: Testing Algorithm for Screening and Diagnosis

Special Instructions

- Hepatitis C: Testing Algorithm for Screening and Diagnosis
- Chronic Hepatitis C Treatment and Monitoring Algorithm: Direct Antiviral Agent (DAA) Combination

Method Name

Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) followed by Hybridization with Sequence-Specific, Fluorescent-Labeled Oligonucleotide Probes

NY State Available

Yes

Specimen

Specimen Type

Serum SST

Shipping Instructions

Ship specimen frozen on dry ice only. If shipment will be delayed for more than 3 days, freeze serum at -20 degrees C or colder (up to 42 days) until shipment on dry ice.

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube: Serum gel (red-top tubes are **not acceptable**)
Submission Container/Tube: Plastic vial
Specimen Volume: 5 mL
Collection Instructions:
Within 2 hours of collection, centrifuge and aliquot serum into a plastic vial.
Additional Information:
1. This test requires a minimum hepatitis C virus viral load of 500 IU/mL within the 30 days preceding collection.
2. Serum specimens previously submitted to other laboratories for non-microbiology tests are **not acceptable** for add-on test requests due to possible sample-to-sample carryover from automation used for those tests.

Forms

If not ordering electronically, complete, print, and send 1 of the following:
-Gastroenterology and Hepatology Test Request (T728)
-Microbiology Test Request (T244)

Specimen Minimum Volume

1.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum SST	Frozen (preferred)	42 days	ALIQUOT TUBE
	Refrigerated	72 hours	ALIQUOT TUBE

Clinical & Interpretive

Clinical Information

Unique nucleotide sequences of certain regions (eg, 5'-noncoding, core, NS5b) of the hepatitis C virus (HCV) genome allow classification of HCV into 6 major genotypes or clades (1-6), based on the most recently proposed HCV genotype nomenclature. In the United States, the most frequently encountered HCV genotypes are 1a and 1b, followed by genotypes 2 and 3. Worldwide geographic distribution, disease outcome, and response to antiviral therapy differ among the genotypes. Therefore, reliable methods for genotype determination are important for proper selection of antiviral

therapy and optimal patient management. Infections with HCV genotypes 2 and 3 have better therapeutic response rates (80%-90%) than genotypes 1 and 4 (40%-50%) to previous standard combination therapy (ribavirin plus pegylated interferon alpha-2a or alpha-2b). Duration of such combination therapy is 24 weeks for chronic HCV genotype 2 and 3 infections in patients who show early virologic response (>2 log or 100-fold decrease in HCV RNA or no detectable HCV RNA at week 12 of therapy), while patients with chronic HCV genotype 1 and 4 infections receive a minimum of 48 weeks of such combination therapy if early virologic response is achieved (undetectable HCV RNA at week 4 of therapy).

Therapeutic response rates for HCV genotype 1 infection are improved significantly (80%-90%) when oral direct acting antiviral agents (eg, daclatasvir, sofosbuvir, ledipasvir + sofosbuvir, velpatasvir + sofosbuvir, glecaprevir + pibrentasvir, elbasvir + grazoprevir, velpatasvir + voxilaprevir + sofosbuvir) are added or used in lieu of interferon-based combination therapy.

The American Association for the Study of Liver Diseases and Infectious Disease Society of America recommendations for testing, managing, and treating hepatitis C are available at www.hcvguidelines.org/contents.

The following algorithms are available:
-Chronic Hepatitis C Treatment and Monitoring Algorithm: Direct Antiviral Antigen (DAA) Combination
-Hepatitis C: Testing Algorithm for Screening and Diagnosis

Reference Values

Undetected

Interpretation

Hepatitis C virus (HCV) genotyping result	Interpretation	Resolution test (reflex test) ordered?
1a	1a is the definitive subtype/genotype	No
1b	1b is the definitive subtype/genotype	No
2	2 is the definitive genotype	No
3	3 is the definitive genotype	No
4	4 is the definitive genotype	No
5	5 is the definitive genotype	No
1	A definitive genotype/subtype (1a, 1b, 6) could not be assigned. Resolution testing ordered.	Yes
1a, 2 (any 2 genotypes)	Result may be due to mixed genotype infection, recombination of HCV genotypes, or assay probe cross-reactivity.	No
1, 3 (2 genotypes with a 1, no subtype)	Result may be due to mixed genotype infection, recombination of HCV genotypes, or assay probe cross-reactivity. Resolution testing ordered.	Yes
HCV not detected	Assay failed to detect HCV RNA.	No
Indeterminate (undetermined genotype)	HCV RNA detected, but genotype could not be determined. Resolution testing ordered.	Yes
Indeterminate (mix)	Result may be due to mixed genotype infection, recombination of HCV genotypes, or assay probe	No

	cross-reactivity.	

