Department of Veterans Affairs **VHA DIRECTIVE 2009-063**
Veterans Health Administration
Washington, DC 20420 **November 25, 2009**

REFLEX CONFIRMATORY TESTING FOR CHRONIC HEPATITIS C VIRUS INFECTION

1. PURPOSE: This Veterans Health Administration (VHA) Directive describes VHA policies on reflex confirmatory testing for chronic hepatitis C virus (HCV) infection.

2. BACKGROUND

a. HCV infection is the most common bloodborne infection in the United States, with an estimated prevalence of over 4 million. It represents a major public health problem both nationally and within VHA because of its ability to cause chronic hepatitis with subsequent development of serious liver disease. Of individuals exposed to HCV as adults, 85 percent will develop chronic hepatitis; of these, 10-20 percent will develop hepatic cirrhosis, putting them at risk for liver failure. Another 1-5 percent will develop hepatocellular carcinoma annually (see subpar. 5d).

b. Laboratory testing for HCV can determine serostatus (evidence of past infection), viral status (evidence of ongoing infection), or both. For clinical decision-making purposes, serologic testing is used to determine serostatus, and ribonucleic acid (RNA) testing is used to identify those patients with chronic infection. In individuals with a positive serologic screening test for HCV infection, the Centers for Disease Control and Prevention recommend confirmatory (also called supplementary) testing to confirm the diagnosis of HCV infection and determine viral status (see subpar. 5b). A 2003 survey of testing and reporting practices at VHA laboratories revealed that while all VHA laboratories surveyed perform confirmatory testing (including RNA tests), the majority did so only when specifically requested (see subpar. 5a). Many times this process results in RNA testing either not being performed on the sample in the laboratory service's possession or results in additional visits of the Veteran for phlebotomy.

c. A solution to streamlining the process of diagnosing chronic HCV infection is to perform reflex RNA testing on a routine basis (i.e., occurring automatically if the initial serologic screening test is positive). The process generally requires that a portion of the initial specimen be stored under suitable conditions, or two different types of specimens be collected, eliminating the need to separately order RNA testing, recall the patient, and obtain a new specimen. VHA research has shown reflex testing to be a cost effective strategy (see subpar. 5c). The standard reflex testing algorithm is shown in Appendix A, and the standard reporting terminology is shown in Appendix B.

d. **Definitions**

(1) **Chronic Hepatitis C.** Chronic Hepatitis C is an active infection with hepatitis C for more than 6 months.

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(2) **Confirmatory HCV Testing.** Confirmatory (also referred to as supplementary) HCV testing is a more specific test (e.g., recombinant immunoblot (RIBA) or RNA) used to verify a positive anti-HCV screening test result.

(3) **HCV RNA Testing**. HCV RNA testing is an assay for the presence of HCV RNA in blood; a positive result confirms prior exposure and the presence of chronic hepatitis C (except in those individuals with acute HCV infection).

(4) **Recombinant Immunoblot Assay (RIBA).** RIBA is more specific serologic testing used for confirmatory testing; a positive result confirms prior exposure but does not confirm or exclude chronic hepatitis C infection.

(5) **Reflex Confirmatory Testing.** Reflex confirmatory testing is additional testing automatically performed on an aliquot of the original specimen in response to a positive screening result.

(6) **Serologic Screening Tests**. Serologic screening tests are serologic immunoassays for detection of anti-HCV antibodies; initial testing methods for diagnosis of HCV infection.

(7) **Serostatus**. Serostatus indicates the presence or absence of anti-HCV antibodies.

(8) **Viral Status.** Viral status indicates the presence or absence of HCV RNA.

3. POLICY: It is VHA policy that reflex confirmatory testing incorporating RNA testing be performed on all specimens that are reactive by initial serologic screening for HCV antibodies.

4. ACTION

a. **Clinical Public Health Program Office, Office of Public Health and Environmental Hazards (13).** Working closely with Diagnostic Services within the Office of Patient Care Services, the Clinical Public Health Program Office is responsible for providing scientific and technical guidance related to the timely and accurate diagnosis of HCV infection. The Clinical Public Health Program Office also produces technical support materials, including examples of existing, successful programs and support to facilitate timely diagnosis of HCV infection.

b. **Facility Director.** The facility Director is responsible for:

(1) Ensuring that reflex confirmatory HCV testing is implemented, as a locally performed test, a fee basis test, or as a test performed by another Department of Veterans Affairs (VA) with established HCV RNA testing capability, and ensuring equal access to reflex confirmatory HCV testing at all points of care at the local health care system where lab testing is provided.

