MAYO CLINIC LABORATORIES

# Test Definition: CRHEP

Chronic Viral Hepatitis (Unknown Type), Serum

## Overview

### Useful For

Diagnosis and evaluation of patients with symptoms of hepatitis lasting more than 6 months

Distinguishing between chronic hepatitis B and C

### Profile Information

| Test Id | Reporting Name | Available Separately | Always Performed |
|---|---|---|---|
| HBC | HBc Total Ab, S | Yes | Yes |
| HBAB | HBs Antibody, S | Yes | Yes |
| HBAG | HBs Antigen, S | Yes | Yes |
| HCVDX | HCV Ab w/Reflex to HCV PCR, S | Yes | Yes |

### Reflex Tests

| Test Id | Reporting Name | Available Separately | Always Performed |
|---|---|---|---|
| HBGNT | HBs Antigen Confirmation, S | No | No |
| HCVQN | HCV RNA Detect/Quant, S | Yes | No |

### Testing Algorithm

If hepatitis C virus (HCV) antibody is reactive, then HCV RNA detection and quantification by real-time reverse transcription polymerase chain reaction will be performed at an additional charge.

If hepatitis B virus surface antigen (HBsAg) is reactive, then confirmation will be performed at an additional charge.

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

### Special Instructions

- Viral Hepatitis Serologic Profiles
- Hepatitis B: Testing Algorithm for Screening, Diagnosis, and Management
- Hepatitis C: Testing Algorithm for Screening and Diagnosis
- Chronic Hepatitis C Treatment and Monitoring Algorithm: Direct Antiviral Agent (DAA) Combination

### Method Name

Electrochemiluminescence Immunoassay (ECLIA)

### NY State Available

No

## Specimen

### Specimen Type

Serum SST

### Necessary Information

**Date of collection is required.**

### Specimen Required

**Patient Preparation:** For 24 hours before specimen collection, patient **should not** take multivitamins or dietary supplements (eg, hair, skin, and nail supplements) containing biotin (vitamin B7).
**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:** 2.5 mL
**Collection Instructions:**
1. Centrifuge blood collection tube per manufacturer's instructions (eg, centrifuge and aliquot within 2 hours of collection for BD Vacutainer tubes).
2. Aliquot serum into plastic vial.

### Forms

If not ordering electronically, complete, print, and send 1 of the following:
-Gastroenterology and Hepatology Test Request (T728)
-Infectious Disease Serology Test Request (T916)

### Specimen Minimum Volume

1.8 mL

### Reject Due To

| | |
|---|---|
| Gross hemolysis | Reject |
| Gross lipemia | Reject |
| Gross icterus | Reject |
| Heat-inactivated specimen | Reject |

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Serum SST | Frozen (preferred) | 84 days | |
| | Refrigerated | 6 days | |

## Clinical & Interpretive

### Clinical Information

Hepatitis B:
Hepatitis B virus (HBV) is a DNA virus that is endemic throughout the world. The infection is spread primarily through percutaneous contact with infected blood products (eg, blood transfusion, sharing of needles among injection drug users). The virus is found in virtually every type of human body fluid and is known to be spread through oral and genital contact. HBV can be transmitted from mother to child during delivery through contact with blood and vaginal secretions; it is not commonly transmitted transplacentally.

After a course of acute illness, HBV persists in approximately 10% of patients. Some of these carriers are asymptomatic while others develop chronic liver disease, including cirrhosis and hepatocellular carcinoma.

Individuals who have recovered from acute hepatitis B (defined as being negative for hepatitis B virus surface [HBs] antigen positive for hepatitis B virus core [HBc] total antibodies, negative or positive for HBs antibody) are lower risk (up to 20%) of HBV reactivation than those with inactive chronic hepatitis B during immunosuppressive therapy or organ transplantation.

For individuals born in regions of the world where HBV prevalence is moderate to high, universal HBV serologic screening before initiation of immunosuppressive therapy is recommended. In the absence of systematic, risk-based testing, universal HBV serologic screening is an option to reduce the risk of missing persons with HBV infection prior to initiation of immunosuppressive treatment.

