INTERPRETATION INFORMATION SHEET

Hepatitis Serology

HBsAg ChLIA: This chemiluminescent assay (ChLIA) detects the presence of Hepatitis B surface antigen (HBsAg). Specimens found repeatedly reactive must be confirmed by a licensed, neutralizing ChLIA antibody test. Only those specimens that can be neutralized by the confirmatory test procedure indicate infection with the Hepatitis B virus or recent vaccination against Hepatitis B. A specimen is considered nonreactive (negative) with a value less than the cutoff and neutralization would not be applicable.

HBsAg EIA: This enzyme immunoassay (EIA) detects the presence of Hepatitis B surface antigen (HBsAg). Specimens found repeatedly reactive must be confirmed by a licensed, neutralizing EIA test. Only those specimens that can be neutralized by the confirmatory test procedure indicate infection with the Hepatitis B virus or recent vaccination against Hepatitis B. A specimen is considered nonreactive (negative) with a value less than the cutoff and neutralization would not be applicable.

HBsAg Confirmatory Neutralization (ChLIA or EIA): These assays use the principle of specific antibody neutralization to confirm the presence of HBsAg in specimens found repeatedly reactive for HBsAg. A specimen is confirmed positive if the reactivity of the neutralized specimen is reduced by at least 50% when compared to the reactivity of the non-neutralized control. A specimen is not confirmed (non-confirmed or non-neutralizable) if the reactivity of the neutralized specimen is NOT reduced by at least 50% when compared to the reactivity of the non-neutralized control. It is acceptable to perform an applicable NAT HBV discriminatory test in place of the HBsAg neutralization assay for confirmation of a specimen that is reactive by both HBsAg and a licensed NAT screening test (refer to Hepatitis NAT information below).

Anti-HBs EIA: This enzyme immunoassay (EIA) detects the presence of antibody to Hepatitis B surface antigen (HBsAg). The detection of anti-HBs is indicative of a prior immunologic exposure to the hepatitis B virus or vaccine. An individual with positive results for anti-HBs is immune to hepatitis B infection. A borderline result indicates other clinical information or subsequent testing is required to determine an individual's immune status relative to Hepatitis B infection. A negative result may indicate that an individual is not immune to infection with Hepatitis B. However, negative or nonreactive results can also be seen in individuals remotely immunized with Hepatitis B vaccination when antibody titers have dropped below the limit of detection. Correlation with the individual's vaccination history, Hepatitis B related test results and current CDC guidelines is recommended.

Anti-HBc ChLIA: This chemiluminescent assay (ChLIA) detects the presence of total antibody (IgM and/or IgG) to Hepatitis B core antigen (HBc) and is used as an aid in reducing the incidence of Hepatitis B transmission by transfusion. Recent studies have shown that a very small proportion of donors reactive for anti-HBc with no other HBV markers (<1%) may also have very low levels of HBV DNA. Additional individual discriminatory HBV NAT results may be useful for donor counseling despite the lack of information about potential infectivity.

Anti-HBc EIA: This enzyme immunoassay (EIA) detects the presence of both IgM and IgG antibody to Hepatitis B core antigen (HBc) and is indicated for screening of blood and blood products intended for transfusion and as an aid in the diagnosis of ongoing or previous Hepatitis B viral infection. Recent studies have shown that a very small proportion of donors reactive for anti-HBc with no other HBV markers (<1%) may also have very low levels of HBV DNA. Additional individual discriminatory HBV NAT results may be useful for donor counseling despite the lack of information about potential infectivity.

Anti-HCV 3.0 ChLIA: This chemiluminescent assay (ChLIA) utilizes recombinant antigens to detect antibody to Hepatitis C virus (HCV). Presence of this antibody indicates that the individual may have been infected with HCV, may harbor infectious HCV and may be capable of transmitting HCV infection. Supplemental tests, such as an alternate licensed screening assay, may assist in more specific determination of antibody status. Use of an appropriate HCV nucleic acid assay (HCV-NAT) may provide more definite indication of current viremia and may substantiate infectivity. The anti-HCV 3.0 version test includes recombinant antigens covering the core, NS3, NS4 and NS5 regions of the HCV genome.

Anti-HCV 3.0 EIA: This enzyme immunoassay utilizes recombinant antigens to detect antibody to Hepatitis C virus (HCV). Presence of this antibody indicates past or present HCV infection, or possibly a carrier state, but does not substantiate infectivity nor immunity. Supplemental tests, such as an alternate licensed screening assay, may assist in more specific determination of antibody status. Use of an appropriate HCV nucleic acid assay (HCV-NAT) may provide more definite indication of current viremia and may substantiate infectivity. The anti-HCV 3.0 version test includes recombinant antigens covering the core, NS3, NS4 and NS5 regions of the HCV genome.