(2) Timely notification of the Veteran tested with final test results and timely referrals for care.

c. **Director, Pathology and Laboratory Medicine Service (P&LMS).** The Director, P&LMS at each facility is responsible for:

(1) Selecting appropriate methodologies for implementation of reflex confirmatory HCV testing, according to the standard HCV testing algorithm in Appendix A.

(2) Creating new laboratory polices and procedures or amendment of existing laboratory policies and procedures to provide reflex testing on positive HCV EIA results to allow timely diagnosis of current viral status.

(3) Reporting results to clinicians using the Computerized Patient Record System (CPRS) according to the standard terminology in Appendix B. ***NOTE:*** *Results for HCV EIA and RNA (and RIBA if performed) should be reported by displaying the entire table in Appendix B as a Word document linked to the CPRS Tools tab, or on a linked intranet site. A comment should be inserted in the interpretation field in File 60 for each assay stating "Refer to HCV test interpretation table" followed by directions on how to access the table within CPRS.*

5. REFERENCES

a. Alter MJ, Kuhnert WL, Finelli WL. Guidelines for laboratory testing and result reporting of antibody to hepatitis C virus. Morbidity and Mortality Weekly Report (MMWR) 2003 (RR-3); 52:1-15.

b. CDC. Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. MMWR 1998; 47 (RR-19):1–33.

c. Chapko MK, Sloan KL, Davison JW, *et al.* Cost effectiveness of testing strategies for chronic hepatitis C. American Journal of Gastroenterology. 2005; 100:607-15.

d. National Institutes of Health. NIH Consensus Statement on Management of Hepatitis C. NIH Consens State Sci Statements 2002; 19:1-46.

6. FOLLOW-UP RESPONSIBILITY: The Chief Consultant of the Public Health Strategic Healthcare Group (13B) is responsible for the contents of this Directive. Questions may be referred to 202-461-1040, or to publichealth@va.gov.

7. RECISSIONS: None. This VHA Directive expires November 30, 2014.

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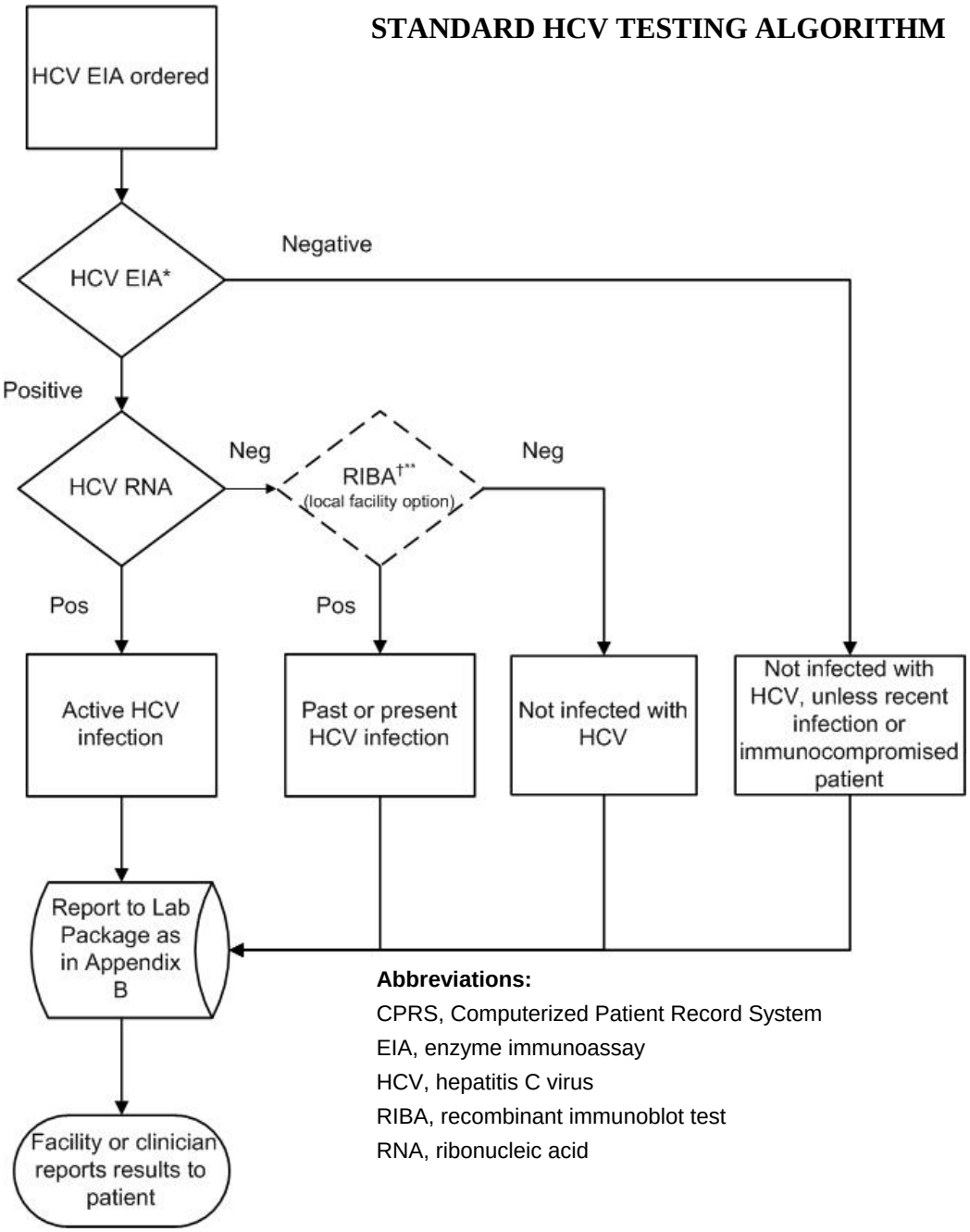
ATTACHMENT A

