

Guideline for the Investigation of Reports of Hepatitis C Virus Infection from Health Care Providers and Laboratories

Purpose: This document provides direction for public health follow up to ensure uniform investigation and classification of hepatitis C virus (HCV) case reports across the State. The process described is designed to ensure thorough investigation of acute hepatitis C infection while allowing prompt classification of chronic cases with a minimum investment of time by health care providers and health department personnel. Although labeled as “Draft,” this guideline should be used for investigation of HCV case reports beginning January 1, 2002.

Introduction: Classification of cases as acute or chronic infection is based on clinical features, health care provider judgement, and laboratory test results. *Classification is for surveillance purposes only and should not be used for clinical decision making.* Acute cases are classified using the Centers for Disease Control and Prevention (CDC) case definition with modifications recommended by the Council of State and Territorial Epidemiologists (CSTE). Although 60-70% of persons with acute hepatitis C infection have no discernible symptoms, only symptomatic cases are included in the CDC surveillance definition of acute cases. Only acute cases are reported to the CDC. Maryland case definitions have been written for chronic hepatitis, including both *confirmed* and *probable* STATUS codes for the Maryland Electronic Reporting and Surveillance System (MERSS). Case reports that cannot be categorized as acute or chronic will be placed into several “Lab Only” categories where the MERSS STATUS code is dependent on the type of laboratory test that was done.

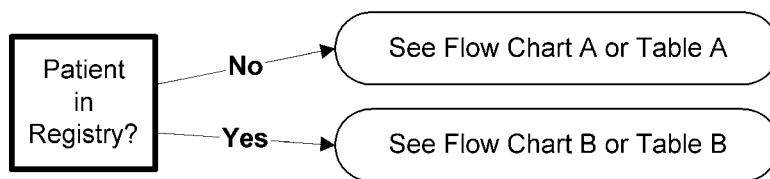
This document uses both tables and flow charts to guide the user in a stepwise fashion through the processes required for case investigation and classification. The tables and flow charts are redundant descriptions of the processes. The user can choose whichever format (tables or flow charts) better fits their working habits and thought processes. Two prominent features of this guide are dependence on the MERSS Hepatitis Registry for knowledge of any prior case classification, and on the alanine aminotransferase (ALT) test result.

Case Investigation - Cases Reported by Health Care Providers (HCPs): All cases reported as acute hepatitis C by a health care provider should be investigated to determine if they meet the criteria defined in the CDC case definition for acute HCV infection. If the HCP merely designates “hepatitis C infection,” then the investigation process is the same as for laboratory cases as described below. For cases that seem likely to meet the CDC criteria, the CDC Viral Hepatitis Case Report (surveillance form) and the new Maryland HCV Supplemental Case Investigation Form should be completed through consultation with the HCP and, if necessary, the patient. You may substitute the Maryland Acute Hepatitis Case Report Form on the EDCP website for the CDC Case Report Form and the Maryland Supplemental Form (i.e., the one form replaces two forms). It is important to collect the case defining clinical and laboratory information as well as the risk factor information for surveillance purposes.

Case Investigation - Cases Reported by Laboratories: The tables and/or flow charts included in this guide should step you through the investigation process. Table A corresponds to Flow Chart A, and Table B to Flow Chart B. You may use either the tables or flow charts (or both), depending on your preference.

Guideline for the Investigation of Reports of Hepatitis C Virus Infection from Health Care Providers and Laboratories

- 1) Begin by ascertaining the patient's correct address and basic demographic information. The "HCV – Initial Case Investigation Form" can be used to collect that information by mailing to the HCP or contacting them by telephone. It should be customized for your health department. This initial contact with the HCP should be used to determine if an ALT test was done and its result.
- 2) Check the MERSS Hepatitis Registry (accessed from the MERSS Main Menu by clicking the "Hepatitis Registry" button) and locate any prior reports on this patient, and if any, how the patient was classified on the earlier report(s).
- 3) Follow the steps outlined in the appropriate table or flow chart.