Hepatitis C:
Hepatitis C virus (HCV) is an RNA virus recognized as the cause of most cases of posttransfusion hepatitis and is a significant cause of morbidity and mortality worldwide. HCV is transmitted through contaminated blood or blood products or close, personal contact. HCV shows a high rate of progression (~75%) to chronic disease. In the United States, HCV infection is quite common, with an estimated 3.5 to 4 million chronic HCV carriers. Cirrhosis and hepatocellular carcinoma are sequelae of chronic HCV.

Laboratory testing for HCV infection usually begins by screening for the presence of HCV-specific antibodies in serum, using an US Food and Drug Administration-approved screening test. Specimens that are repeatedly reactive by screening tests should be confirmed with HCV tests with higher specificity, such as direct detection of HCV RNA by reverse transcription polymerase chain reaction or HCV-specific antibody confirmatory tests.

HCV antibodies are usually not detectable during the first 2 months following infection, but they are usually detectable by the late convalescent stage (>6 months after onset) of infection. These antibodies do not neutralize the virus and they do not provide immunity against this viral infection.

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

-Hepatitis B: Testing Algorithm for Screening, Diagnosis, and Management
-Hepatitis C: Testing Algorithm for Screening and Diagnosis

## Reference Values

HEPATITIS B SURFACE ANTIGEN:
Negative

HEPATITIS B SURFACE ANTIBODY, QUALITATIVE/QUANTITATIVE
Hepatitis B Surface Antibody
Unvaccinated: Negative
Vaccinated: Positive

HEPATITIS B SURFACE ANTIBODY, QUANTITATIVE
Unvaccinated: <8.5 mIU/mL
Vaccinated: > or =11.5 mIU/mL

HEPATITIS B CORE TOTAL ANTIBODIES:
Negative

HEPATITIS C ANTIBODY:
Negative

Interpretation depends on clinical setting. See Viral Hepatitis Serologic Profiles.

## Interpretation

Interpretation depends on clinical setting. See Viral Hepatitis Serologic Profiles

Chronic hepatitis B:
Hepatitis B surface antigen (HBsAg is the first serologic marker appearing in the serum 6 to 8 weeks following hepatitis B viral (HBV) infection. In acute cases, HBsAg usually disappears 1 to 2 months after the onset of symptoms. Persistence of HBsAg for more than 6 months indicates development of either a chronic carrier state or chronic HBV infection.

Hepatitis B virus core IgM and total antibodies (anti-HBc IgM and total) appear shortly after the onset of symptoms of HBV infection and soon after the appearance of HBsAg. The anti-HBc IgM usually falls to undetectable levels within 6 months and anti-HBc total remains detectable for many years.

Anti-HBs usually appears with the resolution of hepatitis B after the disappearance of HBsAg.

If HBsAg and anti-HBc total antibody are positive, testing for HBeAg, anti-HBe, HBV-DNA, and anti-HDV total is recommended.

Chronic hepatitis C:
HCV antibodies (anti-HCV) are almost always detectable by the late convalescent and chronic stage of infection.

Reactive anti-HCV results with cutoff index (COI) values less than or equal to 20.0 with this assay are not predictive of the true HCV antibody status. Additional testing is available to confirm HCV antibody status.

Reactive results with COI values of greater than 20.0 with this assay are highly predictive (95% or greater probability) of the true HCV antibody status, but additional testing is needed to differentiate between past (resolved) and chronic hepatitis C.

A negative screening test result does not exclude the possibility of exposure to or infection with HCV. Negative screening test results in individuals with prior exposure to HCV may be due to low antibody levels that are below the limit of detection of this assay or lack of reactivity to the HCV antigens used in this assay. Patients with acute or recent HCV infections (<2 months from time of exposure) may have false-negative HCV antibody results due to the time needed for seroconversion (average of 8 to 9 weeks). Testing for HCV RNA using HCVQN / Hepatitis C Virus (HCV) RNA Detection and Quantification by Real-Time Reverse Transcription-PCR, Serum is necessary for detection of HCV infection in such patients.