Limitations: It is recognized that presently available methods for hepatitis detection are not sensitive enough to detect all potentially infectious units of blood or all possible cases of hepatitis. A nonreactive result does not exclude infection. It is also recognized that biological false positive results may be obtained with any serologic test.

INTERPRETATION INFORMATION SHEET

Hepatitis C Virus and Hepatitis B Virus Nucleic Acid Testing (NAT)

Procleix HIV/HCV/HBV Assay: This assay utilizes transcription mediated amplification of nucleic acid followed by the use of specific labeled probes for detection of HIV-1, HIV-2 and HCV RNA and HBV DNA. The assay generates a chemiluminescent signal which is measured by a luminometer in Relative Light Units (RLU) and reported as reactive or nonreactive. The screening assay is referred to as "Ultrio Elite" and does not discriminate between HIV-1, HIV-2 and HCV RNA and/or HBV DNA. Specimens found to be reactive with this multiplex assay are then tested in HIV, HCV and HBV Discriminatory Assays (dHIV, dHCV, dHBV assays) to determine if they are reactive for HIV, HCV, and/or HBV. It is possible for all three discriminatory tests to be non-reactive (non-discriminating NAT result or NDR). This may indicate a false positive NAT screening test.

Roche cobas MPX Assay: This assay is based on real time Polymerase Chain Reaction (PCR) technology using a fully automated nucleic acid extraction and purification process followed by PCR amplification of RNA and DNA using specific primers for detection of HIV and HCV RNA and HBV DNA. The assay generates a fluorescent signal produced by labeled detection probes, which is measured by an automated instrument and reported as reactive or nonreactive. The screening assay allows independent identification of HIV and HCV RNA and/or HBV DNA which eliminates the need for individual discriminatory testing. The cobas MPX test may serve as a confirmatory assay in lieu of serology confirmation in "dual-reactive" individuals when discriminated for the applicable RNA or DNA in conjunction with the corresponding antigen or antibody. It is possible for all three cobas MPX discriminatory results to be non-reactive. This may indicate a false positive nucleic acid screening test.

Discriminatory NAT Assays (Procleix dHIV, dHCV, dHBV): These assays utilize specific probe reagent directed against specific conserved regions in the viral genome to determine the presence of virus by TMA. Detection of the chemiluminescent signal is measured by a luminometer in Relative Light Units (RLU) and reported as reactive or nonreactive. Individual Procleix discriminatory assays may be performed for HIV, HCV or HBV and may serve as a confirmatory assay for NAT and serology (dual-reactive) samples in lieu of serology confirmation. Recent studies have shown that a very small proportion of donors reactive for anti-HBc with no other HBV markers (<1%) may also have very low levels of HBV DNA. Additional individual discriminatory HBV NAT results may be useful for donor counseling despite the lack of information about potential infectivity.

Limitations: Detection of HIV, HCV and HBV using nucleic acid tests is dependent on the number of viral particles present in the specimen and may be affected by stage of infection. In addition, some true positive samples may generate invalid results due to a high viral load. Final interpretations of any serology assay should also consider the results from nucleic acid amplification assays and additional medical history. The Ultrio Elite HIV discriminatory assay will not distinguish between samples reactive for HIV-1 and those reactive for HIV-2.

NOTE: Procleix discriminatory HBV triplicate testing or cobas MPX testing is required to provide HBV DNA detection at approximately 2 IU/mL at > 95% probability.

REFERENCES:

Abbott PRISM HBsAg manufacturer's instructions
Abbott PRISM HBsAg confirmatory manufacturer's instructions
Abbott PRISM HCV manufacturer's instructions
Bio-Rad GS HBsAg EIA 3.0 manufacturer's instructions
Bio-Rad GS HBsAg Confirmatory Assay 3.0 manufacturer's instructions
Dodd et al. Transfusion 2018:58:2166-2170.
Ortho HCV Version 3.0 ELISA Test System manufacturer's instructions
Procleix Ultrio Elite Assay manufacturer's instructions
Roche cobas™ MPX manufacturer's instructions
Seed et al. Vox Sanguinis (2019) 114, 397–406.
Terrault et al. HEPATOLOGY, VOL. 67, NO. 4, 2018.

Revision History

Revision	Implemented	Reason
Rev 5	07/07/2020	Replacement of Procleix Ultrio Plus with Ultrio Elite
Rev 4	09/30/19	Replacement of Roche cobas MPX 2.0 with Roche cobas MPX; minor changes to HBc and HBV algorithms
Rev 3	12/17/2018	CTS Algorithm Modification
Rev 2	07/01/2016	Implementation of Roche cobas MPX 2.0 Additional information for anti-HBs
Initial Release	05/01/2013	Revision History added