If using the tables, follow the actions specified according to the case's ALT level (Table A), or their prior Hepatitis Registry entry (Table B). If using the flow charts, begin in the upper left hand corner and go with the flow. Square or rectangular boxes designate decision points and capsule-like boxes (rounded ends) contain the action steps. For cases not found in the registry, you should only need to contact the HCP for follow up (beyond determining demographics and ALT level) if the ALT exceeds seven times the upper limit of normal (ULN). These are the suspect acute cases. The CDC Viral Hepatitis Case Report (surveillance form) and the new Maryland HCV Supplemental Case Investigation Form should be completed through consultation with the HCP and, if necessary, the patient. For cases where the ALT is less than seven times the ULN, entering the cases in MERSS should complete the surveillance process. The table or flow chart will indicate the appropriate MERSS DISEASE and STATUS codes. On the flow charts, the capsule-like boxes with no paths leading out of them are end points. For most cases already in the registry, you should be able to complete your investigation based on the current report and the prior case classification in the registry. You may want to contact the HCP for additional information.

- 4) Determine the appropriate patient follow up using a local health department (LHD) protocol. Until a Maryland Hepatitis C Control Plan is finalized, funded, and put into use, you should determine how you can best follow up with patients in different disease stages according to locally available resources of time, personnel, and funding.
- 5) Complete the paper work. Please send a copy of your completed CDC Hepatitis Case Report and the Maryland HCV Supplemental Case Investigation Form to the MERSS Coordinator in the Division of Communicable Disease Surveillance for all cases classified as **acute HCV infection**. Do NOT send report forms to DHMH for non-acute disease.

Case Definitions: The CDC and Maryland case definitions are listed below, and an attached table, "Available MERSS *DISEASE* and *STATUS* Code Combinations," should be a guide to their use. An additional guide is a flow chart, "Flow Chart – Acute HCV (Case Definition)," designed to help you easily determine if a case meets the CDC surveillance definition for acute disease.

Guideline for the Investigation of Reports of Hepatitis C Virus Infection from Health Care Providers and Laboratories

Surveillance Case Definitions* for Hepatitis C in Maryland

December 3, 2001

Acute

This is the CDC case definition with the CSTE change to the ALT level.

Case STATUS: Confirmed

- 1) An acute illness with discrete onset on symptoms (evidenced in MERSS by an ONSET date)
- 2) Jaundice
- 3) Serum ALT > 7 times the upper limit of normal (ULN)
- 4) IgM anti-HAV negative
- 5) IgM anti-HBc Negative (if done) OR HBsAg Negative
- 6) Anti-HCV positive (repeat reactive) by EIA, verified by an additional more specific assay (e.g. RIBA for anti-HCV or RT-PCR for HCV RNA) or by an average EIA signal to cutoff ratio of ≥ 3.8 ,
OR
Anti-HCV positive by RIBA alone
OR
HCV RNA positive

Chronic

No CDC or CSTE case definitions exist – these are Maryland definitions.

Case Status: Confirmed

HCV RNA Positive on two specimens taken at an interval greater than 6-months

OR

ALT greater than ULN on two specimens taken at an interval greater than 6-months AND anti-HCV Positive (by EIA alone or confirmed by a secondary test)

OR

HCV RNA Positive or ALT > ULN more than 6 months after (Lab Date of) acute HCV infection

Case Status: Probable

HCV RNA Positive OR anti-HCV Positive (by EIA alone or with a confirmatory test)

AND

ULN < ALT \leq 7 times ULN (or ALT > 7 times ULN but fails to meet CDC case definition for acute HCV)

Lab Only

No CDC or CSTE case definitions exist – these are Maryland definitions.

The **Lab Only** code is used for any report that does not result in an acute or chronic classification of the case. There may be insufficient data to classify the case as either acute or chronic, or it could be that the available information is not adequate to advance the patient's current classification. A patient already classified as acute should not be re-entered as acute, therefore a subsequent report might be classified as chronic or lab only. A patient already classified as chronic with a STATUS of *Probable* might be classified on a subsequent report as chronic with a STATUS code of *Confirmed*, but otherwise a subsequent report would be entered as Lab Only.

The STATUS code of *Confirmed* should be used when the test reported is a confirmatory test (e.g., RIBA or RNA), but a STATUS of *Probable* should be used when the reported test is a screening test (e.g., EIA, EIA 2nd generation, etc.).

* These case definitions are only for classification of cases for surveillance purposes. They should not be used in making clinical decisions.