STANDARD HCV TESTING ALGORITHM



Abbreviations:

CPRS, Computerized Patient Record System
EIA, enzyme immunoassay
HCV, hepatitis C virus
RIBA, recombinant immunoblot test
RNA, ribonucleic acid

*EIA may be negative in individuals with *acute* HCV infection. In patients with a negative EIA and no RNA result, clinicians should be advised to order an HCV RNA assay if other evidence indicates acute infection. Similarly, in immunocompromised individuals with chronic HCV infection, EIA may be negative because of impaired immunoglobulin synthesis; if other evidence indicates chronic HCV infection (e.g., elevated serum alanine aminotransferase concentrations, clinicians should be advised to order an HCV RNA assay.

† Facilities may choose to make RIBA available as a local facility option. If RNA is negative, performance of RIBA is strongly encouraged to rule out false positive anti-HCV results. In patients with low anti-HCV s/co ratio (as defined by CDC recommendations at http://www.cdc.gov/hepatitis/HCV/LabTesting.htm#section1), performance of RIBA as initial confirmatory test may be substituted, with RNA performed if RIBA indeterminate or positive.

**If RIBA indeterminate, report that antibody and infection status cannot be determined; repeat anti-HCV or RNA in 1 month.

ATTACHMENT B

STANDARD HCV REPORTING TERMINOLOGY

Results for each assay should be reported individually to clinicians via CPRS in a standardized fashion as shown in the table below. Interpretation and comments should be reported after individual assay result by displaying a link to the following table in the lab test interpretation field.

EIA result	RNA result	RIBA result	Interpretation	Comments
Negative	Not performed	Not performed	Anti-HCV-negative	Unlikely to be infected with HCV; consider ordering HCV RNA if patient is immunocom-promised or acute infection is suspected
Negative	Negative	Not performed	Anti-HCV-negative, HCV RNA-negative	Not infected with HCV
Negative	Positive	Not performed	Anti-HCV-negative, HCV RNA-positive	Acute HCV infection, or chronic infection in an immunocompromised patient
Negative	Positive	Negative	Anti-HCV-negative, HCV RNA-positive	Acute HCV infection, or chronic HCV infection in an immunocompromised patient
Positive	Positive	Not performed	Anti-HCV-positive, HCV RNA-positive	Active HCV infection
Positive	Negative	Not performed	Anti-HCV-positive, HCV RNA-negative	Active infection unlikely; however, a single negative RNA result does not rule out active infection
Positive	Negative	Positive	Anti-HCV-positive, HCV-RNA negative	Past or present HCV infection; however, a single negative RNA result does not rule out active infection
Positive	Negative	Negative	Anti-HCV-negative, HCV RNA-negative	Not infected with HCV
Positive	Negative	Indeterminate	Anti-HCV indeterminate	HCV antibody and infection status cannot be determined; repeat anti-HCV or RNA testing in >1 month