## Cautions

Positive hepatitis B surface antigen (HBsAg) test results should be reported by the attending physician to the State Department of Health as required by law in some states.

Consider administration of hepatitis B immune globulin (HBIG) and hepatitis B vaccine to HBsAg antibody negative individuals exposed to the HBsAg-positive patient's blood or body fluids.

A single negative HCV RNA test result together with a reactive HCV antibody screen result with a cutoff index value greater than 20.0 does not rule out the possibility of chronic HCV infection. Repeat testing for HCV RNA in 1 to 2 months is recommended in patient at risk for chronic hepatitis C.

Infants born to HCV-infected mothers may have false-reactive HCV antibody test results due to transplacental passage of maternal HCV IgG antibodies. HCV antibody testing is not recommended until at least 18 months of age in these infants.

Serum specimens from individuals taking biotin supplements at 20 mg or more per day may have false-positive anti-HBc and false-negative anti-HBs and anti-HCV test results due to interference of biotin with the assay. Such individuals should stop taking these biotin-containing dietary supplements for minimum 12 hours before blood collection for this test.

Assay performance characteristics have not been established for:
-Patients younger than 21 years, pregnant women, or in populations of immunocompromised or immunosuppressed patients for HBC
-Grossly icteric (total bilirubin level of >25 mg/dL)
-Grossly lipemic (intralipid level of >1000 mg/dL)
-Grossly hemolyzed (hemoglobin level of >500 mg/dL)
-Biotin >1200 ng/mL
-Cadaveric specimens
-Those that contain particulate matter

## Clinical Reference

1. LeFevre MLL. Screening for hepatitis B virus infection in nonpregnant adolescents and adults: US Preventive Services Task Force recommendation statement. Ann Intern Med. 2014;161(1):58-66. doi:10.7326/M14-1018
2. Jackson K, Locarnini S, Gish R. Diagnostics of hepatitis B virus: Standard of care and investigational. Clin Liver Dis.

2018;12(1):5-11. doi:10.1002/cld.729
3. Coffin CS, Zhou K, Terrault NA. New and old biomarkers for diagnosis and management of chronic hepatitis B virus infection. Gastroenterology. 2019;156(2):355-368.e3. doi:10.1053/j.gastro.2018.11.037
4. World Health Organization. Guidelines on hepatitis B and C testing. World Health Organization; 2017. Accessed October 8, 2024. Available at www.who.int/publications/i/item/9789241549981
5 Conners EE, Panagiotakopoulos L, Hofmeister MG, et al. Screening and Testing for Hepatitis B Virus Infection: CDC Recommendations - United States, 2023. MMWR Recomm Rep. 2023;72(1):1-25. Published 2023 Mar 10. doi:10.15585/mmwr.rr7201a1
6. American Association for the Study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA): HCV guidance: Recommendations for testing, managing, and treating hepatitis C. AASLD, IDSA; Updated December 19, 2023. Accessed October 8, 2024. Available at www.hcvguidelines.org/contents

## Performance

### Method Description

Hepatitis B surface antigen:
The Elecsys HBsAg (hepatitis B surface antigen) II assay is performed using an electrochemiluminescence immunoassay on the automated cobas e 801 immunochemistry analzyer. HBsAg present in the patient's sample reacts with two biotinylated monoclonal anti-HBs, and a mixture of monoclonal anti-HBs and polyclonal anti-HBsAg antibodies labeled with a ruthenium complex react to form a sandwich complex. After addition of streptavidin-coated microparticles, the complexes become bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode, and unbound substances are washed away. Voltage is applied to the electrode which induces chemiluminescent emissions that are measured by a photomultiplier. Test results for each patient's sample is determined by comparing the electrochemiluminescence signal generated from the reaction product to the cutoff index (COI) value set from reagent lot-specific assay calibrations.(Package insert: Elecsys HBsAG II. Roches Diagnostics; v3.0, 02/2022)

HBsAg confirmation:
The Elecsys HBsAg II Auto Confirm assay is performed using an electrochemiluminescence immunoassay on the automated cobas e 801 immunochemistry analyzer. This test is based on 2 parallel measurements. For the first measurement, the sample is treated with the control pretreatment reagent (PT2) prior to immunoreaction. This measurement serves as a reference. For the second measurement the sample is treated with the confirmatory pretreatment reagent (PT1) prior to immunoreaction. During incubation with confirmatory pretreatment, unlabeled polyclonal anti-HBsAg antibodies are bound to the sample HBsAg and thereby block the binding sites for the labeled antibodies used in the following immunoreaction. The confirmation result (%) is automatically assessed by determining the ratio of both measurements.