Guideline for the Investigation of Reports of Hepatitis C Virus Infection from Health Care Providers and Laboratories

Available MERSS *DISEASE* and *STATUS* Code Combinations for Case Reports of Hepatitis C

DISEASE Code	STATUS Codes	Comments
Hepatitis C Acute	Confirmed	Must meet CDC case definition with ALT level greater than 7 times the upper limit of normal (or greater than 500).
	X-Probable	Not a valid STATUS for acute disease
	Suspect	This is a temporary code for initial categorization of health care provider reported acute disease or partially investigated lab reports where the ALT level is more than 7 times the upper limit of normal (or greater than 500). This should be resolved by investigation to acute DISEASE with STATUS confirmed, or a change of the DISEASE code to chronic HCV or lab only.
Hepatitis C Chronic	Confirmed	Will require paired HCV-RNA or paired ALT above the upper limit of normal (not 7x above) on two tests taken at an interval greater than 6months.
	Probable	See the guide tables and flow charts. This is used for cases without the paired tests described above.
	X-Suspect	Not a valid STATUS for chronic disease
Hepatitis C Lab Only	Confirmed*	Confirmed STATUS designates that the lab test was a “confirmatory” test (RIBA or RNA), rather than a “screening” test (EIA, EIA 2 nd generation).
	Probable	Probable STATUS designates that the lab test was a “screening” test (EIA, EIA 2 nd generation), rather than a “confirmatory” test (RIBA or RNA).
	X-Suspect	Not a valid STATUS for lab only DISEASE.

* If a “confirmed” STATUS seems incongruent when the DISEASE is “lab only,” remember that a STATUS code is always paired with a DISEASE code, and in this case the STATUS code refers to the nature of the lab test, not to whether or not the patient has acute or chronic hepatitis C infection.

Guideline for the Investigation of Reports of Hepatitis C Virus Infection from Health Care Providers and Laboratories

Glossary of Terms

> The algebraic comparison symbol for “greater than.” This is used in this guideline for comparison of lab values (e.g., ALT > Upper Limit of Normal, for an ALT value *greater than* the ULN) or time (e.g., > 6 months, for *more than* 6 months).

ALT Alanine aminotransferase (sometimes referred to as SGPT). A liver enzyme that is often elevated in acute and chronic hepatitis.

AST Aspartate aminotransferase (sometimes referred to as SGOT). A liver enzyme that is often elevated in acute and chronic hepatitis.

Investigated A term used with the Lab Only DISEASE code to indicate that the MERSS Hepatitis Registry was accessed to determine the categorization of any prior reports, and that an attempt was made to find out any clinical or laboratory information necessary to assess the case according to the case definitions.

Lab Only A “lab only” case report is one that does not result in an acute or chronic classification of the case.

SGOT See AST.

SGPT See ALT.

ULN Upper limit of normal. The upper limit of the normal range for a laboratory test. Serum ALT and AST levels are usually reported to the health care provider along with the normal range for the test, or are also designated as within normal limits or exceeding normal limits.

“> ULN” means a value greater than the upper limit of normal; an elevated ALT level might be written as “ALT > ULN”.

“> 7xULN” means a value more than seven times the upper limit of normal such as “ALT > 7xULN”

“ULN < ALT < 7xULN” means an ALT value that is greater than the upper limit of normal (ULN) but less than seven times the ULN.

Uninvestigated A term used with the Lab Only DISEASE code to mean an HCV lab report that is entered into MERSS without accessing the MERSS Hepatitis Registry to determine the categorization of any prior reports, and without an attempt to investigate beyond determining the patient's basic demographic information.

Guideline for the Investigation of Reports of Hepatitis C Virus Infection from Health Care Providers and Laboratories

Table **A** Laboratory Report of HCV – Antibody or RNA – *Without* Prior MERSS Hepatitis C Registry Entry