An "Undetected" result indicates the absence of detectable hepatitis C virus (HCV) RNA in the specimen.

An "Indeterminate" result may be due to one or more of the following causes:
1. Low HCV RNA level (ie, <500 IU/mL)
2. HCV genotype 6
3. Probe reactivity with multiple HCV genotypes
4. Variation in patient's HCV target sequences with mismatches to polymerase chain reaction primers and/or probes.
Specimens generating indeterminate results with this assay will be automatically evaluated with the subsequent test HCVGR / Hepatitis C Virus Genotype Resolution, Serum.

An HCV genotype result of "1" without a subtype result may be due to one or more of the following causes:
1. Low HCV RNA level (ie, <500 IU/mL)
2. Probe reactivity with multiple genotype 1 subtypes
3. Variation in HCV genotype 1 target sequence
4. Misclassification of some true genotype 6 strains

This assay can differentiate between HCV subtypes 1a and 1b. However, subtypes are not reported for HCV genotypes 2 to 5 due to limitations of the current genotyping assay in accurately differentiating the various subtypes of these genotypes.

Results with multiple or mixed HCV genotypes (eg, 1, 5; 1a, 2; or 3, 5) may be due to mixed genotype infection or assay probe cross-reactivity. Only those specimens with multiple or mixed genotype results containing genotype 1 but no subtype will be automatically evaluated with the subsequent test HCVGR / Hepatitis C Virus Genotype Resolution, Serum.

Cautions

An "Undetected" or "Indeterminate" hepatitis C virus (HCV) genotype result does not rule-out active HCV infection. Test results should be correlated with routine serologic and molecular-based testing, as well as clinical presentation. Specimens with indeterminate results will be automatically evaluated with the subsequent test HCVGR / Hepatitis C Virus Genotype Resolution, Serum.

Known cross-reactivity between the assay probes and various HCV genotypes limits the ability of this assay to identify multiple HCV genotypes present in a given specimen. Such cross-reactivity or the actual presence of multiple HCV genotypes in the same specimen may result in an "Indeterminate" or multiple/mixed genotype result.

Clinical Reference

1. Germer JJ, Mandrekar JN, Bendel JL, et al. Hepatitis C virus genotypes in clinical specimens tested at a national reference testing laboratory in the United States. J Clin Microbiol. 2011;49(8):3040-3043
2. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. Updated October 24, 2022. Accessed March 27, 2025. Available at www.hcvguidelines.org

Performance

Method Description

Sample Preparation:
The Abbott mSample Preparation System kit is used with the Abbott m2000sp, an automated sample preparation system using the magnetic microparticle processes to extract and purify viral nucleic acids from human serum specimens. An internal control is incorporated in the nucleic acid extraction and purification procedure for processing the assay controls and clinical specimens. After capture of nucleic acids onto magnetic microparticles, the microparticles are washed to remove unbound sample components. Then, the bound nucleic acids are eluted from the microparticles, and the eluates are transferred to a 96-well microtiter plate containing polymerase chain reaction (PCR) mastermix reagents for amplification and detection.

Amplification, Detection, and Genotyping:
The Abbott RealTime HCV Genotype II assay is used to amplify the 5' noncoding (5' NC), nonstructural 5b (NS5b), and core regions of the hepatitis C virus (HCV) genome, with several PCR primer sets that are optimized to amplify all HCV isolates. An internal control primer set is included to amplify a portion of the hydroxypyruvate reductase gene of the pumpkin plant, *Cucurbita pepo*. The assays positive control is an armored RNA particle diluted in negative human plasma.

During the amplification reaction, complementary DNA (cDNA) sequences are generated from the target RNA sequences by the reverse transcriptase activity of the thermostable rTth DNA polymerase. First, the HCV and internal control reverse primers anneal to their respective target sequences and are extended during a prolonged incubation period. After a denaturation step, in which the temperature of the reaction is raised above the melting point of the double-stranded cDNA:RNA product, a second primer anneals to the cDNA strand and is extended by the DNA polymerase activity of the rTth enzyme to create a double-stranded DNA product. During each round of thermal cycling, amplification products dissociate to single strands at a high temperature, allowing primer annealing and extension as the temperature is lowered. Exponential amplification of the product is achieved through repeated cycling between high and low temperatures, resulting in a billion-fold or greater amplification of target sequences. Fluorescent probes specific for HCV genotypes 1 to 5 and subtypes 1a and 1b anneal to the amplified sequence products in 4 separate reaction wells for each specimen.(Package insert: RealTime HCV Genotype II. Abbott Molecular Inc; R1, 06/2013)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

1 to 6 days

Specimen Retention Time

2 months

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

87902

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HCVG	HCV Genotype, S	32286-7

Result ID	Test Result Name	Result LOINC® Value
81618	HCV Genotype, S	32286-7