During testing, the auto-diluted sample is incubated with control pretreatment and confirmatory pretreatment, followed by formation of sandwich complexes of biotinylated monoclonal anti-HBsAg antibodies and a mixture of monoclonal anti-HBsAg antibody and polyclonal anti-HBsAg antibodies labeled with a ruthenium complex. After addition of streptavidin-coated microparticles, the complexes become bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture is then aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode, and unbound substances are then washed away. Voltage is applied to the

electrode which induces chemiluminescent emissions that are measured by a photomultiplier. Results are determined by comparing the electrochemiluminescence signal generated from the reaction product to the COI value set from reagent lot-specific assay calibration. The confirmation result (%) is calculated from the ratio of the COI obtained for the measurement with confirmatory pretreatment to the COI obtained for the measurement with control pretreatment.(Package insert: Elecsys HBsAg II Auto Confirm. Roche Diagnostics, v1.0, 12/2020)

Hepatitis B core total antibody:
The Elecsys Anti-HBc (hepatitis B core antibody) II assay is performed using an electrochemiluminescence immunoassay on the automated cobas e 801 analyzer. Hepatitis B viral core antibodies (anti-HBc) present in the patient's sample is pretreated first with a reducing reagent, and after the addition of hepatitis B virus core antigen (HBcAg), complexes are formed with anti-HBc in the sample. The remaining unbound sites on the HBcAg become occupied after addition of biotinylated antibodies and ruthenium complex-labeled antibodies specific for HBcAg, together with streptavidin-coated microparticles. The entire complex becomes bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture is then aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. After unbound substances are washed away, voltage is applied to the electrode which induces chemiluminescent emissions that are measured by a photomultiplier. Results are determined by comparing the electrochemiluminescence signal generated from the reaction product of the sample to the COI value set from assay reagent lot-specific assay calibration.(Package insert: Elecsys Anti-HBc II. Roche Diagnostics, v1.0; 04/2022)

Hepatitis C Virus Antibody:
The Elecsys Anti-HCV II assay will be performed on the fully automated cobas e 801 electrochemiluminescence immunoassay analyzer. During the first incubation, antibodies to hepatitis C virus (HCV) in the patient's sample, biotinylated HCV-specific antigens and a reagent containing HCV-specific antigens labeled with a ruthenium complex to form a sandwich complex. In the second incubation, after addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then washed away, and application of a voltage to the electrode then induces chemiluminescent emissions which are measured by a photomultiplier. Test result for each patient's sample is determined automatically by the assay-specific software program by comparing the electrochemiluminescence signal obtained from the sample with the COI value set from reagent lot-specific assay calibrations.(Package insert: Elecsys Anti-HCV II. Roche Diagnostics; v1.0, 03/2023)

### PDF Report
No

### Day(s) Performed
Monday through Sunday

### Report Available
Same day/1 to 2 days

### Specimen Retention Time
14 days

### Performing Laboratory Location
Mayo Clinic Jacksonville Clinical Lab

## 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

86704
86706
86803
87340
87341 (if appropriate)
87522 (if appropriate)

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| CRHEP | Chronic Viral Hepatitis Profile, S | 92889-5 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| HBC | HBc Total Ab, S | 13952-7 |
| HB_AB | HBs Antibody, S | 10900-9 |
| HBSQN | HBs Antibody, Quantitative, S | 5193-8 |
| H_BAG | HBs Antigen, S | 5196-1 |
| HCVA4 | HCV Ab, S | 40726-2 |