Report	Action(s)
Reported Without Alanine Aminotransferase (ALT) Level	<ul style="list-style-type: none"> ◀ Determine the ALT result. If it is unknown, complete the HCV Initial Case Investigation Form by calling or mailing to the Health Care Provider (HCP) <ul style="list-style-type: none"> • With a known ALT result, proceed as below for “Reported With ALT Level.” • If ALT cannot be determined, then Enter into MERSS; DISEASE = HCV Lab Only – Investigated STATUS = <i>Confirmed</i> if a confirmatory test (RIBA, RNA) STATUS = <i>Probable</i> if a screening test (EIA, EIA second generation, etc.)
Reported With Alanine Aminotransferase (ALT) Level	<ul style="list-style-type: none"> ✓ ALT is within normal limits <ul style="list-style-type: none"> ◀ Enter into MERSS; DISEASE = HCV Lab Only - Investigated STATUS = <i>Confirmed</i> if a confirmatory test (RIBA, RNA) STATUS = <i>Probable</i> if a screening test (EIA, EIA second generation, etc.) ◀ Determine appropriate patient follow up using LHD protocol.
	<ul style="list-style-type: none"> ✓ Upper Limit of Normal (ULN) < ALT ≤ 7 times ULN <ul style="list-style-type: none"> ◀ Enter into MERSS; DISEASE = HCV Chronic, STATUS = <i>Probable</i> ◀ Determine appropriate patient follow up using LHD protocol.
	<ul style="list-style-type: none"> ✓ ALT > 7 times ULN <ul style="list-style-type: none"> ◀ Enter into MERSS; DISEASE = HCV Acute, STATUS = <i>Suspect</i> ◀ Send CDC Viral Hepatitis Case Record Form and Maryland HCV Supplemental Case Investigation Form to HCP ◀ Use information from the Viral Hepatitis Case Record Form to determine if the patient meets the CDC case definition for acute HCV infection. <ul style="list-style-type: none"> • If YES: Upgrade MERSS STATUS to Confirmed (DISEASE = HCV Acute) • If NO: Recode DISEASE in MERSS to HCV Chronic with STATUS = <i>Probable</i> ◀ Determine appropriate patient follow up using LHD protocol.

Guideline for the Investigation of Reports of Hepatitis C Virus Infection from Health Care Providers and Laboratories

Table **B** Laboratory Report of HCV – Antibody or RNA – *With* Prior MERSS Hepatitis C Registry Entry

Prior Registry Entry	Action(s)
Acute (only)	<p>Determine if this has become a chronic infection (i.e., six months after acute infection [lab date] the HCV RNA is positive or ALT > ULN)</p> <ul style="list-style-type: none"> ✓ If YES: ◀ Re-enter into MERSS as DISEASE = HCV Chronic with STATUS = <i>Confirmed</i> ▶ Determine appropriate patient follow up using LHD protocol. ✓ If NO: ◀ Re-enter into MERSS as DISEASE = HCV Lab Only – Investigated STATUS = <i>Confirmed</i> if a confirmatory test (RIBA, RNA) STATUS = <i>Probable</i> if a screening test (EIA, EIA second generation, etc.)
Chronic STATUS <i>Confirmed</i>	<ul style="list-style-type: none"> ◀ Re-enter into MERSS as DISEASE = HCV Lab Only - Investigated if resources permit. (Otherwise, just add to the patient’s [paper] record.) STATUS = <i>Confirmed</i> if a confirmatory test (RIBA, RNA) STATUS = <i>Probable</i> if a screening test (EIA, EIA second generation, etc.) ◀ Determine appropriate patient follow up using LHD protocol.
Chronic STATUS <i>Probable</i> (By definition this patient has prior positive RNA or HCV antibody, AND ALT > ULN.)	<p>Determine if this has become a chronic infection with STATUS <i>Confirmed</i> (i.e., HCV RNA Positive on two specimens taken at an interval greater than 6 months OR ALT greater than ULN on two specimens taken at an interval greater than 6 months)</p> <ul style="list-style-type: none"> ✓ If YES: ◀ Re-enter into MERSS as DISEASE = HCV Chronic with STATUS = <i>Confirmed</i> ▶ Determine appropriate patient follow up using LHD protocol. ✓ If NO: ◀ Re-enter into MERSS as DISEASE = HCV Lab Only – Investigated STATUS = <i>Confirmed</i> if a confirmatory test (RIBA, RNA) STATUS = <i>Probable</i> if a screening test (EIA, EIA second generation, etc.)
Lab Only	Proceed as per “No Prior Hepatitis C Registry Entry” - Table A - but use the prior lab work as an aid to classification.